# Annual Reports

## ON THE PROGRESS
## OF CHEMISTRY

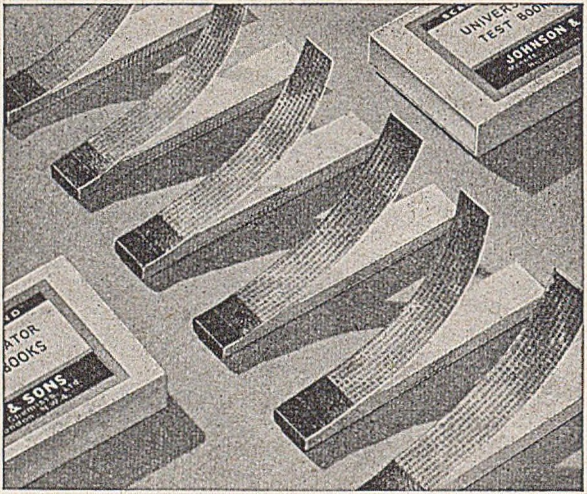
## Committee of Publication

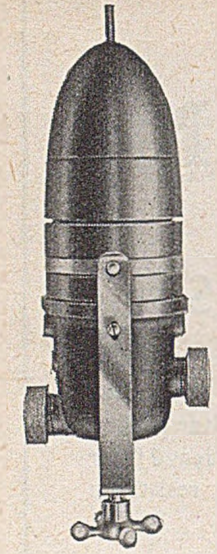
## Editor

## Assistant Editors

## Contributors

A. S. Bailey, B.Sc., M.A., D.Phil.
R. H. Betts, B.Sc., Ph.D.
E. J. Bourne, B.Sc., D.Sc.
E. Boyland, D.Sc., Ph.D.
E. Collinson, M.A., Ph.D.
J. W. Cornforth, M.Sc., D.Phil.
F. S. Dainton, M.A., Ph.D.
S. P. Datta, B.Sc., M.B., B.S.
C. W. Davies, D.Sc., F.R.I.C.
J. D. Dunitz, B.Sc., Ph.D.
D. D. Eley, M.Sc., Ph.D.
F. Fairbrother, D.Sc.
T. G. Halsall, M.Sc., Ph.D.
K. J. Ivin, B.A., Ph.D.
T. J. King, M.A., B.Sc., D.Phil.
J. Lascelles, M.Sc., D.Phil.
J. W. Linnett, M.A., D.Phil.
N. F. Maclagan, D.Sc., M.D., F.R.C.P.
J. F. W. McOmie, M.A., D.Phil.
C. B. Monk, Ph.D., A.R.I.C.
D. M. Needham, M.A., Sc.D., F.R.S.
R. A. Raphael, D.Sc., A.R.C.S., A.R.I.C.
J. H. Robertson, B.Sc., Ph.D.
J. Walker, Ph.D., D.Phil., D.Sc.
W. A. Waters, M.A., Sc.D., F.R.I.C.
B. C. L. Weedon, Ph.D., D.I.C., F.R.I.C.
J. H. Wilkinson, Ph.D., M.P.S., F.R.I.C.
C. L. Wilson, M.Sc., Ph.D., F.R.I.C.





# This is the chemical era of the industrial age

Monsanto Chemicals Limited, one of the largest manufacturers of chemicals in Great Britain, has world-wide manufacturing and selling services. Its products are used in almost all major industries . . .

RUBBER . . . Monsanto's accelerators help speed vulcanisation, add quality. Anti-oxidants improve resistance, prevent early cracking, give increased flexibility.

PLASTICS . . . Monsanto's phenol production makes a major contribution to phenolic plastics production. Plasticizers give more flexible, durable plastics. Lustrex*, Monsanto's polystyrene, is used extensively in refrigeration, electrical, housewares and other fields.

OIL . . . Monsanto's oil additives improve oils, help engines to operate better under all conditions. New additives will meet the demands of future lubricants

TEXTILES . . . Monsanto Syton*, widely used in spinning woollens, worsteds and blends of these fibres, increases yarn strength by 15-20% or more. Other Monsanto products include sizes and preservatives.

PRESERVATIVES . . . Monsanto's pentachlorophenol chemicals help to preserve a wide range of products. Monsanto sodium benzoate helps prevent corrosion — by impregnating wrapping papers for metal articles.

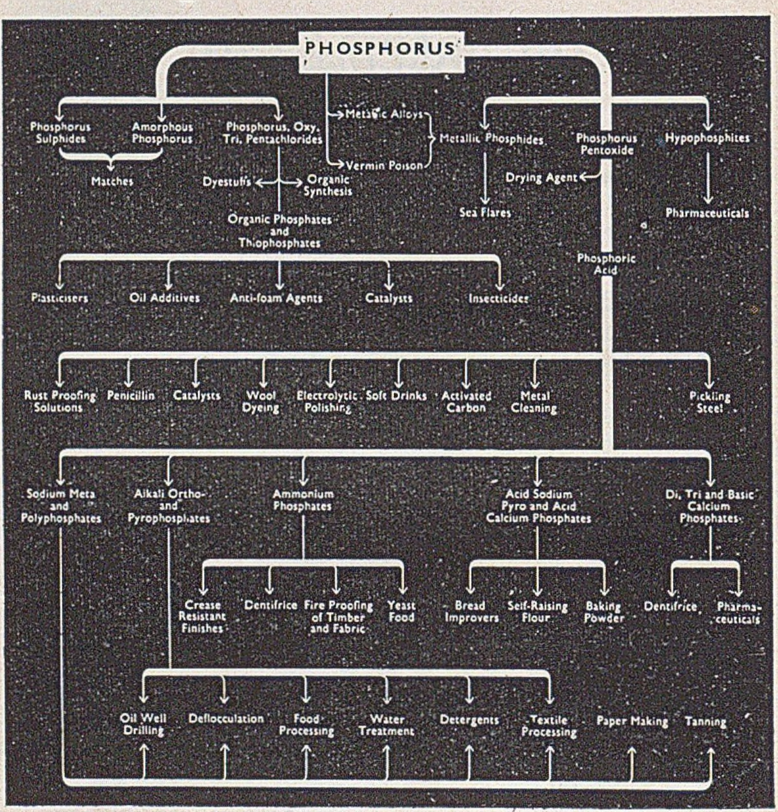
PHARMACEUTICALS . . . Acetyl salicylic acid — of which Monsanto is the largest producer in the U.K. — phenacetin, benzoic acid, phenol, phenolphthalein, germicides are but a few of the many Monsanto products in this field.
If your production programme calls for chemicals, *consult Monsanto first* . . .

*(*Registered Trade Mark)*

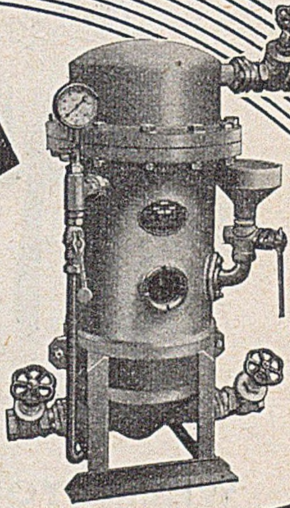
MONSANTO

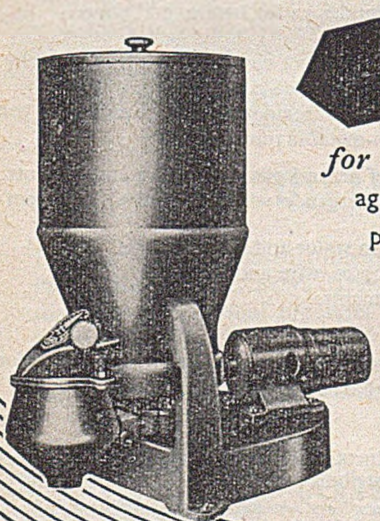
**CHEMICALS FOR EVERY INDUSTRY**

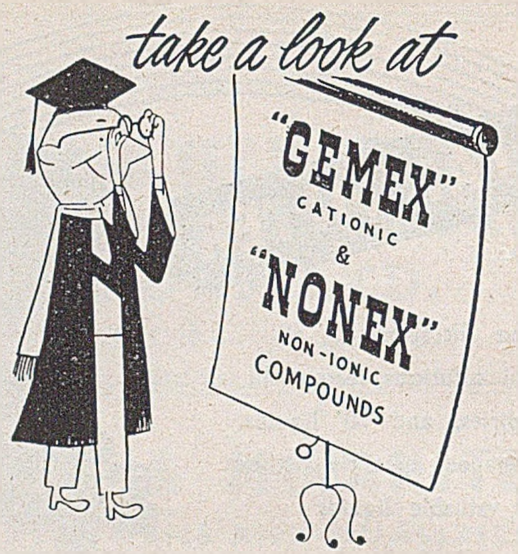
**MONSANTO CHEMICALS LIMITED.**
**8 Waterloo Place, London, S.W.1.**

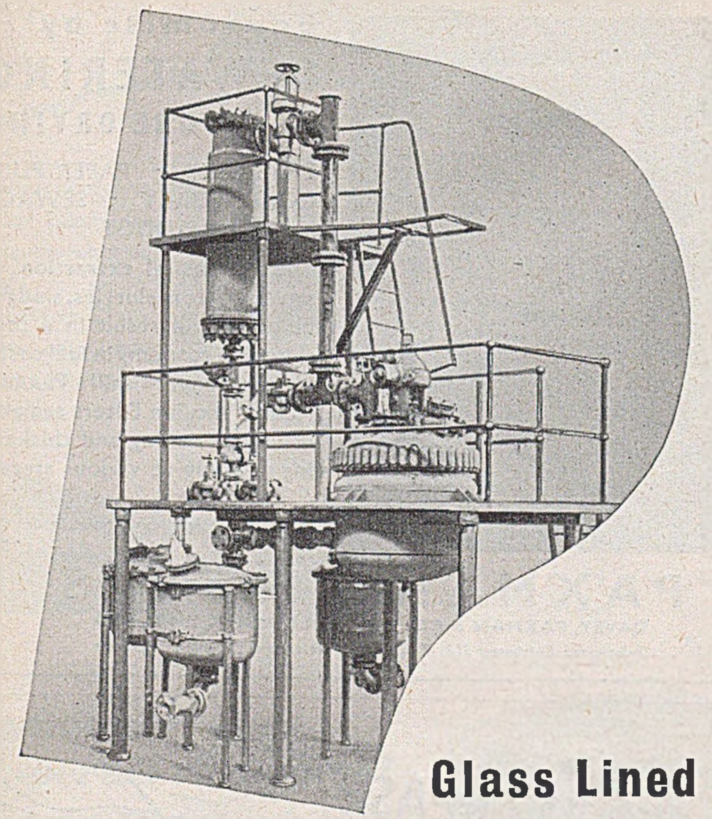


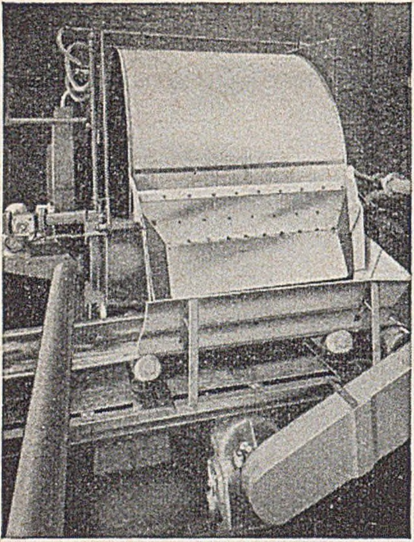
PHOSPHORUS
Phosphorus Sulphides
Amorphous Phosphorus
Matches
Phosphorus, Oxy, Tri, Pentachlorides
Dyestuffs
Organic Synthesis
Organic Phosphates and Thiophosphates
Metallic Alloys
Vermin Poison
Metallic Phosphides
Sea Flares
Phosphorus Pentoxide
Drying Agent
Phosphoric Acid
Hypophosphites
Pharmaceuticals
Plasticisers
Oil Additives
Anti-foam Agents
Catalysts
Insecticides
Rust Proofing Solutions
Penicillin
Catalysts
Wool Dyeing
Electrolytic Polishing
Soft Drinks
Activated Carbon
Metal Cleaning
Pickling Steel
Sodium Meta and Polyphosphates
Alkali Ortho- and Pyrophosphates
Ammonium Phosphates
Acid Sodium Pyro and Acid Calcium Phosphates
Di, Tri and Basic Calcium Phosphates
Crease Resistant Finishes
Dentifrice
Fire Proofing of Timber and Fabric
Yeast Food
Bread Improvers
Self-Raising Flour
Baking Powder
Dentifrice
Pharmaceuticals
Oil Well Drilling
Deflocculation
Food Processing
Water Treatment
Detergents
Textile Processing
Paper Making
Tanning



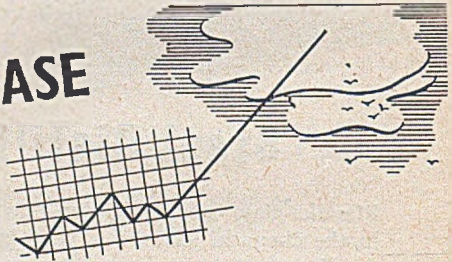



take a look at
"GEMEX"
CATIONIC
&
"NONEX"
NON-IONIC
COMPOUNDS





---



---

## MANSFIELD OIL-GAS PLANT
### FOR LABORATORIES' GAS SUPPLY

Provides a reliable gas supply for laboratories and industrial purposes in localities where a town's gas Service is not available.

Oil-Gas having a calorific value of 1350 B.T.U's per cubic foot, is produced in a simple manner from Solar Oil, Light Diesel Oil, or other suitable oils available at comparatively low cost.

Any of the usual gas burning appliances available for use with Coal gas are readily adapted to give equally good results with Oil gas. Perfect oxidising or reducing flames are obtained.

Full particulars promptly furnished on receipt of estimated number of burners and appliances likely to be used.

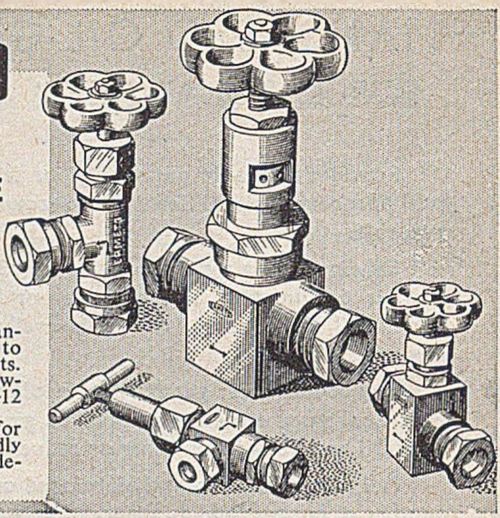
**MANSFIELD & SONS LTD**

62 HAMILTON SQUARE, BIRKENHEAD

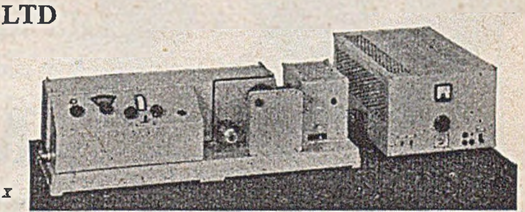
Throughout 1952 **L. LIGHT & Co** continued their policy of placing before scientists interesting compounds, including the following:

**Aleuritic acid**
**2-Amino pyrimidine**
**Behenic acid**
**2 : 3-Benzofluorene**
**Triphenylene**
**Bilverdin**
**α- and β-Conidendrol**
***iso*-Butyraldoxime**
**Cytochrome C**
**Cytosine and Thiocytosine**
**Khellin**
**Eicosane**
**2 : 3-Lutidine**
**1 : 2-Dimethoxy ethane**
**L-Dopa**
**DL-Ethionine**
**Murexide**
**N-Methyl morpholine**
**α-Keto-butyric acid**
***o*-Benzoyl-benzoic acid**
**Erepsin and Ficin**
**Histamine diphosphate**
**Protoporphyrin**
**Pyridoxamine di-HCl**
**Reinecke salt**
**Tetrahydro-carbazole**
**Thiodiglycollic acid**
**2 : 4 : 6-Tri-iodo-phenol**
**Tryptamine**
***iso*-Vanillin**
**4-Vinyl pyridine**
***p*-Terphenyl**

Ask **L. LIGHT & Co Ltd,** **POYLE ESTATE, COLNBROOK, BUCKS,** for your copy of their current catalogue.



---



# ACCURATE CONDUCTIVITY MEASUREMENT

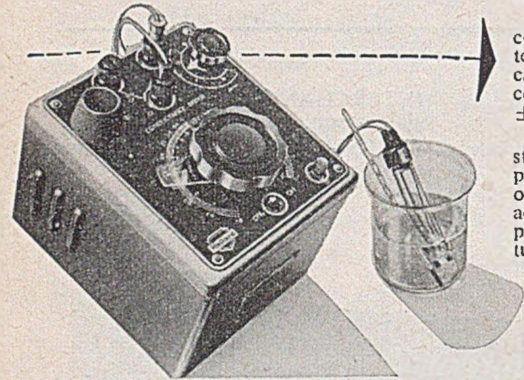
THE Mullard Conductivity Bridge, type E.7566, provides a convenient and sensitive method of checking the chemical concentration of solutions.

This compact, lightweight instrument gives direct reading of conductivity over a range of 0·1 micromhos-10 mhos. It has an accuracy of ± 3 per cent between 10-100,000 micromhos, and is accurate to ± 5 per cent over the rest of the range.

The E.7566 may also be used for the comparison of conductivity between a test and standard solution. In this application it provides automatic temperature compensation, and gives an accuracy of ± 2 per cent.

The instrument incorporates a Wheatstone bridge network, which, to avoid polarisation, is energised at a frequency of 3,000 cycles per second. Rapid and accurate detection of balance is made possible by the use of a cathode ray tuning indicator.

Full technical details of the Mullard Conductivity Bridge and its associated range of Cells are available on request.

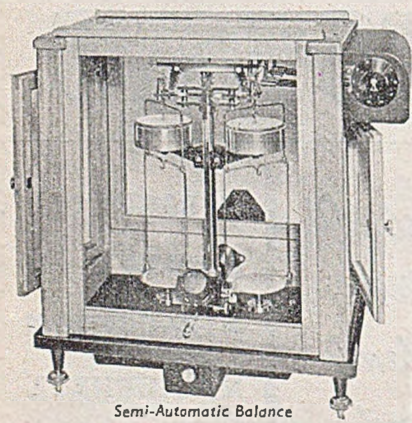


**Mullard**

NORTHERN AGENT: F. C. ROBINSON & PARTNERS, LTD.
287 DEANSGATE, MANCHESTER, 3
SCOTTISH AGENT: LAND, SPEIGHT & CO. LTD.
73 ROBERTSON ST., GLASGOW, C.2

MULLARD LTD · EQUIPMENT DIVISION · CENTURY HOUSE · SHAFTESBURY AVENUE · LONDON · W.C.2
(MI405A)

---



*Semi-Automatic Balance*

Glassware for
every laboratory need:

"PYREX" "HYSIL"
"MONAX" "WOODS"
"E-MIL"

# RALPH CUTHBERT

LIMITED

*Scientific Department*

LORD STREET
HUDDERSFIELD

Telephone 6323
Head Office: WESTGATE

*ESTABLISHED 1870*

**FURNITURE, TITRATION BENCHES AND FITTINGS. PORCELAIN:** Royal Worcester, Doulton. **FILTER PAPERS:** Whatman, Postlip, Greens. **OVENS. PHOTOGRAPHIC EQUIPMENT. TESTING APPARATUS FOR:** Assay and Metallurgy—Cement and Concrete—Coal and Coke—Dairy Products—Paint—Paper—Petroleum products—Rubber—Textiles—Water and Sewage.

*"EVERYTHING FOR THE LABORATORY"*

P.S.—Try the patent "Haleo" tube cutter and marker

## H. K. LEWIS & Co. Ltd.

*SCIENTIFIC AND TECHNICAL BOOKSELLERS*

## SCIENCE DEPARTMENT

Large Stock available of New and Standard Scientific Literature, English and Foreign. A representative Stock of Books on Chemistry—Pure and Applied, Physics, Mathematics, Astronomy, Biology, Psychology, Engineering. Catalogues on request.

Books are sent C.O.D. at the Post Office rates in the British Isles, and throughout the world wherever the system operates.

### SECOND-HAND BOOKS: 23 GOWER PLACE, W.C.1

A constantly changing large stock of Scientific Literature always on view. Libraries, large or small, purchased. Books sought for and reported free of charge.

## SCIENTIFIC LENDING LIBRARY

ANNUAL SUBSCRIPTION—from 25s.

The **LIBRARY** is useful to **SOCIETIES** and **INSTITUTIONS**, and to those engaged on **SPECIAL RESEARCH WORK**, etc. It includes all Recent and Standard works in all branches of Medical and General Science. Every work is the latest edition. New Books and New Editions added to the Library are available to subscribers **immediately on publication.** *Prospectus post free on application.*

The **LIBRARY CATALOGUE** revised to December 1949, containing classified Index of Authors and Titles. Pp. xii + 1152. To subscribers 17*s*. 6*d*. net. To non-subscribers 35*s*. net. Postage 1*s*. 3*d*.

Supplement 1950 to 1952 in preparation.

Bi-Monthly List of new books and new editions added to the Library sent free on request.

**STATIONERY DEPARTMENT.** A Comprehensive range of Designers Sectional Papers, Graph Books and Pads. Sheets and Pads of Logarithmic—"Z" Charts—Circular Percentage—Reciprocal—Triple Co-ordinate—Polar Graph—Time Table (Gantt)—Daily, Weekly and Monthly Charts—Planning Sheets, Lay Out, Tracing Pads etc., held in stock.

*Particulars sent on application*

## H. K. LEWIS & Co. Ltd.

**136 GOWER STREET, LONDON, W.C.1**

Business hours: 9 a.m. to 5 p.m., Saturdays to 1 p.m.
Telephone: EUSton 4282 (seven lines)

*The Polytechnic*

309 REGENT STREET, W.1

*Department of Chemistry and Biology*

DAY AND EVENING COURSES

B.Sc. Degree, Special (Chemistry, Botany, Zoology)
B.Sc. Degree, General (Chemistry, Botany, Zoology, Physiology)
(*University of London, External*)

Associateship of the Royal Institute of Chemistry (A.R.I.C.) Diploma

Diploma in Biology

General Certificate of Education (Advanced Level) and Intermediate Science Courses include Chemistry, Botany, Zoology, and Physics.

Prospectuses may be obtained on application to the undersigned.

J. C. JONES, *Director of Education*

**Safety in the Chemical Laboratory**

*By H. A. J. Pieters and J. W. Creyghton.* Price 15s.
The standard safety manual for all who handle chemicals and gases, whether in the laboratory or in industry. It details correct precautionary measures, and gives all the guidance needed for drafting safety regulations.

**Cooling Towers**

*By J. Jackson, B.Sc.* Price 21s.
This handbook is the result of systematic research and practical experience at the plants of Imperial Chemical Industries Ltd. It sets forth clearly and concisely how cooling towers of the mechanical draught type can be designed, tested, and the test-data interpreted.

**Practical Electron Microscopy**

*By V. E. Cosslett, Cavendish Laboratory, Cambridge.* Price 35s.
An introduction to the basic physical features and to the functioning and operation of the electron microscope.

**REPRINTS**

**Journal of the Chemical Society**

Vols. I–XXIII (1848–1870). Complete set, cloth, £125; paper covers, £115. Selected volumes, paper covers, Vols. I–X, £7 10s. per volume; Vols. XI–XXIII, paper covers, £5 10s. per volume. Memoirs and Proceedings. Vols. I–III (1841–1848). Set of three volumes, £25, paper covers only.

**BUTTERWORTHS SCIENTIFIC PUBLICATIONS**
**BELL YARD TEMPLE BAR LONDON, W.C.2**

# *Publications*

## OF THE CHEMICAL SOCIETY

## JOURNAL OF THE CHEMICAL SOCIETY

| | PRICE (POST FREE) | | | |
|---|---|---|---|---|
| 1848–1870 (Vols. I–XXIII) Reprinted Edition: | £ | *s.* | *d.* | $ |
| Complete Set, cloth binding | 125 | 0 | 0 | (350.00) |
| Complete Set, paper covers | 115 | 0 | 0 | (325.00) |
| Selected Volumes: | | | | |
| 1848–1857 (Vols. I–X), per annum | 7 | 10 | 0 | (21.00) |
| 1858–1870 (Vols. XI–XXIII), per annum | 5 | 10 | 0 | (15.40) |
| 1871–1952, Original edition (including Abstracts, 1871–1923): | | | | |
| per annum | 6 | 0 | 0 | (17.00) |
| per part | | 12 | 0 | (1.60) |
| 1953: | | | | |
| per annum | 10 | 0 | 0 | (28.50) |
| per part | 1 | 0 | 0 | (2.90) |

## ANNUAL REPORTS ON THE PROGRESS OF CHEMISTRY

| | £ | *s.* | *d.* | $ |
|---|---|---|---|---|
| Vol. I (1904)–Vol. XLVIII (1951): | | | | |
| per copy | 1 | 5 | 0 | (3.60) |
| Vol. XLIX (1952) (published 1953): | | | | |
| per copy | 1 | 10 | 0 | (4.30) |

## QUARTERLY REVIEWS

| | £ | *s.* | *d.* | $ |
|---|---|---|---|---|
| Vol. I (1947)–Vol. VII (1953): | | | | |
| per volume | 1 | 10 | 0 | (4.30) |
| per part | | 10 | 0 | (1.40) |

**THE CHEMICAL SOCIETY**
BURLINGTON HOUSE · LONDON, W.1

Annual Reports on the
Progress of Chemistry

# *Cumulative Index*

Vol. I (1904)—Vol. XLVI (1949)

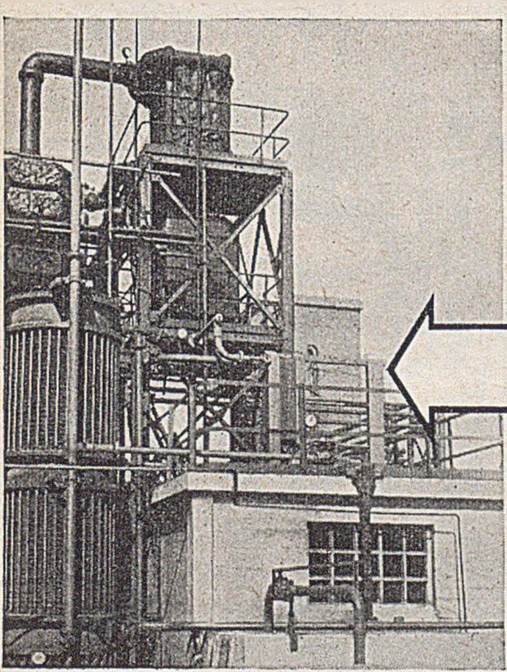
PUBLISHED 1951 PRICE 25s. ($3.50)

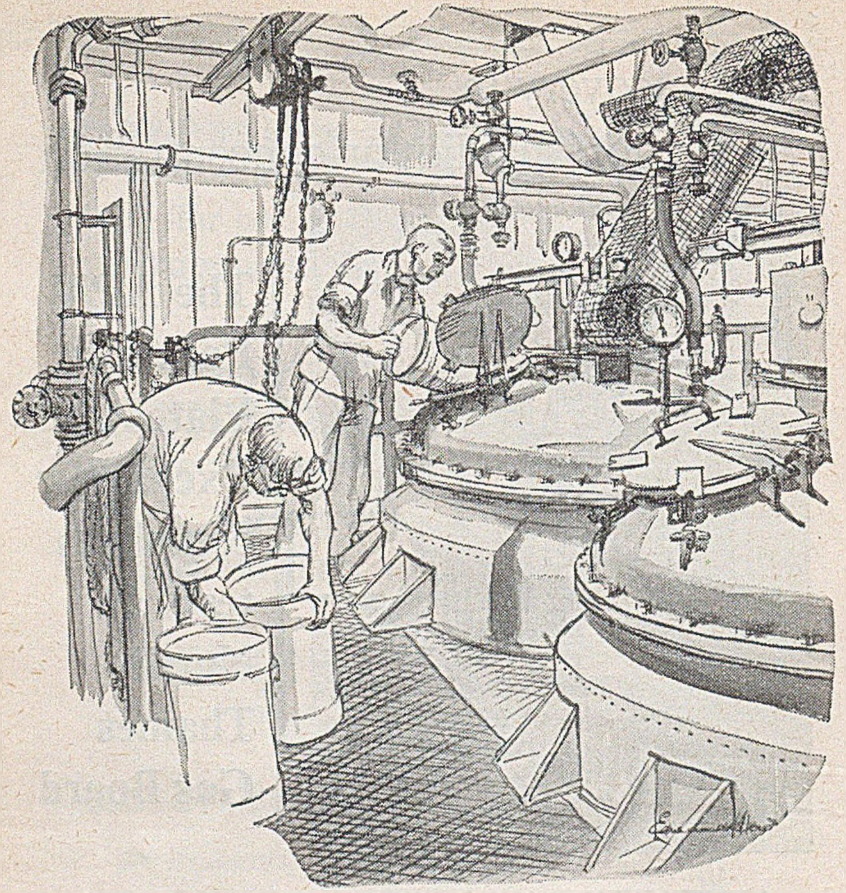
The *Annual Reports* first issued by The Chemical Society in 1904 have long been recognised as containing authoritative summaries of progress in all branches of fundamental chemistry. Every significant new development during the period in question has been described and the very complete references which are provided make it possible to discover the relevant original papers on any particular topic.

A Cumulative Subject Index covering the entire series of Reports, including the volume for 1949 (published 1950), is now published.

It is considered that this Index will be of the greatest value to chemists since those in possession of a series of Annual Reports will be provided, at very moderate cost, with a most useful, yet compact, guide to the chemical literature of the period. The Index is similar in format and binding to the *Annual Reports* and contains nearly 300 pages.

**The CHEMICAL SOCIETY**
**BURLINGTON HOUSE · LONDON, W.1**





THE CHEMICAL SOCIETY

# Annual Reports ON THE PROGRESS OF CHEMISTRY

FOR 1952

Volume XLIX

LONDON 1953

# THE CHEMICAL SOCIETY

## PATRON

HER MAJESTY THE QUEEN

### President

C. K. Ingold, D.Sc., F.R.I.C., F.R.S.

### Vice-Presidents

who have filled the office of President :

F. G. Donnan, C.B.E., D.Sc., LL.D., F.R.S.
Sir Ian Heilbron, D.S.O., D.Sc., LL.D., F.R.S.
Sir Cyril Hinshelwood, M.A., Sc.D., F.R.S.
W. H. Mills, M.A., Sc.D., F.R.S.
Sir Eric Rideal, M.B.E., M.A., D.Sc., F.R.S.
Sir Robert Robinson, O.M., D.Sc., LL.D., F.R.S.

### Vice-Presidents

G. R. Clemo, D.Phil., D.Sc., F.R.S.
D. H. Hey, Ph.D., D.Sc., F.R.I.C.
E. L. Hirst, D.Sc., LL.D., F.R.S.
R. P. Linstead, C.B.E., M.A., D.Sc., F.R.S.
Sir John Simonsen, D.Sc., F.R.I.C., F.R.S.
M. Stacey, Ph.D., D.Sc., F.R.S.

### Treasurer

Sir Wallace Akers, C.B.E., D.C.L., D.Sc., F.R.S.

### Secretaries

H. Burton, Ph.D., D.Sc., F.R.I.C.
E. D. Hughes, D.Sc., F.R.I.C., F.R.S.
L. E. Sutton, M.A., D.Phil., F.R.S.

### Ordinary Members of Council

J. S. Anderson, M.Sc., Ph.D., A.R.C.S.
G. Baddeley, M.Sc., Ph.D., D.Sc.
Wilson Baker, M.A., D.Sc., F.R.S.
D. H. R. Barton, Ph.D., D.Sc., F.R.I.C.
J. Bell, D.Sc., Ph.D., F.R.I.C.
R. P. Bell, M.A., B.Sc., F.R.S.
Neil Campbell, D.Sc., Ph.D.
J. Chatt, M.A., Ph.D., F.R.I.C.
S. J. Gregg, Ph.D., A.R.C.S., F.R.I.C.
S. H. Harper, Ph.D., D.Sc., A.R.C.S.
L. Hunter, Ph.D., D.Sc., F.R.I.C.
F. E. King, M.A., D.Phil., D.Sc.
F. B. Kipping, M.A., Ph.D.
E. A. Moelwyn-Hughes, D.Phil., D.Sc., Sc.D.
L. N. Owen, Ph.D., D.Sc., F.R.I.C.
H. M. Powell, M.A., B.Sc.
A. Robertson, M.A., Ph.D., F.R.S.
M. A. T. Rogers, B.Sc., Ph.D., A.R.I.C.
C. W. Shoppee, D.Sc., D.Phil., F.R.I.C.
J. W. Smith, Ph.D., D.Sc., F.R.I.C.
T. S. Stevens, B.Sc., D.Phil., A.R.I.C.
A. R. J. P. Ubbelohde, M.A., D.Sc., F.R.S.

### Ex-Officio Members of Council

A. Findlay, C.B.E., D.Sc., LL.D., F.R.I.C. (*Chairman of the Chemical Council*).
L. H. Lampitt, D.Sc., F.R.I.C. (*Chairman of the Bureau of Abstracts*).
W. Wardlaw, C.B.E., D.Sc., F.R.I.C. (*Chairman of the Joint Library Committee*).

### General Secretary

J. R. Ruck Keene, M.B.E., T.D., B.A.

### Librarian

A. E. Cummins.

*Telephone Numbers :* Regent 0675/6

# CONTENTS

GENERAL AND PHYSICAL CHEMISTRY

ORGANIC CHEMISTRY

BIOCHEMISTRY

CRYSTALLOGRAPHY

# ANNUAL REPORTS
# ON THE
# PROGRESS OF CHEMISTRY.

## GENERAL AND PHYSICAL CHEMISTRY.

### 1. BOND INTERACTIONS.

THERE are two main methods of obtaining information about bond interactions in polyatomic molecules. The first is to compare bond properties in different molecules. Thus the C–Cl bond is shorter in ClCN (1·67 Å) [1] than in $CH_3Cl$ (1·781 Å),[2] showing the effect of an adjacent triple bond [3] (there is also an increase in the force constant).[4] The second is to study these interactions in a molecule as it vibrates; the usual way of doing this is to determine from the vibration frequencies the function governing the variation of potential energy with distortion. For example Slawsky and Dennison,[5] and Linnett [6] found that, in the methyl halides, the C–X bond interacts with the inter-bond angles in the methyl group, the potential-energy function showing that, as the C–X bond is lengthened, the HCH angle tends to increase. Analogous interaction effects have been found in ethylene,[7] formaldehyde,[8] keten,[8] and diazomethane.[9] Recently other spectroscopic methods of investigating bond interactions have been used. In this Report methods of the second kind will be specially considered.

**Potential-energy Functions.**—Of the two basic force fields the Central has proved less useful than the Valency.[10] In its simplest form the potential-energy function based on the latter involves squared terms in the bond length and inter-bond angle changes but, in its complete form, "cross terms" which take account of the interactions between different parts of the molecule are also included. Thus for the water molecule the complete valency force field (V.F.F.) potential-energy function is [11]

$$V = \tfrac{1}{2}k_1(\Delta r_1{}^2 + \Delta r_2{}^2) + \tfrac{1}{2}k_\alpha\Delta\alpha^2 + k_{1\alpha}(\Delta r_1 + \Delta r_2)\Delta\alpha + k_{11}\Delta r_1\Delta r_2 \quad . \quad (1)$$

where $\Delta r_1$, $\Delta r_2$, and $\Delta\alpha$ are the changes in the bond lengths and H–O–H angle, $k_1$ and $k_\alpha$ are the respective constants, $k_{11}$ measures the interaction

---

[1] J. Y. Beach and A. Turkevich, *J. Amer. Chem. Soc.*, 1939, **61**, 299.

[2] L. E. Sutton and L. O. Brockway, *ibid.*, 1935, **57**, 473; S. L. Miller, L. C. Aamodt, G. Dousmanis, C. H. Townes, and J. Kraitchman, *J. Chem. Phys.*, 1952, **20**, 1112.

[3] A. D. Walsh, *Trans. Faraday Soc.*, 1947, **43**, 60.

[4] J. W. Linnett and H. W. Thompson, *J.*, 1937, 1399.

[5] Z. I. Slawsky and D. M. Dennison, *J. Chem. Phys.*, 1939, **7**, 509.

[6] J. W. Linnett, *ibid.*, 1940, **8**, 91.

[7] H. W. Thompson and J. W. Linnett, *J.*, 1937, 1376. [8] *Idem*, *ibid.*, p. 1384.

[9] B. L. Crawford, W. H. Fletcher, and D. A. Ramsay, *J. Chem. Phys.*, 1951, **19**, 406.

[10] G. Herzberg, "Infra-red and Raman Spectra of Polyatomic Molecules," Van Nostrand, New York, 1945, pp. 159—186.

[11] D. F. Heath and J. W. Linnett, *Trans. Faraday Soc.*, 1948, **44**, 556.

between the bonds, and $k_{1\alpha}$ the interaction between the bonds and the angle. There are four independent constants in the complete quadratic potential-energy function. This is so whatever its form. If there are $n$ fundamental vibrations in a symmetry class, the general potential-energy function governing distortions of that symmetry will contain $\frac{1}{2}n(n + 1)$ independent constants. To obtain the number of independent constants for all distortions of the molecule these must be summed over all symmetry classes. Thus, for water, there are two fundamental symmetric vibrations; for these distortions there are three constants. There is one fundamental antisymmetric vibration; for this there is only one constant. There are therefore four constants in all [cf. (1)].

**Determination of Force Constants.**—The molecule $H_2O$ has only three vibration frequencies, so, from them alone, the four constants cannot be found. This difficulty may be overcome by using isotopes. Thus, for water, deuterium oxide which also has three fundamental frequencies may be used. However, for any pair of isotopic molecules, the Teller–Redlich product rule [12] states that the ratio of the product of the frequencies of all the vibrations of a given symmetry class for one isotopic molecule to the corresponding product for the other is independent of the force field and equal to a function involving the atomic masses and molecular dimensions only. So, since the vibrations of $H_2O$ and $D_2O$ fall into two symmetry classes, $D_2O$ provides only one new independent frequency. This with the three of $H_2O$ makes possible the determination of all four constants. The vibration frequencies of DOH might also be used but, because of relationships between the frequencies of isotopic molecules, they provide no additional information. Decius and Wilson [13] have deduced certain sum rules relating the vibration frequencies of isotopic molecules. For example for water

$$\Sigma\nu^2(\text{HOH}) + \Sigma\nu^2(\text{DOD}) = 2\Sigma\nu^2(\text{HOD}) \quad . \quad . \quad . \quad . \quad . \quad (2)$$

the summations being over all vibration frequencies. Decius [14] has also examined what isotopic substitution is necessary in linear molecules to obtain a unique solution for the force constants.

Hence, if the frequencies of a sufficient number of isotopic molecules are available all the constants may in principle be determined. However the use of isotopic substitution is not always well suited for the accurate determination of force constants. This may be illustrated with hydrogen cyanide. The valency vibration frequencies of HCN are 3312·0 and 2089·0 cm.$^{-1}$.[15] The table lists the frequencies calculated for DCN and $HC^{15}N$ for three values of $k_{12}$ in the function

$$V = \tfrac{1}{2}k_1(\Delta r_{\text{CH}})^2 + \tfrac{1}{2}k_2(\Delta r_{\text{CN}})^2 + k_{12}(\Delta r_{\text{CH}})(\Delta r_{\text{CN}}) \quad . \quad . \quad . \quad . \quad . \quad (3)$$

As one vibration frequency of DCN is 2629·3,[15] $k_{12}$ must have a small negative value. But the figures for $HC^{15}N$ show that it would be necessary to

| | DCN | | | $HC^{15}N$ | | |
|---|---|---|---|---|---|---|
| $k_{12}$ (× $10^{-5}$) | −0·5 | 0 | +0·5 | −0·5 | 0 | +0·5 |
| Frequency (cm.$^{-1}$) | 2648·0 | 2596·1 | 2548·6 | 3309·9 | 3310·8 | 3311·6 |
| | 1881·4 | 1919·1 | 1954·9 | 2056·5 | 2056·0 | 2055·4 |

---

[12] O. Redlich, *Z. physikal. Chem.*, 1935, *B*, 28, 371; see also W. R. Angus *et al.*, *J.*, 1936, 971.

[13] J. C. Decius and E. B. Wilson, *J. Chem. Phys.*, 1951, 19, 1409.

[14] J. C. Decius, *ibid.*, 1952, 20, 511.

[15] G. Herzberg, ref. 10, p. 279.

determine the frequency shifts from $HC^{14}N$ to $HC^{15}N$ very accurately to fix the value of $k_{12}$. The reason why the substitution of deuterium for hydrogen in hydrogen cyanide is so effective in determining $k_{12}$ is that, while the CH "group" frequency is much greater than that of the C–N bond, the CD "group" frequency is close to that of the C–N bond. The closeness of the "group" frequencies in DCN causes the effect of varying $k_{12}$ on the calculated frequencies to be large. Isotopic substitution should therefore be used for calculating force constants only when it is clear that it provides a reliable method.

For $H_2O$, and other bent $AX_2$ molecules, in the absence of isotopic substitution there are only three frequencies to determine four constants. A convenient method of representation has been suggested by Duchesne,[16] and Glockler and Tung,[17] who proposed that the values of three constants should be plotted against values of the fourth which is regarded as an independent variable. It is then found that the graphs are ellipses, and the values of the constants are limited to certain ranges. Such graphical representations have been used by Burnelle and Duchesne,[18] Torkington,[19] Thomas,[20] and Linnett and Heath.[21] However it is often impossible to select from such inadequate data the correct set of values for the constants and it is important that efforts be made to obtain, with complete certainty, all the constants in the general potential-energy function for as many molecules as possible so that reliable conclusions may be drawn from the values.

Another method that has been used for overcoming the difficulty that the number of constants usually exceeds the number of observed frequencies is that of transferring constants from other molecules containing similar bonds. Thus Crawford and Brinkley [22] used the same values for the constant of the C–N bond in hydrogen cyanide and methyl cyanide. This method has been used by Cleveland and Meister and their co-workers in extensive calculations on the halogen derivatives of methane,[23] ethane,[24] and other molecules.[25] However there are often variations in bond lengths from one molecule to another (*e.g.* from methyl chloride to carbon tetrachloride) so that there can be no certainty that force constants can be transferred in the above manner. Caution must be used in making such transfers. Thomas [26] has used constants from related molecules but has made allowance for bond changes on going from one to another. For

[16] J. Duchesne, *Mem. Soc. Roy. Sci., Liège*, 1943, **1**, 429.

[17] G. Glockler and J. Y. Tung, *J. Chem. Phys.*, 1945, **13**, 388.

[18] J. Duchesne and L. Burnelle, *ibid.*, 1951, **19**, 1191.

[19] P. Torkington, *ibid.*, 1949, **17**, 357. [20] W. J. O. Thomas, *J.*, 1952, 2383.

[21] J. W. Linnett and D. F. Heath, *Trans. Faraday Soc.*, 1952, **48**, 592.

[22] B. L. Crawford and S. R. Brinkley, *J. Chem. Phys.*, 1941, **9**, 69.

[23] A. G. Meister, S. E. Rosser, and F. F. Cleveland, *ibid.*, 1950, **18**, 346; S. M. Ferigle, F. F. Cleveland, W. M. Bryer, and R. B. Bernstein, *ibid.*, p. 1073; J. P. Zeitlow, F. F. Cleveland, and A. G. Meister, *ibid.*, p. 1076; J. R. Madigan, F. F. Cleveland, W. M. Bryer, and R. B. Bernstein, *ibid.*, p. 1081; J. R. Madigan and F. F. Cleveland, *ibid.*, 1951, **19**, 119; C. E. Decker, A. G. Meister, and F. F. Cleveland, *ibid.*, p. 784; P. F. Farlon, A. G. Meister, and F. F. Cleveland, *ibid.*, p. 1561; A. Davis, F. F. Cleveland, and A. G. Meister, *ibid.*, 1952, **20**, 454.

[24] F. F. Cleveland, J. E. Lamport, and R. W. Mitchell, *ibid.*, 1950, **18**, 1073; M. Z. El-Sabban, A. G. Meister, and F. F. Cleveland, *ibid.*, 1951, **19**, 855; P. R. McGee, F. F. Cleveland, and S. I. Miller, *ibid.*, 1952, **20**, 1044.

[25] J. S. Ziomek and F. F. Cleveland, *ibid.*, 1949, **17**, 578; F. F. Cleveland, K. W. Greenlee, and E. E. Bell, *ibid.*, 1950, **18**, 355.

[26] W. J. O. Thomas, *ibid.*, 1951, **19**, 1162.

example, the CO force constant in $CO_2$ is known exactly, and, from this and the bond length, using Gordy's formulæ,[27] Thomas calculated the bond order in $CO_2$. From the bond length in cyanic acid he calculated the CO bond order in that molecule, and, from this, using Gordy's formulæ again, he obtained the CO force constant in cyanic acid. So, from the small observed change in bond length (1·163 to 1·170 Å) he determined the small change in the force constant (from 15·5 to 15·0 × $10^5$ dynes/cm.). If accurate bond length values are available from micro-wave or other data this probably provides the best means of making use of the known value of a force constant of a similar bond in a related molecule. It is to be preferred to transferring the value uncorrected.

With molecules having doubly degenerate vibrations there is a further means of obtaining information about force constants. Such vibrations can possess angular momenta by virtue of their internal motions, and the magnitude of the vibrational angular momentum associated with a certain excited level can, in favourable cases, be determined from the structure of the bands associated with the transition to that level from the ground state.[28] This angular momentum is dependent on the force field and may be used to determine force constants. Formulæ for doing this have been published by Boyd and Longuet-Higgins.[29] For the vibrations of a given symmetry class (say the three of the degenerate class of methyl chloride) the sum of the angular momenta associated with all the first excited levels of that class has a particular value independent of the force field. Lord and Merrifield [30] and Boyd and Longuet-Higgins [29] have given some examples of the magnitude of this sum. So, for the degenerate vibrations of methyl chloride there are only two independent angular momenta available for determining the force constants.

As yet the so-called Coriolis coefficients which measure the angular momentum associated with the vibration have not been widely used for determining force constants. Dennison [31] used them with ammonia and he and Hansen [32] used the frequencies of ethane and hexadeuteroethane together with values of the Coriolis coefficients to determine all 21 constants (excluding torsion) in the potential-energy function of that molecule. Lord and Venkateswarlu [33] have pointed out that for allene all ten potential constants associated with distortions corresponding to the degenerate vibrations could be obtained from the eight degenerate vibration frequencies of allene and tetradeuteroallene (only seven are independent because of the Teller–Redlich relation) and the eight Coriolis coefficients (only six are independent because of the sum rules).

It has been assumed so far that the potential-energy function is quadratic

---

[27] W. Gordy, *J. Chem. Phys.*, 1946, **14**, 305; 1947, **15**, 305.

[28] V. M. McConaghie and H. H. Nielsen, *Proc. Nat. Acad. Sci.*, 1948, **34**, 455; D. R. J. Boyd, H. W. Thompson, and R. L. Williams, *Discuss. Faraday Soc.*, 1950, **9**, 154; D. R. J. Boyd, H. W. Thompson, and R. L. Williams, *Proc. Roy. Soc.*, 1952, *A*, **213**, 42; D. R. J. Boyd and H. W. Thompson, *Trans. Faraday Soc.*, 1952, **48**, 493; H. W. Thompson and R. L. Williams, *ibid.*, p. 502; H. H. Nielsen, *J. Chem. Phys.*, 1952, **20**, 759.

[29] D. R. J. Boyd and H. C. Longuet-Higgins, *Proc. Roy. Soc.*, 1952, *A*, **213**, 55.

[30] R. C. Lord and R. E. Merrifield, *J. Chem. Phys.*, 1952, **20**, 1348; M. Johnston and D. M. Dennison, *Phys. Review*, 1935, **48**, 868.

[31] D. M. Dennison, *Review Mod. Phys.*, 1940, **12**, 175.

[32] G. E. Hansen and D. M. Dennison, *J. Chem. Phys.*, 1952, **20**, 313.

[33] R. C. Lord and P. Venkateswarlu, *ibid.*, p. 1237.

and anharmonicity can be neglected. When the aim is to obtain the complete potential-energy function this is not always justifiable. But only in rare cases (*e.g.* water,[34] hydrogen cyanide,[35] nitrous oxide [36]) can sufficient overtones be observed to obtain the zero-order frequencies. In other cases other methods have to be adopted. For instance Dennison corrected the observed fundamentals of methane by assuming a relationship between the anharmonicity coefficients of methane and tetradeuteromethane and by using the Teller–Redlich product rule. Hansen and Dennison treated ethane similarly.

Calculating force constants from vibration frequencies is often tedious. Procedures for making such calculations have been proposed by El'yashevich,[37] Wilson,[38] and Torkington.[39]

**Results for Interaction Constants.**—The simplest type are the bond–bond constants of linear molecules [*e.g.* $k_{12}$ in (3)] for in these the valency vibrations occur independently of the bending ones. In most cases the cross-term constant is positive (*e.g.* in $CO_2$,[8] $CS_2$,[40] $N_3^-$,[40] $N_2O$,[41] OCS,[42] ClCN,[20] BrCN,[20] ICN,[20] and also, regarding the NH as a unit, in HNCO,[20] HNCS,[20] and $HN_3$ [20]). But in HCN,[35] and the bent molecules $H_2O$,[11] $H_2S$,[40] and $H_2Se$,[40] it is negative. The positive value of this constant has been ascribed to the effect of resonance. Thus in carbon dioxide there is resonance between (i) $O{=}C{=}O$, (ii) $\overset{-}{O}{-}C{\equiv}\overset{+}{O}$, and (iii) $\overset{+}{O}{\equiv}C{-}\overset{-}{O}$. The lengthening of the left-hand bond, therefore, favours (ii) and the consequent shortening of the right-hand bond.[8] The potential energy increases less, therefore, when $\Delta r_1$ and $\Delta r_2$ are opposite in sign than when they are of the same sign and this accounts for the cross-term constant being positive; but, when hydrogen is one of the atoms attached to the central atom, the constant is negative. Coulson, Duchesne, and Manneback [43] have suggested that this is due to a charge effect. Hoare and Linnett [40] pointed out that, when the cross-term constant is positive in a triatomic molecule, the diatomic molecule left on dissociating one bond would be expected to be shorter than the corresponding bond in the triatomic molecule. This is found to be so (*e.g.* $r_{CS}$ in $CS_2$ is 1·55 and in CS 1·53 Å). When the constant is negative the reverse is to be expected; this is also found (*e.g.* $r_{OH}$ in $H_2O$ is 0·958 and in OH 0·971 Å). Thomas has confirmed this in the molecules studied by him.[20] The sign of the cross-term constants in the mercury halides is still uncertain and more data for these would be interesting. The positive cross-term constants are always larger than the negative ones so interaction resulting from resonance effects must be greater than that occurring in hydrogen cyanide, water, etc. Heath, Linnett, and

---

[34] L. G. Bonner, *Phys. Review*, 1934, **46**, 458; B. T. Darling and D. M. Dennison, *ibid.*, 1940, **57**, 128.

[35] W. Brookes, *Trans. Faraday Soc.*, 1951, **47**, 1152.

[36] G. Herzberg, ref. 10, p. 278.

[37] El'yashevich, *Compt. rend. Acad. Sci., U.R.S.S.*, 1940, **28**, 604.

[38] E. B. Wilson, *J. Chem. Phys.*, 1939, **7**, 1047; 1941, **9**, 76; J. C. Decius, *ibid.*, 1948, **16**, 1025.

[39] P. Torkington, *ibid.*, 1949, **17**, 357; 1950, **18**, 93, 773; 1951, **19**, 528, 979.

[40] M. F. Hoare and J. W. Linnett, *Trans. Faraday Soc.*, 1949, **45**, 844.

[41] W. S. Richardson and E. B. Wilson, *J. Chem. Phys.*, 1950, **18**, 694.

[42] H. J. Callomon, D. C. McKean, and H. W. Thompson, *Proc. Roy. Soc.*, 1951, *A*, **208**, 341.

[43] C. A. Coulson, J. Duschesne, and J. Manneback, *Nature*, 1947, **160**, 793; "Contribution á l'Etude de la Structure Moleculaire," Liège, 1948, p. 33.

Wheatley[44] pointed out that in $CH_4$, $SiH_4$, $NH_3$, $PH_3$, $H_2O$, and $H_2S$ the bond lengths were always less than in the diatomic molecules AH but, though the cross-term constants are not certain, it seems that they are positive in the Group IV hydrides and in ammonia but negative in the Group VI hydrides and in phosphine and arsine. The contrast between ammonia and arsine has also been noted by Duchesne and Ottelet[45] who suggest that it may be due to the opposing effects of hybridisation changes and H---H interaction which tend to lead to positive and negative cross-term constants, respectively. They also point out that the bond–bond interaction constants involving bonds to hydrogen are small.

From the three valency vibration frequencies of cyanogen and one of the molecule containing one $^{13}C$ atom, Duchesne and Burnelle[18] have found that the (CN)(CC) cross-term constant is positive and the (CN)CN′) cross-term constant negative. The sign of both can be accounted for by the effect of resonance between NC–CN and double-bonded forms, for a shortening of one C–N bond favours the first canonical form and hence a lengthening of the C–C bond (positive constant) and a shortening of the other C–N bond (negative constant) (cf. Longuet-Higgins and Burkitt[46]).

Torkington[47] has suggested a potential-energy function (omitting angle terms) for polyatomic molecules derived from that of Morse for diatomic molecules. This includes bond–bond interaction terms and, for triatomic molecules, Torkington relates the sign of the cross-term constant to the difference between the heat of atomisation and the sum of the bond-dissociation energies (cf. Duchesne[48]). He also considers the sign of the higher-order terms in the potential-energy function.

In methyl chloride the largest interaction constant is that between the C–Cl bond and the H–C–Cl angle. It is positive showing that, as the H–C–Cl angle is increased the C–Cl bond tends to shorten. It is noteworthy that, in cyanogen chloride, where a similar drawing together of the three pairs of electrons opposite to the chlorine atom must also have occurred (relative to methyl chloride in its near-tetrahedral equilibrium configuration), the C–Cl bond has become shorter. A similar effect appears to occur in methane and hydrogen cyanide also.[49] In methane the $(CH_i)(H_jCH_k)$ constant is negative indicating that, as the $H_jCH_k$ angle is reduced the $CH_i$ bond tends to shorten. Also in hydrogen cyanide (and in acetylene) the C–H bond is shorter than in methane.[50] The shortening of the C–Cl bond in cyanogen chloride is often ascribed to resonance, but objections have been made to this explanation by Burawoy[51] and by Duchesne.[52] Burawoy suggests that it is due to changes in electron shielding and other inter-electronic effects, while Duchesne relates it to changes in hybridisation at the chlorine atom. He has explained in a similar manner increases in bond length from carbon tetrachloride to methyl chloride, from silicon tetrachloride to silyl chloride,

---

[44] D. F. Heath, J. W. Linnett, and P. J. Wheatley, *Trans. Faraday Soc.*, 1950, **46**, 137.

[45] J. Duchesne and I. Ottelet, *J. Chem. Phys.*, 1949, **17**, 1354.

[46] H. C. Longuet-Higgins and F. H. Burkitt, *Trans. Faraday Soc.*, 1952, **48**. 1077.

[47] P. Torkington, *J. Chem. Phys.*, 1952, **20**, 1174.

[48] J. Duchesne, *Mem. Acad. Roy. Belg.*, 1952, **26** (7), 1.

[49] J. W. Linnett, *Proc. Roy. Soc.*, 1951, *A*, **207**, 30.

[50] A. D. Walsh, ref. 3; J. W. Linnett, *Trans. Faraday Soc.*, 1945, **41**, 223.

[51] A. Burawoy, *Trans. Faraday Soc.*, 1943, **39**, 79; 1944, **40**, 537; " Contribution á l'Etude de la Structure Moleculaire," Liège, 1948, p. 73.

[52] J. Duchesne, *Trans. Faraday Soc.*, 1950, **46**, 187; *J. Chem. Phys.*, 1951, **19**, 246.

and from carbon tetrafluoride to methyl fluoride, giving nuclear quadrupole coupling data in various molecules in support of this hypothesis. Though the above effects in methyl chloride and cyanogen chloride correspond with those in methane and hydrogen cyanide the bond–bond cross-term constant in the two triatomic molecules are different.

The calculations by Hansen and Dennison[32] for ethane are valuable because they provide a complete treatment of a relatively large molecule. The bond–angle are the largest interaction constants; all the bond–bond constants are small. As with the methyl halides the (CC)(CCH) constant is quite large and positive, but the biggest interaction constant is that associated with the term $(CH_i)(CCH_{i+1})$, the bond and angle being in the same methyl group. It is negative, indicating that, as the $C–H_i$ bond is lengthened, the $CCH_{i+1}$ angle tends to increase. The constant associated with the $(CH_i)(H_{i+1}CH_{i-1})$ cross-term is also negative, indicating that, as the $C–H_i$ bond is lengthened, the $H_{i+1}CH_{i-1}$ angle tends to increase. Thus, as the $CH_i$ bond is lengthened, the angles on the opposite side of the carbon atom tend to increase, so the effect is analogous to that produced by the lengthening of the C–C bond (and the C–Cl bond in methyl chloride[5]). The interactions between the separate methyl groups are of interest because it may be possible to link these to the effects restricting rotation. The molecule being in the staggered form, it is found that increasing one HCC angle tends to cause the opposite one in the other methyl group to increase, and that increasing a C–H bond length in one methyl group tends to cause the adjacent CCH angles in the other methyl group to decrease. The latter could be due to repulsion between non-bonded atoms or between bonds but the former is more difficult to explain, though it might be accounted for by hyperconjugation effects.

Torkington has studied ethylene[53] and its derivatives[54] extensively. Many of his conclusions are unaffected by modifications made to the frequency assignment by Arnett and Crawford,[55] and Rank, Shull, and Axford.[56] For instance he finds that the interaction constant between adjacent C–H bonds is negative (as in water, etc.) and between the *trans*-C–H bonds is probably positive. The latter suggests that as one C–H bond is lengthened the C–H *trans* to it tends to contract. The (C=C)(C–H) interaction constant is positive, and Torkington suggests that this may be a consequence of repulsion between non-bonded hydrogen and carbon atoms (cf. Heath, Linnett, and Wheatley[57]). Torkington also studied the out-of-plane bending constant of the $CH_2$ group in $CH_2=CH_2$, $CH_2=CHX$, and $CH_2=CX_2$, where X = methyl, halogen, cyano, etc.[54] He found that the effect on the constant is twice as great for the $CH_2=CX_2$ molecules as for the corresponding $CH_2=CHX$ molecules (using ethylene as the reference molecule) and also that *ortho*- and *para*-directing groups lower the constant while *meta*-directing ones increase it. This surprising result appears to show that, as electrons are drawn from the double bond, the constant increases. In a later paper[53] Torkington links this effect to the conclusion of Heath, Linnett,

---

[53] P. Torkington, *Proc. Phys. Soc.*, 1951, *A*, **64**, 32.
[54] *Idem*, *Nature*, 1949, **163**, 96; *Proc. Roy. Soc.*, 1950, *A*, **206**, 17.
[55] R. L. Arnett and B. L. Crawford, *J. Chem. Phys.*, 1950, **18**, 118.
[56] D. H. Rank, E. R. Shull, and D. W. E. Axford, *ibid.*, p. 116.
[57] D. F. Heath, J. W. Linnett, and P. J. Wheatley, *Trans. Faraday Soc*, 1949, **45**, 1.

and Wheatley[57] that the out-of-plane bending of the ethylene molecule is easier because the constant associated with the $\pi$-bond is negative. Torkington also studied the out-of-plane bending constant of the CH group in $CH_2{=}CHX$ molecules and found that the order was that of the electronegativities of the attached groups X.[54]

An important factor causing deviations from the simple valency force field is undoubtedly repulsion between non-bonded atoms as has been shown by Urey and Bradley[58] for various $AX_4$ molecules and ions, and by Simanouti[59] in a variety of substituted derivatives of methane and silane. Heath and Linnett also showed the importance of such repulsions in boron halides,[60] various hexafluorides,[61] Group IV halides,[62] and such ions as $SO_4^-$, $NO_3^-$, etc.[63] (see also Coulson, Duchesne, and Manneback,[43] and Sehon and Szwarc[64]). Both Simanouti, and Linnett and Heath compared the repulsion constants with those to be expected from the known van der Waals repulsion between inert gas atoms as calculated by Lennard-Jones.[65] Linnett and Heath,[21] in a general survey, showed that the repulsion constants for a given pair of non-bonded atoms varied regularly in a series of molecules with the distance separating them. Wilson and Polo[66] find that the bond–bond constant in nitrogen trifluoride is probably positive. This could be due to repulsions between the fluorine atoms. Caunt, Short, and Woodward[67] have examined similar repulsion effects in germanium tetrafluoride.

Dennison has determined the five potential constants of methane.[31] For those governing bending only, the main HCH constant is $0{\cdot}42 \times 10^5$ (in dynes/cm.) and the $(H_iCH_j)(H_kCH_l)$ interaction constant is $-0{\cdot}075 \times 10^5$. The negative sign of the latter suggests that reducing one HCH angle tends to cause the opposite one to close up also. This would be an erroneous conclusion, for the six HCH angles cannot be varied independently. Suppose $(\Delta H_iCH_j) = -(\Delta H_kCH_l)$ and the distortion is symmetrical, the other HCH angles will not change, but if $(\Delta H_iCH_j) = +(\Delta H_kCH_l)$ the other four angles decrease by an angle equal to half the increase in the other two. From this it is easy to show that the potential energy increases more rapidly with change in angle for the distortion in which $(\Delta H_iCH_j) = +(\Delta H_kCH_l)$ than for the distortion in which $(\Delta H_iCH_j) = -(\Delta H_kCH_l)$. So the closing of one HCH angle favours the opening of the opposite one. This can be explained by electron correlation effects[68] or by, what is essentially equivalent, hybridisation changes. Difficulties like the above provided one of the reasons for Heath and Linnett's modifying the ordinary valency force field to their orbital force field (O.V.F.F.) in which the central atom is imagined

---

[58] H. C. Urey and C. A. Bradley, *Phys. Review*, 1931, **38**, 1919.

[59] T. Simanouti, *J. Chem. Phys.*, 1949, **17**, 245, 734, 848; D. F. Heath and J. W. Linnett, *ibid.*, 1950, **18**, 147.

[60] D. F. Heath and J. W. Linnett, *Trans. Faraday Soc.*, 1948, **44**, 873.

[61] *Idem, ibid.*, 1949, **45**, 264.

[62] *Idem, ibid.*, 1948, **44**, 561, 878.

[63] *Idem, ibid.*, p. 884.

[64] A. H. Sehon and M. Szwarc, *Proc. Roy. Soc.*, 1951, *A*, **209**, 110.

[65] J. E. Lennard-Jones, *ibid.*, 1924, *A*, **106**, 463; R. A. Buckingham, *ibid.*, 1938, *A*, **168**, 264; R. H. Fowler and E. A. Guggenheim, "Statistical Thermodynamics," C.U.P., 1939, p. 285.

[66] M. K. Wilson and S. R. Polo, *J. Chem. Phys.*, 1952, **20**, 1716.

[67] A. D. Caunt, L. N. Short, and L. A. Woodward, *Nature*, 1951, **168**, 557; *Trans. Faraday Soc.*, 1952, **48**, 873.

[68] (Sir) J. E. Lennard-Jones, *J. Chem. Phys.*, 1952, **20**, 1024; H. Margenau, "The Nature of Physical Reality," McGraw-Hill, 1950, p. 434.

to have its valencies directed in particular directions relative to one another, and the angular deviation of each bond from their directions is used in the potential-energy function.[60] Force fields of the same type had been used by Urey and Bradley [58] and by Howard and Wilson [69] but had never been developed. By this approach difficulties like that for methane will not exist because the impossibility of varying angles independently does not occur in using the O.V.F.F. In terms of cross-terms, a simple O.V.F.F. with no cross-terms, will correspond, in certain cases, to an ordinary V.F.F. including finite angle–angle cross-terms (and *vice versa*).

Some wave-mechanical calculations of force constants and interaction constants have been made. Examples are provided by Warhurst,[70] Coulson and Longuet-Higgins,[71] Parr and Crawford,[72] Parr and Taylor,[73] Wheatley and Linnett,[74] and Longuet-Higgins and Burkitt.[46]

**Intensities of Infra-red Bands.**—Since 1945 an active start has been made in determining the intensities of infra-red bands and in using the data obtained. The procedure is to determine the intensities of the fundamental absorption bands of the molecule and from these to calculate the rate of change of dipole moment with each normal co-ordinate, $\partial\mu/\partial Q$ (see Wilson and Wells [75]; Thorndike, Wells, and Wilson [76]; Callomon, McKean, and Thompson [77]; and Penner and Weber [78]). After a normal co-ordinate treatment these may be converted into values for the rate of change of $\mu$ with bond lengths and angles ($\partial\mu/\partial r$ and $\partial\mu/\partial\alpha$). In most treatments the $\partial\mu/\partial r$ values have been related to a change of moment of a particular bond with length and the $\partial\mu/\partial\alpha$ values used to calculate bond moments supposing that, as the molecule bends, the bonds retain their constant moments which remain directed along the line joining the atoms. The justifiability of these far-reaching assumptions seems to be doubtful. Thorndike,[79] for example, stated that his results for ethane " cast some doubt upon the whole concept of additivity of bond dipole moments " (see also Bell, Thompson, and Vago [80]).

Dipole-moment changes on distortion can also be obtained from measurements of refractive indices using infra-red radiation, as has been done by Rollefson with Rollefson,[81] with Havens,[82] and with Kelly and Schurin.[83] One important difficulty in the interpreting of the change of $\mu$ on distortion is that the magnitude, but not the sign, can be deduced from the data obtained from both refractive-index and absorption measurements.

For carbon dioxide Thorndike [79] found that $\partial\mu'/\partial r$ for the C=O bond was

---

[69] J. B. Howard and E. B. Wilson, *J. Chem. Phys.*, 1934, **2**, 630.

[70] E. Warhurst, *Trans. Faraday Soc.*, 1944, **40**, 26.

[71] C. A. Coulson and H. C. Longuet-Higgins, *Proc. Roy. Soc.*, 1948, *A*, **193**, 447.

[72] R. G. Parr and B. L. Crawford, *J. Chem. Phys.*, 1948, **16**, 526; 1949, **17**, 726.

[73] R. G. Parr and G. R. Taylor, *ibid.*, 1951, **19**, 497.

[74] P. J. Wheatley and J. W. Linnett, *Trans. Faraday Soc.*, 1949, **45**, 897.

[75] E. B. Wilson and A. J. Wells, *J. Chem. Phys.*, 1946, **14**, 578.

[76] A. M. Thorndike, A. J. Wells, and E. B. Wilson, *ibid.*, 1947, **15**, 157.

[77] H. J. Callomon, D. C. McKean, and H. W. Thompson, *Proc. Roy. Soc.*, 1951, *A*, **208**, 332.

[78] S. S. Penner and D. Weber, *J. Chem. Phys.*, 1951, **19**, 807, 817, 974.

[79] A. M. Thorndike, *ibid.*, 1947, **15**, 868.

[80] R. P. Bell, H. W. Thompson, and E. E. Vago, *Proc. Roy. Soc.*, 1948, *A*, **192**, 498.

[81] R. Rollefson and A. H. Rollefson, *Phys. Review*, 1935, **48**, 779.

[82] R. Rollefson and R. Havens, *ibid.*, 1940, **57**, 710.

[83] R. L. Kelly, R. Rollefson, and B. S. Schurin, *J. Chem. Phys.*, 1951, **19**, 1595.

$\pm 6{\cdot}0$ D/Å ($\mu$ and $\mu'$ are used for the dipole moments of molecules and bonds, respectively). This is much bigger than $\partial\mu'/\partial r$ for the C–H bond in methane ($\pm 0{\cdot}55$).[82] He suggests that the large value in carbon dioxide arises because, during the antisymmetric distortion, which is used in the measurement, there is a change in the relative contributions of the various canonical forms which results in a large swing of charge across the molecule (cf. the earlier explanation of the cross-term constant [8]). Such an effect will not occur in methane. In effect, therefore, he ascribes the large value of $\partial\mu'/\partial r$ to an interaction between the two C=O bonds. Eggers and Crawford [84] have investigated the intensities of some combination and overtone bands of carbon dioxide and, by using Crawford and Dinsmore's [85] theoretical treatment, have deduced the coefficients of higher-order terms in the expression for the dipole moment. They find that "electrical anharmonicity seems definitely the predominant factor accounting for the observed intensity of the 3614 and 3716 cm.$^{-1}$ bands" which is further evidence for interaction between the bonds. Unfortunately the sign of the coefficients of these higher-order terms cannot be fixed so that the data do not yet provide definite information regarding the nature of the interaction. An examination of the intensities of the bands of molecules like $^{16}OC^{18}O$ might help in discovering more about electrical interactions between the bonds.[86] Nitrous oxide has been studied by Thorndike, Wells, and Wilson [76] and by Callomon, McKean, and Thompson [77] who found that the values for $\partial\mu/\partial r$ in this molecule are large also. The explanation is probably similar to that for carbon dioxide. Eggers and Crawford [84] have measured the intensities of overtone and combination bands of nitrous oxide (see also Fraser and Price [87]).

Robinson [88] concluded that $\partial\mu/\partial r_{CO}$ in carbonyl sulphide is $-6{\cdot}7 \pm 0{\cdot}5$ compared with $-6{\cdot}0 \pm 0{\cdot}6$ in carbon dioxide and that $\partial\mu/\partial r_{CS}$ is $-4{\cdot}3 \pm 0{\cdot}5$ in the former compared with $-5{\cdot}6 \pm 0{\cdot}5$ in carbon disulphide. He commented on the relative constancy of both these values. Callomon, McKean, and Thompson [42] give a higher value (8·55) for $\partial\mu/\partial r_{CO}$ in carbonyl sulphide.

Hyde and Hornig [89] studied band intensities in hydrogen cyanide and deuterium cyanide and found that $\mu'_{CH}$ and $\partial\mu'/\partial r_{CH}$ are much greater in the former than in methane. They ascribe this to changes in hybridisation of the bond orbitals. Kelly, Rollefson, and Schurin [83] also found $\mu'_{CH}$ to be greater in acetylene than in methane. However they found that $\partial\mu'/\partial r_{CH}$ had about the same value in the two molecules (see Callomon, McKean, and Thompson [42]). Hyde and Hornig found that $\partial\mu'/\partial r_{CN}$ in hydrogen cyanide was similar to that found by Nixon and Cross [90] in cyanogen but much less than that found by them in cyanogen chloride. They ascribed the large value in the latter to the greater polarisability of the C–Cl bond; in effect, to interactions between the bonds (cf. interaction constant). They concluded that $\mu'_{CH}$ in hydrogen cyanide decreases with bond length just as for $\mu_{HCl}$ in hydrogen chloride (Bell and Coop [91]).

---

[84] D. F. Eggers and B. L. Crawford, *J. Chem. Phys.*, p. 1554.
[85] B. L. Crawford and H. L. Dinsmore, *ibid.*, 1950, **18**, 983, 1682.
[86] B. L. Crawford, *ibid.*, 1952, **20**, 977.
[87] R. D. B. Fraser and W. C. Price, *Nature*, 1952, **170**, 490.
[88] D. Z. Robinson, *J. Chem. Phys.*, 1951, **19**, 881.
[89] G. E. Hyde and D. F. Hornig, *ibid.*, 1952, **20**, 647.
[90] E. R. Nixon and P. C. Cross, *ibid.*, 1950, **18**, 1316.
[91] R. P. Bell and I. E. Coop, *Trans. Faraday Soc.*, 1938, **34**, 1209.

Barrow and McKean [92] have examined the methyl halides in detail. Only some of their results can be reported here. They found that $\partial\mu'/\partial r_{CX}$ decreases from the fluoride to the iodide, as would be expected, but that the values are surprisingly large especially for the C–F bond (4·7 D/Å). Such large values have only been observed previously in resonating systems. Robinson [93] has found that the dipole moment of hydrogen chloride depends critically on the hybridisation of the bonding orbitals of the chlorine atom, and they suggest that a similar explanation may account for the large values of $\partial\mu'/\partial r_{CX}$ in the methyl halides (cf. Duchesne [52]). Barrow and McKean also deduce values for $\partial\mu'/\partial r_{CH}$ from the symmetric and degenerate vibrations assuming no interaction between the bonds. In all the halides the values obtained from the symmetric are greater than those from the degenerate vibrations. The lack of agreement between the two values shows that, in all cases, bond interactions must occur. This is similar to the conclusion reached by Thorndike [79] from his study of ethane (cf. Francis [94]). The assumption of additivity of bond dipoles and an independent linear variation of bond dipoles with bond length seems to provide only a poor approximation.[95] There is great need for some further theoretical developments in this field.

**Other Possible Methods of Studying Bond Interactions.**—The intensity and depolarisation factors of Raman lines may be used, together with molecular polarisabilities, for calculating bond polarisabilities and their changes with bond length. This has been done by Wolkenstein [96] for substituted methanes. Cabannes and Rousset [97] have, however, approached the problem differently and regard changes of polarisability during molecular vibrations as resulting from changes in the interactions between centres of polarisability caused by changes in their separation. Further progress here requires an extension of our knowledge of the intensities and depolarisation factors of Raman lines.

The determination of the quadrupole coupling constants provides a valuable means of obtaining information about the electron configuration around a nucleus and changes in this from molecule to molecule caused by changing environment. Examples of important applications of this method have been given recently by Townes and Dailey [98]; Mays and Dailey [99]; Westenberg, Goldstein, and Wilson [100]; Goldstein and Bragg [101]; Gordy [102]; Tetenbaum [103]; Simmons and Goldstein [104]; and Duchesne.[105]

J. W. L.

---

[92] G. M. Barrow and D. C. McKean, *Proc. Roy. Soc.*, 1952, *A*, **213**, 27.

[93] D. Z. Robinson, *J. Chem. Phys.*, 1949, **17**, 1022.

[94] S. A. Francis, *ibid.*, 1950, **18**, 861.

[95] J. A. Pople, *Proc. Roy. Soc.*, 1950, *A*, **202**, 323; C. A. Coulson, *ibid.*, 1951, *A*, **207**, 63; "Valence," O.U.P., 1952, p. 207.

[96] N. V. Wolkenstein, *Acta Physicochem, U.R.S.S.*, 1945, **20**, 161, 174, 525, 544, 835, 883; *J. Exp. Theor. Phys., U.S.S.R.*, 1948, **18**, 138.

[97] J. Cabannes and A. Rousset, *J. Phys. Radium*, 1940, **1**, (8), 138.

[98] C. H. Townes and B. P. Dailey, *J. Chem. Phys.*, 1949, **17**, 782.

[99] L. M. Mays and B. P. Dailey, *ibid.*, 1952, **20**, 1693.

[100] A. A. Westenberg, J. H. Goldstein, and E. B. Wilson, *ibid.*, 1949, **17**, 1319.

[101] J. H. Goldstein and J. D. Bragg, *Phys. Review*, 1949, **75**, 1453.

[102] W. Gordy, *J. Chem. Phys.*, 1951, **19**, 792.

[103] S. J. Tetenbaum, *Phys. Review*, 1952, **86**, 440.

[104] J. W. Simmons and J. H. Goldstein, *J. Chem. Phys.*, 1952, **20**, 122.

[105] J. Duchesne, *ibid.*, p. 1804.

## 2. SURFACE CHEMISTRY.

The solid–liquid interface is the main theme of this section, and since this has not been reported on previously it is necessary to sketch in the main investigations of a decade and a half. Reasons of space have excluded reference to kinetic aspects, to flotation, and adsorption isotherms for solutions. Two monographs, by Gregg [1a] and Bikerman,[1b] have appeared in recent years, and there is considerable research in progress.

**Thermodynamics of the Solid–Liquid Interface.**—The basis of modern work remains the relations due to Young, Dupré, Gibbs, Hardy, and Langmuir, set out in the textbooks on surface chemistry by Rideal [2a] and Adam.[2b] Here we shall start with the work of Harkins and Dahlström [3] and Bangham and Razouk,[4] who pointed out that arguments based on contact angles must take account of the adsorbed film of liquid on the free surface of the solid. This consideration clarified many thermodynamic quantities, especially the work of adhesion. The equations of surface thermodynamics have been systematically reviewed in numerous papers by Harkins,[5,6,7,8] and the following summary largely follows this author, using his nomenclature. Let $\gamma_{SV^\circ}$ denote the surface free energy of the solid surface covered with an adsorbed film in equilibrium with the saturated vapour (pressure $p_0$), $\gamma_{LV^\circ}$ that of the liquid–vapour interface, and $\gamma_{SL}$ that of the solid–liquid interface. If at equilibrium the liquid makes a contact angle $\theta_E$ with the plane surface of the solid, regarded as insoluble in the liquid, then

$$\gamma_{SV^\circ} = \gamma_{SL} + \gamma_{LV^\circ} \cos \theta_E \qquad (1a)$$

If the solid surface has an adsorbed film corresponding to a pressure $p < p_0$, the free energy is

$$\gamma_{SV} = \gamma_{SL} + \gamma_{LV} \cos \theta \qquad (1b)$$

The work of adhesion is *defined* here as the work required to separate 1 cm.$^2$ of solid–liquid interface *in vacuo*,

$$W_{A(SL)} = \gamma_S + \gamma_L - \gamma_{SL} \qquad (2)$$

Here $\gamma_S$ and $\gamma_L$ denote surface tensions *in vacuo* of solid and liquid, respectively. If (1*a*) is substituted in (2), and if $\gamma_{LV^\circ} = \gamma_L$ (except for liquid metals, $\gamma_L$, the surface tension *in vacuo*, is equal to the usual value measured in air), then

$$W_{A(SL)} = \gamma_S - \gamma_{SV^\circ} + \gamma_L(1 + \cos \theta_E) \qquad (3)$$

The spreading pressure of an adsorbed film on a solid is defined by

$$\phi = \gamma_S - \gamma_{SV} \qquad (4a)$$

or for the adsorbed film at saturation pressure

$$\phi_E = \gamma_S - \gamma_{SV^\circ} \qquad (4b)$$

---

[1] (*a*) S. J. Gregg, " The Surface Chemistry of Solids," Chapman and Hall, London, 1951; (*b*) J. J. Bikerman, " Surface Chemistry," Academic Press, New York, 1948.

[2] (*a*) E. K. Rideal, " An Introduction to Surface Chemistry," Cambridge Univ. Press, 1930; (*b*) N. K. Adam, " Physics and Chemistry of Surfaces," Oxford Univ. Press, 1941.

[3] W. D. Harkins and R. Dahlström, *Ind. Eng. Chem.*, 1930, **22**, 897.

[4] D. H. Bangham and R. I. Razouk, *Trans. Faraday Soc.*, 1937, **33**, 1458.

[5] G. E. Boyd and W. D. Harkins, *J. Amer. Chem. Soc.*, 1942, **64**, 1190, 1195.

[6] W. D. Harkins, *J. Chem. Phys.*, 1941, **9**, 552.

[7] W. D. Harkins and H. K. Livingston, *ibid.*, 1942, **10**, 342.

[8] W. D. Harkins and G. Jura, " Colloid Chemistry," Vol. VI, Chapter I (Ed., J. Alexander), Reinhold Publ. Corpn., New York, 1946.

Substituting (4*b*) in (3) yields

$$W_{A(SL)} = \phi_E + \gamma_L(1 + \cos\theta_E) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The equation

$$W^*_{A(SL)} = \gamma_L(1 + \cos\theta_E) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

yields the work required to separate 1 cm.$^2$ of solid and liquid and leave an adsorbed film on the solid. Gregg [1a] calls this the work of adhesion, but in the Reporter's opinion it is preferable to use (5). $\phi_E$ is appreciable for metals and oxides, although for solids such as paraffin it may be very small.

Eqn. (1) is Young's equation, (2) Dupré's equation, and eqn. (5) has been called the corrected Young–Dupré relation.

Further definitions concern the spreading coefficient of a liquid on a solid to give thick (Harkins " duplex " [6]) films. For the initial spreading of a liquid on the clean solid surface

$$S_{L/S} = \gamma_S - \gamma_{SL} - \gamma_L = \phi_E \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7a)$$

Since the film adsorbed at saturation is a duplex film, *i.e.*, has a lower surface with energy $\gamma_{SL}$ and an upper one with energy $\gamma_L$, $S_{L/S}$ is of course equal to $\phi_E$. The final spreading coefficient refers to the film-covered solid.

$$S_{L/S_f} = \gamma_{SV^\circ} - \gamma_{SL} - \gamma_L \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7b)$$

As noted originally by Hardy, if $S_{L/S}$ is positive, the liquid will spread on the solid.

These equations may be adapted to the case where the solid is slightly soluble in the liquid, if one puts the appropriate values $\gamma_{L'V^\circ}$ and $\gamma_{SL'}$ into eqn. (1).

The surface tension may be equated to the free surface energy per cm.$^2$ for liquids and, with qualifications, for solids.* Harkins [9] employs a Gibbs free energy which omits the $\gamma A$ term, *viz.*, $G = U + pV - TS$. The Helmholtz free energy is $F = U - TS$.

In terms of these functions, we have either

$$\gamma = \left(\frac{\partial F}{\partial A}\right)_{T,V} = f \quad \text{or} \quad \gamma = \left(\frac{\partial G}{\partial A}\right)_{T,p} = g \quad . \quad . \quad . \quad . \quad (8)$$

where small letters denote thermodynamic functions for 1 cm.$^2$ of surface. Harkins uses $f$ where the British use $g$, and $\varepsilon$ where the British use $u$.

The Gibbs free energy change of emersion (reverse of immersion) of a solid from a liquid into a vacuum is

$$g_{E(SL)} = g_S - g_{SL} = \gamma_S - \gamma_{SL} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

**Physically Adsorbed Films on Solids.**—Two topics of immediate interest are $\phi_E$ and the surface-area problem. In addition, the discussion of physical adsorption is continued from the Annual Reports for 1950 and 1951.

*The spreading pressure.* Bangham [10] suggested application of the Gibbs adsorption equation for calculating the spreading pressure of an adsorbed

---

[9] W. D. Harkins, " Techniques of Organic Chemistry," Vol. I (Ed., A. Weissberger), Intersci. Publ., New York, 1945.

[10] D. H. Bangham, *Trans. Faraday Soc.*, 1937, 33, 805.

* Thus, surface free energy is correct in eqn. (1) (cf. R. Shuttleworth, *Proc. Phys. Soc.*, 1949, 62, *A*, 167).

film on a solid. If $\Gamma$ is the "surface excess," *i.e.*, the number of moles adsorbed per cm.$^2$ of surface, then

$$\phi = \int_0^p \Gamma \mathrm{d}\mu$$

and, if the perfect gas law can be assumed, then

$$\phi = RT\int_0^p \Gamma \mathrm{d}\ln p = \frac{RT}{AV}\int_0^p \frac{v}{p}\mathrm{d}p \quad . \quad . \quad . \quad . \quad . \quad (10a)$$

where $v$ c.c. of gas are adsorbed on area $A$ at pressure $p$, and $V$ is the molar volume of the gas. To obtain $\phi_E$, the integration is taken up to the saturation vapour pressure $p_0$

$$\phi_E = \frac{RT}{AV}\int_0^{p_0} \frac{v}{p}\mathrm{d}p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10b)$$

Bangham suggested that $\phi_E$ can only be regarded as a true lateral pressure when the film is mobile. Bangham and Razouk [11] applied graphical integration to Coolidge's data for charcoal in order to evaluate $\phi_E$. Harkins and Jura have used this method extensively, and their $\phi_E$ values are listed in the Table on p. 25. A comparison of the third and the fifth column in this Table show that $\phi_E$ may be 50% or more of the work of adhesion.

*Phase changes in monolayers.* Bangham and Razouk [11] found a discontinuity when $\phi\alpha$ was plotted against $p/p_0$ for water on charcoal, which they attributed to formation of a condensed phase. Here $\alpha = 1/\Gamma$ is the area per molecule in the adsorbed film, assumed unimolecular. Gregg,[12] and later Harkins and Jura,[8, 13, 14] have extended this analysis, finding curves analogous to those found for monolayers on water.[2, 15] Following Dervichian, phase changes were classified according to Ehrenfest, *viz.*, a first-order change is a discontinuity in the $v$–$p$ isotherm, a second-order change a discontinuity in $\left(\frac{\partial V}{\partial p}\right)_T$–$p$, etc. First-order phase changes were reported for water on graphite, and for $n$-heptane on silver, ferric oxide, or graphite. Smith [16] has repeated the work on the last two systems and failed to find the transition points, so the matter is still open. However, as originally shown by R. H. Fowler, a first-order condensation process may occur if attractive forces exist between neighbouring molecules in a monolayer. The theoretical aspects of phase changes in adsorbed films have been reviewed by Hill.[17]

Gregg and Maggs [18] plot the function $\beta'$ against log $p$ to reveal more closely the nature of the phase changes involved. $\beta'$ is proportional to the compressibility of the monolayer and is

$$\beta' = -\frac{1}{n_{\mathrm{ads}}}\frac{\mathrm{d}\ln n_{\mathrm{ads}}}{\mathrm{d}\ln p} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

---

[11] D. H. Bangham and R. I. Razouk, *Trans. Faraday Soc.*, 1937, **33**, 1463.

[12] S. J. Gregg, *J.*, 1942, 696.

[13] W. D. Harkins and G. Jura, *J. Chem. Phys.*, 1944, **12**, 112; *J. Amer. Chem. Soc.*, 1944, **66**, 1356.

[14] G. Jura *et al.*, *J. Chem. Phys.*, 1945, **13**, 535; 1946, **14**, 117, 344.

[15] W. D. Harkins, "Colloid Chemistry," Vol. V (Ed., J. Alexander), Reinhold Publ. Corpn., New York, 1944.

[16] R. N. Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 3497.

[17] T. L. Hill, *Adv. in Catalysis*, 1952, **4**, p. 211.

[18] S. J. Gregg and F. A. P. Maggs, *Trans. Faraday Soc.*, 1948, **44**, 123.

where $n_{ads}$ molecules are adsorbed per g. of solid. This method shows a very few true first-order changes, *e.g.*, for *n*-heptane on silver, but most of the changes occur over a range of pressure and fall into Mayer and Streeter's class of diffuse first-order changes.[19] The changes are shown to occur before multi-layer formation sets in. Tompkins [20] suggests that the changes are truly of first order, but blurred by surface heterogeneity.

Coulter and Candela [21] attributed a phase transition, observed for water on silver iodide, to the formation of a hydrate by an impurity. After subtraction of this effect, a type III isotherm was obtained. Bowden and Throssel [22] found that a platinum foil, cleaned *in vacuo* by electron bombardment, adsorbed only a unimolecular layer of water at $p/p_0 = 0{\cdot}9$. The thirty or so layers taken up before cleaning were attributed to traces of hydrophilic impurities. Further work of this kind is urgently needed.

Harkins and Jura [8] discuss empirical equations of state of adsorbed monolayers, and use that for a condensed phase, $\phi = a - b\alpha$, as the basis for their well-known surface area method (H.J. relative method [23]).

**Thermodynamics and Surface Areas.**—The theoretical aspects of physical adsorption have been reviewed by Hill.[17] He advocates [17,24] the usefulness of "adsorption thermodynamics," treating the adsorbed film as a pseudo-one-component system, yielding integral values of energies and entropies of adsorption. Everett [25] discusses solution thermodynamics, treating adsorbed gas and solid as a two-component system, which leads to differential energies and entropies. The thermodynamics of the solid–liquid interface yielding integral energies and entropies of immersion form a third system. Hill and Everett have clarified relations between the solution and adsorption thermodynamics, and a discussion of immersion data has been promised by Hill and Jura.[17] The present approach to adsorption is predominantly thermodynamic. Thus, Hill, Emmett, and Joyner [26] have calculated from isotherms differential and integral energies and entropies of adsorption for nitrogen on graphon. Drain and Morrison [27] have made similar calculations, using calorimetric data, for argon on rutile. The integral entropy of adsorption goes through a minimum at $\theta = 1$, an effect predicted by the Brunauer–Emmett–Teller (B.E.T.) equation for large *c* values, and considered by the authors as justification for use of the B.E.T. equation for determination of surface areas.

It is well known that the B.E.T. equation predicts too high an adsorption for $p/p_0 > 0{\cdot}35$. Cassel [28] showed a related effect, that substitution of the B.E.T. isotherm into eqn. (10) yields $\phi_E = \infty$. Hill [17] attributes this catastrophe to the configuration partition function, and stresses that a proper approach to multilayer theory can only be made through the difficult modern

[19] J. E. Mayer and S. F. Streeter, *J. Chem. Phys.*, 1939, **7**, 1019.

[20] F. C. Tompkins, *Trans. Faraday Soc.*, 1950, **46**, 580.

[21] L. V. Coulter and G. A. Candela, *Z. Elektrochem.*, 1952, **56**, 449.

[22] F. P. Bowden and W. R. Throssel, *Nature*, 1951, **167**, 601, 1038.

[23] W. D. Harkins and G. Jura, *J. Amer. Chem. Soc.*, 1944, **66**, 1366.

[24] T. L. Hill, *J. Chem. Phys.*, 1949, **17**, 520; 1950, **18**, 246; *Trans. Faraday Soc.*, 1951, **47**, 376.

[25] D. H. Everett, *ibid.*, 1950, **46**, 453.

[26] T. L. Hill, P. H. Emmett, and L. G. Joyner, *J. Amer. Chem. Soc.*, 1951, **73**, 5102, 5933.

[27] L. E. Drain and J. A. Morrison, *Trans. Faraday Soc.*, 1952, **48**, 840.

[28] H. M. Cassel, *J. Chem. Phys.*, 1944, **12**, 115; *J. Phys. Chem.*, 1944, **48**, 195.

theory of liquids. He concludes "that, bearing in mind the confirmatory work of Harkins and Jura,[29] B.E.T. areas are the best available at present." The most recent papers do not disturb this conclusion. B.E.T. theory has been applied to water on montmorillonite.[30] Molecular cross-sectional areas $\sigma'$ have been obtained by determination[31] of $V_M$ for anatase of known area (H.J. absolute method[29]) and their deviations from the liquid density $\sigma$ noted, *e.g.*, CO, $-8{\cdot}1\%$, $CO_2$ $+43{\cdot}5\%$. The $k$ of the H.J. relative method was found to be $0{\cdot}251\sigma$. Anderson and Emmett[32] compare the B.E.T. method, its modification,[33] and the H.J. relative method[23] for various gases on a range of carbon blacks. Barrer *et al.*[34] have produced a number of modified B.E.T. equations which fit data up to higher pressures and give consistent $V_M$ values. Corrin, using a solid of known area, has compared H.J. relative areas and B.E.T. areas,[35] and Hüttig and B.E.T. areas.[36] Theimer[37] proposes a semi-empirical equation of the B.E.T. type. A chemisorbed film, depending on its nature, may reduce,[38] or leave unchanged,[39] the isotherm for physical adsorption.

*Heterogeneity.* The thermodynamic properties of argon on rutile up to $\theta = 0{\cdot}6$ may be satisfactorily interpreted on the basis of a localised monolayer on a heterogeneous surface without interactions.[40] The plot of heat of adsorption against $\theta$ for argon on the (111) face of potassium chloride agrees with calculations, and differs markedly from the values for the (100) face.[41] This supplements data on the effect of crystal face on adsorption already advanced by Rhodin[42] for nitrogen on copper. Halsey[43] notes that a comparison of Rhodin's data for single crystal faces and polycrystalline copper, points to intercrystalline boundaries as an important source of heterogeneity. In a review, Halsey[43] concludes that the usual B.E.T. nitrogen isotherm with the well-marked point $B$ corresponds to a state of intermediate heterogeneity. The Sips distribution is different for nitrogen on rutile from that for oxygen and argon.[44] Hüttig and Theimer[45] have discussed lateral interactions and heterogeneity, using the expanded Langmuir equation.

**Porous Solids.**—The pore-size distribution is generally measured[46] by application of Kelvin's equation to the desorption branch of the isotherm. Thus, if the saturation vapour pressure of a liquid be $p_0$, molar volume $V$,

---

[29] W. D. Harkins and G. Jura, *J. Amer. Chem. Soc.*, 1944, **66**, 1362, 1366.

[30] R. W. Mooney, A. G. Keenan, and L. A. Wood, *ibid.*, 1952, **74**, 1367.

[31] H. L. Pickering and H. C. Eckstrom, *ibid.*, p. 4775.

[32] R. B. Anderson and P. H. Emmett, *J. Phys. Chem.*, 1952, **56**, 753, 756.

[33] R. B. Anderson, *J. Amer. Chem. Soc.*, 1946, **68**, 686.

[34] R. M. Barrer, N. Mackenzie, and D. McLeod, *J.*, 1952, 1736.

[35] M. L. Corrin, *J. Amer. Chem. Soc.*, 1951, **73**, 4061.

[36] *Idem*, *J. Phys. Colloid Chem.*, 1951, **55**, 612.

[37] O. Theimer, *Trans. Faraday Soc.*, 1952, **48**, 326.

[38] F. S. Stone and P. F. Tiley, *Nature*, 1951, **167**, 654.

[39] A. S. Joy and T. A. Darling, *ibid.*, 1951, **168**, 433.

[40] L. E. Drain and J. A. Morrison, *Trans. Faraday Soc.*, 1952, **48**, 316; J. A. Morrison, J. M. Los, and L. E. Drain, *ibid.*, 1951, **47**, 1023.

[41] D. M. Young, *ibid.*, 1952, **48**, 548.

[42] T. N. Rhodin, Jr., *J. Amer. Chem. Soc.*, 1950, **72**, 5692.

[43] G. D. Halsey, *Adv. Catalysis*, 1952, **4**, 259.

[44] J. M. Honig and L. H. Reyerson, *J. Phys. Chem.*, 1952, **56**, 140.

[45] G. F. Hüttig and O. Theimer, *Z. Elektrochem.*, 1952, **56**, 490.

[46] A. G. Foster, *Trans. Faraday Soc.*, 1932, **28**, 645; *Proc. Roy. Soc.*, 1934, *A*, **146**, 129.

and surface tension $\gamma$, across a plane surface, then across a meniscus in a capillary, of radius $r$ and with a contact angle $\theta$,

$$p = p_0 \exp - \frac{2V\gamma \cos \theta}{rRT} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

Foster[47] assumed that $\theta = 0$, and that a bimolecular layer of thickness $2\sigma$ is adsorbed on the capillary, so that $r = r_0 - 2\sigma$, where $r_0$ is the actual radius of the capillary. Some success has been achieved in applying this theory to data for ferric oxide gel, where seven liquids lie on a common $r_0$-$v$ curve ($v$ = volume adsorbed). Pore-distribution curves, $dv/dr$ against $r$, are discussed.[47] Wheeler[48] has proposed a theory combining B.E.T. multilayer and capillary-condensation viewpoints with $r = r_0 - t$, $t$ being the multilayer thickness at pressure $p$. Shull[49] points out that B.E.T. theory predicts excessively thick multilayers for gases on *plane* surfaces and recommends obtaining $t$ from experimental data on non-porous solids. This procedure has been followed recently by Juhola, Palumbo, and Smith;[50] they compare pore-size distribution for carbon blacks (1) from nitrogen desorption data[51] and (2) from water desorption data.[52] Since the carbon blacks are free from hydrophilic groups, it is assumed adsorption is negligible, $t = 0$, and $\theta = 60°$. The distributions agreed approximately over the 22—300 Å range, and method (2) was found applicable to the whole range of pores. The importance of pore-distribution in catalytic work has been stressed in an important article by Wheeler.[53]

The open-pore theory of hysteresis[46] has been developed by Cohan,[54] who considers condensation to start by formation of a cylindrical meniscus radius $r_0 - \sigma$, at pressure $p_a$, and desorption at pressure $p_d$ to follow the usual Kelvin equation with $r = r_0$. Thus

$$p_a = p_0 \exp - \frac{\gamma V}{(r_0 - \sigma)RT} \quad \text{and} \quad p_d = p_0 \exp - \frac{2\gamma V}{r_0 RT} \quad . \quad (13a \;\&\; b)$$

Hysteresis commences at $p_d = p_a$, and thus at $r_0 = 2\sigma$. This theory has been discussed by Brunauer[55] and again recently by Foster.[56] Cohan's theory does not consider an adsorbed layer in desorption (eqn. 13*b*), and Foster[56] endeavours to improve this. He considers the adsorption potential as made up of a term for capillary condensation and one for multilayer adsorption. The theory predicts that hysteresis will occur when product $V\gamma/RT\sigma$ for the adsorbed liquid exceeds unity. Pierce and Smith[57] have considered hysteresis in charcoal adsorption, where adsorbed patches are formed on active spots. Everett and Whitton[58] consider the properties of a mechanical model for hysteresis similar to the well-known bimetallic-strip

---

[47] A. G. Foster, *Discuss. Faraday Soc.*, 1948, **3**, 4.

[48] A. Wheeler, Catalyst Symposia, Gibson Island A.A.A.S. Conference, June, 1945, June 1946.

[49] C. G. Shull, *J. Amer. Chem. Soc.*, 1948, **70**, 1405.

[50] A. J. Juhola, A. J. Palumbo, and S. B. Smith, *ibid.*, 1952, **74**, 61.

[51] E. P. Barrett, L. J. Joyner, and P. P. Halenda, *ibid.*, 1951, **73**, 373.

[52] A. J. Juhola and E. O. Wiig, *ibid.*, 1949, **71**, 2069.

[53] A. Wheeler, *Adv. Catalysis*, 1951, **3**, 249.

[54] L. H. Cohan, *J. Amer. Chem. Soc.*, 1944, **66**, 98.

[55] L. Brunauer, "The Adsorption of Gases and Vapours," Vol. I, Oxford Univ. Press, London, 1945.

[56] A. G. Foster, *J.*, 1952, 1806.

[57] C. Pierce and R. N. Smith, *J. Phys. Chem.*, 1950, **54**, 784.

[58] D. H. Everett and W. I. Whitton, *Trans. Faraday Soc.*, 1952, **48**, 749.

thermostat control (cf. also Gregg [1a]). Freezing-point depressions have been measured for liquid held in capillaries.[59, 60] The Kelvin equation has been applied to the contact zones of anatase powder.[61]

Bartell and Bower [62] have applied eqn. (9*a*) to a porous gel (silica gel). They evaluated $A\phi$ by graphical integration and plotted log $A\phi$ against $-\log p/p_0$. They obtained a curve which was interpreted as two straight lines cutting at a point $p_b$, where liquid was formed in the capillaries. The area of the gel was determined by

$$\gamma_{LV^\circ} = \frac{RT}{VA}\int_{p_b}^{T_0} v\,d\ln p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

where everything except $A$ was known.

**Contact Angle and Work of Adhesion.**—To calculate work of adhesion one must insert the equilibrium contact angle $\theta_E$ into eqn. (5), and frequently very large differences have been found between advancing and receding angles, making evaluation of $\theta_E$ impossible. Adam and Jessop [63] ascribe the difference formally to a frictional force opposing motion of the interface. Adam,[2b] and Bartell and Cardwell,[64] suggest that the relatively large advancing angle arises from the need for the liquid to displace lyophobic adsorbed films from the surface. An additional factor is the roughness of the surface.[2] Wenzel [65] writes a modified version of Young's equation for a surface of roughness factor ν (ratio true : apparent areas),

$$\nu(\gamma_{SV^\circ} - \gamma_{SL}) = \gamma_{LV}\cos\theta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

and a thermodynamic proof has recently been advanced for eqn. (15) by Good.[66] An analysis has been made of porous surfaces.[67] Shuttleworth and Bailey [68] show that, on solids whose roughness is formed by isolated pits, subsidiary minima exist apart from that given by eqn. (14), and so hysteresis of the contact angle arises. Cassie [69] attributes hysteresis to a number of possible states of the adsorbed multilayer, which must be in the form of molecular clusters rather than a continuous film. Adam, in the discussion following the last two papers, considered that factors other than roughness must cause hysteresis with varnished surfaces. Hysteresis of the contact angle has been reported at the mercury–benzene–water interface.[70] Solutions of surface-active agents show a unimolecular change of θ with time, associated with adsorption of the agent.[71]

Fowkes and Harkins [72] claim true equilibrium $\theta_E$ values, using a development of Adam's tilting-plate method.[63, 73] Harkins and Livingston [7]

---

[59] M. J. Brown and A. G. Foster, *Nature*, 1952, **169**, 37.

[60] I. Higuti and M. Shimizu, *J. Phys. Chem.*, 1952, **56**, 198; I. Higuti and Y. Iwagami, *ibid.*, p. 921.

[61] I. Higuti and H. Utsugi, *J. Chem. Phys.*, 1952, **20**, 1180.

[62] F. E. Bartell and J. E. Bower, *J. Colloid Sci.*, 1952, **7**, 80.

[63] N. K. Adam and G. Jessop, *J.*, 1925, 1863.

[64] F. E. Bartell and P. H. Cardwell, *J. Amer. Chem. Soc.*, 1942, **64**, 494.

[65] R. N. Wenzel, *Ind. Eng. Chem.*, 1936, **28**, 988.

[66] R. J. Good, *J. Amer. Chem. Soc.*, 1952, **74**, 5041.

[67] A. B. D. Cassie and S. Baxter, *Trans. Faraday Soc.*, 1944, **40**, 546.

[68] R. Shuttleworth and G. L. T. Bailey, *Discuss. Faraday Soc.*, 1948, **3**, 16.

[69] A. B. D. Cassie, *ibid.*, p. 11.

[70] F. G. Bartell and C. W. Bjorklund, *J. Phys. Chem.*, 1952, **56**, 453.

[71] G. A. Wolstenholme and J. H. Schulman, *Trans. Faraday Soc.*, 1950, **46**, 488.

[72] F. M. Fowkes and W. D. Harkins, *J. Amer. Chem. Soc.*, 1940, **62**, 3377.

[73] N. K. Adam and R. S. Morrell, *J. Soc. Chem. Ind.*, 1934, **53**, 255T.

calculated values of $W_{(A)SL}$ from eqn. (5), and showed the importance of $\phi_E$. The most modern data are in the annexed Table.

*Free energies of solid–liquid interaction*, erg/cm.$^2$ (Harkins)

| Solid | Liquid | Spreading coeff. $\phi_E$ | Free energy of emersion $g_{E(SL)}$ | Work of adhesion $W_{A(SL)}$ |
|---|---|---|---|---|
| Anatase [8] | Water | 190 | 262 | 334 |
| ,, [8] | Nitrogen | 56 | 64 | 72 |
| ,, [8] | *n*-Butane | 43 | 58 | 73 |
| ,, [8] | *n*-Heptane | 46 | 66 | 86 |
| Copper [74] | ,, | 29 | 49 | 69 |
| Silver [74] | ,, | 37 | 57 | 77 |
| Lead [74] | ,, | 40 | 69 | 89 |
| Iron [71] | ,, | 53 | 73 | 73 |
| Graphite [71] | ,, | — | — | 69 |

**Low-energy Surfaces.**—Fox, Zisman, and their co-workers are publishing an important series of papers on " The Spreading of Liquids on Low Energy Surfaces." To date, the following have appeared : I, Polytetrafluorethylene (TFE) [75]; II, Copolymers of TFE [76]; III, Hydrocarbon surfaces [77]; IV, Monolayer coatings on platinum [78]; V, Perfluorodecanoic acid monolayers.[79] In each case a very large number of pure liquids was found to give finite values of $\theta_E$, measurable by the sessile-drop method to $\pm 2°$ or better. It was found that the contact angle was unchanged, whether measured in air, or in air saturated with the vapour of the liquid, at least for the less volatile liquids. Thus it was concluded that these low-energy solids did not appreciably adsorb the vapours concerned, *i.e.*, that $\phi_E = 0$ in eqn. (5). It was further found that for each homologous series of liquids and a given solid, $\cos \theta_E$ decreased linearly with the surface tension of the liquid $\gamma_{LV°}$. Extrapolation to $\theta = 0$ yielded a parameter $\gamma_c$, regarded as the critical surface tension, below which spreading of the liquid occurred on the solid concerned, typical values being 33 dynes/cm. for Polythene, and 17·5—20·5 dynes/cm. for TFE. The following order of wettability of groups in the solid surface was found, $\theta_{CF_3} > \theta_{CF_2} > \theta_{CH_3} > \theta_{CH_2}$. Another interesting result was that a monolayer of a long-chain compound effectively changed platinum into a " low-energy " (non-spreading) surface " demonstrating beyond doubt the short-range nature of the forces involved in wetting."

Elton [80] has suggested combining Antonoff's law

$$\gamma_{SL} = |\gamma_{LA} - \gamma_{SA}|$$

with

$$\gamma_{SA} = \gamma_{LA} \cos \theta + \gamma_{SL}$$

to give

$$\gamma_{SA} = \tfrac{1}{2}\gamma_{LA}(1 + \cos \theta)$$

where $\gamma_{SA}$, $\gamma_{LA}$, refer to the surfaces mutually saturated with respect to each other in air. Thus he calculated a value of $\gamma_{SA}$ for paraffin wax of

[74] W. D. Harkins and E. H. Loeser, *J. Chem. Phys.*, 1950, **18**, 556.
[75] H. W. Fox and W. A. Zisman, *J. Colloid Sci.*, 1950, **5**, 514.
[76] *Idem, ibid.*, 1952, **7**, 109. [77] *Idem, ibid.*, p. 428.
[78] E. G. Shafrin and W. A. Zisman, *ibid.*, p. 166.
[79] F. Schulman and W. A. Zisman, *ibid.*, p. 465.
[80] G. A. H. Elton, *J. Chem. Phys.*, 1951, **19**, 1066.

27 dynes/cm., values for water, glycerol, and ethylene glycol agreeing very well. Fox and Zisman [76] point out that the correct equation is

$$\gamma_S = \phi_E + \tfrac{1}{2}\gamma_{LV^\circ}(1 + \cos\theta_E)$$

but since $\phi_E \simeq 0$ for their solids, presumably this introduces little error. They note that $\gamma_S$ varies from 18 to 30 ergs/cm.$^2$ for TFE, and reject the method. Elton [81] concludes that evidence for mutual saturation of phases is lacking and in any case that real differences in $\gamma_S$ may exist. Fowkes and Sawyer [82] assume that $\gamma_{SV^\circ}$ and $\gamma_{SL}$ are the same for a solid perfluorinated oil as for liquid fractions of the same material. Using Young's equation, they calculate $\theta_E$ values for the solid in good agreement with those observed for a number of liquids. They also test the use of Antonov's rule, calculating values of $\gamma_{SV^\circ}$ of 18·3—23·5 erg/cm.$^2$ compared with 22·4 experimentally.

**Displacement Pressure.**—The rate at which a liquid penetrates a capillary is of course determined by $\gamma_L \cos\theta$, but since this quantity is no longer generally equal to $\gamma_S - \gamma_{SL}$, but to $\gamma_S - \gamma_{SL} - \phi_E$, Harkins and Livingston [7] suggested that the use of Freundlich's term, adhesion tension, should be abandoned. Bartell and his co-workers [83] have described a method for relating the pressure required to stop liquid 1 from displacing liquid 2 from a solid, which assumes that

$$A_{S1} = \gamma_S - \gamma_{S1} = \gamma_1 \cos\theta_{S1} \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$
$$A_{S2} = \gamma_S - \gamma_{S2} = \gamma_2 \cos\theta_{S2}$$

for the separate liquids displacing air from the powder, and

$$A_{S1} - A_{S2} = \gamma_{S2} - \gamma_{S1} = \gamma_{12} \cos\theta_{12} \quad . \quad . \quad . \quad . \quad . \quad (17)$$

for liquid 1 displacing liquid 2. Harkins and Livingston [7] have shown that the correct equation derived from (5) is

$$\begin{aligned} A_{S1} - A_{S2} &= (\gamma_{SV_1^\circ} - \gamma_{SV_2^\circ}) + (\gamma_{S1} - \gamma_{S2}) \\ &= \gamma_1 \cos\theta_{S1} + \gamma_2 \cos\theta_{S2} \quad . \quad . \quad . \quad . \quad . \quad . \quad (18) \end{aligned}$$

In one case, eqn. (17) gave 242 ergs/cm.$^2$ while the correct eqn. (18) gave 51 ergs/cm.$^2$ for the difference of two adhesion tensions. Again, the equation $\gamma_{12} \cos\theta_{12} = 242$ is impossible since $\gamma_{12}$ for the system concerned is 51. The experimental aspects of the method have also come under criticism,[84, 85] and a recent worker reports unfavourably on it.[86] A D.C. potential is reported to affect adhesion tension.[87]

**Heats of Wetting.**—The heat of immersion per cm.$^2$ $q_{i(LS)}$ of a solid from *vacuo* into a liquid, which is the enthalpy change of emersion, $h_{E(SL)}$, is [4, 5, 8]

$$q_{i(LS)} = h_{E(SL)} = h_S - h_{SL} = \gamma_S - \gamma_{SL} - T\left(\frac{\partial\gamma_S}{\partial T} - \frac{\partial\gamma_{SL}}{\partial T}\right)_{p,\,A}$$

---

[81] G. A. H. Elton, *J. Colloid Sci.*, 1952, **7**, 450.

[82] F. M. Fowkes and W. M. Sawyer, *J. Chem. Phys.*, 1952, **20**, 1650.

[83] See, *e.g.*, F. E. Bartell and H. J. Osterhof, *Ind. Eng. Chem.*, 1927, **19**, 1277; F. E. Bartell and H. Y. Jennings, *J. Phys. Chem.*, 1934, **38**, 495.

[84] N. S. Davies and H. A. Curtis, *Ind. Eng. Chem.*, 1932, **24**, 1137.

[85] S. H. Bell, J. O. Cutter, and C. W. Price, " Symposium on Wetting and Detergency," Harvey, London, 1937, p. 19.

[86] N. J. de Lollis, *J. Phys. Chem.*, 1952, **56**, 193.

[87] Z. Laszlo, *J. Chem. Phys.*, 1952, **20**, 1807.

If the solid has an adsorbed film

$$q_{i(LS_f)} = h_{E(S_fL)} = h_{S_f} - h_{SL} = \gamma_{SV} - \gamma_{SL} - T\left(\frac{\partial\gamma_{SV}}{\partial T} - \frac{\partial\gamma_{SL}}{\partial T}\right)_{p,\,A}$$

To determine $q_{i(LS)}$ an evacuated bulb of solid is broken under the liquid, whereas if the solid is first equilibriated with vapour at pressure $p$ and then immersed, $q_{i(LS_f)}$ results. In modern work the surface area of the powder is determined, usually by the B.E.T. method, and results are given in ergs/cm.$^2$. Laporte gives a bibliography.[88] Most modern data are due to Harkins, who neglects $pV$ and classifies results as $u_{E(SL)}$ (he writes $\varepsilon_{E(SL)}$).* The liquids examined may be arranged in order of decreasing $u_{E(SL)}$, which is the same for all the solids examined. If $h_{D(VS_f)}$ is the enthalpy change of desorption of the adsorbed film containing $n$ moles, the heat of evaporation from liquid being $\lambda$, then [8, 89]

$$h_{D(VS_f)} = h_{(E)SL} - h_{E(S_fL)} + n\lambda$$

an equation of use in linking heat of wetting to heats of adsorption. Harkins and Jura [89] have plotted $h_{E(S_fL)}$ for water on anatase as a function of film thickness. There is an exponential decrease of $h_{E(S_fL)}$, which becomes constant after five molecular layers. At this stage, *i.e.*, for the saturated film, the heat of emersion is just the surface enthalpy $h_L$ of the bulk liquid, for water 118·5 ergs/cm.$^2$ at 25°. This forms the basis of the H.J. *absolute* method of surface area determination.[8, 29] It gives the specific area of a solid non-porous powder as the ratio of $Q_{i(LS_f)}$, heat of wetting per g. of solid with saturated film, to $h_L$, *i.e.*, $A = Q_{i(LS_f)/h_L}$. Incidentally, the method seems to have been foreseen in a way by Patrick and Grimm [90] in their work on the heat of wetting with silica gel, but the method is nowadays not recommended for porous solids. Heats of wetting for water–graphite confirm discontinuities observed on isotherms.[91]

Heats of wetting on alumina and silica gels have been reported to change with absorbability of the liquid,[92] and with molecular size.[93] The effects may be associated with the failure of larger molecules to penetrate pores (cf. Gregg [1a]). Stowe [94] examined the effect of surface coverage with alumina, and displacement of hydrocarbons by water. The heat of wetting of some surfaces by water is high enough to suggest chemical reaction.[95] The temperature of outgassing of the solid is important, and a balance is usually struck between removal of adsorbed layers and sintering of the internal surface, *e.g.*, with silica gel.[96] It seems that many of the miscellaneous data on heats of wetting apply to porous solids and therefore are difficult to interpret.

D. D. E.

---

[88] F. Laporte, *Ann. Physique*, 1950, **5**, 5.

[89] W. D. Harkins and G. Jura, *J. Amer. Chem. Soc.*, 1944, **66**, 919.

[90] W. A. Patrick and F. V. Grimm, *ibid.*, 1921, **43**, 2144.

[91] P. R. Basford, G. Jura, and W. D. Harkins, *ibid.*, 1948, **70**, 1444.

[92] L. Robert, *Compt. rend.*, 1951, **233**, 1103.

[93] J. G. Miller, H. Heinemann, and W. S. W. McCarter, *Ind. Eng. Chem.*, 1950, **42**, 151.

[94] V. M. Stowe, *J. Phys. Chem.*, 1952, **56**, 484, 487.

[95] F. Howard and J. O. Culbertson, *J. Amer. Chem. Soc.*, 1952, **72**, 1185.

[96] D. T. Ewing and B. T. Bauer, *ibid.*, 1937, **59**, 1548.

* $h_{E(SL)} = u_{E(SL)} + pV$, where $V$ is the associated volume change of emersion.

## 3. ELECTROLYTES.

**Strong Electrolytes.**—*General theory.* In the Debye–Hückel theory of electrolytic solutions, the calculation of the ionic atmosphere surrounding an ion is based on a Boltzmann distribution: $n_r = n \exp(-ze\psi_r/kT)$, where $n_r$ and $\psi_r$ are respectively the number of ions per unit volume and the potential at a distance $r$ from the central ion. According to this, the charge density increases indefinitely with potential, but Wicke and Eigen [1] point out that the space requirements of the ions cannot be neglected except in very dilute solution, and, taking account of these, they derive a new distribution function which departs from Boltzmann's at moderate concentrations, bending over to a limiting saturation value for the charge density. The effect can account for the observed minima in activity data and, with reasonable assumptions concerning ion-hydration, gives good agreement with experiment up to 1M for the alkali halides in water. Falkenhagen is reported as having explained the conductance curves of some alkali halides up to 1M on the same basis, and extensions of the theory to multivalent electrolytes are promised.

Kramers's derivation [2] by statistical mechanics of the Debye–Hückel limiting laws has been modified by Berlin and Montroll,[3] and the new treatment eliminates the low critical concentration at which Kramers's derivation broke down.

Turning to more specialised topics, Barnartt [4] has derived a relation between concentration ($c$) and the velocity ($u$) of sound in electrolytes; by combining the equations of the interionic-attraction theory for the apparent molar volume and isothermal compressibility of the dissolved salt, he obtains for very dilute solutions a relation of the form $u = u_0 + Fc - Gc^{\frac{3}{2}}$. The comparison of this with experimental results is reminiscent of the findings twenty years ago with apparent molar volumes: plots of $\Delta u/c$ are linear against $c^{\frac{1}{2}}$ even up to 4M, but $F$ and $G$ must be replaced by empirical constants. As the experimental data are not accurate below 0·3M, no comparison with the theoretical slope is yet possible. A substantial contribution on polarisation [5] extends Jaffé's earlier theory [6] to electrolytic solutions, and presents results for water and salt solutions with various electrode metals over a wide range of frequencies.

*Conductivity, transport, and diffusion phenomena.* The properties of pure rare-earth salts should be of great interest owing to the close similarities between the compounds; the predominating variable in their electrolytic properties will be the radius of the ion. Spedding and his associates [7] have now published a number of papers on the subject, giving data for the conductivities, transport numbers, and activity coefficients of many of the chlorides and bromides. The equivalent conductances conform with the Onsager limiting slope, and the mobilities derived for the rare-earth ions

---

[1] E. Wicke and M. Eigen, *Naturwiss.*, 1951, **38**, 453; *Z. Elektrochem.*, 1952, **56**, 551.

[2] H. A. Kramers, *Proc. Roy. Acad. Amsterdam*, 1927, **30**, 145.

[3] T. H. Berlin and E. W. Montroll, *J. Chem. Phys.*, 1952, **20**, 75.

[4] S. Barnartt, *ibid.*, p. 278.

[5] H. C. Chang and G. Jaffé, *ibid.*, p. 1071; G. Jaffé and J. A. Rider, *ibid.*, p. 1077.

[6] G. Jaffé, *Ann. Physik*, 1933, **16**, 217, 249.

[7] F. H. Spedding, P. E. Porter, and J. M. Wright, *J. Amer. Chem. Soc.*, 1952, **74**, 2055, 2778, 2781; F. H. Spedding and I. S. Yaffe, *ibid.*, p. 4751. For graph summarising mobility data, see p. 4753.

increase regularly with *decrease* in atomic number up to a flat maximum for cerium, with the value for lanthanum slightly lower. The direction of the curve implies that the effective hydration number is the larger the smaller the ion; the maximum suggests that the larger radius of the first members of the series enables them to accommodate an additional molecule of water in the first hydration sphere, a view to which crystallographic and calorimetric data [8] offer some support.

Gordon and his co-workers [9] have made precision transport-number and conductivity measurements on sodium chloride and potassium chloride in pure methanol at 25° and derive the limiting mobilities: $Cl^-$, 52·38; $Na^+$, 45·22; $K^+$, 52·40. Moving-boundary studies have been made by Dismukes and King,[10] and by Spiro and Parton [11] who have investigated and improved Brady's [12] analytical boundary method. MacInnes and Dayhoff [13] have modified the E.M.F. centrifuge and record new results for sodium iodide and potassium iodide. Measurements continue to appear both of salt diffusion [14] and of tracer-ion diffusion; [15] a novel method has been introduced by Wall, Grieger, and Childers.[16] For a review of the field up to 1950 see Harned.[17]

The Wien effect [18] was discovered twenty-five years ago and, although since then the theory of the increase in conductivity at high field strengths has been worked out, the experimental data remain meagre.[19] Fortunately, new work in the field has now begun at Yale,[20] taking advantage of the recent great advances in techniques at high voltages, and systematic study by the new method should make valuable contributions to electrolyte theory. A completely dissociated electrolyte undergoes a conductivity increase at high voltages because the normal ionic atmosphere, with its retarding effects, virtually disappears at the high ionic velocities engendered. With weak electrolytes there is an additional mass-action increase, since the local concentration of oppositely charged ions is reduced for each ion by the disappearance of its atmosphere, and dissociation proceeds further.[21] Patterson and his co-workers [20] have shown that new results for magnesium, zinc, and copper sulphates are incompatible with the theory for completely dissociated electrolytes, but are in gratifying agreement with theory when the known dissociation constants of the sulphates are taken into account.

[8] F. H. Spedding and C. F. Miller, *J. Amer. Chem. Soc.*, 1952, **74**, 3158.

[9] J. A. Davies, R. L. Kay, and A. R. Gordon, *J. Chem. Phys.*, 1951, **19**, 749; J. P. Butler, H. I. Schiff, and A. R. Gordon, *ibid.*, p. 752.

[10] E. B. Dismukes and E. L. King, *J. Amer. Chem. Soc.*, 1952, **74**, 4798.

[11] M. Spiro and H. N. Parton, *Trans. Faraday Soc.*, 1952, **48**, 263.

[12] A. P. Brady, *J. Amer. Chem. Soc.*, 1948, **70**, 911.

[13] D. A. MacInnes and M. O. Dayhoff, *J. Chem. Phys.*, 1952, **20**, 1034.

[14] R. A. Robinson and C. L. Chia, *J. Amer. Chem. Soc.*, 1952, **74**, 2776; H. S. Hamer and R. S. Hudson, *ibid.*, 1951, **73**, 5083.

[15] J. M. Nielson, A. W. Adamson, and J. W. Cobble, *ibid.*, 1952, **74**, 446; J. H. Wang, *ibid.*, p. 1182; J. H. Wang and S. Miller, *ibid.*, p. 1611.

[16] P. T. Wall, P. F. Grieger, and C. W. Childers, *ibid.*, p. 3562.

[17] H. S. Harned, *Ann. Rev. Phys. Chem.*, 1951, **2**, 37.

[18] M. Wien and J. Malsch, *Ann. Physik*, 1927, **83**, 305.

[19] For review and references see H. C. Eckstrom and C. Schmelzer, *Chem. Reviews*, 1939, **24**, 367.

[20] J. A. Gledhill and A. Patterson, Jr., *J. Phys. Chem.*, 1952, **56**, 999; F. E. Bailey, Jr., and A. Patterson, Jr., *J. Amer. Chem. Soc.*, 1952, **74**, 4426, 4428; D. Berg and A. Patterson, Jr., *ibid.*, p. 4704.

[21] G. S. Hartley and J. W. Roe, *Trans. Faraday Soc.*, 1940, **36**, 101.

*Thermodynamic properties.* Partial molal heat capacities and heat contents have been recorded by Spedding and Miller [8] for aqueous solutions of cerium trichloride and neodymium trichloride at 25°. MacInnes and his co-workers [22] have developed the magnetic float method of density determination, and report partial molal volumes of potassium chloride and iodide and sodium iodide in water at 25°. Salt effects for various organic gases and liquids have been studied,[23] and current theories are analysed in a review by Long and McDevit [23]; the solvation of uranyl nitrate has been examined by both distribution [24] and calorimetric methods,[25] and the activity coefficients in aqueous silver nitrate–nitric acid mixtures have been measured by Davidson and his collaborators [26] using a cell with silver and glass electrodes. E.M.F. measurements have also been used to obtain activities in liquid ammonia [27] and liquid hydrogen fluoride [28] as solvents.

**Incomplete Dissociation in Salt Solutions.**—The applicability of mass-action considerations to ionic association in salt solutions is now widely accepted and a considerable amount of work in this field is being reported, partly filling gaps in the data previously accumulated for the commoner salts and partly supplying information about salts of the new or rarer elements. There is no major theoretical advance to report, but it is clear that the experimental results now being derived from a wide variety of different properties will add to our understanding of the short-range forces between ions. Measurements, unfortunately, are still being largely confined to one temperature, and some, being made in mixed electrolytes at high nominal ionic strengths, cannot be safely used for theoretical comparisons.

Most of the methods so far used are exemplified in the results under review. Conductivity measurements on dilute solutions have yielded dissociation constants for barium thiosulphate [29] and for $SrIO_3^+$.[30] Conductivities on mixed solutions are applicable where extensive association is expected, and this method and the solubility method have both been applied to a number of ferricyanides [31] and tri- and tetra-metaphosphates.[32] Parry and Dubois [33] have used E.M.F. measurements, with copper and glass electrodes, to investigate the interactions of cupric and citrate ions; concentration cells have been used to study the association of stannous with $Cl^-$ and $Br^-$ ions [34] at a nominal ionic strength of 3·0; and equilibrium constants of many bivalent cations with iminodiacetic and related acids [35] have been

---

[22] D. A. MacInnes, M. O. Dayhoff, and B. R. Ray, *Rev. Sci. Instr.*, 1951, **22**, 642; D. A. MacInnes and M. O. Dayhoff, *J. Amer. Chem. Soc.*, 1952, **74**, 1017.

[23] T. J. Morrison, *J.*, 1952, 3814, 3819; W. F. McDevit and F. A. Long, *J. Amer. Chem. Soc.*, 1952, **74**, 1773; A. P. Altshuller and H. E. Everson, *J. Phys. Colloid Chem.*, 1951, **55**, 1368; H. A. C. McKay, *Trans. Faraday Soc.*, 1952, **48**, 1103; J. H. Saylor, A. I. Whitten, I. Claiborne, and P. M. Gross, *J. Amer. Chem. Soc.*, 1952, **74**, 1778. For review see F. A. Long and W. F. McDevit, *Chem. Reviews*, 1952, **51**, 119.

[24] A. W. Garner, H. A. C. McKay, and D. T. Warren, *Trans. Faraday Soc.*, 1952, **48**, 997.

[25] L. I. Katzin, D. M. Simon, and J. R. Ferraro, *J. Amer. Chem. Soc.*, 1952, **74**, 1191.

[26] O. D. Bonner, A. W. Davidson, and W. J. Argersinger, Jr., *ibid.*, p. 1047.

[27] J. Sedlet and T. de Vries, *ibid.*, 1951, **73**, 5808.

[28] G. G. Koerber and T. de Vries, *ibid.*, 1952, **74**, 5008.

[29] T. O. Denney and C. B. Monk, *Trans. Faraday Soc.*, 1951, **47**, 992.

[30] C. A. Colman-Porter and C. B. Monk, *J.*, 1952, 1321.

[31] C. W. Gibby and C. B. Monk, *Trans. Faraday Soc.*, 1952, **48**, 632.

[32] C. B. Monk, *J.*, 1952, 1314, 1317.

[33] R. W. Parry and F. W. Dubois, *J. Amer. Chem. Soc.*, 1952, **74**, 3749.

[34] C. E. Vanderzee and D. E. Rhodes, *ibid.*, pp. 3552, 4806.

[35] S. Chabarek, Jr., and A. E. Martell, *ibid.*, pp. 5052, 5057, 6021.

determined by J. Bjerrum's method. A new departure is the use of cells without transference for studying ion-pair formation in salts.[36] The method is well adapted for work over a range of temperature and should lead to the accumulation of reliable data for the entropy and heat content changes ($\Delta S$, $\Delta H$) of the dissociation process. The values so obtained, with those of some related compounds are (Mal = malonate):

| | $MgSO_4$ | MgMal | ZnMal[37] | $LaSO_4^+$ | $LaFe(CN)_6$[38] |
|---|---|---|---|---|---|
| $\Delta H$, kcal. ............ | −5·7 | −3·2 | −3·1 | −2·5 | −2·0 |
| $\Delta S$, cal./deg. ......... | −31·0 | −23·9 | −27·5 | −26·0 | −23·9 |

Spectrophotometric measurements in the visible and ultra-violet regions are being increasingly employed to study ionic equilibria. The method is experimentally simple and the interpretation straightforward so long as it is remembered that foreign ions which do not affect the absorption may nevertheless interact with the system being studied, especially at high ionic strengths. By measurement of optical densities, Gordon and Schreyer[39] have shown that the deep blue colour given by cobalt in concentrated alkali is due to $Co(OH)_3^-$, and by a similar method Yaffe and Voigt[40] find that Ru(III) and (IV) both give $RuCNS^{2+}$, Ru(IV) being reduced by the thiocyanate. They determine an equilibrium constant for the ion-pair at an ionic strength of approximately 1, and Farrington,[41] in a similar way and at the same ionic strength, has measured the extent of $CuBr^+$ formation. King and Pandow[42] have carried out further work on the ionic state of Ce(IV) in perchloric acid solutions; Beer's law is not obeyed at $H^+$-ion concentrations of 1—2·5M, and the spectra give evidence of polymerisation—presumably dimerisation through oxide or hydroxyl bridging. Anderson and his co-workers[43] have used the method of continuous variations to study the interaction of sulphosalicylic acid with aluminium, nickel, and chromium; a maximum in optical density is given for the 1 : 1 ratio. The copper salt was used as indicator with aluminium, and in a rather similar way Wilson and Taube[44] have studied the interaction of chromium and gallium with the fluoride ion, using ferric ion as indicator.

Raman spectra have been used[45] to study the aluminate and zincate ions; the experimental data are found to be in good agreement with calculations for the tetrahedral ions $Zn(OH)_4^{2-}$ and $Al(OH)_4^-$. The interaction between thorium and various anions has been studied by distribution measurements using the thenoyl–trifluoroacetone complex.[46] Finally, Schubert[47] has continued his application of ion-exchange resins, utilising radio-tracers, to the determination of equilibrium constants, and his most

---

[36] H. W. Jones and C. B. Monk, *Trans. Faraday Soc.*, 1952, **48**, 929; J. I. Evans and C. B. Monk, *ibid.*, p. 934.

[37] J. C. James, *J.*, 1951, 153.

[38] C. W. Davies and J. C. James, *Proc. Roy. Soc.*, 1948, *A*, **195**, 116.

[39] S. Gordon and J. M. Schreyer, *J. Amer. Chem. Soc.*, 1952, **74**, 3169.

[40] R. P. Yaffe and A. F. Voigt, *ibid.*, p. 2500.

[41] P. S. Farrington, *ibid.*, p. 966.

[42] E. L. King and M. L. Pandow, *ibid.*, p. 1966.

[43] A. M. Liebman and R. C. Anderson, *ibid.*, p. 2111; M. B. Lasater and R. C. Anderson, *ibid.*, p. 1429.

[44] A. S. Wilson and H. Taube, *ibid.*, p. 3509.

[45] E. R. Lippincott, J. A. Psellas, and M. C. Tobin, *J. Chem. Phys.*, 1952, **20**, 536.

[46] E. L. Zebroski, H. W. Alter, and F. K. Heumann, *J. Amer. Chem. Soc.*, 1951, **73**, 5646; W. C. Waggener and R. W. Stoughton, *J. Phys. Chem.*, 1952, **56**, 1.

[47] J. Schubert, *ibid.*, p. 113.

recent contribution also reviews earlier work in this field. This completes the list of methods used in the period under review, but, varied as the list is, it is worth noting in addition that conductivities at high field strengths [20] promise to provide a sensitive method of detecting and estimating ion-pairs, and that the same applies, to a lesser degree, to diffusion measurements.[48]

In the main, the measurements enumerated fall well into line with earlier work. In the summary below, numerical values quoted are equilibrium constants for the dissociation process. Some recent writers give the reciprocals of these, but this seems a pity even in cases where it may be the more logical procedure, partly because it is confusing in relation to all the earlier literature and partly because it creates an artificial distinction between acids and other electrolytes.

Ion-pair formation is appreciable but not extensive in cupric bromide,[41] in agreement with data for the chloride.[49] It is somewhat more marked, as might be expected, in Ru(III) thiocyanate; $K_c = 0{\cdot}017$ for $RuCNS^{2+}$ at [40] an ionic strength of approximately 1. An approximate value, $K = 0{\cdot}04$, for $ThCl^{3+}$ is quite high for this valency type [46] and suggests ion-pair formation of the Bjerrum kind between hydrated ions. At M-chloride concentration and an ionic strength of 4·0, however, Waggener and Stoughton [46] report higher association products to be present in the following proportions: $Th^{4+}$, 33·8; $ThCl^{3+}$, 57·5; $ThCl_2^{2+}$, 4·7; $ThCl_3^{+}$, 3·4; $ThCl_4$, 0·6%. The relative figures are not what would be expected from electrostatic theory, and suggest that the further association of $Cl^-$ ions is governed rather by considerations of co-ordination chemistry; this conclusion must be treated with reserve however, in view of our complete ignorance of the activity coefficients and the sensitivity of the results to small experimental errors. The fluorides of metals of high valency are weaker than the other halides, and the dissociation constant [44] of $GaF^{2+}$ is about the same as that of $FeF^{2+}$; the corresponding chromium complex is about five times as strong, so the difficulty in removing water from the hydrated $Cr^{3+}$ ion has no discernible influence here.

The dissociation constants of a number of bivalent metal thiosulphates are normal,[29] being somewhat higher than those of the sulphates, but the cadmium salt is weak ($K = 1{\cdot}2 \times 10^{-4}$), and complex-anion formation is appreciable even in dilute solutions. The sulphosalicylates [43] of copper ($K = 0{\cdot}0022$), aluminium ($K = 5 \times 10^{-4}$), and chromium ($K \approx 10^{-3}$) are of the order of magnitude to be expected for normal ion-pair formation, but the nickel salt ($K = 4 \times 10^{-5}$) is distinctly weak. The dissociation constants for the ion-pairs of the ferricyanides [31] and tri- and tetra-metaphosphates [32] of the alkaline earths are given in the following Table:

| | Mg | Ca | Sr | Ba |
|---|---|---|---|---|
| Ferricyanides ($\times 10^3$) | 1·63 | 1·47 | 1·41 | 1·32 |
| Trimetaphosphates ($\times 10^4$) | 4·89 | 3·56 | 4·43 | 4·50 |
| Tetrametaphosphates ($\times 10^6$) | 6·7 | 3·9 | 7·0 | 10·3 |

It seems that the trimetaphosphate ion, unlike the ferricyanide ion, is able to replace hydration water from the cation, thus giving much smaller

---

[48] H. S. Harned and R. M. Hudson, *J. Amer. Chem. Soc.*, 1951, 73, 3781.

[49] W. H. Banks, E. C. Righellato, and C. W. Davies, *Trans. Faraday Soc.*, 1931, 27, 621.

$K$'s, and reversing the order Ca, Sr, Ba. The magnesium trimetaphosphate is still the strongest salt, presumably because the inner hydration shell of this small ion is particularly stable. This further emphasises the importance of geometrical considerations in any final analysis. Lanthanum trimetaphosphate [32] ($K = 2{\cdot}0 \times 10^{-6}$) is also much weaker than the ferricyanide [38] ($K = 1{\cdot}82 \times 10^{-4}$) and again the non-hydrated cation may be involved. The dissociation constant [32] of the lanthanum tetrametaphosphate ion-pair is $2{\cdot}2 \times 10^{-7}$; this valency product of twelve is the highest yet studied. Analogous considerations concerning the stabilities of complexes involving organic ligands have received active consideration over the past few years. Williams,[50] who has taken the alkaline-earth cations for detailed discussion, shows that the relation between the p$K$ values and ionization potentials, which has so far provided the most satisfactory explanation, fails for magnesium. He considers that short-range repulsion forces must also be considered. In a study of the alkaline earth monocarboxylates by Colman-Porter and Monk,[51] magnesium is again found to be anomalous, and it is suggested that, as detailed above for inorganic salts, the hydration of magnesium may account for this difference.

**Acids and Bases.**—A recent E.M.F. study of the $HSO_4^-$ ion [52] has removed a former discrepancy between the dissociation constant at various temperatures obtained by this method and by other methods ($K = 0{\cdot}0103$ at 25°); the Bureau of Standards [53] have added tartaric and 5 : 5-diethylbarbituric acids to their series of precise E.M.F. data; sulphamic acid has been carefully examined by King,[54] and Jones and Parton [55] have obtained satisfactory results for benzoic acid by using the quinhydrone in place of the hydrogen electrode. A further article on an individual acid is that of Waring,[56] who reviews the thermodynamic properties of formic acid, and two papers devoted to a study of series of acids have been given by Bother-By and Medalia [57] on some substituted benzoic acids and by Peek and Hill [58] on some dicarboxylic acids in 20% methanol; both of these interpret their results in terms of current theories. As opposed to these E.M.F. methods, a spectrophotometric method has been developed for determining the overlapping constants of dibasic acids [59]; this has been applied to several examples and the results are compared with previous data. In the field of non-aqueous solvents, formamide, which is a good solvent of higher dielectric constant than water (109 at room temperature), has been used by Dawson and Griffith [60] for freezing-point studies of several organic acids. Their semi-quantitative calculations suggest that ionization is roughly 10% greater in this solvent than in water.

Two further contributions to the study of base equilibria are those of

---

[50] R. J. P. Williams, *J.*, 1952, 3770.

[51] C. A. Colman-Porter and C. B. Monk, *ibid.*, p. 4363.

[52] C. W. Davies, H. W. Jones, and C. B. Monk, *Trans. Faraday Soc.*, 1952, **48**, 921.

[53] R. G. Bates and R. G. Canham, *J. Res. Nat. Bur. Stand.*, 1951, **47**, 343; G. C. Manov, K. E. Schuette, and F. S. Kirk, *ibid.*, 1952, **48**, 84.

[54] E. J. King and G. W. King, *J. Amer. Chem. Soc.*, 1952, **74**, 1212.

[55] A. V. Jones and H. N. Parton, *Trans. Faraday Soc.*, 1952, **48**, 8.

[56] W. Waring, *Chem. Reviews*, 1952, **51**, 171.

[57] A. K. Bother-By and A. I. Medalia, *J. Amer. Chem. Soc.*, 1952, **74**, 4402.

[58] H. M. Peek and T. L. Hill, *ibid.*, 1951, **73**, 5304.

[59] B. J. Thamer and A. F. Voigt, *J. Phys. Chem.*, 1952, **56**, 225.

[60] L. R. Dawson and E. J. Griffith, *ibid.*, p. 281.

Everett and Wynne-Jones[61] who used a hydrogen electrode for temperature studies of the ammonium and methylammonium ions in 60% aqueous methanol, and a solubility investigation of strontium hydroxide;[30] here ($K = 0{\cdot}11$ for $SrOH^+$) the value fits an equation[62] which relates crystallographic cation radii with the p$K$'s of strong hydroxides.

**Redox Systems.**—Potentials of some of the valency systems of neptunium,[63] americium and praseodymium,[64] and ruthenium[65] have been reported during 1952, and an interesting system, namely, that of the 2 : 2′-dipyridyl derivatives of Os(II–III) has been investigated.[66] The effect of varying the ionic strength ($I$) by indifferent electrolytes gave plots of E.M.F. against $I^{\frac{1}{2}}$ which deviate from those predicted by the Debye–Hückel theory. The authors suggest that the changing nature of the ligand–metal bonds with ionic environment can explain this; however, a consideration of the possible ion-pairs present may well provide a more logical interpretation.

C. W. D.
C. B. M.

## 4. THE KINETICS OF HOMOGENEOUS REACTIONS.

There has been no substantial change in the theory of rate processes. Most of the published work has been based on experiment and concerned either with the elucidation of the mechanisms of various reactions or with the determination of the specific rate constants and energies of activation of simple unimolecular or bimolecular reactions involving ions, molecules, and radicals. The ready availability of suitable radioactive isotopes of most of the common elements has led to an increased understanding of electron- and group- or atom-transfer processes in solution, and also of the nature of the chemical reactions which ensue when nuclear radiations are absorbed by matter. A noteworthy conference has been held on each of these two subjects and the large amount of work which has been carried out is reflected in the size of the appropriate sections of this Report. Three other symposia concerned with (1) the reactivity of free radicals (see ref. 56), (2) combustion and flame, and (3) ionic polymerisation (see ref. 300) have also taken place but the Proceedings of none of these have yet been published.

We have presented the topics in order of increasing complexity of mechanism, and have deliberately omitted any mention of certain fields of work. Thus, oxidation and combustion have not been referred to, but it is hoped that this subject will be covered in next year's Report when the papers submitted to the Boston conference (no. 2 above) will have been printed. Work on reactions in the solid phase and investigations relating to the more physical or dosimetric aspects of radiation chemistry have been omitted as being of only minor interests to chemists.

**General and Theoretical.**—Most reactions which have been reported have been investigated by conventional experimental methods, or by slight

---

[61] D. H. Everett and W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, 1952, **48**, 531.
[62] C. W. Davies, *J.*, 1951, 1256.
[63] D. Cohen and J. C. Hindman, *J. Amer. Chem. Soc.*, 1952, **74**, 4679, 4682.
[64] L. Eyring, H. R. Lohr, and B. B. Cunningham, *ibid.*, p. 1186.
[65] R. E. Connick and C. R. Hurley, *ibid.*, p. 5012.
[66] G. T. Barnes, F. P. Dwyer, and (Miss) E. C. Gyarfas, *Trans. Faraday Soc.*, 1952, **48**, 269.

variants of these. One new method is that of Heitler[1] who used a modified Cottrell apparatus, with a suitably aged thermistor in place of a thermometer to detect the changes of boiling point of the solvent accompanying the changing concentration of a dissolved reactant. By using acetone as the solvent it was possible to record the course of reactions with half-lives of less than one minute. A number of authors developed the mathematical treatment appropriate to the kinetics of complex reactions, such as those involving two consecutive second-order steps,[2] accompanied by diffusion,[3] and autosynthetic reactions.[4]

The principal difficulty in the calculation of velocity constants *a priori*, by the methods of the transition-state theory, is that of obtaining an accurate value for $\Delta E_0^{0\ddagger}$, the increment in internal energy at absolute zero in passing from the reactants to the complex. At best the calculation is semi-empirical and can only be carried through to completion for the simplest systems. There is therefore considerable incentive to find good empirical relations between measured energies of activation and experimentally accessible properties of the reactants. Eyring and Smith[5] have recently shown that there is a linear relation between the activation energy of the reaction of sodium atoms with chlorinated hydrocarbons and the ratio of the net charge on the halogen atom to the polarisability of the carbon–halogen bond which is broken. It has often been pointed out that there is a simple proportionality between the change in activation energy ($\Delta E$) and the change in bond dissociation energy ($\Delta D$) for certain series of simple bimolecular reactions. Bernstein[6] has pointed out, for the case of the reaction

$$CX_{4-n}Y_n + M \longrightarrow M{-}X + CX_{3-n}Y_n$$

where $n = 0, 1, 2$, or $3$, and X is a halogen, that, if all the bonding and non-bonding contributions to the heat of atomisation of the substituted methane $CX_{4-n}Y_n$ are additive, and if the same is also true for the activated complex, then not only is $\Delta E$ proportional to $\Delta D_{C-X}$ but both are proportional to changes in the heat of formation and in the heat of atomisation of the substituted methane.

It is a feature of the transition state theory that, since $\ln A = \alpha \Delta S^{\ddagger}$, variations of the frequency factor ($A$) can be associated with variations of the entropy of activation ($\Delta S^{\ddagger}$). Rollefson[7] has drawn attention to the fact that the $A$ values of many bimolecular gas and solution reactions are within $\simeq 10^{11}$ or $\simeq 10^{7}$ l. mole$^{-1}$ min.$^{-1}$, corresponding to $\Delta S^{\ddagger}$ values of $\simeq -10$ and $\simeq -30$ cal. deg.$^{-1}$ mole$^{-1}$ respectively. The second value of $\Delta S^{\ddagger}$ is of the same order as the translational entropies of many molecules at room temperature, and it is therefore suggested that in the first case the two molecules comprising the activated complex are only loosely bound and that the only condition for formation of the complex is approach of the molecules to within a certain distance, so that only one degree of vibrational freedom is lost; however, in the second case the molecules are tightly bound in the

---

[1] C. Heitler, *Chem. and Ind.*, 1952, 875.

[2] H. G. Higgins and E. J. Williams, *Australian J. Sci. Res.*, 1952, 5, *A*, 572.

[3] F. J. W. Roughton, *Proc. Roy. Soc.*, 1952, *A*, **214**, 564; J. Crank, *Phil. Mag.*, 1952, **43**, 811.

[4] (Sir) Cyril Hinshelwood, *J.*, 1952, 745.

[5] H. Eyring and R. P. Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 229.

[6] R. B. Bernstein, *J. Chem. Phys.*, 1952, **20**, 524.

[7] G. K. Rollefson, *J. Phys. Chem.*, 1952, **56**, 976.

complex and all three degrees of translational freedom have gone. The chemical nature of the reactions in the two groups is considered to be broadly in accord with this view. Another simple deduction from transition-state theory which can readily be demonstrated concerns equilibria.[8] When a reversible reaction is displaced from equilibrium so slightly that the free-energy change is less than the value of $RT$, the rate of approach to equilibrium is directly proportional to the free-energy difference between the reactants and the products.

The transition-state theory has little of quantitative value to offer concerning the pressure dependence of the rate constant of unimolecular reactions, and in the attempts to refine the Lindemann collision theory there are signs of a revived interest in this field and in the problems which underlie this theory. Johnston[9] has carried out a general summation over all quantum states of the individual steps in the Lindemann scheme, whence he obtains the expression.

$$\text{Rate} = \sum_i \frac{a_i c_i (M)}{b_i(M) + c_i}$$

where $a_i$, $b_i$, and $c_i$ are respectively the average values of the rate constants in proceeding from any quantum state of the molecules on the left-hand side of reactions (1), (2), and (3) below, to any quantum state of the molecules on the right-hand side :

$$M + M \xrightarrow{a_i} M + A \quad . \; . \; . \; . \; . \; . \; . \quad (1)$$

$$M + A \xrightarrow{b_i} M + M \quad . \; . \; . \; . \; . \; . \; . \quad (2)$$

$$A \xrightarrow{c_i} C \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (3)$$

and $A$ denotes an activated molecule, $C$ a product molecule, and $M$ the reactant molecule. By assuming these averages to be constant it is possible to set a limit on the value of the rate constant at low concentrations of $M$ from data on the value of the rate constant at high concentrations and *vice versa.* Theory and experiment have been compared for the pyrolyses of nitrous oxide and nitrogen pentoxide. Benson[10] has combined Slater's theory[11] with the Lindemann hypothesis and concludes (*a*) that for molecules containing more than 6 atoms the rate constant is unlikely to change with decreasing pressure until at least 1 mm. Hg is reached and (*b*) that for molecules of identical atomicity but differing shape the fall in rate constant will occur at pressures higher for linear than for non-linear molecules.

**First-order and Unimolecular Gas Reactions.**—Several pyrolytic and isomerisation reactions have recently been shown to be non-chain first-order homogeneous reactions. Notable amongst these are the dehydrohalogenation reactions of halogenated hydrocarbons. Howlett[12] has shown that ethyl chloride, 1 : 1-dichloroethane, *iso*propyl chloride, and *iso*butyl chloride decompose in this manner. Furthermore, below a certain pressure (5 mm. Hg for ethyl chloride at 456°) the order of reaction exceeds unity, but in the presence of sufficient quantities of either product, or added inert gases such as nitrogen and helium, the first-order character can be maintained down to

[8] W. R. Gilkerson, M. M. Jones, and G. A. Gallup, *J. Chem. Phys.*, 1952, **20**, 1182.

[9] H. S. Johnston, *ibid.*, p. 1103. [10] S. W. Benson, *ibid.*, p. 1064.

[11] N. B. Slater, *Proc. Roy. Soc.*, 1948, *A*, **194**, 112.

[12] K. E. Howlett, *J.*, 1952, 3695, 4487; *Chem. and Ind.*, 1952, 1175.

lower pressures. The pyrolysis of 1 : 2-dichloroethane, though a chain reaction, shows similar effects below 20 mm. Hg pressure.[13] This author has examined the results in the light of Rice and Ramsperger's theory and has shown that they are in agreement with the idea that the transformation probability of an activated molecule is a function of the energy possessed in excess of the minimum required for reaction. The relations between the frequency factors and energies of activation of these reactions are regarded as being in accord with the notion that the slow step is the localisation of the energy in the activated molecules. By employing carbon-coated reaction vessels Barton, Head, and Williams [14] have succeeded in suppressing any heterogeneous reaction in the decomposition of (—)-menthyl chloride and demonstrated the unimolecular nature of the residual homogeneous reaction. The usual stereospecificity was observed, the ratio of $\Delta^2$- to $\Delta^3$-olefin in the products being about 0·3.

The isomerisation of di*iso*propenyl ether to allylacetone has been followed spectrophotometrically by Stein and Murphy.[15] At temperatures between 143° and 194° and pressures between 20 and 760 mm. the first-order rate constant has the value $5{\cdot}4 \times 10^{11} \exp(-29{\cdot}3 \text{ kcal.}/RT)$ sec.$^{-1}$, very close to the value which they obtained earlier for allyl vinyl ether. A preliminary account has been given of the kinetics of the isomerisation of *cyclo*propane to propylene between 10 and 0·1 mm.[16] The reaction is quasi-unimolecular, and reasonably good agreement of the data with the predictions based on Kassel's equation [17] is obtained, if in applying the latter, it is assumed that the collision diameter is 3·94 Å and 13 oscillators are involved.

Sir Cyril Hinshelwood and his collaborators have published a series of papers [18] on the decomposition of various straight-chain and branched-chain paraffins in the presence of sufficient nitric oxide to suppress the concurrent chain reaction, and their results are summarised in a final paper.[19] Reactions of hydrocarbons such as ethane, propane, *iso*butane, *iso*pentane, *neo*pentane, and *neo*hexane show a single transition from first to second order as the pressure is reduced, and the energy of activation is independent of pressure. Reactions of other hydrocarbons, including *n*-butane, *n*-pentane, *n*-hexane, 2 : 3-dimethylbutane, and 2- and 3-methylpentane, change from first to second order, return to first order and finally become second order as the pressure is reduced from 1600 to 0·1 mm. This effect could be ascribed to the coexistence of two unimolecular reactions with different pressure dependence, and in agreement with this two distinct activation energies are observed, but the products of these two reactions appear to be the same in the case of *n*-butane. Hydrocarbons in the first category have a frequency factor for decomposition in the normal range of $10^{12}$ to $10^{14}$ sec.$^{-1}$, as also do the hydrocarbons in the second category when the pressure is high. The low-pressure first-order frequency factors for the

---

[13] K. E. Howlett, *Trans. Faraday Soc.*, 1952, **48**, 25.

[14] D. H. R. Barton, A. J. Head, and R. J. Williams, *J*,. 1952, 453.

[15] L. Stein and E. W. Murphy, *J. Amer. Chem. Soc.*, 1952, **74**, 1041.

[16] H. O. Pritchard, R. G. Sowden, and A. F. Trotman-Dickinson, *J. Amer. Chem. Soc.*, 1952, **74**, 4472.

[17] L. S. Kassel, " Kinetics of Homogeneous Reactions," Chem. Catalog. Co., New York, 1932, p. 93.

[18] F. J. Stubbs, K. U. Ingold, B. C. Spall, C. J. Danby, and (Sir) Cyril Hinshelwood, *Proc. Roy. Soc.*, 1952, *A*, **214**, 20; M. G. Peard, F. J. Stubbs, and (Sir) Cyril Hinshelwood, *ibid.*, p. 330, 339. [19] *Idem, ibid.*, p. 471.

latter group of hydrocarbons are however very much higher. A similar high-frequency factor is suggested for the dissociation of vinyl*cyclo*hexene into butadiene.[20] A comparative study of the pyrolysis of nine olefins has been made by Molera and Stubbs.[21] All these reactions are of first order during the initial stages. Marcus [22] has surveyed existing data on atomic cracking reactions and on the deuteration of free radicals, and has deduced the velocity constants for the dissociation of various vibrationally excited alkanes. As would be expected, the rate constant increases with increasing number of degrees of freedom of the decomposing molecule.

The kinetics of decomposition of diethyl peroxide have been investigated in a flow system in the presence of excess of toluene.[23] The products are mainly ethane and formaldehyde with smaller amounts of methane and dibenzyl. The results are interpreted in terms of a non-chain, radical mechanism and the overall first-order constant $[=2{\cdot}1 \times 10^{13} \exp(-31{\cdot}7 \text{ kcal.}/\boldsymbol{R}T) \text{ sec.}^{-1}]$ is shown to refer to the initial break into two ethoxy-radicals. However, the value 31·7 kcal. is rather smaller than the expected value of the bond dissociation energy $D_{\text{EtO–OEt}}$. The possibility that this reaction may be more complicated than has hitherto been supposed has been suggested by Style and Jenkins; [24] and Mortlock and Style [25] have drawn attention to the fact that diethyl peroxide reacts with nitric oxide to form ethyl nitrite. Clearly the nitric oxide method cannot be used to isolate any non-chain decomposition products of this peroxide. The pyrolysis of di-*tert.*-butyl peroxide has been studied mass spectrometrically by Lossing and Tickner at very low pressures (approx. 2 $\mu$) and temperatures up to 350°.[26] These results were combined with those obtained by Vaughan and Szwarc at lower temperatures, and the first-order constant was calculated to be $7{\cdot}10^{15} \exp(-38 \text{ kcal.}/\boldsymbol{R}T) \text{ sec.}^{-1}$. Brinton and Volman [27] have carried out the reaction at much lower temperatures and higher pressures in the presence of ethyleneimine and give values for the rate of fission of the peroxide link in fair agreement with those of Lossing and Tickner.

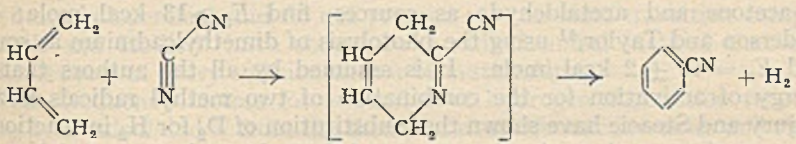
Szwarc and his co-workers have continued their measurements of bond dissociation energies by pyrolysis of the parent compound in a flow system, using toluene as a carrier gas and radical reagent.[28] An interesting point which has emerged from studies of this kind on alkyl and aryl bromides is that, although the rate constants of two C–Br bond dissociation processes may be in the ratio $10^5 : 1$, the frequency factors are of the same order of magnitude.[29]

**Bimolecular Gas Reactions.**—Many bimolecular association reactions are " slow," *i.e.*, have a $P$ factor very much less than unity, and this is attributed to a loss of entropy during formation of the activated complex. Another example of this behaviour is the simple reactions between olefins and ozone

---

[20] N. E. Duncan and G. J. Janz, *J. Chem. Phys.*, 1952, **20**, 1644.
[21] M. J. Molera and F. J. Stubbs, *J.*, 1952, 381.
[22] R. A. Marcus, *J. Chem. Phys.*, 1952, **20**, 352, 359, 364.
[23] R. E. Rebbert and K. J. Laidler, *ibid.*, p. 574.
[24] A. D. Jenkins and D. W. G. Style, *Nature*, 1952, **170**, 706.
[25] H. N. Mortlock and D. W. G. Style, *ibid.*, p. 706.
[26] F. P. Lossing and A. W. Tickner, *J. Chem. Phys.*, 1952, **20**, 907.
[27] R. K. Brinton and D. H. Volman, *ibid.*, p. 25.
[28] M. Ladacki, C. H. Leigh, and M. Szwarc, *Proc. Roy. Soc.*, 1952, *A*, **214**, 273; C. H. Leigh and M. Szwarc, *J. Chem. Phys.*, 1952, **20**, 403, 844; M. Szwarc and D. Williams, *ibid.*, p. 1171.
[29] M. Szwarc and D. Williams, *Nature*, 1952, **170**, 290.

which are characterised by frequency factors of the order $10^3$ to $10^4$ l. mole$^{-1}$ sec.$^{-1}$.[30] The dimerisations of tetrafluoro- and chlorotrifluoro-ethylene are also "slow," with frequency factors similar to those for the dimerisation of dienes, *viz.*, $\simeq 10^7$ l. mole$^{-1}$ sec.$^{-1}$.[31] In marked contrast to these are the addition of butadiene to cyanogen: [32]



and the addition of boron trifluoride to the mono-, di-, and tri-methylamines [33] for which the frequency factors are respectively $1{\cdot}6 \times 10^{12}$ and $\sim 10^{13}$ l. mole$^{-1}$ sec.$^{-1}$. The latter reaction is particularly interesting in that no energy of activation is required, and it is therefore as rapid as the combination of two methyl radicals.[34]

The expectation for bimolecular metatheses is that the *P* factor should be close to unity. This appears to be almost the case in the very rapid reaction $NO_2Cl + NO \longrightarrow NO_2 + NOCl$ which was investigated over the wide range of pressure, 0·2 to 384 mm. Hg, by Freiling, Johnston, and Ogg [35] and for which the velocity constant is $10^9 \exp(-6{\cdot}9 \text{ kcal.}/RT)$ l. mole$^{-1}$ sec.$^{-1}$. This is a particularly interesting reaction in that it is not known whether a chlorine or an oxygen atom is transferred.

**Atomic and Free-radical Reactions.**—Some atomic and free-radical reactions are dealt with in the section on photochemistry. In many cases the photolysis of a compound has been used as a source of free radicals for the purpose of studying the kinetics of inter-radical, and radical–molecule reactions. Such reactions are reported mainly in this section.

Much attention continues to be devoted to the reactions of hydrogen atoms and simple alkyl radicals. Berlie and LeRoy [36] claim to have eliminated the difficulties inherent in previous investigations of reaction (1) and

$$H + C_2H_6 \longrightarrow C_2H_5 + H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

give preliminary values of $E_1 = 6{\cdot}2 \pm 0{\cdot}1$ kcal. and $P_1 = 3{\cdot}3 \times 10^{-3}$. The energy of activation is consistent with the work of Wijnen and Steacie [37] on the reverse reaction (2), where deuterium is used in place of hydrogen.

$$C_2H_5 + D_2 \longrightarrow C_2H_5D + D \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

They find that the value $E_2 = 13{\cdot}3 \pm 0{\cdot}5$ kcal./mole, which after allowance for the difference in zero-point energy of deuterium and hydrogen, leads to $E_1 = 7 \pm 1$ kcal./mole. Wijnen and Steacie did not detect any $C_2H_4D_2$ in their products, but in another system it is claimed [38] that the exchange reaction $CH_3{\cdot}CH_2{\cdot} + D_2 \longrightarrow CH_3{\cdot}CHD{\cdot} + HD$ can occur.

---

[30] R. D. Cadle and C. Schade, *J. Amer. Chem. Soc.*, 1952, **74**, 6002.
[31] J. R. Lacher, G. W. Tompkin, and J. D. Park, *ibid.*, p. 1693.
[32] P. J. Hawkins and G. J. Janz, *ibid.*, p. 1790.
[33] D. Garvin and G. B. Kistiakowsky, *J. Chem. Phys.*, 1952, **20**, 105.
[34] R. Gomer and G. B. Kistiakowsky, *ibid.*, 1951, **19**, 85.
[35] E. C. Freiling, H. S. Johnston, and R. A. Ogg, *ibid.*, 1952, **20**, 327.
[36] M. R. Berlie and D. J. LeRoy, *ibid.*, p. 200.
[37] M. H. J. Wijnen and E. W. R. Steacie, *ibid.*, p. 205.
[38] V. V. Voevodskii, G. K. Lavrovskaya, and R. E. Mardaleishvili, *Dokl. Akad. Nauk. S.S.S.R.*, 1951, **81**, 215; *Chem. Abs.*, 1952, **46**, 1852.

Conflicting values continue to be reported for the energy of activation of the reaction

$$CH_3\cdot + H_2 \longrightarrow CH_4 + H \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Majury and Steacie,[39] using the photolysis of acetone as source of radicals, find $E_3 = 9{\cdot}7 \pm 0{\cdot}6$ kcal./mole; Davidson and Burton,[40] using photolysis of acetone and acetaldehyde as sources, find $E_3 > 13$ kcal./mole; and Anderson and Taylor,[41] using the photolysis of dimethylcadmium as source, find $E_3 = 13 \pm 2$ kcal./mole. It is assumed by all the authors that the energy of activation for the combination of two methyl radicals is zero. Majury and Steacie have shown that substitution of $D_2$ for $H_2$ in reaction (3) causes an increase in activation energy of the order to be expected from the different zero-point energies, while replacement of $CH_3\cdot$ by $CD_3\cdot$ causes a relatively slight reduction in rate.

Lossing and Tickner [26] have developed a mass-spectrographic method for measuring the partial pressure of methyl radicals in thermally decomposing gases. The method differs from previous similar methods in that relatively high-voltage electrons (50 ev) are used, the effect of ionisation of species other than methyl being allowed for by assuming a 100% carbon balance. The combination reaction of methyl radicals was studied and the collision efficiency at 850° estimated as 2—3 $\times 10^{-2}$. A redetermination of the collision efficiency of the reaction between methyl radicals and nitric oxide has been made,[42] by using a radioactive tellurium mirror method. This leads to a collision efficiency of $10^{-2}$ for the combination of methyl radicals at room temperature. Durham and Steacie conclude, from a comparison of the available data, that the true value is between 0·5 and 0·05. The problem has also been discussed theoretically.[22]

The thermal decomposition of di-*tert*.-butyl peroxide has been used as a source of the methyl radical in studies of its reactions with acetone,[43] acetaldehyde, and acraldehyde.[44] The energy of activation of the reaction with acetone was found to be $9{\cdot}5 \pm 1{\cdot}5$ kcal./mole in agreement with other work, while for the reaction with acetaldehyde $E = 7{\cdot}5 \pm 0{\cdot}3$ kcal./mole. Acraldehyde polymerises as well as decomposing in the presence of radicals. The hydrogen abstraction reactions of methyl radicals with various halogenated methane derivates have been found [45] to have the following activation energies: $CH_3F$, 8·7; $CH_2F_2$, 6·2; $CH_3Cl$, 9·4; $CH_2Cl_2$, 7·2; $CHCl_3$, 5·8; $CH_3Br$, 10·1; $CH_2Br_2$, 8·7 kcal./mole. The steric factors lie in the range $10^{-2}$ to $10^{-4}$. The reactions of methyl radicals with oxygen [46] and with *sec*.-butyl chloride [47] have also been studied.

The combination, disproportionation, hydrogen-abstraction, and decomposition reactions of the ethyl radical have been reviewed.[48] There appears to be a real discrepancy between the relative extent of disproportionation and combination of ethyl radicals produced by different methods.

[39] T. G. Majury and E. W. R. Steacie, *Canad. J. Chem.*, 1952, 30, 800.
[40] S. Davidson and M. Burton, *J. Amer. Chem. Soc.*, 1952, 74, 2307.
[41] R. D. Anderson and H. A. Taylor, *J. Phys. Chem.*, 1952, 56, 498.
[42] R. W. Durham and E. W. R. Steacie, *J. Chem. Phys.*, 1952, 20, 582.
[43] M. T. Jaquiss, J. S. Roberts, and M. Szwarc, *J. Amer. Chem. Soc.*, 1952, 74, 6005.
[44] D. H. Volman and R. K. Brinton, *J. Chem. Phys.*, 1952, 20, 1764.
[45] F. A. Raal and E. W. R. Steacie, *ibid.*, p. 578.
[46] F. B. Marcotte and W. A. Noyes, *J. Amer. Chem. Soc.*, 1952, 74, 783.
[47] A. S. Kenyon, *ibid.*, p. 3372.
[48] K. J. Ivin, M. H. J. Wijnen, and E. W. R. Steacie, *J. Phys. Chem.*, 1952, 56, 967.

Bevington[49] has calculated the differences in the heat content, entropy, and free energy of the products resulting from the disproportionation and combination of ethyl and other radicals. It does not follow that the reaction leading to the greatest decrease of free energy will necessarily predominate, since it follows from the work of Wijnen and Steacie[185] that the two reactions are quite independent and do not proceed *via* the same transition complex. Paneth and Hollis[50] have shown by a radiochemical method that ethyl radicals react at every collision with a bismuth mirror.

The frequency factors for a number of hydrogen-abstraction reactions have been calculated[51] from the theory of absolute reaction rates and shown to be in fair agreement with experimental values.

The reactions of sodium vapour with ethyl chloride[52] and trifluorohalogenomethanes[53] have been studied by the diffusion flame method and the following energies of activation found: $C_2H_5Cl$, 10·2 ± 0·5; $CF_3I$, 1·7; $CF_3Br$, 2·3; $CF_3Cl$, 7·4 kcal./mole. In the $CF_3X$ compounds it is the X atom which is preferentially removed. In the case of ethyl chloride the steric factor is unity within experimental error.

In solution the phenyl radical reacts with aromatic compounds to give diphenyl derivatives:

$$\text{Ph}\cdot + \text{PhX} \longrightarrow \text{Ph}\cdot\text{C}_6\text{H}_4\text{X} + \text{H}$$

but in the gas phase at high temperature and low pressure, hydrogen abstraction is preferred in the case of compounds such as toluene:

$$\text{Ph}\cdot + \text{PhMe} \longrightarrow \text{PhH} + \text{Ph}\cdot\text{CH}_2\cdot \longrightarrow (\text{Ph}\cdot\text{CH}_2)_2$$

This difference in behaviour has been investigated by Jaquiss and Szwarc[54] who conclude that the effect is real and advance a tentative explanation.

Kooyman and Farenhorst[55] have given a preliminary account of an experimental study designed to provide a broad test of the predictions of Coulson *et al.* that the free valence number calculated for a given carbon atom in a compound should be related to its ability to interact with a free radical. The correlation is found to be remarkably good for velocity constants varying over a range of more than $10^5$.

A summary of the Toronto conference on the Reactivity of Free Radicals has been published.[56]

**Reactions in Solution.**—*General.*—Kacser[57] has given a theoretical account of the probability factor in uncomplicated ion-dipole reactions. An equation for the "effective shape" of a polar molecule in the field of an ion is developed, which determines the success of reactive approaches of the ion from any given direction. If the field around the molecule is markedly anisotropic, there will be favoured directions of approach for the ion, which will be reflected in the non-exponential factor of the Arrhenius equation. When these concepts are applied to experimental data (reactions of methyl

---

[49] J. C. Bevington, *Trans. Faraday Soc.*, 1952, **48**, 1045.
[50] F. A. Paneth and A. Hollis, *Nature*, 1952, **169**, 618.
[51] S. Bywater and R. Roberts, *Canad. J. Chem.*, 1952, **30**, 773.
[52] R. J. Cvetanovic and D. J. LeRoy, *J. Chem. Phys.*, 1952, **20**, 1016.
[53] J. W. Hodgins and R. L. Haines, *Canad. J. Chem.*, 1952, **30**, 473.
[54] M. T. Jaquiss and M. Szwarc, *Nature*, 1952, **170**, 312.
[55] E. C. Kooyman and E. Farenhorst, *ibid.*, 1952, **169**, 153.
[56] H. W. Melville, *ibid.*, 1952, **170**, 819.
[57] H. Kacser, *J. Phys. Chem.*, 1952, **56**, 1101.

halides with halide ions), they yield the approach distance of reacting molecules, and give information concerning the steric course of the reaction.

The differential rate equations for the kinetics of competitive reactions of the type A + B $\longrightarrow$ C + E, and A + C $\longrightarrow$ D + E have been integrated for the special case where [A] = [B].[58] Measurements of the rates of hydrolysis of ethyl adipate and ethyl succinate were made and used as an illustration of the theory.

Pearson [59] has made a theoretical study of the influence of the solvent on the heats and entropies of reactions in which ions are formed from neutral molecules. Changes in the entropy term appear to be decisive in relating the rates of similar reactions in different solvents.

Curme and Rollefson [60] have compared the rate of quenching of fluorescence of β-naphthylamine by carbon tetrachloride in the gas phase, and in solution in *iso*octane and *cyclo*hexane. Values of the entropy of activation for the process in these three media are essentially identical. They conclude that the rate at which these molecules come together and react is not greatly different in solution in an inert solvent, from what it is in the gas phase.

Franklin [61] has calculated the entropy and heat of formation of alkylcarbonium ions in solution from corresponding values for the gaseous ions, using Latimer's [62] method. These values are used for calculations of $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ for hydrolysis of alkyl halides in aqueous ethanol, and also of the rate of hydration of *iso*butene and dehydration of *tert.*-butanol. The calculations of the rates of these processes are in good agreement with experimental values.

*Isotopic Exchange Reactions in Solution.* Many reactions in solution can be detected only by the use of suitably labelled isotopic species. The increasing availability of both radioactive isotopes of many of the elements, as well as stable isotopes, *e.g.*, $^{18}$O and $^{15}$N, has led to a considerable expansion in the number and variety of studies in this field.

(a) *Electron-transfer processes.* Adamson [63] has suggested that a relation exists between the rate of one-electron transfer and the magnetic properties of the ions concerned. The criterion of this correlation is that if the product of the sum and the difference of the magnetic moments of the couple is high, electron transfer between the couple will be slow. The theoretical basis for this relation is admitted to be obscure.

Libby [64] has considered the probability of isotopic electron transfer from the point of view of the Franck–Condon principle. He suggests that the hydration atmospheres around the ions are unable to move in the time required for electron transfer, thus causing formation of ions in incorrect environment. This requires the later movement of hydration energy from one site to another, and thereby constitutes a barrier which inhibits electron transfer. For large co-ordinated ions such as the ferro- and ferri-cyanides, the energies of hydration are smaller, and the barrier is greatly reduced. Catalysis by small negative ions is explicable on the basis of formation of a linear complex with the anion between the two exchanging cations. This will

---

[58] A. A. Frost and W. C. Schwemer, *J. Amer. Chem. Soc.*, 1952, **74**, 1268.

[59] R. G. Pearson, *J. Chem. Phys.*, 1952, **20**, 1478.

[60] H. G. Curme and G. K. Rollefson, *J. Amer. Chem. Soc.*, 1952, **74**, 3766.

[61] J. L. Franklin, *Trans. Faraday Soc.*, 1952, **48**, 443.

[62] W. M. Latimer, K. S. Pitzer, and C. M. Slansky, *J. Chem. Phys.*, 1939, **7**, 108.

[63] A. W. Adamson, *J. Phys. Chem.*, 1952, **56**, 858.

[64] W. F. Libby, *ibid.*, p. 863.

result in a sharing of the water molecules in the hydration spheres of the cations, with a consequent reduction in height of the energy barrier for electron transfer. As an example of this predicted catalytic effect of small anions, Hornig and Libby [65] have shown that concentrations of fluoride ion as low as $10^{-6}$M exert an accelerating effect on the rate of electron transfer between Ce(III) and Ce(IV) in 6M-nitric acid.

Silverman and Dodson [66] have published a definitive paper on the kinetics of electron transfer between ferrous and ferric ions in aqueous perchloric–hydrochloric acid media. In perchloric acid, the main contribution to exchange comes from the ions $FeOH^{2+}$ and $Fe^{2+}$; the rate constant for exchange between $Fe^{3+}$ and $Fe^{2+}$ is about 1000-fold less. Chloride ion produces a slight catalytic effect, and rate constants were measured for electron transfer between the couples $FeCl^{2+}$–$Fe^{2+}$, and $FeCl_2^{+}$–$Fe^{2+}$. Perchlorate ion plays no specific part in any of the reactions. Molecular oxygen [67] does not affect the rate of electron transfer, and the mechanism suggested by Weiss [68] therefore cannot be operative.

Furman and Garner [69] have found that the rate of electron transfer between V(III) and V(IV) is given by:

$$R = 4{\cdot}5 \times 10^{12} \exp(-20{,}700/RT)[\mathrm{V(III)}][\mathrm{V(IV)}]/[\mathrm{H^+}] \text{ mole l.}^{-1} \text{ sec.}^{-1}$$

The mechanism suggested is: $V^{+3} + H_2O \rightleftharpoons VOH^{2+} + H^+$, $VOH^{2+} + {}^*VO^{2+} \longrightarrow Z^{4+} \longrightarrow {}^*VOH^{2+} + VO^{2+}$, where $Z^{4+}$ is a quadruply charged activated complex of unspecified structure. The exchange between VII and VIII is complete within one minute at 2° C.[70]

Bonner and Hunt [71] have reported that the half-time for electron transfer between Co(II) and Co(III) in aqueous perchloric acid at 0° varies from 4·8 to 22 minutes, depending on the molarity of the solution in the region 0·7 to $3{\cdot}0 \times 10^{-3}$M. The exchange is not catalysed by glass surfaces or by ordinary daylight.

The electron transfer [72] between Eu(II) and Eu(III) in perchloric–hydrochloric acid solutions is of first order in each of the valency states of europium, and also of first order in chloride ion. The over-all energy of activation is 20·8 kcal./mole.

Wolfgang and Dodson [73] have confirmed earlier work that exchange between Hg(I) and Hg(II) is very rapid in perchloric acid solution. They find, however, that addition of cyanide causes the exchange to become slow and measurable. Preliminary kinetic data suggest that the rate-controlling step may be reaction between $Hg_2^{2+}$ and a cyanide complex of Hg(II).

Electron transfer between $K_4Mo(CN)_8$ and $K_3Mo(CN)_8$ has been investigated with $^{99}$Mo as the radioactive tracer.[74] The exchange is complete at all pH values between 1 and 11, and at total molybdenum concentrations as low as $10^{-4}$M.

---

[65] H. C. Hornig and W. F. Libby, *J. Phys. Chem.*, 1952, **56**, 869.
[66] J. Silverman and R. W. Dodson, *ibid.*, p. 846.
[67] L. Eimer, A. I. Medalia, and R. W. Dodson, *J. Chem. Phys.*, 1952, **20**, 743.
[68] J. Weiss, *ibid.*, 1951, **19**, 1066.
[69] S. C. Furman and C. S. Garner, *J. Amer. Chem. Soc.*, 1952, **74**, 2333.
[70] W. R. King, Jr., and C. S. Garner, *ibid.*, p. 3709.
[71] N. A. Bonner and J. P. Hunt, *ibid.*, p. 1866.
[72] D. J. Meier and C. S. Garner, *J. Phys. Chem.*, 1952, **56**, 853.
[73] R. L. Wolfgang and R. W. Dodson, *ibid.*, p. 872.
[74] R. L. Wolfgang, *J. Amer. Chem. Soc.*, 1952, **74**, 6144.

By separating Cr(II) from Cr(III) by an ion-exchange resin, Haissinsky [75] has shown that electron transfer between these ions is complete in hydrochloric acid in the time taken for separation (3—7 minutes). There are some indications that the exchange may not be complete in sulphuric acid in the same time.

The electron transfer between the tris-5 : 6-dimethyl-1 : 10-phenanthroline complexes of ferrous and ferric ions is complete within 15 seconds at 0°, at concentrations $2 \times 10^{-5}$M in each species.[76]

(b) *Atom and group transfer.* Jenkins and Yost [77] have investigated the kinetics of exchange of tritium between hypophosphorous acid and water, and their results indicate that in solution, two forms of this compound exist which differ in position of the hydrogen atom in the $H_3PO_2$ molecule.

$^{14}$C-Labelled acetate has been used in a study of the exchange reactions among sodium acetate, acetic acid, and acetic anhydride in anhydrous acetic acid solutions.[78] Rapid exchange occurs between sodium acetate and the solvent, by direct proton transfer. Only slow exchange occurs between acetic anhydride and acetic acid. Rapid acetate exchange is found between both Pb(II) and Pb(IV) acetates and the solvent. However, contrary to earlier results,[79] no electron exchange occurs between Pb(II) and Pb(IV) in acetic acid at 80° in four hours.

Bonner and Bigeleisen [80] report no exchange of $^{18}$O between water and $N_2O$ in either concentrated alkali or concentrated acid media. No exchange was found between water and sodium hyponitrite at pH above 7·0, or in acid solution, in which this salt slowly decomposes. Similarly, no exchange was observed during the decomposition of sodium "nitrohydroxylamite" (oxyhyponitrite) ($Na_2N_2O_3$) in either acid or alkaline media.

Two independent investigations have shown that there is no exchange between either $CN^-$ or $S^=$ with $CNS^-$ in the pH range 0·5—12·7.[81]

Based on the observations that ozone, $H_2O_2$, and $O_2$ do not exchange $^{18}$O with water, but that addition of hydrogen peroxide to water in presence of ozone causes exchange between water and ozone, Forchheimer and Taube [82] suggest that OH radicals probably undergo exchange with water. This conclusion is reached from a consideration of the mechanism of interaction between hydrogen peroxide and ozone, according to which oxygen atoms in OH radicals finally emerge as oxygen gas.

Atkins and Garner [83] have investigated the exchange of radioactive zinc between zinc ions and seven zinc chelate complexes in pyridine. All " non-fused ring " complexes (*e.g.*, the complex with 8-hydroxyquinoline) showed complete exchange in less than 0·5 minute, while the only " fused ring " complex examined (zinc phthalocyanine) showed no exchange in 35 days. This behaviour is in agreement with earlier predictions [84] relating to the exchange lability of metallo-organic complexes.

[75] M. Haissinsky, *J. Chim. phys.*, 1952, **49**, C 133.

[76] L. Eimer and A. I. Medalia, *J. Amer. Chem. Soc.*, 1952, **74**, 1592.

[77] W. A. Jenkins and D. M. Yost, *J. Chem. Phys.*, 1952, **20**, 538.

[78] E. A. Evans, J. L. Huston, and T. H. Norris, *J. Amer. Chem. Soc.*, 1952, **74**, 4985.

[79] G. von Hevesy and L. Zechmeister, *Z. Elektrochem*, 1920, **26**, 151.

[80] F. Bonner and J. Bigeleisen, *J. Amer. Chem. Soc.*, 1952, **74**, 4944.

[81] A. W. Adamson and P. S. Magee, *ibid.*, p. 1590; G. E. Heisig and R. Holt, *ibid.*, p. 1597.

[82] O. L. Forchheimer and H. Taube, *ibid.*, p. 3705.

[83] D. C. Atkins, Jr., and C. S. Garner, *ibid.*, p. 3527.

[84] S. Ruben, M. D. Kamen, M. B. Allen, and P. Nahinsky, *ibid.*, 1942, **64**, 2297.

Exchange of radio-chromium between the ion $Cr(H_2O)_6{}^{3+}$ and the complexes $(Cr\,en_3)^{3+}$, $Cr(urea)_6{}^{3+}$, and $CrF_3(H_2O)_3$ were found to be very slow.[85] The complex with fluoride ion showed some exchange which increased at lower acidities.

West [86] has continued his studies on the relation between bond type and rate of exchange for cobaltous and cobaltic complexes of the bidentate type. The results in general support the view that covalent bonds display slow exchange of the central metal atom with cobalt ion, and ionic complexes show rapid exchange.

Jones and Long [87] have investigated several exchange reactions between ferrous and ferric ions and their complexes with ethylenediaminetetra-acetic acid ($H_4Y$). $FeY^=$ and $Fe^{2+}$ exchange instantaneously, while the corresponding ferric couple $FeY^-$ and $Fe^{3+}$ exchange slowly. The pair $FeOH^{2+}$–$FeY^-$ exchange at a rate tenfold slower than the couple $Fe^{3+}$–$FeY^-$.

$^{14}C$ has been used by Harris and Stranks [88] to follow the kinetics of exchange between carbonate ion in solution and the carbonate ion in the complex $[Co(NH_3)_4CO_3]^+$. Exchange occurs by two mechanisms, depending on the concentration of carbonate (or bicarbonate) ion in solution. One mechanism involves the ions $[Co(NH_3)_4,HCO_3,H_2O]^{2+}$ and $HCO_3{}^-$, and the other the equilibrium:

$$H_2O + [Co(NH_3)_4HCO_3H_2O]^{2+} \rightleftharpoons Co(NH_3)_4(H_2O)_2{}^{+3} + HCO_3{}^-$$

In a later paper, the effects of ionic strength on the rate of the ion–dipole mechanism and the ion–ion mechanism were investigated.[89] In the concentration range for which the ion–dipole reaction is operative, the equation of Amis and Jaffé [90] accurately described the results up to ionic strength 1·0. For the ion–ion interaction, the Brönsted relation did not describe the effect of the ionic strength on the rate of reaction.

The exchange reaction between water as $H_2{}^{18}O$ and $Cr(H_2O)_6{}^{+3}$ is first order in Cr(III), and the rate increases with concentration of the anion present.[91] With $Cl^-$ as the only anion present, the rate of exchange of water greatly exceeds the rate of formation of the complex ion $[Cr(H_2O)_5Cl]^{2+}$. The rate of exchange is markedly increased by $Cr^{2+}$, and only slightly by $Cr_2O_7{}^{2-}$, and is induced by the reaction between Ce(IV) and Cr(III). The results suggest that electron transfer between Cr(II) and Cr(III) is rapid, and that exchange of water takes place at the Cr(II) stage. The exchange between free and bound water in the complex ion $[Co(NH_3)_5H_2O]^{3+}$ was found to be of first order with respect to the complex ion, and was independent of acidity. A dissociation mechanism is favoured over a bimolecular mechanism involving water as the second reacting species.[92]

Bernstein and Katz [93] have measured the gas-phase exchange between fluorine and the interhalogen compounds $ClF_3$, $BrF_5$, and $IF_7$. Homogeneous exchange occurs at a measurable rate about 100°, probably by

---

[85] W. R. King, Jr., and C. S. Garner, *J. Amer. Chem. Soc.*, 1952, **74**, 5534.

[86] B. West, *J.*, 1952, 3115.

[87] S. S. Jones and F. A. Long, *J. Phys. Chem.*, 1952, **56**, 25.

[88] G. M. Harris and D. R. Stranks, *Trans. Faraday Soc.*, 1952, **48**, 137.

[89] D. R. Stranks, *Trans. Faraday Soc.*, 1952, **48**, 911.

[90] E. S. Amis and G. Jaffé, *J. Chem. Phys.*, 1952, **10**, 598.

[91] R. A. Plane and H. Taube, *J. Phys. Chem.*, 1952, **56**, 33.

[92] A. C. Rutenberg and H. Taube, *J. Chem. Phys.*, 1952, **20**, 825.

[93] R. B. Bernstein and J. J. Katz, *J. Phys. Chem.*, 1952, **56**, 885.

reversible dissociation for the chlorine and iodine compounds, and by an association mechanism for $BrF_5$.

The exchange of $^{131}I$ as sodium iodide has been investigated for the following compounds: (i) allyl iodide in ethyl alcohol; [94] (ii) iodobenzene in *sec.*-octyl alcohol; [95] (iii) *p*-iodophenol in octan-2-ol; [96] (iv) 2-iodonaphthalene in acetyl alcohol; [97] (v) ethyl iodide in acetonitrile [98] and *p*-iodonitrobenzene in octan-2-ol and in acetonitrile.[99]

Exchange between periodate and iodine [100] is slow compared with that reported [101] for exchange between iodate and iodine. The rate varies with acidity in the same way as the chemical reaction between iodide ion and periodate, and the temperature coefficients for the two processes are similar, suggesting similar mechanisms. The exchange between iodate and periodate is very slow and is catalysed by molecular iodine.

*Non-isotopic Reactions in Solution.*— (a) *Electron transfer reactions in aqueous solution.* Dainton [102] has reviewed both thermal and photochemical electron transfers between various cations and anions, on the one hand, and water, hydrogen peroxide, and formic acid, on the other.

Two independent studies have been made of the kinetics of the reaction $Tl(\textsc{iii}) + 2Fe(\textsc{ii}) \longrightarrow Tl(\textsc{i}) + 2Fe(\textsc{iii})$.[103] The hydrolysed forms $TlOH^{2+}$ and $TlO^+$ take part in rate-controlling electron transfers from Fe(II). Tl(II) is suggested as an intermediate in the process.

Carter and Davidson [104] have shown that the oxidation of ferrous ion by bromine in a two-stage process involves the radical-ion $Br_2^-$. The kinetics of the reaction agree with the scheme:

$$Fe^{2+} + Br_3^- \rightleftharpoons Fe^{3+} + Br^- + Br_2^-$$
$$Br_2^- + Fe^{2+} \longrightarrow Fe^{+3} + 2Br^-$$

Fudge and Sykes [105] have shown that the thermal electron transfer between Fe(III) and iodide ion probably occurs by the sequence: $Fe^{3+} + I^- \rightleftharpoons FeI^{2+}$, $FeI^{2+} + I^- \rightleftharpoons Fe^{2+} + I_2^-$, and $Fe^3 + I_2^- \rightleftharpoons Fe^{2+} + I_2$. Ferrous ion inhibits the reaction, by competition with ferric ions for the radical-ion $I_2^-$. In a second paper, Sykes [106] relates the retarding effects of various anions on the process to complex-ion formation with Fe(III), and from the kinetic data, deduces the association constants for formation of the complex ions $FeOH^{2+}$, $FeSO_4^+$, and $FeNO_3^{2+}$.

Adamson [63] has examined the kinetics of oxidation of cyanide ion by $Fe(CN)_6^{3-}$, and suggests a mechanism involving the radical ion $(CN)_2^-$.

A preliminary account has appeared of the reactions of Hg(I) and Hg(II) with formic acid.[107] The rate-controlling steps involve electron transfer from formate ion to Hg(I) or Hg(II), with formation of the free radical

---

[94] S. May, P. Daudel, J. Schottey, M. Sarraf, and A. Vobauré, *J. Chim. phys.*, 1952, **49**, 64.

[95] S. May, M. Sarraf, A. Vobauré, and P. Daudel, *Compt. rend.*, 1951, **233**, 744.

[96] S. May and B. Girandel, *ibid.*, 1952, **234**, 326.

[97] I. Estellés and S. May, *ibid.*, p. 433.

[98] S. May and B. Girandel, *ibid.*, 1952, **235**, 953.

[99] *Idem, ibid.*, 1952, **234**, 2280.

[100] M. Cottin, M. Haissinsky, and D. Peschanski, *J. Chim. phys.*, 1951, **48**, 500.

[101] O. E. Myers and J. W. Kennedy, *J. Amer. Chem. Soc.*, 1950, **72**, 89.

[102] F. S. Dainton, *J.*, 1952, 1533.

[103] C. E. Johnson, Jr., *J. Amer. Chem. Soc.*, 1952, **74**, 959; O. L. Forchheimer and R. P. Epple, *ibid.*, p. 5772.

[104] P. R. Carter and N. Davidson, *J. Phys. Chem.*, 1952, **56**, 877.

[105] A. J. Fudge and K. W. Sykes, *J.*, 1952, 119.

[106] K. W. Sykes, *ibid.*, p. 124.

[107] A. R. Topham and A. G. White, *ibid.*, p. 105.

H·CO·O·. Another thermal electron-transfer reaction leading to free radicals is that between Fe(II) and the *iso*propylcumene and *tert.*-butylcumene hydroperoxide.[108] The rate-controlling step is $Fe^{2+} + R{\cdot}O{\cdot}OH \longrightarrow Fe^{3+} + R{\cdot}O{\cdot} + OH^-$.

Evidence for a two-electron transfer process has been given by Haight and Sager,[109] arising from their studies of the molybdate-catalysed reduction of perchlorate ion by Sn(II). The reaction is very complex, and appears to proceed *via* quadrivalent molybdenum formed by two-electron transfer from Sn(II).

(b) *Reactions of oxygenated anions.* In continuation of his studies of oxygen-transfer reactions involving the use of $^{18}O$, Taube and his co-workers [110] have found that only part of the oxygen in HOCl is transferred to sulphite in this reaction to form $Cl^-$ and $SO_4^{2-}$. He suggests two modes of attack of the hypohalite on $SO_3^{2-}$: $ClO^- + SO_3^{2-} \longrightarrow Cl^- + SO_4^{2-}$; $OCl^- + SO_3^{2-} + H^+ \longrightarrow ClSO_3^- + OH^-$, followed by $ClSO_3^- + H_2O \longrightarrow SO_4^{2-} + 2H^+ + 2Cl^-$. In the first, oxygen transfer is direct, whilst in the second the oxygen atom transferred to the sulphite is derived from the solvent. It was also shown that two atoms of oxygen are transferred to $SO_3^{2-}$ per molecule of hydrogen peroxide reacting.[111] When the same reaction is catalysed by molybdate, only one atom is transferred from $H_2O_2$ to $SO_3^{2-}$. In the former case, permonosulphurous acid is postulated as an intermediate. In the other reaction, oxygen atoms may be transferred from permolybdic acid to $SO_3^{2-}$, with rupture of the O–O bonds in the permolybdate. Transfer of oxygen from $MnO_4^-$ to $SO_3^{2-}$ is very inefficient, and Taube suggests that permanganate acts mainly by electron transfer.

In alkaline solution, pentathionate ion decomposes to thiosulphate, according to $2S_5O_6^{2-} + 6OH^- \longrightarrow 5S_2O_3^{2-} + 3H_2O$.[112] The reaction is of first order in $S_5O_6^{2-}$ and $OH^-$, and displays a kinetic salt effect corresponding to that predicted for a reaction between a singly and a doubly changed anion. The slow stage in the reaction is postulated as $S_5O_6^{2-} + OH^- \longrightarrow S_2O_3^{2-} + HOS{\cdot}S_2O_3^-$, followed by $HOS{\cdot}S_2O_3^- + OH^- \longrightarrow S(OH)_2 + S_2O_3^{2-}$.

Peschanski [113] has made a detailed study of the kinetics of the oxidation of $I_2$ by periodate ion. The mechanism proposed involves successive oxygen transfers from periodate to $I^-$, $IO^-$, $IO_2^-$ (or HOI and $HIO_2$). Iodide ion is present at low concentrations provided by the hydrolysis of iodine.

Abel [114] has discussed the mechanism of the permanganate–oxalate reaction in terms of the relative reactivities of the oxalate ion $(CO_2)_2^{2-}$ and the radical-ion $(CO_2)_2^-$. He suggests that reaction of Mn in oxidation states 6, 5, 4, and 3 is fast with either reagent, and that reaction of $MnO_4^-$ is slow with $(CO_2)_2^{2-}$. The ion-radical is thus the main catalyst, which slowly accumulates during the induction period. Catalysis by Mn(II) is due to reaction with $MnO_4^-$ to give intermediate oxidation states, which then react rapidly with $(CO_2)_2^{2-}$ to give $(CO_2)_2^-$. Malcolm and Noyes [115] suggest that

---

[108] R. J. Orr and H. L. Williams, *Canad. J. Chem.*, 1952, **30**, 985.
[109] G. P. Haight, Jr., and W. F. Sager, *J. Amer. Chem. Soc.*, 1952, **74**, 6056.
[110] J. Halperin and H. Taube, *ibid.*, p. 375. [111] *Idem, ibid.*, p. 380.
[112] J. A. Christiansen, W. Drost-Hansen, and A. E. Nielsen, *Acta Chem. Scand.* 1952, **6**, 333. [113] D. Peschanski, *J. Chim. phys.*, 1951, **48**, 489.
[114] E. Abel, *Monatsh.*, 1952, **83**, 695.
[115] J. M. Malcolm and R. M. Noyes, *J. Amer. Chem. Soc.*, 1952, **74**, 2769.

the kinetics of the $MnO_4^-$–oxalate reaction are consistent with a reaction between $MnO_4^-$ and an oxalate complex of Mn(II), to give Mn(VI), which is rapidly reduced to Mn(III) by either Mn(II) or oxalate. The subsequent reaction involves decomposition of Mn(III) complex oxalates, according to the mechanism suggested by Taube.[116]

The kinetics of the reaction between Mn(II) and periodate have been investigated by Waterbury, Hayes, and Martin.[117] The scheme proposed to account for some aspects of their kinetic results involves oxidation–reduction equilibria between the pairs Mn(II)–$MnO_4^-$, Mn(IV)–Mn(II), accompanied by reaction between Mn(II) and Mn(VI) to form Mn(IV). With these postulated equilibria, together with the assumption that $[Mn(II)] \gg [Mn(III)] \gg [Mn(IV)]$, an expression was obtained which fits the experimental rate law, $R = k[MnO_4^-]^{0 \cdot 5}[Mn(II)][H_5IO_6]$.

A study of the reaction between nitrous acid and hydroxylamine to form nitrous oxide and water has been made by Bothner-By and Friedman.[118] By examining the isotopic composition of the products formed from $^{15}N$-enriched nitrite and $^{18}O$-enriched water, they conclude that the earlier mechanism involving NOH (nitroxyl) is untenable. Hyponitrous acid (HO·N:N·OH) is proposed as the intermediate in neutral solution, and *N*-nitrosohydroxylamine (HO·NH·NO) as the intermediate in acid solution.

A mechanism based on kinetic studies has been proposed for the decomposition of nitrosyldisulphonate ion in water.[119] It involves the formation of OH radicals as an intermediate by reaction of hydrogen-ion with $(SO_3)_2NO^{\cdot 2-}$, followed by reaction of OH with nitrosyl disulphonate ion to produce $N_2O$, nitrous acid, and sulphate ion.

Lister [120] has shown that the decomposition of HOCl is a second-order reaction, and suggests that the rate-controlling step involves disproportionation of HOCl to chloride and chlorite ions. The reaction $HOCl + OCl^- \longrightarrow Cl^- + H^+ + ClO_2^-$ also occurs, but is much slower than the reaction between un-ionised HOCl molecules. Oxygen is generated by a first-order reaction, possibly by reaction of HOCl and water to form $H_2O_2$, followed by a rapid reaction between $OCl^-$ and $H_2O_2$.

(c) *Reaction of complex ions.* Taube [121] has published a comprehensive review of the rates and mechanisms of substitution in inorganic complexes in solution. He stressed the importance in this connection of the electronic structure of the complex ion.

Bjerrum and Poulsen [122] have reported a preliminary study of the rate of formation of several types of complex ions, *e.g.*, the reaction of Ni(II) with dimethylglyoxime and the reaction of Fe(III) with thiocyanate. By using methanol as the solvent, they were able to examine the kinetics of such reactions at temperatures down to 180° K, where the rates are no longer "instantaneous." The results support the idea of a connection between the rate of complex formation and the valency and electron configuration in the transition elements; thus for the same electron configuration, *e.g.*,

---

[116] H. Taube, *J. Amer. Chem. Soc.*, 1948, **70**, 1216; 1947, **69**, 1418.
[117] G. R. Waterbury, A. M. Hayes, and D. S. Martin, Jr., *ibid.*, 1952, **74**, 15.
[118] A. Bothner-By and L. Friedman, *J. Chem. Phys.*, 1952, **20**, 459.
[119] J. H. Murib and D. M. Ritter, *J. Amer. Chem. Soc.*, 1952, **74**, 3394.
[120] M. W. Lister, *Canad. J. Chem.*, 1952, **30**, 879.
[121] H. Taube, *Chem. Reviews*, 1952, **50**, 69.
[122] J. Bjerrum and K. G. Poulsen, *Nature*, 1952, **169**, 463.

$Fe^{3+}$ and $Mn^{2+}$, the higher valency state reacts more slowly. For equal valency, ions with half-completed or completed electron shells give a much higher rate of complex formation. Approximate measurements of the kinetics indicate that most reactions leading to formation of complex ions are instantaneous at room temperature because of a high value of the frequency factor rather than a low value of the activation energy.

Wilmarth and Baes [123] have shown that the paramagnetic complex ions of Cr(III) with water, thiocyanate, urea, ammonia, and other ligands will catalyse the conversion of para- to ortho-hydrogen. By using Wigner's formula relating the approach distance of the paramagnetic ion to the rate of the conversion, deductions regarding the size of these ions were made. It appears likely on this basis that hydrogen must penetrate through most of the atoms in the ligand groups surrounding the central Cr(III) ion.

The mechanism of the acid-catalysed aquation of the complex ion $Co(NH_3)_5CO_3^+$ has been investigated, by means of $H_2{}^{18}O$.[124] By analysing the $^{18}O$ content of the complex ion before and after aquation, it was shown that at least 99% of the change leaves the Co–O bond intact.

Basolo, Bergmann, and Pearson [125] have measured the rates of hydration and hydrolysis of a series of C-substituted acetato-pentammino-cobalt(III) ions in solution. The rates of both processes were dependent on the base strength of the acid ligand, but independent of its size. The authors conclude that the incoming groups approach the complex from a position opposite to the outgoing groups, or that substitution occurs by dissociation. In a second paper,[126] the rate of aquation of the complex ions $[Co(AA)_2Cl_2]^+$ were measured, where AA represents compounds of varying complexity, containing two amino-groups. Increased crowding around the central atom, arising from longer hydrocarbon skeletons in AA, did not retard the reaction, which suggests that aquation does not occur by a seven-co-ordinated $S_N2$ mechanism, but rather by a $S_N1$ mechanism in which the activated complex is penta-co-ordinated.

Price [127] has examined the kinetics of the metal-ion catalysed decarboxylation of acetonedicarboxylic acid, and has shown that the undissociated acid, the univalent anionic form, and the bivalent enol anion react at different rates. The last process is most strongly influenced by metal ions. He suggests that the catalytic activity of cations is due to chelation of the activated complex by the metal ion. In support of this, a relation was found between the catalytic coefficient and the association constant of the chelate compounds formed by these ions with malonate ion. Further, ions which do not form chelate compounds display no catalytic effects.

Brandt and Gullstrom [128] have calculated the stabilities of some 5-substituted 1 : 10-phenanthroline–Fe(II) complexes from the rates of formation and dissociation of the complexes, and also from equilibribium data. The stabilities of the complex formed with Fe(II) decreases in the order methyl, phenyl, chloro, and nitro. Values for the equilibrium constants determined by the two methods for each system were in good agreement.

---

[123] W. K. Wilmarth and C. F. Baes, Jr., *J. Chem. Phys.*, 1952, 20, 116.

[124] J. P. Hunt, A. C. Rutenberg, and H. Taube, *J. Amer. Chem. Soc.*, 1952, 74, 268.

[125] F. Basolo, J. G. Bergmann, and R. G. Pearson, *J. Phys. Chem.*, 1952, 56, 22.

[126] R. G. Pearson, C. R. Boston, and F. Basolo, *J. Amer. Chem. Soc.*, 1952, 74, 2943.

[127] J. E. Prue, *J.*, 1952, 2331.

[128] W. W. Brandt and D. K. Gullstrom, *J. Amer. Chem. Soc.*, 1952, 74, 3532.

(d) *Reactions of hydrogen peroxide.* During the year, a review has appeared of the reactions of hydrogen peroxides with "donor particles," *e.g.*, $BrO_3^-$, $IO_3^-$, $I^-$.[129] At least three papers have been published relating to the source of oxygen evolved from the decomposition of hydrogen peroxide in aqueous solutions containing a variety of other reagents including Fe(II), Fe(III), Ce(IV), $MnO_4^-$, $Br_2$.[130-132] In all cases examined, oxygen comes cleanly from hydrogen peroxide, indicating that the O–O bond in the peroxide remains intact. Measurements of the relative rates of evolution of $^{18}O$ and $^{16}O$ have led to several interesting speculations regarding the detailed mechanism of some of the reactions; thus, Cahill and Taube [131] suggest that a two-electron transfer between Fe(II) and $H_2O_2$ is an important chain-carrying step in the Fe(II)-induced decomposition of this substance. Reactive isomers of $HO_2^-$, arising from decomposition of $FeO{\cdot}OH^{2+}$, have been suggested as intermediates in this reaction.[133, 134]

The reaction between nitrous acid and hydrogen peroxide has been studied by Halfpenny and Robinson.[135] The scheme proposed to account for the kinetics involves peroxynitrous acid ($HO_2NO$) as an intermediate, which decomposes to HO and $NO_2$, followed by reaction of these species to form nitric acid. Shilov also suggests peroxynitrous acid as the intermediate in this reaction.[136]

(e) *Kinetics of other reactions in solution.* The reduction of sodium anthraquinone-2-sulphonate by $Ti^{3+}$ is a composite reaction involving simultaneous reduction of the semiquinone, the semiquinone dimer, and a molecular complex of one molecule of quinone and one of semiquinone. The ratio of reduction of the quinone itself is insignificant compared with these other reactions.[137]

Turgeon and LaMer [138] have published a comprehensive account of the kinetics of formation of the carbinol of crystal-violet. The reaction follows quantitatively the Brönsted–Debye law for primary kinetic salt effects. The energy of activation is 0·9 kcal./mole higher in 40% acetone–water than in pure water. This is contrary to the decrease expected due to the lowering of the coulombic activation energy in a solution of lower dielectric constant. A specific solvent effect may be involved, resulting in preferential solvation of the crystal-violet cation by the organic solvent rather than by water.

Derbyshire [139] has reviewed recent results relating to the rates of bromination and iodination by hypobromous and hypoiodous acid in acid solutions, and suggests that the active entity in such solutions is the halogen cation co-ordinated with a molecule of water, rather than simply a cation hydrated by electrostatic solvation.

The kinetics of the non-isotopic exchange reaction $CH_3Br + I^- \rightleftharpoons CH_3I + Br^-$ have been investigated in ethylene glycol for comparison with

---

[129] J. O. Edwards, *J. Phys. Chem.*, 1952, **56**, 279.

[130] C. A. Bunton and D. R. Llewellyn, *Research*, 1952, **5**, 142.

[131] A. E. Cahill and H. Taube, *J. Amer. Chem. Soc.*, 1952, **74**, 2312.

[132] M. Dole, D. P. Rudd, G. R. Muchow, and C. Comte, *J. Chem. Phys.*, 1952, **20**, 961.

[133] V. S. Anderson, *Acta Chem. Scand.*, 1952, **6**, 1090.

[134] J. A. Christiansen, *ibid.*, p. 1056.

[135] E. Halfpenny and P. L. Robinson, *J.*, 1952, 928.

[136] E. A. Shilov, *Chem. Abs.*, 1952, **46**, 2946.

[137] C. E. Johnson, Jr., and S. Winstein, *J. Amer. Chem. Soc.*, 1952, **74**, 3105.

[138] J. C. Turgeon and V. K. LaMer, *ibid.*, p. 5988.

[139] D. H. Derbyshire, *Research*, 1952, **5**, 240.

earlier measurements of the same system in water, methanol, and acetone.[140] The rates in this solvent were three times greater than in methanol, and four times as great as in water. Values of $\Delta G$ and $\Delta S$ for the equilibrium, as reflected in the ratio of the rate constants, are $-1{\cdot}62$ kcal./mole and 17·3 cal. mole$^{-1}$ deg.$^{-1}$, respectively.

Glew and Moelwyn-Hughes have investigated the kinetics of the alkaline and acid hydrolysis of methyl fluoride in water.[141] The first-order reaction with water is retarded by hydrogen fluoride and by methanol, and kinetic analysis suggests the scheme $CH_3F \rightleftharpoons CH_3{}^{*}F \underset{H_2O}{\rightleftharpoons} CH_3{\cdot}OH + HF$. The alkaline hydrolysis is a second-order process, *viz.*, $CH_3F + OH^- \longrightarrow CH_3{\cdot}OH + F^-$. The energy of activation for alkaline hydrolyses of methyl bromide and fluoride are the same within experimental error, and thus the difference in bond energies of some 30 kcal. is not reflected in this quantity. The authors suggest that the solvent plays an important part in these reactions, and that the energy of activation refers to the escape of the ion from its solvent sheath. For the first-order reaction, this analysis suggests a simultaneous attack by six water molecules surrounding the methyl halide, with reorganisation necessary for the ionisation of a seventh water molecule. The rate-determining step is then the simultaneous ionisation of water and attack on $CH_3X$ by $OH^-$ so formed.

Bell and Clunie [142] have described a thermal method for following fast reactions in solution, which they have used to investigate the kinetics of hydration of acetaldehyde.[143] The results do not support the view [144] that the reaction mechanism involves simultaneous attack by acidic and basic species.

Meadows and Darwent [145] have shown that in neutral and buffered solutions, hemiacetal is the only important product in the reaction between acetaldehyde and methanol; in strongly acid solution, acetal is formed nearly quantitatively. The former reaction exhibits general acid–base catalysis, whilst the latter is catalysed only by hydrogen ions.[146]

Several papers have appeared during the year relating to the kinetics of the reaction of formaldehyde in aqueous solution with urea [147, 148] *N*-methylurea,[149] and phenol.[150]

Bell and Skinner [151] have investigated the kinetics of depolymerisation of paraldehyde in ethereal solutions of proton acids and Lewis acids. The Lewis acids (*e.g.*, $BCl_3$, $SnCl_4$, $TiCl_4$) showed in general more marked catalytic activity than even a very strong proton acid such as HBr. Moreover, these substances appeared to act as catalysts without the co-operation of proton acids. The reactions were initially of first order in paraldehyde and second-order in catalyst.

Bell and Goldsmith [152] have shown that the iodination of 2-keto*cyclo*-

---

[140] J. S. McKinley-McKee and E. A. Moelwyn-Hughes, *J.*, 1952, 838.
[141] D. N. Glew and E. A. Moelwyn-Hughes, *Proc. Roy. Soc.*, 1952, *A*, **211**, 254.
[142] R. P. Bell and J. C. Clunie, *ibid.*, 1952, *A*, **212**, 16. [143] *Idem, ibid.*, p. 33.
[144] C. G. Swain, *J. Amer. Chem. Soc.*, 1950, **72**, 4578.
[145] G. W. Meadows and B. de B. Darwent, *Canad. J. Chem.*, 1952, **30**, 501.
[146] B. de B. Darwent and G. W. Meadows, *Trans. Faraday Soc.*, 1952, **48**, 1015.
[147] J. I. de Jong and J. de Jonge, *Rec. Trav. chim.*, 1952, **71**, 643, 890.
[148] G. Smets and A. Borzee, *J. Polymer Sci.*, 1952, **8**, 371.
[149] L. E. Smythe, *J. Amer. Chem. Soc.*, 1952, **74**, 2713.
[150] L. M. Oebing, G. E. Murray, and R. S. Schatz, *Ind. Eng. Chem.*, 1952, **44**, 354, 356.
[151] R. P. Bell and B. G. Skinner, *J.*, 1952, 2955.
[152] R. P. Bell and H. L. Goldsmith, *Proc. Roy. Soc.*, 1952, *A*, **210**, 322.

hexanecarboxylic acid is of first order with respect to the ester, and zero order in iodine. The reaction is catalysed by water and by anions of carboxylic acids. Catalytic constants for four carboxylic acids obey a relation of the Brönsted type. This ester is iodinated 100—400 times more slowly than the 5-membered analogue. This result is unexpected on the basis of ring-strain considerations, which suggest that the 6-membered ring should be the more reactive of the two compounds.

**Isotope Effects.**—At least three papers have appeared during the year, which consider the theoretical aspects of the effects of isotopic substitution on the rates of chemical reaction.[153] In some cases, an arbitrary choice of model appears necessary to account for the experimental results.[154]

The isotope effect in the hydrolysis of triphenylsilane in moist piperidine has been studied with tritium.[155] The ratio $k_{\mathrm{T}}/k_{\mathrm{H}}$ of the rate constants for the isotopic reactions was 0·8, whilst earlier work with deuterium gave $k_{\mathrm{D}}/k_{\mathrm{H}} = 6$.[156]

The $^{12}$C–$^{12}$C bond in carboxyl-labelled malonic acid is broken about 10% more frequently than the $^{12}$C–$^{14}$C bond by decarboxylation at 138°.[157] This is an intramolecular isotope effect. The temperature coefficient of the intermolecular isotope effect for the same reaction is zero [158] in the temperature range 137—196°. The intermolecular isotope effect is slightly greater in the decarboxylation of [$CO_2H$-$^{14}$C]malonic acid than it is for the corresponding reaction with [α-$^{14}$C]-acid.[159]

Stevens, Pepper, and Lounsbury [160] have measured the relative isotope effects of $^{13}$C and $^{14}$C arising from decarboxylation of mesitoic acid. By using 0·8 mole-% $^{14}$C-compound labelled in the carboxyl position, they were able to measure $^{12}CO_2$, $^{13}CO_2$, and $^{14}CO_2$ in a mass spectrometer. The $^{14}$C isotope effect was more than twice the $^{13}$C isotope effect (1·101 and 1·038 respectively) which is unexpected in view of current theories.[153]

The $^{12}$C-carboxyl group [154] is lost as $^{12}CO_2$ about 10% more frequently than in the $^{14}$C-groups in both α-naphthyl- and phenyl-malonic acid. Decarboxylation of $^{14}$C-labelled anthranilic acid,[161] either by heating it above its melting point, or by boiling it in water, shows no isotope effect. This is considered explicable on the basis of the mechanism proposed, which involves a proton attack on the α-carbon of the zwitterion.

The relative isotope effects in the thermal decomposition of oxalic acid have been investigated with $^{14}$C and $^{13}$C; the isotopes were measured by radiochemical and mass-spectrometric technique, respectively. The $^{13}$C isotope effect was about one-half of the $^{14}$C isotope effect. A small temperature coefficient was noted in the region 80—100°.[162] Bunton and Llewellyn [163] have investigated $^{13}$C isotope effects in the chemical reactions

---

[153] J. Bigeleisen, *Canad. J. Chem.*, 1952, **30**, 443; *J. Phys. Chem.*, 1952, **56**, 823; H. Eyring and F. W. Cagle, Jr., *ibid.*, p. 889.

[154] A. Fry and M. Calvin, *ibid.*, p. 901.

[155] L. Kaplin and K. E. Wilzbach, *J. Amer. Chem. Soc.*, 1952, **74**, 6152.

[156] G. E. Dunn, H. Gilmour, and G. S. Hammond, *ibid.*, 1951, **73**, 4499.

[157] P. E. Yankwich, E. C. Stivers, and R. F. Nystrom, *J. Chem. Phys.*, 1952, **20**, 344.

[158] J. G. Lindsay, A. N. Bourns, and H. G. Thode, *Canad. J. Chem.*, 1952, **30**, 163.

[159] G. A. Ropp and V. F. Raaen, *J. Amer. Chem. Soc.*, 1952, **74**, 4992.

[160] W. H. Stevens, J. M. Pepper, and M. Lounsbury, *J. Chem. Phys.*, 1952, **20**, 192.

[161] *Idem*, *Canad. J. Chem.*, 1952, **30**, 529.

[162] A. Fry and M. Calvin, *J. Phys. Chem.*, 1952, **56**, 897.

[163] C. A. Bunton and D. R. Llewellyn, *Research*, 1952, **5**, 443.

between oxalic acid and bromine, hydrogen peroxide, potassium permanganate, and $KMnO_4$–$Mn^{2+}$. Formation of $^{12}CO_2$ is preferred to that of $^{13}CO_2$, but the effect varies from 1·8 to 3·6%, depending on the reagent used, and appears to be related to the mechanism of attack on oxalic acid by these reagents.

The thermal deammoniation of phthalamide shows an isotope effect, $^{14}NH_3$ being formed more readily than $^{15}NH_3$.[164] The results are related to the effect of isotopic mass of the nitrogen atom in the C–N bonds which are both broken and formed in the reaction.

Schmitt, Myerson, and Daniels have shown that an isotope effect exists in the hydrolysis of urea by urease.[165] $^{12}CO_2$ is evolved 1% more readily than $^{13}CO_2$, and 3·2% more readily than $^{14}CO_2$.

Ropp and Raaen [166] have examined the effect of ring substitution on the isotope effect in hydrolysis of ethyl [$CO_2Et$-$^{14}C$]benzoates. The isotope effect may be greatest in the hydrolysis of those esters in which the largest contributions to the normal state are made by resonance forms of the type $^{+}R{:}C_6H_4{:}{}^{14}C(OEt){\cdot}O^{-}$. Other organic systems for which isotope effects have been detected include (i) the reaction between $^{14}C$-labelled benzophenone and 2 : 4-dinitrophenylhydrazine; [167] (ii) Cannizzaro reaction of $^{14}C$-labelled formaldehyde; [168] (iii) reaction of $^{14}CH_2O$ with dimedone; [169] and (iv) reaction of [1-$^{14}C$]acetone with alkaline hypoiodite.[170] The last reaction is of particular interest, since the isotope effect appears to be opposite to that ordinarily found: the $^{12}C$–$^{14}C$ bond is more easily broken than the $^{12}C$–$^{12}C$ bond.

Yankwich and McNamara [171] find no isotope effects on the equilibrium $Co(en)_2CO_3^{+} + H^{*}CO_3^{-} \rightleftharpoons HCO_3^{-} + Co(en)_2{}^{*}CO_3^{+}$, but find that the lighter isotopes of carbon are exchanged more readily than the heavier. Stranks and Harris [172] have observed just the reverse behaviour in the system $Co(NH_3)_4CO_3^{+}$ : $^{14}C$ becomes concentrated in the anion at equilibrium, while no discrimination is found between $^{12}C$ and $^{14}C$ in the kinetics of the process.

**Photochemistry.**—*Light Sources and Actinometers.*—The influence of several variables on the output of light of wave-length 2537 Å from a quartz–mercury vapour lamp of the low-pressure type has been studied by Heidt and Boyles,[173] who conclude that the output is particularly sensitive to the external temperature and is a maximum at about 45°.

The uranyl oxalate actinometer has been shown to be suitable for measuring intensities up to 1000 times the highest previously used.[174] The quantum yields, at 3650 Å, for the photolysis of seven aromatic diazonium salts [175] have been accurately measured and found to lie in the range 0·20—0·74. The

---

[164] F. W. Stacey, J. G. Lindsay, and A. N. Bourns, *Canad. J. Chem.*, 1952, **30**, 135.
[165] J. A. Schmitt, A. L. Myerson, and F. Daniels, *J. Phys. Chem.*, 1952, **56**, 917.
[166] G. A. Ropp and V. F. Raaen, *J. Chem. Phys.*, 1952, **20**, 1823.
[167] F. Brown and D. A. Holland, *Canad. J. Chem.*, 1952, **30**, 438.
[168] A. M. Downes and G. M. Harris, *J. Chem. Phys.*, 1952, **20**, 196.
[169] A. M. Downes, *Austral. J. Sci. Res.*, 1952, **5**, *A*, 521.
[170] A. Roe and E. L. Albenesius, *J. Amer. Chem. Soc.*, 1952, **74**, 2402.
[171] P. E. Yankwich and J. E. McNamara, *J. Chem. Phys.*, 1952, **20**, 1325.
[172] D. R. Stranks and G. W. Harris, *J. Phys. Chem.*, 1952, **56**, 906.
[173] L. J. Heidt and H. B. Boyles, *J. Amer. Chem. Soc.*, 1951, **73**, 5728.
[174] M. I. Christie and G. Porter, *Proc. Roy. Soc.*, 1952, *A*, **212**, 390.
[175] J. de Jonge, R. Dijkstra, and G. L. Wiggerink, *Rec. Trav. chim.*, 1952, **71**, 846.

photolysis of phenylaminobenzenediazonium sulphate, $\phi = 0{\cdot}36$, has been proposed as an actinometer for 3650 Å. It has the merits (i) that 100% decomposition gives the theoretical amount of nitrogen, (ii) that the nitrogen produced may be blown off by a stream of carbon dioxide and used as a direct measure of the light absorption, and (iii) that the diazonium salts have a high extinction coefficient and 100% absorption of light is easily achieved.

The malachite-green leucocyanide actinometer has been reinvestigated.[176] An improved method of preparation has been described, and it has been confirmed that at all wave-lengths the quantum yield is 1·00, provided the intensity is sufficiently low and the stirring rate sufficiently high.

A new type of Draper–Bunsen actinometer has also been described.[177]

*Direct Photochemical Reactions.*—(a) *Ketones and aldehydes.* The photolysis of keten has been the subject of two papers. By means of $^{13}CO$ it has been found that the $CH_2$ formed by the rupture of the keten molecule readily combines with carbon monoxide to re-form keten. A study of the products of the reaction between $CH_2$ and $(CHD)_2$ indicates the intermediate formation of the trimethylene diradical which then rearranges to give propylene.[178] Norrish and his co-workers[179] have investigated the flash photolysis of keten and discuss attempts to obtain the absorption spectrum of the methylene radical.

Further evidence for the complete free-radical photolysis of acetone vapour, at all temperatures, and wave-lengths between 2300 and 3400 Å, has been published.[180–182] Using radioactive $^{131}I_2$ as radical "catcher," Martin and Sutton have investigated the photolyses of acetone[182] and ethyl methyl ketone.[183] They find that at 3130 Å the relative rates of the two possible primary radical processes, (1) $COMeEt \longrightarrow MeCO + Et$ and (2) $COMeEt \longrightarrow EtCO + Me$, is $R_1/R_2 = 21 \pm 2$ compared with Blacet and Pitts's value of 40, while at 2537 Å the ratio is considerably lower.

The photolysis of diethyl ketone vapour has been extensively investigated between 25° and 300° by Kutschke and by Wijnen and Steacie. Their results, which are in good agreement, are published in a joint paper[184] and support the following mechanism :

$$(1)\qquad (C_2H_5)_2CO + h\nu \longrightarrow C_2H_5{\cdot}CO{\cdot} + C_2H_5{\cdot} \longrightarrow 2C_2H_5{\cdot} + CO$$

$$(2)\qquad 2C_2H_5{\cdot} \longrightarrow C_4H_{10}$$

$$(3)\qquad 2C_2H_5{\cdot} \longrightarrow C_2H_4 + C_2H_6$$

$$(4)\qquad C_2H_5{\cdot} + (C_2H_5)_2CO \longrightarrow C_2H_6 + {\cdot}C_2H_4{\cdot}CO{\cdot}C_2H_5$$

$$(7)\qquad {\cdot}C_2H_4{\cdot}CO{\cdot}C_2H_5 \longrightarrow C_2H_4 + CO + C_2H_5{\cdot}$$

The results indicate that $k_3/k_2 \sim 0{\cdot}10$ at all temperatures, *i.e.*, $E_3 - E_2 = 0$, $E_4 - \frac{1}{2}E_2 = 7{\cdot}4$ kcal./mole, and that reaction (7) only becomes important at high temperature and/or low intensity. The photolysis of $(CH_3{\cdot}CD_2)_2CO$ has confirmed this mechanism[185] and has provided the additional inform-

---

[176] J. G. Calvert and H. J. L. Rechen, *J. Amer. Chem. Soc.*, 1952, **74**, 2011.

[177] E. Cremer and H. Margreiter, *Z. physikal. Chem.*, 1952, **199**, 90.

[178] G. B. Kistiakowsky and W. L. Marshall, *J. Amer. Chem. Soc.*, 1952, **74**, 88.

[179] K. Knox, R. G. W. Norrish, and G. Porter, *J.*, 1952, 1477.

[180] S. W. Benson and C. W. Falterman, *J. Chem. Phys.*, 1952, **20**, 201.

[181] D. H. Volman and W. M. Graven, *ibid.*, p. 919.

[182] G. R. Martin and H. C. Sutton, *Trans. Faraday Soc.*, 1952, **48**, 812.

[183] *Idem, ibid.*, p. 823.

[184] K. O. Kutschke, M. H. J. Wijnen, and E. W. R. Steacie, *J. Amer. Chem. Soc.*, 1952, **74**, 714.

[185] M. H. J. Wijnen and E. W. R. Steacie, *Canad. J. Chem.*, 1951, **29**, 1092.

ation that $E_4 \sim 17$ kcal./mole, that the disproportionation reaction occurs by a head-to-tail mechanism :

$$CH_3{\cdot}CD_2{\cdot} + CH_3{\cdot}CD_2{\cdot} \longrightarrow CH_3{\cdot}CD_2H + CH_2{:}CD_2$$

and that the energy of activation for reaction (4) is greater for the abstraction of a methyl hydrogen than that of a methylenic hydrogen atom.

In the photolysis of di-*n*-propyl ketone, Masson [186] has concluded that about 50% of the activated molecules ultimately decompose by one of the following two processes :

$$(C_3H_7{\cdot}CO{\cdot}C_3H_7)^* \begin{array}{l} \xrightarrow{(1)} C_2H_4 + CH_3{\cdot}CO{\cdot}C_3H_7 \\ \xrightarrow[(2)]{} 2C_3H_7 + CO \end{array}$$

For the reaction $C_3H_7 \longrightarrow C_2H_4 + CH_3$, $E = 20$ kcal./mole was obtained. At 113°, 17% of the propyl radicals disproportionate and 83% combine to give *n*-hexane.

The photolysis of propaldehyde has been studied with steady and intermittent light,[187] and Blacet and Pitts [188] have deduced the relative importance of four possible primary processes from the products obtained in the presence and the absence of iodine.

(b) *Reactions involving halogen atoms.* In the photolysis of the hydrogen halides the energy of the light absorbed may be considerably greater than the energy required to break the hydrogen–halogen bond. Part of the excess of energy will appear as kinetic energy of the hydrogen atom* and might be expected to affect the rates of the reactions, (1) $H + HI \longrightarrow H_2 + I$, and (2) $H + I_2 \longrightarrow HI + I$. However, in the presence of sufficient inert gas the excess of energy will be removed by collision before these reactions occur. Schwarz and his colleagues [189] have interpreted, on the basis of this theory, their results on the photolysis of hydrogen iodide, deuterium iodide, and hydrogen bromide in the presence of helium and hydrogen. They find that, in the presence of inert gas, $k_2/k_1$ is reduced to a limiting value which is independent of the nature of the inert gas, and for thermal hydrogen atoms, $E_2 - E_1 = 4{\cdot}5 \pm 0{\cdot}8$ kcal./mole.

Burns and Dainton [190] have made a complete investigation of the photochemical formation of carbonyl chloride in the presence and absence of nitrosyl chloride as inhibitor, using light of wave-length 3660 Å, between 25 and 55°. Their results confirm the Bodenstein mechanism and the following values for the individual frequency factors ($A$) and energies of activation ($E$) have been obtained :

| | $\log_{10} A$ (l. mole$^{-1}$ sec.$^{-1}$) | $E$ (kcal. mole.$^{-1}$) |
|---|---|---|
| (1) $Cl_2 + h\nu \longrightarrow 2Cl$ | — | — |
| (2) $CO + Cl \longrightarrow COCl$ | $\log A_3/A_2 = 2{\cdot}806$ | $E_3 - E_2 = 6{\cdot}31$ |
| (3) $COCl \longrightarrow CO + Cl$ | | |
| (4) $COCl + Cl_2 \longrightarrow COCl_2 + Cl$ | 9·4 | 2·96 |
| (5) $COCl + Cl \longrightarrow CO + Cl_2$ | 11·6 | 0·83 |
| (6) $Cl + NOCl \longrightarrow NO + Cl_2$ | 10·06 | 1·06 |
| (7) $COCl + NOCl \longrightarrow CO + Cl_2 + NO$ (or $COCl_2 + NO$) | 10·68 | 1·14 |

---

[186] C. R. Masson, *J. Amer. Chem. Soc.*, 1952, 74, 4731.

[187] R. E. Dodd, *J.*, 1952, 878.

[188] F. E. Blacet and J. N. Pitts, *J. Amer. Chem. Soc.*, 1952, 74, 3382.

[189] H. A. Schwarz, R. R. Williams, and W. H. Hamill, *ibid.*, p. 6007.

[190] W. G. Burns and F. S. Dainton, *Trans. Faraday Soc.*, 1952, 48, 39, 52.

* Such atoms are designated as " hot " by the authors.

The results lead to the following heats of reaction :

$$CO + Cl \longrightarrow COCl + 6{\cdot}3 \text{ kcal.}$$
$$COCl + Cl \longrightarrow COCl_2 + 74{\cdot}9 \text{ kcal.}$$

The big difference in the magnitude of the C–Cl bond strengths is in accord with the high energy of reorganisation for the change : $>C{=}O \longrightarrow {}^1\Sigma CO$. The authors have discussed their results in terms of the theory of absolute reaction rates.

Other photochemical reactions involving halogen atoms which have been investigated are the reaction between iodine monochloride and hydrogen,[191] chlorination of toluene,[192] α-deuterotoluene,[193] and 2-deutero*iso*butane $(CH_3)_3CD$,[193] bromination of *n*-pentane,[194] formation of acyl chlorides from oxalyl chloride and paraffins,[195] and reaction of a mixture of chlorine and sulphur dioxide with paraffins.[196] In the liquid-phase photochlorination of $(CH_3)_3CD$ at $-15°$ equimolar amounts of $(CH_3)_3CCl$ and DCl are formed, indicating that no significant rearrangement of free radicals or hydrogen exchange between radicals and hydrocarbon occurs during chlorination.[193] Kharasch and his co-workers [194] dispute Williams and Hamill's claim [197] that lower bromides are formed in the photobromination of *n*-pentane.

The formation of the $H_2^+$ ion has been postulated to explain the effect of pH in the photochemical reactions of aqueous iodide [198] and ferrous solutions [199] respectively.

(c) *Other reactions*. A further study of the photolysis of aqueous hydrogen peroxide has been made at relatively high intensity.[200]

A mechanism of photolysis of methyl nitrite has been put forward which is in complete accord with all work on the decomposition of this compound; [201] the unstable HNO molecule is postulated as an intermediate.

In the photolysis of methylamine [202] it has been shown that 75% of the heavy liquid which is formed consists of a cyclic trimer of $CH_3{\cdot}N{:}CH_2$, and that both the radicals $CH_2{\cdot}NH{\cdot}$ and ${\cdot}CH_2{\cdot}NH_2$ are formed either in the primary process or in a secondary reaction. Booth and Norrish [203] have demonstrated that the photolysis of aliphatic primary and secondary amines gives products arising mainly from a primary process involving rupture of a N–H bond to give free radicals. The same authors have studied the photolysis of amides and conclude that two main types of primary process occur which are molecular, rather than free-radical, in nature.

A novel light-induced reaction of diazomethane with carbon tetrachloride to give $C(CH_2Cl)_4$ has been reported.[204] A free-radical mechanism is proposed. Analogous reactions were observed with chloroform and bromotrichloromethane, the halogens in each case being replaced by a $(CH_2Hal)$ group.

[191] G. G. Palmer and E. O. Wiig, *J. Amer. Chem. Soc.*, 1952, **74**, 2785.

[192] S. Miyazaki, *J. Chem. Soc. Japan*, 1951, **72**, 459, 641.

[193] H. C. Brown and G. A. Russell, *J. Amer. Chem. Soc.*, 1952, **74**, 3995.

[194] M. S. Kharasch, W. Zimmt, and W. Nudenberg, *J. Chem. Phys.*, 1952, **20**, 1659.

[195] F. Runge, *Z. Elektrochem.*, 1952, **56**, 779. [196] F. Povenz, *ibid.*, p. 746.

[197] R. R. Williams and W. H. Hamill, *J. Amer. Chem. Soc.*, 1950, **72**, 1857.

[198] T. Rigg and J. Weiss, *J.*, 1952, 4198. [199] *Idem, J. Chem. Phys.*, 1952, **20**, 1194.

[200] J. P. Hunt and H. Taube, *J. Amer. Chem. Soc.*, 1952, **74**, 5999.

[201] J. A. Gray and D. W. G. Style, *Trans. Faraday Soc.*, 1952, **48**, 1137.

[202] J. S. Watson and B. de B. Darwent, *J. Chem. Phys.*, 1952, **20**, 1041.

[203] G. H. Booth and R. G. W. Norrish, *J.*, 1952, 188.

[204] W. H. Urry and J. R. Eiszner, *J. Amer. Chem. Soc.*, 1952, **74**, 5822.

The action of light on diazoaminobenzene in alcohol,[205] on *meso*azanaphthacene and its angular benzogues,[206] on phosphotungstic acid in the presence of *iso*propyl alcohol,[207] and on aqueous solutions of sodium metaperiodate,[208] has also been studied.

Some work on the photolysis of solid systems has also been reported. Jacobs and Tompkins [209] have shown that the photolysis of potassium azide involves the reaction of pairs of trapped excited azide ions (excitons) of life-time approximately $2 \times 10^{-11}$ sec.; and Linschitz and Rennert [210] have investigated the reversible photobleaching of chlorophyll in glassy solvents at low temperature.

Much recent work is summarised in a symposium on Photochemistry and Photography held in Germany.[211]

*Photosensitised Reactions.*—The mercury($^3P_1$)-sensitised reaction of ethylene has been reinvestigated [212] and the results are compatible with the suggestion that a significant fraction of the quenching collisions of ethylene leads to the formation of metastable ($^3P_0$) atoms. Such atoms have been detected directly not only for ethylene but also when nitrogen, hydrogen, or ethane is the quenching gas.[212a]

The cadmium($^3P_1$)-sensitised decomposition of propane at 300° has been studied.[212b] The mercury-sensitised decomposition of nitric oxide has been shown to be caused by ($6\ ^1P_1$) atoms (1849-Å resonance radiation). It is suggested that Noyes's observation of photosensitised decomposition by light of wave-length 2537 Å was due to "stepwise absorption," *i.e.*, absorption of 4047 Å by ($6\ ^3P_0$) atoms or of 4359 Å by ($6\ ^3P_1$) atoms to give ($7\ ^3S_1$) atoms which then transfer their energy to the nitric oxide molecules.[213]

The products of the mercury-photosensitised reaction of tetrafluoroethylene at 30° are reported to be mainly hexafluoro*cyclo*propane and a linear polymer. The kinetics appear to fit a mechanism involving the rupture of the ethylenic bond to give two difluoromethylene radicals.[214]

The kinetics of reaction of various dienes, furfurylamine, and thiourea with oxygen, photosensitised by fluorescent pigments, have been described.[215] Uri [216] has found it possible to sensitise the polymerisation of methyl methacrylate, using chlorophyll and red light. The rate is enormously increased by certain organic reducing agents such as ascorbic acid, and quantum yields with respect to monomer of the order of 100 may be achieved.

*Fluorescence and Phosphorescence.*—The fluorescence emitted by formic acid, carbonyl chloride, and methylene iodide has been described [217] and

---

[205] H. C. Freeman and R. J. W. Le Fèvre, *J.*, 1952, 2932.
[206] A. Étienne and A. Staehelin, *Compt. rend.*, 1952, **234**, 1453.
[207] L. Chalkley, *J. Phys. Chem.*, 1952, **56**, 1084.
[208] F. S. H. Head and H. A. Standing, *J.*, 1952, 1457.
[209] P. W. M. Jacobs and F. C. Tompkins, *Proc. Roy. Soc.*, 1952, *A*, **215**, 254.
[210] H. Linschitz and J. Rennert, *Nature*, 1952, **169**, 193.
[211] *Idem*, *Z. Elektrochem.*, 1952, **56**, 705.
[212] B. de B. Darwent, *J. Chem. Phys.*, 1952, **20**, 1673.
[212a] B. de B. Darwent and F. G. Hurtubise, *ibid.*, p. 1684.
[212b] P. Agius and B. de B. Darwent, *J. Chem. Phys.*, 1952, **20**, 1679.
[213] J. D. McGilvery and C. A. Winkler, *Canad. J. Chem.*, 1952, **30**, 194.
[214] B. Atkinson, *J.*, 1952, 2684.
[215] G. O. Schenk and K. Kinkel, *Naturwiss.*, 1951, **38**, 355.
[216] N. Uri, *J. Amer. Chem. Soc.*, 1952, **74**, 5808.
[217] P. J. Dyne and D. W. G. Style, *J.*, 1952, 2122.

discussed.[218] In the case of formic acid, the emitter is the radical H·CO·O·. In the case of methylene iodide no evidence has been obtained for the emission of the methylene radical in the region 2400—5000 Å.

The quenching of the fluorescence of β-naphthylamine by carbon tetrachloride in the gas phase has been studied [219] and the phosphorescence emission of benzophenone in light petroleum has been examined and recorded.[220] Two types of emission have been found, the proportion of each depending on the concentration of benzophenone.

**Polymerisation and depolymerisation.** *Nomenclature.*—The International Union of Pure and Applied Chemistry have issued a report [221] on nomenclature in the field of macromolecules. One of the recommendations is that the term "intrinsic viscosity" be replaced by "limiting viscosity number," and that the units in which it is expressed be changed from decilitres/g. to ml./g.

The term "depropagation reaction" has been introduced to denote the exact opposite of the normal propagation reaction in addition polymerisation.[222–224]

*Condensation Polymerisation.*—In some condensation-polymerisation reactions, condensation is preceded by the addition of one reagent to the other, *e.g.*, urea and formaldehyde. References to work on the kinetics of such preliminary reactions are given in another section (p. 51). Work on the kinetics of polycondensation of phenolic alcohols [225] has been published and it is shown that the kinetic treatment of condensation developed by Flory in polyesterification reactions is also applicable to the polyetherification of phenolic alcohols.

*Free-radical Polymerisation.*—(a) Some aspects of the kinetics of radical polymerisation are summarised in the Tilden [102] and Liversidge [226] lectures of the Chemical Society.

(b) *Initiators and initiation rates.* The first-order velocity constant for the decomposition of αα′-azodi*iso*butyronitrile (I) at 82° has been found to be

$$NC{\cdot}CMe_2{\cdot}N\colon N{\cdot}CMe_2{\cdot}CN \quad (I)$$

practically independent of the solvent.[227] By using this initiator for the polymerisation of methyl methacrylate it has been conclusively shown that only about 50% of the radicals produced are effective in initiating polymerisation and that the termination process must be by combination of two radicals. It is inferred that the $RN_2$· radical is capable of initiating the polymerisation of methyl methacrylate but that the R· radical is not.[227] However this cannot be true for the polymerisation of styrene by (I), since the rate of evolution of nitrogen, as calculated from Breitenbach and Schindler's results,[228] is actually slightly greater than that in the solvents used by

---

[218] D. W. G. Style and J. C. Ward, *J.*, 1952, 2125.

[219] H. G. Curme and G. K. Rollefson, *J. Amer. Chem. Soc.*, 1952, **74**, 28.

[220] J. Ferguson and H. J. Tinson, *J.*, 1952, 3083.

[221] *J. Polymer Sci.*, 1952, **8**, 257.

[222] F. S. Dainton and K. J. Ivin, *Proc. Roy. Soc.*, 1952, *A*, **212**, 207.

[223] W. G. Barb, *ibid.*, p. 66.

[224] P. R. E. J. Cowley and H. W. Melville, *ibid.*, *A*, **210**, 461.

[225] H. Kämmerer, *Makromol. Chem.*, 1952, **8**, 72, 85.

[226] H. W. Melville, *J.*, 1952, 1547.

[227] L. M. Arnett, *J. Amer. Chem. Soc.*, 1952, **74**, 2027.

[228] J. W. Breitenbach and A. Schindler, *Monatsh.*, 1952, **83**, 724.

Arnett.[227] The initiator efficiency in various systems has been shown by radioactive tracer [229] and other methods [228, 230] to be generally between 0·5 and 1·0.

The rates of decomposition of the following initiators have also been measured : αα-azobis-(αγ-dimethylvaleronitrile) in xylene,[227] 1 : 1′-azobis-*cyclo*hexanecarbonitrile in xylene,[227] benzoyl peroxide, cumenyl hydroperoxide, and *tert.*-butyl hydroperoxide in methyl methacrylate and styrene respectively,[230] benzoyl peroxide in allyl ethers,[231] and *para*-substituted *tert.*-butyl perbenzoates in diphenyl ether.[232] The effect of structure of diacyl peroxides on the rates of initiation of polymerisation of styrene, and on their radical-induced decomposition has been investigated.[233] Tipper [234] has studied the effect of water on the decomposition of benzoyl peroxide in four solvents. A comparative study has been made [235] of persulphates and benzoyl peroxide as initiators in solution polymerisation.

For some time it has been generally assumed that in the direct photochemical polymerisation of a vinyl monomer, the initial act of absorption would produce a diradical which would then grow in both directions by the addition of monomer. However there is now clear evidence [230, 236] that, in the cases of styrene and methyl methacrylate, photopolymerisation proceeds *via* chains growing in one direction only. There is insufficient evidence to say whether purely thermal polymerisation proceeds by diradicals, and Zimm and Bragg [237] have even suggested that, if there is no transfer process, self-termination of the biradical by cyclisation would prevent the formation of long-chain polymer. However it is possible that the polymerisation of styrene photosensitised by dyes such as trypaflavin, Illuminol RII, and Illuminol U proceeds *via* diradicals.[238]

(c) *Polymerisation of single monomers.* Vaughan [239] has investigated the kinetics of the bulk polymerisation of styrene up to 100% conversion and suggests that the termination and propagation reactions in turn become diffusion-controlled. It has been shown that growing polystyrene chains are terminated mainly by combination.[236] The chain-transfer constants of polystyrene radicals with various halides have been determined.[240, 241] Iodides are more active than bromides which are more active than chlorides. Acid halides are exceptionally active.[240] A preliminary account has been given of a method for the determination of the extent of self-branching in polystyrene and other polymers.[242] $^{14}$C-Styrene is polymerised in the presence of inactive polymers of high molecular weight (500,000). Transfer with the dead polymer occurs and the inactive polymer radical so formed proceeds to add active monomer. The polymerisation is performed under

---

[229] L. M. Arnett and J. H. Peterson, *J. Amer. Chem. Soc.*, 1952, **74**, 2031.

[230] B. Baysal and A. V. Tobolsky, *J. Polymer Sci.*, 1952, **8**, 529.

[231] N. G. Gaylord and F. R. Eirich, *J. Amer. Chem. Soc.*, 1952, **74**, 334.

[232] A. T. Blomquist and I. A. Berstein, *ibid.*, 1951, **73**, 5546

[233] W. Cooper, *J.*, 1951, 3106; 1952, 2408.

[234] C. F. H. Tipper, *J.*, 1952, 2966.

[235] R. Sengupta and S. R. Palit, *J.*, 1951, 3278.

[236] D. H. Johnson and A. V. Tobolsky, *J. Amer. Chem. Soc.*, 1952, **74**, 938.

[237] B. H. Zimm and J. K. Bragg, *J. Polymer Sci.*, 1952, **9**, 476.

[238] M. Koizumi, Z. Kuroda, and A. Watanabe, *J. Inst. Polytech. Osaka City Univ., Ser. C.*, 1951, **2**, 1; *Chem. Abs.*, 1952, **46**, 4915.

[239] M. F. Vaughan, *J. Appl. Chem.*, 1952, **2**, 422; *Trans. Faraday Soc.*, 1952, **48**, 576.

[240] J. A. Gannon, E. M. Feites, and A. V. Tobolsky, *J. Amer. Chem. Soc.*, 1952, **74**, 1854.

[241] J. W. Breitenbach, *Makromol. Chem.*, 1952, **8**, 147.

[242] J. C. Bevington, G. M. Guzman, and H. W. Melville, *Nature*, 1952, **170**, 1026.

conditions such that the polymer produced directly from monomer has a relatively low molecular weight (50,000), and the polymer originally added may then be isolated at the end of the experiment and its content of active monomer units determined. The transfer constant with dead polymer is found to be similar in magnitude to that of other transfer reactions. Preliminary results are also given for vinyl acetate.

A detailed branching mechanism has been proposed for the polymerisation of vinyl acetate, and a simplified kinetic analysis gives an expression for the degree of branching in terms of six ratios.[243] Four of these ratios have been evaluated from experimental results. It appears that part of the branching occurs through ester linkages and that on hydrolysis of the polymer such linkages are broken.[244] No such linkages are present in the polymer initially formed. The kinetics of the bulk and suspension polymerisation,[245] and the inhibited and retarded polymerisation of vinyl acetate have also been studied.[246]

The chain-transfer reaction has been investigated in the catalysed polymerisation of methyl methacrylate,[247] and Matsumoto [248] has discussed the derivation of the mechanism of the termination process in the bulk polymerisation, from the molecular-weight distribution in the polymer.

The rate of the persulphate-catalysed polymerisation of methacrylic acid has been shown by Pinner [249] to decrease with decreasing acidity, and this result is interpreted in terms of copolymerisation of the undissociated acid with its less reactive anion.

The polymerisation of vinyl chloride has been studied in solution by benzoyl peroxide initiation,[250] and in the gas phase [251] by means of photochemical initiation.

In the polymerisation of allyl esters, termination takes place mainly by degradative chain transfer with the monomer, a hydrogen atom being abstracted from the $\alpha$-methylene group. It has been shown that abstraction of hydrogen atoms from the acid-derived portion of the ester may also occur to a small extent.[252] *iso*Propenyl acetate behaves as an allyl compound,[252] whereas methyl *iso*propenyl ketone, containing a conjugated carbonyl group, behaves like methyl methacrylate.[253]

The rate of oxygen uptake in the inhibited polymerisation of acrylonitrile has been measured in four different systems.[254] The products of reaction in aqueous solution were quantitatively analysed and a highly unstable peroxide isolated from non-aqueous systems.

The photo-polymerisation of acetylene has been shown to yield small

[243] O. L. Wheeler, E. Lavin, and R. N. Crozier, *J. Polymer Sci.*, 1952, **9**, 157.

[244] R. Inoue and I. Sakurada, *Chem. High Polymers, Japan*, 1950, **7**, 211; *Chem. Abs.*, 1952, **46**, 4843.

[245] K. Noma and K. Imai, *ibid.*, 1951, **8**, 44; *Chem. Abs.*, 1952, **46**, 11762.

[246] P. D. Bartlett and H. Kwart, *J. Amer. Chem. Soc.*, 1952, **74**, 3969.

[247] S. Basu, J. N. Sen, and S. R. Palit, *Proc. Roy. Soc.*, 1952, *A*, **214**, 247.

[248] M. Matsumoto, *J. Polymer Sci.*, 1952, **8**, 657.

[249] S. H. Pinner, *ibid.*, p. 282.

[250] G. V. Tkachenko, P. M. Khomikovskii, and S. S. Medvedev, *Zhur. Fiz. Khim.*, 1951, **25**, 823; *Chem. Abs.*, 1952, **46**, 3379.

[251] M. Koizumi and K. Nakatsuka, *J. Chem. Soc., Japan, Pure Chem. Sect.*, 1951, **72**, 431; *Chem. Abs.*, 1952, **46**, 4916.

[252] N. G. Gaylord and F. R. Eirich, *J. Amer. Chem. Soc.*, 1952, **74**, 337.

[253] G. Smets and L. Oosterbosch, *Bull. Soc. chim. Belg.*, 1952, **61**, 139.

[254] K. C. Smeltz and E. Dyer, *J. Amer. Chem. Soc.*, 1952, **74**, 623.

amounts of *cyclo*octatetraene.[255] A review of the polymerisation of formaldehyde has been published.[256] The kinetics of polymerisation of methyl acrylate have been studied.[257] 1 : 2-Dichloroethylene has been polymerised by the application of high pressure.[258] The inability of methyl α-*tert*.-butylacrylate to polymerise under a variety of conditions has been ascribed to potential steric hindrance in the polymer.[259]

Some aspects of the kinetics of polymerisation in systems in which polymer is precipitated have been discussed.[260]

(d) *Copolymerisation*. Studies of the composition of copolymers as a function of the composition of the monomer mixture have continued to give information about the relative reactivity of monomers with polymer radicals.[261–268] One of the most interesting reactions investigated was the copolymerisation of ethylene with carbon monoxide at high pressure.[268] Carbon monoxide behaves like maleic anhydride and the copolymer never contains more than 50% of carbon monoxide.

The kinetics of copolymerisation of four further monomer pairs have been investigated: methyl methacrylate and *p*-methoxystyrene, styrene and *m*-hydroxystyrene,[269] but-1-ene and sulphur dioxide,[270] and styrene and sulphur dioxide.[271] In the first system it has been shown that $\phi$ $[=k_{t,12}/(k_{t,11}\cdot k_{t,22})^{0\cdot5}]$, which is a measure of the "cross-termination" process, varies from 12 to 27 as the concentration of *p*-methoxystyrene is increased, whereas in the second system a value $\phi \leqslant 1$ fits the results quite well. In both copolymerisations involving sulphur dioxide it has been found necessary to assume that one of the effective monomers is a 1 : 1 complex, the presence of which has been demonstrated in each case by light-absorption measurements. The ceiling temperature effect in the sulphur dioxide–olefin systems has been shown to be caused by the onset of the depropagation reaction, and the kinetics permit evaluation of the equilibrium constant, and hence of the heat and entropy changes, of the propagation–depropagation reaction.

Gee[272] has subjected to detailed analysis existing data concerning the physical properties of liquid sulphur and has shown that the sudden increase in viscosity at 159° is due to the onset of polymerisation of (principally) $S_8$ molecules. The heat and entropy changes, unlike the values in normal

---

[255] Z. Kuri and S. Shida, *Bull. Chem. Soc., Japan*, 1952, **25**, 116.

[256] R. Sauterey, *Ann. Chim.*, 1952, **7**, 5.

[257] P. S. Shantarovich, *Izvest. Akad. Nauk, S.S.S.R. Otdel. Khim. Nauk*, 1952, 243; *Chem. Abs.*, 1952, **46**, 9384.

[258] K. E. Weale, *J.*, 1952, 2223.

[259] J. W. C. Crawford and S. D. Swift, *J.*, 1952, 1220.

[260] C. H. Bamford, W. G. Barb, and A. D. Jenkins, *Nature*, 1952, **169**, 1044.

[261] H. C. Haas and M. S. Simon, *J. Polymer Sci.*, 1952, **9**, 309.

[262] C. C. Price and R. D. Gilbert, *ibid.*, p. 577.

[263] W. S. Port, E. F. Jordan, J. E. Hansen, and D. Swern, *ibid.*, p. 493.

[264] S. P. Mitzengendler and V. A. Chekhovskaya, *Zhur. Priklad. Khim.*, 1951, **24**, 485; *Chem. Abs.*, 1952, **46**, 9885.

[265] S. N. Ushakov, S. P. Mitzengendler, and B. M. Polyatskina, *ibid.*, p. 289; *Chem. Abs.*, 1952, **46**, 774.

[266] J. W. Vanderhoff, *Microfilm Abs.*, 1951, **11**, 541; *Chem. Abs.*, 1952, **46**, 772.

[267] M. Yoshida and I. Sakurada, *Chem. High Polymers, Japan*, 1950, **7**, 334; *Chem. Abs.*, 1952, **46**, 4844.

[268] D. D. Coffman, P. S. Pinkney, F. T. Wall, W. H. Wood, and H. S. Young, *J. Amer. Chem. Soc.*, 1952, **74**, 3391.

[269] E. P. Bonsall, L. Valentine, and H. W. Melville, *Trans. Faraday Soc.*, 1952, **48**, 763.

[270] F. S. Dainton and K. J. Ivin, *Proc. Roy. Soc.*, 1952, *A*, **212**, 96, 207.

[271] W. G. Barb, *ibid.*, pp. 66, 177.

[272] G. Gee, *Trans. Faraday Soc.*, 1952, **48**, 515.

polymerisations, are both positive and a "floor temperature" rather than a ceiling temperature is therefore found with sulphur.

(e) *Depolymerisation.* A general account of the degradation of polymers has been given by Burgess;[273] and Simha[274] and Madorsky[275] have summarised the behaviour of different polymers in terms of the percentage monomer in the volatile products and the rate of change of molecular weight of the residue. Polymethyl methacrylate is one of the few polymers in which clean reversal to monomer occurs. In this case it has been shown that the depolymerisation can be induced photochemically above 130° and involves initiation, depropagation, and, in most circumstances, mutual termination of chains.[276] Using intermittent light to determine the life of the kinetic chains, and a retarder method to determine the initiation rate, Cowley and Melville[276] were able to deduce, for the first time, an experimental value for a depropagation velocity constant. The value of this is in reasonable agreement with theoretical predictions and leads to an acceptable value for the change of entropy during polymerisation. On the other hand $k_t$ is abnormally small compared with radical-termination reactions in dilute solution and this is attributed to the fact that the reaction is occurring in a highly viscous polymer. Simha[277] has discussed these results in terms of his theoretical treatment.[278] Jellinek[279] has also derived theoretical kinetic equations for the degradation of polymers, and has published a preliminary account of some experiments on the degradation of polystyrene.[280] The products of degradation of polystyrene[281] and polyvinyl acetate[282] have been investigated. In the latter case acetic acid is evolved by a chain reaction proceeding without the agency of free radicals, and a residue of polyacetylene is left. Smets and Tasset[283] have reported data on the degradation of four polymers in the presence of benzoyl peroxide.

*Ionic Polymerisation.*—(a) *Cationic polymerisation.* When Friedel–Crafts catalysts (A) are employed as initiators, it appears that the presence of a trace of a co-catalyst (BC), *e.g.*, water, is generally required for the catalyst to be effective. The catalyst and co-catalyst interact by a reaction such as $A + BC \longrightarrow AB^- + C^+$ to give a cation $C^+$ which initiates polymerisation. A "system" will therefore be defined by monomer–catalyst–co-catalyst–solvent. It is extremely difficult to remove the last traces of water from any system and where there is a possibility of a trace being present this is indicated below by $H_2O$(?).

In the system *iso*butene–$TiCl_4$–$CCl_3{\cdot}CO_2H$–hexane, it has been shown[284] by infra-red analysis that, in agreement with earlier work, the predominant end group is the methylene group. Trisubstituted double bonds and trichloroacetate groups were also found. This suggests that termination

---

[273] A. R. Burgess, *J. Appl. Chem.*, 1952, 78.

[274] R. Simha, *Trans. N.Y. Acad. Sci.*, 1952, **14**, 151.

[275] S. L. Madorsky, *J. Polymer Sci.*, 1952, **9**, 133.

[276] P. R. E. J. Cowley and H. W. Melville, *Proc. Roy. Soc.*, 1952, *A*, **210**, 461; *A*, **211**, 320.

[277] R. Simha, *J. Polymer Sci.*, 1952, 9, 465.

[278] R. Simha and L. A. Wall, *J. Phys. Chem.*, 1952, **56**, 707.

[279] H. H. G. Jellinek, *J. Polymer Sci.*, 1952, **9**, 369.

[280] H. H. G. Jellinek and L. B. Spencer, *ibid.*, 1952, **8**, 573.

[281] B. G. Achhammer, M. J. Reiney, L. A. Wall, and F. W. Reinhart, *ibid.*, p. 555.

[282] N. Grassie, *Trans. Faraday Soc.*, 1952, **48**, 379.

[283] G. Smets and G. Tasset, *Chim. Peintures*, 1952, **15**, 281; *Chem. Abs.*, 1952, **46**, 11762.

[284] M. St. C. Flett and P. H. Plesch, *J.*, 1952, 3355.

occurs by loss of a proton from two possible positions at the end of the growing cation, and by interaction with the trichloroacetate anion.

Although Jordan and Mathieson[285] have reported the consumption of catalyst in the systems M–$AlCl_3$–$H_2O$(?)–$CCl_4$ where M is styrene or α-methylstyrene, there is no evidence that the catalyst fragment is incorporated in the polymer molecule. On the contrary, there is clear evidence[288] that the catalyst is not incorporated in the polymer in the systems: styrene–$SbCl_5$–$H_2O$–nitrobenzene and styrene–$SbCl_5$–$H_2O$(?)–*cyclo*hexane. No radioactivity was detectable in the polymer when radioactive $SbCl_5$ was used as catalyst. Williams and Bardsley[289] have studied the system styrene–$SnCl_4$–HCl–$CCl_4$ at low concentrations of styrene where the main product is 1-phenylethyl chloride. However, although the kinetics are consistent with a carbonium ion mechanism, it is not possible to say whether initiation is by interaction of the catalyst with hydrogen chloride or with styrene.

Jordan and Mathieson have discussed their results on styrene[286] and have made a quantitative comparison with the results on α-methylstyrene.[285] They have also concluded[287] from molecular-weight distribution data[290] that in the latter case termination is by monomer deactivation and solvent transfer.

Norrish and Russell[291] have reported kinetic and molecular-weight measurements in the system *iso*butene–$SnCl_4$–$H_2O$–$C_2H_5Cl$. Water was shown to be essential for reaction. It was concluded that further work was required with very highly purified materials before the mechanism could be fully elucidated.

Further work has been published on the iodine-catalysed polymerisation of vinyl ethers.[292] The effect of a number of side groups has been examined with results which accord with expectation.

(b) *Anionic polymerisation.* Wooding and Higginson[293] have made the first detailed kinetic study of anionic polymerisation. The results for polymerisation of styrene in liquid ammonia, catalysed by potassamide, are in accord with a mechanism involving addition of the amide ion $NH_2^-$ to the monomer, propagation, and termination by reaction of the growing chain with the solvent leading to re-formation of the amide ion. A qualitative survey has been made of the reactivity of various anion bases, and the observed correlation between base strength and reactivity is in accord with the anionic mechanism of polymerisation.

The interesting suggestion has been made that the formation of rhodizonic acid when carbon monoxide reacts with liquid ammonia in the presence of sodium, occurs through an anionic polymerisation in which six carbon monoxide molecules are added to an amide ion.[294]

(c) *Ionic copolymerisation.* The relative ease of addition of two monomers to a growing polymeric entity may be expected to vary according to

[285] D. O. Jordan and A. R. Mathieson, *J.*, 1952, 611, 2354.
[286] *Idem, ibid.*, p. 621. [287] *Idem, ibid.*, pp. 2358, 2363.
[288] R. O. Colclough, *J. Polymer Sci.*, 1952, **8**, 467.
[289] G. Williams and H. Bardsley, *J.*, 1952, 1707.
[290] A. B. Hersberger, J. C. Reid, and R. G. Heiligmann, *Ind. Eng. Chem.*, 1945, **37**, 1073.
[291] R. G. W. Norrish and K. E. Russell, *Trans. Faraday Soc.*, 1952, **48**, 91.
[292] D. D. Eley and J. Saunders, *J.*, 1952, 4167.
[293] N. S. Wooding and W. C. E. Higginson, *J.*, 1952, 760, 774, 1178.
[294] F. Leonard and P. Fram, *Science*, 1952, **116**, 228.

whether such an entity is an anion, a free radical, or a cation, and this has been verified experimentally.[295] The anionic copolymerisation of butyl vinyl sulphone with acrylonitrile[296] and the effect of reaction conditions on the monomer reactivity ratios for the system styrene–*p*-chlorostyrene–$SnCl_4$ have been investigated.[297] Other systems have also been studied[298, 299] and it has been found that for the cationic copolymerisation of a given monomer with a series of substituted styrenes, the reactivity ratio is a function of Hammett's $\sigma$ value.[298]

It is clear from the report[300] of a conference held at Stoke that interesting developments are to be expected in this field.

*Emulsion Polymerisation.*—This does not strictly come into the category of homogeneous reactions but it should be noted that it has been possible to derive from the kinetics,[301] on the basis of Smith and Ewart's theory,[302] values for propagation velocity constants which are similar to those obtained by the more usual methods.

**Radiation Chemistry.**—(a) *Primary Processes.*—Most of the experimental data available on primary products has been obtained by the use of the mass spectrometer. Therefore, strictly speaking, such data apply only to the case of low-energy electron bombardment. Investigations of this kind include the measurement of appearance potentials of ions formed from *cyclo*propane,[303] cyanogen and methyl cyanide,[304] and hydrogen peroxide.[305] Norton[306] has studied the ionisation produced in water vapour in the presence of an excess of hydrogen. An unusually sharp maximum is obtained in the positive current at mass 19. This is due to the ion $H_3O^+$ formed in the following process :

$$H_2O \longrightarrow H_2O^{\ddagger} \longrightarrow H + OH\ (^2\Sigma^+)$$

$$\begin{tikzcd} & OH(^2\pi) \\ OH(^2\Sigma^+) \arrow[ur] \arrow[dr, "H_2"'] & \\ & H_3O \end{tikzcd}$$

$$H_3O \xrightarrow[\text{impact}]{\text{Electron}} H_2O^+ + e$$

There is still no experimental information on the nature of the primary products of high-energy bombardment processes. Until such results are available it will not be clear to what extent the different radiation chemical effects of, say, α-particles and electrons are due to the different spatial distribution of the entities formed or to differences in the entities themselves.

There has also been very little direct experimental investigation of the processes immediately subsequent to the primary act. In the gas phase the probability of electron exchange in hydrogen has been measured.[307] The

---

[295] F. R. Mayo and C. Walling, *Chem. Reviews*, 1950, **46**, 277.

[296] F. C. Foster, *J. Amer. Chem. Soc.*, 1952, **74**, 2299.

[297] C. G. Overberger, L. H. Arond, and J. J. Taylor, *J. Amer. Chem. Soc.*, 1952, **73**, 5541.

[298] C. G. Overberger, L. H. Arond, D. Tanner, J. J. Taylor, and T. Alfrey, *ibid.*, p. 4848. [299] Y. Landler, *J. Polymer Sci.*, 1952, **8**, 63.

[300] P. H. Plesch, *Nature*, 1952, **169**, 828.

[301] M. Morton, P. P. Salatiello, and H. Landfield, *J. Polymer Sci.*, 1952, **8**, 111, 215, 279.

[302] W. V. Smith and R. H. Ewart, *J. Chem. Phys.*, 1948, **16**, 592.

[303] F. H. Field, *J. Chem. Physics*, 1952, **20**, 1734.

[304] C. A. McDowell and J. W. Warren, *Trans. Faraday Soc.*, 1952, **48**, 1084.

[305] A. J. B. Robertson, *ibid.*, p. 228.

[306] F. J. Norton, *Phys. Review*, 1952, **85**, 154.

[307] E. E. Muschlitz and J. H. Simons, *J. Phys. Chem.*, 1952, **56**, 837.

ions $H_3^+$ and $H^+$ do not exchange appreciably with the $H_2$ molecule but the ion $H_2^+$ does so readily. In hydrocarbon gases all the ions $H_3^+$, $H_2^+$, and $H^+$ exchange readily, the explanation probably being that the large molecules can absorb considerable amounts of energy as vibrational energy. It has been found that the formation of the $H_3^+$ ion in hydrogen occurs by the process, $H_2^+ + H_2 \longrightarrow H_3^+ + H$, the $H_2^+$ ion being dissociated.[308]

Hasted[309] has studied the charge-exchange cross-sections of several processes, including that of $O^+$ ions in water, and cross-sections for processes of the type $A^- + B \longrightarrow A + B + C$ have also been measured. Such cross-sections are expected to be negligible unless very energetic ions and atoms are present,[310] but for $O^-$, $Cl^-$, and $F^-$ in various gases unexpectedly large cross-sections were found. This is interpreted as due to the presence of excited states of these ions having low electron affinities. It has been suggested that electron-capture processes in polyatomic molecules generally fall into two classes:[311]

$$AB + e \longrightarrow A + B^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$AB + e \longrightarrow A^+ + B^- + C \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Examples of type (1) are cyanogen and methyl cyanide, whilst type (2) is exemplified by carbon tetrachloride. Processes of type (1) are resonance processes necessitating a suitable crossing in the potential-energy curves of the relevant electronic states of the molecule AB and the ion $AB^-$. Studies of the type of electron capture occurring in given cases may thus yield information about the potential-energy curves of polyatomic molecules. The fact that processes of type (1) are resonance processes is significant in that it opens up the possibility of investigating the ultimate fate of the ion $B^-$ in solution.[312] A review of the reactions of gaseous ions has been presented by Massey.[310]

In a series of papers Magee and Burton have discussed certain initial processes in radiation chemistry. Semiquantitative treatments of simple cases followed by qualitative extension to more complex systems have led to the following general conclusions, and the relevance of each of these to radiation chemistry is discussed. (i) Thermal electron capture by a complex molecule positive ion should lead in most cases to immediate dissociation into two particles, one of which is excited. The particles are more likely to be radicals than molecules.[313] (ii) Under suitable conditions low-energy electrons tend to form negative ions *via* capture by neutral molecules, rather than to neutralise positive ions.[314] (iii) Charge transfers occurring by a resonance process, *e.g.*,

$$A^+ + A \longrightarrow A + A^+$$

may have large cross-sections; non-resonant processes of the type

$$A^+ + B \longrightarrow A + B^+$$

necessitate the crossing of two potential-energy curves of the system $(A + B)^+$

---

[308] R. L. Murray, *J. Appl. Phys.*, 1952, **23**, 6.

[309] J. B. Hasted, *Proc. Roy. Soc.*, 1952, *A*, **212**, 235.

[310] H. S. W. Massey, *Discuss. Faraday Soc.*, 1952, **12**, 24.

[311] J. D. Craggs, C. A. McDowell, and J. W. Warren, *Trans. Faraday Soc.*, 1952, **48**, 1093.

[312] F. S. Dainton, *Discuss. Faraday Soc.*, 1952, **12**, 10.

[313] J. L. Magee and M. Burton, *J. Amer. Chem. Soc.*, 1950, **72**, 1965.

[314] *Idem, ibid.*, 1951, **73**, 523.

and are accompanied by vibrational excitation or dissociation;[315] in general, complex formation is involved, lifetimes may be of the order of seconds, and other processes may therefore compete before the charge transfer is complete.[316] (iv) Simple changes of the type

$$A^+ + B^- \longrightarrow C + D$$

are not expected to occur since charge transfer takes place at a rather large distance. Highly excited states of A + B are expected and the end products should commonly be radicals.[317]

Considerable interest was recently aroused by the work of Dee and Richards.[318, 319] These authors claimed to have shown that an ultra-violet light emission is produced by the α-particle bombardment of liquids. The light is strongly absorbed by the irradiated material and the wave-length involved probably lies between 1500 and 1700 Å. The emission of this light and its subsequent absorption were suggested as a mechanism for the formation of chemically active radicals. Miller and Brown[320] have attempted to confirm these results, without success. They conclude that no appreciable emission of light of wave-length greater than 1800 Å takes place when water is bombarded with α-particles and that appreciable emission of light of shorter wave-lengths is unlikely. Other workers have also been unable to obtain results consistent with those of Dee and Richards.[321, 322] It is interesting that although the ultra-violet light emitted from water exposed to γ- or β-radiation is purely due to the Cerenkov effect[323, 324] and that no ultra-violet emission is found when high-intensity 50 kvp $X$-rays are used,[323] ice at a temperature of −100° to −170° does emit ultra-violet light under the latter type of irradiation and the emission is not of Cerenkov origin.[325] The light intensity is linear with dose rate over a large energy range and has a maximum energy at 3400 Å. In support of these observations tritium-ice is found to be self-luminescent.[325, 326]

A new conception of the processes occurring in liquids upon irradiation has been suggested.[327] Chemical activity is considered to be due to two types of excited species, $M^*$ and $M^‡$. The $M^*$ species is produced in primary processes occurring either in the main particle track or in its "spurs" (δ-ray tracks). It has a much smaller energy than $M^‡$ and is persistent. The $M^‡$ species is considered to result from ion neutralisation. It decomposes near its production site into uncharged radicals. Most of the $M^*$ species are in the lowest excited state but can participate in reactions by exciton or photon transfer if energy traps are present in the solution.

---

[315] J. L. Magee, *J. Phys. Chem.*, 1952, **56**, 555.
[316] M. Burton and J. L. Magee, *ibid.*, p. 842.
[317] J. L. Magee, *Discuss. Faraday Soc.*, 1952, **12**, 33.
[318] P. I. Dee and E. W. T. Richards, *Nature*, 1951, **168**, 736.
[319] E. W. T. Richards, *Discuss. Faraday Soc.*, 1952, **12**, 45.
[320] See N. Miller, *Discuss. Faraday Soc.*, 1952, **12**, 46.
[321] See M. Magat, *ibid.*, p. 48.
[322] M. A. Greenfield, A. Norman, and P. M. Kratz, U.S. Atomic En. Commiss. Report, 1952, UCLA-218.
[323] M. A. Greenfield, A. Norman, A. H. Dowdy, and P. M. Kratz, U.S. Atomic En. Commiss. Report, 1952, UCLA-211.
[324] F. S. Dainton, *Discuss. Faraday Soc.*, 1952, **12**, 44.
[325] L. I. Grossweiner and M. S. Matheson, *J. Chem. Phys.*, 1952, **20**, 1654.
[326] W. M. Jones, *ibid.*, p. 1974.
[327] M. Burton, J. L. Magee, and A. H. Samuel, *ibid.*, p. 760.

(b) *Actinometry*. Owing to their comparative straightforwardness and ease of handling, chemical methods of dosimetry are tending to be almost universally adopted. Of the numerous systems proposed for such measurements the ferrous sulphate system appears to be the most generally satisfactory and has been the subject of the most detailed calibration as yet.[328] A useful review and assessment of the various systems which have been proposed for chemical dosimetry has been given.[329] It is suggested that the term " chemical dosimetry " should be replaced by " actinometry," following the nomenclature of photochemistry. It is unfortunate that a lack of agreement exists between different workers as to the value of the oxidation yield of ferrous ion in aerated solutions which are conventionally 0·8N in sulphuric acid. Most authors agree that for *X*- and $\gamma$-radiation, at dose rates of up to 1000 r./min., the yield for ferrous oxidation is of the order of 20 molecules oxidised per 100 ev energy absorbed ($G = 20$), and Miller and Wilkinson have rechecked this result under varying conditions. However, using $^{60}$Co $\gamma$-radiation, Hochanadel[330] obtained a value of $G = 15{\cdot}5 \pm 0{\cdot}3$, the method of calibration employed being a calorimetric one. As Hochanadel's range of dose rates (1500—15,000 r./min.) was larger than that of the other authors, and since there is general agreement that the yield ultimately falls on increasing the dose rate, it was thought that this may be an explanation of the discrepancy. However, Hardwick[331] found the yield unchanged up to a dose rate of at least 4200 r./min. with 2000 kvp *X*-rays and Rigg, Stein, and Weiss,[332] using a dose rate of $\sim$3000 r./min., found $G = 19{\cdot}9$. Allen,[333] moreover, found a constant yield over a dose-rate range of 100—10,000 r./min. with 2 Mv *X*-rays. It seems clear therefore that this discrepancy is only to be settled by further experiment. Another effect observed in this system, which is confirmed by two investigators,[334, 335] is that the yield falls when low-energy $\beta$-radiation is used. For high-energy $\beta$-radiation the yield remains the same as for *X*-radiation,[336] and the falling yield for low-energy $\beta$-radiation has been explained in terms of the difference of ion density between the two types of radiation.[334] This explanation receives support from the fact that the yield for $\alpha$-radiation in aerated solution is even lower, *viz.*, $G = 6{\cdot}7$—$5{\cdot}9$[337] (depending on the exact value of $W$ for argon). A very marked fall in yield has been observed on increasing the dose rate with 0·92-Mv electrons from $10^3$ to $10^6$ r./min.[338] It has been claimed that ferrous sulphate actinometry is suitable for $\alpha$-radiation,[337] pile radiation,[339, 340] and 24 Mevp *X*-rays.[341] Evidence has been quoted to show that $\alpha$-radiation and lithium recoil particles do not behave additively to the ferrous system.[342] Though a reason for this has been suggested[343] the

[328] N. Miller, *J. Chem. Phys.*, 1950, **18**, 79.
[329] N. Miller and J. Wilkinson, *Discuss. Faraday Soc.*, 1952, **12**, 50.
[330] C. J. Hochanadel, *J. Phys. Chem.*, 1952, **56**, 587.
[331] T. J. Hardwick, *Discuss. Faraday Soc.*, 1952, **12**, 112.
[332] T. Rigg, G. Stein, and J. Weiss, *Proc. Roy. Soc.*, 1952, *A*, **211**, 375.
[333] A. O. Allen, *Discuss. Faraday Soc.*, 1952, **12**, 114.
[334] T. J. Hardwick, *ibid.*, p. 203.
[335] E. J. Hart, U.S. Atomic En. Commiss. Report, AECU-1534.
[336] T. J. Hardwick, *Canad. J. Chem.*, 1952, **30**, 39.
[337] N. Miller, *Discuss. Faraday Soc.*, 1952, **12**, 110. [338] C. B. Amphlett, *ibid.*, p. 272.
[339] E. Saeland and L. Ehrenberg, *Acta Chem. Scand.*, 1952, **6**, 1133.
[340] J. Wright, *Discuss. Faraday Soc.*, 1952, **12**, 60.
[341] R. W. Hummel and J. W. T. Spinks, *J. Chem. Physics*, 1952, **20**, 1056.
[342] J. Wright, *Discuss. Faraday Soc.*, 1952, **12**, 116. [343] M. Burton, *ibid.*, p. 117.

proposal is hardly borne out by the fact that $\alpha$-radiation and 50 kvp *X*-radiation appear to be additive in their effects.[337]

Another actinometer which has been investigated in some detail is the ceric sulphate system.[344] When *X*- or $\gamma$-radiation or high-energy $\beta$-radiation [336] was used this reaction was found to have a lower yield than the ferrous-ion actinometer. However the yield is independent of dose rate up to at least 45,000 r./min. for 2000 kvp *X*-rays or 140,000 r./min. for 50 kvp *X*-rays, independently of the presence or absence of oxygen and independently of the ceric-ion concentration down to the lowest limits which can be studied. It suffers the disadvantages of being more sensitive to impurities, and of exhibiting an increasing yield with decreasing electron energy.[334]

Compared with these two systems the benzene–water system [345] has several disadvantages. Thus the concentration independence of yield is less well fulfilled than for the ferrous system, the yield is much lower, the analysis is clumsy, and the reaction may exhibit a post-irradiation effect.[346] On the other hand this actinometer may prove useful at higher dose-rates.

Other possible systems which have been proposed for actinometry are the formic acid system,[347] the diphenylpicrylhydrazyl system,[348] a phosphate ester system,[349] and the use of polyvinyl chloride films.[350] Many systems have been investigated for possibilities as chemical actinometers.[351] Kanwisher [352] has developed an ingenious method of measuring dose rates with the chloroform–water system.

In order to obtain reasonable standardisation of dose measurements and expressions of yield it has been proposed that: [353] (i) Yields should be expressed as molecules converted per 100 ev energy absorbed. This should be designated by $G$ where the actual energy input is measured. (ii) The yield should be written as $G'$ if energy inputs are obtained from chemical actinometry; in this case full details of conversion factors should be given. (iii) The yield should be written as $G^{20}$ if ferrous sulphate actinometry is employed, the value of $G(\mathrm{Fe}^{2+} \longrightarrow \mathrm{Fe}^{3+})$ being provisionally taken as 20. (iv) The change to which $G$ refers should be indicated, *e.g.*, $G(\mathrm{H_2O_2})$. It is generally felt that the ferrous sulphate system would be the best for universal adoption in the *X*- and $\gamma$-ray dose-rate range from 0 to at least $10^3$ r./min.[354, 355]

(c) *Non-aqueous vapour and liquid systems.* Since the suggestion by Eyring, Hirschfelder, and Taylor [356] it has been commonly assumed that both ionisation and excitation processes play a part in radiation chemical reactions, and the investigations by Essex and his co-workers [357–360] support this view. Nevertheless the polymerisation of acetylene by $\alpha$-particles

---

[344] T. J. Hardwick, *Canad. J. Chem.*, 1952, **30**, 23.

[345] M. J. Day and G. Stein, *Nature*, 1949, **164**, 671.

[346] J. Wright, *Discuss. Faraday Soc.*, 1952, **12**, 114. [347] E. J. Hart, *ibid.*, p. 111.

[348] A. Chapiro, *ibid.*, p. 115. [349] B. E. Conway, *ibid.*, p. 250.

[350] E. J. Henley and A. Miller, *Nucleonics*, 1951, **9**, No. 6, 62.

[351] Illinois Univ. Progress Report No. 2, 1951; *Nuclear Sci. Abs.*, 1952, **6**, No. 4004.

[352] J. W. Kanwisher, *Nucleonics*, 1952, **10**, No. 5, 62.

[353] M. Burton, *Discuss. Faraday Soc.*, 1952, **12**, 317.

[354] F. S. Dainton, *ibid.*, p. 10. [355] N. Miller, *ibid.*, p. 318.

[356] H. Eyring, J. O. Hirschfelder, and H. S. Taylor, *J. Chem. Phys.*, 1936, **4**, 479.

[357] C. Smith and H. Essex, *ibid.*, 1938, **6**, 188.

[358] A. D. Kolumban and H. Essex, *ibid.*, 1940, **8**, 450.

[359] N. T. Williams and H. Essex, *ibid.*, 1948, **16**, 1153.

[360] *Idem*, *ibid.*, 1949, **17**, 995.

seems to provide an exception to this generalisation inasmuch as the whole effect can be accounted for on the basis of ionisation.[361]

A striking contrast between the chemical effects produced by irradiation in the liquid and the gaseous state is provided by a study of the $\alpha$-particle irradiation of *n*-hexane, *cyclo*hexane, and benzene.[362] In the gaseous phase the yields for each substance differ by a maximum factor of three, a completely different result from the effect of electrons on the liquids.[363]

In contrast to earlier findings for the effect of $\alpha$-particle irradiation on ethylene, an investigation of the $\gamma$-irradiation of this gas showed no substantial yield of hydrogen gas or of saturated hydrocarbons.[364] The main reaction is a chain polymerisation having an ionic yield of about 30.[365] The synthesis of ammonia by $\gamma$-irradiation of nitrogen–hydrogen mixtures has also been studied.[366] In this reaction the glass surface area is an important factor.

Three methods have now been used to obtain information concerning the chemically active species produced in organic liquids under the influence of ionising radiations. The first method comprises the use of iodine having a high specific activity of $^{131}I$.[367] Radicals formed during radiolysis combine with iodine to give iodides in small yield. To this product appropriate inactive alkyl iodide carriers are added and fractional distillation, followed by radioactivity measurement, permits an estimation of relative free-radical yields. This method has been applied to the radiolysis of alkanes and alkyl iodides in both the liquid and the gaseous phase.[368] Almost all the radicals formed are considered to react by the process $R + I_2 \longrightarrow RI + I$. A high yield of the parent substance in the case of the vapourised iodides indicates that the C–I bond is that most frequently broken, whilst in the liquid state there is a greater ratio of C–C to C–I bond rupture. Very little hydrogen iodide is formed, indicating only a small probability of C–H bond rupture. With alkanes the radical corresponding to the parent substance is no longer predominant except for methane. The results here obtained are complementary to mass-spectral data.[369] For example, the most important peak in the mass-spectrum of *neo*pentane is $C_4H_9^+$, whilst on radiolysis a large yield of $CH_3$ radical is found. Hence an important primary step appears to be

$$C(CH_3)_4 \rightsquigarrow C(CH_3)_3^+ + CH_3 + e$$

Dose rate variation had no effect on the decomposition patterns but in the case of ethyl iodide there were differences in the ratios of products for 2 Mv *X*-radiation, $\gamma$-radiation, and 50 kvp *X*-radiation. In experiments of this kind an increase of yield at high iodine concentrations can be explained on the basis of higher energy absorption by the heavy iodine atoms.[370]

---

[361] S. C. Lind, *J. Phys. Chem.*, 1952, 56, 920.

[362] V. P. Henri, C. R. Maxwell, W. C. White, and D. C. Peterson, *ibid.*, p. 153.

[363] M. Burton, *ibid.*, 1948, 52, 564.

[364] Yale Univ. Progr. Report, No. 3, 1952, NYO-3309.

[365] Yale Univ. Progr. Report, No. 2, 1952, NYO-3310.

[366] W. A. Selke, C. Kardys, E. V. Sherry, and R. C. Jagel, U.S. Atomic En. Commiss. Report, 1952, NYO-3327.

[367] R. R. Williams and W. H. Hamill, *J. Amer. Chem. Soc.*, 1950, 72, 1857.

[368] L. Gevantman and R. R. Williams, *J. Phys. Chem.*, 1952, 56, 569.

[369] A. Langer, *ibid.*, 1950, 54, 618.

[370] C. C. Schubert and R. H. Schuler, *J. Chem. Phys.*, 1952, 20, 518.

The other two methods so far used in following radical production are the trapping of radicals by (*a*) the initiation of polymerisation, and (*b*) the reaction with diphenylpicrylhydrazyl (DPPH) radicals. Both of these methods have recently been employed for the determination of the number of free radicals produced in a series of organic liquids by given doses of $\gamma$-radiation.[371, 372, 373] Under the conditions of experiment the radical-trapping reaction is considered to be much more probable than radical-recombination reactions and energy yields for radical formation have been evaluated on this basis. Results obtained by the two methods agree reasonably well in most cases, though it has been pointed out that owing to possible breakdown of the hydrazyl radical itself one would not really expect to be able to count the radicals formed with accuracy greater than a factor of 2.[374]

Manion and Burton have studied the radiolysis of mixtures of hydrocarbons in the liquid state.[375] The results are consistent with a mechanism in which both ionisation transfer and excitation transfer play significant roles. Owing to this effect, radiolysis of mixtures yields products which are not predictable on a simple law of averages. In a mixture of two components, whichever component is first ionised, there is known to follow a rapid transfer of ionisation to the species of lower ionisation potential. Manion and Burton's results indicate that excitation transfer usually behaves similarly, this effect being most readily appreciated in the case of radiolysis of *cyclo*hexane–benzene mixtures in which the two effects appear to act in opposition. Fundamental differences in mechanism are shown to exist between radiolyses in the gaseous and the liquid state for *cyclo*hexane–benzene mixtures.*

A mass-spectrometric examination of benzene and deuterobenzene indicated that the ratio of ions $C_mH_n^+/C_mD_n^+$ was constant for different values of $m$ and $n$, whilst the ratio $C_6H_n^+/C_6D_n^+$ tended to increase as $n$ decreased.[376] A different mechanism of formation of the two types of ion was thus indicated. Radiolysis of the two substances by 1·5 Mv electrons gave the result $G(H_2) > G(C_2H_2)$ for benzene, and $G(D_2) < G(C_2D_2)$ for deuterobenzene, again indicating that at least two mechanisms are involved in the radiolysis of benzene and that these do not contribute to the same extent for $C_6H_6$ and $C_6D_6$. The results have been explained in terms of bond rupture and rearrangement of the parent ion, and the difference in zero-point energy between C–D and C–H bonds. It is also shown that the molecules $C_6H_6$ and $C_6D_6$ exhibit mutual protection in a mixture and the implications of this are discussed.

The rate of polymerisation of styrene by $\gamma$-radiation, in the dose-rate range 2400—5500 r./min., has been found to be proportional to the dose rate.[381] This is contrary to earlier reports.[382, 371] Minder and Heydrich[383] have investigated the radiolysis of halogenated hydrocarbons in alcohol and acetone solution. Halogen acids are formed in amount depending on the

---

[371] A. Chapiro, *J. Chim. phys.*, 1950, **47**, 747.

[372] *Idem, Compt. rend.*, 1951, **233**, 792.

[373] A. Prevot-Bernas, A. Chapiro, C. Cousin, Y. Landler, and M. Magat, *Discuss. Faraday Soc.*, 1952, **12**, 98. [374] W. Wild, *ibid.*, p. 127.

[375] J. P. Manion and M. Burton, *J. Phys. Chem.*, 1952, **56**, 560.

[376] S. Gordon and M. Burton, *Discuss. Faraday Soc.*, 1952, **12**, 88.

* Cf. ref. 362.

concentration, the number of halogen atoms in the compound, and the type of binding. It is claimed that, in order to effect decomposition of chloroform by $\gamma$-radiation alone or in solution, oxygen must be present.[377, 378] Good yields of salicylic acid are produced on irradiation of benzyl alcohol in ethyl alcohol with 1-Mev electrons.[379] A bibliography on the effect of $\alpha$-, $\beta$-, $\gamma$-, and $X$-rays on organic compounds has been compiled.[380]

(d) *Water and aqueous solutions.* A widespread interest continues to centre upon radiation effects induced in aqueous systems, consequently no apology is made for devoting most attention to their discussion. Although it has been accepted for some time that the ultimate formation of H atoms and OH radicals seems to offer the most convenient explanation of the behaviour of irradiated water, nevertheless as more experimental data become available there is an increasing feeling that our conceptions regarding the nature of the primary reacting entities, and for that matter the particular form of the substrate with which they react, are too rudimentary. Despite the fact that almost every possible radical or ion has now been invoked to explain this or that aspect of radiation chemical effects in water, together with almost every possible permutation of their formation and breakdown, results continue to appear which meet with no explanation on existing concepts, or which seem incompatible with those of other workers. Just how far the sensitivity of some of the systems to very small changes in experimental conditions is responsible for the discrepancies it would be hard to say at present, but the recent Faraday Society Discussion[384] indicated that several anomalies may in fact be due to this cause.

It has several times been pointed out that the majority of radiation chemical reactions in aqueous solutions are oxidations,[385, 386] and the usual value of the equivalent reduction potential (e.r.p.) of irradiated water, as judged from published experimental results, indicates that the oxidising power of irradiated water cannot be due to a mixture of H atoms and OH radicals alone in equal proportions. It has been shown[387, 388] that any argument based on a difference of distribution of H atoms and OH radicals cannot explain this effect, but the existence of the ions $H_2^+$[389] and $HO^+$[387] (or O atoms) may help to give the observed result. It has also been suggested that all cases of radiation reduction so far observed can be explained by the action of OH radicals or hydrogen peroxide.[390] This indicates that H atoms appear to be very unreactive, and in fact raises the suspicion that they may never have independent existence. From this point of view it has been

---

[377] J. F. Suttle and J. W. Schulte, *Discuss. Faraday Soc.*, 1952, **12**, 317.

[378] J. W. Schulte, J. F. Suttle, and R. Wilhelm, U.S. Atomic En. Commiss. Report, 1952, LA-1438.

[379] B.P., 1952, 665,263.

[380] F. Sachs, Literature Search for Carbide Chemicals Co., 1952, Co(Y-12).

[381] B. Manowitz, R. V. Horrigan, and R. H. Bretton, U.S. Atomic En. Commiss. Report, 1951, BNL-141.

[382] A. Chapiro, *Compt. rend.*, 1949, **228**, 1490.

[383] W. Minder and H. Heydrich, *Discuss. Faraday Soc.*, 1952, **12**, 305.

[384] " Radiation Chemistry," *Discuss. Faraday Soc.*, 1952, **12**.

[385] M. Haissinsky and M. Lefort, *Compt. rend.*, 1949, **228**, 314.

[386] M. Haissinsky, *Discuss. Faraday Soc.*, 1952, **12**, 133.

[387] F. S. Dainton and E. Collinson, *Ann. Rev. Phys. Chem.*, 1951, **2**, 99.

[388] E. Collinson and F. S. Dainton, *Discuss. Faraday Soc.*, 1952, **12**, 251.

[389] J. Weiss, *Nature*, 1950, **165**, 728.

[390] M. Haissinsky and M. Lefort, *Compt. rend.*, 1950, **230**, 1156.

suggested that instead of the $H_2O^-$ ion breaking down in the usually accepted manner :

$$H_2O^- \longrightarrow HO^- + H \tag{3}$$

the breakdown occurs by one of the following processes :

$$H_2O^- \longrightarrow O^- + H_2 \tag{4}$$ [391]

followed by $$O^- + H_2O \longrightarrow HO^- + OH \tag{4a}$$

or $$H_2O^- \longrightarrow H^- + OH \tag{5}$$

followed by $$H^- + H_2O \longrightarrow OH^- + H_2 \tag{5a}$$

Supporting arguments for reactions (5) and (5*a*) have recently been advanced [393] but (5) seems a less likely process energetically than either (3) or (4). It has been argued that process (4) is energetically to be preferred to process (3),[392] but it has also been pointed out that if (4) is energetically favoured with respect to (3) then it cannot be followed by (4*a*).[394] It has been claimed that process (4) offers an alternative explanation to the " hot spot " hypothesis (see next section) for the production of hydrogen gas in nearly constant initial yield and that it also indicates a decreased reducing power of irradiated solutions. Against such a hypothesis the following arguments may be advanced : (*a*) The difficulty of finding a suitable process to follow (4). (*b*) The fact that there is some direct evidence of the participation of D atoms in polymerisations induced in deuterium oxide solution.[395] (*c*) The fact that hydrogen peroxide has been found in greater initial yield than hydrogen in the ferrous sulphate system.[396] (*d*) The fact that it is difficult to explain the reduction of certain organic dyes on this basis. It is certainly not true to assume that reduction occurs by H atoms formed in the process

$$OH + H_2 \longrightarrow H + H_2O \tag{6}$$

as is shown by the enhanced yield produced by the addition of sodium benzoate to such systems.[397, 398]

The theory of Burton, Magee, and Samuel [327] suggests a mechanism somewhat different from that usually accepted for H atom and OH radical formation and it seems likely that the present position may be summarised by the overall expression

$$H_2O \longrightarrow H_2O^* + H + OH + \text{other species as yet ill-defined.}$$

The excited species $H_2O^*$ may be able to oxidise or reduce or play no chemical part, depending on the substrate concerned, and this may be an explanation of the differences in *G* (solute) and *G* (free radical) values found from investigations on different solutes.

(i) *Molecular and radical yield.* The postulate, first advanced by Allen,[399] that the primary effect of ionising radiation on water could be regarded as consisting of two processes :

$$H_2O \longrightarrow \tfrac{1}{2}H_2O_2 + \tfrac{1}{2}H_2 \tag{F}$$
$$H_2O \longrightarrow OH + H \tag{R}$$

---

[391] M. Haissinsky and M. Magat, *Compt. rend.*, 1951, 233, 954.

[392] M. Magat, *Discuss. Faraday Soc.*, 1952, 12, 244.

[393] G. W. R. Bartindale, *ibid.*, p. 246. [394] F. S. Dainton, *ibid.*, p. 245.

[395] E. Collinson and F. S. Dainton, *ibid.*, p. 212.

[396] F. S. Dainton and H. C. Sutton, *ibid.*, p. 121. [397] M. J. Day, *ibid.*, p. 280.

[398] G. Stein, *ibid.*, p. 243. [399] A. O. Allen, *J. Phys. Chem.*, 1948, 52, 479.

has received considerable direct support from measurement of initial hydrogen peroxide yields,[400, 401, 402, 403] and indirect support from the fact that certain results are explicable on mechanisms involving this postulate.[404, 405, 406] On the other hand there have been some dissensions on experimental grounds,[407, 408] hydrogen yields having been found to vary. It is not clear whether or not the yields in these last cases are *initial* yields.

Several attempts have been made to measure the yield for each of the processes ($F$) and ($R$). Hochanadel,[330] using $\gamma$-radiation from a $^{60}$Co source, has examined the rate of production of hydrogen peroxide in acid deaerated potassium bromide solutions and in water containing hydrogen and oxygen. Johnson and Allen [403] found a constant initial yield of hydrogen during the irradiation of several solutions with 2 Mev $X$-rays, and used their results to evaluate the yield due to ($F$). In 0·8N-sulphuric acid lower yields of hydrogen were found, probably owing to direct energy absorption by the acid. Johnson [409] has estimated the percentages of radicals used in the processes ($F$) and ($R$). Hart [406] has made similar estimates from the results of oxidation of formic acid in aerated solution by $^{60}$Co $\gamma$-irradiation and by irradiation with tritium β-rays. This worker also employed the oxidation of ferrous sulphate, in aerated and in air-free solutions, to obtain relative yields of ($R$) and ($F$) [410] for $^{60}$Co $\gamma$- and tritium β-radiation.

Other workers have made estimates of the radical-pair yield alone. Dainton and Rowbottom [411] achieved this by comparison of radiation and photochemical yields for the decomposition of hydrogen peroxide in aqueous solution. Rigg, Stein, and Weiss [332] made an estimate from work on the ferrous sulphate system. The data obtained from these investigations are presented in the table below.

| Reference | Radiation | $G_F$ | $G_R$ | $G_{H_2O}$ | Radicals (%) | | ev per radical pair |
|---|---|---|---|---|---|---|---|
| | | | | | $R$ | $F$ | |
| 330 | $^{60}$Co $\gamma$ | 0·46 | 2·74 | 3·66 | 75 | 25 | 27 |
| 406 | $^{60}$Co $\gamma$ | 0·35 | 2·78 | 3·48 | 79 | 21 | 30·5 |
| 406 | T $\beta$ | | | 3·35 | 70 | 30 | 29·8 |
| 410 | $^{60}$Co $\gamma$ | | | | 62 | 38 | |
| 410 | T $\beta$ | | | | 53 | 47 | |
| 330 | $\gamma + n$ | 1·18 | 1·57 | 3·93 | 40 | 60 | 25·5 |
| 411 | $^{60}$Co $\gamma$ | | | 13·4 | | | 7·5 |
| 332 | 200 kv $X$ | | | | | | 19·4 |
| 403 | 2 Mev $X$ | 0·395 * | | | | | |
| 412 | 2 Mev electrons | | | | 80 | 20 | |
| 413 | 30 kv $X$ | | | 12·3 | | | 8·1 |

* Assuming $G(\mathrm{Fe}^{2+} \longrightarrow \mathrm{Fe}^{3+}) = 20$.

---

[400] A. O. Allen, *Discuss. Faraday Soc.*, 1952, 12, 79.

[401] P. Bonet-Maury, *ibid.*, p. 72.

[402] A. O. Allen, C. J. Hochanadel, J. A. Ghormley, and T. W. Davies, *J. Phys. Chem.*, 1952, 56, 575.

[403] E. R. Johnson and A. O. Allen, *J. Amer. Chem. Soc.*, 1952, 74, 4147.

[404] E. J. Hart, *ibid.*, p. 4174.

[405] E. R. Johnson, U.S. Atomic En. Commiss. Report, 1952, BNL-1209.

[406] E. J. Hart, *J. Phys. Chem.*, 1952, 56, 594.

[407] M. Haissinsky, *Discuss. Faraday Soc.*, 1952, 12, 123. [408] T. Rigg, *ibid.*, p. 119.

[409] E. R. Johnson, U.S. Atomic En. Commiss. Report, 1952, BNL-1209.

[410] E. J. Hart, *J. Amer. Chem. Soc.*, 1951, 73, 1891.

[411] F. S. Dainton and J. Rowbottom, *Nature*, 1952, 169, 370.

[412] E. R. Johnson, *J. Chem. Phys.*, 1951, 19, 1204.

[413] M. Haissinsky and M. Lefort, *J. Chim. phys.*, 1951, 48, 368.

All such values can only represent lower limits to the free-radical yield, owing to the possibility of recombination of some of the radicals to form water. This would account for the different values obtained for different systems, even when the work has been carried out by the same investigator. From this point of view the highest value obtained for the free-radical yield, if subsequently confirmed, bids fair to be the most likely value. Another possible source of variation is the effect of the excited water molecule $H_2O^*$, as discussed earlier.

It has been suggested that the products hydrogen and hydrogen peroxide from (*F*) are formed in regions of high density of energy release (hot spots).[400–402] Bonet-Maury[401] regards each radiation as having some of the property of *X*-radiation and some of the property of α-radiation, the transition from predominantly α-behaviour to predominantly *X*-behaviour occurring at a mean ion density of 200 ion pairs per micron. Such considerations lead to the expectation that an increase in ionisation density of the radiation employed will increase the molecular yield ($G_F$) and decrease the free-radical yield ($G_R$), and that the steady state level of decomposition in pure water will rise.[399] These expectations have been fulfilled experimentally. The steady state level of decomposition of water rises as we pass from *X*-radiation through proton and deuteron radiation to α-radiation,* this being the order of increasing ionisation density. The changing ratios of radicals produced by (*R*) and (*F*) for different radiations as given in the Table are also in agreement with this hypothesis, and Hardwick[334] has shown that on these considerations a correlation between the apparently anomalous results of various workers on the ferrous–ferric and cerous–ceric systems can be achieved.

(ii) *The ferrous–ferric system.* In view of the importance of this system from the point of view of chemical dosimetry it is natural to find that continued attention is paid to it. The effect of several variables on yield in the oxidation of ferrous sulphate produced by *X*-irradiation has been studied by Rigg, Stein, and Weiss[332] who conclude that the effect of increasing pH in reducing the oxidation yield, in air-free solution, can be accounted for by the mechanism :

$$Fe^{2+} + OH \longrightarrow Fe^{3+} + OH^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$H + H^+ \rightleftharpoons H_2^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

$$Fe^{2+} + H_2^+ \longrightarrow Fe^{3+} + H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$H + Fe^{3+} \longrightarrow Fe^{2+} + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

The limiting yield in acid solutions is considered to be due to complete removal of OH radicals and also the complete removal of H atoms, as $H_2{}^+{}_{aq.}$, in oxidation of ferrous ions. At high pH the competing back reaction (10) causes non-linearity of yield. In aerated solutions all hydrogen atoms function as $HO_2$ radicals and the kinetic scheme proposed consists of process (7) together with the following steps :

$$H + O_2 \longrightarrow HO_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

$$HO_2 + Fe^{2+} \longrightarrow Fe^{3+} + HO_2^- \quad . \quad . \quad . \quad . \quad . \quad (12)$$

$$H_2O_2 + 2Fe^{2+} \longrightarrow 2Fe^{3+} + 2OH^- \quad . \quad . \quad . \quad . \quad . \quad (13)$$

$$Fe^{3+} + O_2^- \longrightarrow Fe^{2+} + O_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

---

* Ref. 401, p. 75, Table I.

The fall in yield found on increase of pH is attributed to the back-reaction (14), a reaction established by independent work.[414] The proposed schemes will account for the effect of changing the ferrous-ion concentration in both aerated and deaerated solution and also explains the authors' finding that the limiting yield in aerated acid solutions is about double that in deaerated acid solutions. This experimental result is not in agreement with the findings of several other workers, a value of about 2·8 being more commonly accepted.[410] The reduction of yield caused by addition of hydrogen in deaerated solutions is explained on the basis of the back-reaction (6), a suggestion supported by the fact that hydrogen increases the rate of reduction of ferric ions in deaerated solution.

Though the above mechanism suffices to explain these authors' results, it fails to account for results found by other investigators. Thus Dainton and Sutton [396] have found that hydrogen peroxide is formed during the *X*-irradiation of solutions of ferrous ion at concentrations less than $10^{-5}$M. This tends to support the reaction (*F*) whereas no possible mechanism for the formation of hydrogen peroxide arises from the above postulates. Amphlett [415] has examined the effect of pH on the initial yield of the oxidation of ferrous ions in aerated solutions by *X*- and $\gamma$-irradiation. He finds evidence of a back-reaction as the pH is increased and of an ultimate steady state. The data are not in agreement with those of earlier workers.[416] It is shown that pH effects can only arise from some effect on the $HO_2$ radical, and the process

$$Fe^{3+} + HO_2 \longrightarrow Fe^{2+} + H^+ + O_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

which is equivalent to process (14), is suggested as the pH-dependent step. On the other hand it is found that the pH-dependence of the yield is not fully explained on this basis, and the suggestion is made that possibly the ratio (*R*) : (*F*) changes with pH. Other results still requiring a satisfactory explanation are the steady states at high pH and the fact that the yield of ferric ion produced does not begin to fall immediately after the start of the reaction. So far the suggested kinetics have failed to fit the results completely and it is suggested that there may be a fundamental inadequacy of the proposals. Baxendale [417] has suggested that some of the discrepancies may be cleared up by assuming a non-uniform distribution of radicals. It should be noted here that Collinson and Dainton [395] have also found it necessary to postulate a non-uniform distribution of radicals in order to explain results on the polymerisation of acrylonitrile in aqueous solution by *X*- and $\gamma$-radiations. However, the ferrous oxidation problem is complicated by the fact that Dewhurst [418] was unable to find stationary states and could not obtain reduction of ferric ions, though confirming the effect of pH on both aerated and deaerated solutions. He also found, contrary to Amphlett, that low concentrations of chloride ion had no effect on the reaction, this having been checked on samples of solution from other laboratories. Other work which has appeared on the irradiation of the ferrous–ferric system (apart from that discussed in the section on actinometry) concerns irradiation

---

[414] W. G. Barb, H. J. Baxendale, P. George, and K. R. Hargrave, *Trans. Faraday Soc.*, 1951, **48**, 462.

[415] C. B. Amphlett, *Discuss. Faraday Soc.*, 1952, **12**, 144.

[416] H. Fricke and E. J. Hart, *J. Chem. Phys.*, 1935, **3**, 60.

[417] J. H. Baxendale, *Discuss. Faraday Soc.*, 1952, **12**, 253, 256.

[418] H. A. Dewhurst, *ibid.*, p. 255.

in the presence of other substances. Dewhurst[419] has studied the effect of alcohols on the ferrous oxidation initiated by $\gamma$-radiation, Hart[420] has examined the mechanism of the $\gamma$-ray-induced oxidation of ferrous ion in the presence of formic acid and oxygen, and Cottin, Haissinsky, and Vermeil[421, 422] have investigated the effect of hydrocarbons on the yields of ferric ion produced in aerated aqueous solutions by $\gamma$-rays and 24 kv $X$-rays. The last authors have also examined the effect of alcohols on the $X$-ray-induced oxidation. In each case the yields of oxidation in aerated solutions are appreciably higher than the yields without the added material. In the case of the addition of formic acid the kinetics can be explained on the basis of a chain mechanism including the radical HCO·O. Both alcohols and hydrocarbons appear to give rise to radicals capable of reaction with oxygen to form peroxides. These then oxidise the ferrous ions by chain mechanisms, which in the case of alcohols can be inhibited by the addition of chloride ion.[419] The increase in rate of oxidation due to the presence of primary alcohols is greater the longer the alcohol chain.

Garrison and Rollefson[423] examined the effect of high-energy $\alpha$-particles on aqueous solutions of ferrous ions and carbon dioxide containing $^{14}CO_2$. The aim of this work was to attempt a removal of all the OH radicals by $Fe^{2+}$ ions and hence to study the effect of H atoms on carbon dioxide, these two being assumed to be the active species. The principle products were ferric ions and hydrogen, but a small fraction of the H atoms were used in forming reduction products of carbon dioxide, mainly formic acid, with some formaldehyde and oxalate. A mechanism is given which fits the data over the whole range of observations, and an estimate of the effective concentration of H atoms gives this as $\sim 10^{-3}$M.

(iii) *Other aqueous systems.* The formation and destruction of hydrogen peroxide has been the subject of several investigations.[401, 411, 424–428] Hart and Matheson[424] find the rate of decomposition by $^{60}$Co $\gamma$-radiation to be unmistakably proportional to $[H_2O_2]^{\frac{1}{2}}$ and (dose rate)$^{\frac{1}{2}}$. A mechanism which satisfies the results is proposed which, however, contains an unusual third-order termination step :

$$2HO_2 + H_2O_2 \longrightarrow 2H_2O_2 + O_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

The special efficiency of hydrogen peroxide as a third body in this reaction, rather than water which is present in much greater amounts, is attributed to a hypothetical ring-complex intermediate between $HO_2$ and $H_2O_2$ for which it would seem there is some indirect supporting evidence.[429] Propagation and termination rate constants have been measured in intermittent radiation experiments. Dainton and Rowbottom[411, 430] point out that a rate proportional to $[H_2O_2]^{\frac{1}{2}}$ is contrary to their own findings and to the results of

[419] H. A. Dewhurst, *Trans. Faraday Soc.*, 1952, 48, 905.
[420] E. J. Hart, *J. Amer. Chem. Soc.*, 1952, 74, 4174.
[421] M. Cottin, M. Haissinsky, and C. Vermeil, *Compt. rend.*, 1952, 235, 542.
[422] C. Vermeil, M. Cottin, and M. Haissinsky, *J. Chim. phys.*, 1952, 49, 437.
[423] W. M. Garrison and G. K. Rollefson, *Discuss. Faraday Soc.*, 1952, 12, 155.
[424] E. J. Hart and M. S. Matheson, *ibid.*, p. 169.
[425] M. Ebert and J. W. Boag, *ibid.*, p. 189.
[426] M. Haissinsky and J. Pucheault, *J. Chim. phys.*, 1952, 49, 294.
[427] J. Pucheault, M. Lefort, and M. Haissinsky, *ibid.*, p. 286.
[428] M. Carmo Anta and M. Haissinsky, *Compt. rend.*, 1952, 235, 170.
[429] N. M. Luft, *Discuss. Faraday Soc.*, 1952, 12, 266.
[430] F. S. Dainton and J. Rowbottom, *ibid.*, p. 264.

most of the work which has been done on the photolysis of hydrogen peroxide. They find that the rate of decomposition is proportional to $[H_2O_2]^{1\cdot0}$ × (dose rate)$^{0\cdot5}$ for 1—22M-solutions. This is a major discrepancy only to be resolved by further experimentation. Ebert and Boag [425] have investigated the formation and decomposition of hydrogen peroxide in aqueous solutions by the action of 1 Mev electrons, and 1·2 Mev and 200 kv *X*-radiation. In aerated solutions a higher initial yield of hydrogen peroxide was found with electrons than had previously been found by Lefort [431] with 30 kv *X*-irradiation. Experiments with 200 kv and 1·2 Mev *X*-radiation confirmed that a difference existed between the effect of *X*-rays and of 1 Mev electrons. A subsequent investigation by a group of workers [432] confirmed these findings and showed that for 1 Mev electrons the initial yield of hydrogen peroxide was $G_0 = 1\cdot10$, whilst for 30 kv and 220 kv *X*-radiation $G_0 = 2\cdot28$. Moreover a limiting value was attained for the hydrogen peroxide concentration produced by 1 Mev electrons whereas no limit to the yield was reached for the *X*-irradiations. The results meet with an explanation on the difference of ion density arising from the two types of radiation and it seems possible that the different effects found may arise from a difference in decomposition rate. The effect of pH on the formation and decomposition of hydrogen peroxide in aerated solutions indicates that the effective back-reaction is:

$$O_2^- + H_2O_2 \longrightarrow OH + OH^- + O_2 \quad . \quad . \quad . \quad . \quad . \quad (17)$$

The yields of hydrogen peroxide produced in boric acid solutions by pile irradiation are lower than those produced by α-particle irradiation with radon.[426] The effects of adding various electrolytes in these experiments have also been studied.[427] An investigation of the formation and decomposition of hydrogen peroxide in water by irradiation with α-rays of polonium showed that the results varied according to the acid used.[428] In the presence of 0·8N-sulphuric or -perchloric acid a limiting concentration of hydrogen peroxide, which depends on the polonium concentration, is reached. In 0·8N-nitric acid, no hydrogen peroxide is formed. The effect of polonium and radon in similar experiments is very different, but it is not clear whether this is due to a difference in the radiation emitted or to some effect of the polonium, which was dissolved in the solutions in these experiments. In an interesting extension of earlier work [433] it has been shown that the yield of hydrogen peroxide produced by the α-radiation from radon is the same from both water and a 0·1% solution of carboxypeptidase.[434] This confirms the view previously suggested that hydrogen peroxide production occurs in the core of an α-track and that the small inactivation of carboxypeptidase by α-irradiation is entirely due to δ-rays arising from the main α-track. Weiss has discussed possible results which may arise from the photolysis and radiolysis of hydrogen peroxide with particular reference to reaction in and between tracks.[435]

The exchange reaction between oxygen and water initiated by γ-radiation has been studied by using oxygen enriched in the isotope $^{18}O$.[436] The rate

---

[431] M. Lefort, *J. Chim. phys.*, 1950, 47, 624.

[432] T. Alper, M. Ebert, L. H. Gray, M. Lefort, H. C. Sutton, and F. S. Dainton, *Discuss. Faraday Soc.*, 1952, 12, 266.

[433] W. M. Dale, L. H. Gray, and W. J. Meredith, *Phil. Trans.* 1949, *A*, 242, 33.

[434] W. M. Dale, J. V. Davies, C. W. Gilbert, J. P. Keene, and L. H. Gray, *Biochem. J.*, 1952, 51, 268.

[435] J. Weiss, *Discuss. Faraday Soc.*, 1952, 12, 161.

[436] E. J. Hart, S. Gordon, and D. A. Hutchison, *J. Amer. Chem. Soc.*, 1952, 74, 5548.

of exchange was found to increase with pH and concentration of $^{16,\,18}O_2$ and was inhibited by hydrogen peroxide. The exchange proceeds by a chain mechanism, as many as 40 oxygen molecules being exchanged per free radical pair formed at pH $>9$. The chain is terminated by hydrogen peroxide. An equilibrium is proposed: $HO \rightleftharpoons O^- + H^+$, exchange being then effected by reaction of $O^-$ ions with oxygen molecules and $OH^-$ ions. $HO_2^-$ and $O_2^-$ ions act as chain terminators.

Hardwick[437] has studied the reduction of ceric sulphate in varying concentrations of sulphuric acid, using $\gamma$-rays from $^{60}Co$ and radium, and 2000 kv $X$-rays. The yield of cerous ion ($G = 3{\cdot}2$) remained constant over a wide range of dose rates, ceric ion concentration, and pH, and was independent of the presence or absence of oxygen. The addition of hydrogen gas to air-free solutions increased the yield of cerous ion to $G = 6{\cdot}2$. These results, which can be explained on the basis of reduction by H atoms only or by H atoms and hydrogen peroxide, differ markedly from the results of other workers.[438] However the radiation used by Haissinsky *et al.*[438] was 14 kv $X$-radiation and an attempt has been made to account for these apparent anomalies, and to correlate other results obtained for this system and the ferrous–ferric system, on the basis of the difference in energy of the ionising electrons arising from the different radiations employed.[334] Such an explanation necessitates the assumption that a greater proportion of the reduction of ceric ions proceeds by hydrogen peroxide in the case of the low-energy $X$-rays than in the case of $\gamma$-radiation. It has been pointed out, however, that no such corresponding effects arise in the irradiation of pure water.[439] The effect of radiations ranging from $\gamma$-rays to infra-red rays on methylene-blue in water or glycerol is claimed to be different in the two solvents.[446] Spectrophotometric evidence is given to show that bleaching of the dye takes place *via* the leuco-dye in glycerol; in aqueous solution no leuco-dye is formed, bleaching is much slower and is never complete. In view of other work which has recently been done on this system[397, 440, 441] it seems certain that the effects in aqueous solution were in fact due to incomplete deaeration.

A study has been made of the exchange between deuterium gas and liquid water under the action of $^{60}Co$ $\gamma$-rays,[442] but the full results are not yet available. Experiments have also been started[442] on the mode of formation of hydrogen peroxide in the $\gamma$-ray-induced water–oxygen reaction, with the isotope $^{18}O$ as a tracer. The $X$-irradiation of linoleic acid in aqueous solution leads to a chain reaction.[443] Decrease of dose rate or increase of concentration of the substrate both tend to increase the ionic yield. This is a further demonstration that radiation chemical chain reactions show greater sensitivity to changing conditions than do single molecular changes.* It is suggested that similar reactions may account for the large effects produced by small doses of irradiation in animals. Experiments on the

---

[437] T. J. Hardwick, *Canad. J. Chem.*, 1952, 30, 23.

[438] M. Haissinsky, M. Lefort, and M. Le Bail, *J. Chim. phys.*, 1951, **48**, 209.

[439] M. Lefort, *Discuss. Faraday Soc.*, 1952, **12**, 273.

[440] M. J. Day and G. Stein, *Nature*, 1950, **166**, 146.

[441] E. Collinson, *Discuss. Faraday Soc.*, 1952, **12**, 285.

[442] S. Gordon, E. J. Hart, and P. D. Walsh, U.S. Atomic En. Commiss. Report, 1951, AECU-1742.

[443] J. F. Mead, *Science*, 1952, **115**, 470.

* Cf. ref. 395.

change in viscosity produced in solutions of polymethacrylic acid under the action of $X$-radiation and "nitrogen mustard" indicate that the mechanism is different in the two cases.[444] The change is brought about by coiling of the chains in the case of "nitrogen mustard" and by degradation of the chains with $X$-rays in aerated solution. The fact that there is no appreciable chain breakdown during $X$-irradiation of deaerated solutions seems to indicate that the effective chain-breaking radical may be the $HO_2$ radical. It is suggested that effective biological protective agents function by abstracting an oxygen atom from $HO_2$ since the same agents protect the polymethacrylic acid degradation.[445]

The $X$-irradiation of potassium iodate showed an interesting variation in the ratio of the products formed (iodine and hydrogen peroxide) and in the after-effect observed according to whether the solutions were aerated or deaerated.[446]

Other aqueous systems which have been studied are the decolorisation of chlorophenol-red by $X$-radiation,[447] the $X$-irradiation of ammonia solutions,[448] perchloric acid,[449] mercuric chloride,[450] and indole,[451] the $\gamma$-irradiation of cysteine [452] and benzene,[453] the electron-irradiation of tryptophan, tyrosine, phenylalanine, and cystine,[454] and of fats,[455, 456] the pile-irradiation of cystine,[457] and the $\alpha$-irradiation of formic acid.[458] Other reviews of various aspects of the radiation chemistry of aqueous solutions have appeared during the past year.[459–462]

Alder and Eyring [463] have presented a kinetic analysis of irradiations in solution. Their treatment is not essentially different from that given earlier by Dainton [464] but they have been able to use the resulting expression for ionic yield in terms of solute concentration to fit the curves of experimental results. This means that certain parameters in the expression can be evaluated and the yield of water molecules decomposed per 100 ev of energy absorbed can be estimated for each set of experiments. The highest value of $G(H_2O)$ so obtained is 5·9. This is derived from results on the $X$-irradiation of carboxypeptidase.[433] Formation of hydrogen and hydrogen peroxide is neglected in the treatment. A treatment which is claimed to

---

[444] P. Alexander and M. Fox, *Nature*, 1952, **164**, 572.

[445] *Idem*, *ibid.*, 1952, **170**, 1022.

[446] N. Todd and S. L. Whitcher, *J. Chem. Phys.*, 1952, **20**, 1172.

[447] E. N. Weber and R. H. Schuler, *J. Amer. Chem. Soc.*, 1952, **74**, 4415.

[448] T. Rigg, G. Scholes, and J. Weiss, *J.*, 1952, 3034.

[449] B. Milling, G. Stein, and J. Weiss, *Nature*, 1952, **170**, 710.

[450] G. Stein, R. Watt, and J. Weiss, *Trans. Faraday Soc.*, 1952, **48**, 1030.

[451] C. B. Allsopp and J. Wilson, *Discuss. Faraday Soc.*, 1952, **12**, 299.

[452] A. J. Swallow, *J.*, 1952, 1334.

[453] T. J. Sworski, *J. Chem. Phys.*, 1952, **20**, 1817.

[454] B. E. Proctor and D. S. Bhatia, *Biochem. J.*, 1952, **51**, 535.

[455] R. S. Hannan and J. W. Boag, *Nature*, 1952, **169**, 152.

[456] R. S. Hannan and H. J. Shepherd, *ibid.*, 1952, **170**, 1021.

[457] M. Lipp and H. Weigel, *Naturwiss.*, 1952, **39**, 189.

[458] W. M. Garrison, D. C. Morrison, H. R. Haymond, and J. G. Hamilton, *J. Amer. Chem. Soc.*, 1952, **74**, 4216.

[459] G. Stein, *Discuss. Faraday Soc.*, 1952, **12**, 227.

[460] L. H. Gray, *J. Cellular Comp. Physiol.*, 1952, **39**, Suppl. 1., 57.

[461] W. M. Dale, *ibid.*, p. 39.

[462] A. O. Allen, *Ann. Reviews Phys. Chem.*, 1952, **3**, 57.

[463] M. G. Alder and H. Eyring, *Nucleonics*, 1952, **10**, No. 4, p. 54.

[464] F. S. Dainton, *Ann. Reports*, 1948, **45**, 5.

be simpler[465] and is based on Dee and Richards's theory[318] yields the same expression for the ionic yield as does that of Alder and Eyring. The much lower radical yields deduced for α-irradiations by this method are explained as being due to local quenching of primary photons by molecules directly damaged by the radiation.

R. H. B.
E. C.
F. S. D.
K. J. I.

R. H. BETTS.
E. COLLINSON.
F. S. DAINTON.
C. W. DAVIES.
D. D. ELEY.
K. J. IVIN.
J. W. LINNETT.
C. B. MONK.

---

[465] J. B. Binks, *J. Chem. Phys.*, 1952, 20, 1655.

# INORGANIC CHEMISTRY.

Considerable interest has been sustained in the study of chelate and other complex compounds formed between metal cations and a variety of ligands. The growing interest in this branch of the subject has in part no doubt been stimulated by the increasing importance of these complex compounds in several industrial processes, and great advances have been made in their study in recent years. Although a complete specificity, such that a given chelating agent would form a compound with only one type of ion, may yet be out of reach, the different stabilities of many of these chelates provide a valuable tool for the separation and purification of elements by solvent-extraction, ion-exchange, and other fractional techniques. For example, the use of ion-exchange techniques for the separation and purification of the lanthanons is now well established, several different eluants having been used by individual groups of workers. A quantitative comparison has now been made of the relative value as eluants in this connection, of seven carboxylic acids, *viz.*, acetic, malic, tartaric, citric, aminoacetic, nitrilotriacetic, and ethylenediamine-*NN'N'N'*-tetra-acetic,[1] and the stability constants have been determined for the last-named with several lanthanons.[2]

The effects of the nature of the chelating agent and of the electronic structure of the metal ion on the stability of the complex have been the subjects of numerous investigations. Thus, the effect of a relatively minor change in the structure of the chelating agent is shown by a comparison of the stabilities of the chelates of the anions of iminodiacetic acid and iminodipropionic acid with copper(II), nickel(II), cobalt(II), zinc, and cadmium ions: replacement of the acetate groups by β-propionate groups in the ligand results in a considerable decrease in the stability of the chelate.[3]

A study of the chelates of 2-hydroxyethylaminoacetic acid with a number of bivalent cations [4] has shown, on the other hand, that the stabilities of the chelates of iminodiacetic acid are greatly increased when an amino-hydrogen atom is replaced by the hydroxyl group, though the stability constants are still about 100-fold smaller than those of the corresponding nitrilotriacetic acid.[5]

The effect on chelate stability, of the structure of the chelating agent has also been investigated with the use of 8-hydroxyquinoline and analogous reagents.[6] The steric effect of 8-hydroxyquinaldine, believed to be responsible for the non-reaction of this reagent with aluminium(III), has also been encountered in the case of nickel(II). In the course of this work it was shown that there is an increase of chelate stability in a series of 8-hydroxyquinoline chelates with bivalent ions of transition elements, as the transition electron shell becomes more completely filled.

Evidence of the effect of steric considerations in a chelate compound on

---

[1] R. C. Vickery, *J.*, 1952, 4357. [2] *Idem, J.*, 1952, 1895.

[3] S. Chaberek, Jr., and A. E. Martell, *J. Amer. Chem. Soc.*, 1952, 74, 5052.

[4] S. Chaberek, Jr., R. C. Courtney, and A. E. Martell, *ibid.*, p. 5057.

[5] G. Schwarzenbach, H. Ackermann, and P. Ruckstuhl, *Helv. Chim. Acta*, 1949, 32, 1175; G. Schwarzenbach and E. Freitag, *ibid.*, 1951, 34, 1492.

[6] W. D. Johnston and H. Freiser, *J. Amer. Chem. Soc.*, 1952, 74, 5239.

the reactivity of the central metal atom is also given by the radio-isotopic exchange of zinc between zinc acetate and a number of zinc chelate compounds.[7] There is little or no exchange of the zinc in zinc phthalocyanine—a " fused-ring " type of chelate compound—whereas with others of the " non-fused-ring " type, exchange is rapid.

A further study of the effect of steric hindrance has been made with the chelates of copper(II) and nickel(II) with a series of *N*-alkyldiamines, $R\cdot NH\cdot CH_2\cdot CH_2\cdot NH_2$ (R = H, Me, Et, $Pr^n$, $Bu^n$, and $Pr^i$).[8] Except for the *n*-butyl derivative, there is a general decrease in stability of the straight-chain alkyl complexes as the length of the chain increases, and the complexes with the *iso*propyl derivative are less stable than those containing the straight-chain alkyl groups.

A rather different steric effect of the organic groupings attached to a central metal atom is shown by the physicochemical properties of the alkyloxides of titanium and zirconium. It was established in the first place [9] that the volatility of the amyloxides of these elements depended on the structure of the particular amyl group in question, the branched-chain compounds being in general much more volatile than the straight-chain amyloxides. This effect, it is believed, may be due to the screening by the branched groups inhibiting intermolecular bonding between the central metal atom and oxygen. A number of new tetra-*tert.*-alkoxides of these elements have been prepared.[10] Ebullioscopic measurements show that they all monomeric.

Differences in the stabilities of complex compounds formed by optically active organic stereoisomers with some complex inorganic compounds offer a method of resolution of the racemates. For example, when a racemic mixture of an organic acid reacts with an equimolecular amount of a complex such as *lævo*-carbonatobispropylenediaminecobalt(III) two isomers are formed, one containing the *dextro*- and the other the *lævo*-form of the acid. As these prove to have different stabilities, a partial resolution of the acid becomes possible, and experimental results have been presented for the partial resolution in this way of tartaric, chloropropionic and lactic acid.[11]

A considerable interest has been shown recently in directive influences in the reactions of inorganic co-ordination complexes. In this connection, mention may be made of a review of the extensive experimental work and theoretical considerations relating to the so-called *trans*-effect, especially in relation to the platinum complexes.[12] The *trans*-effect stipulates that the bond holding a group *trans* to an electronegative or other labilising group is weakened thereby, so that the *trans*-group is the first to be removed in a substitution reaction.

A recent example of this effect is seen in the behaviour of dichlorodiethyleneplatinum(II), $(C_2H_4)_2PtCl_2$. In all except the olefin series of platinum(II) complexes, at least one geometric isomer of the simple *non-ionic* compound $L_2PtCl_2$ (L = ligand) is known, and is usually more stable than the corresponding ionic complexes $(LPtCl_3)^-$ and $(L_4Pt)^{+2}$. The olefin

---

[7] D. C. Atkins, Jr., and C. S. Garner, *J. Amer. Chem. Soc.*, 1952, 74, 3527.
[8] F. Basolo and R. K. Murmann, *ibid.*, p. 5243.
[9] D. C. Bradley, R. C. Mehrotra, and W. Wardlaw, *J.*, 1952, 2027.
[10] *Idem, J.*, 1952, 4204.
[11] A. D. Gott and J. C. Bailar, Jr., *J. Amer. Chem. Soc.*, 1952, 74, 4820.
[12] J. V. Quagliano and L. Schubert, *Chem. Reviews*, 1952, 50, 201.

complexes, however, were found to be an exception, and until recently[13] all attempts to prepare $(C_2H_4)_2PtCl_2$ had failed, although $K(C_2H_4PtCl_3)$ has been recognised since 1830.[14] $(C_2H_4)_2PtCl_2$, which may be obtained as a precipitate by passing ethylene into dichlorodiethylene-μμ′-dichlorodiplatinum(II) in acetone at −70°, dissociates at room temperature with the reversal of the reaction and evolution of ethylene. The instability of this new diethylene compound is explained by supposing it to have a *trans*-configuration, the instability being due to the combined effects of the rather weak co-ordinating affinity of ethylene and the strong *trans*-influence, or labilising effect, of an ethylene molecule on the group in the *trans*-position to itself.[15]

Further study has been made of the nature of the co-ordinate link in complex platinum compounds by an examination of the equilibrium between *cis*- and *trans*-bis(triethylphosphine)dichloroplatinum(II) through the measurement of the dielectric polarisation of their solutions as a function of temperature.[16] The highly polar *cis*-isomer is more stable than the *trans*- by about 10 kcal./mol., as are also the *cis*-$(AsEt_3)_2PtCl_2$ and *cis*-$(SbEt_3)_2PtCl_2$ than their corresponding *trans*-isomers.[17]

The influence of the configuration of an ion on its retention by an exchange resin has been made use of for the separation of the *cis*- and *trans*-isomeric dinitrotetramminocobalt(III) ions.[18]

An ion-exchange technique has also been used to demonstrate the formation of some anionic complexes of cadmium and copper.[19] For example, if an anion-exchange resin is pretreated with sodium perchlorate, then cadmium perchlorate is not retained by it and can easily be washed out by water; on the other hand, if the resin is treated with sodium iodide then cadmium iodide is very strongly held, as would be expected from the well-known stability of the cadmium iodide complexes.

In many metal-anion complex ion systems in aqueous solution a number of different complexes exist simultaneously, the separation or identification of which is often very difficult, especially if the equilibria are established rapidly. On the other hand, if the equilibria are established sufficiently slowly and the different species have different ionic charges, then ion-exchange methods offer a convenient method of separation. This has now been carried out in the chromic thiocyanate system from which the species $Cr(H_2O)_6^{+++}$, $Cr(H_2O)_5(SCN)^{++}$, and $Cr(H_2O)_4(SCN)_2^{+}$ have been separated.[20]

The prosthetic groups in cation-exchange resins have usually been sulphonic, carboxylic, or phenolic groups or a combination of these. Resins have now been developed in which the exchange groups are phosphonous and phosphonic. One interesting feature of these new resins is that they appear to show a selectivity for sodium over potassium.[21]

Clathrate compounds of oxygen and of nitric oxide in quinol have been prepared in which some 40—50% of the available spaces are filled.[22] Meas-

---

[13] J. Chatt and R. G. Wilkins, *Nature*, 1950, 165, 859.

[14] Zeise, *Mag. Pharm.*, 1830, 35, 105.

[15] J. Chatt and R. G. Wilkins, *J.*, 1952, 2622.

[16] *Idem*, *J.*, 1952, 273.

[17] *Idem*, *J.*, 1952, 4300.

[18] E. L. King and R. R. Walters, *J. Amer. Chem. Soc.*, 1952, 74, 4471.

[19] I. Lenden, *Svensk Kem. Tidskr.*, 1952, 64, 145; *Chem. Abs.*, 1952, 46, 8563.

[20] E. L. King and E. B. Dismukes, *J. Amer. Chem. Soc.*, 1952, 74, 1674.

[21] J. I. Bregman and Y. Murata, *ibid.*, p. 1868.

[22] D. F. Evans and R. E. Richards, *J.*, 1952, 3295.

urement of the magnetic susceptibility suggests that the paramagnetism of a gas is but little affected by its inclusion in the cage-like structure. It has been pointed out that, in the case of nitric oxide, the clathrate compound offers a method of studying its properties at low temperatures without the complications either of change of state or of dimerisation into diamagnetic dinitrogen dioxide which occurs on liquefaction at 121° K.

A remarkable and unique new iron compound, *di*cyclo*pentadienyliron*, the first compound to be prepared which contains only carbon, hydrogen, and iron, has been described almost simultaneously by two groups of workers.[23] It is a stable orange diamagnetic compound, m. p. 172·5—173°, which vapourises above 100° without decomposition into a monomeric, undissociated vapour which obeys the perfect-gas laws even at 400°.[24] A number of its chemical and physicochemical properties have been studied. On the one hand, it is readily oxidised to a blue cation $Fe(C_5H_5)_2^+$ [25] and, on the other, it undergoes reactions like those of aromatic hydrocarbons.[26] Both chemical evidence [25] and direct $X$-ray examination [27] of single crystals indicate that it possesses a pentagonal antiprismatic structure (Fig. 1), there being no evidence of rotation of the *cyclo*pentadienyl groups.

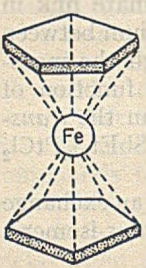


FIG. 1.

The corresponding ruthenium compound, $(C_5H_5)_2Ru$, has also been prepared.[27a] The names ferrocene and ruthenocene have been suggested for these compounds in view of their behaviour as aromatic systems and "ferricinium" and "ruthenicinium" for their unipositive ions, the methods of preparation and properties of these compounds and their salts suggesting that in the neutral compound the metal is in the +2 oxidation state, and in the unipositive ion in the +3 state.

In a similar manner, the reaction of cobaltic acetylacetonate with *cyclo*pentadienylmagnesium bromide gives the unipositive ion $[(C_5H_5)_2Co]^+$ of which several salts have been prepared. This ion, however, cannot be reduced to a neutral cobaltocene.[27b]

The discovery of these compounds opens up a new field in the borderland between inorganic and organic chemistry.

**Group I.**—One of the major difficulties encountered in the laboratory preparation of lithium aluminium hydride by the usual method has been the necessity for the troublesome pulverisation of the lithium hydride. It is reported, however, that by using aluminium bromide instead of the chloride, coarsely powdered lithium hydride can be used.[28]

What is stated to be the first example of a coloured double hydride, namely, $AgAlH_4$, is obtained as a yellow-gold precipitate when ethereal solutions of lithium aluminium hydride and silver perchlorate are shaken together at −80° : the compound decomposes at −50°.[29]

---

[23] T. J. Kealy and P. L. Pauson, *Nature*, 1951, **168**, 1039; S. A. Miller, J. A. Tebboth, and J. F. Tremaine, *J.*, 1952, 632.

[24] L. Kaplan, W. L. Kester, and J. J. Katz, *J. Amer. Chem. Soc.*, 1952, **74**, 5531.

[25] G. Wilkinson, M. Rosenblum, M. C. Whiting, and R. B. Woodward, *ibid.*, p. 2125.

[26] R. B. Woodward, M. Rosenblum, and M. C. Whiting, *ibid.*, p. 3459.

[27] P. F. Eiland and R. Pepinsky, *ibid.*, p. 4971.

[27a] G. Wilkinson, *ibid.*, p. 6146. [27b] *Idem, ibid.*, p. 6148.

[28] E. Wiberg and M. Schmidt, *Z. Naturforsch.*, 1952, **7**, *b*, 59.

[29] E. Wiberg and W. Henle, *ibid.*, p. 250.

A new method of preparation of lithium hydroperoxide monohydrate has been described: dehydration of this compound over phosphoric oxide in a desiccator at 20 mm. gives almost pure lithium peroxide. *X*-Ray diffraction studies indicate that neither the anhydrous hydroperoxide $LiO_2H$ nor the peroxycarbonate $Li_2CO_4$ exists at room temperatures.[30]

An experimental study of the ternary system NaBr–NaCl–6·6M-NaOH has shown that, contrary to some theoretical predictions, these two halides do in fact form a continuous series of solid solutions.[31] It has also been shown, by *X*-ray examination, that when RbCl and KBr, or RbBr and KCl, are melted together in any proportion, a single solid solution is obtained which contains all the ions in the original mixture.[32] Continuous series of solid solutions have also been shown to be formed in the systems $(NH_4)_2SO_4$–$Cs_2SO_4$–$H_2O$, $(NH_4)_2SO_4$–$K_2SO_4$–$H_2O$, and $(NH_4)_2SO_4$–$Rb_2SO_4$.[33] On the other hand, an examination of the system $NH_4F$–NaF–$H_2O$ at 25° has shown that the system is a simple one, with ammonium fluoride and sodium fluoride as solid phases.[34]

The various and widely used sodium metaphosphate polymers have commonly been prepared by thermal dehydration of sodium dihydrogen orthophosphate. It has now been found that the hydration of α-phosphorus(V) oxide at a temperature of 15° or below produces chiefly tetrametaphosphoric acid ($H_4P_4O_{12}$), which offers an alternative method of preparation of the sodium salt of this acid.[35]

Cæsium hexasulphide has been prepared by disproportionation of $Cs_2S_5,H_2O$ in aqueous ethyl alcohol into this and one or more lower polysulphide ions. The crystal structures of $Cs_2S_6$ and of the dehydrated $Cs_2S_5$ prove to be very similar, the polysulphide ions being in the form of non-branched, non-planar, sulphur chains.[36]

A new method of preparation of copper hydride, CuH, has been described.[37] When lithium aluminium hydride in pyridine–ether solution is added to a solution of copper(I) iodide in pyridine, the following reaction takes place: $4CuI + LiAlH_4 = LiI + AlH_3 + 4CuH$, and a blood-red solution is obtained from which the solid may be precipitated as bright red-brown needles on addition of more ether. The dry hydride is stable up to about 60°, above which it decomposes (rapidly at 100°); in water it gives CuOH and hydrogen at a somewhat lower temperature.

The existence of the chlorocuprate ion $CuCl_4^{=}$ in aqueous solution is well known, but until recently evidence of its existence in the solid state has been lacking. *X*-Ray examination of the yellowish-orange $Cs_2CuCl_4$ has now demonstrated the presence of this ion in the solid.[38] In contrast, however, to the more usual planar configuration of quadricovalent copper(II) ions, the chlorine atoms appear to be arranged about the copper in the form of a flattened tetrahedron: the absorption spectrum of the solid is also markedly

---

[30] A. J. Cohen, *J. Amer. Chem. Soc.*, 1952, **74**, 3762.
[31] E. L. Simons, C. A. Orlick, and P. A. Vaughan, *ibid.*, p. 5264.
[32] L. J. Wood and L. J. Breithaupt, Jr., *ibid.*, p. 727.
[33] C. Calvo and E. L. Simons, *ibid.*, p. 1202.
[34] H. M. Haendler and A. Clow, *ibid.*, p. 1843.
[35] R. N. Bell, L. F. Audrieth, and O. F. Hill, *Ind. Eng. Chem.*, 1952, **44**, 568.
[36] S. C. Abrahams, E. Grison, and J. Kalnajs, *J. Amer. Chem. Soc.*, 1952, **74**, 3761.
[37] E. Wiberg and W. Henle, *Z. Naturforsch.*, 1952, **7**, *b*, 250.
[38] L. Helmholz and R. F. Kruh, *J. Amer. Chem. Soc.*, 1952, **74**, 1176.

different from that of the aqueous solution. It would appear therefore that the structure of the aqueous chlorocuprate ion is different from that of the ion in the crystalline state.

Some new copper(I) complexes of methyldiphenylarsine have been prepared. Four types, containing respectively 1, 2, 3, and 4 molecules of the tertiary arsine to each molecule of the copper(I) halide, have been isolated: example of the last two have not been reported previously. Those complexes with an empirical formula $CuX,3AsMePh_2$ are non-electrolytes and contain quadricovalent copper. Those with an empirical formula $CuX,4AsMePh_2$ ($X = I, ClO_4$, or $NO_3$) are salts of the univalent anion X.[39]

A number of complex compounds of silver(I) with polydentate chelating agents have been studied which indicate that the co-ordination number of silver is four in these complexes. When aqueous or alcoholic solutions of silver nitrate are allowed to react with triethylenetetramine (trien), several complexes are formed: $[Ag\ trien]^+$ and $[Ag_2\ trien]^{++}$ are present in both aqueous and alcoholic solutions, and $[Ag\ trien]NO_3$ has been isolated from the latter.[40]

It has been shown that the compound of empirical formula $(C_7H_7)_2SAuBr_2$ probably contains the gold in both univalent and tervalent states: it cannot be formulated as a dimer, as a salt, or as a compound of bivalent gold.[41] An *X*-ray investigation of the corresponding chloride, obtained by the interaction of solutions of " auric chloride " and benzyl sulphide, has shown that the crystal consists of separate molecules of benzyl sulphide–monochlorogold(I), $(C_7H_7)_2S \rightarrow AuCl$, and benzyl sulphide–trichlorogold(III), $(C_7H_7)_2S \rightarrow AuCl_3$, so arranged that a highly disordered structure results.

A study has been made of the preparation and properties of a number of gold imides, of the type $M^I[AuX(imido)_3]$ (X = halogen) from succinimide and of the type $M^I[AuX_2(imido)_2]$ from *o*-benzoicsulphonimide (saccharin) and phthalimide.[42]

**Group II.**—It has been known for some time that the volatility of a number of oxides at high temperatures is greatly increased by the presence of water vapour, a result believed to be due to some reaction between the oxide and water or between the oxide and a decomposition product of water. A study of this increase in the case of beryllium oxide at 1200—1600° has shown that it is due to the reaction $BeO_{(s)} + H_2O_{(g)} \longrightarrow Be(OH)_{2(g)}$.[43]

The dialkyl derivatives of beryllium present some interesting structural and valency problems arising from the fact that they are strongly electron-deficient compounds. A detailed study in this connection has been made of dimethylberyllium and a number of its co-ordination compounds. In the vapour state it appears to polymerise to some extent to the dimer and trimer,[44] and it forms co-ordination compounds with trimethylamine, trimethylphosphine, and dimethyl and diethyl ether, but not with trimethylarsine or dimethyl sulphide.[45] The properties of these compounds indicate that the

---

[39] R. S. Nyholm, *J.*, 1952, 1257.

[40] H. B. Jonassen and P. C. Yates, *J. Amer. Chem. Soc.*, 1952, **74**, 3388.

[41] F. H. Brain, (the late) C. S. Gibson, J. A. J. Jarvis, R. F. Phillips, H. M. Powell, and A. Tyabji, *J.*, 1952, 3686.

[42] A. M. Tyabji and (the late) C. S. Gibson, *J.*, 1952, 450.

[43] L. Grossweiner and R. L. Seifert, *J. Amer. Chem. Soc.*, 1952, **74**, 2701.

[44] G. E. Coates and N. D. Huck, *J.*, 1952, 4496.

[45] *Idem*, *J.*, 1952, 4501.

order of stability is N > P > O. It also reacts with methylamine, dimethylamine, dimethylphosphine, methanol, methanethiol, or hydrogen chloride, but in these cases the products are methane and di-, tri-, or polymeric products. Dimethylamine gives a trimeric compound $(MeBe,NMe_2)_3$ to which a cyclic structure has been assigned.[46]

It is reported that pure magnesium cyanide can be prepared by the passage of hydrogen cyanide over a specially prepared magnesium oxide at 730° : the latter is obtained by ignition of magnesium oxalate at 600°, samples of magnesium oxide prepared by other reactions giving only impure products.[47]

As part of a systematic investigation of isomorphous replacement in hydrated salts, the systems $CdCl_2$–$MCl_2$–$H_2O$ (M = Mg, Mn, $Fe^{II}$, $Cu^{II}$. and Ca) have now been examined. The existence has been established of the double salts $2CdCl_2,MgCl_2,12H_2O$; $CdCl_2,2MgCl_2,12H_2O$; $4CdCl_2,MnCl_2,10H_2O$; $CdCl_2,CuCl_2,4H_2O$ ; and of a number of solid solutions.[48]

Solubility isotherms are reported for the quaternary system $Ba(ClO_3)_2$–$BaBr_2$–$Ba(NO_3)_2$–$H_2O$ at 10° and for the ternary systems $Ba(ClO_3)_2$–$BaBr_2$–$H_2O$ at 10° and 25°, $Ba(ClO_3)_2$–$Ba(NO_3)_2$–$H_2O$ at 10°, 25°, and 45°, and $BaBr_2$–$Ba(NO_3)_2$–$H_2O$ at 10° and 25° : also for a number of other aqueous ternary systems involving barium chlorate, bromate, and iodate.[49]

The solubility of metallic cadmium in fused mixtures of cadmium chloride with some other chlorides has been studied.[50] As a result of this and previous work it emerges that : (1) the solubility of Group II metals in their fused chlorides increases as the cation radius increases, (2) the solubility (for Cd in $CdCl_2$) is decreased by the addition of the chloride of an electropositive element, and (3) the solubility increases as the ratio of the number of anions to cations increases. The last result, *e.g.*, the effect of $CeCl_3$ as compared with KCl, has been interpreted as due to the process of dissolution consisting in the entry of the metal atoms into the octahedral holes of an almost close-packed fused chloride structure, these holes being clearly relatively more abundant when less of them are already occupied by the metal cations.

A re-investigation of the *X*-ray diffraction patterns of the compounds formed in the reactions between mercurous chloride and ammonia has disproved the formation of several mercury(I) compounds which have been suggested by previous workers and has shown that only the well-known mercury(II) compounds $Hg(NH_3)_2Cl_2$, $HgNH_2Cl$, and $Hg_2NCl,H_2O$ are formed in addition to mercury.[51]

**Group III.**—A study of the method of preparation of diborane by the reaction of lithium aluminium hydride with boron trifluoride in ethereal solution has shown that the reaction takes place by at least two successive stages, involving the intermediate formation of lithium borohydride : (*a*) $LiAlH_4 + BF_3 = LiBH_4 + AlF_3$; (*b*) $3LiBH_4 + BF_3 = 2B_2H_6 + 3LiF$.[52]

Diborane can also be prepared by reaction of lithium hydride with the boron trifluoride–ethyl ether complex. An investigation of this reaction

---

[46] G. E. Coates, F. Glockling, and N. D. Huck, *J.*, 1952, 4512.
[47] H. Hartmann and H. Narten, *Z. anorg. Chem.*, 1952, **267**, 37.
[48] H. Bassett and R. N. C. Strain, *J.*, 1952, 1795.
[49] J. E. Ricci and A. J. Freedman, *J. Amer. Chem. Soc.*, 1952, **74**, 1765, 1769.
[50] D. Cubicciotti, *ibid.*, p. 1198.
[51] L. Nijssen and W. N. Lipscomb, *ibid.*, p. 2113.
[52] I. Shapiro, H. G. Weiss, M. Schmich, S. Skolnik, and G. B. L. Smith, *ibid.*, p. 901.

under various conditions has shown that it can proceed by two different courses: (*a*) $6LiH + 8BF_3 = B_2H_6 + 6LiBF_4$ in the absence of promoters, and (*b*) $6LiH + 2BF_3 = B_2H_6 + 6LiF$ if small amounts of the ether-soluble active-hydrogen-containing promoters lithium borohydride and lithium trimethoxyborohydride are present. This offers an explanation of the experimental observation that higher yields of diborane by this reaction are obtained in the presence of methyl ortho-borate.[53]

The preparation of a new type of substituted borohydride containing a quaternary ammonium cation has been described.[54] Tetramethyl-, tetraethyl-, and benzyltrimethyl-ammonium borohydrides have been prepared by metathetical reactions in aqueous solution between sodium or lithium borohydride and the respective quaternary salts or hydroxides.

A number of deuterated boron compounds have been prepared and characterised, including deuterated diborane, borine carbonyl, and dimethylaminodiborane.[55]

A cryoscopic study of mixtures of boron trifluoride and 100% nitric acid has revealed the existence of the solid compound $HNO_3,2BF_3$, m. p. 53°. If boron trifluoride is passed into 100% nitric acid considerable heat is evolved and a water-clear viscous liquid is formed from which large prismatic crystals separate if the boron trifluoride content is sufficiently high: if the composition of the mixture approaches that of the double compound, the whole mass eventually solidifies.[56]

When boron trichloride is passed into 1 : 4-dioxan at 20°, in an otherwise evacuated apparatus, a stable, crystalline, 1 : 1-addition compound $C_4H_8O_2,BCl_3$ is formed. It is noteworthy that such co-ordination with one of the oxygen atoms of dioxan apparently inhibits the other oxygen from acting in like manner, since excess of boron trichloride does not give the 2 : 1-compound $2BCl_3,C_4H_8O_2$ either with dioxan itself or with the 1 : 1-complex.[57]

Methyl orthoborate forms 1 : 1-addition products with mono-, di-, and tri-methylamine, $B(OMe)_3,NH_xMe_{3-x}$.[58]

A further confirmation of the analogy between benzene and borazole ($B_3N_3H_6$) is given by the *X*-ray examination of single crystals of β-trichloroborazole which have been shown to possess a molecular configuration closely resembling that of 1 : 3 : 5-trichlorobenzene.[59]

The sodium salt of a new boron base, $Na_2HBMe_2$, has been prepared by the action of sodium in liquid ammonia at −78° on tetramethyldiborane $B_2H_2Me_4$ which is split equally into $Me_2BH,NH_3$ and this new sodium salt.[60]

An additional contribution to the chemistry of covalent boron–nitrogen compounds has been made by the study of the chemical and physical properties of the monomeric and dimeric dimethylaminoboron dichloride[61]

[53] J. R. Elliott, E. M. Boldebuck, and G. F. Roedel, *J. Amer. Chem. Soc.*, 1953, 74, 5047.

[54] M. D. Banus, R. W. Bragdon, and T. R. P. Gibb, Jr., *ibid.*, p. 2346.

[55] A. B. Burg, *ibid.*, p. 1340.

[56] H. Gerding, P. M. Heertjes, L. J. Revallier, and J. W. M. Steeman, *Rec. Trav. chim.*, 1952, 71, 501.

[57] A. K. Holliday and J. Sowler, *J.*, 1952, 11.

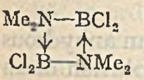
[58] J. Goubeau and R. Link, *Z. anorg. Chem.*, 1952, 267, 27.

[59] D. L. Coursen and J. L. Hoard, *J. Amer. Chem. Soc.*, 1952, 74, 1742.

[60] A. B. Burg and G. W. Campbell, Jr., *ibid.*, p. 3744.

[61] C. A. Brown and R. C. Osthoff, *ibid.*, p. 2340.

and of diethylaminoboron dichloride which, in contrast to the dimethyl compound, does not dimerise.[62] When dimethylaminoboron dichloride is kept at room temperature for several days, it is converted into the crystalline dimer $[Me_2NBCl_2]_2$, the small dipole moment of which confirms the cyclic structure (inset) suggested by previous workers.



Improved methods of preparation of dimethylaminoboron dichloride and of the new difluoride (which also dimerises on storage) have been described : good yields of the dichloride are obtained by the dehydrogenation of the dimethylamine–boron trichloride complex by triethylamine in benzene solution. The difluoride is prepared by refluxing the dimethylamine–boron trifluoride complex at 240—290°, whereby both the dimer of dimethylamine–boron difluoride and the disproportionation products, trimethylamine-boron trifluoride and tetramethylammonium fluoroborate, are obtained.[63]

The structures of dimethylaminodiborane $Me_2NB_2H_5$ and aminodiborane $H_2NB_2H_5$ have been studied by electron diffraction and give further evidence for the bridged structure of the parent diborane. The results of this investigation are in accord with symmetrical structures which have 4-fold co-ordination about the nitrogen atom and may be regarded as derived from diborane by the replacement of one of the bridge hydrogens by $NMe_2$ and $NH_2$ respectively.[64]

It is reported that when an electrodeless discharge is passed through aluminium tri-iodide vapour at low pressures, in a vessel kept at 50°, the tri-iodide undergoes decomposition with formation of a buff-coloured monoiodide.[65] It has also been claimed that potentiometric titration of liquid-ammonia solutions of aluminium tri-iodide with solutions of potassium in the same solvent gives evidence of the existence of $Al^{++}$ and $Al^{+}$ ions.[66]

It had been recorded [67] that when aluminium and other members of this group are anodically oxidised in an electrolyte of ammonium or sodium acetate in anhydrous acetic acid the mean oxidation state of the cations formed was *always* appreciably lower than 3. In contrast to this observation it has now been shown that when the electrolytic oxidation is carried out in liquid ammonia, in a variety of electrolytes, initial valency numbers lower than 3 are only observed when the solution contains nitrate ion.[68]

It has long been known that hydrochloric acid will dissolve more aluminium than corresponds to the equation : $2Al + 6HCl = Al_2Cl_6 + 3H_2$. When a large excess of aluminium is boiled with dilute hydrochloric acid, almost 6 equivalents of aluminium are dissolved to give a clear solution from which the 5/6 basic chloride $Al_2(OH)_5Cl$ can be precipitated by addition of sodium or calcium chloride.[69]

A clarification of the various solid phases formed in equilibrium with an aqueous or sulphuric acid solution of aluminium sulphate has been carried

---

[62] R. C. Osthoff and C. A. Brown, *J. Amer. Chem. Soc.*, 1952, **74**, 2378.
[63] J. F. Brown, Jr., *ibid.*, p. 1219.
[64] K. Hedberg and A. J. Stosick, *ibid.*, p. 954.
[65] W. C. Schumb and H. H. Rogers, *ibid.*, 1951, **73**, 5806.
[66] G. W. Watt, J. L. Hall, and G. R. Choppin, *ibid.*, 1952, **74**, 5920.
[67] A. W. Davidson and F. Jirik, *ibid.*, 1950, **72**, 1700.
[68] W. E. Bennett, A. W. Davidson, and J. Kleinberg, *ibid.*, 1952, **74**, 732.
[69] G. Denk and L. Bauer, *Z. anorg. Chem.*, 1952, **267**, 89.

out by a re-examination, at temperatures from 25° to 60°, of the system $Al_2(SO_4)_3$–$H_2SO_4$–$H_2O$.[70]

Aluminium hypophosphite, $Al(H_2PO_2)_3$, has been obtained as an anhydrous crystalline precipitate by heating aluminium hydroxide, or a solution of an aluminium salt, with 50% hypophosphorous acid at 80—90° for one hour, the precipitation being rather slow.[71]

At −80° anhydrous aluminium chloride neither reacts with toluene nor dissolves appreciably in it. On the addition of excess of anhydrous hydrogen chloride, however, it dissolves reversibly to give a clear, brilliantly green solution in which one mole of hydrogen chloride is apparently taken up per mole of $AlCl_3$ which goes into solution. At −45·4° the amount of hydrogen chloride taken up corresponds to one mole per mole of $Al_2Cl_6$. The reaction is believed to involve the formation of a carbonium cation $[CH_3{\cdot}C_6H_6]^+$ and $AlCl_4^-$ or $Al_2Cl_7^-$ anions.[72]

An *X*-ray and electron-diffraction study has been made of the polymorphism of $Ga_2O_3$ and of the structure of gallia gels.[73]

An examination of the In–$In_2S_3$ system by thermal metallographic and *X*-ray analysis has given evidence of the existence of four definite compounds, $In_2S_3$, ($In_3S_4$), ($In_5S_6$), and InS: the parentheses indicate some uncertainty with regard to composition. No evidence was found for the existence of the sulphide of univalent indium $In_2S$.[74]

Insoluble bistripyridylindium chloride, bromide, and thiocyanate are formed by treating the corresponding indium salts with 2 : 2′ : 2″-tripyridyl [2 : 6-di-(2-pyridyl)pyridine] in dilute aqueous ethanol solution. In a similar manner, 5-nitro-1 : 10-phenanthroline gives the complexes tri-(5-nitro-1 : 10-phenanthrolino)indium chloride, bromide, iodide, and thiocyanate—all relatively insoluble.[75]

Thallium(III) ions react with alkali alkyl xanthates to form the yellow xanthates $(RO{\cdot}CS_2)_3Tl$, which are insoluble in water but soluble in ethanol and other organic solvents. Aqueous or dilute ethanol solutions of 1 : 10-phenanthroline and 2:2′-dipyridyl react with thallium (III) ions to form the insoluble chlorides, bromides, and thiocyanates, $Tl(phenan)X_3$ and $Tl(dipy)X_3$, respectively. Thallium(III) iodide, on the other hand, co-ordinates with two molecules of the chelating agent to form $Tl(phenan)_2I_3$ and $Tl(dipy)_2I_3$. It is reported that the latter compounds are so insoluble that they permit the detection of thallium(III) ions in a dilution of 1 in $10^6$ in the presence of iron.[76]

A new and convenient method of preparation of thallium(III) iodide has been described which consists in the dissolution of thallous iodide in a solution of iodine in concentrated hydriodic acid followed by evaporation to constant weight at room temperature *in vacuo* over silica gel. It may be noted that the solution yields $TlI_3$ and not the anhydrous hypothetical acid $HTlI_4$. The only intermediate phase in the thermal decomposition of $TlI_3$ to TlI and $I_2$ is $Tl_3I_4$.[77]

A study has been made of a number of aqueous ternary and quaternary

---

[70] D. Taylor and H. Bassett, *J.*, 1952, 4431. [71] D. A. Everest, *J.*, 1952, 2945.

[72] H. C. Brown and H. W. Pearsall, *J. Amer. Chem. Soc.*, 1952, **74**, 191.

[73] R. Roy, V. G. Hill, and E. F. Osborn, *ibid.*, p. 719.

[74] M. F. Stubbs, J. A. Schufle, A. J. Thompson, and J. M. Duncan, *ibid.*, p. 1441.

[75] G. J. Sutton, *Austral. J. Sci. Res.*, 1951, **4**, *A*, 651.

[76] *Idem*, *ibid.*, p. 654. [77] A. G. Sharpe, *J.*, 1952, 2165.

systems involving thallous, ammonium, potassium, and cupric sulphates at 25° in order to compare the behaviour of thallous salts with those of the corresponding silver and alkali-metal salts. Despite certain well-known similarities between argentous and thallous salts, it is found that $Tl_2SO_4$ forms a continuous series of solid solutions at room temperature with $(NH_4)_2SO_4$ and $K_2SO_4$, whereas $Ag_2SO_4$ does not form solid solutions with either of these salts. Thallous sulphate also forms the double salt $Tl_2SO_4,CuSO_4,6H_2O$, which is isomorphous with the corresponding double salts $(NH_4)_2SO_4,CuSO_4,6H_2O$ and $K_2SO_4,CuSO_4,6H_2O$. On the other hand, thallous sulphate does not form a solid solution with sodium sulphate at 25° or 45°, whereas argentous salts form solid solutions with a variety of corresponding sodium salts, including the sulphate.[78]

It is reported [79] that thallous sulphide $Tl_2S$, free from the oxidation products which usually accompany it when it is precipitated in aqueous solution, may be obtained by the action of dry hydrogen sulphide on an alcoholic solution of thallous ethoxide.

*Lanthanons.* The well-known fact that metals usually exhibit their highest oxidation states as fluorides has suggested that higher oxidation states of praseodymium and neodymium might be obtained by the use of chlorine trifluoride or bromine trifluoride as fluorinating agents. With $ClF_3$ both $Pr_6O_{11}$ and $PrO_2$, as well as the trioxides $Pr_2O_3$ and $Nd_2O_3$, however, yielded only the trifluorides: $BrF_3$ proved to be relatively inactive towards the freshly ignited oxides.[80]

The occurrence of the lanthanon elements as uranium-fission products has stimulated interest in the properties of the pure metals themselves. Kilogram quantities of lanthanum and cerium, and somewhat less of praseodymium and neodymium, have been prepared by the reduction of the anhydrous chlorides by calcium in refractory-oxide lined crucibles, the reaction being initiated by the exothermic reaction between the calcium and a trace of added iodine.[81] A technique for the preparation of smaller quantities (40 g.) of the highly pure metals has also been developed which also consists in the reduction of the anhydrous chlorides by calcium, the reaction being carried out, however, in tantalum crucibles and the resulting metal vacuum-cast in tantalum containers. Pure lanthanum, cerium, praseodymium, neodymium, and gadolinium have been prepared by this method. It is noteworthy that samarium, europium, and ytterbium, those lanthanons which exhibit stable bivalent oxidation states, are only reduced to the bivalent chlorides by this reaction, which can therefore be used for their removal.[82]

A good yield (85%) of the mixed anhydrous lanthanon chlorides has been obtained by the direct chlorination of a mixture of monazite sand and carbon at 900°. At this temperature the majority of impurities form volatile products, and the mixed chlorides can be drained away from the reaction mixture.[83]

---

[78] J. E. Ricci and J. Fischer, *J. Amer. Chem. Soc.*, 1952, **74**, 1443, 1607.

[79] B. Reuter and A. Goebel, *Z. anorg. Chem.*, 1952, **268**, 101.

[80] A. I. Popov and G. Glockler, *J. Amer. Chem. Soc.*, 1952, **74**, 1357.

[81] F. H. Spedding, H. A. Wilhelm, W. H. Keller, D. H. Ahmann, A. H. Daane, C. C. Hach, and R. P. Ericson, *Ind. Eng. Chem.*, 1952, **44**, 553.

[82] F. H. Spedding and A. H. Daane, *J. Amer. Chem. Soc.*, 1952, **74**, 2783.

[83] F. R. Hartley, *J. Appl. Chem.*, 1952, **2**, 24.

The preparations of cerous ammonium acetylacetonate, m. p. 143—144° (decomp.), and of praseodymium ammonium acetylacetonate, m. p. 145°, have been described. These compounds are only very slightly soluble (~1 mg./ml.) in carbon tetrachloride, acetone, and benzene, and are insoluble in light petroleum, hexane, and *iso*octane.[84]

**Group IV.**—The preparation and crystal structures of a further number of disilicides of the lanthanon elements have been reported, namely, $LaSi_2$, $CeSi_2$, $PrSi_2$, $NdSi_2$, $SmSi_2$, and of $YSi_2$.[85]

The reactions between carbon, silicon, and germanium tetrafluorides and $Al_2Cl_6$, $Al_2Br_6$, $Al_2I_6$, $MgCl_2$, $CaCl_2$, and $BaCl_2$ have been investigated.[86] At high temperatures the reaction between $SiF_4$ and $Al_2Cl_6$ goes to completion, but at lower temperatures a mixture of $SiCl_4$, $SiFCl_3$, $SiF_2Cl_2$, and $SiF_3Cl$ is obtained: similar results are obtained when $Na_2SiF_6$ is substituted for $SiF_4$, and it is possible to prepare $SiCl_4$, $SiBr_4$, and $SiI_4$ by the reaction of $SiF_4$ or $Na_2SiF_6$ and aluminium in the presence of the appropriate halogen.

Interest has revived, largely in connection with its technical applications, in the chemistry of the so-called silicon oxyhydride, the solid, highly cross-linked, polymeric hydrolysis product, with an empirical formula $SiHO_{3/2}$, which is obtained as a precipitate when a benzene solution of $SiHCl_3$ is poured into cold water or when the trichlorosilane vapour is hydrolysed at 450° with steam. As might be inferred from its formula, it has very strong reducing properties, and when heated it gives hydrogen and silicon sesquioxide $Si_2O_3$: $2SiHO_{3/2} = Si_2O_3 + H_2$.[87]

Evidence has been presented [88] to show that the hydrated sodium silicates, commonly formulated as $Na_2SiO_3$,9, 6, and $5H_3O$, and $Na_6Si_2O_7,11H_2O$ are in fact acid salts of orthosilicic acid and their hydrates, *viz.*, $Na_2[H_2SiO_4]$, 8, 5, and $4H_2O$; $Na_3[HSiO_4],5H_2O$.

Convenient methods have been described for the preparation, as a continuous process, of monosilane by the reduction of silicon tetrachloride with lithium aluminium hydride and the subsequent alkylation and alkoxylation of the silane by reaction of the monosilane with the appropriate organolithium compound: tetraphenyl-, tetraethyl-, triethyl-, diethyl-, tri*iso*propyl-, tetra-2-naphthyl-, and tri-1-naphthyl-silane have been prepared in this manner. Phenylsodium reacts with silane to give tetraphenylsilane and sodium hydride. Silane has been found to react with various alcohols in the presence of alkoxide ions to give tetra-alkoxysilanes, $(RO)_4Si$, and hydrogen.[89]

A number of new alkylgermanium and alkylsilicon compounds have been prepared and their reactions studied,[90] and further work has been carried out on the synthesis of dialkylamino-germanes and -silanes.[91]

Trichlorodimethylaminosilane and chlorobisdimethylaminosilane have been prepared from dimethylamine and silicon tetrachloride. Both com-

---

[84] J. R. Seehof, *J. Amer. Chem. Soc.*, 1952, **74**, 3960, 3961.

[85] G. Brauer and H. Haag, *Z. anorg. Chem.*, 1952, **267**, 198.

[86] M. Schmeisser and H. Jenker, *Z. Naturforsch.*, 1952, **7**, *b*, 191; W. C. Schumb and D. W. Breck, *J. Amer. Chem. Soc.*, 1952, **74**, 1754.

[87] G. H. Wagner and A. N. Pines, *Ind. Eng. Chem.*, 1952, **44**, 321.

[88] E. Thilo and W. Miedreich, *Z. anorg. Chem.*, 1952, **267**, 76.

[89] J. S. Peake, W. H. Nebergall, and Y. T. Chen, *J. Amer. Chem. Soc.*, 1952, **74**, 1526.

[90] H. H. Anderson, *J. Amer. Chem. Soc.*, 1951, **73**, 5798, 5800, 5802, 5804.

[91] *Idem, ibid.*, 1952, **74**, 1421.

pounds give silane instead of the expected dimethylaminosilane on reduction with lithium aluminium hydride. They are sufficiently basic to form several hydrochlorides but do not form quaternary salts with methyl iodide.[92]

Several methods have been described for the preparation of the new compounds $TiCl_4,CH_3{\cdot}CO_2Et$; $TiCl_3{\cdot}OEt,CH_3{\cdot}CO_2Et$; and $TiCl_3{\cdot}OPr^i,CH_3{\cdot}CO_2Et$; these can be distilled under reduced pressure without change in composition, which suggests the possibility of a quinquecovalent titanium. A new series of titanium trichloride monoalkoxides $TiCl_3{\cdot}OR$ (R = Me, Et, $Pr^i$, and $Bu^n$) has also been obtained by the rapid radical-interchange reaction between titanium tetrachloride and the appropriate tetra-alkoxide.[93]

The preparation of a number of new alkoxides of zirconium and hafnium and the effect of molecular complexity on their properties has already been mentioned.[10]

When a solution of zirconyl chloride, $ZrOCl_2,6H_2O$, in alcoholic hydrogen chloride is treated with pyridine, a quantitative yield of pyridinium chlorozirconate $(C_5H_6N)_2ZrCl_6$ is obtained. This compound forms a very convenient starting material for the preparation of the zirconium alkoxides $Zr(OR)_4$ (where R = Et, $Pr^i$, $Bu^s$, and $Bu^n$), which have been obtained in a pure state by passing ammonia into a suspension of $(C_5H_6N)_2ZrCl_6$ in a mixture of benzene and the appropriate alcohol.[94]

A study of the thermal decomposition of ammonium heptafluorozirconate has shown that the decomposition takes place in three distinct stages, *viz.*, $(NH_4)_3ZrF_7 \longrightarrow (NH_4)_2ZrF_6 \longrightarrow NH_4ZrF_5 \longrightarrow ZrF_4$. The decomposition temperatures for the three successive decompositions are a function of the pressure: at 760 mm. they are 297°, 357°, and 410°, respectively.[95]

Details have been given of a method of purification of zirconium from common impurities, and especially iron, by the alternate precipitation of $Zr(SO_4)_2,4H_2O$ by the addition of concentrated sulphuric acid to an aqueous zirconium sulphate solution in the presence of hydrochloric acid (essential for the removal of iron) and the dissolution of the precipitate in water again.[96]

The complexes formed by zirconium(IV) with 2-nitroso-1-naphthol have been investigated in aqueous ethanol and aqueous dioxan solutions, in the absence and in the presence of $HClO_4$. In the absence of $HClO_4$ a 1 : 1 complex is formed, whereas if the solution is 3M or stronger with respect to $HClO_4$ and $3 \times 10^{-3}$M in Zr(IV), a 1 : 4 complex is formed.[97]

A detailed investigation has been carried out on the chemistry of zirconium in nitric, hydrochloric, perchloric, and sulphuric acid solutions by a combination of ion-exchange, radiochemical, and other techniques. The results indicate the presence at lower acid concentrations of a variety of polynuclear hydrolysis products, and at higher acidities of such complexes (in nitric acid) as $[Zr(NO_3)_2H_2O)_4]^{++}$, $[Zr(OH)_2(NO_3)(H_2O)_3]^{+}$, $[Zr(OH)_2(NO_3)_2(H_2O)_2]^{++}$, and $[Zr(OH)_2(NO_3)_4]^{-}$.[98]

---

[92] R. Cass and G. E. Coates, *J.*, 1952, 2347.

[93] D. C. Bradley, D. C. Hancock, and W. Wardlaw, *J.*, 1952, 2773.

[94] D. C. Bradley, F. M. Abd-el-Halim, E. A. Sadek, and W. Wardlaw, *J.*, 1952, 2032.

[95] H. M. Haendler, C. M. Wheeler, Jr., and D. W. Robinson, *J. Amer. Chem. Soc.*, 1952, 74, 2352.

[96] W. S. Clabaugh and R. Gilchrist, *ibid.*, p. 2104.

[97] H. B. Jonassen and W. R. de Monsabert, *ibid.*, p. 5298.

[98] B. A. J. Lister and (Miss) L. A. McDonald, *J.*, 1952, 4315.

A process has been developed for the concentration of hafnium from a mixture of zirconium and hafnium in which it occurs only to the extent of 2% by weight up to about 90% in two cycles. Each cycle consists of the adsorption of the mixed zirconium and hafnium chlorides in methanol solution on activated silica gel, followed by extraction with 1·9N-anhydrous hydrogen chloride in methanol (which preferentially removes the zirconium), followed by 7N-sulphuric acid which removes the remaining adsorbate.[99] This follows the earlier experiments reported [100] that silica gel adsorbs hafnium in strong preference to zirconium from a methanol solution of the tetrachlorides.

It has long been known [101] that zirconium and hafnium tetrachlorides form addition products with phosphorus pentachloride and phosphorus oxychloride which, since they can be distilled, are of interest in connection with the separation of the metals. From this point of view a wider study has now been made of the reactions of these tetrahalides with phosphorus oxychloride and the oxyfluorides $POFCl_2$, $POF_2Cl$, and $POF_3$;[102] with $POCl_3$ and $POFCl_2$ the tetrahalides give addition products with the composition $2POX_3,MCl_4$, which decompose when heated under reduced pressure ($<$ 0·1 mm.) to give the 1 : 1 addition products $POX_3,MCl_4$. With $POF_2Cl$ and $POF_3$, however, the metal tetrahalides give only $POX_3,MCl_4$ at room temperature. The introduction of fluorine not only decreases the thermal stability of the addition products but also introduces the possibility of halogen exchange. If the tetrahalides are kept sufficiently long in contact with excess of $POFCl_2$ or $POF_2Cl$, complete halogen exchange takes place within the phosphoryl molecule and $2POCl_3,MCl_4$ crystallises from solution, whilst if the 1 : 1 addition products with $POF_2Cl$ or $POF_3$ are heated, some fluorination of the metal halide takes place.

Whilst an *f* electron in thorium is not essential to the general actinide hypothesis, the existence of a tervalent fluoride isostructural with uranium(III) fluoride might be expected on the basis of an electron in the 5*f* orbital paralleling cerium(III) fluoride with an electron in the 4*f* orbital. In contrast, however, to the preparation of the other lower halides [103] by reduction of the tetrahalides, especially the iodide, by the metal, a number of attempts, by a variety of methods, to reduce $ThF_4$ by the metal at temperatures up to 1600° have failed. There was some indication, however, that thorium dissolves slightly in its tetrafluoride at high temperatures as do a number of other metals in their molten halides.[104]

Thermal, metallographic, *X*-ray, and chemical analysis have demonstrated the existence of four definite phases in the binary Th–Se system, *viz.*, ThSe, $Th_2Se_3$, $Th_7Se_{12}$, and $ThSe_2$.[105]

Distribution measurements of thorium ion between aqueous solutions and a solution of thenoyltrifluoroacetone in benzene have confirmed that

---

[99] G. H. Beyer, A. Jacobs, and R. D. Masteller, *J. Amer. Chem. Soc.*, 1952, **74**, 825.

[100] R. S. Hansen, K. Gunnar, A. Jacobs, and C. R. Simmons, *ibid.*, 1950, **72**, 5043; *Ann. Reports*, 1950, **47**, 108, ref. 91.

[101] A. E. Van Arkel and J. H. de Boer, *Z. anorg. Chem.*, 1924, **141**, 289.

[102] E. M. Larsen, J. Howatson, A. M. Gammill, and L. Wittenberg, *J. Amer. Chem. Soc.*, 1952, **74**, 3489.

[103] J. S. Anderson and R. W. M. D'Eye, *J.*, 1949, S244; E. Hayek and Th. Rehner, *Experientia*, 1949, **5**, 114; E. Hayek, Th. Rehner, and A. Frank, *Monatsh.*, 1951, **82**, 575.

[104] J. C. Warf, *J. Amer. Chem. Soc.*, 1952, **74**, 1864.

[105] R. W. M. D'Eye, P.G. Sellman, and (Miss) J. R. Murray, *J.*, 1952, 2555.

thorium(IV) is present as a simple, hydrated, tetrapositive ion in perchlorate solutions of an acidity greater than about 0·08M. The same technique has been used to measure the association constants of some complexes formed between thorium ion and fluoride, chloride, nitrate, sulphate, and phosphate ions, severally.[106]

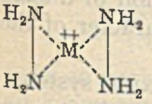
Some investigations have been reported in connection with bivalent germanium. Freshly prepared hydrous germanous oxide, obtained by precipitation with alkali in the cold, is yellow and retains its colour if stored under water at room temperature. It is, however, thermodynamically unstable and on boiling or treatment with aqueous hydrochloric acid changes to dark brown. Potential measurements give $GeO_{(yellow)} = GeO_{(brown)}$, $\Delta G^\circ = -7{\cdot}2$ kcal./mole and $GeO_2 + 2H^+ + 2e^- = GeO_{(brown)}$, $E^\circ = -0{\cdot}118 \pm 0{\cdot}010$ volt at 25°.[107] Measurements have also been made of the heat of oxidation of $GeI_2$ to germanic acid [108] and of the equilibrium $Ge(s) + GeO_2(s) = 2GeO(g)$.[109]

Several additional new complex compounds of bivalent germanium have been prepared: $GeI_2,2NH_2Me$; $Ge(H_2PO_2)_2,GeCl_2$; $3Ge(H_2PO_2)_2,GeBr_2$. These resemble the corresponding compounds of bivalent tin. If germanium dioxide is heated alone with hypophosphorous acid it goes into solution and is reduced to bivalent germanium. This is in contrast to the behaviour of stannic hydroxide which, although soluble in hypophosphorous acid, is not reduced in the absence of hydrochloric acid.[110]

It is well known that ordinary tin is converted into the low-temperature grey (α) modification at temperatures around 0° if a few particles of previously prepared grey tin are also present. The difficulty usually met with is to obtain some of the latter to initiate the transition. It has now been shown that if a small cylinder of pure white tin is surrounded by solid carbon dioxide, and cold-worked at this temperature (*e.g.*, submitted to a pressure of several tons), and then kept at −78°, it is almost completely transformed into the grey variety in 24 hours.[111]

An examination of the reaction between stannic chloride and hydrazine mono- or di-hydrochloride in varying amounts, has shown that monohydrazinium chlorostannate, $N_2H_4,H_2SnCl_6$, or $N_2H_6SnCl_6$, although reported in the literature, does not appear to exist. The only product isolated from these reactions is dihydrazinium chlorostannate, $(N_2H_5)_2SnCl_6$.[112]

**Group V.**—If hydrazine is added to an aqueous solution of a metal ion, such as $Zn^{++}$ or $Ni^{++}$, one usually obtains a precipitate in which the proportion of hydrazine to metal ion is half that to be expected from the usual co-ordination number of the metal, *e.g.*, $Zn(N_2H_4)_2X_2$, $Ni(N_2H_4)_2X_2$, $Ni(N_2H_4)_3X_2$. This has led to the supposition that in these compounds both nitrogen atoms of a given hydrazine molecule are involved with the same metal ion in the formation of a three-membered chelate ring (inset). Evidence has now been obtained which suggests that these metal hydrazine complexes may be in



---

[106] E. L. Zebroski, H. W. Alter, and F. K. Heumann, *J. Amer. Chem. Soc.*, 1951, 73, 5646.

[107] W. L. Jolley and W. M. Latimer, *ibid.*, 1952, 74, 5751.

[108] *Idem, ibid.*, p. 5752.

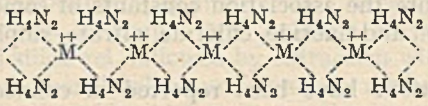
[109] *Idem, ibid.*, p. 5754.

[110] D. A. Everest, *J.*, 1952, 1670.

[111] E. S. Hedges and J. Y. Higgs, *Nature*, 1952, 169, 622.

[112] W. Pugh and A. M. Stephen, *J.*, 1952, 4138.

fact not chelate compounds, but endless networks in which each hydrazine molecules is bound to two metal cations :



In two cases no precipitate is obtained—those of the perchlorates and of the fluoroborates. The former are too explosive for investigation, but it has been shown that in the fluoroborates, where the system remains homogeneous, $Ni^{++}$ ion co-ordinates six molecules of hydrazine, and $Zn^{++}$ four, the hydrazine functioning therefore as a monodentate group.[113]

Further progress has been made in the study of the liquid dinitrogen tetroxide solvent system. The properties of a solution of diethylnitrosamine, which behaves as a " base " in this solvent, indicate that the double compound $N_2O_4,2Et_2N{\cdot}NO$, which is formed between solvent and solute, undergoes electrolytic dissociation according to the scheme : [114]

$$N_2O_4 + 2Et_2N{\cdot}NO \rightleftharpoons N_2O_4,2Et_2N{\cdot}NO \rightleftharpoons (Et_2N{\cdot}NO)_2NO^+ + NO_3^-$$

Metallic zinc has been found to react rapidly with solutions of " bases " in liquid dinitrogen tetroxide. With a solution of diethylnitrosamine, nitric oxide is evolved and a red liquid is formed which is immiscible with the dinitrogen tetroxide. This red liquid is indistinguishable from the product obtained by dissolving the compound $Zn(NO_3)_2,2N_2O_4$ in diethylnitrosamine or by adding dinitrogen tetroxide to a solution of anhydrous zinc nitrate in diethylnitrosamine. The reactions which take place are analogous to the reactions of metallic zinc and of zinc hydroxide with aqueous solutions of alkali : [115]

$$Zn + 4N_2O_4 + 4Et_2N{\cdot}NO \rightleftharpoons [(Et_2N{\cdot}NO)_2NO^+]_2[Zn(NO_3)_4] + 2NO$$
$$Zn(NO_3)_2 + 2N_2O_4 + 4Et_2N{\cdot}NO \rightleftharpoons [(Et_2N{\cdot}NO)_2NO^+]_2[Zn(NO_3)_4]$$

Dinitrogen tetroxide also forms addition compounds with ethers, of which a number have been prepared ; [116] with diethyl ether $N_2O_4,2(C_2H_5)_2O$, m. p. $-74{\cdot}8°$ ; with tetrahydrofuran $N_2O_4,C_4H_8O$, m. p. $-20{\cdot}5°$, and $N_2O_4,2C_4H_8O$ (incongruent melting) ; with tetrahydropyran $N_2O_4,2C_5H_{10}O$, m. p. $-56{\cdot}8°$ ; and with dioxan $N_2O_4,O[C_2H_4]_2O$, m. p. $45{\cdot}2°$. The structures of these compounds have been studied by spectroscopic and magnetic methods. It is of interest that a suggested explanation of the relatively high melting point of the dioxan compound is the use of both oxygens of the dioxan molecule to make possible the formation of an indefinitely extended aggregation. It may be recalled [57] that co-ordination of dioxan with one molecule of boron trichloride inhibits the donor character of the other oxygen atom.

In connection with the study of liquid dinitrogen tetroxide systems, evidence has been obtained for the existence of a new series of nitrogen oxyacid compounds of the general formula $Na_2N_2O_x (x = 3—6)$.[117] The first member of this series $Na_2N_2O_2$, the familiar sodium hyponitrite, is

---

[113] G. Schwarzenbach and A. Zobrist, *Helv. Chim. Acta*, 1952, 35, 1291.
[114] C. C. Addison and C. P. Conduit, *J.*, 1952, 1390.
[115] *Idem, J.*, 1952, 1399.
[116] B. Rubin, H. H. Sisler, and H. Shechter, *J. Amer. Chem. Soc.*, 1952, 74, 877.
[117] C. C. Addison, G. A. Gamlen, and R. Thomson, *J.*, 1952, 338, 346.

rapidly oxidised by liquid dinitrogen tetroxide to sodium β-oxyhyponitrite (β-$Na_2N_2O_3$) which differs in chemical properties from the α-compound, of the same empirical formula, prepared from hydroxylamine and ethyl nitrate. The latter, sodium α-oxyhyponitrite, also undergoes rapid oxidation to the compound $Na_2N_2O_4$ which again is a different compound from sodium nitrite. $Na_2N_2O_4$ undergoes a further slow oxidation in liquid dinitrogen tetroxide to a compound of empirical formula $NaNO_3$ which may be the dimer $Na_2N_2O_6$, and a silver salt believed to have the formula $Ag_2N_2O_6$ has been prepared. Sodium β-oxyhyponitrite undergoes slow oxidation in liquid dinitrogen tetroxide to the compound $Na_2N_2O_5$ which is also formed rapidly by the action of nitrogen dioxide gas at 100° on sodium hyponitrite, and is further oxidised slowly under these conditions to the $NaNO_3$ (or $Na_2N_2O_6$) stage. Ultra-violet absorption spectra of aqueous solutions of the hydrolysis products of these compounds have been examined and an attempt has been made to formulate structures for them.

Hydrogen peroxide has been shown to react with nitrous acid, nitric oxide, and nitrogen dioxide with the formation of pernitrous acid, $HNO_3$. From the behaviour of the products of these reactions in initiating the polymerisation of methyl methacrylate and in hydroxylating and nitrating benzene, it has been suggested that pernitrous acid undergoes homolytic fission to give OH radicals and nitrogen dioxide.[118]

Further studies have been made of nitrosyl chloride as an acid–base ionising solvent and of the behaviour in solution of several nitrosyl double compounds: $NOFeCl_4$, $NOAlCl_4$, $NOBF_4$, $(NO)_2SnCl_6$. Nitrosyl compounds react in nitrosyl chloride solution with the slightly soluble $(CH_3)_4NCl$ in the sense of the acid–base neutralisation $NO^+ + Cl^- = NOCl$ as demonstrated by a conductometric titration of $NOFeCl_4$ by $(CH_3)_4NCl$ and by the partial neutralisation equilibria of $NOBF_4$, $NOClO_4$, and $(NO)_2S_2O_7$, each with $(CH_3)_4NCl$. The idea that $NO^+$ represents "acid" and $Cl^-$ "base" is further justified by the electrolysis of $NOFeCl_4$ in NOCl, which gives NO at the cathode and $Cl_2$ at the anode.[119]

Some work has been carried out on the constitution and reactions of nitryl chloride, $NO_2Cl$. On hydrolysis and alcoholysis this behaves as a nitrosyl hypochlorite.[120] By the reaction of nitryl chloride with antimony pentachloride in liquid chlorine, one can obtain a compound $NO_2Cl,SbCl_5$ which behaves as nitrosyl chloroantimonate $[NO_2]^+[SbCl_6]^-$: it dissolves in liquid sulphur dioxide to give a conducting solution and undergoes ionic reactions with tetramethylammonium perchlorate and fluoroborate to give nitryl perchlorate and fluoroborate respectively:[121]

$$[NO_2][SbCl_6] + [NMe_4]ClO_4 = [NO_2]ClO_4 + [NMe_4]SbCl_6$$
$$[NO_2][SbCl_6] + [NMe_4]BF_4 = [NO_2]BF_4 + [NMe_4]SbCl_6$$

An investigation of the behaviour of nitryl chloride towards ammonia and a number of Lewis acids suggests that the nitrogen–chlorine bond is not so strongly polarised as to act as a source of negative chlorine, except towards exceedingly strong electron acceptors such as sulphur trioxide, with which it forms $NO_2Cl,2SO_3$, presumably nitronium chlorodisulphate

---

[118] E. Halfpenny and P. L. Robinson, *J.*, 1952, 928.

[119] A. B. Burg and D. E. McKenzie, *J. Amer. Chem. Soc.*, 1952, **74**, 3143.

[120] F. Seel and J. Nógrádi, *Z. anorg. Chem.*, 1952, **269**, 188.

[121] F. Seel, J. Nógrádi, and R. Posse, *ibid.*, p. 197.

$NO_2(ClS_2O_6)$. Thus, on reaction with ammonia it yields chloroamine and ammonium nitrite, rather than nitramide and ammonium chloride, and it does not react with $SnCl_4$ or $BF_3$, which might be expected to co-ordinate a negative chlorine. It has been suggested that the addition of the second oxygen atom in going from nitrosyl chloride to nitryl chloride either greatly reduces the polarity of the N–Cl bond or actually reverses its direction, so that the chlorine becomes positive.[122]

Dinitrogen tetrasulphide, $N_2S_4$, which has been known for a long time,[123] has received renewed attention. This compound, which is prepared by the action of sulphur in $N_4S_4$ (*e.g.*, in $CS_2$ solution in an autoclave at 100—120°), is a dark red, fairly unstable solid, m. p. 23°. It is soluble in many organic solvents and is diamagnetic. The latter excludes a dissociation into $NS_2$ molecules, which would be paramagnetic, whilst its chemical behaviour towards a variety of reagents suggests that its structural formula is quite different from that of its oxygen analogue dinitrogen tetroxide.[124]

The two new double compounds $Li_3AlP_2$ and $Li_3AlAs_2$ have been prepared.[125] In their chemical reactions these compounds behave more like $Li_3P$ and $Li_3As$ than as AlP or AlS respectively.

It is reported that compounds of the type $PX_5,IY$, where X and Y are different halogens, can be synthesised directly, either by fusion together of the components $PX_5$ and IY, or by dissolving these in $CCl_4$. $PBr_5ICl$ has been prepared by the latter method and forms cherry-red needle-shaped crystals, m. p. 112·8°. It is formulated by the authors as $[PBr_4^+][BrICl^-]$. $PCl_5IBr$ forms yellow crystals, m. p. 140° (decomp.).[126]

A spectrophotometric study of phosphorus hexachloroiodide and hexabromoiodide has shown that these compounds dissociate in carbon tetrachloride solution into their component molecules, $PCl_6I \rightleftharpoons PCl_5 + ICl$; $PBr_6I \longrightarrow PBr_3 + IBr + Br_2$, whereas in polar solvents such as acetonitrile the dissociation is ionic: $PCl_6I \longrightarrow PCl_4^+ + ICl_2^-$ and $PBr_6I \longrightarrow PBr_4^+ + IBr_2^-$.[127]

Solubility measurements of antimonous oxide in water and in dilute solutions of hydrochloric acid and of sodium hydroxide show that in both acid and alkaline solutions the antimony is present as a univalent ion, $SbO^+$ and $SbO_2^-$, respectively.[128]

Antimony pentafluoride, a compound with some remarkable physical properties,[129] appears to possess a power of compound formation which is much greater than that of arsenic pentafluoride. Some unusual chemical compounds which include antimony pentafluoride have been reported. It dissolves sulphur, selenium, and tellurium to give blue, yellow, and red solutions, respectively, from which the stable crystalline compounds $(SbF_5)_2S$, $(SbF_5)_2Se$, and $(SbF_5)_2Te$ can be isolated. Sulphur dioxide forms $SbF_5SO_2$, and $NO_2$ forms $SbF_5NO_2$.[130]

---

[122] H. H. Batey and H. H. Sisler, *J. Amer. Chem. Soc.*, 1952, **74**, 3408.

[123] F. L. Usher, *J.*, 1925, 730.

[124] M. Goehring, H. Herb, and H. Wissemeir, *Z. anorg. Chem.*, 1952, **267**, 238.

[125] R. Juza and W. Schulz, *ibid.*, 1952, **269**, 1.

[126] I. D. Muzyka and Ya. A. Fialkov, *Doklady Akad. Nauk. S.S.S.R.*, 1952, **83**, 415; *Chem. Abs.*, 1952, **46**, 6983.

[127] A. I. Popov and E. H. Schmorr, *J. Amer. Chem. Soc.*, 1952, **74**, 4672.

[128] K. H. Gayer and A. B. Garrett, *ibid.*, p. 2353.

[129] A. A. Woolf and N. N. Greenwood, *J.*, 1950, 2200.

[130] E. E. Aynsley, R. D. Peacock, and P. L. Robinson, *Chem. and Ind.*, 1951, 1117.

It is reported[131] that almost pure vanadium monoxide (99·68%) has been prepared by heating a compressed intimate mixture of $V_2O_3$ and finely divided vanadium in a vacuum at 1750°. The product is described as having a specific gravity of 5·55, a hardness of 8—9 on Mohs' scale, and to dissolve in acids to give the blue or violet solutions characteristic of hypovanadous salts.

The monoboride VB and the mononitride VN have also been examined, the former being prepared[132] as the product of the simultaneous reduction of $V_2O_5$ and $B_2O_3$ with carbon in a graphite crucible at 1650° in an atmosphere of hydrogen, and VN in a crystalline form by the action of nitrogen and hydrogen on the vapour of vanadium tetrachloride in the presence of a heated filament. The latter technique has also been used to prepare niobium mononitride NbN, though in the form of smaller crystals than the vanadium nitride.[133]

A preliminary report has been made of a new solvent extraction method for the separation of niobium and tantalum. It has been found, by using a tracer technique, that niobium can be extracted almost quantitatively from concentrated hydrochloric acid solution by a solution of methyldioctylamine in xylene : under these conditions the extraction of tantalum appears to be almost negligible. The niobium can then be extracted from the organic phase with nitric, sulphuric, or dilute hydrochloric acid.[134]

An inorganic chromatographic separation of these two elements from one another and from other elements present in complex minerals, and suitable for their quantitative determination, has been developed. This method is based on the adsorption of the metals as fluorides on a cellulose column in a Polythene tube, and selective extraction by ethyl methyl ketone containing hydrofluoric acid.[135]

The elution by 7·0M-hydrochloric acid of carrier-free $^{95}$Nb, adsorbed from a 10·0M-hydrochloric acid solution on a Dowex 2 anion-exchange resin, instead of giving the usual symmetrical curve of activity of eluant versus volume of eluant, gives a curve which shows several peaks. As these can be identified by the characteristic disintegration rate of $^{95}$Nb, the presence of any other species, or of isotopic separation, may be excluded. This result has been attributed to the slow establishment of equilibrium among the various ionic species present, which would not necessarily have different charges as in the case of the thiocyanate complexes of chromium, which have been separated by this kind of technique,[20] but may contain different numbers of chloro-, oxy-, and hydroxy-groups. Elution with 6·0M-hydrochloric acid gives the usual symmetrical elution curve.[136]

It has been shown that niobium pentachloride and tantalum pentachloride form a continuous series of mixed crystals.[137]

When niobium pentachloride is heated at 350—400° with niobium metal, in a molar ratio greater than 4 : 1, niobium tetrachloride may be obtained

---

[131] M. Frandsen, *J. Amer. Chem. Soc.*, 1952, **74**, 5046.

[132] H. Blumenthal, *ibid.*, p. 2942.

[133] F. H. Pollard and G. W. A. Fowles, *J.*, 1952, 2444.

[134] G. W. Leddicotte and F. L. Moore, *J. Amer. Chem. Soc.*, 1952, **74**, 1618.

[135] F. H. Burstall, P. Swain, A. F. Williams, and G. A. Wood, *J.*, 1952, 1497; A. F. Williams, *J.*, 1952, 3155; R. A. Mercer and A. F. Williams, *J.*, 1952, 3399.

[136] E. H. Huffman and G. M. Iddings, *J. Amer. Chem. Soc.*, 1952, **74**, 4714.

[137] H. Schäfer and C. Pietruck, *Z. anorg. Chem.*, 1952, **267**, 174.

as large needles. With a greater proportion of metal, the trichloride is obtained, or some lower chloride which disproportionates near 600° into the metal and the trichloride.[138]

Niobium tetrachloride also disproportionates on heating, and the equilibrium pressure of the decomposition $2NbCl_4 = NbCl_3 + NbCl_5$ has been measured.[139]

Although quinquevalent tantalum is much less easily reduced than quinquevalent niobium, $TaCl_5$ being unaffected by hydrogen at temperatures up to 400°, there is evidence that at temperatures over 500° some reduction of $TaCl_5$ does occur. Similarly, if hydrogen chloride or hydrogen bromide is passed over the metal at about 400° only the pentahalide is formed. At higher temperatures (between 600° and 800°), however, lower halides are formed which may undergo some disproportionation with the deposition of films of metallic tantalum on the walls of the apparatus.[140]

The reduction of niobium and tantalum pentoxides, and mixtures of the two, to the quadrivalent dioxides by moist hydrogen at 900°, has been investigated.[141]

**Group VI.**—A comprehensive review has been published [142] of the methods used for the production and determination of abundance of isotopic oxygen and of its applications. Details have also been given [143] of the construction and operation of a number of fractionating columns for the enrichment of $^{18}O$ in water. One of these is reported as being capable of producing per day, 200 c.c. of 0·6% $H_2{}^{18}O$, or 50 c.c. of 1·7% $H_2{}^{18}O$ or 20 c.c. of 3·2% $H_2{}^{18}O$ : another, operating as a second stage, gives 10 c.c. of 12% $H_2{}^{18}O$ per week.

The isotope $^{18}O$ has been used as a tracer in the study of the mechanism of oxidation of hydrogen peroxide.[144] The oxygen liberated when $H_2O_2$ is oxidised in aqueous solution by Ce(IV), $MnO_4^-$, $Cl_2$, HClO, and $Cr_2O_7^=$ is derived wholly from the hydrogen peroxide and not from the water. Similarly, the oxygen liberated in the catalytic decomposition of $H_2O_2$ by Fe(III), $I^-$, $I_2$, $Br^-$, $Br_2$, $MnO_2$, and Pt is derived only from the $H_2O_2$.

A series of higher sulphur chlorides with the composition $S_xCl_2$ (where $x$ can have values up to about 100, depending upon the temperature of reaction), and consisting of long sulphur chains terminated at the ends by the two chlorine atoms, has been prepared by a " hot-cold " tube method from $S_2Cl_2$ and hydrogen.[145]

Some new trifluoromethyl derivatives of sulphur have been prepared. Trifluoroiodomethane, $CF_3I$, reacts with sulphur to give bistrifluoromethyl disulphide $(CF_3)_2S_2$, carbon disulphide, thiocarbonyl fluoride, and polysulphides. Bistrifluoromethyl disulphide undergoes an unusual type of hydrolysis in aqueous alkali, the first stage of which consists in the hydrolytic fission of the S–S bond to give trifluoromethanethiol and trifluoromethane-

---

[138] H. Schäfer, C. Göser, and L. Bayer, *Z. anorg. Chem.*, 1951, **265**, 258; C. H. Brubaker, Jr., and R. C. Young, *J. Amer. Chem. Soc.*, 1952, **74**, 3690.

[139] H. Schäfer, L. Bayer, and H. Lehmann, *Z. anorg. Chem.*, 1952, **268**, 268.

[140] R. C. Young and C. H. Brubaker, Jr., *J. Amer. Chem. Soc.*, 1952, **74**, 4967.

[141] H. Schäfer and B. Breil, *Z. anorg. Chem.*, 1952, **267**, 265.

[142] M. Dole, *Chem. Reviews*, 1952, **51**, 263.

[143] I. Dostrovsky, D. R. Llewellyn, and B. H. Vromen, *J.*, 1952, 3509; I. Dostrovsky, J. Gillis, D. R. Llewellyn, and B. H. Vromen, *J.*, 1952, 3517.

[144] A. E. Cahill and H. Taube, *J. Amer. Chem. Soc.*, 1952, **74**, 2312.

[145] F. Féher and M. Baudler, *Z. anorg. Chem.*, 1952, **267**, 293.

sulphenic acid which subsequently break up to give fluoride, carbonate, and sulphide ions :

$$\begin{tikzcd}
CF_3\cdot S\cdot S\cdot CF_3 \arrow[r, "NaOH"] & CF_3\cdot SH \arrow[d] & + & CF_3\cdot S\cdot OH \arrow[d] \\
F^-, CO_3^{=}, S^{=} & F_2C{:}S + HF \arrow[l] & & F^-, CO_3^{=}, S^{=}
\end{tikzcd}$$

On irradiation in the presence of mercury, the disulphide yields bis(trifluoromethylthio)mercury $(CF_3S)_2Hg$ : in the absence of mercury it gives bistrifluoromethyl sulphide which, in contrast to the disulphide, is quite stable to aqueous alkali.[146]

It is reported that the chloride of trichlorophosphazosulphuric acid, $ClSO_2N{:}PCl_3$, has been prepared by the reaction at 100° between sulphamic acid and phosphorus pentachloride.[147]

New methods have been described for the preparation of selenium oxyfluoride and selenium tetrafluoride. The latter is prepared by the action of dilute fluorine on selenium at 0°. It is a liquid, m. p. $-9{\cdot}5°$, b. p. 106°, with some remarkable solvent properties. It dissolves the fluorides of sodium, potassium, rubidium, and cæsium to form complexes with a composition approaching $MSeF_5$ which is different from that of any of the other complex selenium halides, *viz.*, $M_2SeX_6$.[148]

Selenium, diselenium, and triselenium di(benzenesulphinate) and di(toluenesulphinate), $Se(SO_2R)_2$, $Se_2(SO_2R)_2$, and $Se_3(SO_2R)_2$, have been prepared, and represent a new class of selenium compounds of which the sulphur analogues have been known for a long time. In their reactions they behave as derivatives of $Se^{++}$, $Se_2^{++}$, and $Se_3^{++}$, respectively.[149] Selenium and tellurium di(benzenethiosulphonate) and di(toluene-*p*-thiosulphate) have also been prepared.[150]

Conductivity measurements have shown that tellurium tetrachloride behaves as an " acid " in arsenic trichloride solution and may be titrated conductimetrically in this solvent with $(CH_3)_4NCl$. Compounds can be isolated from the resulting solution which are probably the " acid " and " normal " salts respectively, $(NMe_4)(AsCl_2)(TeCl_2)$ and $(NMe_4)_2TeCl_6$.[151]

The system chromium(III) oxide–water has been studied in the temperature range 145—560° by the hydrothermal method. A definite blue-grey compound, CrO(OH), $d = 4{\cdot}12$, is formed below 419—424°. This decomposes sharply and endothermically at about 430°. Rhombohedral $Cr_2O_3$ is the stable phase above 450°.[152]

The products obtained when chromium(VI) trioxide is heated in a vacuum have been investigated by *X*-ray and chemical analysis.[153] Evidence has been obtained of the existence of three definite compounds intermediate between $CrO_3$ and $Cr_2O_3$, *viz.*, $Cr_3O_8$, $Cr_2O_5$, and $CrO_2$.

Pure chromyl fluoride, $CrO_2F_2$, has been prepared for the first time, by the reaction between $CrO_3$ and anhydrous hydrogen fluoride in an apparatus built out of copper, silica-free glass, and Kel-F tubing. It forms violet-red

---

[146] G. A. R. Brandt, H. J. Emeléus, and R. N. Haszeldine, *J.*, 1952, 2198.

[147] A. V. Kirsanov, *Zhur. Obshchei Khim.*, 1952, **22**, 88; *Chem. Abs.*, 1952, **46**, 6984.

[148] E. E. Aynsley, R. D. Peacock, and P. L. Robinson, *J.*, 1952, 1231.

[149] O. Foss, *Acta Chem. Scand.*, 1952, **6**, 508.

[150] *Idem, ibid.*, p. 521.

[151] V. Gutmann, *Monatsh.*, 1952, **83**, 159.

[152] A. W. Laubengayer and H. W. McCune, *J. Amer. Chem. Soc.*, 1952, **74**, 2362.

[153] R. S. Schwartz, I. Fankuchen, and R. Ward, *ibid.*, p. 1676.

crystals which have a v. p. of 760 mm. at 29·6° and melt to an orange-red liquid at 31·6° under a pressure of 885 mm.[154]

An examination of the spectra of chromic acid and chromic acid–phosphoric acid systems has indicated the formation of two chromate–phosphate complex ions, $HCrPO_7^{-}$ and $H_2CrPO_7^{-}$.[155]

The alkali-metal compounds of chromium of the type $MCr_3O_8$ have been prepared and examined.[156] The oxidation states of chromium in these compounds, which are obtained by heating mixtures of the composition $M_2Cr_2O_7 + 2CrO_3$ at 350° in air for two hours and extracting the excess of the dichromate with water, appear somewhat problematical. The black metallic appearance of, for example, the potassium compound suggests that it is not a compound containing chromium in its two usual and independent states of oxidation 3 and 6, $K_2Cr_2(CrO_4)_4$ or $K_2(CrO)_2(Cr_2O_7)_2$, but that there is some interaction between the chromium ions so that the effective overall oxidation state is +5.

A compound of univalent chromium $(dipy_3Cr^{I})(ClO_4)$ (dipy = 2 : 2′-dipyridyl) is reported to be formed by reduction of the bivalent compound $(dipy_3Cr^{II})(ClO_4)_2$ by magnesium in the presence of ammonium perchlorate, and with exclusion of air.[157]

On treating chromium hexacarbonyl with alcoholic potassium hydroxide, a brilliantly yellow derivative is obtained, which on acidification yields a white, volatile, unstable, crystalline substance, the properties of which suggest that it is $Cr(CO)_5H_2$.[158]

The term " tungsten bronze " is used to describe the non-stoicheiometric compounds of general formula $M_xWO_3$ (where M is an alkali metal and $x$ is less than unity) obtained on reduction of the alkali tungstates. These have been considered (*a*) as solutions of tungsten(VI) oxide in a hypothetical tungsten(V) compound $MWO_3$, and also (*b*), on account of their high electrical conductivity, low magnetic moment, and general metallic appearance, as solid solutions of alkali metal in $WO_3$. The essential difference between these two models is that in (*a*) the electron from the alkali metal is considered to be strongly associated with the tungsten(V) ion, which would therefore be paramagnetic, whereas in (*b*) the electron from the alkali metal is part of the electron gas that is associated with the whole lattice. To distinguish between these two models, the magnetic susceptibilities of a very wide series of lithium tungsten bronzes have been measured.[159] The values of the susceptibilities are very low and actually become diamagnetic as the concentration of lithium is decreased. The results are in agreement with those calculated for an electron-gas model.

Studies have been made of the alkali-metal molybdate systems, $K_2MoO_4$–$MoO_3$, $Rb_2MoO_4$–$MoO_3$, and $Cs_2MoO_4$–$MoO_3$,[160] and of the alkali fluoride molybdenum(V) systems, LiF–$MoO_3$, NaF–$MoO_3$, KF–$MoO_3$, RbF–$MoO_3$, and $CsMoO_3$.[161]

---

[154] A. Engelbrecht and A. V. Grosse, *J. Amer. Chem. Soc.* 1952, **74**, 5262.

[155] F. Holloway, *ibid.*, p. 224.

[156] L. Suchow, I. Fankuchen, and R. Ward, *ibid.*, p. 1678.

[157] Fr. Hein and S. Herzog, *Z. anorg. Chem.*, 1952, **267**, 337.

[158] M. G. Rhomberg and B. B. Owen, *J. Amer. Chem. Soc.*, 1951, **73**, 5904.

[159] L. E. Conroy and M. J. Sienko, *ibid.*, 1952, **74**, 3520.

[160] V. I. Spitsyn and I. M. Kuleshov, *J. Gen. Chem. U.S.S.R.*, 1951, 1493; *Chem. Abs.*, 1952, **46**, 9006.

[161] O. Schmitz-Dumont and I. Heckmann, *Z. anorg. Chem.*, 1952, **267**, 277.

*Uranium and the trans-uranic elements.* Further investigation has been made of the sodium uranates. Chemical, *X*-ray diffraction, pH, and conductivity data indicate that when sufficient sodium hydroxide is added to uranyl nitrate solutions, two compounds $Na_2U_7O_{22}$ and $Na_6U_7O_{24}$ (or mixtures of these) are precipitated. In the first place, when just insufficient sodium hydroxide to produce precipitation is added (which requires 1 mol. or more of NaOH per mol. of $UO_2^{++}$), basic uranyl ions $UO_3UO_2^{++}$ and $(UO_3)_2UO_2^{++}$ are formed. Further addition of NaOH to a mole ratio NaOH/U of 2·29, causes the quantitative precipitation of the uranium as $Na_2U_7O_{22}$. This in turn may react with excess of alkali to give $Na_6U_7O_{24}$.[162]

The diuranates of the alkaline-earth metals have been prepared by the ignition of the corresponding metal uranyl acetates, a method of preparation which has been found to give a product free from an excess of either the alkaline-earth metal or uranium oxide. The thermal stabilities in vacuum and in oxygen up to 1100° have been investigated and the results have shown that the metal diuranate–oxygen systems are reversible below this temperature.[163]

The magnetic susceptibilities of $UF_4$–$ThF_4$ solid solutions reported earlier,[164] which seemed to indicate the presence of two 5*f* electrons in $UF_4$, have been corrected by the author. The amended values [165] show that, within experimental error, both the susceptibility at room temperature and the moment extrapolated to infinite dilution agree with the values predicted for two unpaired spins with the orbital contribution to the moment completely quenched. These results therefore fall into line with those obtained for the $UO_2$–$ThO_2$ solid solutions [166] and imply a configuration of $6d^2$ for the $U^{4+}$ ion.

The magnetic susceptibilities of plutonium dioxide and tetrafluoride have also been measured, over the temperature range 90—450° K. Measurements made on the solid solutions of $PuF_4$ in the isomorphous $ThF_4$ lead to an extrapolated susceptibility at infinite dilution in agreement with a $5f^4$ configuration. The dioxide has approximately the same susceptibility at infinite dilution, but the behaviour with increasing concentration is more complex and some of the evidence may indicate that 6*d* levels are occupied.[167] The sexavalent plutonium ion should have two unpaired electrons, and in order to determine whether these are in the 5*f* or the 6*d* level, the magnetic susceptibility of sodium plutonyl acetate has been measured over the temperature range 90—300° K. The results agree with the theoretical value for spin-only for two electrons, which therefore may be taken as evidence that the ground state of the plutonyl ion has a $6d^2$ configuration.[168]

The potentials of the couples $Am_{(aq)}{}^{4+} + \frac{1}{2}H_{2(g)} = Am_{(aq)}{}^{3+} + H_{(aq)}{}^{+} = +2{\cdot}4$ v, and $Pr_{(aq)}{}^{++} + \frac{1}{2}H_{2(g)} = Pr_{(aq)}{}^{3+} + H_{(aq)}{}^{+} = +2{\cdot}9$ v have been estimated from thermodynamical data and measurements of the heats of reaction of the oxides with nitric acid and fluoroboric acid in a micro-calorimeter.[169]

---

[162] C. A. Wamser, J. Belle, E. Bernsohn, and B. Williamson, *J. Amer. Chem. Soc.*, 1952, **74**, 1020. [163] H. R. Hoekstra and J. J. Katz, *ibid.*, p. 1683.

[164] J. K. Dawson, *J.*, 1951, 2889; *Ann. Reports*, 1951, **48**, 102, ref. 146.

[165] *Idem*, *J.*, 1952, 1185.

[166] W. Trzebiatowski and P. W. Selwood, *J. Amer. Chem. Soc.*, 1950, **72**, 4504; *Ann. Reports*, 1950, **47**, 116, ref. 164.

[167] J. K. Dawson, *J.*, 1952, 1882. [168] *Idem*, *J.*, 1952, 2705.

[169] L. Eyring, H. R. Lohr, and B. B. Cunningham, *J. Amer. Chem. Soc.*, 1952, **74**, 1186.

An interesting feature of this work was that the primary objective was the evaluation of the $Am^{4+}$–$Am^{3+}$ potential and that the chemically similar but more abundant praseodyminium was used—as the authors express it—as a " stand-in " for the perfection of the technique.

A further study has been made of the chemistry of sexavalent americium, which has been shown to resemble that of U(VI), Np(VI), and Pu(VI).[170]

A search has been made in aqueous solution for oxidation states of curium higher than $Cm^{3+}$ by using macro-amounts (up to 238 μg. per experiment) of the element, and using americium(III), which does exhibit the higher oxidation states +5 and +6 in solution, as an internal check. No evidence was found for the existence of $Cm^{4+}$, $Cm^{5+}$, or $Cm^{6+}$ in the oxidation of $Cm^{3+}$–$Am^{3+}$ mixtures in either acid or alkaline solutions, under conditions where the $Am^{3+}$ was oxidised quantitatively to $Am^{5+}$ or $Am^{6+}$.[171]

**Group VII.**—The conditions and products of reaction of elementary fluorine with zinc, zinc oxide, zinc bromide, zinc sulphide, nickel, nickel(II) oxide, nickel(III) oxide, and nickel(II) sulphate have been investigated. There was no evidence of the production of a higher fluoride of nickel by the fluorination of the so-called nickel(III) oxide, $Ni_2O_3$: in all cases the bivalent fluorides were the only non-volatile products observed.[172]

Silver tetrafluoroborate can be simply prepared by the action of bromine trifluoride on dry silver borate, and undergoes rapid decomposition at 200° into silver fluoride and boron trifluoride. These reactions form a convenient method of preparation of small quantities of anhydrous silver fluoride, and can be carried out in quartz apparatus.[173]

The magnetic susceptibilities of a number of simple and complex fluorides of transition metals have been measured, *viz.*, $K_2TiF_6$; $K_2TiF_6,H_2O$; $VF_3$; $K_3VF_6$; $K_2CrF_5,H_2O$; $KCrOF_4$; $K_2MnF_5,H_2O$; $Li_3FeF_6$; $Na_3FeF_6$; $K_2FeF_5$; $CsFeF_4$; $CuF_2,2H_2O$; $TaF_3$; $RhF_4$; $Na_3RhF_7$; $PdF_3$; $PtF_4$; $K_2PtF_6$; $AuF_3$; $AgAuF_4$. Compounds of the first transition series, except when magnetically concentrated, show the number of unpaired electrons which would be expected for ionic binding. For the second and third transition series, however, when the number of electrons in the metal ion is even, the compounds are diamagnetic, and paramagnetic when the number is odd, but with a moment which corresponds to only one unpaired electron, which shows that for these two series, minimum multiplicity is the rule even for fluorides.[174]

The commercial availability of chlorine trifluoride, and the ease with which it can be used, offer the possibility of its substitution for elementary fluorine as a fluorinating agent in a number of reactions, and a number of metal fluorides have been prepared from the metals by its use. Details have now been given of the preparation of cobalt(III), nickel(II), and silver(II) fluorides from chlorine trifluoride and cobalt(II), nickel(II), and silver(I) chlorides, respectively.[175]

The existence of bromine monochloride in carbon tetrachloride solution

---

[170] L. B. Asprey, S. E. Stephanou, and R. A. Penneman, *J. Amer. Chem. Soc.*, 1951, 73, 5715.

[171] S. E. Stephanou and R. A. Penneman, *ibid.*, 1952, 74, 3701.

[172] H. M. Haendler, W. L. Patterson, Jr., and W. J. Bernard, *ibid.*, p. 3167.

[173] A. G. Sharpe, *J.*, 1952, 4538.

[174] R. S. Nyholm and A. G. Sharpe, *J.*, 1952, 3579.

[175] E. G. Rochow and I. Kukin, *J. Amer. Chem. Soc.*, 1952, 74, 1615.

was clearly proved nearly 25 years ago,[176] and described as probably highly dissociated. The extent of this dissociation has now been re-investigated spectrophotometrically and found to amount to 43·2±1% at 25°. The equilibrium constant for the reaction $2BrCl \rightleftharpoons Br_2 + Cl_2$ in carbon tetrachloride has been calculated to be $0{\cdot}145 \pm 0{\cdot}006$.[177]

Alkali hypobromites are familiar in aqueous solution, but no solid hypobromites appear to have been isolated.[178] It is reported, however, that at −5° it is possible to isolate the crystalline alkali hypobromites $NaBrO,5H_2O$ and $7H_2O$, and $KBrO,3H_2O$ from the products of the action of bromine on solutions of the respective hydroxides at this temperature.[179]

It was pointed out several years ago [180] that molecular iodine formed brown solutions, and was polarised, in electron-donor or " basic " solvents, which included aromatic and olefinic hydrocarbons. It was subsequently demonstrated that iodine formed 1 : 1 addition compounds with several aromatic hydrocarbons.[181] Ultra-violet absorption measurements have now shown that iodine forms 1 : 1 addition compounds also with olefins at low temperatures.[182]

The system $MnSO_4$–$H_2SO_4$–$H_2O$ has been investigated at 0°, 20°, 25°, 45°, 65°, and 95·7°, and the following solid phases identified: $MnSO_4,5H_2O$, $MnSO_4,H_2O$, $MnSO_4,H_2SO_4,H_2O$, $MnSO_4,H_2SO_4$, and $MnSO_4,3H_2SO_4$.[183]

The separation of technetium from uranium-fission product wastes has made this element available in weighable amounts and therefore made possible the investigation of its chemistry by ordinary analytical methods instead of only by tracer techniques. Approximately 0·6 g. of the spectrographically pure metal has been prepared by the hydrogen reduction of ammonium pertechnetate [184] and it has been established that the light yellow crystalline oxide (m. p. 119·5° ± 0·1°) obtained when technetium is heated in dry oxygen at 400—600° is $Tc_2O_7$. The pertechnetate ion possesses an intense ultra-violet absorption (molar extinction at 2470 Å = 4000) which can be used for its spectrophotometric determination—as little as $10^{-8}$ g. of technetium can be detected in this way.[185] Technetium heptasulphide, previously assumed to be $Tc_2S_7$ on the basis of analogy with $Re_2S_7$, has also been examined and its formula confirmed by chemical analysis.[186]

The existence of rhenium in aqueous solution in the −1 oxidation state is now accepted on the basis of the stoicheiometry of its reduction. A solid rhenide, however, has recently been reported for the first time. When potassium perrhenate is reduced by potassium in ethylenediamine, a white solid is deposited which is stated to contain rhenium in the −1 oxidation state, together with some potassium hydroxide.[187]

---

[176] A. E. Gillam and R. A. Morton, *Proc. Roy. Soc.*, 1929, *A*, **124**, 604.

[177] A. I. Popov and J. J. Mannion, *J. Amer. Chem. Soc.*, 1952, **74**, 222.

[178] N. V. Sidgwick, " The Chemical Elements and Their Compounds," Oxford, 1950, p. 1221.

[179] R. Scholder and K. Krauss, *Z. anorg. Chem.*, 1952, **268**, 279.

[180] F. Fairbrother, *J.*, 1948, 1051.

[181] H. A. Benesi and J. H. Hildebrand, *J. Amer. Chem. Soc.*, 1949, **71**, 2703.

[182] S. Freed and K. M. Sancier, *ibid.*, 1952, **74**, 1273.

[183] D. Taylor, *J.*, 1952, 2370.

[184] J. W. Cobble, C. M. Nelson, G. W. Parker, W. T. Smith, Jr., and G. E. Boyd, *J. Amer. Chem. Soc.*, 1952, **74**, 1852.

[185] G. E. Boyd, J. W. Cobble, C. M. Nelson, and W. T. Smith, Jr., *ibid.*, p. 556.

[186] C. L. Rulfs and W. W. Meinke, *ibid.*, p. 235.

[187] E. Griswold, J. Kleinberg, and J. B. Bravo, *Science*, 1952, **115**, 375.

**Group VIII.**—The bicentenary of the discovery of nickel in 1751 by Cronstedt has been marked by a symposium on recent developments in the chemistry and applications of nickel and its compounds.[188]

A detailed *X*-ray examination of the compound $Ni(CN)_2,NH_3,C_6H_6$, which is obtained as a precipitate when benzene is added to a solution of nickel cyanide in ammonia, has shown that the benzene—which exhibits no detectable vapour pressure at room temperature—is not linked to the nickel complex by chemical bonds, but that the benzene molecules are held in cavities formed by the solid structure of the complex.[189]

A study of the reaction between nickel tetracarbonyl and *o*-phenylenebisdimethylarsine has shown that two of the carbonyl groups are readily replaced by the chelate group to yield a stable, crystalline, diamagnetic compound of the formula $Ni(CO)_2$(diarsine) : attempts to replace all four carbonyl groups, however, were unsuccessful. Oxidation of this complex with iodine liberates carbon monoxide, giving the compound $NiI_2$(diarsine), the first of a previously unknown class of *cis*-planar bivalent nickel complexes. The corresponding chloride and bromide are much less stable. By oxidation of the bromide with excess of bromine, a tervalent nickel complex bromide of the formula $NiBr_3$(diarsine) has been prepared.[190]

Details have been given of a convenient laboratory method of preparation of nickel and cobalt carbonyls and of a number of their derivatives, which is based on the reaction between carbon monoxide, at atmospheric pressure, and aqueous ammoniacal solutions of nickel and cobalt salts in the presence of sodium dithionite.[191]

Several new reactions of sodium in liquid ammonia with the carbonyls of cobalt and iron have been reported.[192]

Cobalt(II) chloride is well known to form a mono-, a di-, and a hexahydrate, but there is less definite evidence of the existence of a tetrahydrate. An investigation of the system $CoCl_2$–$H_2O$–acetone has now shown that the tetrahydrate and a hitherto unreported trihydrate also exist over narrow ranges of water activity.[193]

A spectrophotometric study of the deep blue solution obtained when a cobalt(II) salt is dissolved in strongly alkaline solution has shown that the colour is due to a trihydroxycobalt(II) ion, $Co(OH)_3^-$.[194]

The products of the reduction of cobalt(II) nitrate with two equivalents of potassium in liquid ammonia are (i) insoluble cobalt(II) amide and (ii) a mixture of soluble nitrate and nitrite. If a large excess of potassium is used, however, almost all the nitrate is reduced to nitrite, and the insoluble product consists principally of potassium hydroxide and elemental cobalt. The cobalt which is obtained by the reduction of cobalt(III) bromide in liquid ammonia in this way exhibits a marked activity as a catalyst for the hydrogenation of allyl alcohol at room temperature.[195]

Some preliminary results have been published of an investigation of the

---

[188] Symposium, *Ind. Eng. Chem.*, 1952, **44**, 949.

[189] J. H. Rayner and H. M. Powell, *J.*, 1952, 319.

[190] R. S. Nyholm, *J.*, 1952, 2906.

[191] W. Hieber, E. O. Fischer, and E. Böckley, *Z. anorg. Chem.*, 1952, **269**, 308.

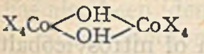
[192] H. Behrens, *Z. Naturforsch.*, 1952, **7**, *b*, 321.

[193] L. I. Katzin and J. R. Ferraro, *J. Amer. Chem. Soc.*, 1952, **74**, 275.

[194] S. Gordon and J. M. Schreyer, *ibid.*, p. 3169.

[195] G. W. Watt and C. W. Keenan, *ibid.*, p. 2048.

preparation and properties of the curious compound known as "cobaltic acetate"—the product obtained by anodic oxidation of cobalt(II) acetate tetrahydrate in glacial solution. The elucidation of the structure of this compound presents some difficulties, but its properties seem to indicate a possibility that it may be a binuclear complex containing the μ-dihydroxo-bridge grouping (inset).[196]



$X_4Co\!<\!{}^{OH}_{OH}\!>\!CoX_4$

Tracer experiments with $H_2{}^{18}O$ have shown that in the aquation of carbonatopentamminocobalt(III) ion

$$[Co(NH_3)_5CO_3]^+ + 2H^+ = [Co(NH_3)_5H_2O]^{+++} + H_2CO_3$$

which takes place rapidly in water, and still more rapidly when the solution is acidified, the cobalt–oxygen bond remains intact, the removal of carbonate from the complex ion taking place by the removal of carbon dioxide, *i.e.*, by the breaking of the carbon–oxygen bond.[197] The mechanism is therefore similar to that observed in the hydrolysis of an ester.[198]

A study of the type of bonding in a number of bidentate chelate cobalt complexes has been made by a radio-isotope exchange technique, using $^{60}Co$. Where the bonding is mainly ionic, a rapid exchange occurs and as the covalent character of the bonding increases so one can expect a diminution in the rate of exchange of the cobalt. The same technique has been used to study the behaviour of bis(salicylideneaniline)cobalt(II) and cobalt(II) acetate in pyridine solution on alumina and similar surfaces and on an ion-exchange resin. The break-up of the complex on these surfaces points to the considerable ionic nature of the binding of the cobalt atom in such complexes.[199]

Further sexadentate cobalt(III) compounds have been prepared by the use as ligands of condensation products of a series of sulphur-containing αω-diamines of the general formula: $NH_2\cdot[CH_2]_x\cdot S\cdot[CH_2]_y\cdot S\cdot[CH_2]_z\cdot NH_2$, where $x$, $y$, and $z$ are 2 or 3, with salicylaldehyde or 2-hydroxy-1-naphthaldehyde. Most of the complex salts prepared have been resolved into optical isomers, some with extremely high rotations.[200]

In connection with a study of the magnetic moments of octahedral complexes of Cr, Mn, Ni, Co, and Fe, with the chelate agents dipyridyl, and *o*-phenylenebisdimethylarsine, $C_6H_4(AsMe_2)_2$, the following new compounds have been prepared: $[Co(diarsine)_3](ClO_4)_2$, $[Co(diarsine)_3](ClO_4)_3$, $[Co(diarsine)_2(OAc)_2](ClO_4)$, $[Co(dipy)_3](ClO_4)_3,3H_2O$, and $[Cr(dipy)_2Cl_2]Cl,2H_2O$. Also the co-ordination of tervalent chromium with a tertiary arsine has been reported for the first time. In compounds of the type $M^{II}(dipy)_3X_2$ the bonds are ionic $4s4p^34d^2$ when $M^{II}$ = Mn or Co and covalent $3d^24s4p^3$ when the metal is Fe or Cr. The paramagnetism of the corresponding nickel compounds indicates that the bonds are ionic rather than covalent. In the dipyridyl complexes of tervalent iron or cobalt, the bonds are covalent, as are also the bonds in the stable octahedral complexes of the ditertiary arsine with Ni, Co, and Fe in their bi- and tervalent states.[201]

---

[196] J. A. Sharp and A. G. White, *J.*, 1952, 110.

[197] J. P. Hunt, A. C. Rutenberg, and H. Taube, *J. Amer. Chem. Soc.*, 1952, **74**, 268.

[198] M. Polanyi and A. L. Szabo, *Trans. Faraday Soc.*, 1934, **30**, 508.

[199] B. West, *J.*, 1952, 3115, 3123.

[200] F. P. Dwyer, N. S. Gill, E. C. Gyarfas, and F. Lions, *J. Amer. Chem. Soc.*, 1952, **74**, 4188.

[201] F. H. Burstall and R. S. Nyholm, *J.*, 1952, 3570.

Potentiometric titrations in aqueous solution show that cobalt tetracarbonyl hydride, $Co(CO)_4H$, is a strong acid and that iron tetracarbonyl dihydride, $Fe(CO)_4H_2$, is a weak dibasic acid.[202]

A new method has been described for the preparation of nitrosylcobalt tricarbonyl $Co(NO)(CO)_3$ and of dinitrosyliron dicarbonyl $Fe(NO)_2(CO)_2$; it consists in the acidification of solutions of the alkali salts of the respective carbonyl hydrides in the presence of corresponding amounts of nitrite,[203] *e.g.*

$$Fe(CO)_5 + 3NaOH \longrightarrow Fe(CO)_4HNa + Na_2CO_3 + H_2O$$

$$Fe(CO)_4HNa + 2NaNO_2 + 3HOAc \longrightarrow Fe(NO)_2(CO)_2 + 2CO + 3NaOAc + 2H_2O$$

Iron can be removed from solutions of ferric phosphate by either cation- or anion-exchange resins. Evidence has been obtained which indicates that the extraction of the iron as an anion is due to the formation of a complex ion containing 3 phosphate groups to each iron atom, the phosphate groups presumably behaving as bidentate groups, forming $H_3[Fe(HPO_3)]$ or $H_6[Fe(PO_4)_3]$.[204]

What is claimed to be the first cationic iron(III) complex to be obtained in enantiomorphic forms has been prepared by the ceric ammonium nitrate–nitric acid oxidation of (+)- and (−)-tris-2 : 2′-dipyridyliron(II) perchlorates. The resolution of the latter compounds was carried out through the iodide antimonyl tartrate: (+)- and (−)-tris-1 : 10-phenanthrolineosmium(III) perchlorates have also been prepared by oxidation of the corresponding osmium(II) compounds by chlorine.[205]

The stabilities of some 5-substituted 1 : 10-phenanthrolineiron(II) complexes have also been determined.[206]

A contribution has been made to the preparation of trinuclear ruthenium compounds by that of the basic acetate, $[Ru_3(OAc)_6(OH)_2](OAc),7H_2O$, by the reduction of ruthenium tetroxide by acetaldehyde in anhydrous acetic acid–carbon tetrachloride solution. This compound dissolves in water to give an intensely blue solution, and rapidly in pyridine to give a solution which becomes green when warmed. Addition of chloroplatinic acid to the aqueous solution of the pyridyl derivative precipitates $[Ru_3(OAc)_6py_5]ClPtCl_6$.[207]

Sexavalent ruthenium is commonly met with as an anion in the form of alkali-metal ruthenates $M_2RuO_4$, which are stable in alkali but immediately disproportionate on treatment with acid, into the +4 and +8 oxidation states; no simple salts of the ruthenyl cation $RuO_2^{++}$ have hitherto been isolated. The reduction of ruthenium tetroxide by a variety of reducing agents in sulphuric acid solution has given evidence that a sexavalent state is capable of existence, as a green solution, in this medium, but decomposes in a few hours at room temperature, probably by the above disproportionation. The experiments suggest, however, that even in these solutions the ruthenium is present as the anionic complex $[RuO_2(SO_4)_2]^{=}$ rather than as the ruthenyl ion $RuO_2^{++}$.[208]

A study has been made by spectrophotometric methods of the solution

---

[202] W. Hieber and W. Hübel, *Z. Naturforsch.*, 1952, **7**, *b*, 322.

[203] F. Seel, *Z. anorg. Chem.*, 1952, **269**, 40.

[204] J. E. Salmon, *J.*, 1952, 2316.

[205] F. P. Dwyer and E. C. Gyarfas, *J. Amer. Chem. Soc.*, 1952, **74**, 4699.

[206] W. W. Brandt and D. L. Gullstrom, *ibid.*, p. 3532.

[207] F. S. Martin, *J.*, 1952, 2682. [208] *Idem*, *J.*, 1952, 3055.

chemistry of ruthenium in the +6, +7, and +8 oxidation states. The +7 state, which is known in the solid compounds $NaRuO_4,H_2O$ and $KRuO_4$, has also been identified in aqueous solution, and its properties studied.[209]

Spectrophotometric techniques have also been used to study the formation of a number of complex compounds of ruthenium. The orange-coloured complex formed by the reaction of ruthenium(IV) perchlorate with thiosemicarbazide was identified as $Ru[SC(:NH)\cdot NH\cdot NH_2]^{+2}$, and the bright red complex with 4-phenylthiosemicarbazide as $Ru[SC(:NPh)\cdot NH\cdot NH_2]^{+2}$. Both the thiosemicarbazide and the 4-phenylthiosemicarbazide behaved as weak acids, liberating a hydrogen ion for each molecule of ligand which entered the complex.[210]

With a number of complexing ions, both ruthenium(IV) and ruthenium(III) form the same coloured complex, the quadrivalent ruthenium being reduced in each case by the ligand before complexing occurs; *i.e.*, with thiocyanate, the same deep blue $[Ru(CNS)]^{+2}$, with thiourea the blue-green complexes, $Ru[SC(:NH)\cdot NH_2]^{+2}$ and $Ru[SC(:NH)\cdot NH_2]_3$,[211] and with dithio-oxamide, the blue-green complexes $Ru[SC(:NH)\cdot CS\cdot NH_2]^{+2}$ and $Ru[SC(:NH)\cdot CS\cdot NH_2]_3$.[212]

A new series of a nitrosopentamminoruthenium(III) ion $[Ru(NH_3)_5\cdot NO]^{+3}$ has been prepared: the salts are diamagnetic.[213]

A number of salts of tetracyanopalladic(II) acid have been studied:[214] the acid, which is prepared by acidification of a solution of palladium(II) cyanide in excess of cyanide ions, forms insoluble salts with silver and copper(II) ions or with their ammines. It also forms normal salts with benzidine, naphthaquinoline, and oxine, and the salts of nitron. Palladium(II) cyanide itself also forms co-ordination compounds with a large number of nitrogen-containing organic compounds.

A number of fluoro-complexes of palladium and gold of the type $M_2[PdF_6]$ and $M[AuF_4]$ (M = alkali metal) have been prepared, *viz.*, $Cs_2PdF_6$, $Rb_2PdF_6$, $K_2PdF_6$, and $KAuF_4$, by the fluorination of the corresponding chlorine compounds. All these compounds are bright orange to yellow and, in contrast to the corresponding chlorine or bromine compounds, are immediately hydrolysed by water. During the fluorination of the alkali-metal chloroaurates red intermediate products—possibly mixed fluorochloroaurates—were obtained: these were more stable towards water.[215]

The reactions of *NN*-diethylglycine and *N*-ethyl-*N*-methylglycine with cobalt(III) and platinum(II) have been studied, and dinitro-(*N*-ethyl-*N*-methylglycine)platinate(II) has been prepared; this has been shown to contain an asymmetric nitrogen atom through its resolution by fractionation with (—)-quinine and treatment with optically active quartz powder.[216]

F. FAIRBROTHER.

[209] R. E. Connick and C. R. Hurley, *J. Amer. Chem. Soc.*, 1952, **74**, 5012.
[210] R. P. Yaffe and A. F. Voigt, *ibid.*, p. 5043.
[211] *Idem, ibid.*, pp. 2500, 2503.
[212] *Idem, ibid.*, p. 3163.
[213] K. Gleu and I. Buddecker, *Z. anorg. Chem.*, 1952, **268**, 202.
[214] F. Feigl and G. B. Heisig, *J. Amer. Chem. Soc.*, 1951, **73**, 5630.
[215] R. Hoppe and W. Klemm, *Z. anorg. Chem.*, 1952, **268**, 364.
[216] J. R. Kuebler and J. C. Bailar, Jr., *J. Amer. Chem Soc.*, 1952, **74**, 3535.

# ORGANIC CHEMISTRY.

## 1. INTRODUCTION.

THE following report on organic chemistry covers work published during the year except for the theoretical topics which are better reviewed at longer intervals than one year, so that the work discussed can be considered critically in relation to contemporary views. The section on theoretical organic chemistry, therefore, deals with the more salient features of the chemistry of free radicals in solution, since that rapidly advancing field has not been reviewed since 1948. The mechanism of the ozonisation of aromatic compounds, which was last reported in 1947, now merits special attention in view of the wider application of recent theories to other contemporary studies of the reactivity of polynuclear aromatic systems.

Perhaps the most novel discoveries of the year are the recognition of iron di*cyclo*pentadienyl as a new type of symmetrical structure showing typical aromatic behaviour, and the use of clathrate compounds for optical resolutions. In synthetic organic chemistry the year has been notable for a stereospecific total synthesis of cortisone, a synthesis of flavin-adenine-dinucleotide, a synthesis of morphine, and a synthesis of all-*trans*-methylbixin; each of these considerable achievements exemplifies in some way or other the high degree of specificity of modern techniques in organic chemistry, to which has been added a welcome catalytic hydrogenation method for reducing triple bonds to double bonds. The structure of lanosterol has now been established and the stereochemistry of the β-amyrin and lupeol groups of triterpenes has been elucidated, while appreciation of the rich variety of types of substance found to occur naturally is increased by the isolation of an antibiotic incorporating every known type of carbon–carbon unsaturation.

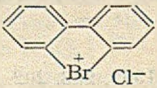
The increasing use of enzymic methods for the study of organic chemical problems is seen in recent work on nucleotides and macromolecules, while expanding facilities for infra-red spectroscopy are reflected in the increasing use being made of this tool in structural problems.

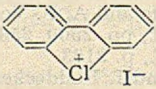
J. W.
W. A. W.

## 2. THEORETICAL ORGANIC CHEMISTRY.

**Bromonium Cations.**—Though iodonium salts have long been known, stable bromine and chlorine analogues (I) and (II) have been prepared by

(I)





(II)

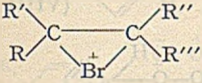
R. B. Sandin and A. S. Hay [1] only in the year under review. The corresponding iodonium salts were made by L. Mascarelli in 1907.[2] Previously,

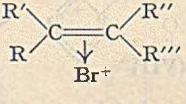
---

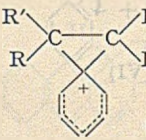
[1] *J. Amer. Chem. Soc.*, 1952, **74**, 274.

[2] *Atti R. Accad. Lincei*, 1907, **16**, II, 562; 1908, **17**, II, 580; 1912, **21**, II, 617; *Gazzetta*, 1908, **38**, 624.

cyclic bromonium cations (III) had been postulated by I. Roberts and G. E. Kimball[3] in order to explain *trans*-addition to olefins. Their theory had received strong support from the work of S. Winstein and H. J. Lucas[4] and other American investigators of the stereochemistry of the reactions of olefins, 1 : 2-glycols, and their derivatives.[5] M. J. S. Dewar has advocated the π-bond formula (IV) but there now seems to be no special need for it, since it depends on the assumption that a halogen atom can only form a single covalent bond.[6] Related studies of neighbouring group displacement reactions[7] have led D. J. Cram to postulate the transient existence of a "phenonium ion" (V), but a detailed report of this subject is deferred until next year.


(III)


(IV)


(V)

**Ozonisation. The Action of Double-bond Reagents.**—Continuation of the detailed studies of ozonisation by J. P. Wibaut and his school in Amsterdam[8] has in the past two years led to results of major theoretical significance. Kinetic measurements of the velocities of ozonisation of several benzene, pyridine, quinoline, and *iso*quinoline derivatives have been made.[9–14] The velocity of addition of ozone to benzene is proportional to the concentration of the ozone as well as to that of the benzene.[11–13] Apparently benzene triozonide is formed in successive stages, the velocity of the first being much less than that of the subsequent ones. Alkyl substituents increase the reaction velocity,[9, 10] whilst halogens have the opposite effect, as the following sequences show:[10, 14] $C_6H_6 < C_6H_5Me < C_6H_5Et$; $p\text{-}C_6H_4Me_2 > m(o)\text{-}C_6H_4Me_2 > C_6H_5Me$; $C_6H_6 > C_6H_5F > C_6H_5Cl \simeq C_6H_5Br$; $C_6H_5Me > C_6H_5{\cdot}CH_2Cl > C_6H_5{\cdot}CHCl_2 > C_6H_5{\cdot}CCl_3$. Anisole is attacked exceedingly rapidly whilst pyridine derivatives do not react as fast as their benzene analogues.[14] This has led J. P. Wibaut and F. L. J. Sixma[10, 15] to conclude that the first stage in the ozonisation of an aromatic compound is an electrophilic reaction in which the central, electropositively polarised, oxygen atom of the ozone molecule (VI) becomes attached to the activated aromatic system, giving the primary transition state (VII). In this, only four electrons remain distributed over the five carbon centres, 2—6, of the benzene ring, which is thus positively charged, whilst the two terminal oxygen atoms of the ozone residue are negatively charged. Consequently, stabilisation of (VII) occurs very rapidly, to give the structures (VIII) and (IX) which, in the case of benzene alone, will be identical and correspond to H. Staudinger's

---

[3] *J. Amer. Chem. Soc.*, 1937, **59**, 947. [4] *Ibid.*, 1939, **61**, 1576.

[5] See E. R. Alexander, "Ionic Organic Reactions," J. Wiley & Sons, New York, 1950, pp. 100—102. [6] See *Ann. Reports*, 1950, **47**, 133; 1951, **48**, 118.

[7] *J. Amer. Chem. Soc.*, 1949, **71**, 3863, 3871, 3883; 1952, **74**, 2129, 2137, 2149, 2152, 2159. [8] *Ann. Reports*, 1947, **44**, 127.

[9] J. van Dijk, *Rec. Trav. chim.*, 1948, **67**, 945.

[10] J. P. Wibaut, F. L. J. Sixma, L. W. F. Kampschmidt, and H. Boer, *ibid.*, 1950, **69**, 1355. [11] H. Boer, F. L. J. Sixma, and J. P. Wibaut, *ibid.*, 1951, **70**, 509, 1005.

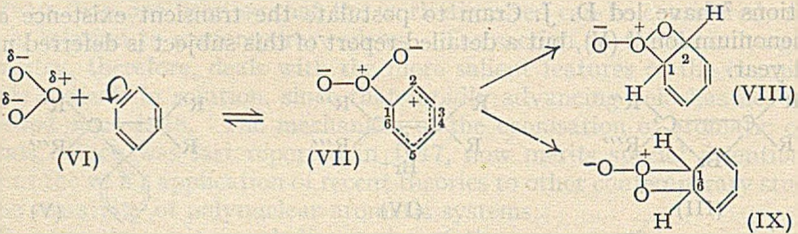
[12] H. Boer and F. L. J. Sixma, *ibid.*, p. 997.

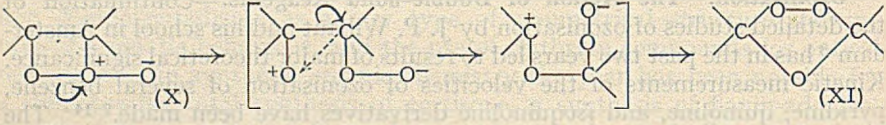
[13] J. P. Wibaut and F. L. J. Sixma, *ibid.*, 1952, **71**, 761.

[14] F. L. J. Sixma, *ibid.*, p. 1124.

[15] J. P. Wibaut and F. L. J. Sixma, *Proc. K. Ned. Akad. Wet.*, 1948, **51**, 776.

" molozonides." [16] The conversion of these initial molozonides of olefins (X) into the stable structures (XI), which have been established by the work of A. Rieche with simple olefins [17] and of B. Witkop and J. B. Patrick [18] in the indole series, has been explained by R. Criegee as an intramolecular change.[19] This completes the fission of the carbon–carbon double bond; opening up of the ozonide finally occurs by an acid–base-catalysed hydrolysis [20] which has a mechanism similar to that involved in the acid-catalysed decompositions of hydroperoxides.[21]





The electrophilic nature of the attack of ozone on aromatic compounds (VI ⟶ VII) has been substantiated [10, 11] by showing that the reaction can be catalysed by the " Lewis acids " aluminium chloride, ferric chloride, and boron fluoride. These electron-deficient molecules enhance the electrophilic character of the ozone :

$$\mathrm{O{=}\overset{+}{O}{-}\overset{-}{O} + AlCl_3 \rightleftharpoons O{=}\overset{+}{O}{-}O{-}\overset{-}{Al}Cl_3}$$
$$\mathrm{Cf.\ RCl + AlCl_3 \rightleftharpoons R^+[AlCl_4]^-}$$

The view that the initial stage in the ozonisation of an aromatic compound resembles nitration, or the Friedel–Crafts reaction, has been challenged by G. M. Badger [22] who maintains that ozone, osmium tetroxide, and diazoacetic ester differ from cations such as $NO_2^+$ in that they attack the $\pi$-electrons of double bonds and not localised electrons at the site of individual carbon atoms.[23] It is characteristic of these " double-bond reagents " that they can often attack polycyclic aromatic systems at bonds of high electron density which sometimes do not correspond to the carbon centres attacked by typical electrophilic substituting agents. Pyrene exemplifies this; ozonisation occurs at the " K " *bonds* 1—2 and 6—7 whereas nitration occurs almost exclusively at *atoms* 3 or 5. Though they concede that the formation of a " $\pi$-complex " [24] may possibly precede the formation of the transition structure, Sixma and Wibaut [25] counter Badger's argument by pointing out that the reversible formation of the transition structure (VII) is followed in ozonisation by a process different from that which occurs in

---

[16] *Ber.*, 1925, **58**, 1088. [17] *Ibid.*, 1932, **65**, 1274; *Annalen*, 1942, **553**, 187.

[18] *J. Amer. Chem. Soc.*, 1952, **74**, 3855. Cf. this vol., p. 123.

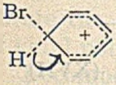
[19] *Annalen*, 1948, **560**, 127; cf. J. E. Leffler, *Chem. Reviews*, 1949, **45**, 385.

[20] B. Witkop and J. B. Patrick, *J. Amer. Chem. Soc.*, 1952, **74**, 3861.

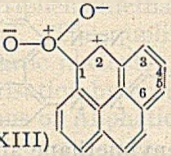
[21] See p. 129. [22] *Rec. Trav. chim.*, 1952, **71**, 468. [23] *Quart. Reviews*, 1951, **5**, 147.

[24] M. J. S. Dewar, " Electronic Theory of Organic Chemistry," Oxford Univ. Press, 1949, pp. 17, 169. [25] *Rec. Trav. chim.*, 1952, **71**, 473.

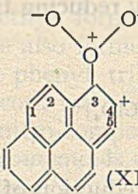
bromination or nitration. Ozonisation involves ring closure by stabilisation of vicinal electrostatic charges of opposite sign (VII→VIII, IX), whereas bromination involves stabilisation by extrusion of a proton, (XII), and the re-formation of the aromatic sextet. The Dutch workers calculate that if the stabilising effects of vicinal charges are taken into account then the transition structure (XIII) has a slightly lower energy content than (XIV), though in pyrene itself the electron density is higher at atom 3 than at atom 1, since the localisation of the nuclear positive charge in (XIII) gives an activated phenanthrene structure with an energy level below that of the activated naphthalene arrangement in (XIV). Ring closure of (XIII) thus



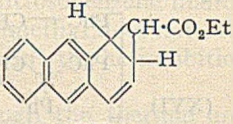
(XII)



(XIII)



(XIV)



(XV)

gives a more stable product than that which could be derived from (XIV), and consequently ozonisation of pyrene is to be expected at bond 1—2. Sixma and Wibaut[25] suggest that the whole conception of mechanistically distinct "double-bond reagents" is untenable.

Ethyl diazoacetate has been considered to be another reagent of this type[26] since it adds to the 1 : 2-positions of anthracene. However, the reaction products, e.g., (XV), which have localised double bonds since they easily add on bromine, are much less reactive towards ethyl diazoacetate than are the aromatic molecules from which they have been formed: here again "double-bond character" cannot be a satisfactory explanation of the chemical reactivity. It is evident to the Reviewer that ethyl diazoacetate is typically a reagent which attacks *polarisable* bonds and that the final ring closure would favour reaction *via* a particular transition state; osmium tetroxide is a reagent with similar characteristics. All these reagents thus exemplify the theoretical dangers inherent in attempts to assess the energy levels of the transition states of organic reactions by calculations which take into account the detailed electronic structure of only one of the participating molecules.

### Free radicals and their reactions.

**Triphenylmethyl and Related Compounds.**—Of the methods available for determining the degree of dissociation of compounds of the hexaphenylethane series, most reliance has, in recent years, been placed on magnetic susceptibility measurements. G. W. Wheland[27] and P. W. Selwood and R. M. Dobres[28] have pointed out that this method has a serious inherent error: molecular diamagnetic susceptibility is compounded of both atomic and resonance terms, and the latter, which may be large for stable mesomeric radicals, is incalculable and has hitherto been neglected. Consequently if the paramagnetism, $\chi_\mu$, due to an unpaired electron is estimated as $\chi_\mu = \chi_{\textit{paramag., found}} + \chi_{\textit{diamag., atomic, calc.}}$ it gives results which may be much too

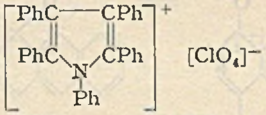
---

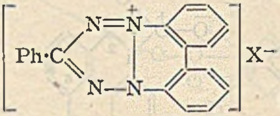
[26] G. M. Badger, J. W. Cook, and A. R. M. Gibb, *J.*, 1951, 3456.

[27] "Advanced Organic Chemistry," J. Wiley & Sons, New York, 1949, p. 696.

[28] *J. Amer. Chem. Soc.*, 1950, 72, 3860.

low. The discrepancy is noticeable when observations are made over a range of temperatures. This difficulty may however be overcome by measuring the paramagnetic resonance absorption.[29] Colorimetric measurements, on absorption bands characteristic of the free radicals themselves, show the expected temperature dependence and are considered to be trustworthy.[28] Magnetic-susceptibility methods however are still valuable for measuring reaction velocities [30] and for the qualitative detection of free radicals. New radicals which have been examined in this way include pentaphenylpyrrolium perchlorate (XVI) [31] and the uncharged reduction product of the tetrazolium salt (XVII).[32] Somewhat similar in reactions are the free radicals obtained by reducing triphenylmethane dyes with zinc dust in pyridine solution.[33]

(XVI) 

 (XVII)

Stepwise polarographic reduction of triphenylmethane and acridine dyes has been studied by R. C. Kaye and H. I. Stonehill [34] who consider that the free-radical stage is of biological significance. They point out that the chemotherapeutically active dyes give radicals which are stable over a considerable pH range, and they suggest that these radicals may act by stopping reaction chains essential for bacterial metabolism.[35] Polarographic reduction of coenzymes has also been examined from this viewpoint.[36] Chemical one-electron reduction of pyridinium salts has also been discussed.[37]

K. Ziegler and W. Deparade [38] have shown that many compounds such as 2 : 3-dimethyl-2 : 3-diphenylbutane slowly evaporate at temperatures well below their normal boiling points owing to dissociation and disproportionation :

$$\mathrm{CPhMe_2{-}CPhMe_2} \overset{\text{Slow}}{\rightleftharpoons} 2\,\cdot\mathrm{CPhMe_2} \overset{\text{Fast}}{\rightleftharpoons} \mathrm{CHPhMe_2} + \mathrm{CPhMe{:}CH_2}$$

The immediate addition of the transient radicals to the oxygen atoms of chloranil [39] can be used to determine rates of dissociation, and in this way the results tabulated have been obtained. The activation energies, $E$,

| Groups in $R_3C{\cdot}CR_3$ | Temp. of noticeable decomp. | $E$ (kcal.) |
|---|---|---|
| 4Me, 2Ph | +240° | 50 |
| 4Et, 2Ph | 142 | — |
| $4Pr^n$, 2Ph | 110 | 34—38 |
| $4Bu^n$, 2Ph | 110 | 37—39 |
| 2Me, 4Ph | 60 | 30 |
| 4-*cyclo*hexyl, 2Ph | 30 | 21 |
| 6Ph | −20 | 19 |

---

[29] C. A. Hutchison, A. Kowalsky, R. C. Pastor, and G. W. Wheland, *J. Chem. Phys.*, 1952, **20**, 1485.

[30] H. Boardman and P. W. Selwood, *J. Amer. Chem. Soc.*, 1950, **72**, 1372; R. M. Dobres and P. W. Selwood, *ibid.*, p. 5731.

[31] R. Kuhn and H. Kainer, *Chem. Ber.*, 1952, **85**, 498.

[32] R. Kuhn and D. Jerchel, *Annalen*, 1952, **578**, 1.

[33] E. Weitz, L. Müller, and K. Dinges, *Chem. Ber.*, 1952, **85**, 878.

[34] *J.*, 1951, 27, 2638; 1952, 3231, 3240.

[35] R. C. Kaye, *J. Pharm. Pharmacol.*, 1950, **2**, 902.

[36] R. C. Kaye and H. I. Stonehill, *J.*, 1952, 3244.

[37] F. Kröhnke, *Chem. Ber.*, 1950, **83**, 35.

[38] *Annalen*, 1950, **567**, 123.

[39] See p. 117.

which accord excellently with theoretical predictions,[40] are consistent with measurements made by other methods. Thus a value of 48 kcal. has been obtained for the dissociation energy of dibenzyl.[41]

The radicals of the compounds $CR_3{\cdot}CR_3$ are polymerisation catalysts: chain-starting rates can be followed by substituting the aromatic nuclei with iodine or, better, radio-active iodine.[42]

The infra-red spectrum of triphenylmethyl favours a planar structure.[43]

G. S. Hammond and A. Ravve [44] have made an interesting study of the reaction between triphenylmethyl and nitrobenzene. The latter is immediately reduced to a complex mixture of nitrosobenzene, azoxybenzene, and azobenzene, whilst the triphenylmethyl forms the peroxide; diphenyl, terphenyl, and triphenylmethanol are also formed. Nitrosobenzene mainly yields azobenzene. Thus, unlike free phenyl, triphenylmethyl does not substitute the aromatic nucleus. The work may be relevant to the inhibition of vinyl polymerisation by aromatic nitro-compounds.[45]

**Decompositions of Aliphatic Azo-compounds.**—Though the thermal and photochemical decomposition of azomethane, MeN:NMe, has been used since 1933 for generating free methyl radicals in the gas phase,[46] the use of aliphatic azo-compounds for preparing active free radicals in the liquid phase has only developed since 1949, when Madison Hunt, in a patent for the du Pont Co.,[47] introduced them as catalysts for the polymerisation of olefins. The simplest of these compounds, αα'-azo*iso*butyronitrile (XVIII; X = CN) which now has several trade names (Porofor-N, ADIB, AZDN), was first prepared in 1896 by J. Thiele and K. Heuser [48] by condensing acetone, hydrazine, and hydrogen cyanide, and oxidising the resulting symmetrical hydrazine with bromine-water. Many ditertiary azo-compounds can be prepared satisfactorily in this way; [49] in difficult cases hydrogen cyanide can be added to the azines RR'C:N·N:CRR' under pressure.[50] Some primary and secondary azo-compounds can be prepared by similar methods,[51] but they are less useful for the preparation of free radicals since they may isomerise to hydrazones in polar solvents.

When heated at 80—120° in an indifferent solvent, or on exposure to light of λ 3000—3700 Å,[52] these azo-compounds evolve nitrogen quantitatively giving the free aliphatic radicals (XIX) which react together to form the dimer (XX), together with smaller amounts of products of disproportionation reactions (XXI, XXII). The olefin (XXI), however, so rapidly reacts with the free radicals that only the products (XXIII) and (XXIV)

---

[40] M. Szwarc, *Quart. Reviews*, 1951, **5**, 22.

[41] C. Horrex and S. E. Miles, *Discuss. Faraday Soc.*, 1951, **10**, 187.

[42] K. Ziegler, W. Deparade, and W. Kulhorn, *Annalen*, 1950, **567**, 151.

[43] G. Karagounis, *Helv. Chim. Acta*, 1951, **34**, 994.

[44] *J. Amer. Chem. Soc.*, 1951, **73**, 1891.

[45] Cf. P. D. Bartlett and H. Kwart, *ibid.*, 1952, **74**, 3969.

[46] J. A. Leermakers, *J. Amer. Chem. Soc.*, 1933, **55**, 3499; F. O. Rice and D. V. Sickman, *ibid.*, 1935, **57**, 1384.

[47] U.S.P. 2,471,959; *Chem. Abs.*, 1949, **43**, 6002. [48] *Annalen*, 1896, **290**, 1.

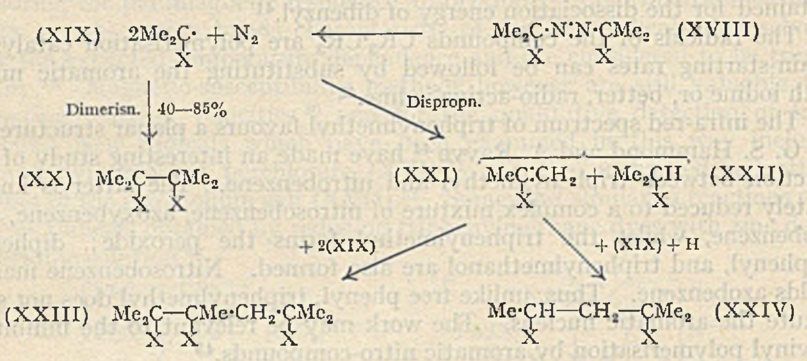
[49] A. W. Dox, *J. Amer. Chem. Soc.*, 1925, **47**, 1471; C. G. Overberger, M. T. O'Shaughnessy, and H. Shalit, *ibid.*, 1949, **71**, 2661; A. F. Bickel and W. A. Waters, *Rec. Trav. chim.*, 1950, **69**, 312, 1490.

[50] U.S.P. 2,469,385; C. G. Overberger and M. B. Berenbaum, *J. Amer. Chem. Soc.*, 1951, **73**, 2618; C. G. Overberger and H. Biletch, *ibid.*, p. 4880.

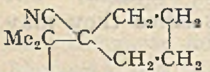
[51] S. G. Cohen, S. J. Groszos, and D. B. Sparrow, *ibid.*, 1950, **72**, 3947.

[52] F. M. Lewis and M. S. Matheson, *ibid.*, 1949, **71**, 747.

indicate that it has been formed.[53] Disproportionation is much more evident with the ester (XVIII; X = $CO_2Me$) than with the nitrile (XVIII; X = CN). Since the radicals (XIX) are the prototypes of the growing chains of acrylic polymers ($R{\cdot}CH_2{\cdot}\dot{C}XMe$) it has been suggested that this work is indicative of the extents to which chain-ending in vinyl polymerisation occurs by combination and by disproportionation. A thermodynamic study[54] indicates that, on account of the opposition of energy and entropy factors, the favoured radical–radical reaction depends upon the temperature; disproportionation is favoured at high temperatures.



From an unsymmetrical ketone there can be prepared both *meso*- and racemic forms of an azo-compound, RR'C(CN)·N:N·C(CN)RR', but, provided that the free radicals have planar configurations, each of these should give the *same*, inactive, free radicals RR'C(CN)·, and consequently they should give identical mixtures of *meso*- and racemic dimers [cf. (XX)]. C. G. Overberger and M. B. Berenbaum[55] have shown that this is indeed the case. Moreover, from a mixture of two different azo-compounds, αα'-azo*iso*butyronitrile and 1 : 1'-azo-(1-cyano-*cyclo*pentane), they have been able to isolate the dimer (XXV) resulting from the cross-linkage of the two different radicals. Similar results had been reported by H. Bretschneider and N. Ajtai[56] who made use of the decomposition of azo-compounds in a synthesis of hexœstrol. Clear experimental evidence for (*a*) the independent existence, and (*b*) the planar structure, of aliphatic free radicals in solution has thus been obtained.


(XXV)

Many kinetic investigations have established that the aliphatic azo-compounds decompose by strictly first-order reactions: rates of decomposition and activation energies have been determined for the purpose of selecting appropriate catalysts for particular technical uses.[49—52] C. E. H. Bawn and S. F. Mellish,[57] who used αα-diphenyl-β-picrylhydrazyl to combine with the free radicals, consider that the activation energy for the dissociation of αα'-azo*iso*butyronitrile is independent of the solvent. L. M. Arnett,[58]

---

[53] A. F. Bickel and W. A. Waters, ref. 49.
[54] J. C. Bevington, *Trans. Faraday Soc.*, 1952, **48**, 1045.
[55] *J. Amer. Chem. Soc.*, 1951, **73**, 2618, 4883.
[56] *Ber.*, 1941, **74**, 571.
[57] *Trans. Faraday Soc.*, 1951, **47**, 1216.
[58] *J. Amer. Chem. Soc.*, 1952, **74**, 2027, 2031.

from polymer studies with an azonitrile labelled with $^{14}C$ in the CN group, considers that stepwise decomposition occurs:

$$RN{:}NR \xrightarrow{\text{Slow}} R\cdot + \cdot N{:}NR \xrightarrow{\text{Fast}} N_2 + \cdot R$$

and thinks that only one of the radicals, probably $RN{:}N\cdot$, operates in polymerising methyl methacrylate, though both may be effective with styrene and acrylonitrile. E. P. Bonsall, L. Valentine, and H. W. Melville[59] consider that only about 25% of the generated $\cdot CMe_2\cdot CN$ radicals may be effective chain-starters in liquid styrene, whilst L. Bateman and A. L. Morris[60] reach a similar conclusion in regard to their chain-starting ability in the autoxidation of olefins. In this case the chain-starting reaction may perhaps be $O_2 + \cdot CMe_2X \longrightarrow \cdot O\cdot O\cdot CMe_2X$, since the tertiary aliphatic radicals do not easily attack C–H bonds, even in aldehydes,[61] and resemble triphenylmethyl much more closely than they do free methyl or free phenyl. O–H bonds too are not attacked, even in quinol,[53, 62] but dehydrogenation of S–H bonds is quite effective.[63] The resulting $RS\cdot$ radicals are surprisingly good dehydrogenators[64] and so thiols, by chain transfer, can catalyse the dehydrogenations of hydrocarbons and of aldehydes by alkyl radicals. In the latter case the chain reaction, $R\cdot + HSR' \longrightarrow RH + \cdot SR'$; $R'S\cdot + R\cdot CHO \longrightarrow R'SH + R\cdot CO\cdot$; $R\cdot CO\cdot \longrightarrow R\cdot + CO$, can be promoted.[65]

Reactions of the tertiary alkyl radicals with halogens and halogen compounds have been studied by M. C. Ford and W. A. Waters.[66] Direct combination occurs with both bromine and iodine. The reaction with sulphuryl chloride can be used to initiate the radical-chain chlorination of compounds such as toluene;[67] this chain can be inhibited by iodine and by chloranil. Homolytic bromination by *N*-bromosuccinimide can be catalysed in the same way, and is then so effective that even *cyclo*hexane can be substituted. Amongst alkyl halides only so-called "positive halogen compounds" have been found to react metathetically, $Z\text{–}Br + \cdot CMe_2X \longrightarrow Z\cdot + Br\text{–}CMe_2X$, and this is ascribed to their tendency to undergo homolysis rather than heterolysis.

In view of their relevance to the inhibition of polymerisation and of autoxidation, the reactions between $\cdot CMe_2X$ radicals ($X = CN, CO_2Me$) and quinones have been investigated in detail.[62] The initial combination occurs regularly at oxygen, though in the case of 1 : 4-naphthaquinone there is a little substitution. The main products are the quinol mono- and di-ethers (XXVII, XXVIII), the latter arising from dehydrogenation of $\cdot CMe_2X$ by the semi-quinone radical (XXVI). Since this radical is a mesomeric hybrid (*a–b*) addition of the second radical to carbon is also possible and products of type (XXIX) have been isolated from substituted quinones. Though in

---

[59] *Trans. Faraday Soc.*, 1952, **48**, 763. [60] *Ibid.*, p. 1149.

[61] E. F. P. Harris and W. A. Waters, *J.*, 1952, 3108.

[62] A. F. Bickel and W. A. Waters, *J.*, 1950, 1764; F. J. Lopez Aparicio and W. A. Waters, *J.*, 1952, 4666; K. Ziegler, E. Eimers, W. Hechelhammer, and H. Wilms, *Annalen*, 1950, **567**, 62.

[63] P. Bruin, E. C. Kooyman, and A. F. Bickel, *Rec. Trav. chim.*, 1952, **71**, 3108.

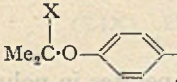
[64] A. F. Bickel and E. C. Kooyman, *Nature*, 1952, **170**, 211; E. F. P. Harris and W. A. Waters, *ibid.*, p. 212.

[65] K. E. J. Barrett and W. A. Waters, *Discuss. Faraday Soc.*, 1953, **14**, 221.

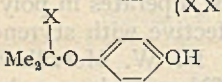
[66] *J.*, 1951, 1851; 1952, 2240.

[67] Cf. M. S. Kharasch and H. C. Brown, *J. Amer. Chem. Soc.*, 1939, **61**, 2142.

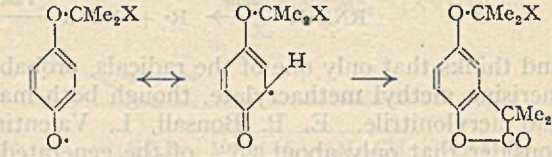
general it is the quinones of highest redox potential which most effectively add ·$CMe_2X$ radicals, steric effects of vicinal substituents are important.



(XXVIII)

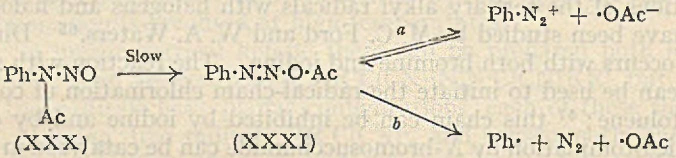


(XXVII)



(XXVIa) (XXVIb) (XXIX)

**Decompositions of Aromatic Diazo-compounds.**—In their first paper on homolytic aromatic substitution W. S. M. Grieve and D. H. Hey[68] reported that benzenediazoacetate (XXXI) decomposed unimolecularly at approximately the same rate in a wide range of aromatic solvents and inferred therefrom that its homolysis (*b* below) was the rate-controlling process, the subsequent reactions of the resulting free radicals, Ph· and ·OAc, with surrounding solvent molecules being very fast. This single postulate is no longer tenable, for R. Huisgen and G. Horeld,[69] who emphasise that benzene diazoacetate is always prepared in the isomeric form of nitrosoacetanilide (XXX), have shown that the rate-determining stage is the *intramolecular* rearrangement of (XXX) to (XXXI) and not the subsequent decompositions of the latter,



(XXX) (XXXI)

which may be either heterolytic and reversible (*a*), or homolytic and irreversible (*b*). Their conclusions have been substantiated by D. F. de Tar[70] and have been accepted and much elaborated by D. H. Hey and his colleagues.[71]

The nitroso-compound (XXX) does not couple with β-naphthol, but in an ionising solvent dye formation is a first-order process, explicable as a slow change (XXX ⟶ XXXI), followed by the rapid ionisation (*a*) to the reactive diazonium cation. In non-ionising solvents, homolysis (*b*) preponderates and the rate of nitrogen evolution then approaches that of the isomerisation (XXX ⟶ XXXI), but in acetic acid process (*a*) removes (XXXI) without loss of nitrogen so that gas evolution is very much slower. The isomerisation can also be followed by measuring the rate of formation of benzenediazonium picrate.[72] Since the rate of change from (XXX) to (XXXI) is not noticeably solvent-dependent or greatly dependent on changes in the nature of the alkyl and aryl groups,[71] it is probably *intramolecular*. This should yield the *trans*-form of the diazoate, though it is now generally accepted that it is the *cis*- rather than the *trans*-diazoates which readily lose nitrogen. However, in the presence of a base such as piperidine, a bimolecular conversion of (XXXII) into a (*cis*?)-diazoate can also occur.[71, 72]

---

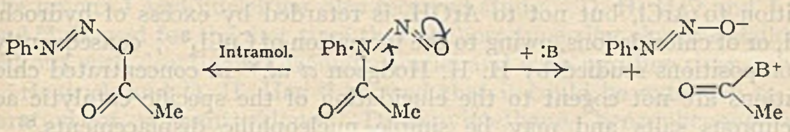
[68] *J.*, 1934, 1797. [69] *Annalen*, 1949, **562**, 137.

[70] *J. Amer. Chem. Soc.*, 1951, **73**, 1446.

[71] *Nature*, 1951, **167**, 725; *Research*, 1951, **4**, 385; *J.*, 1952, 4657.

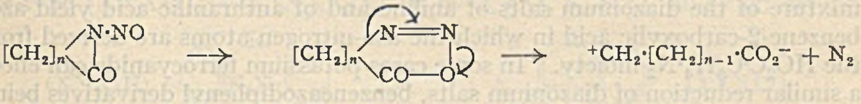
[72] R. Huisgen *et al.*, *Annalen*, 1951, **573**, 163, 181; **574**, 157, 171, 184.

Similar rearrangements have been studied with aliphatic nitroso-lactams.[73] Though these can be formulated as yielding diazoates, aliphatic free radicals



(XXXII)

do not appear to be formed, since the decomposing mixture has no effect on αα-diphenyl-β-picrylhydrazyl [$Ph_2N{\cdot}\dot{N}{\cdot}C_6H_2(NO_2)_3$] which is quickly decolorised by benzene solutions of (XXX). Since aliphatic diazonium cations are unstable the nitrogen evolution may, in these compounds, occur heterolytically.



Huisgen and Horeld[68, 74] point out further that when benzenediazoacetate decomposes in aromatic solvents acetic acid is formed in about 95% yield and that free hydrogen atoms are only formed to a very slight extent.[75] Consequently they suggest that the reaction

$$Ph{\cdot}N_2{\cdot}OAc + PhH \longrightarrow Ph_2 + N_2 + AcOH$$

occurs mainly between vicinal molecules without the liberation of many truly *free* radicals. The induction of vinyl polymerisation, however, gives clear proof that both Ph· and AcO· radicals can, to some extent, have independent existence in this system.[77] Since the acetate radical slowly decomposes in warm solutions ($Me{\cdot}CO{\cdot}O{\cdot} \longrightarrow Me{\cdot} + CO_2$) de Tar[70, 76] examined the extent of carbon dioxide evolution from nitrosoacetanilide solutions. It is greatest (17%) in acetic anhydride, and just detectable in benzene or acetic acid, but does not occur in methanol. The main role of the AcO· radical is thus that of hydrogen abstraction, and in the case of toluene-*o*-diazoacetate this may come from the side-chain; in chloroform solution a 90% yield of indazole can be obtained, though in ethanol only 10%, and none in acetic acid.[78]

Decompositions of diazonium salts have also been studied. Their fluorosilicates may be used to introduce fluorine into the aromatic nucleus.[79] R. Huisgen and H. Nataken[78] suggest that the replacement by hydrogen, $Ph{\cdot}N_2Cl + EtOH \longrightarrow PhH + N_2 + HCl + Me{\cdot}CHO$, is a reaction of the covalent diazo-chloride whilst the reaction, $Ph{\cdot}N_2Cl + EtOH \longrightarrow PhOEt + N_2 + HCl$, probably involves the $Ph{\cdot}N_2^+$ cation. It has now been established

---

[73] R. Huisgen and J. Reinertshofer, *Annalen*, 1952, **575**, 174, 197; G. Nischk and E. Müller, *ibid.*, p. 232.

[74] Cf. R. Huisgen and G. Sorge, *Annalen*, 1950, **566**, 162.

[75] Cf. D. R. Augood, D. H. Hey, and G. H. Williams, *J.*, 1952, 2100.

[76] D. F. de Tar and H. J. Scheifele, Jr., *J. Amer. Chem. Soc.*, 1951, **73**, 1442.

[77] D. H. Hey and G. S. Misra, *Discuss. Faraday Soc.*, 1947, **2**, 279.

[78] *Annalen*, 1951, **573**, 181.

[79] R. D. Beaty and W. K. R. Musgrave, *J.*, 1952, 875.

by two independent groups of workers[80, 81] that the true Sandmeyer reaction is a decomposition of the specific double salt $\mathrm{Ar{\cdot}N_2{\cdot}CuCl_2}$. The decomposition to ArCl, but not to ArOH, is retarded by excess of hydrochloric acid, or of chloride ions, owing to the formation of $\mathrm{CuCl_4{}^{3-}}$; consequently the decompositions studied by H. H. Hodgson *et al.*[82] in concentrated chloride solutions are not cogent to the elucidation of the specific catalytic action of cuprous salts and may be simple nucleophilic displacements.[83] The cyclic single-electron-transfer mechanism proposed by W. A. Waters[84] provides a rational interpretation of this specific action, but the transfer must occur within the molecule of the complex salt so that no *free* aryl radicals are formed. Reduction to an azo-compound, or to a symmetrical diaryl, is favoured if the cuprous salt is added to the diazonium salt solution.[85] By using $^{15}\mathrm{N}$, P. F. Holt and (Mrs.) B. I. Hopson-Hill[86] have shown that a mixture of the diazonium salts of aniline and of anthranilic acid yield azobenzene-2-carboxylic acid in which the azo-nitrogen atoms are derived from the $\mathrm{HO_2C{\cdot}C_6H_4{\cdot}N_2}$ moiety. In some cases potassium ferrocyanide can effect a similar reduction of diazonium salts, benzeneazodiphenyl derivatives being formed.[87]

The decomposition of concentrated aqueous solutions of diazonium salts $\mathrm{Ar{\cdot}N_2X}$ always yields a little of the hydrocarbon ArH, together with the ether ArOAr, but never the diaryl $\mathrm{Ar_2}$.[88] Electron-abstracting substituents favour formation of hydrocarbon. In dilute, weakly acid solutions when undissociated $\mathrm{Ar{\cdot}N{\vdots}N{\cdot}OH}$ might be present ArH is not formed. This supports the view[85] that the hydrocarbon ArH is produced in the tar phase since free phenyl radicals dimerise when generated in aqueous solution.[89]

Hypophosphorous acid is probably the best reagent for reducing diazonium salts to the hydrocarbon ArH : phosphorous acid is much less effective.[90] Small amounts of oxidising agents, *e.g.*, $\mathrm{KMnO_4}$, $\mathrm{K_2Cr_2O_7}$, $\mathrm{Cu^{++}}$, $\mathrm{NO_2{}^-}$, and also copper powder and $\mathrm{Fe^{++}}$, catalyse the reduction with hypophosphorous acid, whilst benzoquinone, but not quinol, inhibits it.[91] Consequently the following radical-chain mechanism has been suggested :

*Initiation :*
$$\underset{\substack{\text{Covalent;}\\ \text{a trace suffices}}}{\mathrm{Ar{\cdot}N{\vdots}N{\cdot}PO_2H_2}} \longrightarrow \mathrm{Ar{\cdot}} + \mathrm{N_2} + \mathrm{O{\vdots}\dot{P}H{\cdot}OH}$$

*Chain :*
$$\mathrm{Ar{\cdot}} + \mathrm{H_3PO_2} \longrightarrow \mathrm{Ar{\cdot}H} + \mathrm{O{\vdots}\dot{P}H{\cdot}OH}$$
$$\mathrm{O{\vdots}\dot{P}H{\cdot}OH} + \mathrm{Ar{\cdot}N_2{}^+} \longrightarrow \mathrm{Ar{\cdot}} + \mathrm{N_2} + [\mathrm{H_2PO_2}]^+$$
$$[\mathrm{H_2PO_2}]^+ + \mathrm{OH^-} \longrightarrow \mathrm{H_3PO_3}$$

*Catalysis :*
$$\mathrm{Cu^{2+}} + [\mathrm{HPO_2}]^- \longrightarrow \mathrm{Cu^+} + \mathrm{O{\vdots}\dot{P}H{\cdot}OH}$$

Since aliphatic amino-groups are not rapidly attacked by nitrous acid at pH >3, whilst diazotisation of aromatic amino-groups is then still possible,

---

[80] W. A. Cowdrey and D. S. Davies, *J.*, 1949, S 48; *Quart. Reviews*, 1952, **6**, 358.
[81] E. Pfeil and O. Velten, *Annalen*, 1949, **562**, 163; **565**, 183.
[82] *J.*, 1941, 770; 1942, 376, 720; 1944, 18, 393.
[83] Cf. E. S. Lewis and W. H. Hinds, *J. Amer. Chem. Soc.*, 1952, **74**, 304.
[84] *J.*, 1942, 266. [85] K. H. Saunders and W. A. Waters, *J.*, 1946, 1154.
[86] *J.*, 1952, 4251. [87] M. C. Ford, W. A. Waters, and H. T. Young, *J.*, 1950, 833.
[88] H. Gies and E. Pfeil, *Annalen*, 1952, **578**, 11; J. H. Gorvin, *J.*, 1951, 1693.
[89] J. H. Merz and W. A. Waters, *J.*, 1949, 2427.
[90] N. Kornblum, A. E. Kelley, and G. D. Cooper, *J. Amer. Chem. Soc.*, 1952, **74**, 3074.
[91] N. Kornblum, G. D. Cooper, and J. E. Taylor, *ibid.*, 1950, 72, 3013.

selective elimination of the latter can be effected by the hypophosphite method.[92]

The union of aryl nuclei has also received study. D. H. Hey and J. M. Osbond [93] showed for the first time that Pschorr-type ring closures could be carried out with deactivated aromatic nuclei and with pyridine rings, whilst R. A. Heacock and D. H. Hey [94] showed that it could be extended to the preparation of phenanthridones. Diphenylmethane, benzophenone, and diphenylamine derivatives can also be cyclised by their methods.[95] The best experimental procedure is to use a suspension of the solid diazonium sulphate, or preferably the fluoroborate, in acetone with copper powder as the catalyst. The success of the reaction in linking up deactivated rings, such as pyridine, is indicative of a homolytic mechanism. However, D. F. de Tar and S. V. Sigmanli,[96] who have also carried out ring closures of the type (XXXIII) ⟶ (XXXIV) (R = O, CO, S, $SO_2$), find that strong acid conditions are helpful and favour an ionic mechanism. Diazonium fluoroborates can also be used, together with phosphorous or arsenious chloride, for preparation of aryl-phosphonic and -arsonic acids.[97]

(XXXIII)  (XXXIV)

L. Horner and H. Stöhr have reported evidence indicating that the photochemical decomposition of diazonium salts may be homolytic in type.[98]

**Homolytic Aromatic Substitution.**—This subject has been reviewed by D. H. Hey in his Tilden lecture.[99] Consistent quantitative values for arylation of nitrobenzene, chlorobenzene, and pyridine by (i) benzoyl peroxide, (ii) sodium benzenediazoate, and (iii) nitrosoacetanilide are now available.[100, 101] They show that in each case nearly 60% of the substitution occurs in the *ortho*-position. By using binary mixtures it has been possible to evaluate the following " partial rate factors " which measure the relative rates of arylation at the individual positions of the molecules $C_6H_5R$ with respect to attack at any one carbon centre in benzene. These values are so very different from the relative rates of aromatic substitution by electrophilic reagents, such as $NO_2^+$, that it is quite clear that the aryl radical approaches the reaction site without exerting any polarising influence on the aromatic molecule. Nevertheless the partial rate factors show that the reactivities of the *ortho*-, *meta*-, and *para*-positions are by no means equal, as

| Substituted molecule | Partial rate factor | | | Total rate of substitution relative to benzene : | |
|---|---|---|---|---|---|
| | *ortho* | *meta* | *para* | arylation | nitration |
| Nitrobenzene ............ | 7·0 | 1·2 | 7·9 | 4·0 | $10^{-4}$ |
| Chlorobenzene ......... | 2·7 | 1·03 | 1·2 | 1·44 | $3 \times 10^{-2}$ |
| Pyridine .................. | — | — | — | 1·15 | Minute |

---

[92] N. Kornblum and D. C. Iffland, *J. Amer. Chem. Soc.*, 1949, **71**, 2137.

[93] *J.*, 1949, 3164, 3172.

[94] *J.*, 1952, 1508, 4059.

[95] D. H. Hey and R. D. Mulley, *J.*, 1952, 2276.

[96] *J. Amer. Chem. Soc.*, 1950, **72**, 965.

[97] G. O. Doak and L. D. Freedman, *J. Amer. Chem. Soc.*, 1951, **73**, 5656, 5658.

[98] *Chem. Ber.*, 1952, **85**, 993.

[99] *J.*, 1952, 1974.

[100] D. H. Hey, A. Nechvatal, and T. S. Robinson, *J.*, 1951, 2892; D. R. Augood, D. H. Hey, and G. H. Williams, *J.*, 1952, 2094.

[101] D. F. de Tar and H. J. Scheifele, Jr., *J. Amer. Chem. Soc.*, 1951, **73**, 1442.

would be the case if homolytic substitution were controlled entirely by the frequency of collision.

These measured partial rate factors are in qualitative accord with the calculations of G. W. Wheland [102] and of the subsequent elaborators of his concepts [103] which relate the ease of homolytic attack on an aromatic system $C_6H_5R$ to the energy increment needed to localise a single electron at any particular carbon atom or permit calculations of the free valence number at particular carbon centres.[104] Though these calculations predicted that both chlorobenzene and nitrobenzene should react more easily than benzene, and mainly in the *ortho*- and *para*-positions, and also that there should be a preponderance of *ortho*-substitution though, since this had not been substantiated by experimental evidence, the theorists had not drawn particular attention to this interesting feature of homolytic aromatic substitution. Earlier qualitative work had been indicative of prevalent *para*-substitution, since *para*-compounds can always be isolated from mixtures much more easily than their isomers.

Quantitative results for the hydroxylations of nitrobenzene,[105] chlorobenzene,[106] and benzoic acid [107] by the radical ·OH generated by (*a*) Fenton's reagent and (*b*) *X*-ray decomposition of water have also been reported by H. Loebl, G. Stein, and J. Weiss. Unlike those considered above they indicate that the relative rates of substitution are much more uniform and follow the order *para* > *ortho* > *meta*, the *meta*-substitution being 20—25%.

Controversial views as to whether homolytic aromatic substitution proceeds by initial hydrogen abstraction, $R\cdot + HAr \longrightarrow RH + \cdot Ar$, or by an addition mechanism, $R\cdot + HAr \longrightarrow {}^{R}_{H}\!\rangle Ar \xrightarrow{R'} RAr + HR'$, are still being presented,[100,108] though the latter is generally favoured. It may well be that the detailed mechanism of homolytic substitution depends on the natures of the radicals involved and perhaps on their mode of generation. Novel substitutions by hydroxyl and nitro-groups have been reported by E. Halfpenny and P. L. Robinson [109] who find that, in dilute acid solutions, hydrogen peroxide and nitrous acid combine to give yellow pernitrous acid which soon decomposes with generation of radicals capable of inducing vinyl polymerisation :

$$H_2O_2 + HNO_2 \xrightarrow{H^+} H_2O + HO\cdot O\cdot NO \longrightarrow HO\cdot + \cdot NO_2 \longrightarrow HNO_3$$

Their results are consistent only with aromatic substitution by an addition mechanism. Attack on benzene by the $\cdot NH_2$ free radical also seems to occur additively.[110]

Unlike nitrobenzene and chlorobenzene, phenol is attacked by ·OH only in the *ortho*- and *para*-positions.[111] Extension of similar work to alkylated

---

[102] *J. Amer. Chem. Soc.*, 1942, **64**, 900.

[103] C. A. Coulson, *Trans. Faraday Soc.*, 1946, **42**, 265; *Research*, 1951, **4**, 317; M. J. S. Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3357; J. D. Roberts and A. Streitweiser, *ibid.*, p. 4723.

[104] See D. H. Hey and G. H. Williams, *Discuss. Faraday Soc.*, 1953, **14**, 216.

[105] *J.*, 1949, 2074. [106] *J.*, 1951, 3275. [107] *J.*, 1949, 3245; 1951, 405.

[108] D. F. de Tar, *J. Amer. Chem. Soc.*, 1950, **72**, 1028; A. F. Bickel and E. C. Kooyman, *Rec. Trav. chim.*, 1952, **71**, 1137; cf. *Discuss Faraday Soc.*, 1953, **14**, 147.

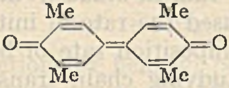
[109] *J.*, 1952, 928, 939.

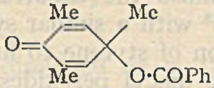
[110] P. Davis, M. G. Evans, and W. C. E. Higginson, *J.*, 1951, 2563.

[111] G. Stein and J. Weiss, *J.*, 1951, 3265.

phenols [112] indicates that the initial reaction may give a mesomeric aryloxy-radical, $Ar{\cdot}OH + {\cdot}OH \longrightarrow ArO{\cdot} + H_2O$, which may either dimerise or pick up a further hydroxyl radical according to the selected reaction conditions. These reactions of phenols show some significant resemblances to oxidations effected by the enzymes tyrosinase and peroxidase. However, comparable studies which have been carried out with aromatic amines [113] stress differences between Fenton's reagent and peroxidase, though again the initial formation of mesomeric aromatic radicals has been postulated. From reactions of phenols with benzoyl peroxide in boiling chloroform the benzoate radical, $Ph{\cdot}CO{\cdot}O{\cdot}$, can be substituted into the nucleus.[114] Both *m*- and *p*-cresol give 4-benzoyloxy-*m*-cresol (Me = 1), *m*-2-xylenol gives the diphenoquinone (XXXV), and mesitol gives the quinole (XXXVI). *tert.*-Butyl hydroperoxide attacks phenols in a somewhat similar way.[115]

(XXXV)





(XXXVI)

F. R. Mayo and W. B. Hardy [116] have attempted to distinguish between homolytic and heterolytic brominations of naphthalene. R. Huisgen and G. Sorge find that the relative rate factor for naphthalene substitution is about 22.[117] R. L. Dannley and M. Gippin [118] have shown that benzoyl peroxide introduces the benzoyloxy-group into naphthalene, and not phenyl as with the less active benzene derivatives. Again, nitro-, chlorine, and bromine are activating groups, promoting attack at positions 4 and 5. With this reagent I. M. Roitt and W. A. Waters [119] find that, even in dilute solutions in chlorobenzene, benzoyloxy-groups are substituted into *meso*-positions of anthracene, 1 : 2-benzanthracene, and 3 : 4-benzpyrene but not into 1 : 2-5 : 6-dibenzanthracene. 9-Methylanthracene is in part substituted at position 10 and in part dimerises to 1 : 2-di-9′-anthranylethane after hydrogen abstraction from the methyl group. In the benzene series a similar formation of dibenzyl derivatives occurs with *p*-xylene and mesitylene, though not with toluene.[120] In contrast, A. F. Bickel and E. C. Kooyman [108] find that 2-cyano-2-propyl radicals *add* to the *meso*-positions of anthracene, and so strongly advocate an addition mechanism for all homolytic aromatic substitutions. E. C. Kooyman and E. Farenhorst [121] have successfully related the ease of radical addition to the polycyclic aromatic hydrocarbons to calculations of " free valence numbers " [122] and by extending these concepts E. C. Kooyman and J. W. Heringa [123] suggest that extended mesomerism, jointly involving both the anthracenoid *meso*-positions and the olefinic " K " regions, of the polycyclic aromatic hydrocarbons and not the latter alone, must be taken into account in deriving

---

[112] S. L. Cosgrove and W. A. Waters, *J.*, 1951, 1726.

[113] D. G. H. Daniels and B. C. Saunders, *J.*, 1951, 2112, 3433.

[114] S. L. Cosgrove and W. A. Waters, *J.*, 1949, 3189; 1951, 388.

[115] T. W. Campbell and G. M. Coppinger, *J. Amer. Chem. Soc.*, 1952, **74**, 1469.

[116] *Ibid.*, p. 911.

[117] *Annalen*, 1950, **566**, 162.

[118] *J. Amer. Chem. Soc.*, 1952, **74**, 332.

[119] *J.*, 1952, 2695.

[120] D. R. Augood, D. H. Hey *et al.*, *Research*, 1951, **4**, 387.

[121] *Nature*, 1952, **169**, 153.

[122] F. H. Burkitt, C. A. Coulson, and H. C. Longuet-Higgins, *Trans. Faraday Soc.*, 1951, **47**, 553.

[123] *Nature*, 1952, **170**, 661.

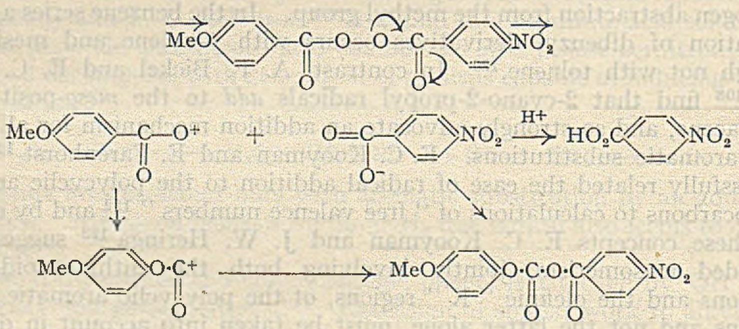
experimentally satisfactory relations between chemical reactivity and carcinogenic action for these molecules.[124]

**Reactions of Peroxides.**—Several aspects of the chemistry of organic peroxides have been discussed in recent reviews [125] to which reference can be made for information published before 1950.

*Acyl peroxides.* By kinetic studies, several investigators have attempted to discriminate between the initial homolytic decomposition of benzoyl peroxide, $(Ph{\cdot}CO{\cdot}O{\cdot})_2 \rightleftharpoons 2Ph{\cdot}CO{\cdot}O{\cdot}$, and the induced decomposition, $R{\cdot} + (Ph{\cdot}CO{\cdot}O{\cdot})_2 \longrightarrow R{\cdot}O{\cdot}COPh + Ph{\cdot}CO{\cdot}O{\cdot}$ (where R· may be Ph· or a radical resulting from attack on a solvent molecule) which may follow.[126]

C. G. Swain, W. H. Stockmayer, and J. T. Clarke [127] have measured the rate of the direct decomposition of a number of substituted benzoyl peroxides by using 3 : 4-dichlorostyrene to combine with the Ph·CO·O· radicals and so minimise the occurrence of the radical-induced decomposition. W. Cooper,[128] with a similar system, has used the rate of initiation of the polymerisation of styrene to find the decomposition rate of both aliphatic and aromatic diacyl peroxides and, by studying chain transfer, has also measured the speed of radical-induced decompositions.[129] Symmetrical substitution of the aryl nucleus alters the reaction velocities in a way that can be interpreted by the Hammett relationships, which have hitherto been tested only for heterolytic reactions. Electron-repelling substituents (Me, OMe) increase the rate of the initial decomposition, but reduce the rate of the radical-induced decompositions. *ortho*-Substituents greatly increase the rate of the direct decomposition. Allyl esters have also been used as chain-stopping solvents,[130] and effects of solvents and of added water have been examined.[131]

Decidedly unsymmetrical diacyl peroxides have been studied by J. E. Leffler [132] who has shown that an acid-catalysed heterolytic decomposition, followed by a molecular rearrangement, is then prone to occur :



---

[124] Cf. G. M. Badger, *Quart. Reviews*, 1951, **5**, 147; R. D. Brown, *ibid.*, 1952, **6**, 63.

[125] D. Swern, *Chem. Reviews*, 1949, **45**, 1 (per-acids); J. E. Leffler, *ibid.*, p. 385 (reaction mechanisms); E. G. E. Hawkins, *Quart. Reviews*, 1950, **4**, 251 (aliphatic peroxides); R. Criegee, *Fortschr. Chem. Forschung*, 1950, **1**, 508; Houben–Weyl, " Methoden der Organischen Chemie," 1952, 4th Edn., Vol. VIII, pp. 3—74.

[126] See *Ann. Reports*, 1948, **45**, 143—145.

[127] *J. Amer. Chem. Soc.*, 1950, **72**, 5426. [128] *J.*, 1951, 3106. [129] *J.*, 1952, 2408.

[130] N. G. Gaylord and F. F. Eirich, *J. Amer. Chem. Soc.*, 1952, **74**, 334.

[131] C. F. H. Tipper, *J.*, 1952, 2966.

[132] *J. Amer. Chem. Soc.*, 1950, **72**, 67, 3809.

The direct combinations of Ph·CO·O· radicals with iodine,[133] triphenylmethyl,[134] and αα-diphenyl-β-picrylhydrazyl[57] have also been studied, though the nature of the colourless product formed from the last radical has not been investigated. Iodine is not very suitable as a chain-breaking agent since the initial reaction product, benzoyl hypoiodite, Ph·CO·O·I, is a very powerful electrophilic iodinating agent and promptly attacks the solvent. With triphenylmethyl in benzene solution the products are triphenylmethyl benzoate (60—70%), benzoic acid (30%), and tetraphenylmethane; no carbon dioxide is evolved. Instead of being a chain-breaker the triphenylmethyl promotes the homolytic decomposition of the benzoyl peroxide:

$$\begin{aligned} \mathrm{Ph_3C\cdot} + (\mathrm{Ph{\cdot}CO{\cdot}O})_2 &\longrightarrow \mathrm{Ph_3C{\cdot}O{\cdot}CO{\cdot}Ph} + \mathrm{Ph{\cdot}CO{\cdot}O\cdot} \\ \mathrm{Ph_3C\cdot} + \mathrm{Ph{\cdot}CO{\cdot}O\cdot} &\longrightarrow \mathrm{Ph_3C{\cdot}O{\cdot}CO{\cdot}Ph} \\ \mathrm{Ph{\cdot}CO{\cdot}O\cdot} + \mathrm{C_6H_6} &\longrightarrow \mathrm{Ph{\cdot}CO{\cdot}OH} + \mathrm{C_6H_5\cdot} \\ \mathrm{Ph_3C\cdot} + \mathrm{C_6H_5\cdot} &\longrightarrow \mathrm{Ph_4C} \end{aligned}$$

Other reactions of benzoyl peroxide are discussed on p. 123. Decompositions of lauroyl peroxide[135] and of *tert.*-butyl perbenzoate have also been examined;[136] they too yield active radicals. In contrast the decompositions of phenylacetyl peroxide, $(\mathrm{Ph{\cdot}CH_2{\cdot}CO{\cdot}O})_2$,[137] and of coumariloyl peroxide[138] show little evidence of free-radical formation.

The decomposition of acetyl peroxide in alcohols, and in glycols, is a chain reaction in which hydrogen atoms are removed from CH and not from OH groups;[139] lead tetra-acetate attacks glycols in a different way.[140] This dehydrogenation is due to free methyl and not to $\mathrm{CH_3{\cdot}CO{\cdot}O\cdot}$ radicals. Again, by methyl-radical attack, acetyl peroxide dehydrogenates chloro- and dichloro-alkanes in preference to abstracting chlorine, the ease of attack on groups being *tert.*-CH > $\mathrm{R{\cdot}CH_2Cl}$ > $\mathrm{RR'CH_2}$ > primary and *sec.*-Cl > *tert.*-Cl, $\mathrm{CH_3}$.[141] In most cases dimeric alkanes can be isolated in good yield. Allyl bromide acts abnormally,[142] the first reaction being

$$\mathrm{Me\cdot} + \mathrm{CH_2{:}CH{\cdot}CH_2Br} \longrightarrow \mathrm{Me.CH_2{\cdot}CH{:}CH_2} + \mathrm{\cdot Br}$$

F. G. Edwards and F. R. Mayo,[143] by studying the decomposition of acetyl peroxide in mixtures of compounds, $\mathrm{CHR_3}$ and carbon tetrachloride, and measuring the relative yields of methane and of methyl chloride, have attempted to determine the relative reactivities of free methyl towards different C–H bonds of organic liquids by direct comparison with its reactivity towards C–Cl in carbon tetrachloride. Their results do not accord with the relative reactivities of the same liquids towards the hydrocarbon radicals of the growing chains of polymerising ethylene or styrene, and they

---

[133] G. S. Hammond, *J. Amer. Chem. Soc.*, 1950, **72**, 3737; G. S. Hammond and L. M. Soffer, *ibid.*, p. 4711.

[134] G. S. Hammond, J. T. Rudesill, and F. J. Modic, *ibid.*, 1951, **73**, 3929.

[135] W. E. Cass, *ibid.*, 1950, **72**, 4915.

[136] A. T. Blomquist and A. F. Ferris, *ibid.*, 1951, **73**, 3408, 3412; A. T. Blomquist and I. A. Berstein, *ibid.*, p. 5546.

[137] P. D. Bartlett and J. E. Leffler, *J. Amer. Chem. Soc.*, 1950, **72**, 3030.

[138] M. C. Ford and W. A. Waters, *J.*, 1951, 824.

[139] M. S. Kharasch, J. L. Rowe, and W. H. Urry, *J. Org. Chem.*, 1951, **16**, 905; M. S. Kharasch and H. N. Friedlander, *ibid.*, 1949, **14**, 239.

[140] M. S. Kharasch, H. N. Friedlander, and W. H. Urry, *ibid.*, 1951, **16**, 533.

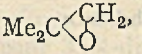
[141] M. S. Kharasch and G. Buchi, *J. Amer. Chem. Soc.*, 1951, **73**, 632.

[142] *Idem, J. Org. Chem.*, 1949, **14**, 84.

[143] *J. Amer. Chem. Soc.*, 1950, **72**, 1265.

consequently suggest that acetyl peroxide may not liberate *free* methyl, $CH_3{\cdot}CO{\cdot}O{\cdot} \longrightarrow CH_3{\cdot} + CO_2$, in an independent reaction from that in which carbon dioxide is lost, $CH_3{\cdot}CO{\cdot}O{\cdot} + CHR_3 \longrightarrow CH_3{-}H + CO_2 + {\cdot}CR_3$.

E. W. R. Steacie and his colleagues [144] continue to amass data concerning activation energies for reactions of methyl radicals with H–C and Cl–C bonds in vapour-phase reactions, but discussion of them is outside the scope of this report.

*Dialkyl peroxides.* The thermal and photochemical reactions of *tert.*-butyl peroxide continue to receive careful study.[145] The $Me_3C{\cdot}O{\cdot}$, which is formed thermally at about 140°, easily breaks down to acetone and free methyl, the latter dehydrogenates more $Me_3C{\cdot}O{\cdot}$ and consequently epoxy-*iso*butane,  $Me_2C{<}\overset{CH_2}{\underset{O}{|}}$, is a major product of the decomposition of the pure liquid. The peroxide, which has frequently been used as a catalyst, can induce the " polymerisation " of compressed mixtures of ethylene and carbon monoxide to polyketones.[146] The radical $Me_3C{\cdot}O{\cdot}$ reacts without further decomposition with *cyclo*hexene, 1-methyl*cyclo*hexene, and other methyl-substituted olefins, forming *tert.*-butyl alcohol and olefinic dimers, *e.g.*, di*cyclo*hex-2-enyl, through allylic attack.[147] The action on natural rubber resembles vulcanisation. Toluene yields dibenzyl, and ethylbenzene yields both the *meso*- and the racemic form of 2 : 3-diphenylbutane. Ketones also lose hydrogen from α-positions and form 1 : 4-diketones.[148]

The relative stabilities of alkoxy-radicals, $RO{\cdot}$, as judged by the decompositions of a series of unsymmetrical peroxides $RO{\cdot}O{\cdot}CMe_3$, follow the order $MeO > EtO > BuO > Pr^i > Bu^iO = Bu^tO$,[149] whilst the radicals from α-cumyl peroxide $(Ph{\cdot}CMe_2O{\cdot})_2$, *tert.*-butyl α-cumyl peroxide, and *tert.*-butyl triphenylmethyl peroxide invariably break down by loss of methyl radicals and can effect similar dehydrogenations of hydrocarbons.[150] M. S. Kharasch, A. Fono, and W. Nudenberg [150] point out that here again the decompositions may involve reactions not necessarily generating *free* methyl radicals (cf. above), *e.g.*, $Me_2C{\cdot}O{\cdot} + H{\cdot}CMe_2Ph \longrightarrow Me_2CO + MeH + {\cdot}CMe_2Ph$, and consider that it is profitless to compare the reactivities of free radicals which have not been prepared in the same way and at similar temperatures. They also stress the necessity of isolating, and accounting quantitatively for, all the reaction products, pointing out that for this reason the measurements of M. Szwarc and J. S. Roberts,[151] who decomposed *tert.*-butyl peroxide in toluene vapour at 120—160° and measured only the gas evolved, have little precise meaning.

Decompositions of optically active peroxides have been studied.[152] They show that alkoxy-radicals can remove hydrogen from CH or SH groups without loss of optical activity of the carbon centre of the original

---

[144] *J. Amer. Chem. Soc.*, 1950, **72**, 2310; *J. Chem. Phys.*, 1950, **18**, 1097; 1951, **19**, 169; 1952, **20**, 578; *J. Phys. Colloid Chem.*, 1951, **55**, 908.

[145] E. R. Bell, F. F. Rust, and W. E. Vaughan, *J. Amer. Chem. Soc.*, 1950, **72**, 337; J. H. Raley, L. M. Porter, F. F. Rust, and W. E. Vaughan, *ibid.*, 1951, **73**, 15; L. M. Dorfmann and Z. W. Salsburg, *ibid.*, p. 255.

[146] M. M. Brubaker, D. D. Coffman, and H. H. Hoehn, *ibid.*, 1952, **74**, 1509.

[147] E. H. Farmer and C. G. Moore, *J.*, 1951, 131, 142.

[148] C. G. Moore, *J.*, 1951, 236.

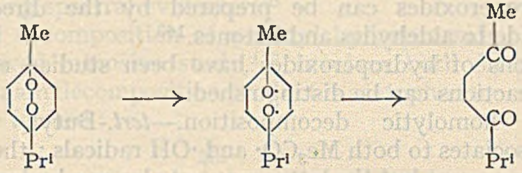
[149] F. F. Rust, F. H. Seubold, and W. E. Vaughan, *J. Amer. Chem. Soc.*, 1950, **72**, 338.

[150] *J. Org. Chem.*, 1951, **16**, 105, 1458. [151] *J. Chem. Phys.*, 1950, **18**, 561.

[152] N. Kornblum and H. E. De la Mare, *J. Amer. Chem. Soc.*, 1952, **74**, 3079.

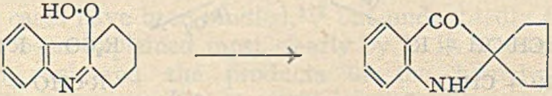
radical. Alkoxy-radicals with identical characteristics can be obtained by the pyrolysis of alkyl nitrites : $R{\cdot}O{\cdot}NO \longrightarrow R{\cdot}O{\cdot} + {\cdot}NO$.[153] Decompositions of unsaturated peroxides, such as $Me_3C{\cdot}O{\cdot}O{\cdot}CH_2{\cdot}CH{:}CH_2$, have also been studied,[154] and acetylenic peroxides have been prepared.[155]

The decomposition of the cyclic peroxide, dihydroascaridole (XXXVII), has been examined by C. G. Moore; [156] it yields the diketone (XXXVIII) and a gas (possibly ethylene). H. Hock and F. Depke [157] have made, by autoxidation, a number of transannular peroxides from compounds such as *cyclo*pentadiene, *cyclo*hexadiene, indene, and dihydronaphthalene, and have characterised the products of their decompositions. The evidence presented is, however, insufficient to decide whether or not some of them may really be hydroperoxides.

(XXXVII)


(XXXVIII)

*Hydroperoxides.* These are the normal products of autoxidations and several accounts of isolations of pure products from such reactions have been reported.[158] J. E. Coleman, H. B. Knight, and D. Swern [159] have described a novel way of concentrating the autoxidation product of methyl oleate. They remove the unoxidised material as its clathrate complex with urea : the residue may then contain 70—90% of peroxide. The yellow autoxidation product of benzaldehyde phenylhydrazone is thought now to be $Ph{\cdot}CH(O{\cdot}OH){\cdot}N{:}NPh$, derived from the mesomeric radical $Ph{\cdot}CH{:}N{\cdot}\dot{N}{\cdot}Ph \longleftrightarrow Ph{\cdot}\dot{C}H{\cdot}N{:}NPh$.[160] The hydroperoxide (XXXIX) of 1 : 2 : 3 : 4-tetrahydrocarbazole, the decomposition of which has received detailed study,[161] probably arises through a similar mesomeric radical containing nitrogen. When decomposed it yields *cyclo*pentane*spiro*-2-ψ-indoxyl (XL). Alkyl hydroperoxides can also be prepared by the action of hydrogen peroxide on alkyl sulphates, or on tertiary alcohols in the presence of concentrated sulphuric acid. A. G. Davies and A. M. White [162] have shown that they can

(XXXIX)


(XL)

---

[153] N. Kornblum and E. P. Oliveto, *J. Amer. Chem. Soc.*, 1949, **71**, 226.

[154] T. W. Campbell and G. M. Coppinger, *J. Amer. Chem. Soc.*, 1951, **73**, 1788.

[155] N. A. Milas and O. L. Mageli, *ibid.*, 1952, **74**, 1471.

[156] *J.*, 1951, 234. [157] *Chem. Ber.*, 1950, **83**, 227, 317; 1951, **84**, 122, 349.

[158] H. Hock *et al.*, *ibid.*, 1950, **83**, 227, 238, 327; 1951, **84**, 356; R. Criegee and H. Zogel, *ibid.*, p. 215; D. B. Sharp *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 5600; 1952, **74**, 1802; J. Fugger *et al.*, *ibid.*, 1951, **73**, 2861; J. H. Skellon and P. E. Taylor, *J.*, 1952, 1813.

[159] *J. Amer. Chem. Soc.*, 1952, **74**, 4886.

[160] R. Criegee and G. Lohaus, *Chem. Ber.*, 1951, **84**, 219.

[161] R. J. S. Beer, L. McGrath, and A. Robertson, *J.*, 1950, 2118, 3283; R. J. S. Beer, T. Broadhurst, A. Robertson, and L. McGrath, *J.*, 1952, 4351; S. G. P. Plant and Sir R. Robinson, *Nature*, 1950, **165**, 36; B. Witkop, *et al.*, *J. Amer. Chem. Soc.*, 1950, **72**, 614, 633; R. J. S. Beer, T. Broadhurst, and A. Robertson *J.*, 1952, 4946.

[162] *J.*, 1952, 3300; *Nature*, 1952, **170**, 168.

regularly be prepared by the $S_N1$ mechanism from carbonium ions and hydrogen peroxide, as for example from (+)-tetrahydro-α-naphthyl hydrogen phthalate, with concurrent racemisation. Another interesting preparation is from 2-methylbut-2-ene with 90% hydrogen peroxide and a trace of sulphuric acid :

$$Me_2C{:}CHMe + H^+ \longrightarrow Me_2\overset{+}{C}{\cdot}CH_2Me \longrightarrow Me_2C(O{\cdot}OH){\cdot}CH_2Me$$

1-Hydroxy-hydroperoxides can be prepared by the direct addition of hydrogen peroxide to aldehydes and ketones.[163]

Decompositions of hydroperoxides have been studied extensively and three types of reactions can be distinguished.

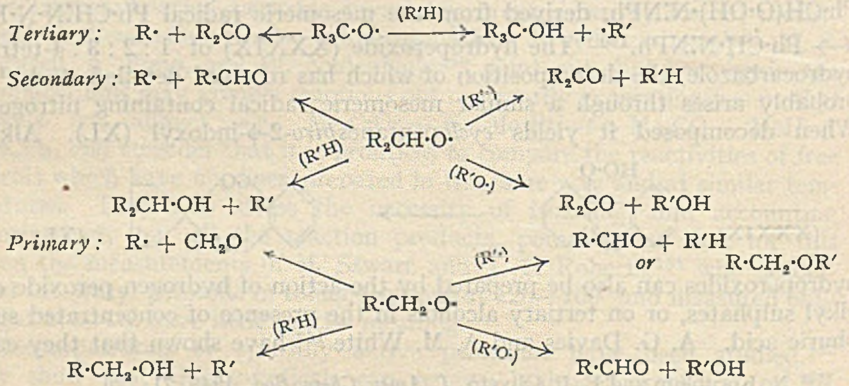
(*a*) Thermal homolytic decomposition.—*tert.*-Butyl hydroperoxide, $Me_3C{\cdot}O{\cdot}OH$, dissociates to both $Me_3CO{\cdot}$ and ${\cdot}OH$ radicals : the former acts as a dehydrogenating agent but the latter may act also as a hydroxylating agent. Thus the decomposition in *cyclo*hexene [164] gives *cyclo*hex-2-enol, *cyclo*hexane-1 : 2-diol, and dimeric coupling products. Radical-induced decompositions of the hydroperoxide also occur even in the vapour phase,[165] *e.g.* :

$$Me{\cdot} + Me_3C{\cdot}O{\cdot}OH \longrightarrow Me{\cdot}H + Me_3C{\cdot}O{\cdot}O{\cdot}$$

$$Me_3C{\cdot}O{\cdot}O{\cdot} + {\cdot}Me \longrightarrow Me_3C{\cdot}O{\cdot}OMe \longrightarrow Me_3C{\cdot}O{\cdot} + {\cdot}OMe$$

$$MeO{\cdot} + Me_3C{\cdot}O{\cdot}OH \longrightarrow MeO{\cdot}H + Me_3C{\cdot}O{\cdot}O{\cdot}$$

The hydrogen abstraction was confirmed by the use of the deuteroperoxide, $Me_3C{\cdot}O{\cdot}OD$, whereby both $CH_3D$ and $CH_3OD$ were isolated. The alkoxy-radicals formed by the foregoing decompositions of hydroperoxides can then undergo further reactions which can be summarised as shown : [166]



Degradations of this type can account for the course of the low-temperature oxidation of paraffin hydrocarbons.

Similar reactions can be induced by other free radicals in solutions of organic hydroperoxides.[167] For this reason kinetic studies of hydroperoxide

---

[163] W. Cooper, *J.*, 1951, 1340; 1952, 1180.

[164] E. H. Farmer and C. G. Moore, *J.*, 1951, 149.

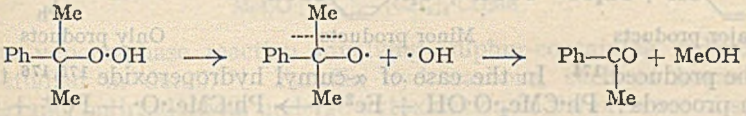
[165] F. H. Seubold, F. F. Rust, and W. E. Vaughan, *J. Amer. Chem. Soc.*, 1951, **73**, 18.

[166] E. R. Bell, J. H. Raley, F. F. Rust, F. H. Seubold, and W. E. Vaughan, *Discuss. Faraday Soc.*, 1951, **10**, 242.

[167] V. Stannett and R. B. Mesrobian, *J. Amer. Chem. Soc.*, 1950, **72**, 4125.

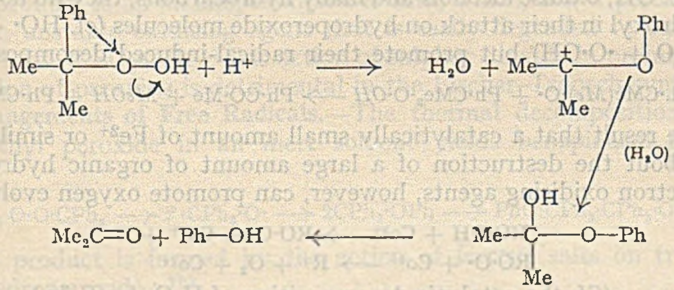
decompositions show that the reaction is complex,[168–171] though at low concentrations in solution it closely simulates a first-order reaction, indicating that the primary decomposition of the hydroperoxide, RO·OH ⟶ RO· + ·OH, then becomes the rate-controlling process. Olefinic peroxides, however, seem to decompose by second-order reactions[169] until very low concentrations are reached, and this has been ascribed to molecular association of the hydroperoxide to a hydrogen-bonded dimer for the existence of which there is supporting spectral evidence.[170]

The thermal decomposition of α-cumyl hydroperoxide, $Ph{\cdot}CMe_2{\cdot}O{\cdot}OH$, which has received intensive study,[171] involves both direct and induced reactions: the main decomposition product is acetophenone, whilst methanol also seems to be formed:



$$Ph\text{—}\overset{Me}{\underset{Me}{C}}\text{—}O{\cdot}OH \longrightarrow Ph\text{—}\overset{Me}{\underset{Me}{C}}\text{—}O{\cdot} + {\cdot}OH \longrightarrow Ph\text{—}\underset{Me}{CO} + MeOH$$

(*b*) Acid-catalysed decompositions.—These are heterolytic and lead to molecular rearrangement by migration of an anionoid hydrocarbon group. In marked contrast to the homolytic decomposition (above) the sole products from α-cumyl hydroperoxide are acetone and phenol:



Several of these cases have been studied,[172] but undoubtedly the course of the reaction has been explained most clearly by P. D. Bartlett and J. D. Cotman[173] who compared the products of the homolytic and the acid-catalysed decompositions of *p*-nitrotriphenylmethyl hydroperoxide. With mineral acids it gave exclusively *p*-nitroacetophenone and phenol, owing to preferential migration of the phenyl group, which more easily provides electrons, whereas from thermal decomposition there resulted a mixture in which *p*-nitrophenol slightly predominated, $NO_2{\cdot}C_6H_4{\cdot}$ being a somewhat more stable radical than $C_6H_5{\cdot}$ and therefore requiring less activation energy for liberation.

(*c*) Decompositions catalysed by one-electron transfer.—These decompositions resemble the decomposition of hydrogen peroxide and of inorganic

---

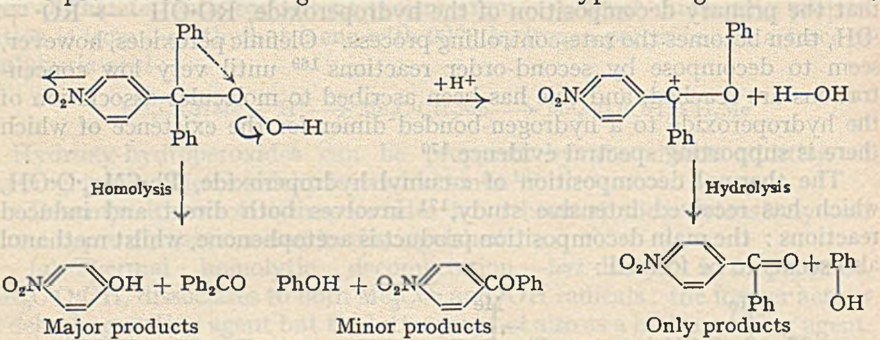
[168] Alan Robertson and W. A. Waters, *J.*, 1948, 1578; S. Farkas and E. Passaglia, *J. Amer. Chem. Soc.*, 1950, **72**, 3333. [169] J. L. Bolland, *Quart. Reviews*, 1949, **3**, 1.

[170] L. Bateman and (Mrs.) H. Hughes, *J.*, 1952, 4594.

[171] M. S. Kharasch, A. Fono, and W. Nudenberg, *J. Org. Chem.*, 1951, **16**, 113; J. W. L. Fordham and H. L. Williams, *Canad. J. Res.*, 1949, **27**, *B*, 943.

[172] M. S. Kharasch *et al.*, *J. Org. Chem.*, 1951, **16**, 113, 128, 150.

[173] *J. Amer. Chem. Soc.*, 1950, **72**, 3095.



per-salts by electron transfer, whereby free hydroxyl radicals, which have pronounced oxidising actions on almost all types of organic molecules, may be produced.[174] In the case of α-cumyl hydroperoxide [175,176] the reaction proceeds: $Ph{\cdot}CMe_2{\cdot}O{\cdot}OH + Fe^{2+} \longrightarrow Ph{\cdot}CMe_2{\cdot}O{\cdot} + Fe^{3+} + {\cdot}OH^-$, giving an alkoxy-radical which may be detected by addition to chloroprene, isoprene, or butadiene, from which dimers, *e.g.*, $(Ph{\cdot}CMe_2{\cdot}O{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot})_2$, are produced.[176] This system is today the catalyst generally adopted for emulsion polymerisation. Though alkoxy-radicals produced in this way can, like ·OH, oxidise alcohols and many hydrocarbons, they do not resemble free hydroxyl in their attack on hydroperoxide molecules (cf. $HO{\cdot} + HO{\cdot}OH \longrightarrow H_2O + {\cdot}O{\cdot}OH$) but promote their radical-induced decomposition:

$$Ph{\cdot}CMe(\mathit{Me}){\cdot}O{\cdot} + Ph{\cdot}CMe_2{\cdot}O{\cdot}\mathit{OH} \longrightarrow Ph{\cdot}CO{\cdot}Me + \mathit{MeOH} + Ph{\cdot}CMe_2{\cdot}O{\cdot}$$

with the result that a catalytically small amount of $Fe^{2+}$ or similar ion can bring about the destruction of a large amount of organic hydroperoxide. One-electron oxidising agents, however, can promote oxygen evolution:

$$RO{\cdot}OH + Co^{3+} \longrightarrow RO{\cdot}O{\cdot} + Co^{2+} + H^+$$
$$RO{\cdot}O{\cdot} + Co^{3+} \longrightarrow R^+ + O_2 + Co^{2+}$$

(Cf. the catalytic decomposition of $H_2O_2$ by $Fe^{3+}$.)

All these reactions are markedly susceptible to chain transfer. Thus with a fatty acid, or its anion, reactions of the type $HO{\cdot} + R{\cdot}CO_2^- \longrightarrow HO^- + R{\cdot}CO_2{\cdot}$ easily occur,[174,177] rapidly lowering the activity of the free radicals remaining in the system, with results of great technical importance in connection with polymerisation processes. These more complicated systems are, however, too involved to be discussed here: they have little novel theoretical interest. Attention may, however, be directed to the rather surprising observations by H. J. Kauffmann [178] who has apparently found

---

[174] J. H. Merz and W. A. Waters, *J.*, 1949, S 15, 2427; I. M. Kolthoff and A. I. Medalia, *J. Amer. Chem. Soc.*, 1949, **71**, 3777, 3784; I. M. Kolthoff, A. I. Medalia, and H. P. Raaen, *ibid.*, 1951, **73**, 1733; J. W. L. Fordham and H. L. Williams, *ibid.*, p. 4855; A. E. Cahill and H. Taube, *ibid.*, 1952, **74**, 2312; G. Stein and J. Weiss, *J.*, 1951, 3265; S. L. Cosgrove and W. A. Waters, *J.*, 1951, 1726.

[175] I. M. Kolthoff and A. I. Medalia, *J. Amer. Chem. Soc.*, 1949, **71**, 3789; J. W. L. Fordham and H. L. Williams, *ibid.*, 1950, **72**, 4465; 1951, **73**, 1634.

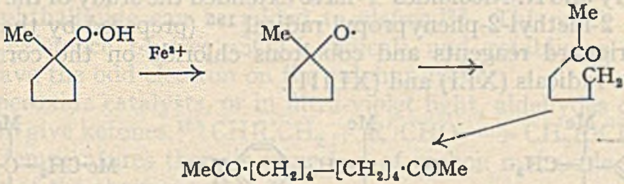
[176] M. S. Kharasch, W. Nudenberg *et al.*, *J. Org. Chem.*, 1951, **16**, 113, 129, 1458, 1556; 1952, **17**, 207.

[177] I. M. Kolthoff and I. K. Miller, *J. Amer. Chem. Soc.*, 1951, **73**, 5118.

[178] *Ibid.*, 1951, **73**, 4311; 1947, **69**, 899.

chain reactions which can promote the radical oxidation of organic dyes. Similar inexplicable features of radical reactions have been observed in radiation chemistry.[179]

The following bond-breaking and radical-coupling reaction is also illustrative of actions of the free alkyloxy-radicals which can be obtained by electron-transfer from cyclic hydroperoxides.[180]



One vapour-phase reaction involving sulphur-containing radicals has been studied in detail.[181] Paraffin hydrocarbons, such as hexane and *cyclo*hexane, on irradiation, undergo autoxidation in the presence of sulphur dioxide, and the following chain mechanism has been proposed :

$$R\cdot + SO_2 \longrightarrow R\cdot SO_2\cdot ;\quad R\cdot SO_2\cdot + O_2 \longrightarrow R\cdot SO_2\cdot O\cdot O\cdot$$
$$R\cdot SO_2\cdot O\cdot O\cdot + RH \longrightarrow R\cdot SO_2\cdot O\cdot OH + R\cdot$$

The first product is an alkanepersulphonic acid, which, like a percarboxylic acid, is an unstable oxidising agent that is easily degraded to an alkanesulphonic acid, $R\cdot SO_2\cdot OH$. This action of sulphur dioxide in promoting the autoxidation of paraffins is detrimental in the Fischer–Tropsch synthesis.

**Rearrangements of Free Radicals.**—The thermal decomposition of triphenylmethyl peroxide in an inert solvent yields benzpinacol diphenyl ether : [182]

$$CPh_3\cdot O\cdot O\cdot CPh_3 \longrightarrow 2\,\cdot CPh_3\cdot O\cdot \longrightarrow 2CPh_2\cdot OPh \longrightarrow PhO\cdot CPh_2\cdot CPh_2\cdot OPh$$

The same product is formed by the action of ferrous salts on triphenylmethyl hydroperoxide : [183]

$$CPh_3\cdot O\cdot OH + Fe^{2+} \longrightarrow Fe^{3+} + OH^- + CPh_3\cdot O\cdot \longrightarrow \cdot CPh_2\cdot OPh \longrightarrow \text{Dimer}$$

whilst the decomposition of *tert.*-butyl triphenylmethyl peroxide in cumene yields 2-methyl-3-phenoxy-2 : 3 : 3-triphenylpropane :

$$\begin{tikzcd}
CPh_3\cdot O\cdot O\cdot CMe_3 \arrow[r] & CMe_3\cdot O\cdot + CPh_3\cdot O\cdot \arrow[r] & \cdot CPh_2\cdot OPh \arrow[d] \\
CMe_3\cdot O\cdot + H\cdot CMe_2Ph \arrow[r] & CMe_3\cdot OH + \cdot CMe_2Ph \arrow[r] & CPhMe_2\cdot CPh_2\cdot OPh
\end{tikzcd}$$

Aryloxy-compounds of this type can be hydrolysed by acetic–perchloric acid : the aryloxy-group is quantitatively eliminated as a phenol, and an olefin is formed by stabilisation, in the normal way, of the resulting tertiary carbonium ion by 1 : 2-migration of a methyl group. In this way M. S. Kharasch, A. C. Poshkus, A. Fono, and W. Nudenberg [183] have compared the migratory aptitudes of a number of aryl groups in unsymmetrical per-

---

[179] *Discuss. Faraday Soc.*, 1952, **12**, 133—312; see also A. J. Swallow, *J.*, 1952, 1334.

[180] E. G. E. Hawkins and D. P. Young, *J.*, 1950, 2804; cf. E. G. E. Hawkins, *Quart. Reviews*, 1950, **4**, 251.

[181] R. Graf, *Annalen*, 1952, **578**, 50.

[182] H. Wieland, *Ber.*, 1911, **44**, 2553.

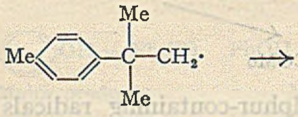
[183] *J. Org. Chem.*, 1951, **16**, 1458.

oxides, using either bromination or condensation with chloroacetic acid to separate the phenolic products.

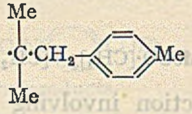
$$ArPh_2C{\cdot}O{\cdot}O{\cdot}CMe_3 \longrightarrow CPhMe_2{\cdot}CPh_2{\cdot}OAr \longrightarrow ArOH + CH_2{:}CPh{\cdot}CMePh_2$$

They find that *p*-diphenylyl and α-naphthyl groups migrate about six times as fast as phenyl, whilst *p*-tolyl migrates almost as readily as phenyl.

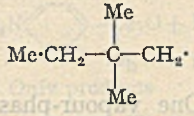
W. H. Urry and N. Nicolaides[184] have extended the study of the rearrangement of the 2-methyl-2-phenypropyl radical[185] (prepared by the combined action of Grignard reagents and cobaltous chloride on the corresponding halide) to the radicals (XLI) and (XLIII).



(XLI)



(XLII)



$$Me{\cdot}CH_2{-}\overset{\displaystyle Me}{\underset{\displaystyle Me}{C}}{-}CH_2{\cdot}$$

(XLIII)

They find that (XLI) in part rearranges to (XLII) by migration of the *p*-tolyl group, but that there is no evidence of the migration of the ethyl group of (XLIII). Similar conclusions have been reached by D. Y. Curtin and M. J. Hurwitz[186] who have prepared radicals, $CPh_3{\cdot}CHR{\cdot}$, by treating the aldehyde $CPh_3{\cdot}CHR{\cdot}CHO$ (R = H, Me) with *tert.*-butyl peroxide at 140°.[187] The aldehyde, $CPh_3{\cdot}CH_2{\cdot}CHO$, after this decarbonylation gave only $CHPh_2{\cdot}CH_2Ph$, showing that rearrangement of $CPh_3{\cdot}CH_2{\cdot}$ to ${\cdot}CPh_2{\cdot}CH_2Ph$ was complete, whilst $CPh_3{\cdot}CHMe{\cdot}CHO$ gave equal amounts of $CHPh_2{\cdot}CHMePh$ and $CPh_2{:}CMePh$. Decarbonylation of (XLIV) to (XLV) occurred in 85% yield, without rearrangement, whilst (XLVI) gave (XLVII), the dimer of the rearranged radical.

$$\text{(XLIV)}\quad p\text{-}MeO{\cdot}C_6H_4{\cdot}CHPh{\cdot}CH_2{\cdot}CHO \longrightarrow MeO{\cdot}C_6H_4{\cdot}CHPhMe\quad\text{(XLV)}$$

$$\text{(XLVI)}\quad CPh_2Me{\cdot}CH_2{\cdot}CHO \longrightarrow CH_2Ph{\cdot}CPhMe{\cdot}CPhMe{\cdot}CH_2Ph\quad\text{(XLVII)}$$

From these results they conclude that only aryl radicals can migrate. A similar conclusion has been reached by C. G. Overberger and M. B. Berenbaum[188] who formed the radical (XLVIII) from the azo-nitrile derived from pinacolone, and found that it dimerised to a mixture of the *meso*- and racemic forms of (XLIX) without any migration of methyl groups:

$$\text{(XLVIII)}\quad CMe_3{\cdot}CMe(CN){\cdot} \longrightarrow CMe_3{\cdot}CMe(CN){\cdot}CMe(CN){\cdot}CMe_3\quad\text{(XLIX)}$$

Again H. C. Brown and G. A. Russell[189] who have investigated the photochemical chlorinations of $CMe_3D$ and $CH_2PhD$ find no evidence for deuterium migration (*e.g.*, $CMe_2D{\cdot}CH_2{\cdot} \longrightarrow {\cdot}CMe_2{\cdot}CH_2D$) or even for deuterium exchange between molecules.

**Addition Reactions.**[190]—Few novel homolytic additions have been reported in the period under review, but there has been a great deal of study of reaction mechanisms. By catalysis with *tert.*-butyl peroxide, or ultra-violet light, phosphine can be added to olefins to give products of types $R{\cdot}PH_2$, $R_2PH$, and $R_3P$.[191] Free oxygen is able to catalyse the

---

[184] *J. Amer. Chem. Soc.*, 1952, **74**, 5163.

[185] *Ann. Reports*, 1948, **45**, 148.

[186] *J. Amer. Chem. Soc.*, 1952, **74**, 5381.

[187] See p. 133.

[188] *J. Amer. Chem. Soc.*, 1952, **74**, 3293.

[189] *Ibid.*, p. 3995.

[190] See *Ann. Reports*, 1948, **45**, 149—157.

[191] A. R. Stiles, F. F. Rust, and W. E. Vaughan, *J. Amer. Chem. Soc.*, 1952, **74**, 3282.

addition of thiols to olefins [192] and consequently can indirectly promote vinyl polymerisation. The reactions

$$RSH + O_2 \longrightarrow RS{\cdot} + HO_2 \text{ and } RSH + HO_2{\cdot} \longrightarrow RS{\cdot} + H_2O_2$$

have been suggested as the initiating reactions. Benzoyl-peroxide-catalysed addition of sulphuryl chloride to olefins can lead to the formation of a dichlorinated sulphone, $(R{\cdot}CHCl{\cdot}CH_2)_2SO_2$ [193, 194] and, similarly, *N*-chlorosulphonylphthalimide can be added to olefins.[195] This work confirms the transient existence of free $\cdot SO_2Cl$ radicals and establishes that $R{\cdot}SO_2{\cdot}$ radicals have the odd electron on the sulphur atom.

With peroxide catalysts, or in ultra-violet light, aldehydes can be added to olefins to give ketones,[196] $CHR{:}CH_2 + R'{\cdot}CHO \longrightarrow CH_2R{\cdot}CH_2{\cdot}COR'$, but at higher temperatures there is some loss of carbon monoxide owing to the occurrence of the chain reaction [197]

$$R'{\cdot}CO{\cdot} \longrightarrow R'{\cdot} + CO;\ R'{\cdot} + R'{\cdot}CHO \longrightarrow R'H + R'{\cdot}CO{\cdot}.$$

This leads to racemisation of optically active aldehydes.[198] Aldehydes can also be added to αβ-unsaturated esters and ketones.[199] Mesityl oxide, $CMe_2{:}CHAc$, gives $R{\cdot}CO{\cdot}CMe_2{\cdot}CH_2Ac$ and $R{\cdot}CO{\cdot}CHAc{\cdot}CHMe_2$ in the ratio 10 : 1, indicating that the $R{\cdot}CO{\cdot}$ radical adds preferentially to give the more stable radical, *viz.*, $R{\cdot}CO{\cdot}CMe_2{\cdot}\dot{C}H{\cdot}COMe$, and not at the point of higher electron density. Both A. L. Henne and M. Nager [200] and R. N. Haszeldine [201] stress the same features in relation to additions to 3 : 3 : 3-trifluoropropene, $CF_3{\cdot}CH{:}CH_2$, and 3 : 3 : 3-trifluoropropyne, $CF_3{\cdot}C{\vdots}CH$. In ultra-violet light these molecules add hydrogen bromide to give the 1-bromo-compounds, $CF_3{\cdot}CH_2{\cdot}CH_2Br$ and $CF_3{\cdot}CH{:}CHBr$. These are also formed under polar conditions (a reversal of the normal mode of addition to propylene) though much less easily, owing to the exceptionally strong electrophilic action of fluorine. Similar photochemical additions can be effected by $CF_3Br$ and $CF_3I$, which resemble $CCl_3Br$ in their ease of homolysis.[202] Kinetic features of the benzoyl peroxide- and photochemically-catalysed additions of both bromotrichloromethane [203, 204] and carbon tetrachloride [205] to olefins have received detailed examination. The olefins most active towards the $\cdot CCl_3$ radical are those which tend to give the most stable radical adducts, but these tend to yield dimers, rather than to continue reaction chains by abstracting a halogen atom from $CCl_4$ or $CCl_3{\cdot}Br$. Since the $\cdot CCl_3$ radical can also attack C–H bonds,[205, 206] chain ending is often due to the formation of resonance-stabilised allylic radicals, $\cdot CHR{\cdot}CH{:}CHR'$.[207] The reactions with allyl

---

[192] M. S. Kharasch, W. Nudenberg, and G. J. Mantell, *J. Org. Chem.*, 1951, **16**, 524.

[193] M. S. Kharasch, 8th Solvay Report, 1951, pp. 177—196 (R. Stoops, Brussels).

[194] M. S. Kharasch and A. F. Zavist, *J. Amer. Chem. Soc.*, 1951, **73**, 964.

[195] M. S. Kharasch and R. A. Mosher, *J. Org. Chem.*, 1952, **17**, 453.

[196] M. S. Kharasch, W. H. Urry, and B. M. Kuderna, *J. Org. Chem.*, 1949, **14**, 248.

[197] See p. 117. S. Winstein and F. H. Seubold, *J. Amer. Chem. Soc.*, 1947, **69**, 2916.

[198] W. E. Doering, M. Farber, M. Sprecher, and K. I. Wiberg, *ibid.*, 1952, **74**, 3000.

[199] T. M. Patrick, *J. Org. Chem.*, 1952, **17**, 1009, 1269.

[200] *J. Amer. Chem. Soc.*, 1951, **73**, 5527. [201] *J.*, 1952, 2504, 3490.

[202] R. N. Haszeldine, *J.*, 1949, 2856; 1950, 2037; 1952, 3483.

[203] M. S. Kharasch and H. N. Friedlander, *J. Org. Chem.*, 1949, **14**, 239; M. S. Kharasch and M. Sage, *ibid.*, p. 538.

[204] H. W. Melville, J. C. Robb, and R. C. Tutton, *Discuss. Faraday Soc.*, 1951, **10**, 154.

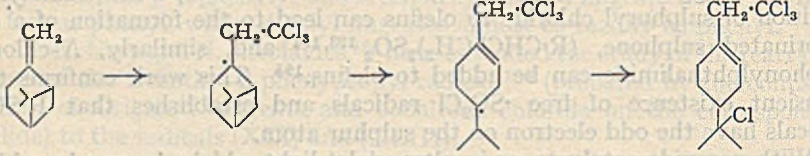
[205] E. C. Kooyman, *ibid.*, p. 163.

[206] E. C. Kooyman and E. Farenhorst, *Rec. Trav. chim.*, 1951, **70**, 867.

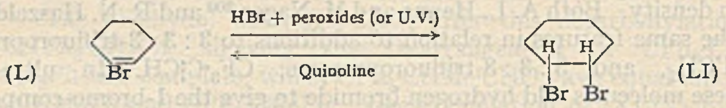
[207] E. C. Kooyman, *ibid.*, 1950, **69**, 492.

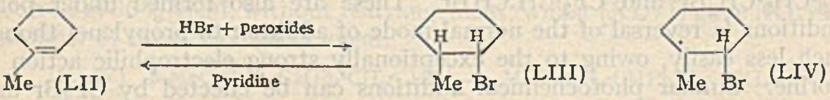
chloride [208] exemplify particularly clearly the influence of electrophilic groups on radical reactivity.[193]

Addition of carbon tetrachloride to (+)-limonene is followed by elimination of hydrogen chloride,[209] whilst that to β-pinene leads to ring fission.[210]



The stereochemistry of homolytic addition has been investigated by H. L. Goering, P. I. Abell, and B. F. Aycock.[211] Addition of hydrogen bromide to simple olefins is not stereospecific because the addition of atomic bromine is reversible [212, 213] and promotes isomerisation more than addition. Since *cis*- and *trans*-1 : 2-dibromo*cyclo*hexane give different (*trans*-)elimination products on treatment with quinoline, a discrimination can be made by examining the addition products to 1-bromo*cyclo*hexene (L). With hydrogen bromide in the presence of benzoyl peroxide, or in ultra-violet light, it gives *cis*-1 : 2-dibromo*cyclo*hexane (LI) which is, thermodynamically, the less stable isomer. 1-Methyl*cyclo*hexene (LII) behaves similarly, giving (LIII).





The intermediate radical (LIV) might be expected to give a mixture of *cis*- and *trans*-isomers if the free radical has a planar structure with the methyl group coplanar with the ring; but evidently *trans*-addition of the hydrogen bromide is favoured. Resonance between the unpaired electron of the carbon radical and the unshared electrons of the bromine atom is invoked to explain why (LIV) should react with hydrogen bromide in the direction remote from the bromine atom. In discussion of addition of trichlorobromomethane to *cyclo*hexene, F. S. Fawcett [214] suggests that steric hindrance may favour the *trans*-addition which has been observed. Stereochemical specificity, however, cannot be a general feature of free-radical addition, since the copolymers of vinyl acetate with the *cis*- and the *trans*-form of 1 : 2-dichloroethylene have the same steric configuration, though the two isomers react at different speeds.[215]

Studies of copolymerisation give important information concerning the relative speeds of addition to different olefinic compounds, and F. R. Mayo

---

[208] M. S. Kharasch and M. Sage, *J. Org. Chem.*, 1949, **14**, 79.
[209] S. Israelashvili and E. Diamant, *J. Amer. Chem. Soc.*, 1952, **74**, 3185.
[210] D. M. Oldroyd, G. S. Fisher, and L. A. Goldblatt, *ibid.*, 1950, **72**, 2407.
[211] *J. Amer. Chem. Soc.*, 1952, **74**, 3588.
[212] D. H. Derbyshire and W. A. Waters, *Trans. Faraday Soc.*, 1949, **45**, 749.
[213] H. Steinmetz and R. M. Noyes, *J. Amer. Chem. Soc.*, 1952, **74**, 4141.
[214] *Chem. Reviews*, 1950, **47**, 235. [215] *Ibid.*, 1950, **46**, 191.

and C. Walling [215] have provided a valuable review of this subject. Many olefinic compounds which do not polymerise alone can be made to form copolymers when admixed with other polymerisable olefins. It turns out to be a general rule that whenever a mixture of two olefins, $M^1$, $M^2$, is induced to polymerise by a catalysing radical, $R\cdot$, the growing chain $R\cdot[M]_n\cdot M^{1}\cdot$, with $M^1$ as the terminal component, has a greater tendency to add to the *different* monomer, $M^2$; similarly $R\cdot[M]_n\cdot M^{2}\cdot$ preferentially adds to $M^1$. Cross-combination rates are much greater than those for union of like monomers,[216] and it has been suggested that this effect is due to differences in polarity of the monomers.[217] Mayo and Walling [215, 218] suggest that even in free-radical reactions contributions to the transition state from canonical structures in which electron transference has occurred should be taken into account; this, they think, explains why, in general, free-radical reactions occur most easily between molecules of different polar character.[219]

**Formation of Radicals by Oxidations and Reductions.**—The possibilities of radical formation by one-electron oxidation and reduction processes have been discussed by F. S. Dainton in his Tilden lecture.[220] Their transient existence has often been inferred from kinetic studies. Thus C. E. H. Bawn and A. G. White [221] conclude that free radicals must be formed during the oxidations of formic acid, formaldehyde, and methanol by cobaltic salts, and F. R. Duke and R. F. Bremer [222] formulate a free-radical intermediate in the fission of butane-2 : 3-diol by ceric salts. Radical formation has often been postulated in the initial stages of the permanganate–oxalic acid reaction which has been examined afresh.[223] Particularly interesting results have been reported by G. Parravano [224] who found that the polymerisation of methyl methacrylate can be brought about at the surface of catalytically active metals, such as platinum and palladium, by adsorbed hydrogen, and by the catalysed decompositions of hydrazine and of formic acid. This confirms earlier surmises [225] of the atomic nature of " nascent hydrogen." He has also shown that a similar polymerisation can be induced by active suspensions of *B. coli*, and by the formaldehyde–xanthine oxidase system, thus supporting free-radical concepts of the mechanism of enzyme oxidation.[226]

Polarographic measurements of organic compounds, which have been reviewed by J. E. Page,[227] indicate that the reduction of ketones, if carried out at pH $\not> 5$, proceeds in one-electron transfer stages.[228] H. A. Levine and M. J. Allen [229] have substantiated this by showing that a cross-linked pinacol can be obtained by the reduction at a mercury cathode of a mixture of *p*-dimethylaminoacetophenone and *p*-methoxyacetophenone.

---

[216] E. P. Bonsall, L. Valentine, and H. W. Melville, *Trans. Faraday Soc.*, 1952, **48**, 763, and earlier papers.

[217] C. C. Price, " Reactions at Carbon–Carbon Double Bonds," Intersci. Publ., New York, 1946, pp. 95—105; E. J. Arlman, H. W. Melville, and L. Valentine, *Rec Trav. chim.*, 1949, **68**, 945.

[218] *J. Amer. Chem. Soc.*, 1948, **70**, 1537.

[219] See F. R. Mayo, *Discuss. Faraday Soc.*, 1953 **14**, 254.

[220] *J.*, 1952, 1533.

[221] *J.*, 1951, 331, 339, 343; cf. C. E. H. Bawn, *Discuss. Faraday Soc.*, 1953 **14**, 181.

[222] *J. Amer. Chem. Soc.*, 1951, **73**, 5179.

[223] J. M. Malcolm and R. M. Noyes, *ibid.*, 1952, **74**, 2769.

[224] *Ibid.*, 1950, **72**, 3857, 5546; 1951, **73**, 183, 628.

[225] W. A. Waters, " The Chemistry of Free Radicals," Oxford Univ. Press, 1946 pp. 215—217.

[226] *Op. cit.*, pp. 267—284.

[227] *Quart. Reviews*, 1952, **6**, 262.

[228] D. M. Coulson and R. W. Crowell, *J. Amer. Chem. Soc.*, 1952, **74**, 1290, 1294.

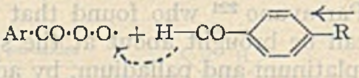
[229] *J.*, 1952, 254.

R. Pummerer[230] has confirmed his earlier suggestions[231] of the formation of free aryloxy-radicals by the oxidation of phenols with potassium ferricyanide by showing that that oxidation product of tetrachloro-*p*-cresol can be added to styrene, *cyclo*hexene, dimethylfulvene, 2 : 3-dimethylbutadiene, *cyclo*pentadiene, and benzoquinone.

Further kinetic studies of quinone reduction have been interpreted by postulating the existence of semiquinone radicals.[232]

Anodic oxidations (the Kolbe reaction), which have recently been extended for the preparation of many coupled, and cross-coupled, dibasic acids, have been reviewed by B. C. L. Weedon[233] who concludes " there is good reason for assuming that free radicals are involved in many, if not all, of the anodic reactions of carboxylic acids."

Kinetic studies of the radicals involved in aldehyde[234] and olefin[235] autoxidation continue to provide data concerning relative reactivities in radical–molecule interactions. J. L. Bolland[235] concludes that for olefins the activation energy of the process $R{\cdot}O{\cdot}O{\cdot} + HR' \longrightarrow R{\cdot}O{\cdot}OH + {\cdot}R'$ can be correlated with the resonance energy of the resulting hydrocarbon radical $R'{\cdot}$. C. Walling and E. A. McElhill,[236] who have studied the autoxidations of substituted benzaldehydes in acetic anhydride solution, which give mixed diacyl peroxides, $Ar{\cdot}CO{\cdot}O{\cdot}O{\cdot}COMe$, find that effects of polar substituents accord with the Hammett relation : electron-donating groups (*e.g.*, MeO) increase the susceptibility of an aldehyde to autoxidation, showing that electron release by the aldehyde molecule to the peroxy-radical is significant :



When mixtures of aldehydes are used, the peroxy-radicals react preferentially with aldehydes containing different substituent groups, the polar influences being similar to those found in copolymerisation (see p. 135).

W. A. Waters and C. Wickham-Jones[237] find that the retardation of benzaldehyde autoxidation by *m*-2-xylenol leads, through the dimerisation of the aryloxy-radical of the phenol, to 3 : 5 : 3′ : 5′-tetramethyl-4 : 4′-diphenoquinone (XXXV ; p. 123) which then inhibits the autoxidation by combining with benzoyl radicals ; the final reaction product has been isolated from this system.[238]

**Sulphur Radicals.**—It has frequently been suggested that organic disulphides may dissociate to thiyl radicals $RS{\cdot}$ when heated ; thiols may also yield such radicals on pyrolysis.[239] Hot solutions of di(benzothiazol-2-yl) disulphide (LV) do not obey Beer's law and are paramagnetic.[240] C. G. Moore has now found that this compound reacts with *cyclo*hexene, yielding

---

[230] *Chem. Ber.*, 1952, **85**, 535. [231] *Ber.*, 1928, **61**, 1102.

[232] J. E. Lu Valle, *J. Amer. Chem. Soc.*, 1952, **74**, 2920 ; C. E. Johnson and S. Winstein, *ibid.*, pp. 755, 3105 ; J. H. Baxendale, H. R. Hardy, and L. H. Sutcliffe, *Trans. Faraday Soc.*, 1951, **47**, 963. [233] *Quart. Reviews*, 1952, **6**, 380.

[234] H. R. Cooper and H. W. Melville, *J.*, 1951, 1984, 1994.

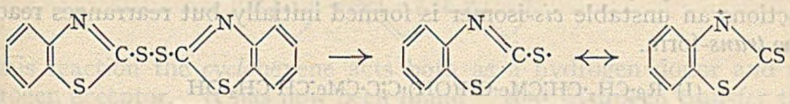
[235] J. L. Bolland, *Quart. Reviews*, 1949, **3**, 1 ; *Trans. Faraday Soc.*, 1950, **46**, 358 ; L. Bateman and G. Gee, *ibid.*, 1951, **47**, 155, 274 ; L. Bateman and A. L. Morris, *ibid.*, 1952, **48**, 1149. [236] *J. Amer. Chem. Soc.*, 1951, **73**, 2927.

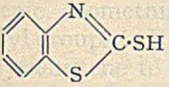
[237] *J.*, 1952, 2420, 2427. [238] R. F. Moore and W. A. Waters, *J.*, 1952, 2432.

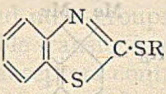
[239] C. J. Thompson, R. A. Meyer, and J. S. Ball, *J. Amer. Chem. Soc.*, 1952, **74**, 3284.

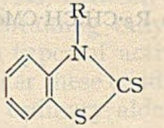
[240] H. G. Cutforth and P. W. Selwood, *ibid.*, 1948, **70**, 278.

(LVII—LIX) (R = *cyclo*hexenyl) by a chain reaction. This is indicative of the participation of the mesomeric radical (LVI) with the free valency distributed between sulphur and nitrogen:[241]


(LV) (LVI)


(LVII)


(LVIII)


(LIX)

Pyrolysis of (LVIII; R = alkyl or benzyl) yields a mixture of (LVII), (LIX) and an olefin (*e.g.*, stilbene), but this decomposition is thought to be heterolytic.[242]

When discussing the mechanism of thiochrome formation from aneurin, P. Sykes and A. R. Todd[243] suggested that aneurin disulphide dissociates to the thiyl radical and that the sulphur then adds to the carbon atom of an adjacent C:N bond. They find that thiochrome is most easily prepared by oxidising aneurin with alkaline ferricyanide, which, being a one-electron-abstracting agent, would convert the thiol into the thiyl radical. Very little is known, as yet, about the possibilities of radical addition to C:N bonds, though the molecular rearrangement involved in the decomposition of tetrahydrocarbazole hydroperoxide (see p. 127) seems to afford another instance of it.

Other reactions of thiyl radicals have been mentioned on pp. 117, 127 and 133, and it appears that by the use of free alkyl radicals in solution thiyl radicals may now become more accessible.

W. A. W.

## 3. GENERAL METHODS.

**Reduction.**—*Catalytic hydrogenation.* Of recent years acetylenes have featured extensively in syntheses of polyenes such as vitamin A[1] and β-carotene.[2] The routes employed have usually involved at some stage the partial reduction of a triple bond conjugated with one or more double bonds. Selective hydrogenations of this type are fraught with considerable difficulty, and therefore the publication[3] of details of the lead- and quinoline-poisoned palladium catalyst, developed for the commercial synthesis of vitamin A, is most welcome. When this catalyst is used the partial hydrogenation of (I) to (II) in the vitamin A synthesis is accomplished almost quantitatively,[3] while surprisingly good yields are obtained in the conversion of dehydro-β-carotene (III) into β-carotene,[4] of bisdehydromethylbixin into methylbixin[5]

---

[241] *J.*, 1952, 4232.
[242] C. G. Moore and E. S. Waight, *J.*, 1952, 4237.
[243] *J.*, 1951, 534.
[1] Cf. *Ann. Reports*, 1949, 46, 175.
[2] Cf. *Ann. Reports*, 1950, 47, 166; 1951, 48, 158.
[3] H. Lindlar, *Helv. Chim. Acta*, 1952, 35, 446.
[4] H. H. Inhoffen, F. Bohlmann, K. Bartram, G. Rummert, and H. Pommer, *Annalen*, 1950, 570, 54; H. H. Inhoffen, F. Bohlmann, and G. Rummert, *ibid.*, 1951, 571, 75.
[5] R. Ahmad and B. C. L. Weedon, *Chem. and Ind.*, 1951, 882.

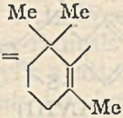
(see p. 153), and in similar hydrogenations.[6] A Raney nickel catalyst, partly poisoned with piperidine and zinc acetate, is also suitable for the hydrogenation of some polyene-acetylenes to the corresponding polyenes.[7] In these reductions an unstable *cis*-isomer is formed initially but rearranges readily to the *trans*-form.

(I) $R_\beta\cdot CH_2\cdot CH{:}CMe\cdot CH(OH)\cdot C{\vdots}C\cdot CMe{:}CH\cdot CH_2\cdot OH$

(II) $R_\beta\cdot CH_2\cdot CH{:}CMe\cdot CH(OH)\cdot CH{:}CH\cdot CMe{:}CH\cdot CH_2\cdot OH$

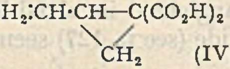
(III) $R_\beta\cdot CH{:}CH\cdot CMe{:}CH\cdot CH{:}CH\cdot CMe{:}CH\cdot C{\vdots}C\cdot CH{:}CMe\cdot CH{:}CH\cdot CH{:}CMe\cdot CH{:}CH\cdot R_\beta$

$R_\beta$ =



The formerly troublesome partial reduction of $\Delta^{5:7}$- to $\Delta^{7}$-sterols, important intermediates for the preparation of 11-oxygenated steroids *via* $\Delta^{7:9(11)}$-dienes, is accomplished in good yield by using a Raney nickel catalyst. Thus 7-dehydrocholesterol yields cholest-7-enol,[8] and ergosterol is converted quantitatively into the 5 : 6-dihydro-derivative, the side-chain double bond being unattacked.[9]

It has been found that a *cyclo*propane ring, when conjugated with a double bond, may undergo reductive fission with surprising ease. Thus the dicarboxylic acid (IV) rapidly absorbs 2 mols. of hydrogen over platinum to



$$CH_2{:}CH\cdot\underset{\diagdown\ CH_2\ \diagup}{CH{-}C}(CO_2H)_2 \qquad (IV)$$

give *n*-butylmalonic acid in almost quantitative yield.[10] No ring fission of 2-*cyclo*propylalkenes occurs, however, on hydrogenation over a barium-promoted copper chromite catalyst.[11]

Studies have been made on the stereochemical course of some Raney nickel hydrogenolyses. Desulphuration of both sulphides[12] and sulphoxides,[13] in which the sulphur atom is directly attached to an asymmetric carbon atom, gives racemic products, but only slight racemisation is observed with the corresponding sulphones.[12] Dehydroxylation of substituted benzyl alcohols also takes place with practically complete retention of configuration.[14]

The activity of a platinum catalyst which has been poisoned with thiophen, methyl sulphide, or mercury or zinc ions, may be restored completely by simple washing. Similar desorption of thiophen from a nickel surface can be accomplished, though less readily.[15]

*Hydrogen transfer.* It has long been known that the metal-catalysed

---

[6] C. F. Garbers, C. H. Eugster, and P. Karrer, *Helv. Chim. Acta*, 1952, **35**, 1850.

[7] W. Oroshnik, G. Karmas, and A. D. Mebane, *J. Amer. Chem. Soc.*, 1952, **74**, 295, 3807; P. Karrer and J. Kebrle, *Helv. Chim. Acta*, 1952, **35**, 2570.

[8] L. F. Fieser, J. E. Herz, and W.-Y. Huang, *ibid.*, 1951, **73**, 2397.

[9] G. D. Laubach and K. J. Brunings, *ibid.*, 1952, **74**, 705; W. V. Ruyle, E. M. Chamberlin, J. M. Chemerda, G. E. Sita, L. M. Aliminosa, and R. L. Erickson, *ibid.*, p. 5929.

[10] R. W. Kierstead, R. P. Linstead, and B. C. L. Weedon, *J.*, 1952, 3610.

[11] V. A. Slabey and P. H. Wise, *J. Amer. Chem. Soc.*, 1952, **74**, 3887.

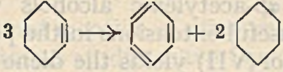
[12] W. A. Bonner, *ibid.*, 1952, **74**, 1034.

[13] *Idem, ibid.*, p. 5089.

[14] W. A. Bonner, J. A. Zderic, and G. A. Casaletto, *ibid.*, p. 5086.

[15] E. B. Maxted and G. T. Ball, *J.*, 1952, 4284.

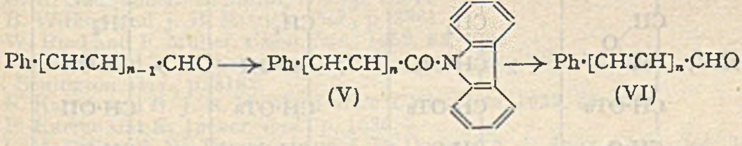
disproportionation of *cyclo*hexene to benzene and *cyclo*hexane occurs rapidly under mild conditions : [16]



In this reaction the *cyclo*hexene acts both as a hydrogen donor and as a hydrogen acceptor. It has now been found [17] that hydrogen transfer takes place, below 100° and in the presence of palladium catalysts, between *cyclo*hexene and a wide range of "foreign" acceptors containing ethylenic, acetylenic, azomethine, azo- and nitro-groups, or certain types of activated carbonyl groups. No appreciable transfer is observed under these conditions from *cyclo*hexene to potential acceptors containing only ordinary aldehyde, keto-, carboxyl, or cyano-groups, or from *cyclo*hexene to naphthalene, anthracene, or phenanthrene. In the positive reactions, competition occurs between disproportionation and transfer. The latter often predominates, even though it may proceed more slowly than disproportionation in the absence of the foreign acceptor.

Hydrogen transfer thus represents a useful alternative to catalytic hydrogenation. No special apparatus is required and the products are readily isolated in high yield. With compounds containing several potential acceptor functions, transfer-hydrogenation is often more highly specific than ordinary catalytic hydrogenation. Thus *m*-dinitrobenzene, for example, is converted into *m*-nitroaniline almost quantitatively.

*Lithium aluminium hydride.* The flood of literature on this reagent continues in full spate. Whereas previous attempts to reduce derivatives of carboxylic acids with lithium aluminium hydride to give aldehydes directly have met with little success, except in isolated instances,[18, 19] two processes have now been developed which promise to be of wide application. Reduction, in tetrahydrofuran, of the diphenylylene-amides (V; $n = 1, 2, 4, 6$) of ω-phenylpolyene-carboxylic acids gives good yields of the corresponding polyene-aldehydes (VI).[20] The starting material can be made either from the appropriate acid chloride and carbazole, or by a Doebner type of condensation between an aldehyde and the half diphenylylene-amide of malonic acid. These reactions thus provide a means of converting an unsaturated aldehyde into its vinylogue :



(V)
(VI)

The second method for the preparation of aldehydes consists in the reduction of *N*-methylanilides,[20, 21] but few details are as yet available. It is

[16] J. Boeseken, *Rec. Trav. chim.*, 1928, **37**, 255; N. D. Zelinsky and G. S. Pawlow, *Ber.*, 1933, **66**, 1420.

[17] R. P. Linstead, E. A. Braude, P. W. D. Mitchell, K. R. H. Wooldridge, and L. M. Jackman, *Nature*, 1952, **169**, 100.

[18] Cf. *Ann. Reports*, 1951, **48**, 145; L. Birkofer and A. Birkofer, *Chem. Ber.*, 1952, **85**, 286; cf. L. Friedmann, Abstr. Papers 116th Meeting Amer. Chem. Soc., 1949.

[19] M. Mousseron, R. Jacquier, M. Mousseron-Canet, and R. Zagdoun, *Bull. Soc. chim.*, 1952, 1042.

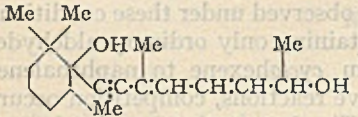
[20] G. Wittig and P. Hornberger, *Annalen*, 1952, **577**, 11.

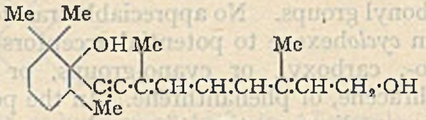
[21] F. Weygand and G. Eberhardt, *Angew. Chem.*, 1952, **64**, 458.

claimed to give high yields of aliphatic, aromatic, and heterocyclic aldehydes, and also dialdehydes such as those from succinic and malic acid.

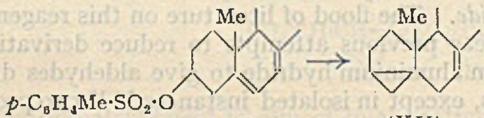
Partial reduction of αβ-acetylenic alcohols with lithium aluminium hydride [22] has found two useful extensions in the polyene field. The readily available diacetylenic glycol (VII) yields the diene (VIII),[23] an intermediate for the synthesis of carotenoids. Both the glycols (IX) and (X) are selectively reduced to the corresponding polyene glycols, from which new routes to vitamin A have been developed.[24]

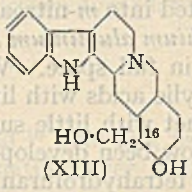
$$\underset{\text{(VII)}}{HO{\cdot}CHMe{\cdot}C\vdots C{\cdot}C\vdots C{\cdot}CHMe{\cdot}OH} \longrightarrow \underset{\text{(VIII)}}{HO{\cdot}CHMe{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CHMe{\cdot}OH}$$


(IX)

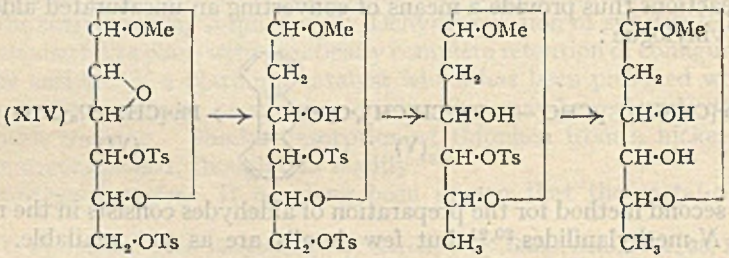

(X)

The reaction of toluene-*p*-sulphonates with lithium aluminium hydride has been the subject of further study. While cholesteryl toluene-*p*-sulphonate gives mainly cholest-5-ene and some 3 : 5-*cyclo*cholestane,[27] the epimer is reported to yield predominantly cholesta-3 : 5-diene and some cholest-5-ene, but none of the *cyclo*-steroid.[28] With ergosteryl and 7-dehydroergosteryl toluene-*p*-sulphonates, the *cyclo*-derivatives (XII) are the main products.[29]


(XII)


(XIII)

Reduction of the mono- and tri-toluene-*p*-sulphonyl derivatives of yohimbine (XIII) gives 16-methylyohimbol and 16-methylyohimbane respectively.[30] With 4 : 6-ditoluene-*p*-sulphonyl 2 : 3-anhydro-α-methyl-D-alloside (XIV), reduction can be arrested at each of the stages shown :



* Ts = $p$-$C_6H_4Me{\cdot}SO_2$.

---

[22] J. D. Chanley and H. Sobotka, *J. Amer. Chem. Soc.*, 1949, **71**, 4140.

[23] R. Ahmad, F. Sondheimer, B. C. L. Weedon, and R. J. Woods, *J.*, 1952, 4089.

[24] J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J.*, 1952, 1094.

[27] H. Schmid and P. Karrer, *Helv. Chim. Acta*, 1949, **32**, 1371.

[28] H. Schmid and K. Kägi, *ibid.*, 1952, **35**, 2194.

[29] P. Karrer and H. Asmis, *ibid.*, p. 1926.

[30] P. Karrer and R. Saemann, *ibid.*, p. 1932.

This selectivity has been utilised to develop convenient syntheses of the 2 : 6-bisdesoxy-sugars, digitoxose and cymarose,[31] present in some cardiac glycosides.

Space permits only a brief mention of other recent applications of lithium aluminium hydride. Detailed studies have been made of the reduction of oximes to primary amines.[32] Acyl cyanides [33] and cyanohydrins [34] are converted into primary amines and hydroxyamines respectively. Diacylamines,[35] *iso*cyanates, and *iso*thiocyanates [36] yield monoalkylamines. Reduction of nitrosamines affords a useful synthesis of 1 : 1-disubstituted hydrazines.[37] Normal reduction of each of the functional groups occurs in diazoacetic ester,[36] and acyl derivatives of simple peptides.[38] Organic phosphates,[39] nitrates, nitrites,[40] and peroxides [41] furnish the corresponding alcohols. Keten dimers yield β-hydroxy-ketones,[42] and tropolone methyl ether gives, unexpectedly, benzaldehyde.[43]

In the heterocyclic field, attempts to reduce carbethoxy-, formyl, and acetyl groups directly attached to a pyrrole nucleus have met with little success.[44] Acid [44, 45] and amide [46] groups in alkyl side chains can, however, be reduced normally, as can the propionic acid side chains in chlorins and porphyrins.[47] Quinoline- and pyridine-carboxylic esters furnish the expected hydroxymethyl derivatives.[48]

Under appropriate conditions, heterocyclic nuclei themselves undergo partial reduction. Thus pyridine, quinoline, acridine, phenazine, and benziminazole yield dihydro-derivatives.[49] Quinoxalines [49] and 1 : 2-dihydro-2-ketoquinoxalines [50] yield tetrahydroquinoxalines.

*Lithium and sodium borohydrides.* Although it is generally recognised that lithium and sodium borohydrides show greater selectivity in action than lithium aluminium hydride, the use of these reagents has been greatly restricted by their relative inaccessibility and high cost. Both these drawbacks should to a large extent be remedied now that the borohydrides may be obtained simply, and in excellent yield, by reduction of the boron tri-

---

[31] H. R. Bolliger and P. Ulrich, *Helv. Chim. Acta*, 1952, **35**, 93; H. R. Bolliger and M. Thürkauf, *ibid.*, p. 1426.

[32] D. R. Smith, M. Maienthal, and J. Tipton, *J. Org. Chem.*, 1952, **17**, 294; C. R. Walter, *J. Amer. Chem. Soc.*, 1952, **74**, 5185.

[33] A. Burger and E. D. Hornbaker, *ibid.*, p. 5514.

[34] H. R. Nace and B. B. Smith, *ibid.*, p. 1861.

[35] B. Witkop and J. B. Patrick, *ibid.*, p. 3861.

[36] W. Ried and F. Müller, *Chem. Ber.*, 1952, **85**, 470.

[37] C. Hanna and F. W. Schueler, *J. Amer. Chem. Soc.*, 1952, **74**, 3693; R. H. Poirier and F. Benington, *ibid.*, p. 3192.

[38] P. Karrer and B. J. R. Nicolaus, *Helv. Chim. Acta*, 1952, **35**, 1581.

[39] P. Karrer and E. Jucker, *ibid.*, p. 1586.

[40] L. M. Soffer, E. W. Parrotta, and J. Di Domenico, *J. Amer. Chem. Soc.*, 1952, **74**, 5301.

[41] A. Mustafa, *J.*, 1952, 2435; M. Meta and D. A. Sutton, *J.*, 1952, 2679.

[42] A. S. Spriggs, C. M. Hill, and G. W. Senter, *J. Amer. Chem. Soc.*, 1952, **74**, 1555.

[43] J. W. Cook, R. A. Raphael, and A. I. Scott, *J.*, 1952, 4416.

[44] A. Treibs and H. Scherer, *Annalen*, 1952, **577**, 139.

[45] B. R. Baker, R. E. Schaub, and J. H. Williams, *J. Org. Chem.*, 1952, **17**, 116.

[46] O. Klamerth and W. Kutscher, *Chem. Ber.*, 1952, **85**, 444.

[47] A. Kalojanoff, *Annalen*, 1952, **577**, 147.

[48] K. W. Rosenmund and F. Zymalkowski, *Chem. Ber.*, 1952, **85**, 152; R. G. Jones and E. C. Kornfeld, *J. Amer. Chem. Soc.*, 1951, **73**, 107.

[49] F. Bohlmann, *Chem. Ber.*, 1952, **85**, 380.

[50] J. Druey and A. Hüni, *Helv. Chim. Acta*, 1952, **35**, 2301.

fluoride–ether complex with lithium and sodium hydride respectively,[20] *e.g.*, $BF_3,Et_2O + 4LiH \longrightarrow LiBH_4 + 3LiF$.

Sodium borohydride has recently been used very successfully to reduce aldehydo-cardiac glycosides, and aglycones, to the corresponding alcohols, the sugar and unsaturated lactone groups being unaffected.[51]

With steroids, it has been found that 3-keto-groups are reduced with sodium borohydride much more readily than are those at $C_{(17)}$ or $C_{(20)}$. This enables 3α-hydroxy-testan-17-one (-*ætio*cholan-17-one), one of the principal urinary steroids, to be prepared in one operation from the readily available testane-3 : 17-dione.[52]

The greater selectivity of lithium and sodium borohydride, as compared with lithium aluminium hydride, has also been utilised, for example, for reduction of ketones to alcohols, the cyano-,[53] semicarbazono-,[53, 54] nitro-,[55] amido-,[56, 57] and ester [52] groups being left intact. The use of sodium borohydride in the elucidation of the structure of peptides is mentioned below (p. 149).

**Oxidation.**—Shaking an alcohol of the allylic type in light petroleum with manganese dioxide is proving to be a valuable method of wide application for the preparation of αβ-unsaturated aldehydes [58, 59] and ketones.[24, 59–61] It is noteworthy that *neo*vitamin A is thereby converted into *neo*retinene,[62] indicating that a *cis*-double bond is preserved under the conditions of the reaction. The method can be used successfully with the simple acetylenic alcohol, oct-3-yn-2-ol, but fails with hex-1-yn-3-ol, possessing an ethynyl group ($\cdot C\vdots CH$).[24]

These oxidations with manganese dioxide are not confined to petroleum solutions, as was originally inferred, and can be carried out in other non-hydroxylic solvents, such as carbon tetrachloride [24] and acetone,[5, 23] acetone being particularly suitable for the oxidation of petroleum-insoluble glycols.

Samples of manganese dioxide differ widely in their ability to effect oxidation, but may be simply and quickly graded by measuring the yield of cinnamaldehyde (as the 2 : 4-dinitrophenylhydrazone) from cinnamyl alcohol under standard conditions.[59] Details have been given for the preparation of manganese dioxide with high activity.[24, 61]

It has been shown that light accelerates the periodate oxidation of a number of simple organic substances such as formaldehyde and formic acid.[63] This has an important bearing on the use of periodate for the estimation of α-glycols and the chain length of polysaccharides.

[51] A. Hunger and T. Reichstein, *Chem. Ber.*, 1952, **85**, 635.

[52] E. Elisberg, H. Vanderhaeghe, and T. F. Gallagher, *J. Amer. Chem. Soc.*, 1952, **74**, 2814.

[53] N. L. Wendler, R. P. Graber, R. E. Jones, and M. Tishler, *J. Amer. Chem. Soc.*, 1952, **74**, 3630. [54] Huang-Minlon and R. H. Pettebone, *ibid.*, p. 1562.

[55] H. Shechter, D. E. Ley, and L. Zeldin, *ibid.*, p. 3664.

[56] E. C. Hermann and A. Kreuchunas, *ibid.*, p. 5168.

[57] K. Schlögl, F. Wessely, and G. Korger, *Monatsh.*, 1952, **83**, 493.

[58] S. Ball, T. W. Goodwin, and R. A. Morton, *Biochem. J.*, 1948, **42**, 516; N. L. Wendler, H. L. Slates, N. R. Trenner, and M. Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 719; K. R. Farrar, J. C. Hamlet, H. B. Henbest, and E. R. H. Jones, *J.*, 1952, 2657; H. R. Canna, P. D. Dalvi, R. A. Morton, M. K. Salah, G. R. Steinberg, and A. L. Stubbs, *Biochem. J.*, 1952, **52**, 535. [59] B. C. L. Weedon and R. J. Woods, *J.*, 1951, 2687.

[60] E. A. Braude and W. F. Forbes, *J.*, 1951, 1755.

[61] E. A. Braude and J. A. Coles, *J.*, 1952, 1430.

[62] P. D. Dalvi and R. A. Morton, *Biochem. J.*, 1952, **50**, 43.

[63] F. S. H. Head and G. Hughes, *J.*, 1952, 2046.

**Halogenation.**—In the presence of alkylammonium salts, olefins such as *cyclo*hexene undergo addition of bromine on treatment with *N*-bromosuccinimide,[64] the normal allylic substitution [65] being largely suppressed. Like benzoyl peroxide,[66] tertiary aliphatic azo-compounds catalyse homolytic brominations with *N*-bromosuccinimide.[67]

Direct bromination of polymethoxybenzenes frequently leads to complex mixtures. Monobromo-derivatives are, however, obtained in excellent yield by bromination, catalysed by ferric chloride, in acetic anhydride with pyridinium bromide perbromide.[68]

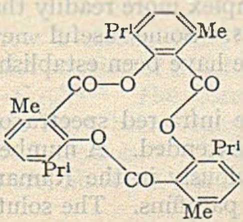
Solutions of trifluoroacetyl hypohalites (*e.g.*, $CF_3{\cdot}CO_2I$), prepared from silver trifluoroacetate and iodine or bromine, have been used to effect electrophilic halogenation of several aromatic compounds.[69] Further examples have been given of the direct iodination of benzene derivatives in sulphuric acid with iodine and silver sulphate.[70]

**Urea and Thiourea Complexes.**[71]—The crystal structure of urea adducts of *n*-paraffins has been examined in detail.[72]

By precipitation of the non-peroxidic portion of methyl oleate autoxidation mixtures as urea complexes, concentrates containing 70—90% of peroxides are readily isolated.[73] Vinyl esters of long-chain fatty acids may be purified by means of urea complexes.[74]

Thiourea, which forms complexes with a wide variety of branched-chain compounds, also yields adducts with *n*-paraffins containing fourteen or more carbon atoms.[75]

**Optical Resolutions.**—The study of molecular compounds of the clathrate type has led to remarkable new procedures for the resolution of some racemic compounds. Although tri-*o*-thymotide (XV) [76] crystallises as a racemate, resolution takes place on formation of its crystalline adduct with *n*-hexane, benzene, or chloroform.[77] Racemisation occurs rapidly in solution, and therefore all the trithymotide can be removed in the (+)- or the (—)-form by



(XV)

---

[64] E. A. Braude and E. S. Waight, *J.*, 1952, 1116.

[65] C. Djerassi, *Chem. Reviews*, 1948, 43, 271.

[66] H. Schmid and P. Karrer, *Helv. Chim. Acta*, 1946, **29**, 573.

[67] M. C. Ford and W. A. Waters, *J.*, 1952, 2240.

[68] E. C. Horning and J. A. Parker, *J. Amer. Chem. Soc.*, 1952, **74**, 2107.

[69] R. N. Haszeldine and A. G. Sharpe, *J.*, 1952, 993.

[70] I. R. L. Barker and W. A. Waters, *J.*, 1952, 150.

[71] *Ann. Reports*, 1949, **46**, 156; 1950, **47**, 165; 1951, **48**, 155; R. W. Schiessler and D. Flitter, *J. Amer. Chem. Soc.*, 1952, **74**, 1720.

[72] A. E. Smith, *Acta Cryst.*, 1952, **5**, 224.

[73] J. E. Coleman, H. B. Knight, and D. Swern, *J. Amer. Chem. Soc.*, 1952, **74**, 4886.

[74] D. Swern and W. S. Port, *ibid.*, p. 1738.

[75] R. L. McLaughlin and W. S. McClesnahan, *ibid.*, p. 5804.

[76] W. Baker, B. Gilbert, and W. D. Ollis, *J.*, 1952, 1443.

[77] A. C. D. Newman and H. M. Powell, *ibid.*, p. 3747.

slow, controlled growth of a single crystal or homogeneous crop. When an adduct is formed with a compound which is itself a (±)-mixture, one enantiomorph of the latter is enclosed preferentially in the asymmetric cavities of a trithymotide crystal. In this way *sec.*-butyl bromide can be resolved.[78] This trithymotide process should be applicable to a range of substances, and does not require a functional group in the molecule to be resolved; it will of course fail with molecules which are too large for the cavities. A further notable feature of the method is that it does not depend on the use of asymmetric substances; it has even been suggested that somewhat similar processes may be responsible for the much debated origin of optical activity in Nature.[78]

In a similar way, (±)-2-chloro-octane has been resolved by the preferential formation of the urea–(+)-chloride or urea–(−)-chloride complex; the urea inclusion compounds have a screw-like lattice.[78a]

Many racemic aromatic amino-acids are separated into their enantiomorphs on paper chromatograms.[79] These resolutions are probably due to a higher degree of adsorption of one isomer of the solute on the surface of the optically active cellulose. Partial resolution of camphorsulphonic acid and mandelic acid on silica gel, prepared in the presence of an enantiomorph of the acid to be resolved, has been claimed.[80]

It is known that if a cobalt complex contains two optically active bidentate groups, a third optically active group co-ordinates more firmly if it has the same configuration as those already present.[81] Advantage of this principle has been taken to effect partial resolutions of (±)-tartaric, α-chloropropionic, and lactic acids; on reaction of the (±)-acids with carbonatobis-*l*-propylenediaminocobalt(III) chloride, the D-forms enter the co-ordination sphere of the complex more readily than do the L-forms.[82]

**Spectrophotometric Methods.**—Some useful new correlations between spectra and molecular structure have been established recently in the fatty-acid and the steroid field.

Earlier observations on the infra-red spectra of fatty acids, and their esters, have been considerably extended. A number of the phenomena now reported have been noted previously in the Raman spectra of fatty acids, and in the infra-red spectra of paraffins. The solution spectra of saturated fatty acids consist largely of broad bands and are of very similar appearance, but the intensity of the methylene rocking band (720 cm.$^{-1}$) increases progressively as the chain is lengthened. The solid-phase spectra show much more fine structure, and significant differences are observed between the spectra of homologues, and of polymorphic modifications of the same acid.[83, 84]

A number of solution spectra of branched chain fatty acids have been

---

[78] H. M. Powell, *Nature*, 1952, **170**, 155.

[78a] W. Schlenck, *Experientia*, 1952, **8**, 337.

[79] M. Kotake, T. Sakan, N. Nakamura, and S. Senoh, *J. Amer. Chem. Soc.*, 1951, **73**, 2973; C. E. Dalgliesh, *J.*, 1952, 137, 3940; *Biochem. J.*, 1952, **52**, 3; M. Mason and C. P. Berg, *J. Biol Chem.*, 1952, **195**, 515.

[80] R. Curti and U. Colombo, *J. Amer. Chem. Soc.*, 1952, **74**, 3961.

[81] J. C. Bailar, H. B. Jonassen, and A. D. Gott, *ibid.*, p. 3131.

[82] A. D. Gott and J. C. Bailar, *ibid.*, p. 4820.

[83] R. N. Jones, A. F. McKay, and R. G. Sinclair, *ibid.*, pp. 2570, 2575.

[84] N. K. Freeman, *ibid.*, p. 2523.

recorded.[84] Branching within five carbon atoms of the carboxyl group, particularly at $C_{(\alpha)}$, can be recognised. The number of side-chain (terminal methyl) groups can be deduced with reasonable certainty, and it is tentatively claimed that indications of the presence of ethyl, propyl, and *gem.*-dimethyl groups can be obtained.

It has been found that the absorption band (966 cm.$^{-1}$) [85] characteristic of a *trans*-double bond in the environment $-CH_2 \cdot CH{:}CH \cdot CH_2-$ is displaced by 12—18 cm.$^{-1}$ to higher frequencies in *trans*-αβ-unsaturated fatty acids and *iso*butylamides.[86, 87] The corresponding *cis*-isomers absorb very weakly in this region. The *cis*- and the *trans*-isomers of αβ-unsaturated acids may also be distinguished by a small, but definite, difference in the C=C stretching frequency.[86, 87]

Absorption bands of steroids in the 1350—1500 cm.$^{-1}$ region have been assigned to the various types of methylene and methyl groups in the molecule.[88] The cyclic methylene groups of the steroid system absorb at a different frequency from those in the linear side chain. Methylene groups adjacent to carbonyl groups and to double bonds absorb at characteristic positions. Angular methyl groups, terminal side-chain methyl groups, and those in acetoxy-substituents, all absorb at different wave-lengths and can be distinguished.

The degree of substitution of an isolated (unconjugated) double bond in a steroid can be determined by ultra-violet light absorption measurements, the presence of either of the two tetra-substituted bond types ($\Delta^{8(9)}$ and $\Delta^{8(14)}$) being easily detected.[89] A $\Delta^5$-double bond in 3β-acetoxy-steroids with the normal configuration, and without other substituents in the vicinity of the double bond, may be recognised [90] by means of two characteristic peaks near 800 and 812 cm.$^{-1}$.

3-Hydroxy-steroids show a strong band (C—OH stretching) between 995 and 1055 cm.$^{-1}$, the exact position of which depends on the stereochemical configuration at $C_{(3)}$ and $C_{(5)}$.[91, 92] The correlations established earlier [93] with the 3-acetoxy-steroids have been found to hold quite well with the acetates of the four isomeric 2-decalols.[94] The differences between the spectra of the decalols themselves are, however, not so well-defined as with those of the hydroxy-steroids.

The infra-red and Raman spectra of acetylenic and ethylenic hydrocarbons have been reviewed.[95]

**Aliphatic Acids.**—Pimelic acid is formed in good yield when *cyclo*hex-3-enecarboxylic acid, from butadiene and acrylic acid, is heated with aqueous alkali under pressure.[96]

---

[85] L. Crombie, *Quart. Reviews*, 1952, 6, 101. [86] L. Crombie, *J.*, 1952, 2997, 4338.

[87] R. G. Sinclair, A. F. McKay, G. S. Myers, and R. N. Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 2578.

[88] R. N. Jones and A. R. H. Cole, *ibid.*, p. 5648; R. N. Jones, A. R. H. Cole, and B. Nolin, *ibid.*, p. 5662.

[89] P. Bladon, H. B. Henbest, and G. W. Wood, *J.*, 1952, 2737.

[90] H. Hirschmann, *J. Amer. Chem. Soc.*, 1952, **74**, 5357.

[91] A. R. H. Cole, R. N. Jones, and K. Dobriner, *ibid.*, p. 5571.

[92] H. Rosenkrantz, A. T. Milhorat, and M. Farber, *J. Biol. Chem.*, 1952, **195**, 509.

[93] R. N. Jones, P. Humphries, F. Herling, and K. Dobriner, *J. Amer. Chem. Soc.*, 1951, **73**, 3215.

[94] W. G. Dauben, E. Hoerger, and N. K. Freeman, *ibid.*, 1952, **74**, 5206.

[95] N. Sheppard and D. M. Simpson, *Quart. Reviews*, 1952, 6, 1.

[96] F. X. Werber, J. E. Jansen, and T. L. Gresham, *J. Amer. Chem. Soc.*, 1952, **74**, 532.

Fatty acids are converted quantitatively into their anhydrides on treatment in pyridine with thionyl chloride.[97]

**Ketones.**—The malonates (XVI; R′ = tetrahydro-2-pyranyl), readily prepared from dihydropyran and the appropriate malonic acid under the influence of an acidic catalyst, are used in an elegant new route to a wide variety of saturated and unsaturated ketones:[98]

$$\text{(XVI)}\quad R\cdot CH(CO_2R')_2 \xrightarrow{R''\cdot COCl} R''\cdot CO\cdot CR(CO_2R')_2 \longrightarrow R''\cdot CO\cdot CH_2R$$

The process can be modified to give β-keto-esters. The advantage of using the tetrahydropyranyl and also *tert.*-butyl[99] esters lies in the ease with which the derived acylmalonates are converted on being warmed, preferably with a trace of acetic acid, into the required ketone with evolution of carbon dioxide and dihydropyran or *iso*butene.

Peroxide-catalysed addition of aldehydes to unsaturated esters and ketones yields keto-esters and diketones difficult to prepare in other ways;[100] thus acetylsuccinic ester is obtained from acetaldehyde and ethyl maleate.

**Peptide Syntheses.**[101]—Further details and examples have been published of the methods, mentioned in previous reports,[102] using an acylaminoacylthiophenol,[103] a mixed anhydride of an acylamino-acid with either sulphuric acid[104] or carbonic acid,[105] or an α-carbethoxy-*iso*cyanate.[106]

In the carbobenzyloxy-method,[107] the substitution of benzyl chloroformate by *p*-nitrobenzyl chloroformate is sometimes advantageous.[108] The latter reagent is a stable low-melting solid, and with amino-acids gives derivatives which crystallise readily. *o*-Nitrophenoxyacetyl and chloroacetyl derivatives of amino-acids can be used[109] in the azide[110] and the chloroformate[105, 111] method of peptide synthesis respectively; the subsequent removal of the protecting groups is accomplished by methods described on p. 156. Amino-acids and peptides are regenerated from their *N*-phthaloyl derivatives more conveniently by the action of phenylhydrazine[112] than by the usual hydrazine procedure.[113]

A modification of the azide method[110] of peptide synthesis has been

---

[97] W. Gerrard and A. M. Thrush, *J.*, 1952, 741.

[98] R. E. Bowman and W. D. Fordham, *J.*, 1952, 3945.

[99] G. S. Fonken and W. S. Johnson, *J. Amer. Chem. Soc.*, 1952, **74**, 831.

[100] T. M. Patrick, *J. Org. Chem.*, 1952, **17**, 1009; A. Mondon, *Angew. Chem.*, 1952, **64**, 224.

[101] For recent reviews see B. L. Shapiro, *Chem. and Ind.*, 1952, 1119; T. Wieland, *Angew. Chem.*, 1951, **63**, 7.

[102] *Ann. Reports*, 1950, **47**, 162; 1951, **48**, 151.

[103] T. Wieland and W. Schäfer, *Annalen*, 1952, **576**, 104.

[104] G. W. Kenner and R. J. Stedman, *J.*, 1952, 2069.

[105] J. R. Vaughan and R. L. Osato, *J. Amer. Chem. Soc.*, 1952, **74**, 676.

[106] D. Goldschmidt and M. Wick, *Annalen*, 1952, **575**, 217.

[107] M. Bergmann and L. Zervas, *Ber.*, 1932, **65**, 1192.

[108] F. H. Carpenter and D. T. Gish, *J. Amer. Chem. Soc.*, 1952, **74**, 3818.

[109] R. W. Holley and A. D. Holley, *ibid.*, p. 3069.

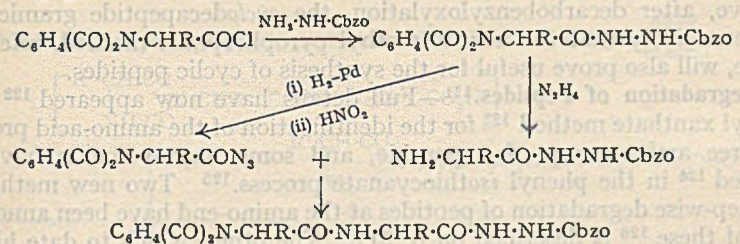
[110] T. Curtius, *J. pr. Chem.*, 1904, **70**, 73.

[111] R. A. Boissonnas, *Helv. Chim. Acta*, 1951, **34**, 874.

[112] I. Schumann and R. A. Boissonnas, *ibid.*, 1952, **35**, 2235, 2237; *Nature*, 1952, **169**, 154.

[113] See, for example, J. C. Sheehan, D. W. Chapman, and R. W. Roth, *J. Amer. Chem. Soc.*, 1952, **74**, 3822; F. E. King and D. A. A. Kidd, *J.*, 1949, 3315.

outlined which makes use of the previously unknown azides of phthalimido-acids and peptides,[114] *e.g.* :



Cbzo = $Ph{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}$

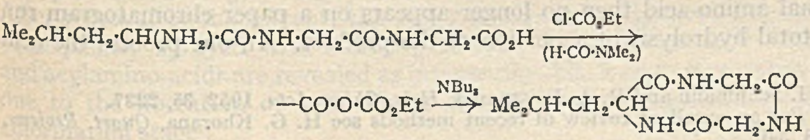
An attractive new peptide synthesis has been developed[115] which consists simply in the addition of tetraethyl pyrophosphate to a solution in diethyl phosphite of an acylamino-acid (or peptide) and an amino-acid (or peptide) ester :

$$R{\cdot}CO{\cdot}NH{\cdot}CHR'{\cdot}CO_2H + NH_2{\cdot}CHR''{\cdot}CO_2Et \xrightarrow{[(EtO)_2P]_2O} R{\cdot}CO{\cdot}NH{\cdot}CHR'{\cdot}CO{\cdot}NH{\cdot}CHR''{\cdot}CO_2Et$$

$$\text{(XVII)}\quad R{\cdot}CO{\cdot}NH{\cdot}CHR'{\cdot}CO{\cdot}O{\cdot}P(OEt)_2 \qquad (EtO)_2P{\cdot}NH{\cdot}CHR''{\cdot}CO_2Et\quad \text{(XVIII)}$$

Modifications of this " standard " procedure, which may prove advantageous in special cases, involve treating the pyrophosphate initially with either of the two amino-acid components. The diethyl phosphite anhydride (XVII) (" anhydride route ") or diethylphosphamidite (XVIII) (" amide route ") thus formed is then treated with the second amino-acid derivative. When an optically active acyl dipeptide is used racemisation is observed only in the " anhydride route." The same intermediates (XVII)[116] and (XVIII)[117] may also be prepared, though less conveniently, by the action of diethyl chlorophosphite on the acylamino-acid or amino-acid respectively.

Of recent years considerable interest in cyclic polypeptides has been aroused by the recognition that a number of natural compounds belong to this class. It is therefore particularly noteworthy that, by a modification of the chloroformate method,[105, 111] and by application of the Ziegler dilution principle,[118] a synthesis of a cyclic polypeptide, *cyclo*leucylglycyl glycyl (XIX), has been achieved.[119] While the formation of larger rings will



(XIX)

probably prove more difficult, owing to less favourable steric factors, it nevertheless seems feasible. Attempts to cyclise two molecules of the

---

[114] K. Hofmann, A. Lindenmann, M. Z. Magee, and N. H. Khan, *J. Amer. Chem. Soc.*, 1952, **74**, 470.

[115] G. W. Anderson, J. Blodinger, and A. D. Welcher, *ibid.*, p. 5309.

[116] G. W. Anderson and R. W. Young, *ibid.*, p. 5307.

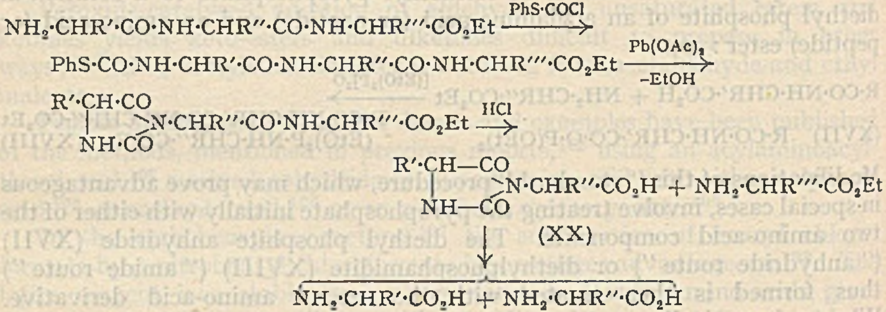
[117] G. W. Anderson, J. Blodinger, R. W. Young, and A. D. Welcher, *ibid.*, p. 5304.

[118] K. Ziegler, H. Eberle, and H. Ohlinger, *Annalen*, 1933, **504**, 94.

[119] R. A. Boissonnas and I. Schumann, *Helv. Chim. Acta*, 1952, **35**, 2229.

recently prepared[120] pentapeptide, L-valyl-L-δ-carbobenzyloxyornithyl-L-leucyl-D-phenylalanyl-L-proline will doubtless be made in the near future, to give, after decarbobenzyloxylation, the *cyclo*decapeptide gramicidin S. It seems likely that the new tetraethyl pyrophosphate method, referred to above, will also prove useful for the synthesis of cyclic peptides.

**Degradation of Peptides.**[121]—Full details have now appeared[122] of the dialkyl xanthate method[123] for the identification of the amino-acid providing the free amino-group of a peptide, and some improvements have been effected[124] in the phenyl *iso*thiocyanate process.[125] Two new methods for the step-wise degradation of peptides at the amino-end have been announced. One of these[126] is described on p. 211. The other, which to date has only been applied to two model tripeptides, enables the terminal and the penultimate amino-acid to be identified simultaneously:[127]



To establish the order of the end two amino-acids in the original peptide, the structure of the hydantoin (XX) is determined by reduction of its acid chloride with sodium borohydride, and subsequent hydrolysis to an amino-acid and an amino-alcohol. The more readily available *N*-carbalkoxy-derivative (XXI) of the peptide may also be used as shown below, but, as the final ring closure can occur in two ways, the structure of the hydantoin does not necessarily indicate the actual sequence of the two amino-acids in the peptide chain.[128, 129]

Of the new methods for the degradation of the acid end of a peptide, two involve destruction of the free carboxyl group in an *N*-derivative; the terminal amino-acid then no longer appears on a paper chromatogram run after total hydrolysis of a portion of the product. In one process the acid

---

[120] I. Schumann and R. A. Boissonnas, *Helv. Chim. Acta*, 1952, **35**, 2237.

[121] For an excellent review of recent methods see H. G. Khorana, *Quart. Reviews*, 1952, **6**, 340.

[122] G. W. Kenner and H. G. Khorana, *J.*, 1952, 2076.

[123] *Ann. Reports*, 1951, **48**, 154.

[124] B. Dahlerup-Petersen, K. Linderstrøm-Lang, and M. Ottesen, *Acta Chem. Scand.*, 1952, **6**, 1135.

[125] *Ann. Reports*, 1950, **47**, 165.

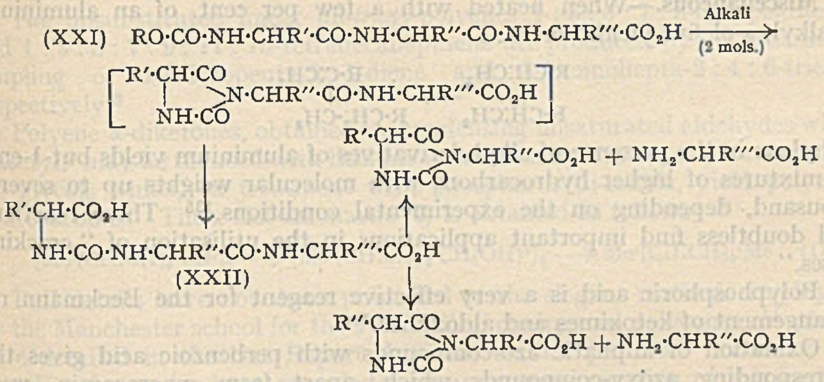
[126] R. W. Holley and A. D. Holley, *J. Amer. Chem. Soc.*, 1952, **74**, 5445.

[127] F. Wessely, K. Schlögl, and E. Wawersich, *Monatsh.*, 1952, **83**, 1439; A. Lindenmann, N. H. Khan, and K. Hofmann, *J. Amer. Chem. Soc.*, 1952, **74**, 476.

[128] F. Wessely, K. Schlögl, and G. Korger, *Monatsh.*, 1952, **83**, 1156; *Nature*, 1952, **169**, 708.

[129] F. Wessely, K. Schlögl, and E. Wawersich, *Monatsh.*, 1952, **83**, 1426.

chloride of an *N*-carbalkoxypeptide (XXI), or the derived urea peptide (XXII), is reduced with sodium borohydride.[129, 129a] In the other,[130] *N*-



carbobenzyloxy- and *N*-dinitrophenyl-peptides (XXIII) are subjected to the anodic methoxylation reaction discovered earlier with α-acylamino-acids:[131]

$$\begin{tikzcd} \underset{\text{(XXIII)}}{\text{—CHR}''\text{·CO·NH·CHR}'\text{·CO}_2\text{H}} \arrow[r] & \underset{\text{(XXIV)}}{\text{—CHR}''\text{·CO·NH·CHR}'\text{·OMe} + \text{CO}_2} \arrow[d, "\text{HCl}"] \\ & \text{—CHR}''\text{·CO}_2\text{H} + \text{NH}_3 + \text{R}'\text{·CHO} + \text{MeOH} \end{tikzcd}$$

The second method has the advantage that hydrolysis of the methoxy-compound (XXIV) yields a substituted peptide on which the process can be repeated. The terminal amino-acid of an *N*-dinitrophenylpeptide can also be identified after removal by partial enzymic hydrolysis with carboxypeptidase.[132]

Treatment of silk fibroin with concentrated sulphuric acid at room temperature results in an average transfer of *ca.* 60% of the peptide chains linked to the nitrogen atoms of the serine residues to the hydroxyl groups of these residues. After acetylation of the product, the *O*-peptidyl bonds may be hydrolysed with alkali.[133] This method of hydrolysis of specific peptide bonds is probably applicable to other polypeptides containing serine or threonine residues.

A valuable new process has been introduced for the detection of all kinds of peptides, including cyclic peptides and proteins, on paper chromatograms. After removal of the solvent, the paper is exposed to gaseous chlorine and subsequently sprayed with starch–potassium iodide solution.[134] Peptides and acylamino-acids are revealed as intense blue-black spots, the colour being due to the liberation of iodine from the *N*-chloropeptides formed in the chlorination stage :

$$\text{-CO·NH-} \xrightarrow{\text{Cl}_2} \text{-CO·NCl-} \xrightarrow{\text{KI}} \text{-CO·NH-} + \text{HCl} + \text{I}$$

The great merit of the new method, compared with that using ninhydrin, is that the colour developed is as intense with proteins and peptides of high

---

[129a] Cf. J. L. Bailey, *Biochem. J.*, 1952, **52**, iv.

[130] R. A. Boissonnas, *Helv. Chim. Acta*, 1952, **35**, 2226.

[131] R. P. Linstead, B. R. Shephard, and B. C. L. Weedon, *J.*, 1951, 2854.

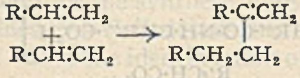
[132] E. Waldschmidt-Leitz and K. Gauss, *Chem. Ber.*, 1952, **85**, 353.

[133] D. F. Elliot, *Biochem. J.*, 1952, **50**, 542.

[134] H. N. Rydon and P. W. G. Smith, *Nature*, 1952, **169**, 922.

molecular weight as it is with those of low molecular weight. Most amino-acids also give positive results.

**Miscellaneous.**—When heated with a few per cent. of an aluminium trialkyl, α-olefins yield dimers :



$$\begin{array}{c} R{\cdot}CH{:}CH_2 \\ + \\ R{\cdot}CH{:}CH_2 \end{array} \longrightarrow \begin{array}{l} R{\cdot}C{:}CH_2 \\ \quad | \\ R{\cdot}CH_2{\cdot}CH_2 \end{array}$$

Ethylene in the presence of alkyl derivatives of aluminium yields but-1-ene, or mixtures of higher hydrocarbons with molecular weights up to several thousand, depending on the experimental conditions.[135] These reactions will doubtless find important applications in the utilisation of " cracking gases."

Polyphosphoric acid is a very effective reagent for the Beckmann rearrangement of ketoximes and aldoximes.[136]

Oxidation of aliphatic azo-compounds with perbenzoic acid gives the corresponding azoxy-compounds which, apart from macrozamin, were formerly unknown.[137]

Solutions of fuming nitric acid in trifluoroacetic anhydride can be used to synthesise nitrate esters from polyhydric alcohols, and nitro-derivatives from aromatic compounds, including those possessing deactivating groups.[138]

B. C. L. W.

## 4. ALIPHATIC COMPOUNDS.

**Hydrocarbons.**—The saturated hydrocarbons *n*-do-octacontane, $C_{82}H_{166}$, and *n*-hectane, $C_{100}H_{202}$, have been prepared by the Wurtz reaction on 1-iodohentetracontane and 1-iodopentacontane respectively.[1] A series of hydrocarbons containing recurrent groups has been obtained by standard methods involving anodic coupling of ββ-disubstituted glutaric half-esters and reduction of the ester groupings in the product to methyl.[2]

The original Boord synthesis of terminally unsaturated olefins [3] has been rendered more convenient by a much improved preparation of the starting αβ-dibromo-ethers, involving addition of bromine to the commercially available alkyl vinyl ethers.[4]

Mass-spectrometric methods have been applied to the problem of competitive olefin formation from quaternary ammonium hydroxides; [5] the results confirm the generalisation derived earlier that the alkyl group having the most acidic β-hydrogen is preferentially eliminated as olefin.[6] The simplest hydrocarbon with three cumulated double bonds, butatriene,

---

[135] K. Ziegler, *Angew. Chem.*, 1952, **64**, 323.

[136] E. C. Horning and V. L. Stromberg, *J. Amer. Chem. Soc.*, 1952, **74**, 2680, 5151; E. C. Horning, V. L. Stromberg, and H. A. Lloyd, *ibid.*, p. 5153.

[137] B. W. Langley, B. Lythgoe, and L. S. Rayner, *J.*, 1952, 4191.

[138] E. J. Bourne, M. Stacey, J. C. Tatlow, and J. M. Tedder, *ibid.*, p. 1695.

[1] G. Ställberg, S. Ställberg-Stenhagen, and E. Stenhagen, *Acta Chem. Scand.*, 1952, **6**, 313.

[2] S. F. Birch, V. E. Gripp, D. T. McAllan, and W. S. Nathan, *J.*, 1952, 1363.

[3] *Ann. Reports*, 1930, **27**, 83.

[4] D. C. Rowlands, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Org. Chem.*, 1952, **17**, 807.

[5] P. A. S. Smith and S. Frank, *J. Amer. Chem. Soc.*, 1952, **74**, 509.

[6] W. Hanhart and C. K. Ingold, *J.*, 1927, 997.

$CH_2{:}C{:}C{:}CH_2$, has been obtained by debromination of 1 : 4-dibromobutyne with zinc.[7]

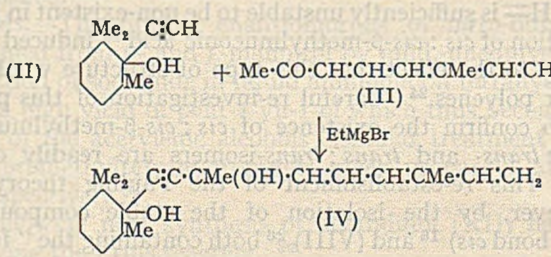
The unsubstituted linear all-*trans*-polyenes 1 : 3 : 5 : 7 : 9-decapentaene and 1 : 3 : 5 : 7 : 9 : 11 : 13-tetradecaheptaene are produced by the sodamide coupling of 1-chloropenta-2 : 4-diene and 1-bromohepta-2 : 4 : 6-triene respectively.[8]

Polyene α-diketones, obtained by condensing unsaturated aldehydes with diacetyl,[9] may be reduced with lithium aluminium hydride to the corresponding glycols which, on treatment with phosphorus di-iodide, yield polyene hydrocarbons. Thus, eicosanonaene (I) is obtained as follows : [10]

$$[Me\cdot(CH{:}CH)_4\cdot CO\cdot]_2 \longrightarrow [Me\cdot(CH{:}CH)_4\cdot CH(OH)\cdot]_2 \longrightarrow Me\cdot[CH{:}CH]_9\cdot Me \quad \text{(I)}$$

Full details have now been published of the elegant methods employed by the Manchester school for the synthesis of conjugated poly-ynes; [11] these were detailed in the last Report.[14] Some similar processes involving diacetylene have also been recorded; an unexpected reaction of this hydrocarbon involves formation of vinyldiacetylene [13] from the monosodium derivative and vinyl bromide.

**Carotenoids.**—An æsthetically satisfying synthesis of vitamin $A_1$ from *cyclo*hexanone has been evolved. The key step involves condensation of the $C_{11}$ ethynyl-alcohol (II) with the $C_9$ ketone (III) to give the $C_{20}$ glycol (IV) whence, by standard processes of anionotropic rearrangement, acetylation of the primary hydroxyl group, partial hydrogenation, and dehydration of the tertiary hydroxyl group, vitamin $A_1$ acetate is obtained.[15] Variants of this procedure have also been investigated and the paper is remarkable for its scrupulous attention to detail.



It has been established that the acid-catalysed rearrangement-dehydration of β-ionols (*e.g.*, V) gives only small yields (3%) of the β-ionylidene compound (VI), the main product (90%) being the isomeric substance (VII) which is termed a *retro*ionylidene compound. Several other examples of this type of

---

[7] W. M. Schubert, T. H. Liddicoet, and W. A. Lanka, *J. Amer. Chem. Soc.*, 1952, **74**, 569.

[8] A. D. Mebane, *ibid.*, p. 5227.

[9] P. Karrer and C. Cochand, *Helv. Chim. Acta*, 1945, **28**, 1181.

[10] F. Bohlmann, *Chem. Ber.*, 1952, **85**, 386.

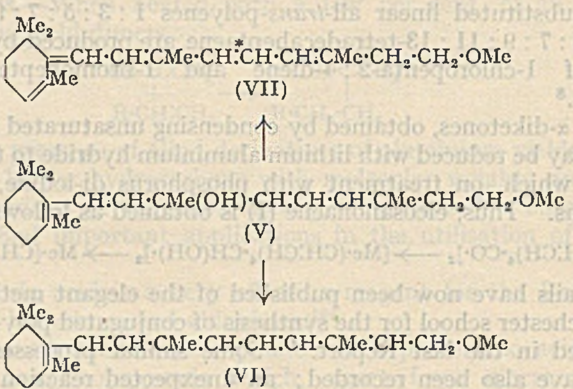
[11] J. B. Armitage, E. R. H. Jones, and M. C. Whiting, *J.*, 1952, 1993, 2014; J. B. Armitage, C. L. Cook, N. Entwhistle, E. R. H. Jones, and M. C. Whiting, *ibid.*, p. 1998; J. B. Armitage and M. C. Whiting, *ibid.*, p. 2005; J. B. Armitage, C. L. Cook, E. R. H. Jones, and M. C. Whiting, *ibid.*, p. 2010; C. L. Cook, E. R. H. Jones, and M. C. Whiting, *ibid.*, p. 2883.

[13] T. Herbertz, *Chem. Ber.*, 1952, **85**, 475.

[14] *Ann. Reports*, 1951, **48**, 157.

[15] J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J.*, 1952, 1094.

rearrangement are described and it is pointed out that some previous work in the vitamin $A_1$ field needs reassessment on this basis.[16]



(VII)

(V)

(VI)

The use of *cyclo*hexenyl- and 6 : 6-dimethyl*cyclo*hexenyl-lithium for obtaining substances related to vitamin $A_1$ has been recorded.[17]

Details of the synthesis of vitamin $A_2$ described in last year's Report [18] have now appeared.[19] Manganese dioxide oxidation of both the synthetic [19] and natural [20] vitamins has furnished the corresponding aldehyde which is identical with the retinene$_2$ isolated from the retinas of fresh-water fish. The isomeric $C_{20}H_{26}O$ aldehyde obtained by Oppenauer oxidation of vitamin $A_1$ is not identical with retinene$_2$ and an allene structure is suggested for it.[21]

Pauling has postulated that the highly hindered system $=\!CMe\cdot CH\overset{cis}{=}CH\cdot CH\!=$ is sufficiently unstable to be non-existent in polyenes.[22] The reported isolation of *cis* : *cis*-β-methylmuconic acid [23] induced a modification of the theory to the effect that this type of structure would be more stable in the lower polyenes.[24] Careful re-investigation of this point, however, has failed to confirm the existence of *cis* : *cis*-β-methylmuconic acid although the *cis* : *trans*- and *trans* : *trans*-isomers are readily obtainable, stable entities.[25] This re-establishment of the Pauling theory is again jeopardised, however, by the isolation of the stable compounds (VII; " starred " double bond *cis*) [16] and (VIII) [26] both containing the " forbidden " structural feature. It appears that caution should be exercised in using this theory to eliminate isomers.

The hydrocarbon (VIII) is obtained from the diacetylenic tetraol (IX) by

---

[16] W. Oroshnik, G. Karmas, and A. D. Mebane, *J. Amer. Chem. Soc.*, 1952, **74**, 295, 3807; P. Karrer and J. Kebrle, *Helv. Chim. Acta*, 1952, **35**, 2570.

[17] E. A. Braude, T. Bruun, B. C. L. Weedon, and R. J. Woods, *J.*, 1952, 1414, 1419.

[18] *Ann. Reports*, 1951, **48**, 160.

[19] K. R. Farrar, J. C. Hamlet, H. B. Henbest, and E. R. H. Jones, *J.*, 1952, 2657.

[20] H. R. Cama, P. D. Dalvi, R. A. Morton, M. K. Salah, G. R. Steinberg, and A. L. Stubbs, *Biochem. J.*, 1952, **52**, 535; H. R. Cama, P. D. Dalvi, R. A. Morton, and M. K. Salah, *ibid.*, p. 540.

[21] H. R. Cama, A. C. Field, J. Glover, R. A. Morton, and M. K. Salah, *ibid.*, p. 548.

[22] L. Pauling, *Fortschr. Chem. org. Naturstoffe*, 1939, **3**, 203; L. Zechmeister, *Chem. Reviews*, 1944, **34**, 267.

[23] P. Karrer. R. Schwyzer, and A. Neuwirth, *Helv. Chim. Acta*, 1948, **31**, 1210.

[24] L. Pauling, *ibid.*, 1949, **32**, 2241.

[25] J. A. Elvidge, R. P. Linstead, and P. A. Sims, *J.*, 1951, 3386, 3398.

[26] C. F. Garbers, C. H. Eugster, and P. Karrer, *Helv. Chim. Acta*, 1952, **35**, 1179, 1850.

dehydration and subsequent partial catalytic hydrogenation of the triple bonds; stereomutation with iodine furnishes the all-*trans*-isomer, the phenyl analogue of carotene.[26] Two isomeric by-products from the dehydration of

$$\begin{tikzcd}[row sep=large]
\text{(Ph·CH:CH·CMe:CH·CH}\overset{cis}{=\!=}\text{CH·CMe:CH·CH:)}_2 \quad \text{(VIII)} \\
\text{[Ph·CH:CH·CMe(OH)·CH}_2\text{·C⋮C·CMe(OH)·CH}_2\text{·CH:]}_2 \quad \text{(IX)} \arrow[u, "\text{(i) }-\text{H}_2\text{O}", "\text{(ii) Pd–H}_2"'] \arrow[d, "-\text{H}_2\text{O}"] \\
\text{(Ph·CH:CH·CMe:C:C:CH·CMe:CH·CH:)}_2 \quad \text{(X)}
\end{tikzcd}$$

(IX) are considered to possess cumulene structures, one of which (X) is shown.[26]

The most notable event of the current year in the synthetic carotenoid field has been the total synthesis of all-*trans*-methylbixin (XI) by the reactions shown (R = tetrahydro-2-pyranyl).[27]

$$\text{2RO·CH}_2\text{·CMe:CH·C⋮CH + Me·CO·CH}_2\text{·CH:CH·CH}_2\text{·CO·Me} \longrightarrow$$

$$\text{(RO·CH}_2\text{·CMe:CH·C⋮C·CMe:CH·CH:)}_2 \xrightarrow[\text{(ii) MnO}_2]{\text{(i) H}^+} \text{(OCH·CMe:CH·C⋮C·CMe:CH·CH:)}_2$$

$$\xrightarrow[\text{(ii) MeOH}]{\text{(i) Malonic acid}} \text{(MeO}_2\text{C·CH:CH·CMe:CH·C⋮C·CMe:CH·CH:)}_2 \xrightarrow[\text{(ii) I}_2]{\text{(i) Pd–H}_2}$$

$$\text{(MeO}_2\text{C·CH:CH·CMe:CH·CH:CH·CMe:CH·CH:)}_2 \quad \text{(XI)}$$

A review of geometrical isomerism about carbon–carbon double bonds has been published.[28]

**Alcohols.**—The optical enantiomorphs of *threo*-butane-2 : 3-diol have been obtained from D- and L-mannitol by mild, unequivocal reactions.[29]

The action of sodamide in liquid ammonia on tetrahydrofurfuryl chloride furnishes a high yield of pent-4-yn-1-ol which thus becomes one of the most accessible of the acetylenic alcohols; similar treatment of epichlorohydrin and 2-chloromethyltetrahydropyran gives propargyl alcohol and hex-5-yn-1-ol respectively.[30]

The following neat synthesis of lavandulol (XII) has been achieved[31] by employing the Prins reaction :[32]

$$\text{AcO·CMe}_2\text{·CH}_2\text{·CH}_2\text{·CH:CMe}_2 \xrightarrow[\text{AcOH–H}_2\text{SO}_4]{\text{(CH}_2\text{O)}_n}$$

$$\text{AcO·CMe}_2\text{·CH}_2\text{·CH}_2\text{·CH(CH}_2\text{·OAc)·CMe}_2\text{·OAc} \xrightarrow[\text{(ii) hydrolysis}]{\text{(i) Pyrolysis;}}$$

$$\text{Me}_2\text{C:CH·CH}_2\text{·CH(CH}_2\text{·OH)·CMe:CH}_2 \quad \text{(XII)}$$

The growing family of the remarkable naturally occurring polyenynes (see p. 160) has been further augmented by the isolation of the glycols

---

[27] R. Ahmad and B. C. L. Weedon, *Chem. and Ind.*, 1952, 882.

[28] L. Crombie, *Quart. Reviews*, 1952, 6, 101.

[29] L. J. Rubin, H. A. Lardy, and H. O. L. Fischer, *J. Amer. Chem. Soc.*, 1952, 74, 424.

[30] G. Eglinton, E. R. H. Jones, and M. C. Whiting, *J.*, 1952, 2873; R. Paul and S. Tschelitcheff, *Bull. Soc. chim.*, 1952, 808.

[31] H. Grütter and H. Schinz, *Helv. Chim. Acta*, 1952, 35, 1656

[32] *Ann. Reports*, 1951, 48, 154.

oenanthetoxin (XIII or XIV; R = OH) and cicutoxin (XV or XVI; R = OH) and the closely related alcohols oenanthetol (XIII or XIV; R = H) and cicutol (XV or XVI; R = H) from the umbelliferous plants *Oenanthe crocata* and *Cicuta virosa*.[33] A related ketone, oenanthetone, is probably 14-dehydro-1-deoxyoenanthetoxin.

$$\left\{\begin{array}{ll}\mathrm{HO{\cdot}CH_2{\cdot}CH{:}CH{\cdot}[C{\vdots}C]_2{\cdot}[CH{:}CH]_2{\cdot}[CH_2]_2{\cdot}CHRPr^n} & \mathrm{(XIII)} \\ \mathrm{HO{\cdot}CH_2{\cdot}[CH{:}CH]_2{\cdot}[C{\vdots}C]_2{\cdot}CH{:}CH{\cdot}[CH_2]_2{\cdot}CHRPr^n} & \mathrm{(XIV)}\end{array}\right.$$

$$\left\{\begin{array}{ll}\mathrm{HO{\cdot}[CH_2]_3{\cdot}[C{\vdots}C]_2{\cdot}[CH{:}CH]_3{\cdot}CHRPr^n} & \mathrm{(XV)} \\ \mathrm{HO{\cdot}[CH_2]_3{\cdot}[CH{:}CH]_3{\cdot}[C{\vdots}C]_2{\cdot}CHRPr^n} & \mathrm{(XVI)}\end{array}\right.$$

**Halogeno-compounds.**—The formation of bromides by the treatment of the corresponding alkyl toluene-*p*-sulphonates with sodium bromide has been shown to proceed without rearrangement.[34]

In spite of the highly reactive nature of its chlorine atom, propargyl chloride has been found to react with sodio-derivatives of ketones to yield the corresponding acetylenic alcohols of the general type $\mathrm{HO{\cdot}CRR'{\cdot}C{\vdots}C{\cdot}CH_2Cl}$.[35]

The geometrical isomers of 3-bromo-1 : 2-dichloroprop-1-ene have been obtained by the action of *N*-bromosuccinimide on 1 : 2-dichloroprop-1-ene; the corresponding alcohols and chlorides were also prepared by hydrolysis and reaction with phosphorus trichloride.[36]

Investigations on fluorinated aliphatic compounds proceed apace [37] and only a brief selection can be reviewed in detail. As expected, nucleophilic addition to trifluoropropyne takes place in an anti-Markovnikov manner, the adducts being of the type $\mathrm{CF_3{\cdot}CH{:}CHX}$ (X = F, Cl, Br, I, CN, OMe, OEt, or $\mathrm{NEt_2}$); mercury-catalysed hydration, however, gives predominantly trifluoroacetone (65%) together with the expected 3 : 3 : 3-trifluoropropaldehyde (35%).[38, 39] 3 : 3 : 3-Trifluoropropyne reacts normally with ethylmagnesium bromide and the resulting Grignard reagent undergoes the expected condensation with ketones.[38] Sodium borohydride reduction of 3-bromo-1 : 1 : 1-trifluoroacetone furnishes the corresponding bromohydrin which may be readily dehydrobrominated to 2 : 3-epoxy-1 : 1 : 1-trifluoropropane; the ethylene oxide ring in this compound is much more resistant to fission than that in 1 : 2-epoxypropane itself.[40] Perfluoroaldehydes may be obtained directly from the corresponding acids by lithium aluminium hydride reduction.[41]

---

[33] E. Anet, B. Lythgoe, M. H. Silk, and S. Trippett, *Chem. and Ind.*, 1952, 756.

[34] H. Pines, A. Rudin, and V. N. Ipatieff, *J. Amer. Chem. Soc.*, 1952, **74**, 4063.

[35] J. Colonge and R. Gelin, *Compt. rend.*, 1952, **235**, 577.

[36] L. F. Hatch, J. J. D'Amico, and E. V. Ruhnke, *J. Amer. Chem. Soc.*, 1952, **74**, 123.

[37] J. A. Cuculo and L. A. Bigelow, *ibid.*, p. 710; K. E. Rapp, J. T. Barr, R. L. Pruett, C. T. Bahner, J. D. Gibson, and R. H. Lafferty, *ibid.*, p. 749; M. Hauptschein, C. S. Stokes, and A. V. Grosse, *ibid.*, p. 848; M. Hauptschein, R. L. Kinsman, and A. V. Grosse, *ibid.*, p. 849; H. D. Mallory, *ibid.*, p. 839; W. L. Mosby, *ibid.*, p. 844; M. Hauptschein, E. A. Nodiff, and A. V. Grosse, *ibid.*, p. 1347; E. T. McBee, J. F. Higgins, and O. R. Pierce, *ibid.*, p. 1387; E. T. McBee and T. M. Burton, *ibid.*, p. 3902; R. N. Haszeldine, *J.*, 1952, 3423, 4259, 4423.

[38] A. L. Henne and M. Nager, *J. Amer. Chem. Soc.*, 1952, **74**, 650.

[39] R. N. Haszeldine and K. Leedham, *J.*, 1952, 3483; R. N. Haszeldine, *ibid.*, p. 3490.

[40] E. T. McBee and T. M. Burton, *J. Amer. Chem. Soc.*, 1952, **74**, 3022.

[41] D. R. Husted and A. H. Ahlbrecht, *ibid.*, p. 5422.

**Aldehydes and Ketones.**—The violet-leaf perfume, nona-*trans*-2 : *cis*-6-dienal (XVII) has been synthesised from dipropargyl by the process shown.[42]

$$\mathrm{CH{\vdots}C{\cdot}[CH_2]_2{\cdot}C{\vdots}CH} \xrightarrow[\text{(ii) –EtI}]{\text{(i) NaNH}_2} \mathrm{Et{\cdot}C{\vdots}C{\cdot}[CH_2]_2{\cdot}C{\vdots}CH} \xrightarrow[\text{(ii) –CH(OEt)}_3]{\text{(i) EtMgBr}}$$

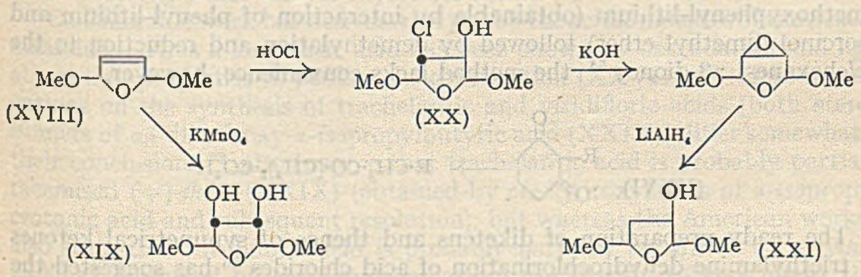
$$\mathrm{Et{\cdot}C{\vdots}C{\cdot}[CH_2]_2{\cdot}C{\vdots}C{\cdot}CH(OEt)_2} \xrightarrow{\text{Pd–H}_2} \mathrm{Et{\cdot}CH\overset{\textit{cis}}{=\!=}CH{\cdot}[CH_2]_2{\cdot}CH\overset{\textit{cis}}{=\!=}CH{\cdot}CH(OEt)_2}$$

$$\xrightarrow{\text{H}^+} \mathrm{Et{\cdot}CH\overset{\textit{cis}}{=\!=}CH{\cdot}[CH_2]_2{\cdot}CH\overset{\textit{trans}}{=\!=}CH{\cdot}CHO} \quad \text{(XVII)}$$

A convenient preparation of lævulaldehyde diethyl acetal is afforded by the peroxide-catalysed addition of acetaldehyde to acraldehyde diethyl acetal.[43]

A series of straight chain αω-hydroxy-aldehydes has been obtained by lead tetra-acetate fission of the corresponding carbocyclic acyloins, and their ring-chain tautomerism has been studied.[44]

Substituted succinic dialdehydes have been produced from 2 : 5-dihydro-2 : 5-dimethoxyfuran (XVIII) which is readily prepared from furan. Mild acid hydrolysis of (XVIII) furnishes a mixture of the liquid maleic dialdehyde and the crystalline fumaric dialdehyde.[45] Hydroxylation of (XVIII) by potassium permanganate gives the cyclic acetal of *meso*tartaric dialdehyde (*meso*-tetrahydro-3 : 4-dihydroxy-2 : 5-dimethoxyfuran) (XIX) [46] while the hypochlorous acid adduct (XX) by treatment with potassium hydroxide followed by reductive fission of the resulting epoxide produces malic dialdehyde cyclic acetal (tetrahydro-3-hydroxy-2 : 5-dimethoxyfuran) (XXI).[46] The latter product is more conveniently procured by Raney nickel hydrogenolysis of the bromohydrin corresponding to (XX); [47] malic dialdehyde is also formed by lithium aluminium hydride reduction of malic bismethylanilide.[48] Epoxysuccinic dialdehyde has been produced by lead tetra-acetate or periodic acid fission of epoxyconduritol (5 : 6-epoxy*cyclo*hexane-1 : 2 : 3 : 4-tetrol); [49] the preparation of its cyclic acetal is described above.[46] Condensation of these dialdehydes with acetonedicarboxylic acid and methylamine to yield tropane alkaloids has been investigated.[46, 47, 49]



A convenient route has been developed for the preparation of octa-3 : 5-diene-2 : 7-dione (XXIII) a key intermediate for carotenoid syntheses, by

---

[42] F. Sondheimer, *ibid.*, p. 4040; see also F. Zobrist and H. Schinz, *Helv. Chim. Acta*, 1952, **35**, 2380. [43] A. Mondon, *Angew. Chem.*, 1952, **64**, 224.

[44] C. D. Hurd and W. H. Saunders, *J. Amer. Chem. Soc.*, 1952, **74**, 5324.

[45] D. L. Hufferd, D. S. Tarbell, and T. R. Koszalka, *ibid.*, p. 3014.

[46] J. C. Sheehan and B. M. Bloom, *ibid.*, p. 3825.

[47] A. Stoll, B. Becker, and E. Jucker, *Helv. Chim. Acta*, 1952, **35**, 1263.

[48] F. Weygand and G. Eberhardt, *Angew. Chem.*, 1952, **64**, 458.

[49] C. Schöpf and A. Schmetterling, *ibid.*, p. 591; see also C. Schöpf and W. Arnold, *Annalen*, 1947, **558**, 109.

partial reduction of the readily available diacetylenic glycol (XXII) followed by manganese dioxide oxidation of the resulting diene glycol; other approaches to the diketone were also investigated.[50]

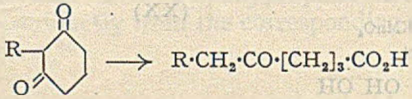
$$\text{(XXII)}\quad \mathrm{HO{\cdot}CHMe{\cdot}[C{:}C]_2{\cdot}CHMe{\cdot}OH} \xrightarrow[\text{(ii) MnO}_2]{\text{(i) LiAlH}_4} \mathrm{Me{\cdot}CO{\cdot}[CH{:}CH]_2{\cdot}CO{\cdot}Me}\quad \text{(XXIII)}$$

**Fatty Acids and their Derivatives.**—*Saturated acids.* Optimum conditions have been established for the preparation of pimelic acid by alkaline isomerisation and cleavage of *cyclo*hex-3-ene-1-carboxylic acid and the mechanism of the process is discussed.[51] Pimelic acid may also be obtained by subjecting the aldehydo-ester (XXIV) (formed by Michael addition of diethyl malonate to acraldehyde) to reductive condensation with ethyl cyanoacetate with subsequent hydrolysis and decarboxylation of the product (XXV); α-substituted pimelic acids result when a substituted malonic ester is used.[52]

$$\underset{\text{(XXIV)}}{\mathrm{(EtO_2C)_2CH{\cdot}[CH_2]_2{\cdot}CHO}} \xrightarrow[\text{Pd-H}_2]{\mathrm{NC{\cdot}CH_2{\cdot}CO_2Et;}} \underset{\text{(XXV)}}{\mathrm{(EtO_2C)_2CH{\cdot}[CH_2]_3{\cdot}CH(CN){\cdot}CO_2Et}}$$

A useful method of preparing δ-keto-acids and thence the non-ketonic acids involves alkaline fission of 2-alkyl*cyclo*hexane-1 : 3-diones (XXVI) followed by Huang-Minlon reduction. These two stages may be conveniently telescoped since the hydrazine reduction medium is itself sufficiently alkaline to effect the ring scission.[53] Application of this process to 2-methylenebis(*cyclo*hexane-1 : 3-dione) (readily obtainable by interaction of formaldehyde and *cyclo*hexane-1 : 3-dione) furnishes a quantitative yield of brassylic acid, $\mathrm{CO_2H{\cdot}[CH_2]_{11}{\cdot}CO_2H}$.[53] The yields in this procedure are very high but preparation of the starting materials of type (XXVI), involving the reaction of an alkyl halide with *cyclo*hexane-1 : 3-dione, is complicated by the occurrence of concomitant *O*-alkylation. An attempt to eliminate this restriction has been made by effecting the condensation of the alkyl halide with 2 : 6-dimethoxyphenyl-lithium (obtainable by interaction of phenyl-lithium and resorcinol dimethyl ether) followed by demethylation and reduction to the *cyclo*hexane-1 : 3-dione;[54] the method lacks convenience, however.

(XXVI)



$$\longrightarrow \mathrm{R{\cdot}CH_2{\cdot}CO{\cdot}[CH_2]_3{\cdot}CO_2H}$$

The ready preparation of diketens and thence of symmetrical ketones by triethylamine dehydrochlorination of acid chlorides[55] has suggested the extension of this process to ω-carbethoxy-acid chlorides.[55, 56] The symmetrical keto-esters (XXVII) thus obtained may be readily hydrolysed and

---

[50] R. Ahmad, F. Sondheimer, B. C. L. Weedon, and R. J. Woods, *J.*, 1952, 4089.

[51] F. X. Werber, J. E. Jansen, and T. L. Gresham, *J. Amer. Chem. Soc.*, 1952, **74**, 532.

[52] D. T. Warner and O. A. Moe, *ibid.*, p. 371.

[53] H. Stetter and W. Dierichs, *Chem. Ber.*, 1952, **85**, 61, 290, 1061.

[54] H. Lettré and A. Jahn, *ibid.*, p. 346.

[55] J. C. Sauer, *J. Amer. Chem. Soc.*, 1947, **69**, 2444.

[56] A. T. Blomquist, J. R. Johnson, L. I. Diuguid, J. K. Shillington, and R. D. Spencer, *ibid.*, 1952, **74**, 4203.

reduced to the corresponding αω-dicarboxylic acids containing an odd number of carbon atoms:

$$\mathrm{EtO_2C{\cdot}[CH_2]_{\mathit{n}}{\cdot}COCl \xrightarrow{Et_3N} Diketen \xrightarrow[-CO_2]{H_2O;} EtO_2C{\cdot}[CH_2]_{\mathit{n}}{\cdot}CO{\cdot}[CH_2]_{\mathit{n}}{\cdot}CO_2Et}$$

(XXVII)

Attention has been drawn to the convenience of using ethylene glycol as a solvent in nitrile preparations involving the metathesis of an alkyl halide with sodium cyanide; even secondary nitriles are preparable by this technique.[57]

A series of long-chain β-hydroxy-acids has been obtained by catalytic hydrogenation of the corresponding β-keto-esters and the crystal structure of the compounds examined.[58]

It had been deduced from knowledge of the Walden inversion and the stereochemistry of double-bond addition reactions that the higher-melting 9 : 10-dihydroxystearic acid (m. p. 131°) possesses the *erythro*-configuration whilst the lower-melting acid (m. p. 95°) is the *threo*-isomer. This conclusion has been most elegantly confirmed by a study of the urea inclusion compounds of the two acids. Measurements show that the *erythro*-acid, with its hydroxyl groups on opposite sides of the zig-zag carbon chain, cannot readily fit into the urea lattice cavity, while the *threo*-acid can do so with great ease. In practice it is found that the lower-melting acid forms a crystalline urea complex in quantitative yield whilst the higher-melting isomer does not form an adduct.[59] This use of the urea crystal lattice as " molecular calipers " has wide potentialities for the direct determination of molecular configurations. (It should perhaps be pointed out that the Fischer projection formula for the *erythro*-acid shows both hydroxyl groups on the *same* side of the carbon chain. This is in accordance with the tenets of the convention which require the molecule to be " normalised " from the stable zig-zag configuration before projection is carried out.[60])

Configurational relations have been worked out between the 2 : 3-epoxy-, -bromoacetoxy-, and -dihydroxystearic acids.[61]

Considerable work has been carried out on the acidic moieties of the *Senecio* alkaloids. Thus α-longinecic acid has been shown by degradation and light absorption properties to possess the constitution (XXVIII).[62] Two investigations on the synthesis of trachelantic and viridifloric acids [both stereoisomers of αβ-dihydroxy-α-*iso*propylbutyric acid (XXIX)] differ somewhat in their conclusions.[63] Both agree that trachelantic acid is probably partially racemised (+)-*threo*-(XXIX) (obtained by *cis*-hydroxylation of α-*iso*propylcrotonic acid and subsequent resolution), but whereas the American workers also state that viridifloric acid is probably partially racemised (+)-*erythro*-(XXIX) (obtained by *trans*-hydroxylation) the British workers report that the enantiomorphs of the latter acid show no measurable rotation. The structure of monocrotalic acid (XXX) deduced from degradation reactions

---

[57] R. N. Lewis and P. V. Susi, *J. Amer. Chem. Soc.*, 1952, **74**, 840.

[58] M. Skogh, *Acta Chem. Scand.*, 1952, **6**, 809.

[59] D. Swern, L. P. Witnauer, and H. B. Knight, *J. Amer. Chem. Soc.*, 1952, **74**, 1655.

[60] C. S. Hudson, *Adv. Carbohydrate Chem.*, 1948, **3**, 1.

[61] G. S. Myers, *J. Amer. Chem. Soc.*, 1952, **74**, 1390.

[62] R. Adams, T. R. Govindachari, J. H. Looker, and J. D. Edwards, *ibid.*, p. 701.

[63] R. Adams and B. L. Van Duuren, *ibid.*, p. 5349; J. L. Dry and F. L. Warren, *J.*, 1952, 3445.

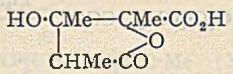
has been confirmed by a synthesis involving hydroxylation of αβγ-trimethylglutaconic acid.[64]

$Me{\cdot}CH{:}C(CO_2H){\cdot}CH{:}CMe{\cdot}CMe(OH){\cdot}CO_2H$

(XXVIII)

$Me{\cdot}CH(OH){\cdot}CPr^i(OH){\cdot}CO_2H$

(XXIX)



(XXX)

Two groups of workers have shown by synthesis that a pyruvate oxidation factor of certain bacteria, α-lipoic (or thioctic) acid, is the dextrorotatory enantiomorph of the cyclic disulphide from 5 : 8-dimercapto-*n*-octanoic acid (*i.e.*, 3-3′-carboxypropyl-1 : 2-dithian).[65]

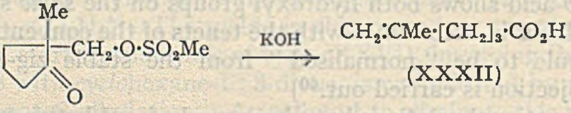
A convenient and reproducible procedure for preparing oxaloacetic acid has been evolved.[66]

Cholesteryl esters of the branched-chain 28-methyltriacontanoic, 26-methyloctacosanoic, and 24-methylhexacosanoic acids have been isolated from wool wax.[67] The steric effects involved in the acid-catalysed esterification of highly-branched acids have been investigated.[68]

*Unsaturated acids.* An interesting synthesis of 5-methylhex-5-enoic acid (XXXII), in high yield, involves the base-catalysed fission of the methanesulphonate of 2-hydroxymethyl-2-methyl*cyclo*pentanone (XXXI).[69]

By use of the Bowman " acyloin " and " methoxy-ketone " methods [70] the pure *cis*- and *trans*-forms of myristoleic, palmitoleic, gadoleic, octadec-4-enoic, and undec-9-enoic acids have been obtained.[71] Tariric (octadec-6-ynoic) acid and thence, by partial hydrogenation, petroselinic acid has been synthesised [72] by Strong's method.[73]

(XXXI)



(XXXII)

Reaction of two molecules of acetylene with one of methyl acrylate under pressure in the presence of triphenylphosphine–nickel carbonyl catalyst gives a high yield of methyl hepta-2 : 4 : 6-trienoate, $CH_2{:}CH{\cdot}[CH{:}CH]_2{\cdot}CO_2Me$; the corresponding nitrile is similarly obtained from acrylonitrile.[74]

The earlier claim [23] to have obtained *cis* : *cis*-β-methylmuconic acid by hydrolysis of its anhydride has now been shown [25] to be a misinterpretation (cf. p. 152), the product being in fact the *cis* : *trans*-isomer; hot alkali converts this isomer into the *trans* : *trans*-compound. By contrast all the

---

[64] R. Adams, B. L. Van Duuren, and B. H. Braun, *J. Amer. Chem. Soc.*, 1952, 74, 5608; see also R. Adams and F. B. Hauserman, *ibid.*, p. 694.

[65] M. W. Bullock, J. A. Brockman, E. L. Patterson, J. V. Pierce, and E. L. R. Stokstad, *ibid.*, p. 1868; C. S. Hornberger, R. F. Heitmiller, I. C. Gunsalus, G. H. F. Schnakenberg, and L. J. Reed, *ibid.*, p. 2382. [66] J. C. Roberts, *J.*, 1952, 3315.

[67] J. Tiedt and E. V. Truter, *Chem. and Ind.*, 1952, 402.

[68] K. L. Loening, A. B. Garrett, and M. S. Newman, *J. Amer. Chem. Soc.*, 1952, 74, 3929. [69] A. Eschenmoser and A. Frey, *Helv. Chim. Acta*, 1952, 35, 1660.

[70] *Ann. Reports*, 1950, 47, 171; 1951, 48, 161.

[71] B. W. Boughton, R. E. Bowman, and D. H. Ames, *J.*, 1952, 671; D. E. Ames and R. E. Bowman, *ibid.*, p. 677.

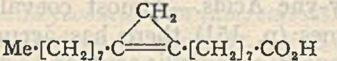
[72] P. B. Lumb and J. C. Smith, *Chem. and Ind.*, 1952, 358.

[73] *Ann. Reports*, 1949, 46, 165.

[74] T. L. Cairns, V. A. Engelhardt, H. L. Jackson, G. H. Kalb, and J. C. Sauer, *J. Amer. Chem. Soc.*, 1952, 74, 5636.

three geometrically isomeric αα′-dimethylmuconic acids are isolatable entities.[75]

Following the isolation of a *cyclo*propane acid,[76] now named lactobacillic acid,[77] from *Lactobacillus arabinosus* and *L. casei*, an even more remarkable related acid, the *cyclo*propene derivative sterculic acid (XXXIII), has been obtained from the kernel oil of *Sterculia foetida* by way of its urea complex.[78] The constitution is confirmed by ozonolysis to 9 : 11-diketononadecanoic acid.


(XXXIII)

$$Me\cdot[CH_2]_7\cdot C{=}C\cdot[CH_2]_7\cdot CO_2H \quad (\text{with } CH_2 \text{ bridging})$$

The fatty acids of *L. arabinosus* also contain *cis*-octadec-11-enoic acid,[77] the second occurrence of this compound in Nature; [76] another synthesis of the *trans*-isomer (" vaccenic acid " [76]) has been reported.[79]

A new hydroxy-acid, 9-hydroxyoctadec-12-enoic acid, isomeric with ricinoleic acid, has been isolated from the seed oil of *Strophanthus sarmentosus*.[80]

An ethylenic-acetylenic acid, ximenynic acid, obtained from the kernel oil of several species of *Ximenia*, has been shown to be octadec-11-en-9-ynoic acid, a constitution suggestive of a possible biogenesis from ricinoleic acid.[81]

The decarboxylation and re-formation of linoleic acid (XXXIV) has been carried out by the annexed method, the process being admirably suited for the production of the " labelled " acid.[82]

$$\text{(XXXIV)} \xrightarrow{Br_2} C_5H_{11}\cdot[CHBr]_2\cdot CH_2\cdot[CHBr]_2\cdot[CH_2]_7\cdot CO_2H \xrightarrow{Br_2\text{ on Ag salt}}$$

$$C_5H_{11}\cdot[CHBr]_2\cdot CH_2\cdot[CHBr]_2\cdot[CH_2]_7\cdot Br \xrightarrow{Zn}$$

$$C_5H_{11}\cdot CH{:}CH\cdot CH_2\cdot CH{:}CH\cdot[CH_2]_7\cdot Br \xrightarrow{Mg;\ CO_2} \text{(XXXIV)}$$

A similar, but less convenient, procedure has been devised for oleic acid.[83]

The synthesis of the *trans* : *trans*- and *cis*-2 : *trans*-8-isomers of the structure (XXXV) has been reported; [84] like the previously synthesised *cis* : *cis*- and *trans*-2 : *cis*-8-isomers,[85] neither is identical with the naturally occurring insecticide herculin for which constitution (XXXV) had previously been suggested. Attempted re-isolation of herculin from the bark of *Xanothoxylum clava-herculis* L. gave only a new conjugated triethylenic *iso*butylamide for which the name *iso*herculin is proposed.[84] A similar situation obtains in the case of the insecticide pellitorine for which the structure (XXXVI) had been derived, none of the four possible geometrical isomers [85, 86] being identical with the natural product. In this case, how-

---

[75] J. A. Elvidge, R. P. Linstead, and J. F. Smith, *J.*, 1952, 1026.

[76] *Ann. Reports*, 1950, **47**, 171; for suggested biogenesis see E. M. Kosower, *Science*, 1951, **113**, 605.

[77] K. Hoffmann, R. A. Lucas, and S. M. Sax, *J. Biol. Chem.*, 1952, **195**, 473.

[78] J. R. Nunn, *J.*, 1952, 313.

[79] W. J. Gensler and G. R. Thomas, *J. Amer. Chem. Soc.*, 1952, **74**, 3942.

[80] F. D. Gunstone, *J.*, 1952, 1274.

[81] S. P. Ligthelm, H. M. Schwartz, and M. M. von Holdt, *ibid.*, p. 1088.

[82] D. R. Howton, R. H. Davis, and J. C. Nevenzel, *J. Amer. Chem. Soc.*, 1952, **74**, 1109.

[83] S. Bergstrom, K. Pääbo, and M. Rottenberg, *Acta Chem. Scand.*, 1952, **6**, 1024.

[84] L. Crombie, *J.*, 1952, 2997.

[85] *Ann. Reports*, 1949, **46**, 166; 1950, **47**, 172; 1951, **48**, 162.

[86] L. Crombie, *J.*, 1952, 4338.

ever, pellitorine was successfully re-isolated from *Anacyclus pyrethrum*[86] and has been shown to possess the fully conjugated structure (XXXVII);[87] the synthetic *trans* : *trans*-(XXXVII) is markedly similar in properties to the natural product.[88]

$\mathrm{Me{\cdot}[CH_2]_2{\cdot}CH{:}CH{\cdot}[CH_2]_4{\cdot}CH{:}CH{\cdot}CO{\cdot}NHBu^i}$ (XXXV)
$\mathrm{Me{\cdot}[CH_2]_2{\cdot}CH{:}CH{\cdot}[CH_2]_2{\cdot}CH{:}CH{\cdot}CO{\cdot}NHBu^i}$ (XXXVI)
$\mathrm{Me{\cdot}[CH_2]_4{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CO{\cdot}NHBu^i}$ (XXXVII)

**Naturally Occurring Poly-yne Acids.**—Almost coevally with the recent studies on synthetic poly-ynes (p. 151) there has accumulated a growing family of natural products, usually carboxylic acids and esters (but see p. 153), containing such systems. This phenomenon is not wholly coincidental as the striking and characteristic ultra-violet absorption of these systems (as determined from the synthetic compounds) has greatly facilitated their detection in plant extracts. Much of this work has been carried out by N. A. Sörensen and his collaborators,[88] who have established the wide occurrence of such poly-ynes in plants of the Compositae family. Thus the essential oil of *Matricaria inodora* L. has yielded *cis*-dihydromatricaria ester[88h] (XXXVIII), *cis*-2 : *trans*-8-[88h] and *cis* : *cis*-matricaria ester[88a, b, f] (XL), while the closely related dehydromatricaria ester[88e, g] (probably XLI) is a constituent of *Artemisia vulgaris* L. The allied *cis*-lachnophyllum ester (XXXIX) is obtained from *Lachnophyllum gossypinum* Bge.[88c, 89] A number of these compounds and their geometrical isomers have been synthesised by the standard acetylenic coupling reactions.[88c, f, g, i]

A highly interesting compound of this type is the strongly lævorotatory $C_{13}$ acid, mycomycin (XLII) which is an antibiotic metabolic product of *Norcardia acidophilus*.[90] Its almost incredible structure involves a conjugate diyne-allene-diene system, *i.e.*, it incorporates every known type of carbon–carbon unsaturation. The van't Hoff prediction of the resolvability of asymmetric allenes is thus exemplified for the first time by a natural product. When the allene function is destroyed, either by complete hydrogenation to *n*-tridecanoic acid or by alkaline rearrangement to the isomeric triynediene, *iso*mycomycin (XLIII), the optical activity disappears. Since the double bonds of the allene link are at right angles mycomycin contains two discrete chromophores, an enediyne and a triene system, which are non-interacting; this conception is confirmed by its ultra-violet absorption.

$\mathrm{Me{\cdot}CH{:}CH{\cdot}C{\vdots}C{\cdot}C{\vdots}C{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Me}$ (XXXVIII)
$\mathrm{Me{\cdot}CH_2{\cdot}CH_2{\cdot}C{\vdots}C{\cdot}C{\vdots}C{\cdot}CH{:}CH{\cdot}CO_2Me}$ (XXXIX)
$\mathrm{Me{\cdot}CH{:}CH{\cdot}C{\vdots}C{\cdot}C{\vdots}C{\cdot}CH{:}CH{\cdot}CO_2Me}$ (XL)
$\mathrm{Me{\cdot}CH{:}CH{\cdot}C{\vdots}C{\cdot}C{\vdots}C{\cdot}C{\vdots}C{\cdot}CO_2Me}$ (XLI)
$\mathrm{CH{\vdots}C{\cdot}C{\vdots}C{\cdot}CH{:}C{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2H}$ (XLII)

$$\Big\downarrow{\scriptstyle \mathrm{KOH}}$$

$\mathrm{Me{\cdot}C{\vdots}C{\cdot}C{\vdots}C{\cdot}C{\vdots}C{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2H}$ (XLIII)

---

[87] L. Crombie, *Chem. and Ind.*, 1952, 1034; M. Jacobson, *Chem. Eng. News*, 1952, 30, 4131.

[88] (*a*) *Annalen*, 1941, 549, 80; (*b*) *Acta Chem. Scand.*, 1950, 4, 416, (*c*) 851, (*d*) 1081, (*e*) 1567, 1575; (*f*) *ibid.*, 1951, 5, 1244; *ibid.*, 1952, 6, (*g*) 602, (*h*) 883, (*i*) 893.

[89] W. Wiljams, V. S. Smirnov, and V. P. Goljmov, *J. Gen. Chem. U.S.S.R.*, 1935, 5, 1195.

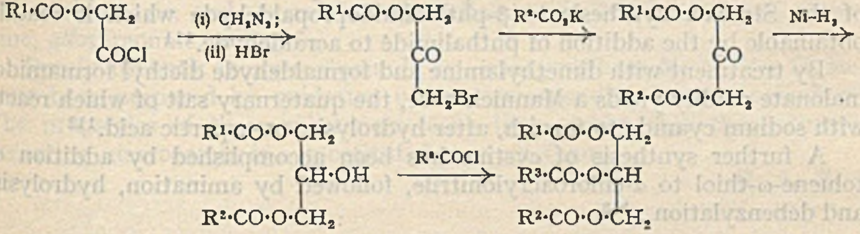
[90] W. D. Celmer and I. A. Solomons, *J. Amer. Chem. Soc.*, 1952, 74, 1870, 2245, 3838.

Allied poly-ynes have been detected in the culture liquids of various species of *Basidiomycetes*,[91] and in *Centaurea cyanus* L.[92]

**Acids from the Diphtheria and Tubercle Bacillus.**—Corynomycolic acid, isolated from the lipids of the diphtheria bacillus *Corynebacterium diphtheriae*,[93] has been identified by degradation and synthesis as (+)-2-*n*-tetradecyl-3-hydroxystearic acid,[94] *i.e.*, it is of the same general type as the mycolic acids obtained from human tubercle. Further degradative work on α-mycolic acid has been reported.[95] An analogous keto-acid, mycolonic acid, has been isolated from bovine *Mycobacterium tuberculosis*.[96]

**Phosphatides and Derived Compounds.**—Full details have now appeared [97] of the synthesis of α-cephalins mentioned in the last Report.[98] An improved procedure has been worked out [99] for the processes involved in the synthesis of α-lecithins.[100]

A most flexible procedure for the synthesis of glycerides has been devised whereby the alcohol groups of the glycerol are successively built up and become available one by one for reaction with individual fatty acids.[101]



Two further syntheses of racemic dihydrosphingosine have been reported [102, 103] which are essentially practical improvements of the Swiss and the British syntheses reported last year.[104] A footnote records the successful extension of the method to furnish sphingosine (XLIV) itself.[102] The synthetic dihydrosphingosine has been resolved with L-glutamic acid, the lævorotatory enantiomorph being identical with the natural product.[105] Infra-red examination has shown the configuration about the double bond of sphingosine to be *trans*.[106]

(XLIV) $\mathrm{Me{\cdot}[CH_2]_{12}{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}CH(NH_2){\cdot}CH_2{\cdot}OH}$

**Amino-acids.***—An unsaturated amino-dicarboxylic acid, probably γ-methyleneglutamic acid, $\mathrm{CO_2H{\cdot}CH(NH_2){\cdot}CH_2{\cdot}C({:}CH_2){\cdot}CO_2H}$, and the corre-

---

[91] M. Anchel, *J. Amer. Chem. Soc.*, 1952, **74**, 1588.

[92] B. Hellström and N. Löfgren, *Acta Chem. Scand.*, 1952, **6**, 1024.

[93] E. Lederer and J. Pudles, *Bull. Soc. Chim. biol.*, 1951, **33**, 1003.

[94] E. Lederer, J. Pudles, S. Barbezat, and J. J. Trillat, *Bull. Soc. chim.*, 1952, 93; E. Lederer, V. Portelance, and K. Serck-Hanssen, *ibid.*, p. 413.

[95] J. Asselineau, *ibid.*, p. 557.

[96] H. Demarteau and E. Lederer, *Compt. rend.*, 1952, **235**, 265.

[97] E. Baier, J. Maurukas, and M. Russell, *J. Amer. Chem. Soc.*, 1952, **74**, 152.

[98] *Ann. Reports*, 1951, **48**, 163.

[99] E. Baer and J. Maurukas, *J. Amer. Chem. Soc.*, 1952, **74**, 157.

[100] *Ann. Reports*, 1950, **47**, 172.

[101] H. Schlenk, B. G. Lamp, and B. W. De Haas, *J. Amer. Chem. Soc.*, 1952, **74**, 2550.

[102] M. J. Egerton, G. I. Gregory, and T. Malkin, *J.*, 1952, 2272.

[103] N. Fisher, *Chem. and Ind.*, 1952, 130. [104] *Ann. Reports*, 1951, **48**, 164.

[105] C. A. Grob and E. F. Jenny, *Helv. Chim. Acta*, 1952, **35**, 2106.

[106] K. Mislow, *J. Amer. Chem. Soc.*, 1952, **74**, 5155.

* All amino-acids, not only the aliphatic ones, are dealt with in this section.

sponding amide have been isolated from the vegetative material of groundnut plants.[107]

An isomer of lysine, βε-diamino-*n*-hexanoic acid, $NH_2{\cdot}CH_2{\cdot}[CH_2]_2{\cdot}CH(NH_2){\cdot}CH_2{\cdot}CO_2H$, termed *iso*lysine or β-lysine, has been obtained by degradation of the antibiotics streptolin, streptothricin, and viomycin;[108] its structure has been confirmed synthetically by standard methods.

(+)-β-Aminobutyric acid has been produced by Arndt–Eistert homologation of *N*-phthaloyl-L-alanine.[109] A satisfactory synthesis of *N*-β-alanyl-2-mercaptoethylamine (XLV) has been developed involving the condensation of carbobenzyloxy-β-alanine azide with 2-benzylthioethylamine and removal of both protecting groups in the product with sodium in liquid ammonia; reaction of (XLV) with D-pantolactone yields pantotheine (*Lactobacillus bulgaricus* factor).[110]

$$NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}SH \quad (XLV)$$

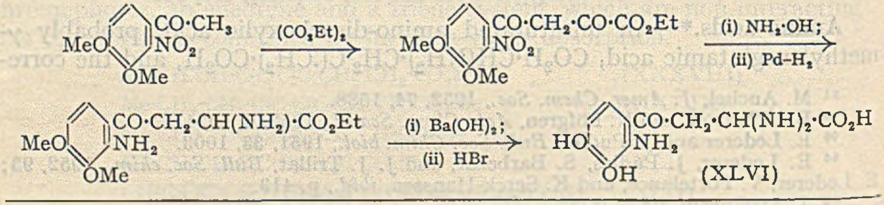
A convenient synthesis of DL-αγ-diaminobutyric acid involves application of the Strecker synthesis to β-phthalimidopropaldehyde which is readily obtainable by the addition of phthalimide to acraldehyde.[111]

By treatment with dimethylamine and formaldehyde diethyl formamidomalonate readily yields a Mannich base, the quaternary salt of which reacts with sodium cyanide to furnish, after hydrolysis, DL-aspartic acid.[112]

A further synthesis of cystine has been accomplished by addition of toluene-ω-thiol to α-chloroacrylonitrile, followed by amination, hydrolysis, and debenzylation:[113]

$$CH_2{:}CCl{\cdot}CN \xrightarrow{Ph{\cdot}CH_2{\cdot}SH} Ph{\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}CHCl{\cdot}CN \longrightarrow HS{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CO_2H$$

A study of the condensation of ω-bromoacetophenones with sodio-*N*-acylaminomalonates has led to an improved technique, hydrolysis of the products furnishing β-benzoylalanines; the process has been used for the synthesis of kynurenin.[114] Suitable conditions have been evolved for the exclusive formylation of the aromatic amino-group of kynurenin, to give *N'*-formylkynurenin, the first identifiable intermediate in the normal biological degradation of tryptophan.[114] 3 : 4-Dihydroxykynurenin (XLVI)



(XLVI)

---

[107] J. Done and L. Fowden, *Biochem. J.*, 1952, **51**, 451.

[108] E. E. van Tamelen and E. E. Smissman, *J. Amer. Chem. Soc.*, 1952, **74**, 3713; H. E. Carter, W. R. Hearn, E. M. Lansford, A. C. Page, N. P. Salzman, D. Shapiro, and W. R. Taylor, *ibid.*, p. 3704.

[109] K. Balenović, D. Cerar, and Z. Fuks, *J.*, 1952, 3316.

[110] J. Baddiley and E. M. Thain, *ibid.*, p. 800.

[111] R. O. Atkinson and F. Poppelsdorf, *ibid.*, p. 2448.

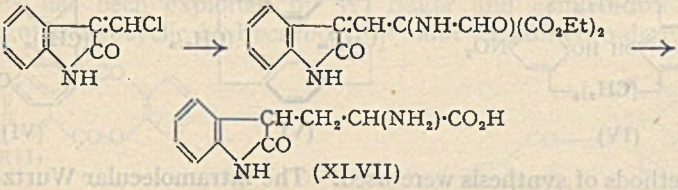
[112] R. O. Atkinson, *ibid.*, p. 3317.

[113] K.-D. Gundermann and F. Micheel, *Annalen*, 1952, **578**, 45.

[114] C. E. Dalgliesh, *J.*, 1952, 137; O. Wiss and H. Fuchs, *Helv. Chim. Acta*, 1952, **35**, 407.

has been synthesised from 3 : 4-dimethoxy-2-nitroacetophenone in the manner shown.[115]

An interesting synthesis of 3-oxindolylalanine [116] (XLVII) involves condensation of the readily accessible chloromethyleneoxindole with sodioformamidomalonic ester, followed by reduction with sodium dithionite and hydrolysis.[117]



(XLVII)

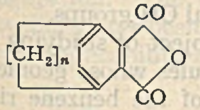
**Miscellaneous.**—The preparation of a wide variety of "labelled" aliphatic compounds has been reported.[118] These include $^{14}$C-labelled formaldehyde, acetone, glycerol, dimethylaminoethanol, glyoxylic, citric, succinic, malic, fumaric, tartaric, and several branched-chain acids, leucine, alanine, threonine, *allo*threonine, and urea.

Purely aliphatic azoxy-compounds, *e.g.*, azoxymethane Me·N:N(→ O)·Me, have been prepared by oxidation of the corresponding azo-compounds.[119] The properties of these substances leave little doubt that the naturally occurring macrozamin is a substituted azoxymethane.

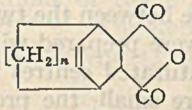
R. A. R.

## 5. AROMATIC COMPOUNDS.

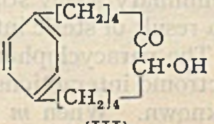
**Bridged Benzene Rings.**—*para*-Bridged benzene rings (I; $n = 9$, 10, and 14) have been prepared by the Diels–Alder reaction of maleic anhydride with large ring dienes, followed by dehydrogenation.[1-3] The tetrahydrophthalic anhydride intermediates (II) were dehydrogenated readily when $n = 10$ and 14, and with difficulty when $n = 9$, but not at all when $n = 8$—models shows that (I; $n = 8$) would be highly strained. Details of the acyloin synthesis of (III) [4] have now been published.[2]



(I)



(II)



(III)

The condensation of nitromalondialdehyde with *cyclo*octanone and larger cyclic ketones gives a six-membered ring with a *meta*-bridge.[4] The same reagent with *cyclo*hexadecane-1 : 9-dione yields the compound (IV)

---

[115] A. Butenandt and H.-G. Schlossberger, *Chem. Ber.*, 1952, **85**, 565.

[116] *Ann. Reports*, 1951, **48**, 66.

[117] H. Behringer and H. Weissauer, *Chem. Ber.*, 1952, **85**, 743.

[118] Atomic Energy Commission Supplement, *J. Amer. Chem. Soc.*, 1952, **74**, 2389 *et seq.*

[119] B. W. Langley, B. Lythgoe, and L. S. Rayner, *J.*, 1952, 4191.

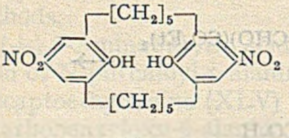
[1] R. B. Ingraham, D. M. MacDonald, and K. Wiesner, *Canad. J. Res.*, 1950, **28**, *B*, 453.

[2] K. Wiesner, D. M. MacDonald, R. B. Ingraham, and R. B. Kelly, *ibid.*, p. 561.

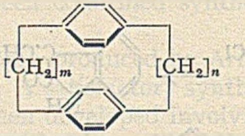
[3] M. F. Bartlett, S. K. Figdor, and K. Wiesner, *Canad. J. Chem.*, 1952, **30**, 291.

[4] *Ann. Reports*, 1950, **47**, 190.

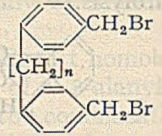
which incorporates two benzene rings as part of the large ring structure.[5] Other examples of a similar type, incorporating two to four benzene rings united by methylene bridges joined to their *para*-positions have been prepared, *viz.*, (V) and (XI). The name "paracyclophane" was suggested for this class of compound.[6]



(IV)

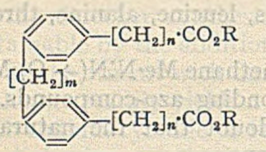


(V)

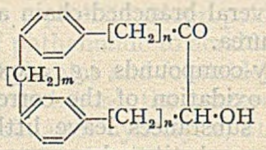


(VI)

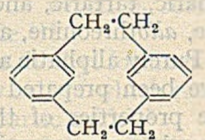
Two methods of synthesis were used. The intramolecular Wurtz reaction with the dibromides (VI; $n = 2, 3, 4$) gave the corresponding hydrocarbons (V; $m = 2$, $n = 2, 3, 4$) in yields of 2·1, 4·6, and 0·5% respectively.[6] The acyloin reaction with the diesters (VII; $m = 2$, $n = 3, 5$, and 9;[7] $m = 3$,



(VII)



(VIII)

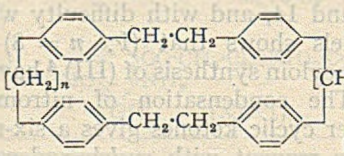


(IX)

$n = 2$;[6] and $m = 5$, $n = 2$[8]) gave the corresponding ketols (VIII), of which the last two were reduced in stages to the paracyclophanes (V; $m = 3$ and 5; $n = 6$).[6, 8] The properties of (V; $m = n = 2$) agree well with those of di-*p*-xylylene prepared by the pyrolysis of *p*-xylene.[4] Production of this highly strained compound in comparatively good yield is reminiscent of that of di-*m*-xylylene (IX) from *m*-xylylene dibromide.[9] Preliminary *X*-ray studies[10] show that (IX) also has distorted benzene rings as a result of steric interference between the two internal CH groups.

The paracyclophanes (V) were prepared with the object of studying the electronic interactions of unsaturated centres in molecules whose geometry is known. When $m$ and $n$ are small, the proximity of the benzene rings results in $\pi$-orbital overlap which produces a change in the ultra-violet and infra-red spectra from those of the open-chain analogues (X). This effect

(X)



(XI)

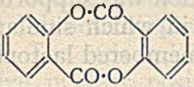
disappears in (V) when $n = 5$, $m = 6$. Steric repulsion, causing buckling of the aromatic rings, is present in the smaller macrocycles (V; $m = 2$, $n = 2$, 3, and possibly 4) but absent in the larger ones. This distortion also

---

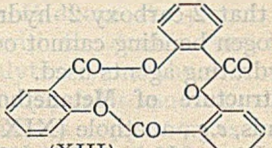
[5] V. Prelog, K. Wiesner, and O. Häflinger, *Coll. Czech. Chem. Comm.*, 1951, **15**, 900.
[6] D. J. Cram and H. Steinberg, *J. Amer. Chem. Soc.*, 1951, **73**, 5691.
[7] R. C. Fuson and G. P. Speranza, *ibid.*, 1952, **74**, 1621.
[8] H. Steinberg and D. J. Cram, *ibid.*, p. 5388.
[9] *Ann. Reports*, 1951, **48**, 184.
[10] C. J. Brown, unpublished.

affects the absorption spectra. In the reaction of (VI; $n = 1$ and 3) with sodium the polynuclear paracyclophanes (XI; $n = 1$ and 3) were produced in minute quantities. They exhibit normal ultra-violet absorption spectra.

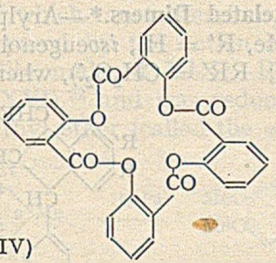
The syntheses of the foregoing cyclic hydrocarbons and acyloins illustrates the beneficial effect of the rigid groups in facilitating ring closure by restricting the rotational possibilities of the chain. This "rigid group principle" has been exploited by W. Baker and collaborators for the synthesis of macrocyclic hydrocarbons [9, 11] and the anhydro-derivatives of *o*-hydroxy- and *o*-mercapto-benzoic acids. Removal of the elements of water from salicylic acid gave mixtures of di- (XII), tri- (XIII), tetra- (XIV), and hexa-salicylide (XV) in yields varying according to the method of dehydration and the experimental conditions.[12]



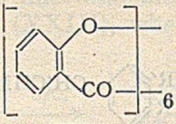
(XII)



(XIII)

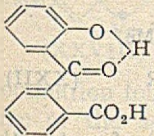


(XIV)

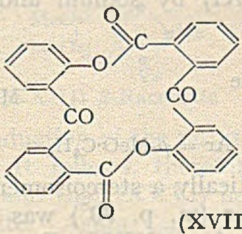


(XV)

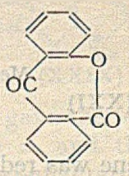
*o*-, *m*-, and *p*-Cresotic acids [13] and thiosalicylic acid [14] yielded di-, tri-, and tetra-anhydro-derivatives; *o*-thymotic acid (2-hydroxy-6-methyl-3-*iso*propylbenzoic acid) [15] gave di- and tri-thymotides. The dipole moments [16, 17] show that the di-anhydro-derivatives possess the *cis*-configuration. The conformations of the 8-, 12-, 16-, and 24-membered salicyclides have been discussed.[12–17] The stereochemistry of tri-*o*-thymotide and its applicability as a resolving agent is discussed on p. 143.



(XVI)



(XVII)



(XVIII)

Dehydration of 2-carboxy-2′-hydroxybenzophenone (XVI) by acetic anhydride gave the 7-membered lactone (XVIII) whereas other dehydrating

---

[11] W. Baker, J. F. W. McOmie, and W. D. Ollis, *J.*, 1951, 200; W. Baker, *Ind. chim. belge*, 1952, 17, 633.

[12] W. Baker, W. D. Ollis, and T. S. Zealley, *J.*, 1951, 201.

[13] W. Baker, B. Gilbert, W. D. Ollis, and T. S. Zealley, *J.*, 1951, 209.

[14] W. Baker, A. S. El-Nawawy, and W. D. Ollis, *J.*, 1952, 3163.

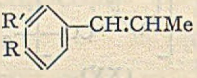
[15] W. Baker, B. Gilbert, and W. D. Ollis, *J.*, 1952, 1443.

[16] *Ann. Reports*, 1951, **48**, 141.

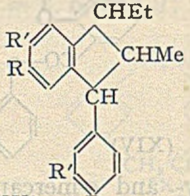
[17] L. E. Sutton and M. F. Saxby, unpublished.

agents such as phosphoric anhydride, trifluoroacetic anhydride, etc., gave only the 14-membered lactide (XVII).[18] It was suggested that intramolecular hydrogen bonding occurs as shown in (XVI), thereby causing the molecules to take up a configuration unfavourable for lactonisation but favourable for intermolecular lactide formation. Acetic anhydride first acetylates the phenolic hydroxyl group and the resulting acetate is rapidly converted into the lactone (XVIII) by an exchange reaction. Other dehydrating agents probably react first with the carboxyl group to give mixed anhydrides or acylium ions. This explanation was supported by the fact that 2-carboxy-2′-hydroxydiphenylmethane, in which similar internal hydrogen bonding cannot occur, gave only the 7-membered lactone with all dehydrating agents used.

**Structure of Metanethole and Related Dimers.***—Arylpropenyl compounds, *e.g.*, anethole (XIX; R = OMe, R′ = H), *iso*eugenol (XIX; R = OH, R′ = OMe), and *iso*safrole (XIX; RR′ = $CH_2O_2$:), when treated with



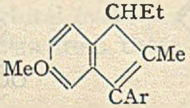
(XIX)

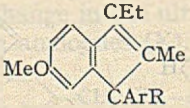


(XX)

acids, give stable saturated dimerides which are now known to be derivatives of phenylindane; *e.g.*, metanethole, the dimer of anethole, is one of the four possible racemates of 1-ethyl-5-methoxy-3-*p*-methoxyphenyl-2-methylindane (XX; R = OMe, R′ = H). These structures for the dimers were deduced from degradative studies [19–21] and confirmed by the step-wise syntheses of metanethole [20] and di*iso*eugenol dimethyl ether (XX; R = R′ = OMe) (see below) in the correct stereochemical configurations: earlier syntheses had given stereoisomers. The last step in the synthesis of metanethole (m. p. 135°) involved the reduction of 1-ethyl-5-methoxy-3-*p*-methoxyphenyl-2-methylindene (XXI) by sodium and alcohol. When the same

(XXI)





(XXII)

Ar = $p$-MeO·$C_6H_4$–.

indene was reduced catalytically a stereoisomer (m. p. 99°) of metanethole was obtained. This isomer (m. p. 99°) was produced by the catalytic reduction of the isomeric indene (XXII; R = H), and must have the *cis*-

---

[18] W. Baker, D. Clark, W. D. Ollis, and T. S. Zealley, *J.*, 1952, 1452.

[19] W. Baker and J. Enderby, *J.*, 1940, 1094; M. Pailer, *Monatsh.*, 1947, **77**, 45; M. Pailer, U. Müller, and K. Porschinski, *ibid.*, 1948, **79**, 620; J. M. van der Zanden and G. de Vries, *Rec. Trav. chim.*, 1949, **68**, 261, 407; A. Müller *et al.*, *Ber.*, 1942, **75**, 692, and later papers; W. von E. Doering and J. A. Berson, *J. Amer. Chem. Soc.*, 1950, **72**, 1118.

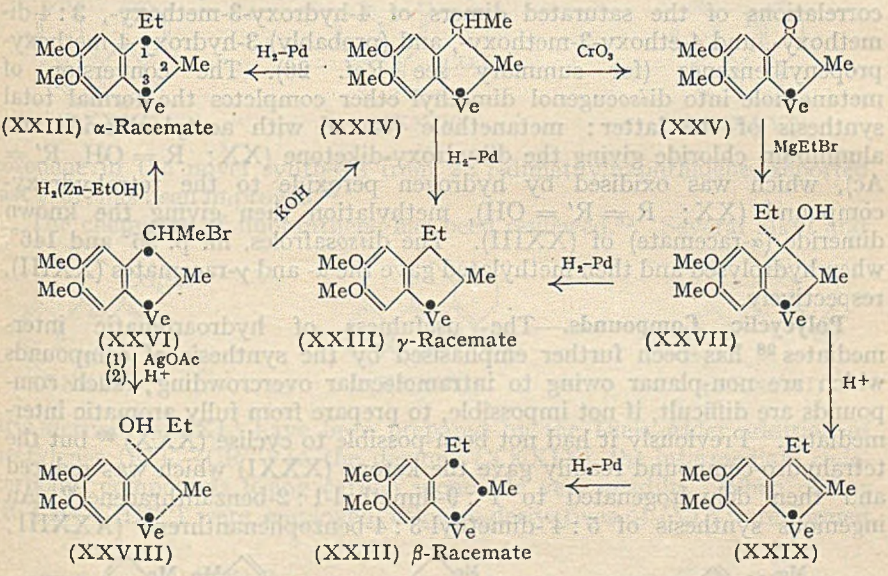
[20] J. M. van der Zanden and G. de Vries, *Rec. Trav. chim.*, 1952, **71**, 733.

[21] N. J. Cartwight and R. D. Haworth, *J.*, 1947, 948.

* [Added in proof.] For a comprehensive review see A. Müller, *Acta Chim. Hung.*, 1952, **2**, 231.

*cis*-configuration, since catalytic reduction of cyclic olefins results in *cis*-addition. Bromination of the indene (XXI) gave a monobromo-compound *assumed* to be (XXII; R = Br).* Reduction of (XXII; R = Br) by sodium and alcohol gave metanethole (m. p. 135°). Van der Zanden and de Vries assumed that reduction under these conditions gave a *trans*-compound and since the same stereoisomer (m. p. 135°) is obtained from (XXI), metanethole must have the *trans-trans*-configuration.[20]

Three of the four possible racemates of di*iso*eugenol dimethyl ether are known;[22] their relations are shown in formulæ (XXIII)—(XXIX), where Ve = 3 : 4-dimethoxyphenyl, and • represents H above the plane of the ring. (1) The indene (XXIX) and its isomer with the double bond in the alternative nuclear position are reduced catalytically to the β-racemate (XXIII)[21–23] which must therefore be *cis-cis*. (2) A bromo-derivative of (XXIII), prepared by the action of finely divided copper on *iso*eugenol dibromide (dibromide of XIX; R = R′ = OMe),[24] was shown to have structure (XXVI)[22] and was reduced by zinc dust and alcohol to di*iso*eugenol dimethyl ether (called the α-racemate) (XXIII), whereas dehydrobromination followed by reduction of the resulting (XXIV) gave the γ- and some of the α-racemate. It follows, therefore, that the α- and the γ-racemate are $C_{(1)}$-epimers, and that (XXVI) has the same configuration at $C_{(2)}$ and $C_{(3)}$ as the α-racemate. Again, $C_{(2)}$ and $C_{(3)}$ in these compounds must be *trans*, otherwise reduction of (XXIV) would have given some of the *cis-cis*, β-racemate. (3) The hydrolysis of (XXVI) involves a retropinacol



---

[22] A. Müller, M. Mészáros, K. Körmendy, and A. Kucsman, *J. Org. Chem.*, 1952, **17**, 787.

[23] A. Müller and G. Gal, *Ber.*, 1944, **77**, 343; A. Müller, L. Toldy, G. Halmi, and M. Mészáros, *J. Org. Chem.*, 1951, **16**, 481.

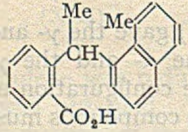
[24] J. Haraszti and T. Széki, *Annalen*, 1933, **503**, 294.

* If the bromo-compound is formed by allyl substitution it might have the alternative structure (XXI; Br in place of H at $C_{(1)}$) and the argument for the *trans-trans*-configuration would no longer be valid.—J. F. W. McO.

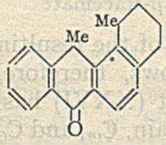
rearrangement and yields the indanol (XXVIII). The latter is not dehydrated by acid whereas the epimeric (XXVII) readily gives the indene (XXIX). Dehydration normally occurs more readily when the H and OH are *trans*, whence follow the configurations shown for (XXVIII) and (XXVII). (4) Conversion of the bromo-compound (XXVI) into the indanol (XXVIII) almost certainly involves inversion at $C_{(1)}$, and thus the bromo-compound and the α-racemate must both have the H atoms at $C_{(1)}$–$C_{(2)}$ and $C_{(2)}$–$C_{(3)}$ in *trans*-relations. Similarly the hydrogenolysis of the *trans-trans*-indanol (XXVII) gives, by inversion at $C_{(1)}$, the γ-racemate (XXIII) which must then be the *cis-trans*-stereoisomer.

A. Müller has discussed the mechanism of the acid dimerisation of phenyl propenyl ethers and concludes that it is highly stereospecific and leads to the all-*trans*-configuration.[22, 25] That most, if not all, of these dimers have the same configuration has been shown by (1) the conversion of metanethole,[26] di*iso*safrole,[27] and the dimer of 1 : 2-dibenzyloxy-4-propenylbenzene [26] into di*iso*eugenol dimethyl ether by reactions which are unlikely to affect the stereochemical configuration, and (2) the previously known correlations of the saturated dimers of 4-hydroxy-3-methoxy-, 3 : 4-dimethoxy-, and 4-ethoxy-3-methoxy-, and (probably) 3-hydroxy-4-methoxy-propenylbenzenes (for summary see Ref. 26). The conversion of metanethole into di*iso*eugenol dimethyl ether completes the formal total synthesis of the latter: metanethole reacted with acetyl chloride and aluminium chloride giving the dihydroxy-diketone (XX; R = OH, R′ = Ac), which was oxidised by hydrogen peroxide to the tetrahydroxy-compound (XX; R = R′ = OH), methylation then giving the known dimeride (α-racemate) of (XXIII). The di*iso*safroles, m. p. 95° and 146°, when hydrolysed and then methylated gave the α- and γ-racemates (XXIII), respectively.

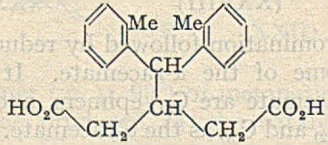
**Polycyclic Compounds.**—The usefulness of hydroaromatic intermediates [28] has been further emphasised by the synthesis of compounds which are non-planar owing to intramolecular overcrowding; such compounds are difficult, if not impossible, to prepare from fully aromatic intermediates. Previously it had not been possible to cyclise (XXX) [29] but the tetrahydro-compound readily gave the ketone (XXXI) which was reduced and then dehydrogenated to 1′ : 9-dimethyl-1 : 2-benzanthracene.[30] An ingenious synthesis of 5 : 4′-dimethyl-3 : 4-benzophenanthrene (XXXIII; R = H) involved a double cyclisation of the glutaric acid (XXXII) to the diketone, which was converted into (XXXIII; R = H) by reduction and



(XXX)



(XXXI)

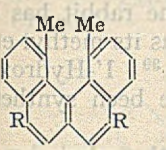


(XXXII)

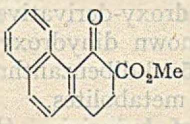
---

[25] A. Müller, *J. Org. Chem.*, 1952, **17**, 1077.
[26] W. Baker, C. N. Haksar, J. F. W. McOmie, and T. L. V. Ulbricht, *J.*, 1952, 4310.
[27] W. Baker, J. A. Godsell, J. F. W. McOmie, and T. L. V. Ulbricht, unpublished.
[28] A. J. Birch, *Ann. Reports*, 1950, **47**, 180.
[29] J. Cason and J. D. Wordie, *J. Org. Chem.*, 1950, **15**, 617.
[30] J. Cason and D. D. Phillips, *ibid.*, 1952, **17**, 298.

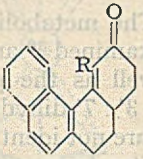
dehydrogenation.[31] The diketone was also treated with methylmagnesium iodide, the product yielding the 2 : 5 : 9 : 4′-tetramethyl compound (XXXIII; R = Me). The intermediate acid (XXXII) was prepared in good yield by the addition of *o*-tolylmagnesium bromide to *o*-methylbenzylidenemalonic ester, followed by homologation (Arndt–Eistert) of both carboxyl groups. The Robinson–Mannich base synthesis has been applied to the synthesis of the same ring system. The keto-ester (XXXIV) was treated with methyl vinyl ketone in the presence of a small amount of sodium methoxide; ring closure with elimination of the carbomethoxy-group then gave (XXXV; R = H), which was converted into the parent hydrocarbon and its 2-methyl and 2-ethyl derivatives by ordinary methods.[32] Alkylation of (XXXIV) by the methiodide of 1-diethylamino-3-pentanone, followed by cyclisation, gave (XXXV; R = Me). Similarly 4-methylchrysene (XXXVIII) has been prepared from (XXXVI) and the methiodide of 1-diethylamino-3-pentanone, *via* (XXXVII).[33] The yield of coronene in the novel synthesis from 2 : 7-dimethylnaphthalene, reported last year, has been improved.[34]



(XXXIII)

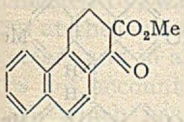


(XXXIV)

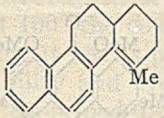


(XXXV)

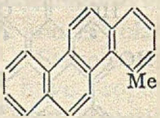
The chemistry of fluoranthene has been reviewed.[35] Several alkyl and aryl derivatives (XL) have been prepared by the Diels–Alder addition of acetylenes ($R''C{\equiv}CR'''$) to the dienone (XXXIX), the intermediate *endo*-carbonyl compounds losing carbon monoxide very readily. When olefins ($R''CH{=}CHR'''$) were employed, dihydro-derivatives of (XL) were formed and were converted by oxidation or dehydrogenation into (XL).[36] The fluoranthene derivatives (XLIII) and (XLVI) are the first hydrocarbons



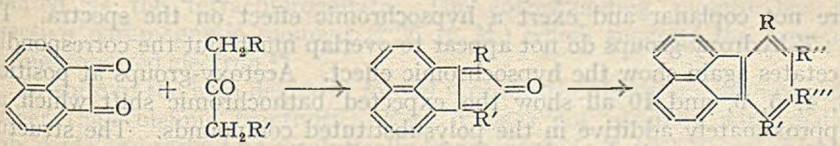
(XXXVI)



(XXXVII)



(XXXVIII)



(XXXIX) (XL)

---

[31] M. S. Newman and M. Wolf, *J. Amer. Chem. Soc.*, 1952, **74**, 3225.

[32] A. L. Wilds and R. G. Werth, *J. Org. Chem.*, 1952, **17**, 1154.

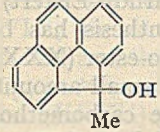
[33] *Idem, ibid.*, p. 1149.

[34] W. Baker, J. F. W. McOmie, and W. K. Warburton, *J.*, 1952, 2991.

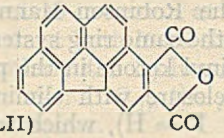
[35] S. H. Tucker, and M. Whalley, *Chem. Reviews*, 1952, **50**, 483.

[36] C. F. H. Allen and J. A. Van Allan, *J. Org. Chem.*, 1952, **17**, 845.

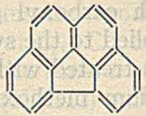
with four aromatic nuclei annealed directly to a *cyclo*pentane ring.[37] The alcohol (XLI) with maleic anhydride gave the adduct (XLII) directly and thence (XLIII). The dibenzo-derivative was obtained from (XLIV) *via* (XLV) as shown.



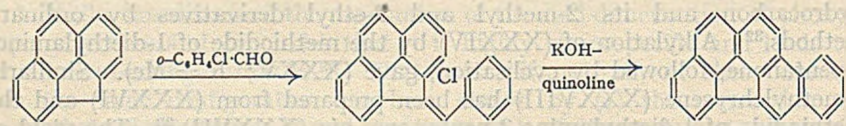
(XLI)



(XLII)



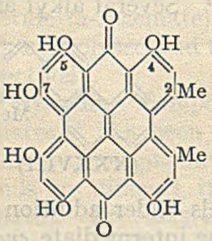
(XLIII)



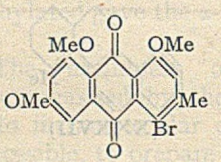
(XLIV) (XLV) (XLVI)

The metabolism of 1 : 2-5 : 6-dibenzanthracene in the rabbit has been re-examined[38] and a monohydroxy-derivative isolated (as its methyl ether) as well as the previously known dihydroxy-derivative.[39] 1′-Hydroxy-[38] and 3′ : 7′-dihydroxy[40]-1 : 2-5 : 6-dibenzanthracene have been synthesised but are not identical with the metabolites.

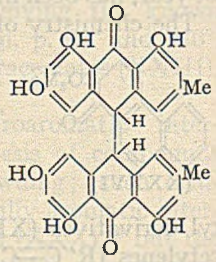
*Structure and synthesis of hypericin.* Hypericin, the photodynamic colouring matter of St. John's wort,[41] has been shown to have the structure (XLVII),[42] on chemical and spectroscopic evidence. As a result of steric hindrance the 2 : 2′-methyl groups in this and related polycyclic compounds are not coplanar and exert a hypsochromic effect on the spectra. The 7 : 7′-hydroxy-groups do not appear to overlap much but the corresponding acetates again show the hypsochromic effect. Acetoxy-groups at positions 3, 4, 5, 6, and 10 all show the expected bathochromic shift which are approximately additive in the polysubstituted compounds. The structure (XLVII) for hypericin has been confirmed by synthesis, albeit in very poor yield, from 1-bromoemodin trimethyl ether (XLVIII).[43] The closely related



(XLVII)



(XLVIII)



(XLIX)

---

[37] N. Campbell and D. H. Reid, *J.*, 1952, 3281.

[38] J. W. Cook and R. Schoental, *J.*, 1952, 9.

[39] E. Boyland, A. A. Levi, E. H. Mawson, and E. Roe, *Biochem. J.*, 1941, **35**, 184.

[40] L. S. Hornig, *J. Amer. Chem. Soc.*, 1952, **74**, 4572.

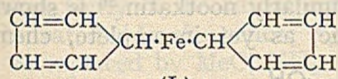
[41] *Ann. Reports*, 1941, **38**, 214.

[42] H. Brockmann, E. H. F. von Falkenhausen, R. Neeff, A. Dorlars, and G. Budde, *Ber.*, 1951, **84**, 865.

[43] H. Brockmann and F. Kluge, *Naturwiss.*, 1951, **38**, 141.

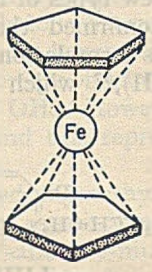
pigment penicilliopsin[41] has been converted by oxidation followed by irradiation into hypericin. This and other evidence leads to (XLIX) as the probable structure of penicilliopsin.[44]

**Di*cyclo*pentadienyliron.**—The discovery of a completely new type of compound possessing aromatic properties merits special notice. Di*cyclo*pentadienyliron has been prepared by two different methods. The reaction of *cyclo*pentadiene with reduced iron, in the form of the "doubly-promoted synthetic ammonia catalyst" in nitrogen at 300° (at atmospheric pressure) gave an orange-yellow compound formulated as (L).[45] As a possible route to fulvalene[46] (LI) the Grignard reagent prepared from *cyclo*pentadiene was treated with ferric chloride.[47] The reaction product, m. p. 173—174°, was also formulated as (L) or a resonance hybrid thereof. This, the first known compound containing only carbon, hydrogen, and iron, is remarkably stable and can be recrystallised from organic solvents. It is insoluble in, and unaffected by, water, sodium hydroxide, or concentrated hydrochloric acid even at the boiling point. At 100° the compound sublimes and is volatile in steam and in alcohol vapour; it resists pyrolysis at 470°. Structure (L) does not account for this stability and Woodward *et al.*[48] have proposed (LII), which has since been confirmed by preliminary *X*-ray structural studies.[49] The anti-prismatic structure (LII) agrees with the diamagnetism, the zero dipole moment, and the fact that the infra-red absorption spectrum indicates C–H bonds of only one type.[48] The name *ferrocene* has been proposed for this unique iron compound.[50] Oxidation of ferrocene by a variety of reagents gives the blue cation $[Fe(C_5H_5)]_2^+$ which has been isolated as the tetrachlorogallate. The corresponding picrate has an effective paramagnetic moment (2·26 B. M.) which suggests the presence of one unpaired electron.[48]



(L)

(LI)



(LII)

In spite of the high degree of formal unsaturation ferrocene has aromatic rather than olefinic reactivity. *E.g.*, it does not combine with maleic anhydride and cannot be catalytically hydrogenated;[50] with acetyl chloride in the presence of aluminium chloride a red diacetyl derivative is formed, which gives a dioxime, and can be oxidised to a dicarboxylic acid; β-chloro-

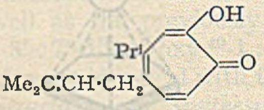
---

[44] H. Brockmann and R. Neeff, *Naturwiss*, 1951, **38**, 47.
[45] S. A. Miller, J. A. Tebboth, and J. F. Tremaine, *J.*, 1952, 632.
[46] R. D. Brown, *Nature*, 1950, **165**, 566.
[47] T. J. Kealy and P. L. Pauson, *ibid.*, 1951, **168**, 1039.
[48] G. Wilkinson, M. Rosenblum, M. C. Whiting, and R. B. Woodward, *J. Amer. Chem. Soc.*, 1952, **74**, 2125.
[49] P. F. Eiland and R. Pepinsky, *ibid.*, p. 4971.
[50] R. B. Woodward, M. Rosenblum, and M. C. Whiting, *ibid.*, p. 3458.

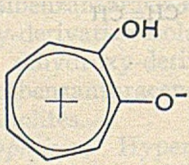
propionyl chloride and phthalic anhydride react similarly. Strongly oxidising species, such as $NO_2^+$ and $Br^+$, convert ferrocene into the cation instead of effecting substitution.[50]

From the vapour pressures and vapour densities the normal boiling point (249°), molecular weight (186), heats of sublimation (16·8 kcal./mole) and vaporisation (11·3 kcal./mole), the latent heat of fusion (5·5 kcal./mole), and the triple point (183°) have been calculated.[51] From the measured heat of combustion of ferrocene the combined energies of resonance of the five-membered rings and that of the C–Fe bonds have been calculated to be 113 kcal.[52] This high value is in accordance with the unusual stability of ferrocene.

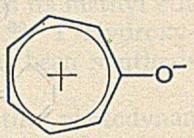
**Tropolones.**—These compounds continue to attract much attention and some new types of reaction have been revealed. *X*-Ray structural studies have confirmed the accepted structure of purpurogallin [53] and proved Dewar's formulation of colchicine.[54, 55] Similarly nootkatin [56] is shown to be (LIII),[57] which is in accord with the, as yet incomplete, chemical evidence.[58] The symbol (LIV) is suggested as more adequately representing the electron distribution in tropolone than the classical structure or any single canonical form.[59] In this way the *cyclo*heptatrienylium ion $C_7H_7^+$ is recognised as the major source of aromatic resonance energy, and *cyclo*heptatrienone (LV) (" *cyclo*heptatrienylium oxide; " tropone) as the parent of the new aromatic series, tropolone being related to it as phenol is to benzene. The high dipole moment (4·3 D) [60] and chemical properties [61] of *cyclo*heptatrienone indicate considerable stability of the polar structure (LV).



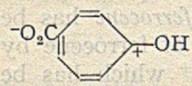
(LIII)



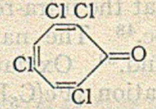
(LIV)



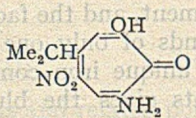
(LV)



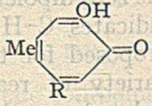
(LVI)



(LVII)



(LVIII)



(LIX)

4-Keto*cyclo*heptatrienecarboxylic acid has been prepared by the hydrolysis of the reaction product of diazoacetic ester with anisole; [62] it chars but does not melt at 250° and probably exists as a zwitter-ion (LVI).

---

[51] L. Kaplan, W. L. Kester, and J. J. Katz, *J. Amer. Chem. Soc.*, 1952, **74**, 5531.
[52] F. A. Cotton and G. Wilkinson, *ibid.*, p. 5764.
[53] C. A. Taylor, *Nature*, 1952, **169**, 1087; J. D. Dunitz, *ibid.*, p. 1088.
[54] M. J. S. Dewar, *ibid.*, 1945, **155**, 141.
[55] M. V. King, J. L. de Vries, and R. Pepinsky, *Acta Cryst.*, 1952, **5**, 437.
[56] *Ann. Reports*, 1950, **57**, 184.
[57] R. B. Campbell and J. M. Robertson, *Chem. and Ind.*, 1952, 1266.
[58] H. Erdtman and W. E. Harvey, *ibid.*, p. 1267.
[59] W. von E. Doering and L. H. Knox, *J. Amer. Chem. Soc.*, 1952, **74**, 5683.
[60] Al Di Giacomo and C. P. Smyth, *ibid.*, p. 4411.
[61] *Ann. Reports*, 1951, **48**, 187.
[62] J. R. Bartels-Keith, A. W. Johnson, and A. Langemann, *J.*, 1952, 4461.

2-Phenyl*cyclo*heptatrienone resulted from the action of phenyl-lithium [63] or phenylmagnesium bromide [64] on tropolone or its methyl ether. The bromination of *cyclo*heptanone yielded a mixture from which 2 : 4 : 7-tribromotropone could be isolated. When the mother-liquor from the latter was treated with sodium hydrogen carbonate the sodium salts of α-bromo- and αα′γ-tribromo-tropolone were isolated.[65] The hydroxyl group of tropolones can be replaced by bromine or chlorine by using phosphorus tribromide [66] or thionyl chloride respectively.[59, 63, 66] With α-bromotropolone thionyl chloride yielded 2 : 3- or 2 : 7-dichlorotropone.[66] Similarly αα′γ-tribromotropolone yielded 2 : 3 : 5 : 7-tetrachlorotropone (LVII), the orientation being deduced from its alkaline isomerisation to 2 : 4 : 6-trichlorobenzoic acid.[59] This halogen replacement is acid-catalysed and when 2-chloro*cyclo*heptatrienone is heated in acetic acid with hydrogen bromide or potassium iodide the corresponding bromo- and iodo-ketone is formed.[59, 63] This reactivity of the halogens resembles that in chloro-*p*-benzoquinone or (*op*-)nitrated chlorobenzenes; *e.g.*, the chlorine in 2-chloro*cyclo*heptatrienone can be replaced by MeO, $NH_2$, *p*-$Me{\cdot}C_6H_4S$, CN, and OH. However, the main product of alkaline hydrolysis is benzoic acid and this represents a fifth type of ring contraction in the tropolone series.

Studies on the iodination,[67] bromination,[68, 69] and hydroxymethylation [70] of tropolones have been reported. In contrast to other α-aminotropolones, which rearrange to salicylic acids when diazotised,[71] α′-amino-γ-nitro-β-*iso*propyltropolone (LVIII) can be converted into the corresponding bromo- and chloro-compounds by the Sandmeyer reaction.[72] The action of nitrous acid on the β-aminotropolone (LIX; $R = NH_2$) gave (LIX; $R = OH$) but no intermediate diazonium compound could be detected even at −20°.[73] Tropolone reacted with chloroform and sodium hydroxide giving the γ-aldehyde which was orientated by oxidation to tropolone-γ-carboxylic acid.[74] This acid was obtained directly when carbon tetrachloride was used in the Reimer–Tiemann reaction. Reduction of tropolone by lithium aluminium hydride gave a small yield of a compound which was thought to be *cyclo*hept-4-ene-1 : 2-dione.[74] Under similar conditions tropolone methyl ether gave benzaldehyde; a possible mechanism for this ring contraction was put forward.[74] The oxidation of β-methyltropolone by potassium persulphate gave γ-hydroxy-β-methyltropolone together with a small amount of the isomeric α- or α′-hydroxy-compound.[73]

Details of the preparation of αβ-benzotropolone (LX) from benzo*cyclo*heptene-3 : 4-dione have been published.[75] Dehydrogenation of (LXI)

---

[63] W. von E. Doering and C. F. Hiskey, *J. Amer. Chem. Soc.*, 1952, **74**, 5688.

[64] T. Nozoe, T. Mukai, and J. Minegishi, *Proc. Japan Acad.*, 1951, **27**, 419.

[65] T. Nozoe, Y. Kitahara, T. Andô, and S. Masamune, *ibid.*, p. 415.

[66] B. J. Abadir, J. W. Cook, J. D. Loudon, and D. K. V. Steel, *J.*, 1952, 2350.

[67] Y. Kitahara and T. Arai, *Proc. Japan Acad.*, 1951, **27**, 423.

[68] T. Nozoe, S. Seto, S. Itô, and M. Satô, *ibid.*, p. 426; T. Mukai, M. Kunori, H. Kishi, T. Moroi, and K. Matsui, *ibid.*, p. 410; T. Nozoe, S. Seto, H. Takeda, S. Morosawa, and K. Matsumoto, *ibid.*, p. 556.

[69] H. Fernholz, E. Hartwig, and J.-C. Salfeld, *Annalen*, 1952, **576**, 131.

[70] T. Nozoe, T. Mukai, and K. Takase, *Proc. Japan Acad.*, 1951, **27**, 561.

[71] *Ann. Reports*, 1951, **48**, 186.

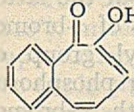
[72] T. Nozoe, H. Akino, and K. Sato, *Proc. Japan Acad.*, 1951, **27**, 565.

[73] W. D. Crow, R. D. Haworth, and P. R. Jefferies, *J.*, 1952, 3705.

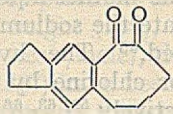
[74] J. W. Cook, R. A. Raphael, and A. I. Scott, *J.*, 1952, 4416.

[75] J. W. Cook, A. R. M. Gibb, R. A. Raphael, and A. R. Somerville, *J.*, 1952, 603.

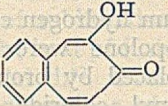
gave the corresponding indano(5 : 6-α : β)tropolone.[76] Some substitution reactions of (LX) have been described by Nozoe *et al.*[77] The synthesis of βγ-benzotropolone (LXII) has been improved by condensing phthalaldehyde



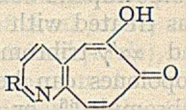
(LX)



(LXI)



(LXII)



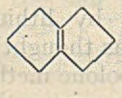
(LXIII)

with bromoacetone[69] or better with methoxyacetone[78] (followed by demethylation) in place of acetol, previously used.[56] Substitution reactions of (LXII) and the isomerisations to derivatives of β-naphthoic acid are analogous to those of the simpler tropolones.

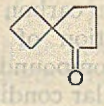
Pyridinotropolones, *e.g.*, (LXIII), have been prepared from γ-aminotropolone, the parent compound by the Skraup reaction,[79] the homologue (LXIII; R = Me) by the Doebner–Miller reaction;[80] ethoxymethylenemalonic ester yielded 5-carbethoxy-4-hydroxypyridino(3 : 2-β : γ)tropolone.[80]

A further review of tropolone chemistry has recently been published.[81]

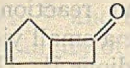
**Other Non-benzenoid Aromatic Compounds.**—The great interest in the theoretical calculation of the physical properties of this class of compound continues and many new types have been predicted.[82] Experimental work has received a stimulus from the discovery of ferrocene (see above) and the synthesis of dibenzopentalene (see p. 174). Several hydro-derivatives of *pseudo*aromatic compounds have been synthesised but their aromatisation always presents difficulties and it is clear that new, mild methods of dehydrogenation, direct or otherwise, are required. The hexahydropentalene (LXIV) was synthesised from *cyclo*butanone, which was first



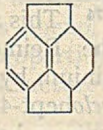
(LXIV)



(LXV)



(LXVI)



(LXVII)

converted into the pinacol. Rearrangement of the latter gave (LXV), which on reduction followed by dehydration underwent a retropinacol rearrangement thereby yielding (LXIV).[83] A mixture of tetrahydropentalenes resisted dehydrogenation to pentalene.[84] The starting point for their synthesis was the adduct (LXVI) from *cyclo*pentadiene and keten.

[76] A. D. Campbell and S. N. Slater, *J.*, 1952, 4353.

[77] T. Nozoe, Y. Kitahara, and T. Andô, *Proc. Japan Acad.*, 1951, **27**, 107.

[78] D. S. Tarbell and J. C. Bill, *J. Amer. Chem. Soc.*, 1952, **74**, 1234.

[79] J. W. Cook, J. D. Loudon, and D. K. V. Steel, *Chem. and Ind.*, 1952, 562.

[80] R. Slack and C. F. Attridge, *ibid.*, p. 471.

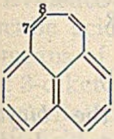
[81] G. B. R. de Graaff, *Chem. Weekblad*, 1952, **48**, 525, 541.

[82] J. F. Tinker, *J. Chem. Phys.*, 1951, **19**, 981; B. Pullman, A. Pullman, G. Berthier, and J. Pontis, *J. Chim. phys.*, 1952, **49**, 20; B. Pullman, A. Pullman, E. D. Bergmann, G. Berthier, E. Fischer, Y. Hirschberg, and J. Pontis, *ibid.*, p. 24; B. Pullman, A. Pullman, E. D. Bergmann, H. Berthod, E. Fischer, Y. Hirschberg, D. Lavie, and M. Mayot, *Bull. Soc. chim.*, 1952, **73**; J. D. Roberts, A. Streitwieser, and C. M. Regan, *J. Amer. Chem. Soc.*, 1952, **74**, 4579; K. Mislow, *J. Chem. Phys.*, 1952, **20**, 1489; R. D. Brown, *Quart. Reviews*, 1952, **6**, 63.

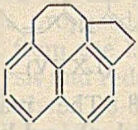
[83] E. Vogel, *Chem. Ber.*, 1952, **85**, 25.

[84] J. D. Roberts and W. F. Gorham, *J. Amer. Chem. Soc.*, 1952, **74**, 2278.

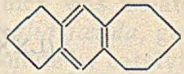
Expansion of the four-membered ring *via* the cyanohydrin and the derived aminomethyl-hydroxy-compound gave a mixture of ketones which was reduced by lithium aluminium hydride and dehydrated. Other experiments directed towards the synthesis of pentalene starting from octahydro-1 : 4-diketopentalene and from its 2 : 5-diketo-isomeride were also fruitless.[85] It is interesting that pyracene and not pyracylene was obtained by dehydrogenation of (LXVII),[86] although the related 1 : 2-5 : 6-dibenzopyracylene was easily synthesised and is very stable.[87] In contrast to the synthesis of acepleiadiene reported last year,[88] it has not yet been possible to prepare *cyclo*hepta[*de*]naphthalene (pleiadene) (LXVIII) from its 7 : 8-dihydro-derivative, nor has it been possible to dehydrogenate (LXIX) [89] or (LXX).[90] The octahydrobenzoheptalene (LXXI) has been described,[91] but heptalene and its derivatives are still unknown.



(LXVIII)

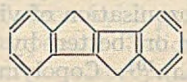


(LXIX)

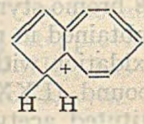


(LXX)

(LXXI)



(LXXII)



(LXXIII)

The bronze-coloured 1 : 2-4 : 5-dibenzopentalene has been prepared [92] after many unsuccessful attempts.[88] The dibromide from the known compound (LXXII) was dehydrobrominated by silver acetate in dry boiling benzene. Dibenzopentalene is insoluble in orthophosphoric acid, unlike azulene and does not form a picrate or a complex with 2 : 4 : 7-trinitrofluorenone; it is easily polymerised and behaves like a conjugated diene. There is, as yet, no chemical evidence that dibenzopentalene is more "aromatic" than *cis-cis*-1 : 4-diphenylbutadiene which is its open-chain analogue. However, the ultra-violet absorption spectrum of dibenzopentalene indicates some degree of resonance interaction in the excited state.

The azulenes have been comprehensively reviewed,[93] and their basic properties studied.[94] The azulenium ion is formulated as (LXXIII) (only one canonical form shown). The first known "fully aromatic" tetracyclic azulene (LXXIV) has been prepared by the Buchner synthesis from 1 : 2-benzofluorene; [95] it forms bright green crystals. Benzazulenes with the

---

[85] C. T. Blood and R. P. Linstead, *J.*, 1952, 2255.

[86] A. G. Anderson and R. H. Wade, *J. Amer. Chem. Soc.*, 1952, **74**, 2274.

[87] H. W. D. Stubbs and S. H. Tucker, *J.*, 1951, 2936. [88] *Ann. Reports*, 1951, **48**, 191

[89] P. D. Gardner and W. J. Horton, *J. Amer. Chem. Soc.*, 1952, **74**, 657.

[90] A. D. Campbell and S. N. Slater, *J.*, 1952, 4353.

[91] A. G. Anderson and H. F. Greef, *J. Amer. Chem. Soc.*, 1952, **74**, 5124.

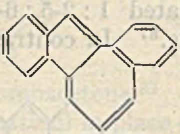
[92] C. T. Blood and R. P. Linstead, *J.*, 1952, 2263.

[93] M. Gordon, *Chem. Reviews*, 1952, **50**, 127.

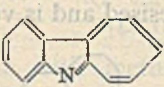
[94] P. A. Plattner, E. Heilbronner, and S. Weber, *Helv. Chim. Acta*, 1952, **35**, 1036; E. Heilbronner and M. Simonetta, *ibid.*, p. 1049; L. H. Chopard-dit-Jean and E. Heilbronner, *ibid.*, p. 2170. [95] W. Treibs, *Annalen*, 1952, **577**, 201.

diethylamino-group attached to the nucleus or to a side-chain have also been described.[96] The synthesis of 3-aza-1 : 2-benzazulene (LXXV) has been repeated[97] but the properties now ascribed to it are quite different from those previously reported.[98]

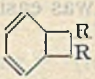
In the polymerisation of acetylenes to *cyclo*octatetraene two compounds $C_{10}H_{10}$ are also formed. These have been identified as vinyl*cyclo*octatetraene



(LXXIV)

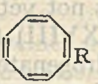


(LXXV)



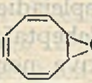
(LXXVI)

and *cis*-1-phenylbuta-1 : 3-diene.[99] The reaction between the *bicyclo*-octadiene (LXXVI; R = Cl) and phenyl-lithium yields chloro*cyclo*octatetraene (LXXVII; R = Cl) and a similar reaction occurs with the di-



(LXXVII)

(LXXVIII)



(LXXIX)

bromide. The monohalogeno-compounds are isomerised by heat to β-chloro- and β-bromo-styrene.[100] The monocarboxylic acid (LXXVII; R = $CO_2H$) was obtained in poor yield by ozonisation of vinyl*cyclo*octatetraene followed by oxidation with silver oxide, or, better, by carboxylation of the lithium compound (LXXVII; R = Li).[101] Copolymerisation of mono- and di-substituted acetylenes with acetylene has provided a direct synthesis of mono- and 1 : 2-di-substituted *cyclo*octatetraenes.[102] Alternatively the alkyl and aryl compounds can be prepared by the action of metal alkyls and aryls on *cyclo*octatetraene.[103] The reaction with lithium alkyls has been shown to proceed by addition, followed by the transfer of the equivalent of lithium hydride to another molecule of *cyclo*octatetraene, the products being (LXXVII; R = alkyl) and a mixture of 1 : 3 : 5- and 1 : 3 : 6-*cyclo*octatrienes. In the hope of preparing (LXXVIII) which might be dehydrated to (LXXVII; R = Ph), *cyclo*octatetraene epoxide (LXXIX) was treated with phenyl-lithium. However, the reaction took an unexpected course and resulted in isomerisation to *cyclo*octa-2 : 4 : 6-trienone.[104]

*cyclo*Octa-1 : 3 : 5-triene has now been shown to be in mobile equilibrium with the *bicyclo*octadiene (LXXVI; R = H). The monocyclic form can be isolated *via* its silver nitrate complex.[105]

F. J. W. McO.

---

[96] W. Treibs, W. Ziegenbein, H. Wetzel, and H. Böhm, *Annalen*, 1952, **577**, 207.

[97] A. G. Anderson and J. Tazuma, *J. Amer. Chem. Soc.*, 1952, **74**, 3455.

[98] W. Treibs, *Annalen*, 1952, **576**, 110.

[99] L. E. Craig and C. L. Larrabee, *J. Amer. Chem. Soc.*, 1951, **73**, 1191, 5471; A. C. Cope and S. W. Fenton, *ibid.*, p. 1195; D. W. Withey, *J.*, 1952, 1930.

[100] A. C. Cope and M. Burg, *J. Amer. Chem. Soc.*, 1952, **74**, 168.

[101] A. C. Cope, M. Burg, and S. W. Fenton, *ibid.*, p. 173.

[102] A. C. Cope and H. C. Campbell, *ibid.*, 1951, **73**, 3536; 1952, **74**, 179; A. C. Cope and D. S. Smith, *ibid.*, p. 5136.

[103] A. C. Cope and M. R. Kinter, *ibid.*, 1951, **73**, 3424; A. C. Cope and H. O. Van Orden, *ibid.*, 1952, **74**, 175.

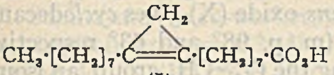
[104] A. C. Cope and B. D. Tiffany, *ibid.*, 1951, **73**, 4158.

[105] A. C. Cope, A. C. Haven, F. L. Ramp, and E. R. Trumbull, *ibid.*, **74**, 4867

## 6. ALICYCLIC COMPOUNDS.

**Small and Large Rings.**—Syntheses of *cyclo*propane-1 : 2 : 3-triamine,[1] 1 : 1 : 2-trimethyl*cyclo*propane,[2] and di*cyclo*propyl[3] have been described. Dehydration of 1-*cyclo*propylethanol over alumina gives vinyl*cyclo*propane,[4] derivatives of which may also be obtained by a new route involving the malonate condensation with 1 : 4-dibromobut-2-ene.[5] Vinyl*cyclo*propane has been converted into *cyclo*propylacetylene.[6]

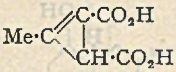
Evidence has been presented for the presence of a *cyclo*propene ring in sterculic acid, for which (I) is proposed.[7] The acid, which was isolated by means of its urea complex from the kernel oil of *Sterculia fœtida*, gave a 1 : 3-diketone (II) on ozonolysis and reduction of the ozonide by catalytic hydrogenation. Oxidation of the 1 : 3-dione with hydrogen peroxide in acetic acid gave pelargonic and azelaic acids.

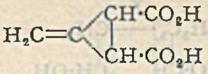


(I)

$CH_3\cdot[CH_2]_7\cdot CO\cdot CH_2\cdot CO\cdot[CH_2]_7\cdot CO_2H$
(II)

The molecular structure of *cyclo*propene has been determined by electron-diffraction studies.[8] The length of the –C=C– bond is rather short, being 1·28 ± 0·04 Å. The dicarboxylic acid obtained by Feist[9] by the action of alkali on ethyl 3-bromo-4 : 6-dimethyl-2-pyrone-5-carboxylate, previously formulated as 1-methyl*cyclo*propene-2 : 3-dicarboxylic acid (III), has now been shown to be 1-methylene*cyclo*propane-*trans*-2 : 3-dicarboxylic acid (IV).[10]

(III)




(IV)

The use of methylene*cyclo*butane as a source of isoprene for diene syntheses has been described.[11]

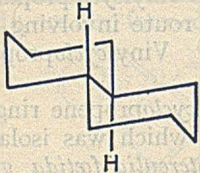
Energy differences between the " chair " and the " boat " conformation of *cyclo*hexane, and between *trans*-decalin (V) and *cis*-decalin in the conformations (VI) and (VII) have been calculated by a new method.[12] The differences between (V) and (VI), and between (VI) and (VII), are found to be 2·4 and at least 8·8 kcal. respectively. Introduction of an angular methyl group into *cis*- and *trans*-decalin (VI and V) lowers the energy difference from 2·4 to 0·8 kcal.

The preparations of *cyclo*nonyne and *cis*- and *trans*-*cyclo*nonene,[13] and of *cyclo*decyne and *cis*- and *trans*-*cyclo*decene,[14, 15] have been described in

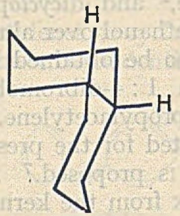
---

[1] H. A. Hoffman and A. Burger, *J. Amer. Chem. Soc.*, 1952, **74**, 5485.
[2] R. G. Kelso, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *ibid.*, p. 287.
[3] V. A. Slabey, *ibid.*, p. 4928. [4] *Idem*, *ibid.*, p. 4930.
[5] R. W. Kierstead, R. P. Linstead, and B. C. L. Weedon, *J.*, 1952, 3610.
[6] Ya. M. Slobodin and I. N. Shokhor, *Zhur. Obshchei Khim.* (*J. Gen. Chem., U.S.S.R.*), 1952, **22**, 195. [7] J. R. Nunn, *J.*, 1952, 313.
[8] J. D. Dunitz, H. G. Feldman, and V. Schomaker, *J. Chem. Phys.*, 1952, **20**, 1708.
[9] F. Feist, *Ber.*, 1893, **26**, 747.
[10] M. G. Ettlinger, *J. Amer. Chem. Soc.*, 1952, **74**, 5805.
[11] K. Alder and H. A. Dortmann, *Chem. Ber.*, 1952, **85**, 556.
[12] R. B. Turner, *J. Amer. Chem. Soc.*, 1952, **74**, 2118.
[13] A. T. Blomquist, L. H. Liu, and J. C. Bohrer, *ibid.*, p. 3643.
[14] A. T. Blomquist, R. E. Burge, Jr., and A. C. Sucsy, *ibid.*, p. 3636.
[15] V. Prelog, K. Schenker, and Hs. H. Günthard, *Helv. Chim. Acta*, 1952, **35**, 1598.

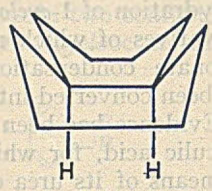
detail, and the oxides of *cis*- and *trans*-*cyclo*decene have been prepared.[16] Because of the conformation of their rings the oxides do not undergo normal $S_N2$ hydrolysis to 1 : 2-glycols. From the *cis*-oxide (VIII), *cyclo*dec-2-en-1-ol, two compounds of the formula $C_{10}H_{18}O_2$ (m. p. 98° and 74° respectively) and, by a transannular reaction involving the $C_{(6)}$–$CH_2$ group, *cyclo*decane-1 : 6-diol (IX) have been obtained. The *trans*-oxide (X) gives *cyclo*decanone, two compounds of the formula $C_{10}H_{18}O_2$ (m. p. 98° and 63° respectively) and, also by transannular reactions involving the $C_{(6)}$–$CH_2$ group, an isomeric *cyclo*decane-1 : 6-diol (XI) and *trans*-α-decalol (XII).



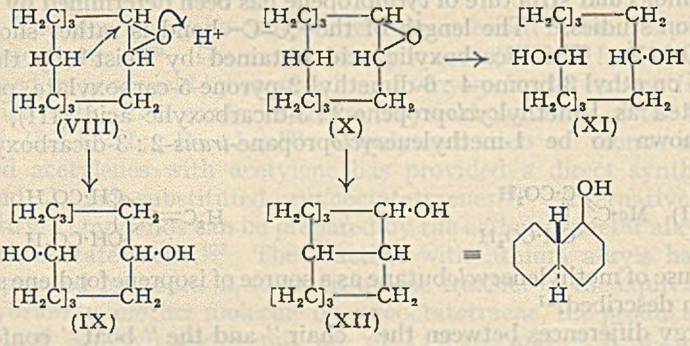
(V)



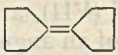
(VI)



(VII)

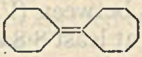


Compounds (XIII), (XIV), and (XV), with intercyclic double bonds, have been prepared.[17]



(XIII)

(XIV)



(XV)

**Terpenes.**—The work of the famous terpene chemist Komppa has been reviewed by W. Hückel.[18]

3-Methylcitronellal has been prepared by selective hydrogenation of 3-methylcitral,[19] the stereoisomers of which and of citral have been characterised.[20] A by-product isolated from the cyclisation of citral anil with 95% sulphuric acid has been shown to be 1-acetyl-4 : 4-dimethyl*cyclo*hexene.[21] 3 : 7-Dimethyl-6-methyleneoct-2-enal has been synthesised.[22]

Further evidence has been presented [23] in support of the currently

---

[16] V. Prelog and K. Schenker, *Helv. Chim Acta.*, 1952, 35, 2044.

[17] R. Criegee, E. Vogel, and H. Höger, *Chem. Ber.*, 1952, 85, 144.

[18] W. Hückel, *Chem. Ber.*, 1952, 85, S I.

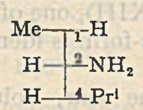
[19] Y.-R. Naves, *Bull. Soc. chim.*, 1952, 519. [20] *Idem, ibid.*, p. 521.

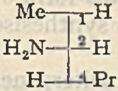
[21] H. B. Henbest, B. L. Shaw, and G. Woods, *J.*, 1952, 1154.

[22] M. Stoll and B. Willhalm, *Helv. Chim. Acta*, 1952, 35, 775.

[23] N. L. McNiven and J. Read, *J.*, 1952, (*a*) 153, (*b*) 159, (*c*) 2067.

accepted configurations of the menthols,[24] menthylamines,[25] and carvomenthone.[26] (+)-Carvomenthylamine has been shown to have configuration (XVI) and *neo*carvomenthylamine (XVII).[23a] The structures (XVI) and (XVII) have been confirmed by conformational analysis.[27] Application

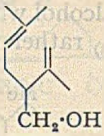
(XVI)




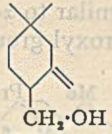
(XVII)

of this method [27] to *iso*carvomenthol and *neoiso*carvomenthol is invalid, however, as there is no *prima facie* reason for distinguishing between the polar and the equatorial conformation for the methyl group of these *iso*carvomenthols. Pure (—)-*cis*- and (+)-*trans*-piperitol have been prepared from (—)-piperitone and converted into (—)-*neo*menthol and (+)-*iso*menthol by hydrogenation.[28]

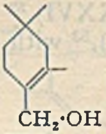
H. Schinz and his co-workers have continued their study of the cyclisation of unsaturated terpenes.[30–38, 45] Their work has also included new syntheses of lavandulol (XVIII) [29, 30] and of *cyclo*lavandulol (XIX),[34, 39] and the preparation of a number of compounds related to the latter, including β-*cyclo*lavandulol (XX),[40] β-*cyclo*lavandulal,[40] β-*cyclo*lavandulic acid,[30, 40] β-*cyclo*lavandulylideneacetone (XXI),[40] 5-methyl-,[41] 6-methyl-,[42] and 5 : 5-dimethyl*cyclo*lavandulylideneacetone,[43] and 5 : 5-dimethyl*apocyclo*lavandulylideneacetone (XXII).[43]



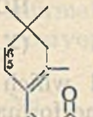
(XVIII)

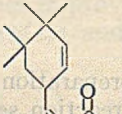


(XIX)



(XX)

(XXI)




(XXII)

5-Keto-α-ionone, prepared by oxidation of α-ionone with *tert.*-butyl chromate, has been converted into diols A and B, ketone C, and diketone D which have been isolated from pregnant-mare's urine.[44] Further syntheses

---

[24] Cf. Sir John Simonsen and L. N. Owen, "The Terpenes," 2nd Edn., Cambridge Univ. Press, Vol. I, p. 242.

[25] Cf. *Idem, op. cit.*, p. 245.

[26] Cf. Sir John Simonsen and D. H. R. Barton, *op. cit.*, Vol. III, p. 516.

[27] A. K. Bose, *Experientia*, 1952, 8, 458.

[28] A. K. Macbeth and J. S. Shannon, *J.*, 1952, 2852.

[29] H. Grütter and H. Schinz, *Helv. Chim. Acta*, 1952, 35, 1656.

[30] W. Kuhn and H. Schinz, *ibid.*, p. 2009.

[31] Cf. H. Schinz, *Chimia*, 1951, 5, 107.

[32] L. Williman and H. Schinz, *Helv. Chim. Acta*, 1952, 35, 2401.

[33] R. Helg and H. Schinz, *ibid.*, p. 2406.

[34] A. Brenner, U. Steiner, and H. Schinz, *ibid.*, p. 1336.

[35] L. Comombi and H. Schinz, *ibid.*, p. 1066.

[36] W. Kuhn and H. Schinz, *ibid.*, p. 2395.

[37] A. Caliezi and H. Schinz, *ibid.*, p. 1637.

[38] *Idem, ibid.*, p. 1649.

[39] A. Brenner and H. Schinz, *ibid.*, p. 1333.

[40] *Idem, ibid.*, p. 1615.

[41] R. Vonderwahl and H. Schinz, *ibid.*, p. 1997.

[42] *Idem, ibid.*, p. 2005.

[43] *Idem, ibid.*, p. 2368.

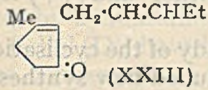
[44] V. Prelog and M. Osgan, *ibid.*, p. 986.

of α- and β-irone have been described,[45] and mixtures of natural and of synthetic irones have been separated by fractional distillation.[46] 1 : 1 : 6-Trimethyl*cyclo*hexan-3-one, a degradation product of γ-irone, has been synthesised.[47]

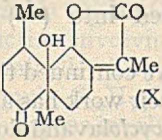
The *cis*- and the *trans*-form of jasmone (XXIII), one of which is dihydropyrethrone, have been synthesised.[48] The *cis*-form is identical with natural jasmone.

**Sesquiterpenes and Diterpenes.**—During the year, Volume III of "The Terpenes"[26] has appeared, providing a systematic survey of the chemistry of the sesquiterpenes and diterpenes up to 1950.

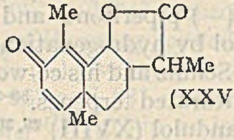
An αβ-unsaturated γ-lactone grouping has been shown to be present in $\psi$-santonin by infra-red examination, leading to structure (XXIV).[49] This has been confirmed since ozonolysis of $\psi$-santonin in chloroform gives a mixture containing pyruvic acid. Attempts to synthesise the structural features of santonin (XXV) have been described.[50, 51]



(XXIII)

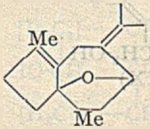


(XXIV)

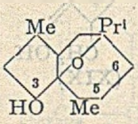


(XXV)

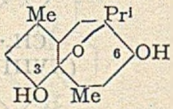
A number of sesquiterpene oxides with the guaiazulene skeleton have been investigated. Germacrol, from Bulgarian geranium oil, has been shown to be (XXVI).[52] It is similar to α-kessyl alcohol which is now known to be (XXVII),[53] with the hydroxyl group at $C_{(3)}$ rather than $C_{(5)}$.[54] This follows from its preparation from kessoglycol which is formulated as (XXVIII).[55] The reaction sequence involves the formation of kessoglycol diacetate, partial hydrolysis to kessoglycol 3-monoacetate, oxidation to the 6-ketone, and Wolff–Kishner reduction to (XXVII). Lederene is also probably an oxide of guaiazulene type.[56]



(XXVI)



(XXVII)



(XXVIII)

β-Caryophyllene[57] has now been shown to be (XXIX) with reasonable certainty,[58] and criticism of its formulation as (XXIX)[59] rather than as

---

[45] H. Grütter, R. Helg, and H. Schinz, *Helv. Chim. Acta*, 1952, **35**, 771; H. Favre and H. Schinz, *ibid.*, p. 1627.

[46] Hs. H. Günthard, C. F. Seidel, and L. Ruzicka, *ibid.*, p. 1820; C. F. Seidel and L. Ruzicka, *ibid.*, 1826.

[47] H. Favre and H. Schinz, *ibid.*, p. 2388.

[48] L. Crombie and S. H. Harper, *J.*, 1952, 869.

[49] W. Cocker, B. E. Cross, and D. H. Hayes, *Chem. and Ind.*, 1952, 314.

[50] F. D. Gunstone and R. M. Heggie, *J.*, 1952, 1354, 1437.

[51] G. R. Clemo and F. J. McQuillin, *J.*, 1952, 3835, 3839.

[52] W. Treibs, *Annalen*, 1952, **576**, 116.

[53] T. Ukita, *J. Pharm. Soc. Japan*, 1945, **65**, No. 5/6*A*, 7.

[54] Cf. *Ann. Reports*, 1950, **47**, 197.

[55] T. Ukita, *J. Pharm. Soc. Japan*, 1944, **64**, 285.

[56] K. Takeda and T. Shimada, *ibid.*, p. 132.

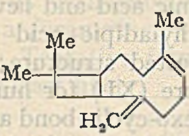
[57] Cf. *Ann. Reports*, 1951, **48**, 194.

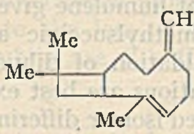
[58] D. H. R. Barton, T. Bruun, and A. S. Lindsey, *J.*, 1952, 2210.

[59] T. L. Dawson, G. R. Ramage, and R. Whitehead, *Chem. and Ind.*, 1952, 450.

(XXX) has been answered.[60] Formula (XXIX) includes the key grouping $-CH_2\cdot CMe{:}CH-$ which is present in β-caryophyllene, and leads to (XXXI)

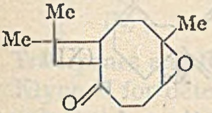
(XXIX)



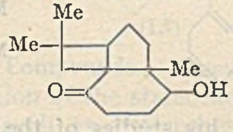


(XXX)

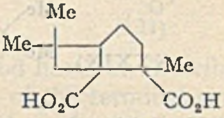
for Treibs's oxido-ketone,[61] to (XXXII) for the cyclised keto-alcohol obtained by the action of alkali on (XXXI), and to (XXXIII) for the dicarboxylic acid derived from (XXXII).



(XXXI)



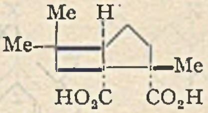
(XXXII)

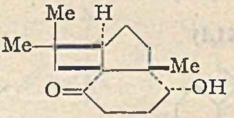


(XXXIII)

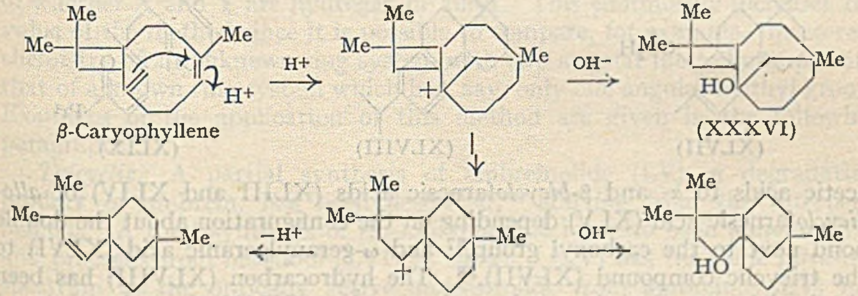
The stereochemistry of some of the above-mentioned compounds has been elucidated.[58] The easy formation of (XXXII) indicates that its *cyclo*butane ring is fused *cis*, while the properties of (XXXIII) are those of a *cis*-*cyclo*pentane-1 : 2-dicarboxylic acid. This leads to (XXXIV) for the dicarboxylic acid. Structure (XXXV) has been put forward for the keto-alcohol from which it follows that the *endo*cyclic double bond of β-caryophyllene is *cis*. Confirmation of its *cis*-nature is provided by comparison of the properties of β-caryophyllene with those of *cis*- and *trans*-*cyclo*nonene.[13]

(XXXIV)





(XXXV)



β-Caryophyllene

(XXXVI)

(XXXVIII)

(XXXVII)

β-Caryophyllene readily cyclises under the influence of acid to a number of tricyclic compounds, the most important being α- and β-caryophyllene alcohol, and clovene.[62] These are to be formulated as (XXXVI), (XXXVII), and (XXXVIII).[58, 62]

---

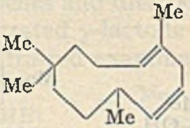
[60] D. H. R. Barton, T. Bruun, and A. S. Lindsey, *Chem. and Ind.*, 1952, 691.

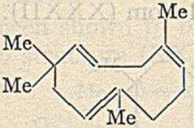
[61] W. Treibs, *Chem. Ber.*, 1947, **80**, 56.

[62] A. Eschenmoser and Hs. H. Günthard, *Helv. Chim. Acta*, 1951, **34**, 2338.

The monocyclic triene, humulene (α-caryophyllene, didymocarpene), and a number of its partially hydrogenated derivatives have been oxidised.[63] Ozonolysis of humulene gives αα-dimethylsuccinic acid and lævulaldehyde, while αα-dimethylsuccinic acid and ββ-dimethyladipic acid result from vigorous oxidation of dihydrohumulene (suggested structure; XXXIX). The observations are best explained by structure (XL) for humulene or a closely related isomer differing only in an endo-exo-cyclic bond arrangement. The eleven-membered ring is directly derivable by opening of the four-membered ring of β-caryophyllene (XXIX).

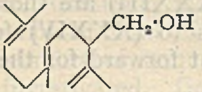
(XXXIX)



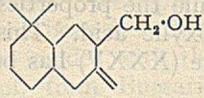


(XL)

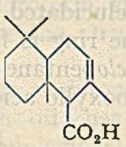
H. Schinz has extended his studies of the cyclisation of unsaturated terpenes to sesqui- and di-terpenes. Sesquilavandulol (XLI) has been cyclised to (XLII),[35, 36] farnesic acid and dihydro-α- and β-ionylidene-acetic acids to α- and β-*bicyclo*farnesic acids (XLIII and XLIV) or *allo-bicyclo*farnesic acid (XLV) depending on the configuration about the double bond next to the carboxyl group,[37] and ω-geranylgeranic acid (XLVI) to the tricyclic compound (XLVII).[38] The hydrocarbon (XLVIII) has been obtained by treating the condensation product (XLIX) from farnesal and methyl *iso*propyl ketone with iodine.[38] These examples indicate that the cyclisation method is of great potential value for the syntheses of naturally occurring diterpenes and related compounds (cf. the synthesis of *rac*-ambreinolide, p. 183).



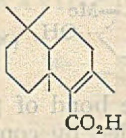
(XLI)



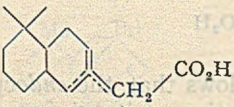
(XLII)



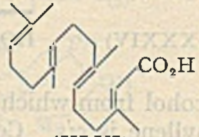
(XLIII)



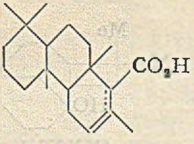
(XLIV)



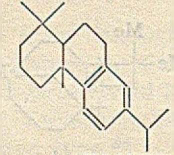
(XLV)



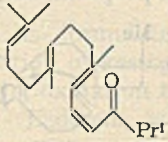
(XLVI)



(XLVII)



(XLVIII)



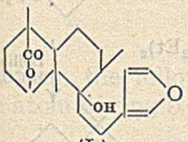
(XLIX)

*Marrubiin.* Marrubiin, $C_{20}H_{28}O_4$, is a diterpene which has previously been shown to possess a tertiary hydroxyl group, and a lactone ring, and

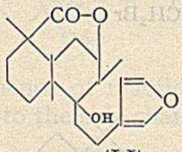
---

[63] G. R. Clemo and J. O. Harris, *J.*, 1952, 665.

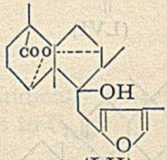
probably an oxide ring and two double bonds, and to give 1 : 2 : 5-trimethylnaphthalene on dehydrogenation.[64] Infra-red data now indicate that the lactone ring is six-membered and that the oxido-oxygen atom is probably present in a furan ring.[65] Oxidation leads to the loss of three carbon atoms.[65, 66] Tentative formulations for marrubiin are (L), (LI), or LII). The third is least likely.



(L)

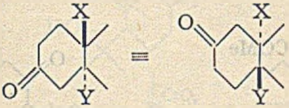


(LI)

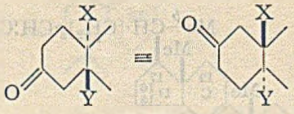


(LII)

**Triterpenes and Related Compounds.**—A new method has been described by Klyne [67] for determination of the stereochemistry of the terminal rings of polycyclic compounds such as triterpenes. He has shown that the molecular-rotation contribution of a terminal ring unit is, in the main, independent of the nature of the rest of the molecule provided the penultimate ring is saturated and unsubstituted. For each type of terminal unit, *e.g.*, for the *trans*-β-decalone type (LIII and LIV), the molecular-rotation contribution has a characteristic magnitude, being either positive or negative depending on which of the two enantiomeric forms (*e.g.*, LIII or LIV) is



(LIII)



(LIV)

under review. The molecular-rotation contribution is taken as the difference: ($[M_D]$ of ketone) minus ($[M_D]$ of corresponding deoxy-compound). The sign and size of the contribution are, to a first approximation, independent of whether X and Y are hydrogen or alkyl. This enormously increases the value of the method since it is possible to compare, for example, the stereochemistry of an unknown ring system with two angular methyl groups with that of a known ring system which has, say, only one angular methyl group. Examples of the application of this method are given in the following paragraphs.

*Tricyclic.* A partial synthesis of ambreinolide (LV), a degradation product of ambrein, has been described,[68] starting from the diterpene manoöl. A total synthesis of *rac*-ambreinolide has also been announced,[69] and proceeds from nerolidol (LVI) as shown. (LV) has the same infra-red spectrum as the optically active ambreinolide from ambrein. (LV) has been converted into the racemic unsaturated acid (LVII), from an optically active form of which ambratriene (LVIII), a dehydration product of ambrein,

---

[64] Cf. Sir John Simonsen and D. H. R. Barton, ref. 26, p. 479.

[65] W. Cocker, B. E. Cross, S. R. Duff, and T. F. Holley, *Chem. and Ind.*, 1952, 827.

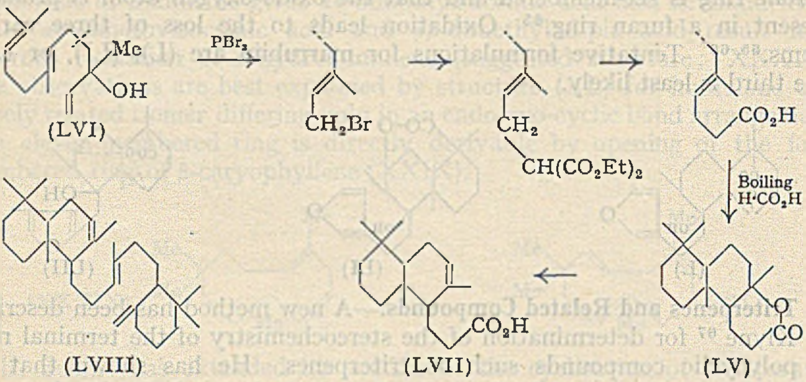
[66] E. Ghigi, *Gazzetta*, 1948, 78, 865; 1951, 81, 336.

[67] W. Klyne, *J.*, 1952, 2916.

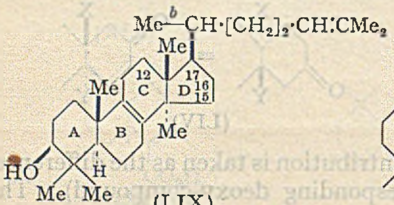
[68] H. R. Schenk, H. Gutmann, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1952, 35, 817.

[69] P. Dietrich and E. Lederer, *ibid.*, p. 1148.

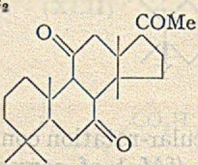
has already been obtained.[70] The way is thus open for a total synthesis of (LVIII).



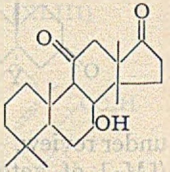
*Tetracyclic.* The structure of lanosterol (lanostadienol) has now been completely elucidated [71-77] and shown to be (LIX). It follows from the *X*-ray analysis of lanostenyl iodoacetate,[71] and from a series of chemical degradations which have shown that ring D is five-membered [72-74] and that the side chain is attached to $C_{(17)}$.[75, 76] Proof concerning ring D follows



(LIX)

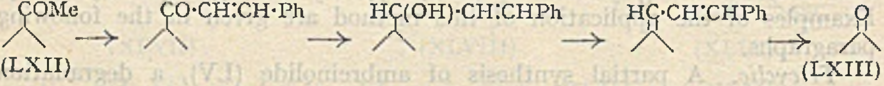


(LX)



(LXI)

from the conversion [72] of the methyl ketone (LX) [78] into (LXI) by several steps including (LXII) to (LXIII). The infra-red spectrum of (LXI) has a band at 1745 cm.$^{-1}$ corresponding to a carbonyl group on a five-membered



ring. The apparent integrated absorption intensity at 1412 cm.$^{-1}$ of a similar degradation product (LXIV) shows that there is only one $CH_2$

---

[70] O. Dürst, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1949, **32**, 46.

[71] R. G. Curtis, J. Fridrichsons, and A. McL. Mathieson, *Nature*, 1952, **170**, 321.

[72] W. Voser, Hs. H. Günthard, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1952, **35**, 66.

[73] W. Voser, O. Jeger, and L. Ruzicka, *ibid.*, p. 503.

[74] C. S. Barnes, D. H. R. Barton, J. S. Fawcett, and B. R. Thomas, *J.*, 1952, 2339.

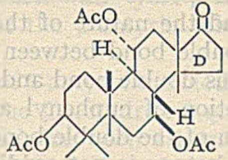
[75] C. S. Barnes, D. H. R. Barton, A. R. H. Cole, J. S. Fawcett, and B. R. Thomas, *Chem. and Ind.*, 1952, 426.

[76] W. Voser, Hs. H. Günthard, H. Heusser, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1952, **35**, 2065.

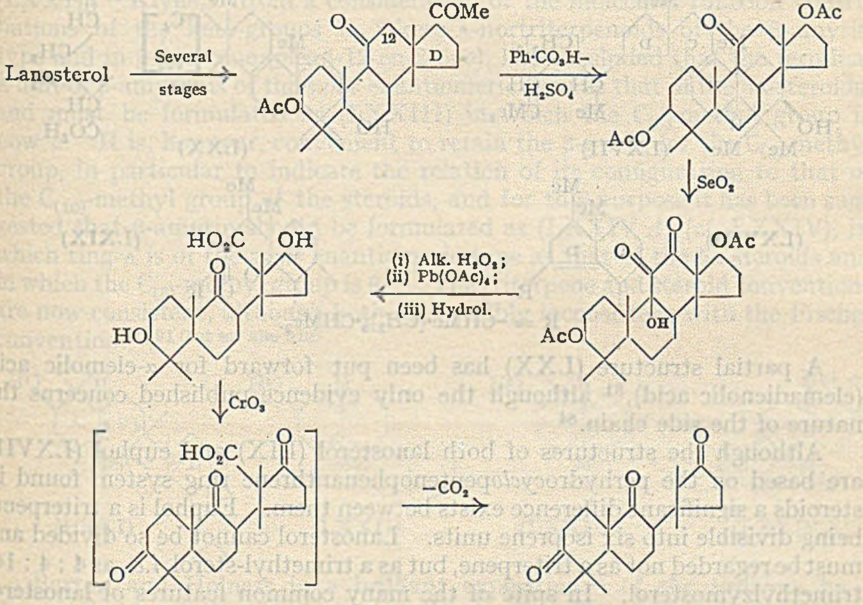
[77] W. Voser, M. V. Mijović, H. Heusser, O. Jeger, and L. Ruzicka, *ibid.*, p. 2414.

[78] Cf. *Ann. Reports*, 1951, **48**, 196.

group α to the carbonyl group, which therefore cannot be at $C_{(16)}$.[75] A decision between $C_{(15)}$ and $C_{(17)}$ as the point of attachment of the side chain results from the following sequence of reactions which indicate that the carbon atom of ring D attached to the side chain must be β to $C_{(12)}$.

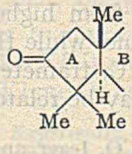


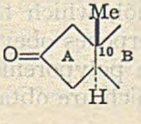
(LXIV)



The inter-relation of the asymmetric centres of lanosterol (LIX) is indicated by the *X*-ray structure analysis [71] and confirmed by chemical evidence,[77, 79] which also relates the configuration at the carbon atom carrying the Me group common to rings A/B to that at $C_{(10)}$ in the steroids as follows. Ring A of lanostenone is opened to give a dicarboxylic acid, cyclisation of

(LXV)





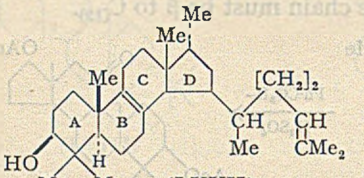
(LXVI)

which gives the nor-ketone (LXV).[80] The molecular-rotation contribution of its keto-group indicates that (LXV) is a *trans*-indan-2-one of the *same* enantiomeric type as that (LXVI) derived from steroids by a similar route.[67]

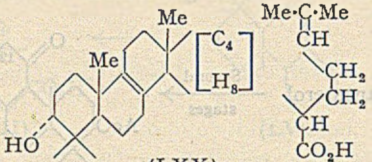
[79] D. H. R. Barton, J. S. Fawcett, and B. R. Thomas, *J.*, 1951, 3147.

[80] L. Ruzicka, E. Rey, and A. C. Muhr, *Helv. Chim. Acta*, 1944, **27**, 472.

A complete structure (LXVII) has been put forward[81] for euphol (euphadienol) although detailed evidence in support of all its features has not yet been published. Further points established during the year[82] include the structure of ring A and the nature of the A–B ring fusion, the environment of the unreactive double bond between rings B and C, and a relation between the position of this double bond and the side chain. This follows from the acidic isomerisation of euphenyl acetate to *iso*euphenyl acetate (LXVIII)[83] and the fission of the double bond in the *iso*-acetate to give the diketone (LXIX). This ketone is not oxidised by alkaline hypoiodite.

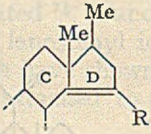


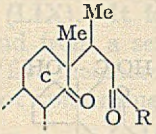
(LXVII)



(LXX)

(LXVIII)





(LXIX)

R = $-CHMe·[CH_2]_3·CHMe_2$.

A partial structure (LXX) has been put forward for α-elemolic acid (elemadienolic acid),[81] although the only evidence published concerns the nature of the side chain.[84]

Although the structures of both lanosterol (LIX) and euphol (LXVII) are based on the perhydro*cyclo*pentenophenanthrene ring system found in steroids a significant difference exists between them. Euphol is a triterpene, being divisible into six isoprene units. Lanosterol cannot be so divided and must be regarded not as a triterpene, but as a trimethyl-sterol, *i.e.*, as 4 : 4 : 14-trimethylzymosterol. In spite of the many common features of lanosterol and euphol this difference appears to be fundamental and may result from their formation by different biogenetic routes. Euphol is obtained from plant resins in which many other triterpenes occur, whereas lanosterol is produced by the sebaceous glands of sheep[85] and by yeast from which no triterpenes have yet been obtained. These facts suggest that other tetracyclic compounds such as euphorbol, elemadienolic acid, tirucallol, handianol, and butyrospermol, which have been isolated from higher plant sources, may also be triterpenes obeying the isoprene rule, while the triterpene-like acids such as the polyporenic acids A, B, and C, trametenolic acid,[86] and eburicoic acid which are obtained from fungi may be related to lanosterol.

---

[81] E. Kyburg, M. V. Mijović, W. Voser, H. Heusser, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*., 1952, **35**, 2073.

[82] K. Christen, M. Dünnenberger, C. B. Roth, H. Heusser, and O. Jeger, *ibid.*, p. 1756.

[83] M. Vilkas, G. Dupont, and R. Dulon, *Bull. Soc. chim.*, 1949, 813.

[84] Y. Mazur, E. Koller, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1952, **35**, 181.

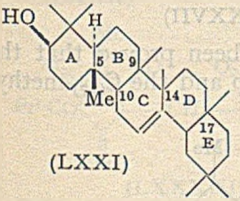
[85] Cf. E. Lederer, *J.*, 1949, 2120.

[86] Cf. W. Gruber and G. Proske, *Monatsh.*, 1951, **82**, 255.

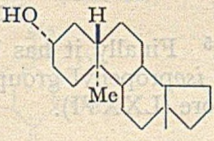
The non-identity of dihydroeuphol and dihydrobasseol has been discussed.[87]

*Pentacyclic triterpenes.* The year has seen the complete elucidation of the stereochemistry of the β-amyrin (olean-12-en-2β-ol) and lupeol groups of triterpenes.

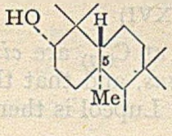
From the relation of β-amyrin to abietic acid [88] it follows that the junction A–B is *trans*, while the $C_{(2)}$-hydroxyl group is considered to be *cis* to the $C_{(5)}$-methyl group which has been arbitrarily assigned the β-configuration.[89] Using the classical representation of β-amyrin, with ring A at the upper left-hand side of the structure, rings A and B are to be formulated as in (LXXI), in which the terminal A unit is the enantiomer of that of the 5α-steroids (LXXII). Klyne,[67] from a consideration of the molecular-rotation contributions of the keto-groups in 2-keto-A-nortriterpenoids of the β-amyrin type and in β-amyrone (olean-12-en-2-one), has concluded that the terminal A unit of β-amyrin is of the *same* enantiomeric type as that of the 5α-steroids, and must be formulated as (LXXIII) in which the $C_{(5)}$-methyl group is now α. It is, however, convenient to retain the β-prefix for the $C_{(5)}$-methyl group, in particular to indicate the relation of its configuration to that of the $C_{(10)}$-methyl group of the steroids, and for this purpose it has been suggested that β-amyrin should be formulated as (LXXIV *A*) (cf. LXXIV), in which ring A is of the *same* enantiomeric type as that of the 5α-steroids and in which the $C_{(5)}$-methyl group is β.[90] The triterpene and steroid conventions are now consistent, although both are possibly inconsistent with the Fischer convention.[90, 91 (but see also 91a)]



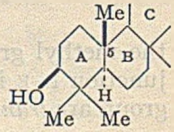
(LXXI)



(LXXII)



(LXXIII)



(LXXIV *A*)

Barton and Holness in a brilliant exposition [92] of the problem have discussed the relative configurations in rings C, D, and E of β-amyrin and concluded that the junction D–E is *cis*, and that the $C_{(10)}$-hydrogen atom and the $C_{(14)}$-methyl group are both *trans* to the $C_{(17)}$-methyl group (cf. LXXIV and LXXV). The junction B–C is in the more stable arrangement.[92, 93]

Making the probable assumption that the $C_{(5)}$- and the $C_{(9)}$-methyl group are *cis*, Barton concluded that there are only two structures (LXXIV and LXXV) for β-amyrin which will accommodate the facts described above. Now, (LXXIV) and (LXXV) have terminal ring E units which are enantiomeric. Klyne [67] has distinguished between these two structures

---

[87] F. A. Alves, *Experientia*, 1952, 8, 10.

[88] Cf. D. H. R. Barton, *Quart. Reviews*, 1949, 3, 36; O. Jeger, " Fortschritte der Chemie organischer Naturstoffe," Springer-Verlag, 1950, Vol. VII.

[89] D. H. R. Barton, *Experientia*, 1950, 6, 316.

[90] T. G. Halsall, E. R. H. Jones, and G. D. Meakins, *J.*, 1952, 2862.

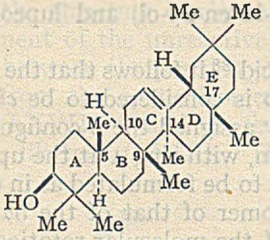
[91] Cf. A. Lardon and T. Reichstein, *Helv. Chim. Acta*, 1949, 32, 2003.

[91a] J. A. Mills, *J.*, 1952, 4982.

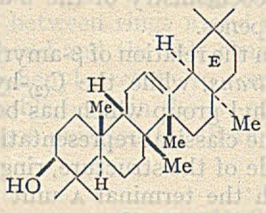
[92] D. H. R. Barton and N. J. Holness, *J.*, 1952, 78.

[93] R. Budziarek, W. Manson, and F. S. Spring, *J.*, 1951, 3336.

by showing that the terminal ring E of β-amyrin is of the same enantiomeric type as that in (LXXIV), which therefore is the correct formulation of β-amyrin.

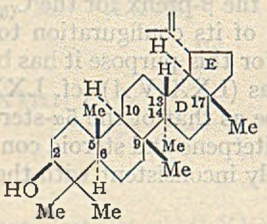


(LXXIV)

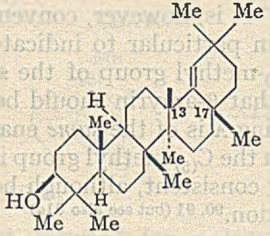


(LXXV)

The configurations of $C_{(2)}$, $C_{(5)}$, $C_{(6)}$, $C_{(9)}$, $C_{(10)}$, $C_{(14)}$, and $C_{(17)}$ of lupeol (cf. LXXVI) are the same as in β-amyrin.[94] Lupeol has also been converted into germanicol (LXXVII)[90] in which the hydrogen atom at $C_{(13)}$ and

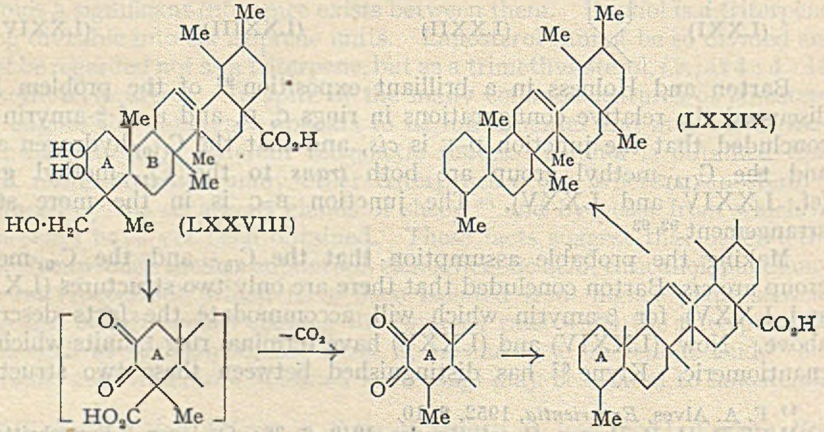


(LXXVI)



(LXXVII)

the methyl group at $C_{(17)}$ are *cis*.[95] Finally it has been proved that the junction D–E is *trans*, and that the *iso*propenyl group and the $C_{(17)}$-methyl group are *trans*.[90] Lupeol is therefore (LXXVI).



Asiatic acid, the aglycone of asiaticoside, has been shown to be (LXXVIII).[96] This structure is supported by proof of the presence of

---

[94] T. R. Ames, T. G. Halsall, and E. R. H. Jones, *J.*, 1951, 450.

[95] D. H. R. Barton and C. J. W. Brooks, *J.*, 1951, 257.

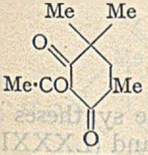
[96] (Mme.) Judith Polonsky, *Bull. Soc. chim.*, 1952, 649, 1015; *Compt. rend.*, 1949, 228, 1450; 1950, 230, 485, 1784; 1951, 232, 1878; 1951, 233, 93, 671.

an α-glycol group, the formation of a lactone involving the carboxyl group and the double bond, and the conversion of (LXXVIII) into 23-nor-α-amyrene (LXXIX) as shown.

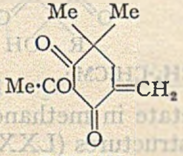
Zeorin, a pentacyclic secondary-tertiary diol, has been fully characterised.[97] It forms a monoacetate, dehydration of which with phosphorus oxychloride in pyridine gives *iso*zeorinin acetate. This contains the grouping ($>C{=}CH_2$). The secondary hydroxyl group is not at the typical triterpene 2-position.

New triterpenes isolated include gratiogenin (as its glycoside gratioside) which may be 21-keto-olean-12-ene-2 : 19 : 29-triol,[98] and psidiolic acid, $C_{30}H_{48}O_4$.[99] δ-Amyrin, hitherto not found in Nature, has been isolated from Spanish broom.[100] The sô-called crataegolic acid [101] is a mixture of known triterpenes.[102]

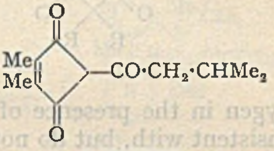
**β-Triketones.**—Considerable progress has recently been made in the chemistry of the group of naturally occurring alkali-soluble substances which owe their acidity to the presence of a β-triketone system. Birch [103] has considered the evidence concerning angustione, dehydroangustione, and calythrone, and concluded that they are best represented by structures (LXXX), (LXXXI), and (LXXXII). Flavaspidic acid, which was formulated by Boehm [104] as (LXXXIII) with a *cyclo*butane ring, is now believed to be (LXXXIV),[103] the quinonoid nature of which would account for the yellow colour of the acid.



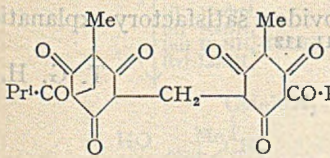
(LXXX)



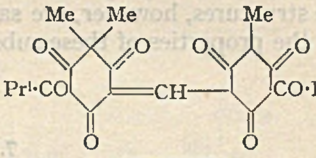
(LXXXI)



(LXXXII)



(LXXXIII)



(LXXXIV)

Protokosin, isolated from the anthelmintic drug kousso, was originally formulated as $C_{22}H_{28}O_7$ and also thought to have a *cyclo*butane ring. The formula has now been modified to $C_{25}H_{32}O_8$, and structure (LXXXV) has been proposed.[105] (LXXXVI) and (LXXXVII) follow for α- and β-kosin which result from the action of zinc and alkali on protokosin.

The hop constituents lupulone and humulone have been synthesised : [106]

---

[97] D. H. R. Barton and T. Bruun, *J.*, 1952, 1683.

[98] R. Tschesche and A. Heesch, *Chem. Ber.*, 1952, 85, 1067.

[99] G. Soliman and M. K. Farid, *J.*, 1952, 134; H. R. Arthur and W. H. Hui, *Chem. and Ind.*, 1952, 693.

[100] O. C. Musgrave, J. Stark, and F. S. Spring, *J.*, 1952, 4393.

[101] R. Tschesche and R. Fugmann, *Chem. Ber.*, 1951, 84, 810.

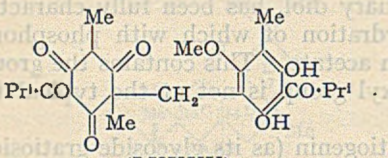
[102] T. Bersin and A. Müller, *Helv. Chim. Acta*, 1952, 35, 1891.

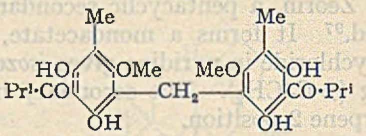
[103] A. J. Birch, *J.*, 1951, 3026. [104] R. Boehm, *Annalen*, 1903, 329, 310.

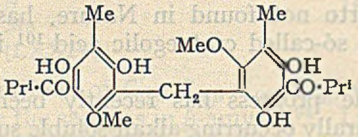
[105] A. J. Birch and A. R. Todd, *J.*, 1952, 3102.

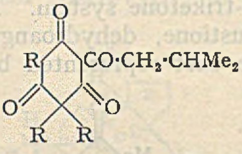
[106] W. Riedl, *Chem. Ber.*, 1952, 85, 692.

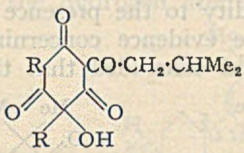
lupulone by trialkylation of 2 : 4 : 6-trihydroxy*iso*valerophenone with 1-bromo-3-methylbut-2-ene, and humulone by similar dialkylation of the same trihydroxy*iso*valerophenone followed by oxidation of the product with oxygen in the presence of lead acetate in methanol. These syntheses are consistent with, but do not prove, structures (LXXXVIII) and (LXXXIX) which have been proposed for lupulone[107, 108] and humulone.[106, 108–110] These structures, however, are said not to provide a satisfactory explanation of all the properties of these substances.[109, 111, 112]


(LXXXV)


(LXXXVI)


(LXXXVII)

(LXXXVIII)



(LXXXIX)

$R = -CH_2{\cdot}CH{:}CMe_2.$

T. G. H.

## 7. STEROIDS.

**Total Syntheses.**—The year's outstanding achievement in synthetic chemistry is a stereospecific total synthesis of cortisone by Sarett and his associates[1] at the Merck Laboratories in New Jersey. "Stereospecific" is defined by the authors to mean that in each reaction producing a fixed asymmetric centre the ratio, to all other isomers, of the isomer having the configuration of the end product is greater than unity; they add that in the present synthesis there is no such ratio less than 8 : 1.

An account of earlier stages in the synthesis, leading to the hydroxydiketone monoketal (I) is still in the press. This ketone was alkylated, first with methyl iodide and then with 2-methylallyl iodide. The product (II) after oxidation to the diketone was condensed with ethoxyethynylmagnesium bromide; rearrangement of the acetylenic ether (III) gave the unsaturated

---

[107] M. Verzele and F. Govaert, *Bull. Soc. chim. Belg.*, 1950, **58**.

[108] J. F. Carson, *J. Amer. Chem. Soc.*, 1951, **73**, 4652.

[109] G. Harris, G. A. Howard, and J. R. A. Pollock, *J.*, 1952, 1906.

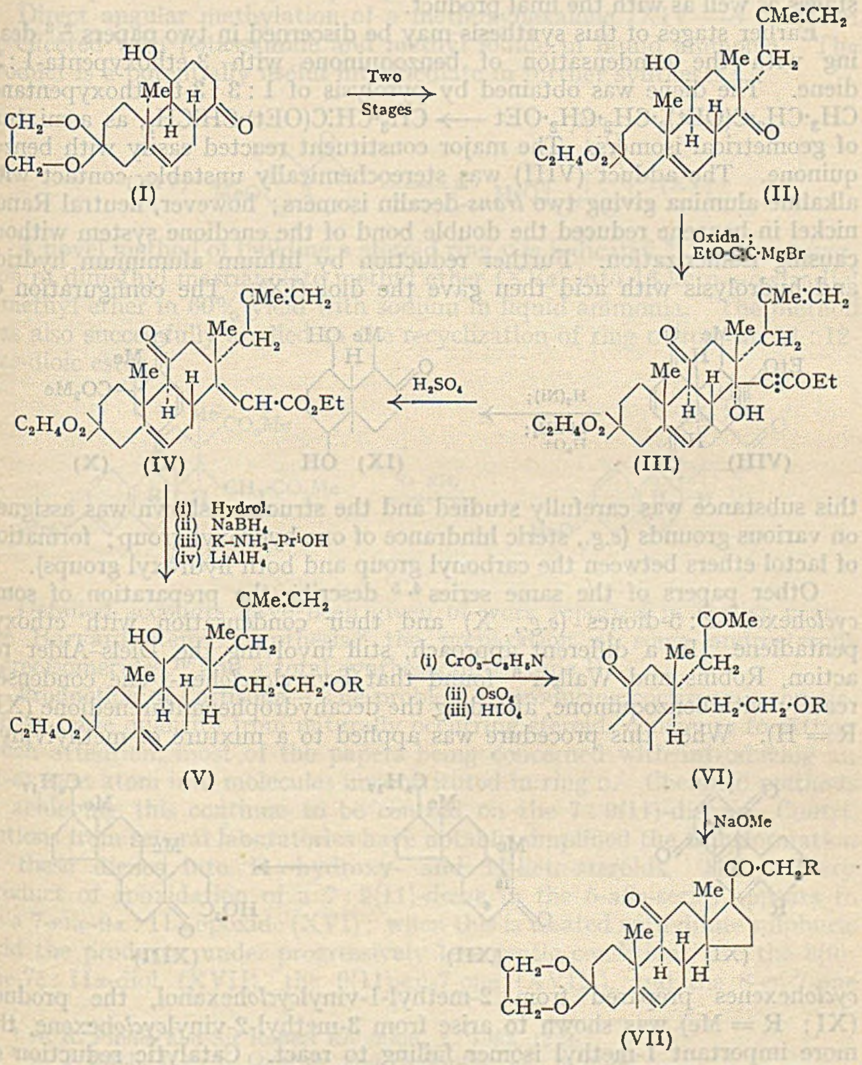
[110] A. H. Cook and G. Harris, *J.*, 1950, 1873.

[111] Cf. G. A. Howard and J. R. A. Pollock, *J.*, 1952, 1902.

[112] Cf. S. David and C. Imer, *Bull. Soc. chim.*, 1951, 634.

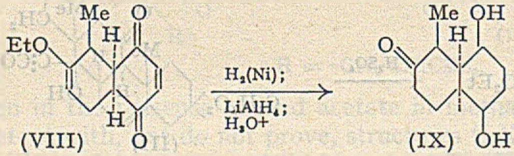
[1] L. H. Sarett, R. M. Lukes, R. E. Beyler, G. I. Poos, W. F. Johns, and J. M. Constantin, *J. Amer. Chem. Soc.*, 1952, **74**, 4974.

ester (IV). This was hydrolysed to the acid and reduced stepwise by three selective reagents: first, sodium borohydride (carbonyl group), then potassium and *iso*propanol in liquid ammonia (conjugated double bond), and finally lithium aluminium hydride (carboxyl group). The resulting diol (V; R = H) formed a monotoluene-*p*-sulphonyl derivative (V; R = $C_6H_4Me{\cdot}SO_2$) which was then oxidized stepwise by three selective reagents: chromium trioxide–pyridine ($>CH{\cdot}OH \longrightarrow >CO$), osmium tetroxide

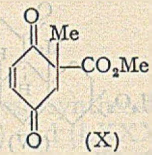


[$>C{:}CH_2 \longrightarrow >C(OH){\cdot}CH_2{\cdot}OH$], and periodic acid [$>C(OH){\cdot}CH_2{\cdot}OH \longrightarrow >CO + CH_2O$]. Cyclization with sodium methoxide of the toluene-*p*-sulphonyloxy-ketone (VI) and isomerization with alkali of the initially formed 17α-stereoisomer gave the 3-ethylene ketal (VII; R = H) of (±)-11-ketoprogesterone. Resolution was achieved by way of the strychnine salt of the 21-oxalyl acid (VII; R = $CO{\cdot}CO_2H$): the (+)-acid, on removal of the oxalyl group and hydrolysis of the ketal, gave 11-ketoprogesterone. Synthesis of cortisone from the (+)-oxalyl acid (VII; R = $CO{\cdot}CO_2H$) was completed by iodination and acetoxylation to the 21-iodo-compound (VII; R = I) and 21-acetate (VII; R = OAc); the remaining stages followed established procedures. Comparison of the synthetic compounds with material derived from natural sources was made at several of the intermediate stages as well as with the final product.

Earlier stages of this synthesis may be discerned in two papers [2, 3] dealing with the condensation of benzoquinone with 3-ethoxypenta-1 : 3-diene. The diene was obtained by pyrolysis of 1 : 3 : 3-triethoxypentane, $CH_3{\cdot}CH_2{\cdot}C(OEt)_2{\cdot}CH_2{\cdot}CH_2{\cdot}OEt \longrightarrow CH_3{\cdot}CH{:}C(OEt){\cdot}CH{:}CH_2$, as a mixture of geometrical isomers. The major constituent reacted easily with benzoquinone. The adduct (VIII) was stereochemically unstable, contact with alkaline alumina giving two *trans*-decalin isomers; however, neutral Raney nickel in benzene reduced the double bond of the enedione system without causing isomerization. Further reduction by lithium aluminium hydride and hydrolysis with acid then gave the diol (IX). The configuration of this substance was carefully studied and the structure shown was assigned on various grounds (*e.g.*, steric hindrance of one hydroxyl group; formation of lactol ethers between the carbonyl group and both hydroxyl groups).

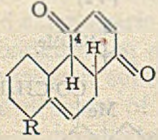


(VIII) (IX)

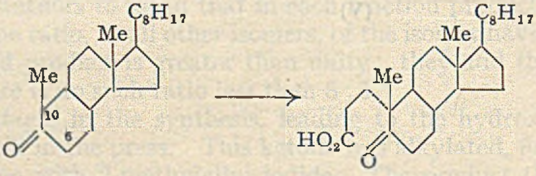


(X)

Other papers of the same series [4, 5] describe the preparation of some *cyclo*hexene-2 : 5-diones (*e.g.*, X) and their condensation with ethoxypentadiene. In a different approach, still involving the Diels–Alder reaction, Robins and Walker [6] found that 1-vinyl*cyclo*hex-1-ene condensed readily with benzoquinone, affording the decahydrophenanthrenedione (XI; R = H). When this procedure was applied to a mixture of methylvinyl*cyclo*hexenes prepared from 2-methyl-1-vinyl*cyclo*hexanol, the product (XI; R = Me) was shown to arise from 3-methyl-2-vinyl*cyclo*hexene, the more important 1-methyl isomer failing to react. Catalytic reduction of



(XI)



(XII) (XIII)

---

[2] L. H. Sarett, R. M. Lukes, G. I. Poos, J. M. Robinson, R. E. Beyler, J. M. Vandegrift, and G. E. Arth, *J. Amer. Chem. Soc.*, 1952, 74, 1393.

[3] R. E. Beyler and L. H. Sarett, *ibid.*, p. 1406. [4] *Idem, ibid.*, p. 1397.

[5] R. M. Lukes, G. I. Poos, and L. H. Sarett, *ibid.*, p. 1401.

[6] P. A. Robins and J. Walker, *J.*, 1952, 642, 1610; see also N. C. Deno and J. D. Johnston, *J. Org. Chem.*, 1952, 17, 1466.

(XI; R = H and Me) was studied: it is interesting that of the two keto-groups that at $C_{(4)}$ was reduced preferentially.

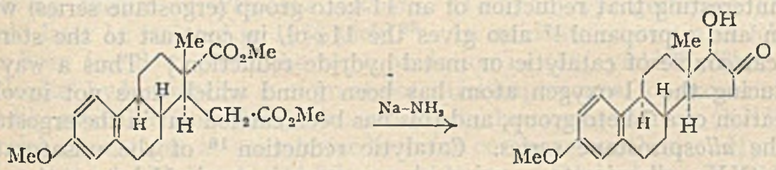
A partial synthesis of the "Windaus acid" (XIII; derived from, and reconvertible into, cholestenone) from the ketone (XII) is reported.[7] It was necessary to block the methylene group at position 6 (steroid numbering) with a methylanilinomethylene group in order to induce reaction with acrylonitrile at position 10. Hydrolytic procedures then gave the acid (XIII).

Direct angular methylation of a methoxyhexalone (XIV ⟶ XV) can be effected with potassamide and methyl iodide in liquid ammonia. The product is a potentially useful intermediate in further syntheses.[8]

(XIV)

(XV)

A novel method of building a steroid ring D is indicated [8a] by the conversion of dimethyl marrianolate methyl ether (XV*a*) into 16-keto-α-œstradiol 3-methyl ether in 60% yield with sodium in liquid ammonia. The method was also successfully applied to the recyclization of ring C from an 11 : 12-*seco*-dioic ester.



(XV*a*)

Detailed accounts have been given of work reported in earlier years: the Harvard steroid synthesis,[9] the preparation of some androsterone stereoisomerides,[10] and a total synthesis of œstrone.[11]

**Production of Cortisone.**—The problem of producing cortisone economically in large quantity from naturally occurring steroids continues to attract much attention, most of the papers being concerned with introducing an 11-oxygen atom into molecules unsubstituted in ring C. Chemical methods of achieving this continue to be centred on the 7 : 9(11)-dienes. Contributions from several laboratories have notably simplified the transformation of these dienes into 11α-hydroxy- and 11-keto-steroids. The primary product of epoxidation of a 7 : 9(11)-diene in the 5-*allo*-series appears to be a 7-ene-9α : 11α-epoxide (XVI); when this is treated with dilute sulphuric acid the products, under progressively less gentle conditions, are the 8(9)-ene-7ξ : 11α-diol (XVII), the 9(11)-en-7-one (XVIII), and the 8-en-7-one

---

[7] A. R. Pinder and Sir Robert Robinson, *J.*, 1952, 1224.

[8] A. J. Birch, J. A. K. Quartey, and H. Smith, *ibid.*, p. 1768.

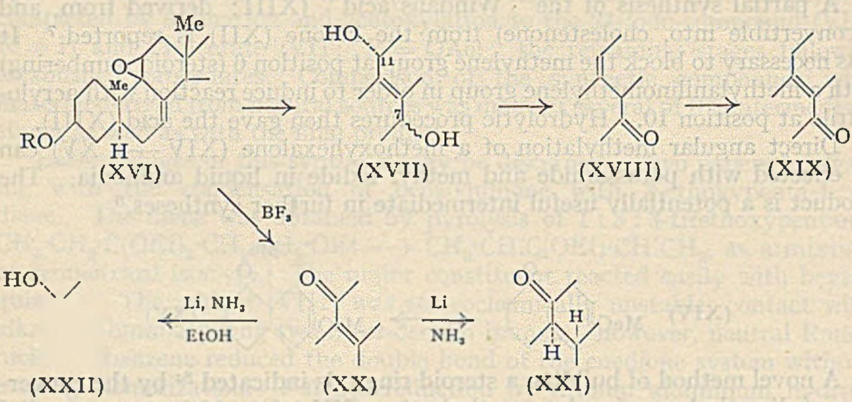
[8a] J. C. Sheehan, R. C. Coderre, L. A. Cohen, and R. C. O'Neill, *J. Amer. Chem. Soc.*, 1952, 74, 6155.

[9] R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. McLamore, *J. Amer. Chem. Soc.*, 1952, 74, 4223.

[10] J. R. Billeter and K. Miescher, *Helv. Chim. Acta*, 1951, 34, 2053.

[11] W. S. Johnson, D. K. Bannerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg, and L. J. Chin, *J. Amer. Chem. Soc.*, 1952, 74, 2833.

(XIX).[12, 13, 14, 15] When, however, the epoxide is treated with the boron trifluoride–ether complex,[12, 13] or with ferric chloride,[14] in benzene, the



product is the 8-en-11-one (XX) and this can be reduced to the saturated ketone of "natural" configuration (XXI) by lithium in liquid ammonia;[15, 16] when ethanol is present, reduction proceeds as far as the 11α-ol (XXII). [It is interesting that reduction of an 11-keto-group (ergostane series) with sodium and *n*-propanol[17] also gives the 11α-ol, in contrast to the stereochemical course of catalytic or metal-hydride reduction.] Thus a way of introducing the 11-oxygen atom has been found which does not involve elimination of a 7-keto-group, and this has been carried out in the ergostane and the *allo*spirostane series. Catalytic reduction[16] of the unsaturated ketone (XX; *allo*spirostane series) gives a stereoisomeric 11-ketone thought to have the "unnatural" configuration at $C_{(8)}$ and $C_{(9)}$.

On the other hand, epoxidation of 7 : 9(11)-dienes in the 5-normal (bile acid) series seems to occur preferentially at the 7 : 8-double bond. This is indicated both by molecular-rotation differences between the diene and its epoxide and by the formation of an 8-en-7-one from the epoxide with boron trifluoride.[12, 14]

Improvements and elucidations of methods for making 11-oxygenated steroids from 7 : 9(11)-dienes *via* 7 : 11-dioxygenated derivatives have been published,[18–23] but space to review them is lacking. A method which does not start from the usual diene involves oxidation of ergosta-7 : 22-dienyl acetate (XXIII) with *tert.*-butyl chromate; the 8 : 9-epoxy-7-one (XXIV) is

---

[12] H. Heusser, K. Eichenberger, P. Kurath, H. R. Dällenbach, and O. Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106.

[13] H. Heusser, K. Heusler, K. Eichenberger, C. G. Honegger, and O. Jeger, *ibid.*, 1952, **35**, 295.

[14] H. Heusser, R. Anliker, K. Eichenberger, and O. Jeger, *ibid.*, p. 936.

[15] E. Schoenewaldt, L. Turnbull, E. M. Chamberlin, D. Reinhold, A. E. Erickson, W. V. Ruyle, J. M. Chemerda, and M. Tishler, *J. Amer. Chem. Soc.*, 1952, **74**, 2696.

[16] F. Sondheimer, R. Yashin, G. Rosenkranz, and C. Djerassi, *ibid.*, p. 2696.

[17] H. Heusser, R. Anliker, and O. Jeger, *Helv. Chim. Acta*, 1952, **35**, 1537.

[18] C. Djerassi, E. Batres, M. Velasco, and G. Rosenkranz, *J. Amer. Chem. Soc.*, 1952, **74**, 1712.

[19] J. Romo, G. Stork, G. Rosenkranz, and C. Djerassi, *ibid.*, p. 2918.

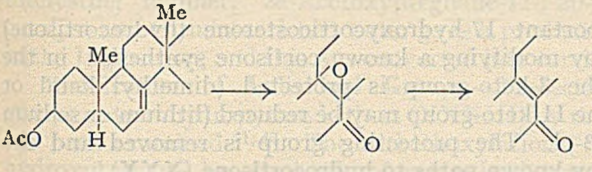
[20] R. Budziarek, G. T. Newbold, R. Stevenson, and F. S. Spring, *J.*, 1952, 2892.

[21] R. C. Anderson, R. Stevenson, and F. S. Spring, *ibid.*, p. 2901.

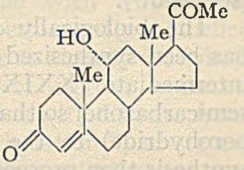
[22] R. Budziarek, F. Johnson, and F. S. Spring, *ibid.*, p. 3410.

[23] R. Budziarek and F. S. Spring, *Chem. and Ind.*, 1952, 1102.

formed (along with the 8 : 14-epoxy-7-one in comparable amount) and this is reduced to the 8-en-7-one (XXV) by zinc and acetic acid.[24] A method already exists [25] for the conversion of 8-en-7-ones into 11-ones.

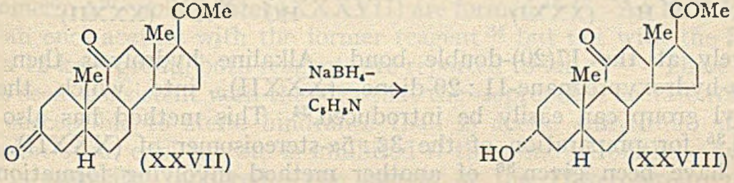


(XXIII) (XXIV) (XXV)



(XXVI)

Some important work has appeared on the biosynthetic hydroxylation of ring C. A detailed study has been made of optimum conditions for hydroxylation, by adrenal homogenates, of deoxycorticosterone and its 17α-hydroxy-analogue to corticosterone and 17α-hydroxycorticosterone (hydrocortisone) respectively.[26] A similar hydroxylation in the 11β-position was effected by the mould *Streptomyces fradiae*, 17α-hydroxy-11-deoxycorticosterone being converted in small yield into hydrocortisone.[27] Certain moulds of the order *Mucorales*, on the other hand, are capable of hydroxylation in the 11α-position : thus when progesterone was introduced into a growing culture of *Rhizopus arrhizus*, 11α-hydroxyprogesterone (XXVI) could later be isolated in 10% yield.[28] An unidentified strain of *Rhizopus* has been found to effect the same oxidation in 45% yield.[29] This microbiological hydroxylation is of great potential importance, for progesterone is readily available from diosgenin, and 11α-hydroxyprogesterone (XXVI) has special advantages as an intermediate for cortisone synthesis. Hydrogenation of the double bond in $\Delta^4$-3-ketones having an 11β-hydroxy-[30] or 11-keto-substituent [31] affords largely the 5-*allo*(A/B *trans*)-configuration, but with 11α-hydroxyprogesterone the product is the 5-normal(A/B *cis*)-compound and on oxidation affords pregnane-3 : 11 : 20-trione (XXVII),[29] and a later



(XXVII) (XXVIII)

---

[24] H. Heusser, G. Saucy, R. Anliker, and O. Jeger, *Helv. Chim. Acta*, 1952, **35**, 2090.

[25] C. Djerassi, O. Mancera, G. Stork, and G. Rosenkranz, *J. Amer. Chem. Soc.*, 1951, **73**, 4496; *idem* and M. Velasco, *ibid.*, 1952, **74**, 3321.

[26] F. W. Kahnt and A. Wettstein, *Helv. Chim. Acta*, 1951, **34**, 1790.

[27] D. R. Collingsworth, M. P. Brunner, and W. J. Haines, *J. Amer. Chem. Soc.*, 1952, **74**, 2381. [28] D. H. Peterson and H. C. Murray, *ibid.*, p. 1871.

[29] O. Mancera, A. Zaffaroni, B. A. Rubin, F. Sondheimer, G. Rosenkranz, and C. Djerassi, *ibid.*, p. 3711.

[29a] D. H. Peterson, H. C. Murray, S. H. Eppstein, L. M. Reinecke, A. Weintraub, P. D. Meister, and H. M. Leigh, *ibid.*, p. 5933.

[30] J. Pataki, G. Rosenkranz, and C. Djerassi, *J. Biol. Chem.*, 1952, **195**, 751.

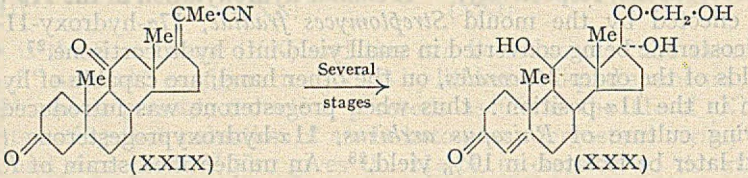
[31] J. M. Chemerda, E. M. Chamberlin, E. H. Wilson, and M. Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 4052; E. Wilson and M. Tishler, *ibid.*, 1952, **74**, 1609; E. P. Oliveto, C. Gerold, and E. B. Hershberg, *ibid.*, p. 2248. A trace of alkali favours formation of the (A/B *cis*)-isomer : cf. Julian, " Recent Progress in Hormone Research," Academic Press, New York, 1951, Vol. VI, pp. 207, 212.

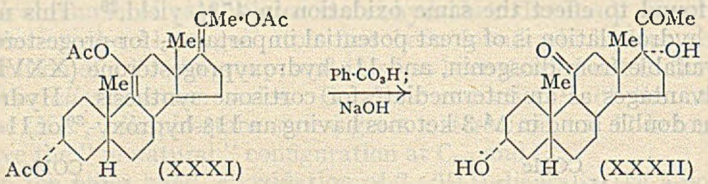
paper [29a] reports 85—95% yields with *Rhizopus nigricans*. Preferential reduction of the 3-keto-group is possible with sodium borohydride in pyridine; [29] the resulting 3α-ol (XXVIII) can be converted into cortisone (see below).

The biologically important 17-hydroxycorticosterone (hydrocortisone) has been synthesized [32] by modifying a known cortisone synthesis: in the intermediate (XXIX) the 3-keto-group is protected (dimethyl ketal or semicarbazone) so that the 11-keto-group may be reduced (lithium or sodium borohydride) to the 11β-ol. The protecting group is removed and the synthesis then proceeds by known paths to hydrocortisone (XXX).

The 11α-epimer of hydrocortisone has also been synthesised.[33]

Further progress is reported with methods for elaborating the cortisone side chain. From 3α-hydroxypregnane-11 : 20-dione (XXVIII) with acetic anhydride–toluene-*p*-sulphonic acid a dienol triacetate (XXXI; or the $\Delta^{11(12)}$-isomer) is obtainable which can be epoxidized with perbenzoic acid selectively at the 17(20)-double bond. Alkaline hydrolysis then gives 3α : 17α-hydroxypregnane-11 : 20-dione (XXXII), into which the 21-hydroxyl group can easily be introduced.[34] This method has also been applied [35] for preparation of the 3β : 5α-stereoisomer of (XXXII). Full details have been given [36] of another method involving formation and epoxidation of a 16 : 17-double bond.





The tertiary 17α-hydroxyl group in (XXXII) has been acetylated (acetic anhydride–toluene-*p*-sulphonic acid); the 17-acetoxy- is comparable with a 21-acetoxy-group in ease of hydrolysis.[37, 38] The $CH_2{\cdot}OH$ group in the cortisone side chain has been oxidized [39] to CHO: pyridine and toluene-*p*-sulphonyl chloride, followed by *p*-nitrosodimethylaniline gave the nitrone, $-CH{=}N({\rightarrow}O)C_6H_4{\cdot}NMe_2$; this was hydrolysed by dilute acid to the aldehyde,

---

[32] N. L. Wendler, R. B. Graber, R. E. Jones, and M. Tishler, *J. Amer. Chem. Soc.*, 1952, 74, 3630.

[33] J. Romo, A. Zaffaroni, J. Hendrichs, G. Rosenkranz, C. Djerassi, and F. Sondheimer, *Chem. and Ind.*, 1952, 783.

[34] T. H. Kritchevsky, D. L. Garmaise, and T. F. Gallagher, *J. Amer. Chem. Soc.*, 1952, 74, 483. [35] J. Pataki, G. Rosenkranz, and C. Djerassi, *ibid.*, p. 5615.

[36] F. B. Colton, W. R. Nes, D. A. van Dorp, H. L. Mason, and E. C. Kendall, *J. Biol. Chem.*, 1952, 194, 235; F. B. Colton and E. C. Kendall, *ibid.*, p. 247.

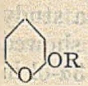
[37] Huang-Minlon, E. Wilson, N. L. Wendler, and M. Tishler, *J. Amer. Chem. Soc.*, 1952, 74, 5394. [38] R. B. Turner, *ibid.*, p. 4220.

[39] E. F. Rogers, J. B. Conbere, K. Pfister, and W. J. Leanza, *ibid.*, p. 2946.

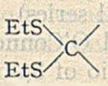
which proved approximately as effective as cortisone in the rat-liver glycogen test.

A radioactive cortisone labelled with tritium has been prepared[40] in an interesting manner. 3α-Acetoxypregnane-11 : 20-dione with a platinum catalyst and tritium-enriched water gave a product " permanently " labelled in the 16-position, and this was converted into cortisone as already described.

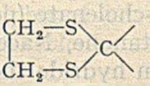
**Modification of Individual Groups.**—Protection of steroid hydroxyl groups as tetrahydropyranyl ethers (XXXIII) by reaction with dihydropyran has been examined.[41, 42] The carbethoxylation (" cathylation ") of steroid hydroxyl groups by ethyl chloroformate is shown to be a selective process, esters ($R{\cdot}O{\cdot}CO_2Et$) being formed preferentially from " equatorial " hydroxyl groups. Thus of the three hydroxyl groups in methyl cholate only one (the equatorial 3α) reacts even when excess of reagent is available.[43] Experience with the formation of thioketals (XXXIV or XXXV) from cyclic steroid ketones and ethanethiol (EtSH) or ethanedithiol ($HS{\cdot}CH_2{\cdot}CH_2{\cdot}SH$) may be summarized thus :[44] the ketones which reacted with both thiols had the carbonyl group in ring A or D ; ketones with a carbonyl group in ring B or C reacted with ethanedithiol only, except the 11-keto-group which was inert to both thiols.



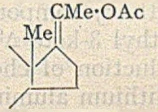
(XXXIII)



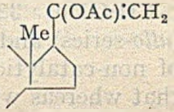
(XXXIV)



(XXXV)



(XXXVI)



(XXXVII)

Some interesting data on the formation of enol acetates are now available. 20-Ketones are well known to give $\Delta^{17(20)}$-enol acetates (XXXVI) with acetic anhydride–toluene-*p*-sulphonic acid,[45] but with *iso*propenyl acetate the isomeric $\Delta^{20}$-enol acetates (XXXVII) are formed.[46, 47] An 11-keto-group gives an enol acetate with the former reagent[34] but not with the latter.[46] With a 12-keto-group, both reagents are reported to fail.[46, 48] These curious results seem consistent with the idea that the *iso*propenyl acetate reagent is more susceptible to steric hindrance than is acetic anhydride, and that formation of an enol acetate is inhibited if the removal of the α-hydrogen atom is sterically hindered. The inertia of the 12-keto-group may be utilized to eliminate the 7-substituent in 3α-hydroxy-7 : 12-diketocholanic acid by catalytic hydrogenolysis of the 7-monoenol acetate which it forms.[48]

Shoppee and Summers[49] have devised a route to the *epi*cholesteryl halides. 3β-Hydroxycholestan-6-one (XXXVIII) with phosphorus pentachloride or pentabromide gave the 3α-halides (XXXIX) which were reduced with lithium aluminium hydride to the 6β-ols ; these were dehydrated to the desired halides (XL). The normal (3β) cholesteryl halides were obtainable

[40] D. K. Fukushima, T. H. Kritchevsky, M. L. Eidinoff, and T. F. Gallagher, *J. Amer. Chem. Soc.*, 1952, **74**, 487.

[41] W. G. Dauben and H. L. Bradlow, *ibid.*, p. 559.

[42] A. C. Ott, M. F. Murray, and R. L. Pederson, *ibid.*, p. 1239.

[43] L. F. Fieser, J. E. Herz, M. W. Klohs, M. A. Romero, and T. Utne, *ibid.*, p. 3309.

[44] H. Hauptmann and M. Moura Campos, *ibid.*, p. 3179.

[45] T. F. Gallagher and T. H. Kritchevsky, *J. Biol. Chem.*, 1949, **179**, 507.

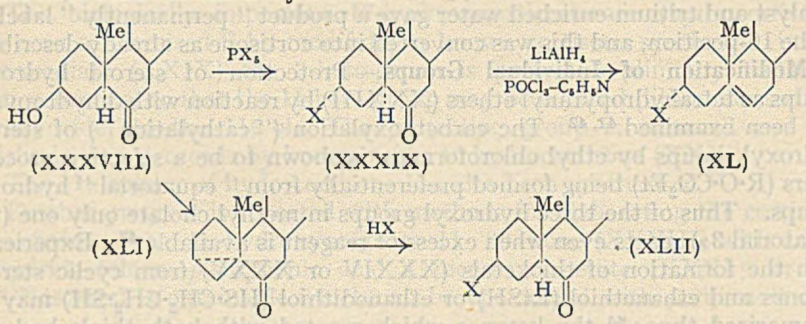
[46] R. B. Moffett and D. I. Weisblat, *J. Amer. Chem. Soc.*, 1952, **74**, 2183.

[47] H. Vanderhaeghe, E. R. Katzenellenbogen, K. Dobriner, and T. F. Gallagher, *ibid.*, p. 2810.

[48] R. Hirschmann, M. Brown, and N. L. Wendler, *ibid.*, 1951, **73**, 5373.

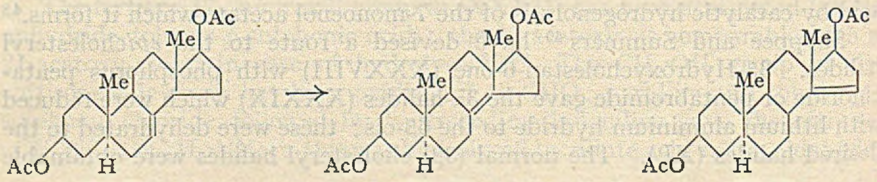
[49] C. W. Shoppee and G. H. R. Summers, *J.*, 1952, 1786, 1790.

by a modification of the same process: 3 : 5-*cyclo*cholestan-6-one (XLI) [from the toluene-*p*-sulphonyl derivatives of (XXXVIII) and potassium hydroxide] with hydrogen halides gave 3β-halogenocholestan-6-ones (XLII) which were reduced and dehydrated.



A discovery [50] which may prove generally useful is that steroid 3-ketones undergo "reductive methylation" on catalytic hydrogenation in methanol containing hydrogen bromide, the product being a methyl ether: $>CO \longrightarrow >CH{\cdot}OMe$. 3β-Methoxy-compounds were produced from both cholestanone (*allo*-series) and methyl 3-keto-$\Delta^{9(11)}$-cholenate (normal series). In a study of non-catalytic reduction of cholestanone, Nace and O'Connor [51] showed that whereas with lithium aluminium hydride the ratio of 3β-ol to 3α-ol in the product was 7·3 : 1, with aluminium alkoxides $Al(OR)_3$ more of the 3α-ol was formed. This effect could be exaggerated by increasing the bulk of the R group: with di-*tert.*-butylcarbinol $Me_3C{\cdot}CH(OH){\cdot}CMe_3$ and its aluminium alkoxide the reduction product contained 55% of 3α-ol. The results are attributed to steric hindrance in formation of an intermediate complex.

**Some Reactions involving Double Bonds.**—The diacetate of androst-7-enediol (XLIII) was found [52] to be rearranged by hydrogenation catalysts in the known manner to the $\Delta^{8(14)}$-isomeride (XLIV), but further isomerization by hydrogen chloride to the $\Delta^{14}$-isomeride (XLV) did not occur. This failure to isomerize, in contrast to the results obtained with cholesterol and ergosterol analogues, has also been observed with $\Delta^{8(14)}$-*allo*pregnenolone and with $\Delta^{8(14)}$-dehydrotigogenin.[53]

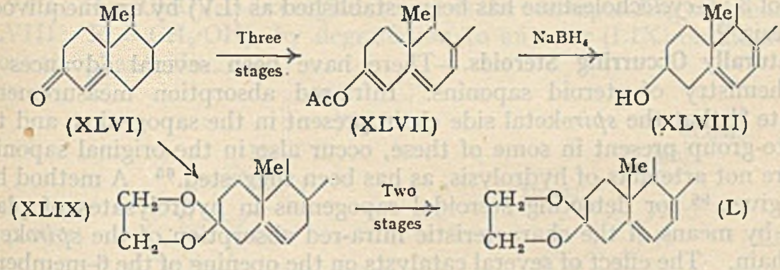


Two methods of obtaining $\Delta^{5:7}$-steroids from $\Delta^4$-3-ketones (XLVI) have been elaborated. By bromination and dehydrobromination the 4 : 6-dien-3-one can be made, the enol acetate (XLVII) of which with sodium boro-

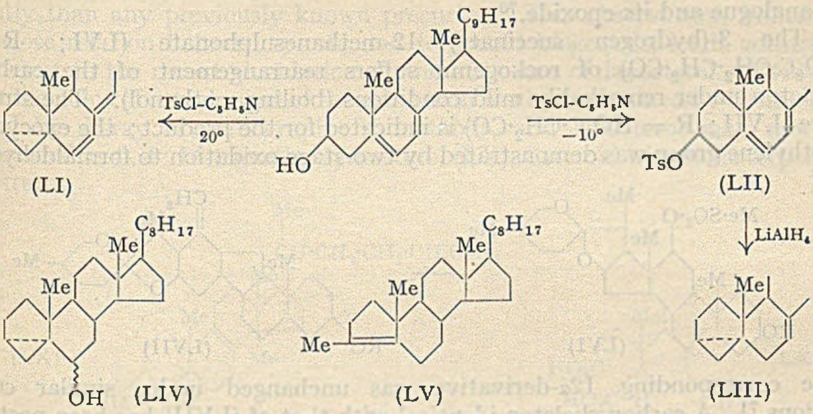
---

[50] J. C. Babcock and L. F. Fieser, *J. Amer. Chem. Soc.*, 1952, **74**, 5472.
[51] H. R. Nace and G. L. O'Connor, *ibid.*, 1951, **73**, 5824.
[52] R. Antonucci, S. Bernstein, D. Giancola, and K. J. Sax, *J. Org. Chem.*, 1951, **16**, 1891.
[53] O. Mancera, D. H. R. Barton, G. Rosenkranz, and C. Djerassi, *J.*, 1952, 1021.

hydride affords the 5 : 7-dien-3β-ol (XLVIII). This has been done in the cholestane [54] and 22-*iso-allo*spirostane [55] series. Alternatively one can obtain the $\Delta^5$-ketal (XLIX) from the unsaturated ketone (XLVI; cholestenone, progesterone, 21-acetoxyprogesterone) and ethylene glycol; [56] bromination and dehydrobromination then give an unusually high yield of the 5 : 7-diene (L)[56, 57]



**3 : 5-*cyclo*Steroids.**—A hydrocarbon obtained from ergosterol with toluene-*p*-sulphonyl chloride and pyridine, and formerly thought to be an ergostatetraene, is now shown [58] to be 3 : 5-*cyclo*ergosta-6 : 8(14) : 22-triene (LI). By working at −10°, ergosterol and 7-dehydrocholesterol can be converted into toluene-*p*-sulphonyl derivatives (LII) and these with lithium aluminium hydride give 3 : 5-*cyclo*-7-enes (LIII).[59]



(Ts = $p$-$C_6H_4Me\cdot SO_2$)

Wagner, Wolff, and Wallis report [60] that both epimers of 3 : 5-*cyclo*-cholestan-6-ol (LIV) are rearranged under acidic conditions to give the same (3β) cholesterol derivatives, and have advanced arguments that the 3 : 5-

---

[54] W. G. Dauben, J. F. Eastham, and R. A. Micheli, *J. Amer. Chem. Soc.*, 1951, 73, 4496.

[55] H. J. Ringold, G. Rosenkranz, and C. Djerassi, *ibid.*, 1952, 74, 3441.

[56] R. Antonucci, S. Bernstein, R. Littell, K. J. Sax, and J. H. Williams, *J. Org. Chem.*, 1952, 17, 1341; cf. E. Fernholz and H. E. Stavely, Abstr. 102nd meeting, Amer. Chem. Soc., Sept. 1941, M 39.

[57] R. Antonucci, S. Bernstein, R. Lenhard, K. J. Sax, and J. H. Williams, *J. Org. Chem.*, 1952, 17, 1369.

[58] M. Fieser, W. E. Rosen, and L. F. Fieser, *J. Amer. Chem. Soc.*, 1952, 74, 5397.

[59] P. Karrer and H. Asmis, *Helv. Chim. Acta*, 1952, 35, 1926.

[60] A. F. Wagner, N. E. Wolff, and E. S. Wallis, *J. Org. Chem.*, 1952, 17, 529; N. E. Wolff and E. S. Wallis, *ibid.*, p. 1361.

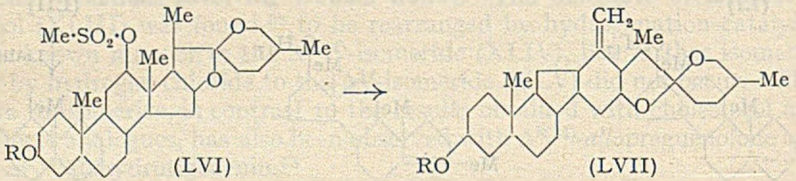
*cyclo*-6-ols (the *iso*-steroids) prepared by rearrangement of 3β-hydroxy-$\Delta^5$-steroids have the 6α-configuration. However, *iso*cholesterol can be hydrogenated[61] to cholestan-6β-ol (its epimer gives cholestan-6α-ol) and should therefore be 3 : 5-*cyclo*cholestan-6β-ol. The mechanisms of *iso*cholesterol rearrangements have been discussed.[60, 61]

The structure of the unsaturated hydrocarbon obtained [62] by acid treatment of 3 : 5-*cyclo*cholestane has been established as (LV) by an unequivocal synthesis.[63]

**Naturally Occurring Steroids.**—There have been several advances in the chemistry of steroid saponins. Infra-red absorption measurements indicate [64] that the *spiro*ketal side chain present in the sapogenins, and the 12-keto-group present in some of these, occur also in the original saponins and are not artefacts of hydrolysis, as has been suggested.[65] A method has been given [66] for detecting steroidal sapogenins in hydrolysates of plant tissue by means of the characteristic infra-red absorption of the *spiro*ketal side chain. The effect of several catalysts on the opening of the 6-membered heterocyclic ring in sapogenins by acetic anhydride has been studied.[67] Reductive fission of this ring (to give a primary alcohol) can be effected with lithium aluminium hydride and ether saturated with hydrogen chloride. Without the acid no cleavage occurs.[68]

Manogenin (2α? : 3β-dihydroxy-22-*isoallo*spirostan-12-one [69]) has been converted into hecogenin (3β-hydroxy-22-*isoallo*spirostan-12-one) *via* the $\Delta^3$-analogue and its epoxide.[70]

The 3-(hydrogen succinate) 12-methanesulphonate (LVI; R = $HO_2C{\cdot}CH_2{\cdot}CH_2{\cdot}CO$) of rockogenin suffers rearrangement of the carbon skeleton under remarkably mild conditions (boiling methanol). The structure (LVII; R = $HO_2C{\cdot}CH_2{\cdot}CO$) is indicated for the product; the exocyclic methylene group was demonstrated by two-stage oxidation to formaldehyde.



(LVI) (LVII)

The corresponding 12α-derivative was unchanged under similar conditions.[71] A carbon skeleton identical with that of (LVII) has been postulated for the alkaloid jervine.[72]

---

[61] C. W. Shoppee and G. H. R. Summers, *J.*, 1952, 3361.

[62] H. Schmid and K. Kägi, *Helv. Chim. Acta*, 1950, **33**, 1582; cf. F. S. Prout and B. Riegel, *J. Amer. Chem. Soc.*, 1952, **74**, 3190.

[63] C. W. Shoppee and G. H. R. Summers, *J.*, 1952, 2528.

[64] E. S. Rothman, M. E. Wall, and C. R. Eddy, *J. Amer. Chem. Soc.*, 1952, **74**, 4013.

[65] R. E. Marker and J. Lopez, *ibid.*, 1947, **69**, 2390.

[66] M. E. Wall, C. R. Eddy, M. L. McClennan, and M. E. Klumpp, *Analyt. Chem.*, 1952, **24**, 1337.

[67] D. H. Gould, H. Staeudle, and E. B. Hershberg, *J. Amer. Chem. Soc.*, 1952, **74**, 3685.

[68] H. M. Doukas and T. D. Fontaine, *ibid.*, 1951, **73**, 5918.

[69] For some evidence of configuration see J. Pataki, G. Rosenkranz, and C. Djerassi, *ibid.*, p. 5375.

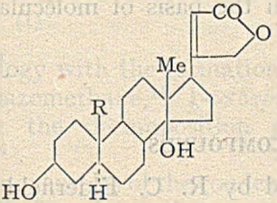
[70] N. L. Wendler, H. L. Slates, and M. Tishler, *ibid.*, 1952, **74**, 4894.

[71] R. Hirschmann, C. S. Snoddy, and N. L. Wendler, *ibid.*, p. 2694.

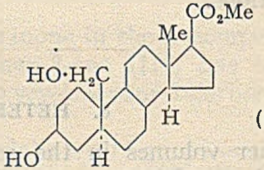
[72] J. Fried, O. Wintersteiner, M. Moore, B. M. Iselin, and A. Klingsberg, *ibid.*, 1951, **73**, 2970.

Reichstein and his collaborators have published numerous papers adding to the systematic knowledge of naturally occurring cardiac glycosides. Two glycosides from *Gomphocarpus fruticosus*, gofruside and frugoside, were respectively hydrolysed[73] to the aglycones corotoxigenin and coroglaucigenin previously obtained by Stoll, Pereira, and Renz[74] from *Coronilla glauca*. Corotoxigenin has been identified as a 5-deoxystrophanthidin (LVIII; R = CHO), and coroglaucigenin as the corresponding strophanthidol (LVIII; R = $CH_2{\cdot}OH$), by degradation to an ester (LIX) obtainable also from strophanthidin.

(LVIII)



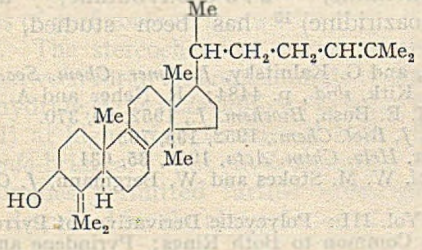
(LIX)



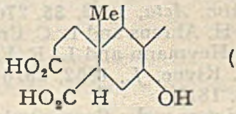
The cholesterol isomer, cholest-7-en-3β-ol, has been isolated from the skin of albino rats.[75]

**Biogenesis of Steroids.**—Langdon and Bloch[76] have shown that $^{14}C$-labelled squalene, obtained from the tissues of rats fed with $^{14}C$-labelled acetic acid, when fed to other rats is converted into cholesterol more efficiently than any previously known precursor. This observation, indicating a close relation between steroid and terpenoid biogenesis, lends additional interest to the recent elucidation of the structure of lanosterol. Evidence on the point of attachment of the side-chain has been obtained by chemical[77] and by *X*-ray crystallographic[78] methods, and lanosterol may now be regarded as 4 : 4 : 14-trimethylzymosterol (LX), a steroid with some terpenoid features.

(LX)



(LXI)



**Physical Properties of Steroids.**—Several papers on the infra-red spectra of steroids have appeared, and features of the spectra have been correlated with the configuration of 3-hydroxyl groups,[79] with methyl and methylene groups,[80] and with the $\Delta^5$-3β-hydroxy-system.[81] Several methods for paper

---

[73] A. Hunger and T. Reichstein, *Helv. Chim Acta*, 1952, **35**, 1073.

[74] A. Stoll, A. Pereira, and J. Renz, *ibid.*, 1949, **32**, 293.

[75] D. R. Idler and C. A. Baumann, *J. Biol. Chem.*, 1952, **195**, 623.

[76] R. G. Langdon and K. Bloch, *J. Amer. Chem. Soc.*, 1952, **74**, 1869.

[77] W. Voser, M. V. Mijovic, H. Heusser, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1952, **35**, 2414.

[78] R. G. Curtis, J. Fridrichsons, and A. McL. Mathieson, *Nature*, 1952, **170**, 321.

[79] A. R. H. Cole, R. N. Jones, and K. Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 5571.

[80] R. N. Jones and A. R. H. Cole, *ibid.*, p. 5648; *idem* and B. Nolin, *ibid.*, p. 5662.

[81] H. Hirschmann, *ibid.*, p. 5357.

chromatography of steroids have been reported.[82] A fractionation of ox bile by counter-current distribution showed, among other things, that no unconjugated bile acids are present in fresh bile.[83]

**Stereochemistry of Steroids.**—Chemical evidence for the assignment of configurations to the two 7-hydroxycholesterols has been provided by Heymann and Fieser;[84] the *seco*-3 : 4-dioic acid (LXI) obtained by hydrogenation and oxidation of the more dextrorotatory epimer forms a $\gamma$-lactone, which is only possible with a 7β-hydroxyl group.

Klyne[85] has published a paper correlating the stereochemistry of the triterpenoids with that of the steroids on the basis of molecular-rotation contributions.

J. W. C.

## 8. HETEROCYCLIC COMPOUNDS.

Further volumes in the series edited by R. C. Elderfield[1] and by A. Weissberger[2] have appeared, and a comprehensive tabular survey[3] of thiazoles has been published.

**Three- and Four-membered Ring Systems.**—Studies on the fission of the oxiran ring by a variety of reagents[4] continue to be reported. *o*-, *m*-, and *p*-Nitrostyrene oxides react with the phenoxide ion to give predominantly the secondary alcohols,[5] while, under suitable conditions in the presence of excess of phenol as solvent, styrene oxide can give the primary alcohol almost exclusively.[6] The secondary alcohol is the major product from styrene oxide and benzylamine,[7] and *p*-nitrostyrene oxide and diethyl sodiomalonate give the lactone (I),[8] indicating steric factors to be then a controlling influence.[9] The reaction between Grignard reagents and the oxiran ring have been reviewed.[10] The stereochemistry of the opening and closure of the ring in 2 : 3-dimethylethyleneimine,[11] 2 : 3-epoxybutane,[12] and *cyclo*hexeneimine (2 : 3-*cyclo*hexanoaziridine)[13] has been studied, both re-

---

[82] R. B. Davis, J. M. McMahon, and G. Kalnitsky, *J. Amer. Chem. Soc.*, 1952, **74**, 4483; D. Kritchevsky and M. R. Kirk, *ibid.*, p. 4484; R. Neher and A. Wettstein, *Helv. Chim. Acta*, 1952, **35**, 276; I. E. Bush, *Biochem. J.*, 1952, **50**, 370.

[83] E. H. Ahrens and L. C. Craig, *J. Biol. Chem.*, 1952, **195**, 763.

[84] H. Heymann and L. F. Fieser, *Helv. Chim. Acta*, 1952, **35**, 631.

[85] W. Klyne, *J.*, 1952, 2916; cf. W. M. Stokes and W. Bergmann, *J. Org. Chem.*, 1951, **16**, 1817.

[1] "Heterocyclic Compounds. Vol. III: Polycyclic Derivatives of Pyrrole; Polycyclic Systems with One Nitrogen Common to Both Rings; Pyrindene and Related Compounds. Vol. IV: Quinoline, Isoquinoline, and Their Benzo Derivatives." J. Wiley and Sons, Inc., New York, 1952.

[2] "Thiophene and its Derivatives," by H. D. Hartough. "Five-membered Heterocyclic Compounds with Nitrogen, Sulphur and Oxygen (except Thiazole)," by L. L. Bambas. Intersci. Publ., New York, 1952.

[3] Kartothek der Thiazolverbindungen (in 4 vols.), by B. Prijs. S. Karger, Basel, 1951.

[4] Cf. *Ann. Reports*, 1950, **47**, 220.

[5] C. O. Guss, *J. Org. Chem.*, 1952, **17**, 678.

[6] C. O. Guss and H. R. Williams, *ibid.*, 1951, **16**, 1809.

[7] C. L. Browne and R. E. Lutz, *ibid.*, 1952, **17**, 1187.

[8] S. J. Cristol and R. F. Helmreich, *J. Amer. Chem. Soc.*, 1952, **74**, 4083.

[9] Cf. also R. Rothstein and J. Ficini, *Compt. rend.*, 1952, **234**, 1293, 1694.

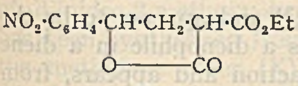
[10] N. G. Gaylord and E. I. Becker, *Chem. Reviews*, 1951, **49**, 413.

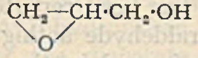
[11] F. H. Dickey, W. Fickett, and H. J. Lucas, *J. Amer. Chem. Soc.*, 1952, **74**, 944.

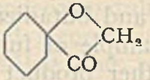
[12] G. K. Helmkamp and H. J. Lucas, *ibid.*, p. 951.

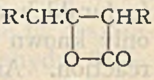
[13] O. E. Paris and P. E. Fanta, *ibid.*, p. 3007.

actions being accompanied, as would be expected, by Walden inversion. Alkaline hydrolysis of either the *O*- or the *S*-acetyl derivative of 2-mercaptoethanol gives ethylene sulphide and polymeric material, and *cyclo*hexene sulphide is similarly obtainable.[14] Glycidol (II) is obtained in high yield from glycerol and ethylene carbonate, or phenyl carbonate, a cross-linked poly(glycerol carbonate) being presumably an intermediate.[14a]


(I)


(II)


(III)


(IV)

In analogy with the formation of coumaranone in the decomposition of *o*-anisoyldiazomethane,[15] 1-oxa*spiro*[3 : 5]nonan-3-one (III) has been obtained by the decomposition of 1-acetoxy*cyclo*hexane-1-carbonyldiazomethane.[16]

Further examples of the condensation of indoles with β-propiolactone have been described, and pyrrole gave β-2-pyrrolylpropionic acid.[17] Confirmatory evidence has been produced to show that monosubstituted keten dimers are β-lactones (IV) containing a semicyclic double bond.[18]

**Five- and Six-membered Ring Systems.**—A detailed analysis has been made of the stereochemical factors governing the synthesis of cyclic acetals of polyhydric alcohols, and a theoretical basis has been provided [19] for certain empirical rules [20] developed to enable the pattern of condensation between a given carbonyl compound and a given polyhydric alcohol to be predicted.

γ-Valerolactone has been used in the Friedel–Crafts reaction with the isomeric xylenes for the synthesis of various polymethylnaphthalenes.[21] Perfluorobutyrolactone, the main product of the degradation of silver hexafluoroglutarate with excess of iodine, is a highly reactive compound and reacts with water, ethanol, ammonia, hydriodic acid, and ethanethiol to give derivatives of perfluorosuccinic acid.[22]

*Furan.* The stereochemical course of the temperature-dependent reaction [23] between furan and maleinimide is similar to that between furan and maleic anhydride,[24] the *endo*-adduct (V) being formed at 25° and the *exo*-compound (VI) at higher temperatures; both adducts are relatively unstable, having *endo*-bridges,[25] but hydrogenation to the hexahydro-3 : 6-*endo*-oxophthalimides permitted further investigation.[23] Electrolytic methods have been described for the alkoxylation of furan and substituted furans with

[14] L. W. C. Miles and L. N. Owen, *J.*, 1952, 817.

[14a] H. A. Bruson and T. W. Riener, *J. Amer. Chem. Soc.*, 1952, **74**, 2100.

[15] E. R. Marshall, J. A. Kuck, and R. C. Elderfield, *J. Org. Chem.*, 1942, **7**, 444; A. K. Bose and P. Yates, *J. Amer. Chem. Soc.*, 1952, **74**, 4703.

[16] J. R. Marshall and J. Walker, *J.*, 1952, 467.

[17] J. Harley-Mason, *J.*, 1952, 2433.

[18] C. M. Hill, M. E. Hill, H. I. Schofield, and L. Haynes, *J. Amer. Chem. Soc.*, 1952, **74**, 166.

[19] S. A. Barker, E. J. Bourne, and D. H. Whiffen, *J.*, 1952, 3865.

[20] S. A. Barker and E. J. Bourne, *ibid.*, p. 905.

[21] W. L. Mosby, *J. Amer. Chem. Soc.*, 1952, **74**, 2564.

[22] M. Hauptschein, C. S. Stokes, and A. V. Grosse, *ibid.*, p. 1974.

[23] H. Kwart and I. Burchuk, *ibid.*, p. 3094.

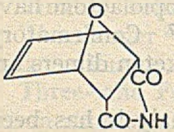
[24] R. B. Woodward and H. Baer, *ibid.*, 1948, **70**, 1161.

[25] Cf. *Ann. Reports*, 1950, **47**, 179; M. Kloetzel, *Organic Reactions*, 1948, **4**, 9.

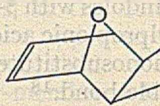
the production of 2 : 5-dialkoxy-2 : 5-dihydrofurans;[26] with methanol, maleinaldehyde tetramethylacetal is a by-product. Acyloxylation of furans is effected with lead tetra-acyloxylates[27] and pyrolysis of 2 : 5-diacetoxy-2 : 5-dihydrofuran gives 2-acetoxyfuran,[28] while conversion of the dialkoxydihydrofurans into 1-arylpyrroles proceeds in good yield.[29]

The Willgerodt reaction is applicable in the furan series if lower temperatures are used than is customary.[30] Formation of a 1 : 2-adduct (VII) of furfuraldehyde and butadiene has been reported,[31] and appears to be the only known example of furfuraldehyde acting as a dienophile in a diene reaction. Another product is formed in the reaction and appears, from various degradations, to be (VIII).[32] The reaction of diazonium salts with furylacrylic acid[33] leads mainly to 5-aryl-2-styrylfurans, 2-styrylfurans and β-(5-aryl-2-furyl)acrylic acids being formed as by-products.

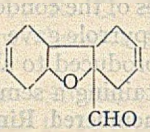
The methylenedihydrofuran, obtained together with 2-methylfuran by applying the Wolff–Kishner reaction to furfuraldehyde, has been shown by ultra-violet absorption to be the conjugated 2 : 5-dihydro-2-methylenefuran.[34] The reaction between the two stereoisomeric forms of tetrahydro-5-hydroxy-3-methyl-2-propenylfuran and aniline is said to give selectively the two forms of the corresponding anilinotetrahydrofurans.[35]



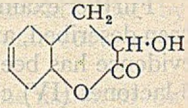
(V)



(VI)



(VII)



(VIII)

*Pyran.* Further experience has been obtained of the use of dihydropyran for the protection of secondary alcohol groups in steroids.[36] Other novel reactions in this series include the reaction of 2-alkoxy-3 : 4-dihydropyrans[37] with ammonia over alumina at 400°, which gives pyridine, and thermal cleavage over an alumina–silica catalyst to isomeric 5-alkoxypent-4-enals.[38] Addition of alcohols, carboxylic acids, phenol, and hydrogen cyanide yields the appropriate 6-alkoxy-, 6-acyloxy-, 6-phenoxy-, and 6-cyano-derivatives of 2-alkoxytetrahydropyran.[38] Hydrogenation of 2-alkoxydihydropyrans over Raney nickel gave 2-alkoxytetrahydropyrans and hydrolysis followed by hydrogenation gave the corresponding pentane-1 : 5-diols.[39] The latter

---

[26] N. Clauson-Kaas *et al.*, *Acta Chem. Scand.*, 1952, **6**, 531, 545, 551, 556, 569; N. Elming, *ibid.*, p. 572.

[27] N. Elming and N. Clauson-Kaas, *ibid.*, p. 535; N. Elming, *ibid.*, p. 578.

[28] N. Clauson-Kaas and N. Elming, *ibid.*, p. 560.

[29] N. Elming and N. Clauson-Kaas, *ibid.*, p. 867; N. Clauson-Kaas and Z. Tyle, *ibid.*, p. 667.

[30] J. A. Blanchette and E. V. Brown, *J. Amer. Chem. Soc.*, 1952, **74**, 2098.

[31] J. C. Hillyer, S. Swadesh, M. L. Leslie, and A. P. Dunlop, *Ind. Eng. Chem.*, 1948, **40**, 2216. [32] J. C. Hillyer and J. T. Edmonds, *J. Org. Chem.*, 1952, **17**, 600.

[33] W. Freund, *J.*, 1952, 3068; cf. D. M. Brown and G. A. R. Kon, *J.*, 1948, 2150.

[34] H. L. Rice, *J. Amer. Chem. Soc.*, 1952, **74**, 3193.

[35] C. Glacet, *Compt. rend.*, 1952, **234**, 2371.

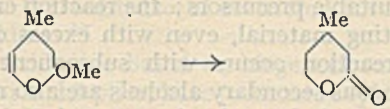
[36] A. C. Ott, M. F. Murray, and R. L. Pederson, *J. Amer. Chem. Soc.*, 1952, **74**, 1239; E. Elisberg, H. Vanderhaeghe, and T. F. Gallagher, *ibid.*, p. 2814.

[37] *Ann. Reports*, 1950, **47**, 226; 1951, **48**, 211.

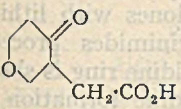
[38] C. W. Smith, D. G. Norton, and S. A. Ballard, *J. Amer. Chem. Soc.*, 1952, **74**, 2018.

[39] R. I. Longley, W. S. Emerson, and T. C. Shafer, *ibid.*, p. 2012.

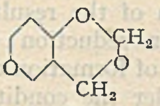
are also obtained directly by hydrogenation over copper chromite in the presence of water,[39] the saturated δ-lactone [40] being a by-product in the case



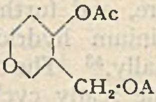
of dihydro-2-methoxy-4-methylpyran. Dihydrodeoxypatulinic acid (IX) has been synthesised from Δ$^3$-dihydropyran and formaldehyde by way of the methylene ether (X) or the diacetate (XI),[41] and tetrahydro-3 : 4-dihydroxypyran is accessible from erythrol (but-1-ene-3 : 4-diol) and formaldehyde.[42]



(IX)

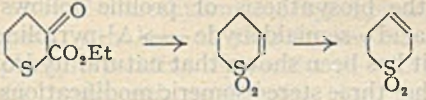


(X)

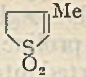


(XI)

Dieckmann ring-closure of ethyl γ-carbethoxymethylthiobutyrate gives ethyl tetrahydro-3-ketothiapyran-2-carboxylate (XII), converted by a series of stages into Δ$^2$-dihydrothiopyran 1 : 1-dioxide (XIII); the latter readily passes irreversibly into the Δ$^3$-sulphone (XIV) [43] in contrast with the situation arising with isoprene sulphone (XV). Vapour-phase reaction of tetrahydropyran with primary aromatic amines gives 1-arylpiperidines in high yield.[44]



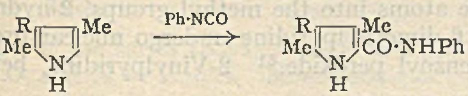
(XII) (XIII) (XIV)

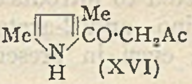


(XV)

Deuterated γ-pyrones have been prepared by exchange and synthesis, and exchange, rather surprisingly, takes place only at the α-position.[45]

*Pyrrole.* The molecular structures of pyrrole and some of its simple derivatives have been studied by electric dipole-moment measurements [46] and fit into a general pattern with indole derivatives.[47] Pyrroles react with *iso*cyanates with *C*-substitution at previously unsubstituted positions in the nucleus. The imino-group is unreactive and no reaction takes place with





(XVI)

1-methylpyrrole in accordance with the rule that *N*-substitution deactivates the pyrrole nucleus generally.[48] Similarly, diketen reacts with pyrroles to give *C*-acetoacetylpyrroles (*e.g.*, XVI), hydrolysed by alkali to *C*-acetyl-

---

[40] Cf. L. P. Kyrides and F. B. Zienty, *J. Amer. Chem. Soc.*, 1946, 68, 1385.

[41] S. Olsen, *Acta Chem. Scand.*, 1951, 5, 1326.

[42] *Idem, ibid.*, p. 1339.

[43] E. Fehnel, *J. Amer. Chem. Soc.*, 1952, 74, 1569.

[44] A. N. Bourns, H. W. Embleton, and M. K. Hansuld, *Canad. J. Chem.*, 1952, 30, 1.

[45] R. C. Lord and W. D. Phillips, *J. Amer. Chem. Soc.*, 1952, 74, 2429.

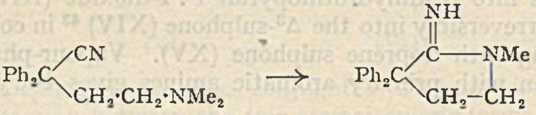
[46] H. Kofod, L. E. Sutton, and J. Jackson, *J.*, 1952, 1467.

[47] E. F. J. Janetzky and M. C. Lebret, *Rec. Trav. chim.*, 1944, 63, 123.

[48] A. Treibs and W. Ott, *Annalen*, 1952, 577, 119.

pyrroles.[49] Hydroxymethylpyrroles containing only alkyl groups as other substituents are unknown and are not even accessible by lithium aluminium hydride reduction of suitable precursors; the reaction either fails completely with recovery of starting material, even with excess of reagent in boiling tetrahydrofuran, or reaction occurs with subsequent destruction of the labile product. Analogous secondary alcohols are also not accessible by this means, 3-acetyl-2 : 4-dimethylpyrrole, for example, yielding cryptopyrrole (3-ethyl-2 : 4-dimethylpyrrole).[50] When the reducible functional groups are not directly attached to the pyrrole nucleus reduction with lithium aluminium hydride proceeds normally.[51]

Substituted pyrrolidines are prepared by the addition of aliphatic nitro-compounds to acrylic ester, followed by reduction of the $\gamma$-nitro-esters, ring closure, and further reduction of the resulting pyrrolidones with lithium aluminium hydride.[52] Similar reduction of alkylsuccinimides proceeds normally.[53] The relative ease of formation of the pyrrolidine ring is shown by the ready cyclisation, under the conditions of amidine formation, of 3-chloro-1-phenyl-, 3-chloro-1 : 1-diphenyl-,[54] and 3-dimethylamino-1 : 1-diphenyl-propyl cyanide[55] to iminopyrrolidines, ring closure in the last instance being accompanied by loss of a methyl group. Evidence has been obtained to suggest that the biosynthesis of proline follows the path: glutamic acid ⟶ glutamic acid $\gamma$-semialdehyde ⟶ $\Delta^1$-pyrroline-5-carboxylic acid ⟶ proline,[56] and it has been shown that natural hydroxy-L-proline can be converted into the other three stereoisomeric modifications by selective inversions.[57]



*Pyridine.* The Tschitschibabin synthesis of pyridines has been improved by carrying out the reaction in acetic acid–ammonium acetate,[58] and certain 2 : 3 : 5-trisubstituted pyridines are conveniently prepared by disproportionation of 2 : 3 : 5-trisubstituted 1-benzyl-1 : 2-dihydropyridines obtained by condensation of aldehydes with *N*-benzylaldimines.[59] A kinetic study has been carried out on the reaction between butadiene and cyanogen, by which 2-cyanopyridine is formed.[60] Although *N*-bromosuccinimide would be expected to introduce bromine atoms into the methyl groups, 2-hydroxy-, 2-amino-, and 2-acetamido-4 : 6-dimethylpyridine undergo nuclear bromination even in presence of benzoyl peroxide.[61] 2-Vinylpyridine, being a

---

[49] A. Treibs and K. H. Michl, *Annalen*, 1952, **577**, 129.

[50] A. Treibs and H. Scherer, *ibid.*, p. 139.

[51] O. Klamerth and W. Kutscher, *Chem. Ber.*, 1952, **85**, 444; W. Kutscher and O. Klamerth, *Z. physiol. Chem.*, 1952, **289**, 229.

[52] R. B. Moffett and J. L. White, *J. Org. Chem.*, 1952, **17**, 407.

[53] D. E. Ames and R. E. Bowman, *J.*, 1952, 1057.

[54] F. E. King, K. G. Latham, and M. W. Partridge, *ibid.*, p. 4268.

[55] W. Wilson, *J.*, 1950, 2173; 1952, 3524; J. Cymerman and W. S. Gilbert, *ibid.*, p. 3529.

[56] H. J. Vogel and B. D. Davis, *J. Amer. Chem. Soc.*, 1952, **74**, 109.

[57] D. S. Robinson and J. P. Greenstein, *J. Biol. Chem.*, 1952, **195**, 383.

[58] M. Weiss, *J. Amer. Chem. Soc.*, 1952, **74**, 200.

[59] T. M. Patrick, *ibid.*, p. 2984.

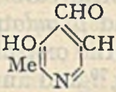
[60] P. J. Hawkins and G. J. Janz, *ibid.*, p. 1790.

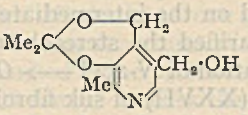
[61] R. P. Mariella and E. P. Belcher, *ibid.*, p. 1916.

vinylogue of acrylonitrile, takes part in Michael addition reactions to give appropriate pyridylethyl derivatives.[62] Ultra-violet absorption characteristics have shown the existence of restricted rotation in 4-aryl-3 : 5-dicarbethoxy-2 : 6-lutidines.[63]

A synthesis of pyridoxine based on biogenetic considerations has been described,[64] and pyridoxal 5-phosphate (codecarboxylase) (XVII), which may be purified as the acridine salt,[65] has been obtained from *OO-iso*propylidenepyridoxine (XVIII) by reaction with phosphoric oxide in phosphoric acid, and subsequent oxidation of pyridoxine 5-phosphate.[66] Anhydrous phosphoric acid also converts pyridoxamine into the crystalline 5-phosphate.[67] (—)-Pipecolinic acid has been recognised as a natural amino-acid of relatively wide occurrence.[68]

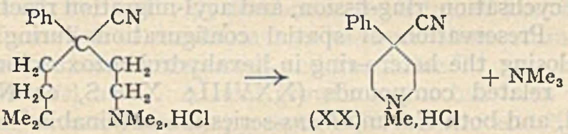
(XVII)



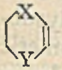


(XVIII)

(XIX)

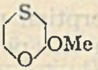


Convenient syntheses of alkylpiperidines,[53] piperidin-4-ol,[69] 3 : 3-disubstituted 2 : 6-diketopiperidines,[70] substituted 3-piperidones [71] and 1-alkyl-3-hydroxypiperidines [72] have been described, while a novel ring-closure of αα-bis-2-dimethylaminoethyl-α-phenylacetonitrile hydrochloride (XIX) proceeds with loss of trimethylamine and formation of 4-cyano-1-methyl-4-phenylpiperidine hydrochloride (XX) in 78% yield.[73]

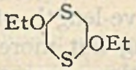


(XXI)

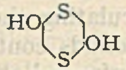
(XXII)



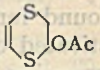
(XXIII)



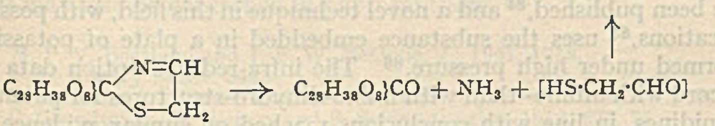
(XXIV)



(XXV)



(XXVI)



Uscharin Uscharidin

*Monocyclic compounds with more than one hetero-atom.* Preliminary studies of the series (XXI) and (XXII) have been reported where X = S, Y = O, and X = Y = S. Monothioglycol (2-mercaptoethanol) and chloro-

---

[62] R. Levine and M. H. Wilt, *J. Amer. Chem. Soc.*, 1952, **74**, 342.

[63] A. P. Phillips and P. L. Graham, *ibid.*, p. 1552.

[64] A. Cohen, J. W. Haworth, and E. G. Hughes, *J.*, 1952, 4374.

[65] M. Viscontini and P. Karrer, *Helv. Chim. Acta*, 1952, **35**, 1924.

[66] J. Baddiley and A. P. Mathias, *J.*, 1952, 2583.

[67] E. A. Peterson, H. A. Sober, and A. Meister, *J. Amer. Chem. Soc.*, 1952, **74**, 570.

[68] R. M. Zacharius, J. F. Thompson, and F. C. Steward, *ibid.*, p. 2949; G. Harris and J. R. A. Pollock, *Chem. and Ind.*, 1952, 931.

[69] K. Bowden and P. N. Green, *J.*, 1952, 1164.

[70] E. Tagmann, E. Sury, and K. Hoffmann, *Helv. Chim. Acta*, 1952, **35**, 1235.

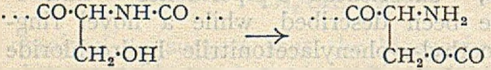
[71] F. F. Blicke and J. Krapcho, *J. Amer. Chem. Soc.*, 1952, **74**, 4001.

[72] J. H. Biel, H. L. Friedman, H. A. Leiser, and E. P. Sprengeler, *ibid.*, p. 1485.

[73] F. F. Blicke, J. A. Faust, J. Krapcho, and E. Tsao, *ibid.*, p. 1844.

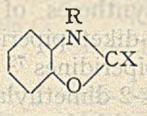
acetaldehyde dimethyl acetal gave 2-methoxy-1 : 4-oxathian (XXIII), converted by catalytic decomposition over phosphoric oxide into 1 : 4-oxathien (XXI; X = S, Y = O).[74] 2-Mercaptoacetal, $HS\cdot CH_2\cdot CH(OEt)_2$, passes slowly into 2 : 5-diethoxy-1 : 4-dithian (XXIV). The latter is hydrolysed to mercaptoacetaldehyde, which dimerises to give the two stereoisomeric forms of 2 : 5-dihydroxy-1 : 4-dithian (XXV), and the derived acetates pass when heated into the same acetoxy-1 : 4-dithien (XXVI).[75] The heterocyclic fragment of the African arrow poison uscharin consists apparently of a thiazoline ring since hydrolysis gives uscharidin, ammonia, and dimeric mercaptoacetaldehyde (XXV).[76]

*Oxazoline; thiazoline.* Applications of intermediate oxazoline formation in stereochemical problems have already been reviewed.[77] Analogous studies based on the intermediate formation of the tetrahydro-1 : 3-oxazine ring have clarified the stereochemistry of tropine and *pseudo*tropine.[78] A novel application of *N*-acyl ⟶ *O*-acyl migration *via* the oxazoline is in the degradation (XXVII) of silk fibroin at serine residues,[79] and an account has been given of cyclisation, ring-fission, and acyl-migration reactions involving thiazolines.[80] Preservation of spatial configuration during various procedures for closing the hetero-ring in hexahydrobenzoxazolones (XXVIII; X = O) and related compounds (XXVIII; X = S, or NH) has been demonstrated, and both *cis*- and *trans*-series are obtainable.[81]

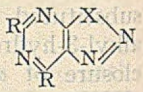


$$\ldots CO\cdot\underset{\displaystyle CH_2\cdot OH}{\underset{|}{CH}}\cdot NH\cdot CO\ldots \longrightarrow \ldots CO\cdot\underset{\displaystyle CH_2\cdot O\cdot CO}{\underset{|}{CH}}\cdot NH_2$$

(XXVII)



(XXVIII)



(XXIX)

*Pyrimidine.* Further studies of the ultra-violet light absorption of pyrimidine derivatives have been reported,[82] and an empirical rule has been found for calculating the wave-length of absorption maxima of polysubstituted compounds containing not more than one potentially tautomeric grouping.[83] Infra-red absorption characteristics of a wide range of derivatives have been published,[84] and a novel technique in this field, with possible wide applications,[85] uses the substance embedded in a plate of potassium bromide formed under high pressure.[86] The infra-red absorption data are more in accord with amino- than with imino-dihydro-structures for potential aminopyrimidines, in line with conclusions reached on similar evidence for aminopyridines.[87]

---

[74] W. E. Parham, I. Gordon, and J. D. Swalen, *J. Amer. Chem. Soc.*, 1952, **74**, 1824.

[75] G. Hesse and I. Jörder, *Chem. Ber.*, 1952, **85**, 924.

[76] G. Hesse and H. W. Gampp, *ibid.*, p. 933.

[77] *Ann. Reports*, 1951, **48**, 217; cf. G. Fodor and K. Koczka, *J.*, 1952, 850.

[78] G. Fodor and K. Nádor, *Nature*, 1952, **169**, 462; A. Nickon and L. F. Fieser, *J. Amer. Chem. Soc.*, 1952, **74**, 5566.

[79] D. F. Elliott, *Biochem. J.*, 1952, **50**, 542.

[80] J. C. Crawhall and D. F. Elliott, *J.*, 1952, 3094.

[81] M. Mousseron, F. Winternitz, and M. Mousseron-Canet, *Compt. rend.*, 1952, **235**, 373.

[82] D. Shugar and J. J. Fox, *Biochim. Biophys. Acta*, 1952, **9**, 199; M. P. V. Boarland and J. F. W. McOmie, *J.*, 1952, 3716.

[83] *Idem, ibid.*, p. 3722.

[84] L. N. Short and H. W. Thompson, *ibid.*, p. 168.

[85] Cf. U. Schiedt and H. Reinwein, *Z. Naturforsch.*, 1952, **7b**, 270.

[86] M. M. Stimson and M. J. O'Donnell, *J. Amer. Chem. Soc.*, 1952, **74**, 1805.

[87] C. L. Angyal and R. L. Werner, *J.*, 1952, 2911; J. D. S. Goulden, *ibid.*, p. 2939; cf. also S. J. Angyal and C. L. Angyal, *ibid.*, p. 1461.

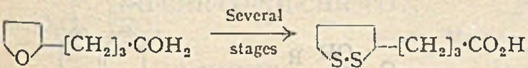
Although 5-aminopyrimidine itself fails to undergo diazotisation,[88] the presence of other suitable substituents allows normal diazonium salt formation to occur, and in the presence of a 4(6)-mercapto-, -hydroxy-, or primary-amino-group, ring closure to pyrimidino-thiadiazoles (XXIX; X = S), -oxadiazoles (XXIX; X = O), and -triazoles (XXIX; X = NH) occurs;[89] ring closure even takes place with a 4(6)-alkyl group, giving 1 : 2 : 4 : 6-tetra-azaindenes (XXIX; X = $CH_2$), isomeric with purines.

A new reaction of acetylene with nitriles, *e.g.*, propionitrile, results in the formation of 2 : 4-diethylpyrimidine and the isomeric aminopyridine; a carbanion mechanism is suggested for the reaction.[90]

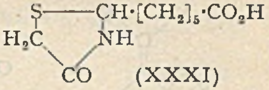
*Triazine.* Insight into the mechanism of formation of *s*-triazines from nitriles has been obtained since all nitriles which form triazines readily give primary products containing two molecules of nitrile to one of hydrogen halide, their properties being compatible with ionic structures.[91] Besides the use of strong acids, nitriles may also be trimerised in the presence of methanol or weak bases at high pressures (7000—8500 atm.); besides the triazine, the isomeric 4-amino-2 : 6-dimethylpyrimidine is also obtained from acetonitrile.[92]

The novel formation of aminotriazines has been observed in the reaction between α-cyano-carbonyl compounds and guanidine.[93]

*α-Lipoic* (*thioctic*) *acid.* A new growth factor has been isolated and described under several names: protogen A,[94] thioctic acid,[94] and α-lipoic acid.[95] Degradation [94-96] and synthesis [97, 98] of α-lipoic acid (from γ-tetrahydro-2-furylbutyric acid) and of some of its isomers [99] have shown it to be "5 : 8-dithio-octanoic acid" (3-3′-carboxypropyl-1 : 2-dithian) (XXX). Another growth factor, protogen B, is possibly a closely related sulphoxide.[100 (95)] The amide of α-lipoic acid with thiamine pyrophosphate appears to be a coenzyme in the oxidative decarboxylation of α-keto-acids,[101] and it may also be concerned in photosynthesis.[102]



(XXX)



(XXXI)

---

[88] M. P. V. Boarland and J. F. W. McOmie, *J.*, 1951, 1218.

[89] F. L. Rose, *J.*, 1952, 3448.

[90] T. L. Cairns, J. C. Sauer, and W. K. Wilkinson, *J. Amer. Chem. Soc.*, 1952, 74, 3989.

[91] C. Grundmann, G. Weisse, and S. Seide, *Annalen*, 1952, 577, 77.

[92] T. L. Cairns, A. W. Larchar, and B. C. McCusick, *J. Amer. Chem. Soc.*, 1952, 74, 5633.

[93] P. B. Russell, G. H. Hitchings, B. H. Chase, and J. Walker, *ibid.*, p. 5403.

[94] J. A. Brockman, E. L. R. Stokstad, E. L. Patterson, J. V. Pierce, M. Macchi, and F. P. Day, *ibid.*, p. 1868.

[95] L. J. Reed, B. G. DeBusk, I. C. Gunsalus, and G. H. F. Schnakenberg, *ibid.*, 1951, 73, 5920.

[96] L. J. Reed, Q. F. Soper, G. H. F. Schnakenberg, S. F. Kern, H. Boaz, and I. C. Gunsalus, *ibid.*, 1952, 74, 2383.

[97] M. W. Bullock, J. A. Brockman, E. L. Patterson, J. V. Pierce, and E. L. R. Stokstad, *ibid.*, p. 1868.

[98] C. S. Hornberger, R. F. Heitmiller, I. C. Gunsalus, G. H. F. Schnakenberg, and L. J. Reed, *ibid.*, p. 2382.

[99] M. W. Bullock, J. A. Brockman, E. L. Patterson, J. V. Pierce, and E. L. R. Stokstad, *ibid.*, p. 3455.

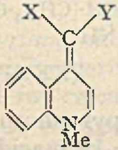
[100] E. L. Patterson, J. A. Brockman, F. P. Day, J. V. Pierce, M. E. Macchi, C. E. Hoffman, C. T. O. Fong, E. L. R. Stokstad, and T. H. Jukes, *ibid.*, 1951, 73, 5919.

[101] L. J. Reed and B. G. DeBusk, *ibid.*, 1952, 74, 3457, 3964, 4727; *J. Biol. Chem.*, 1952, 199, 881. [102] M. Calvin and J. A. Barltrop, *ibid.*, p. 6153.

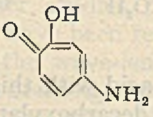
*Actithiazic acid.* Two other groups[103] have independently isolated a novel antibiotic, $C_9H_{15}O_3NS$, from *Streptomyces* spp. · Treatment with mercuric chloride [104] or alkali [105] removed the nitrogen, the sulphur, and two carbon atoms to give the semialdehyde of pimelic acid; the substance was therefore (—)-2-5′-carboxypentylthiazolid-4-one (XXXI), and the (±)-form was synthesised by condensation of this aldehyde with thioglycollamide [104, 106] and resolved with brucine.[104]

**Condensed Ring Systems.**—*Quinoline.* Dihydroquinoline is obtainable from quinoline by reduction with lithium aluminium hydride, a reagent which generally converts heterocyclic compounds into dihydro-derivatives which are often difficult of access and unstable.[107] Several instances of lability of halogen substituents in the *Bz*-ring of quinoline have been reported: the bromine atoms in 8-amino-5 : 7-dibromoquinoline are replaced by chlorine during diazotisation and deamination in hydrochloric acid; [108] 8-amino-5-bromo-6-methoxyquinoline is converted into the 7-bromo-isomer by boiling hydrobromic acid; [109] 5-chloro-8-hydroxy-7-iodoquinoline is said to undergo disproportionation in boiling dioxan to give 8-hydroxy-5 : 7-di-iodo- and 5 : 7-dichloro-8-hydroxy-quinoline.[110] Reactive halogen atoms in the heterocyclic rings of 2-chloro- and 4 : 7-dichloro-quinoline, and of 2-chlorobenzothiazole, undergo the Friedel–Crafts reaction with resorcinol to give the corresponding dihydroxyphenyl derivatives.[111]

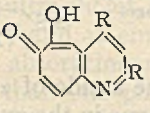
The base-catalysed condensation of quinolinium methiodide with substances containing a reactive methylene group is now well-established, the products being derivatives (XXXII) of 1 : 4-dihydro-1-methyl-4-methylene-quinoline.[112] γ-Aminotropolone (XXXIII) undergoes the Gould–Jacobs modification of the Conrad–Limpach reaction,[113] the Doebner–Miller reaction,[113] and the Skraup reaction [114] to give the appropriate pyridinotropolones (XXXIV).



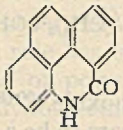
(XXXII)



(XXXIII)



(XXXIV)



(XXXV)

Three of five antibiotics produced by *Pseudomonas aeruginosa* have been

---

[103] W. E. Grundy, A. L. Whitman, E. G. Rdzok, E. J. Rdzok, M. E. Hanes, and J. C. Sylvester, *Antibiotics and Chemotherapy*, 1952, **2**, 399; B. A. Sobin, *J. Amer. Chem. Soc.*, 1952, **74**, 2947.

[104] W. M. McLamore, W. D. Celmer, V. V. Bogert, F. C. Pennington, and I. A. Solomons, *ibid.*, p. 2946.

[105] J. R. Schenck and A. F. De Rose, *Arch. Biochem. Biophys.*, 1952, **40**, 263.

[106] R. K. Clark and J. R. Schenck, *ibid.*, p. 270.

[107] F. Bohlmann, *Chem. Ber.*, 1952, **85**, 390.

[108] R. C. Elderfield and E. F. Claflin, *J. Amer. Chem. Soc.*, 1952, **74**, 2953.

[109] W. M. Lauer, C. J. Claus, R. W. Von Korff, and S. A. Sundet, *ibid.*, p. 2080.

[110] T. Nógrádi, *Chem. Ber.*, 1952, **85**, 104.

[111] G. Illuminati and H. Gilman, *J. Amer. Chem. Soc.*, 1952, **74**, 2896.

[112] N. J. Leonard, H. A. DeWalt, and G. W. Leubner, *J. Amer. Chem. Soc.*, 1951, **73**, 3325; N. J. Leonard and R. L. Foster, *ibid.*, 1952, **74**, 2110, 3671.

[113] R. Slack and C. F. Attridge, *Chem. and Ind.*, 1952, 471.

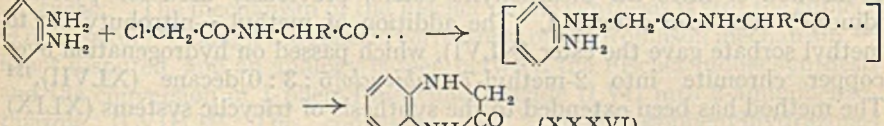
[114] J. W. Cook, J. D. Loudon, and D. K. V. Steel, *ibid.*, p. 562.

shown by degradation[115] and synthesis[116] to be 2-heptyl-, 2-nonyl-, and 2-non-1′-enyl-quinolin-4-ol. 1 : 2-Dihydro-2-keto-1-azapyrene (XXXV) has been isolated from the pitch fraction, b. p. 470°, of coal tar.[117]

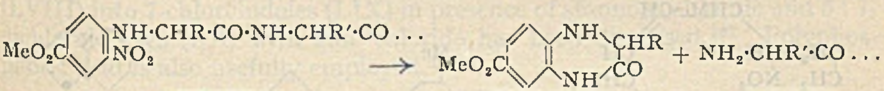
*Quinazoline; quinoxaline; benzoxazine.* The infra-red absorption spectra of 4-hydroxy-, 2 : 4-dihydroxy-, and 4-mercapto-quinazolines support the tautomeric carbonyl and thiocarbonyl structures.[118]

Relatively high pH values have been found to favour the formation of monoacyl derivatives of tetrahydroquinoxaline,[119] which is conveniently prepared from *o*-amino-*N*-2-hydroxyethylaniline.[120]

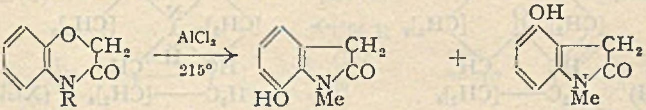
Elegant methods for the removal of terminal protecting *N*-chloroacetyl groups or terminal amino-acid residues from peptides have been described. Reaction of the chloroacetyl derivatives with *o*-phenylenediamine affords 1 : 2 : 3 : 4-tetrahydro-2-ketoquinoxaline (XXXVI) and the free peptide directly.[121] The reaction is not conveniently applied by reduction of dinitrophenyl peptides prepared by the standard method,[122] but condensation of a peptide with methyl 4-fluoro-3-nitrobenzoate affords the appropriate substituted phenylpeptide (XXXVII), passing on reduction into the tetrahydroketoquinoxaline (XXXVIII), characteristic of the terminal amino-acid residue, and the lower peptide (XXXIX).[123, 124] Terminal *o*-nitrophenoxyacetyl groups are similarly eliminated from peptides, reduction affording the lactam (XL; R = H) of *o*-aminophenoxyacetic acid and the free peptide.[121, 123] The ready formation of the ring system (XL) was also seen in the formation of 2 : 3-dihydro-3-keto-4-methylbenz-1 : 4-oxazine (XL; R = Me) when the normal conditions for the Stollé oxindole synthesis were applied to *N*-α-halogenoacetyl-*N*-methyl-*o*-anisidine, though rearrangement



(XXXVI)



(XXXVII) (XXXVIII) (XXXIX)



(XL) (XLI) (XLII)

---

[115] I. C. Wells, W. H. Elliott, S. A. Thayer, and E. A. Doisy, *J. Biol. Chem.*, 1952, **196**, 321. [116] I. C. Wells, *ibid.*, p. 331.

[117] O. Kruber and R. Oberkobusch, *Chem. Ber.*, 1952, **85**, 433.

[118] H. Culbertson, J. C. Decius, and B. E. Christensen, *J. Amer. Chem. Soc.*, 1952, **74**, 4834. [119] J. S. Morley, *J.*, 1952, 4004.

[120] G. R. Ramage and G. Trappe, *ibid.*, p. 4406.

[121] R. W. Holley and A. D. Holley, *J. Amer. Chem. Soc.*, 1952, **74**, 3069.

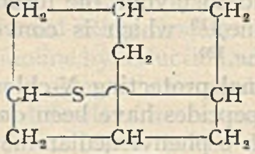
[122] F. Sanger, *Biochem. J.*, 1945, **39**, 507.

[123] R. W. Holley and A. D. Holley, *loc. cit.*, p. 1110.

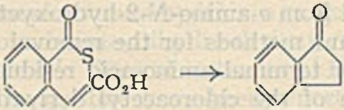
[124] *Idem*, *ibid.*, p. 5445.

to the isomeric oxindoles (XLI) and, surprisingly, (XLII) took place at higher temperatures.[125]

*Miscellaneous sulphur-containing compounds.* The properties of an interesting compound, $C_9H_{14}S$, from Middle East oil distillates recall adamantane in some respects and, as desulphurisation gave *bicyclo*[1 : 3 : 3]nonane, it is formulated as thia-adamantane (XLIII).[126] Raney nickel desulphurisation of 1 : 2-dihydro-1-keto-2-thianaphthalenes (*e.g.*, XLIV) gave indanones (*e.g.*, XLV).[127]



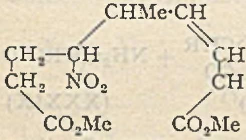
(XLIII)



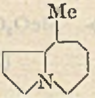
(XLIV) (XLV)

Full details have now been given of the isolation [128] of biocytin from yeast and its recognition by degradation [129] and synthesis [130] as ε-*N*-biotinyl-L-lysine.

*Ring systems with a nitrogen atom common to two rings.* The reductive cyclisation of nitro ωω′-dicarboxylic esters, previously used for pyrrolizidines,[131] has been extended. The addition of methyl γ-nitrobutyrate to methyl sorbate gave the ester (XLVI), which passed on hydrogenation over copper chromite into 2-methyl-7-aza*bicyclo*[5 : 3 : 0]decane (XLVII).[132] The method has been extended to the synthesis of tricyclic systems (XLIX) from the oximes of keto-dicarboxylic esters (XLVIII) under similar conditions.[133] The hexahydrojulolidine obtained in this way (where $x = y = z = 2$) was identical with one of the stereoisomers obtained on catalytic reduction of julolidine,[134] and gave evidence of resolution [133] over a column



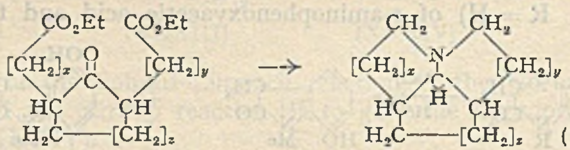
(XLVI)



(XLVII)

(LI)

(L)



(XLVIII) (XLIX)

---

[125] J. W. Cook, J. D. Loudon, and P. McCloskey, *J.*, 1952, 3904.

[126] S. F. Birch, T. V. Cullum, R. A. Dean, and R. L. Denyer, *Nature*, 1952, **170**, 629.

[127] D. J. Dijksman and G. T. Newbold, *J.*, 1952, 13; J. J. Brown and G. T. Newbold, *ibid.*, p. 4397.

[128] L. D. Wright, E. L. Cresson, H. R. Skeggs, T. R. Wood, R. L. Peck, D. E. Wolf, and K. Folkers, *J. Amer. Chem. Soc.*, 1952, **74**, 1996.

[129] R. L. Peck, D. E. Wolf, and K. Folkers, *ibid.*, p. 1999.

[130] D. E. Wolf, J. Valiant, R. L. Peck, and K. Folkers, *ibid.*, p. 2002.

[131] N. J. Leonard and D. L. Felley, *ibid.*, 1950, **72**, 2537.

[132] N. J. Leonard, D. L. Felley, and E. D. Nicolaides, *ibid.*, 1952, **74**, 1700.

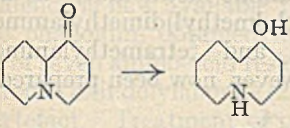
[133] N. J. Leonard and W. J. Middleton, *ibid.*, p. 5114.

[134] M. Protiva and V. Prelog, *Helv. Chim. Acta*, 1949, **32**, 621.

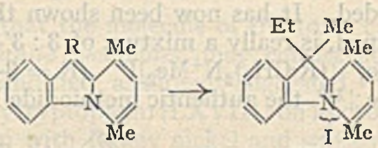
of D-lactose, indicating the *cis* : *trans*-structure (L), the *cis* : *cis*- and *trans* : *trans*-stereoisomers being *meso*-forms.

(−)-Octahydropyrrocoline (LI) has been correlated with (+)-coniine and D(+)-pipecolinic acid and therefore belongs to the D-series.[135]

The electrolytic reduction of α-amino-ketones[136] has now been applied to bicyclic representatives in a new synthesis of medium-sized nitrogen-containing rings, octahydro-1-ketopyridocoline (LII) giving 5-hydroxyaza*cyclo*decane (LIII).[137]



(LII) (LIII)

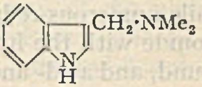


(LIV) (LV)

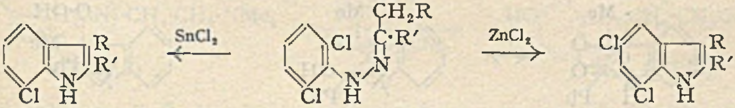
The "ethiodide" of 1 : 5 : 8-trimethyl-2 : 3-benzopyrrocoline (LIV; R = Me) and the "methiodide" of 1-ethyl-5 : 8-dimethyl-2 : 3-benzopyrrocoline (LIV; R = Et) are identical, indicating alkylation at the β-carbon atom of the indole ring system and the salt is therefore the pyridinium compound (LV).[138]

*Indole*. The mechanism of the Fischer indole synthesis is still the subject of discussion[139] though the general correctness of the Robinson mechanism[140] is not disputed, and an analogy is seen between the Fischer indole synthesis and the conversion of 1-phenylthiosemicarbazide (LVI) into 2-aminobenzothiazole (LVII).[141] The conversion of 2 : 6-dichlorophenylhydrazones (LVIII) into 7-chloroindoles (LIX) in presence of stannous chloride and 5 : 7-dichloroindoles (LX) with zinc chloride has been discussed.[142] Polyphosphoric acid is also usefully employed.[143]

(LVI) (LVII)



(LXI)



(LIX) (LVIII) (LX)

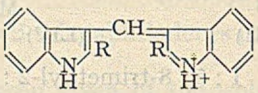
Indole-3-aldehyde has been obtained by improved methods; these are the reaction of potassium indole with carbon monoxide at high temperatures and pressures,[144] a modification[144] of the *N*-methylformanilide process,[145]

---

[135] N. J. Leonard and W. J. Middleton, *loc. cit.*, p. 5776.
[136] *Ann. Reports*, 1951, 48, 223.
[137] N. J. Leonard, S. Swann, and J. Figueras, *J. Amer. Chem. Soc.*, 1952, 74, 4620.
[138] Sir R. Robinson and J. E. Saxton, *J.*, 1952, 976.
[139] R. B. Carlin, *J. Amer. Chem. Soc.*, 1952, 74, 1077.
[140] G. M. Robinson and R. Robinson, *J.*, 1924, 125, 827.
[141] K. Clusius and H. R. Weisser, *Helv. Chim. Acta*, 1952, 35, 400.
[142] R. B. Carlin, J. G. Wallace, and E. E. Fisher, *J. Amer. Chem. Soc.*, 1952, 74, 990.
[143] H. M. Kissman, D. W. Farnsworth, and B. Witkop, *ibid.*, p. 3948.
[144] F. T. Tyson and J. T. Shaw, *ibid.*, p. 2273.
[145] A. C. Shabica, E. E. Howe, J. B. Ziegler, and M. Tishler, *ibid.*, 1946, 68, 1156.

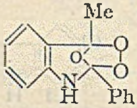
and the reaction between hexamethylenetetramine and gramine (LXI) in aqueous acetic or propionic acid.[146] The red pigment (urorosein) obtained by the action of acids on indole-3-aldehydes has been shown to be the methene (LXII), recalling pterorhodin formation amongst pterins, and the carbon atom which is lost is eliminated as formic acid.[147] αα'-Di-indolyl-methane and -methene have also been described.[148]

Although " gramine methiodide " has frequently been used, its recorded properties have varied and no significant analytical data have hitherto been recorded. It has now been shown that " gramine methiodide," as usually obtained, is really a mixture of 3 : 3'-bis(indolylmethyl)dimethylammonium iodide, $[(R{\cdot}CH_2)_2N^+Me_2]I^-$ (R = 3-indolyl) and tetramethylammonium iodide; [149] the authentic methiodide has, however, now been prepared.[149]



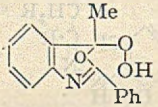
(LXII)

The oxidation of indoles has been further extensively studied and reviewed with special reference to the biological oxidation of tryptophan.[150] Hydrogen peroxide in the presence of ammonium molybdate affords derivatives of anthranilic acid in the case of indoles unsubstituted in the 3-position, and the appropriate ketones from 3-substituted derivatives.[151] Treatment with osmium tetroxide followed by hydrolysis of the resulting esters gave 2 : 3-dihydro-2 : 3-dihydroxyindoles,[152] and further study of the autoxidation of tetrahydrocarbazoles to give derivatives of *cyclo*pentane*spiro*-2-*ψ*-indoxyl is reported.[153] The reactions of the stable ozonide (LXIII) formed by 2-phenylskatole have been interpreted in terms of an equilibrium between this structure (LXIII) and the tautomeric hydroperoxide form (LXIV), while numerous reductive transformations have been carried out linking the ozonide with the hydroperoxide (LXV) derived from the same parent compound, and acid- and base-catalysed rearrangements of the ozonide have also been examined.[154]

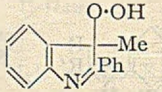


(LXIII)

↔



(LXIV)



(LXV)

A novel synthetic route to the eserine (physostigmine) ring system has emerged; [150] 3-methyl- or -hydroxy-indolenines with an alanine side-chain undergo an internal condensation at pH < 6 to give eseroline derivatives and

---

[146] H. R. Snyder, S. Swaminathan, and H. J. Sims, *J. Amer. Chem. Soc.*, 1952, **74**, 5110.

[147] J. Harley-Mason and J. D. Bu'Lock, *Biochem. J.*, 1952, **51**, 430.

[148] H. Dobeneck and G. Maresch, *Z. physiol. Chem.*, 1952, **289**, 271.

[149] T. A. Geissman and A. Armen, *J. Amer. Chem. Soc.*, 1952, **74**, 3916.

[150] A. Ek, H. Kissman, J. B. Patrick, and B. Witkop, *Experientia*, 1952, **8**, 36.

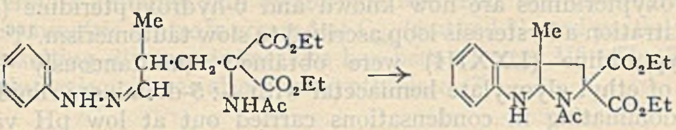
[151] C. Mentzer and Y. Berguer, *Compt. rend.*, 1952, **234**, 627; *Bull. Soc. chim.*, 1952, 218.

[152] D. W. Ockenden and K. Schofield, *Nature*, 1951, **168**, 603.

[153] R. J. S. Beer, T. Broadhurst, A. Robertson, and L. McGrath, *J.*, 1952, 4351; R. J. S. Beer, T. Broadhurst, and A. Robertson, *ibid.*, p. 4946.

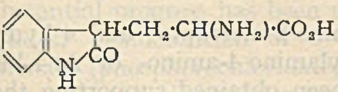
[154] B. Witkop, J. B. Patrick, and H. M. Kissman, *Chem. Ber.*, 1952, **85**, 949; B. Witkop and J. B. Patrick, *J. Amer. Chem. Soc.*, 1952, **74**, 3855, 3861.

it is impossible to synthesise β-methyl-ψ-tryptophan by the Fischer indole synthesis from (LXVI), as (LXVII) results instead.

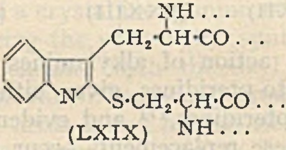


(LXVI) (LXVII)

Evidence is now available to show that the molecule of the toxic cyclic peptide phalloidin, obtained from *Amanita phalloides*, may consist not of six but of seven amino-acid residues,[155] and that, as already suggested,[156] the formation of oxindolylalanine (2-hydroxytryptophan) (LXVIII) on hydrolysis is an artefact. Treatment of phalloidin with Raney nickel and subsequent hydrolysis have afforded tryptophan,[155] indicating the presence of the fragment (LXIX) in phalloidin, and, as the ratio, after hydrolysis, of oxindolylalanine to cysteine appears to be 2 : 1, it may be that the hydroxyl group of threonine or that of *allo*hydroxyproline may participate in an analogous structure, while the amino-acid residue next to the cysteine may be alanine.[157] A simple new synthesis of oxindolylalanine has been described.[158]

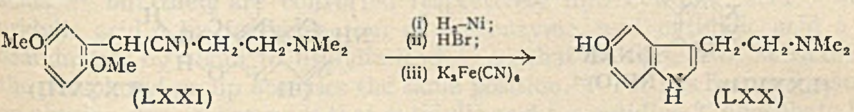


(LXVIII)



(LXIX)

Convenient syntheses of 5- and 7-hydroxyindole have been recorded[159] and bufotenine (LXX), the pressor amine from the skin of the toad, has been obtained from 2 : 5-dimethoxybenzyl cyanide by way of the nitrile (LXXI) and the derived phenylethylamine.[160] The biological effects of serotonin (5-hydroxytryptamine)[161] are reversed by 2 : 3-dialkyl-5-aminoindoles.[162]



(LXXI) (LXX)

3-Indolylacetonitrile has been recognised as a naturally occurring plant-growth hormone[163] and the related aldehyde has been synthesised and studied for such activity.[164]

---

[155] T. Wieland and G. Schmidt, *Annalen*, 1952, **577**, 215.

[156] J. W. Cornforth, C. E. Dalgliesh, and A. Neuberger, *Biochem. J.*, 1951, **48**, 598.

[157] F. Šorm and B. Keil, *Coll. Czech. Chem. Comm.*, 1951, **16**, 366.

[158] H. Behringer and H. Weissauer, *Chem. Ber.*, 1952, **85**, 743; this vol., p. 163.

[159] R. I. T. Cromartie and J. Harley-Mason, *J.*, 1952, 2525; J. Harley-Mason, *Chem. and Ind.*, 1952, 173.

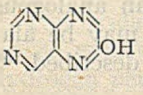
[160] J. Harley-Mason and A. H. Jackson, *Chem. and Ind.*, 1952, 954.

[161] New synthesis: B. Asero, V. Colò, V. Erspamer, and A. Vercellone, *Annalen*, 1952, **576**, 69.

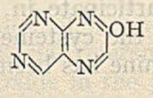
[162] D. W. Woolley and E. Shaw, *J. Amer. Chem. Soc.*, 1952, **74**, 2949; cf., however, T. D. Spies, and R. E. Stone, *J. Amer. Med. Assoc.*, 1952, **150**, 1599.

[163] E. R. H. Jones, H. B. Henbest, G. F. Smith, and J. A. Bentley, *Nature*, 1952, **169**, 485. [164] J. B. Brown, H. B. Henbest, and E. R. H. Jones, *J.*, 1952, 3172.

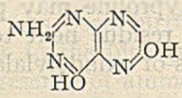
*Pteridine.* The pteridines have recently been reviewed [165] and progress has been made in the study of some of the simpler representatives. All four monohydroxypteridines are now known and 6-hydroxypteridine (LXXII) shows on titration a hysteresis loop ascribed to slow tautomerism.[166] 6- and 7-Hydroxypteridine (LXXIII) were obtained simultaneously by condensation of ethyl glyoxylate hemiacetal with 4 : 5-diaminopyrimidine, the latter predominating in condensations carried out at low pH values.[166] Similarly, xanthopterin (LXXIV) is obtained from 2 : 4 : 5-triamino-6-hydroxypyrimidine and diacetoxyacetic acid in concentrated sulphuric acid at 90°; [167] xanthopterin is also conveniently obtained from leucopterin (2-amino-4 : 6 : 7-trihydroxypteridine) *via* dihydroxanthopterin.[168] " β-Dihydroxanthopterin " has now been identified as 2 : 6-diamino-5′-hydroxy-1′ : 4′-oxazino(2′ : 3′-4 : 5)pyrimidine (LXXV),[169] and attempts to prepare pteridines by reduction and cyclisation of 4 : 2′-chloroethylamino-5-nitropyrimidines gave instead the tetrahydroglyoxalinopyrimidines (LXXVI).[170]



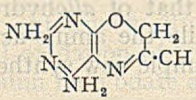
(LXXII)



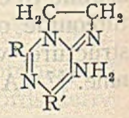
(LXXIII)



(LXXIV)

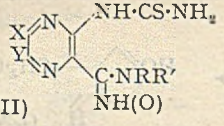


(LXXV)

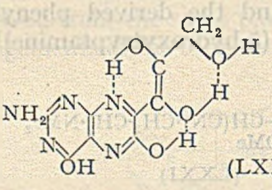


(LXXVI)

The action of alkylamines on 4-amino-2-mercapto- and 4-hydroxy-2-mercapto-pteridines gives either 2-alkylamino-4-amino- or 2 : 4-bisalkylamino-pteridines,[171] and evidence has been obtained supporting the view that these replacements occur with ring cleavage to a thioureidopyrazine intermediate (LXXVII) and subsequent ring-closure; [172] a similar mechanism is advanced for the formation of 2 : 4-bisalkylamino- from 2 : 4-diaminopteridines and alkylamines.[173]



(LXXVII)



(LXXVIII)

Pterorhodin formation from pterins, linking two pteridine ring-systems through the 7-position by a methine bridge, is possible if there is present a molecule capable of providing the methine bridge under oxidative conditions,[174] and a novel formula (LXXVIII) [175] for erythropterin is believed to account for the notable stability of this ene-diol compound.

[165] A. Albert, *Quart. Reviews*, 1952, **6**, 197.

[166] A. Albert, D. J. Brown, and G. Cheesman, *J.*, 1952, 1620.

[167] F. Korte, *Chem. Ber.*, 1952, **85**, 1017; F. Korte and E. G. Fuchs, *ibid.*, 1953, **86**, 114.

[168] A. Albert and H. C. S. Wood, *J. Appl. Chem.*, 1952, **2**, 591.

[169] G. B. Elion and G. H. Hitchings, *J. Amer. Chem. Soc.*, 1952, **74**, 3877.

[170] G. R. Ramage and G. Trappe, *J.*, 1952, 4410.

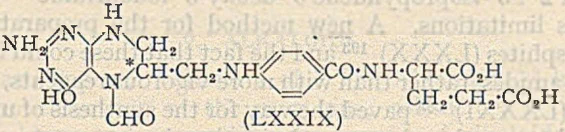
[171] E. C. Taylor and C. K. Cain, *J. Amer. Chem. Soc.*, 1951, **73**, 4384; 1952, **74**, 1644.

[172] E. C. Taylor, *ibid.*, p. 1651. [173] *Idem*, *ibid.*, p. 1648.

[174] R. Tschesche and F. Korte, *Chem. Ber.*, 1952, **85**, 139.

[175] Due to H. G. Khorana; cf. R. Tschesche and F. Korte, *loc. cit.*

Further descriptions of the chemistry [176] and the synthesis [177] of leucovorin (LXXIX) have been published. In the preparation of leucovorin from pteroyl-L-glutamic acid by formylation, reduction and rearrangement, a new asymmetric centre is created at $C_{(6)}$ (marked *), and partial separation of the resulting diastereoisomerides has been effected.[178] The 7-isomer of pteroylglutamic acid has also been synthesised.[179]



(LXXIX)

*Nucleotides and related compounds.* Physical and physico-chemical aspects of pyrimidines, purines, and nucleic acids have been reviewed, together with such other studies as bear on structure.[180] Spectrophotometric patterns have been presented enabling distinction to be made between ribofuranosides and their deoxyribofuranoside analogues; similarly, differences are reported between pyrimidine glycopyranosides and glycofuranosides.[181] Riboflavin-5′ phosphate is simply obtained by warming riboflavin with metaphosphoric acid,[182] and diphosphopyridine nucleotide (cozymase) has been obtained in the form of a crystalline quinine salt.[183]

Substantial progress has been made during the year in the synthesis of nucleotides. Condensation of 5′-trityl adenosine with dibenzyl chlorophosphonate (phosphorochloridate) and removal of protecting groups gave two adenylic acids, identical with adenylic acids *a* and *b* from ribonucleic acids; these are formulated as adenosine-2′ phosphate and -3′ phosphate (not necessarily respectively), and ready phosphoryl migration under acid conditions enables interconversion to take place by way of the cyclic 2′ : 3′-phosphate.[184] Cyclic 2′ : 3′-phosphates of adenosine, cytidine, and uridine have been synthesised. The cytidine and uridine derivatives have been identified as products of incomplete ribonuclease digestion of ribonucleic acids [185] but they are converted respectively into cytidylic acid *b* and uridylic acid *b* by further action of the enzyme, and cytidylic acid *b* is deaminated by alkali to uridylic acid *b*, so that in these two substances the phosphoryl group occupies the same position.[186] It has been suggested on physico-chemical grounds that cytidylic acid *b* is cytidine-3′ phosphate.[187]

---

[176] D. B. Cosulich, B. Roth, J. M. Smith, M. E. Hultquist, and R. P. Parker, *J. Amer. Chem. Soc.*, 1952, **74**, 3252.

[177] B. Roth, M. E. Hultquist, M. J. Fahrenbach, D. B. Cosulich, H. P. Broquist, J. A. Brockman, J. M. Smith, R. P. Parker, E. L. R. Stokstad, and T. H. Jukes, *ibid.*, p. 3247.

[178] D. B. Cosulich, J. M. Smith, and H. P. Broquist, *ibid.*, p. 4215.

[179] C. W. Waller, M. J. Fahrenbach, J. H. Boothe, R. B. Angier, B. L. Hutchings, J. H. Mowat, J. F. Poletto, and J. Semb, *ibid.*, p. 5405; cf. J. H. Boothe, J. H. Mowat, C. W. Waller, R. B. Angier, J. Semb, and A. L. Gazzola, *ibid.*, p. 5407.

[180] D. O. Jordan, *Ann. Rev. Biochem.*, 1952, **21**, 209.

[181] J. J. Fox and D. Shugar, *Biochem. Biophys. Acta*, 1952, **9**, 369.

[182] M. Viscontini, C. Ebnöther, and P. Karrer, *Helv. Chim. Acta*, 1952, **35**, 457.

[183] K. Wallenfels and W. Christian, *Angew. Chem.*, 1952, **64**, 419.

[184] D. M. Brown and A. R. Todd, *J.*, 1952, 44.

[185] D. M. Brown, D. I. Magrath, and A. R. Todd, *ibid.*, p. 2708.

[186] D. M. Brown, C. A. Dekker, and A. R. Todd, *ibid.*, p. 2715.

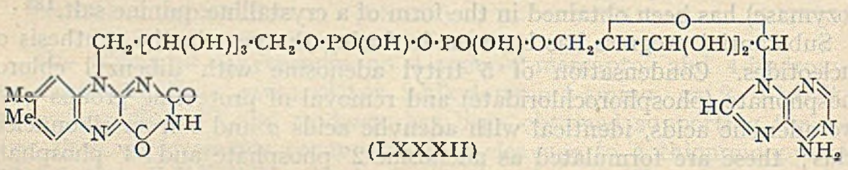
[187] L. F. Cavalieri, *J. Amer. Chem. Soc.*, 1952, **74**, 5804.

Uridine-5′ pyrophosphate has been synthesised [188, 189] and found to be identical with "uridine diphosphate" from the naturally occurring coenzyme "uridine-diphosphate-glucose," [190] and uridine-5′ pyrophosphate linked to an amino-sugar through the reducing group has been isolated from penicillin-treated *Staphylococcus aureus* cells.[191] Adenosine-5′ uridine-5′ phosphate has been synthesised from a suitably protected silver adenosine-5′ phosphate and 2′ : 3′-*iso*propylidene 5′-deoxy-5′-iodouridine [192] but this type of method has limitations. A new method for the preparation of mixed secondary phosphites (LXXX) [193] and the fact that these could be chlorinated with *N*-chloro-amides, rather than with more vigorous reagents, to the chlorophosphonates (LXXXI) [189] paved the way for the synthesis of unsymmetrical diribonucleoside pyrophosphates, culminating in an outstanding achievement: [194] the synthesis of flavin-adenine-dinucleotide ($P_1$-riboflavin-5′ $P_2$-adenosine-5′ dihydrogen pyrophosphate, FAD) (LXXXII), identical with the naturally occurring coenzyme, by condensation of 2′ : 3′-*iso*propylidene adenosine-5′ benzyl chlorophosphonate with the monosilver salt of riboflavin-5′ phosphate and subsequent removal of protecting groups.

(LXXX)

$\mathrm{(RO)(CH_2Ph)P(O)H} \longrightarrow \mathrm{(RO)(CH_2Ph)P(O)Cl}$

(LXXXI)



(LXXXII)

*Vitamin* $B_{12}$. In this field the situation has been complicated by the appearance of *pseudo*vitamin $B_{12}$,[195, 196] which contains adenine instead of 5 : 6-dimethylbenziminazole in the nucleotide portion of the molecule.[195] Fresh spectroscopic evidence has been produced, however, to show that the benziminazole chromophore is present in intact vitamin $B_{12}$ itself,[197] and the spectroscopic examination of authentic synthetic benziminazolo-cobaltous and -cobaltic co-ordination compounds has proved the validity of criteria previously employed in establishing the presence of the related complex in the vitamin.[198] Details have been published of the degradation of vitamin $B_{12}$ to 5 : 6-dimethyl-1-α-D-ribofuranosylbenziminazole (α-ribazole) [199] and of the syntheses of the four 1-D-ribosides of 5 : 6-dimethylbenziminazole.[200]

[188] N. Anand, V. M. Clark, R. H. Hall, and A. R. Todd, *J.*, 1952, 3665.

[189] G. W. Kenner, A. R. Todd, and F. J. Weymouth, *ibid.*, p. 3675.

[190] A. C. Paladini and L. F. Leloir, *Biochem. J.*, 1952, **51**, 426.

[191] J. T. Park, *J. Biol. Chem.*, 1952, **194**, 885.

[192] D. T. Elmore and A. R. Todd, *J.*, 1952, 3681.

[193] N. S. Corby, G. W. Kenner, and A. R. Todd, *ibid.*, p. 3669.

[194] S. M. H. Christie, G. W. Kenner, and A. R. Todd, *Nature*, 1952, **170**, 924.

[195] H. W. Dion, D. G. Calkins, and J. J. Pfiffner, *J. Amer. Chem. Soc.*, 1952, **74**, 1108.

[196] U. J. Lewis, D. V. Tappan, and C. A. Elvehjem, *J. Biol. Chem.*, 1952, **194**, 539; 1952, **199**, 517.

[197] G. H. Beaven and E. R. Holiday, *J. Pharm. Pharmacol.*, 1952, **4**, 344.

[198] M. T. Davies, P. Mamalis, V. Petrow, B. Sturgeon, G. H. Beaven, E. R. Holiday, and E. A. Johnson, *ibid.*, p. 448.

[199] N. G. Brink and K. Folkers, *J. Amer. Chem. Soc.*, 1952, **74**, 2856.

[200] F. W. Holly, C. H. Shunk, E. W. Peel, J. J. Cahill, J. B. Lavigne, and K. Folkers, *ibid.*, p. 4521.

A crystalline 2′- or 3′-phosphate of α-ribazole has now been obtained both by degradation of vitamin $B_{12}$ and by synthesis.[201]

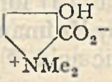
**Macrocyclic Compounds.**—A report on this field must be deferred because of limitations of space, but it may be noted that the subject of chlorophyll has been reviewed exhaustively for the period 1938—1951.[202]

J. W.

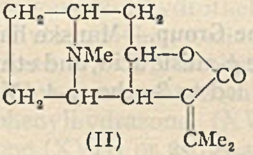
## 9. ALKALOIDS.

Since the last Report,[1] volume 2 of " The Alkaloids " [2] has appeared. This covers the chemistry of the morphine, colchicine, acridine, indole, erythrina, strychnos, and amaryllidaceae groups of alkaloids up to 1951. The biogenesis of alkaloids has been reviewed [3] and has been investigated by means of radioactive carbon.[4]

**Simple Bases.**—Cornforth and Henry have isolated (—)-stachydrine from the fruit of *Capparis tomentosa* Lam. and from the fruit of *Courbonia virgata* A. Brongn. ; both *cis*- and *trans*-3-hydroxystachydrine (I) have been isolated.[5] Both compounds were dehydrated to the same optically inactive anhydro-compound which was reduced to (±)-stachydrine and oxidised to β-dimethylaminopropionic acid.



(I)



(II)

Simple syntheses of mezcaline and trichocereine (*NN*-dimethylmezcaline) [6, 7] and of arecoline [8] have been described. Mezcaline containing $^{14}$C has been prepared.[9]

**Tropane Group.**—The stereochemistry of the tropane alkaloids has been discussed.[10] Lithium aluminium hydride reduction of tropinone gives entirely $\psi$-tropine.[11] The Robinson synthesis has been used for the preparation of 6-hydroxytropinone [12, 13] and 6 : 7-dihydroxytropinone,[13] the intermediate aldehydes being obtained from furan. Pinder has isolated

---

[201] E. A. Kaczka, D. Heyl, W. H. Jones, and K. Folkers, *J. Amer. Chem. Soc.*, 1952, **74**, 5549.

[202] A. Stoll and E. Wiedemann, *Fortschr. chem. Forsch.*, 1952, **2**, 538.

[1] *Ann. Reports*, 1951, **48**, 228.

[2] Ed., R. H. F. Manske and H. L. Holmes; Academic Press, New York, 1952.

[3] (Sir) R. Robinson, *Bull. World Hlth. Org.*, 1952, **6**, 211.

[4] K. Bowden and L. Marion, *Canad. J. Chem.*, 1951, **29**, 1037, 1043; E. Leete, S. Kirkwood, and L. Marion, *ibid.*, 1952, **30**, 749; S. A. Brown and R. U. Byerrum, *J. Amer. Chem. Soc.*, 1952, **74**, 1523.

[5] J. W. Cornforth and A. J. Henry, *J.*, 1952, 597, 601.

[6] K. Banholzer, T. W. Campbell, and H. Schmid, *Helv. Chim. Acta*, 1952, **35**, 1577.

[7] L. Reti and J. A. Castrillón, *J. Amer. Chem. Soc.*, 1951, **73**, 1767.

[8] A. Dobrowsky, *Monatsh.*, 1952, **83**, 443.

[9] W. Block and K. Block, *Chem. Ber.*, 1952, **85**, 1009.

[10] G. Fodor, *Nature*, 1952, **170**, 278; G. Fodor, Ö. Kovács, and L. Mészáros, *Research*, 1952, **5**, 534; B. L. Zenitz, C. M. Martini, M. Priznar, and F. C. Nachod, *J. Amer. Chem. Soc.*, 1952, **74**, 5564; A. Nickon and L. F. Fieser, *ibid.*, p. 5566.

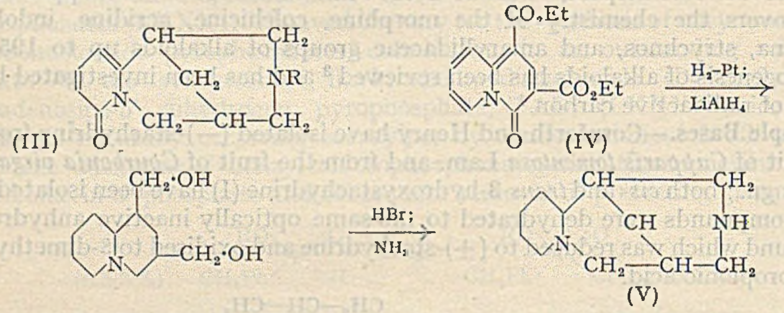
[11] R. Mirza, *Nature*, 1952, **170**, 630.

[12] A. Stoll, B. Becker, and E. Jucker, *Helv. Chim. Acta*, 1952, **35**, 1263.

[13] J. C. Sheehan and B. M. Bloom, *J. Amer. Chem. Soc.*, 1952, **74**, 3825.

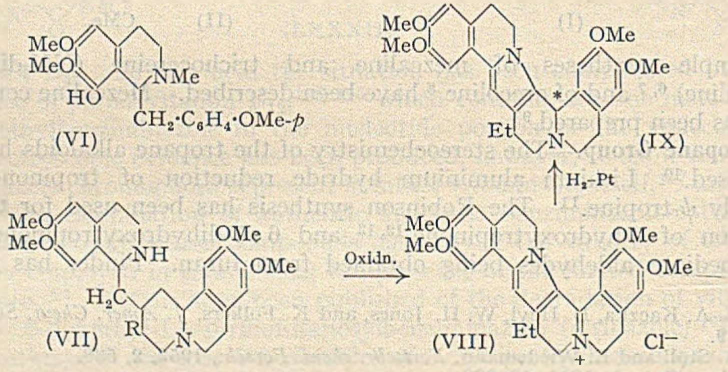
an alkaloid, probably dioscorine, from *Dioscorea hispida* Dennst.;[14] the alkaloid does not appear to have the structure (II) suggested by Gorter[15] since it gave no acetone on ozonolysis. It is an αβ-unsaturated lactone (at least a six-membered ring) containing a *C*-methyl group.

**Lupinane Group.**—Rhombifoline has been shown to possess structure (III; $R = CH_2{\cdot}CH_2{\cdot}CH{:}CH_2$). When heated with hydrogen iodide it gave cytisine (III; R = H); and the latter re-formed rhombifoline on alkylation with but-3-enyl bromide.[16] Deoxytetrahydrocytisine (V) has been synthesised from 1 : 3-dicarbethoxy-4-quinolizone (IV) and resolved *via* the tartrate.[17]



(III) (IV) (V)

*iso***Quinoline Group.**—Manske has deduced formula (VI) for corpaverine; oxidation gave *p*-anisic acid, and ethylation followed by Hofmann degradation and oxidation led to 3-ethoxy-4 : 5-dimethoxyphthalic acid.[18]



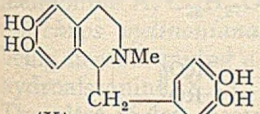
(VI) (IX) (VII) (VIII)

*Emetine* (VII; R = Et).[19] Openshaw and Wood have shown[20] that rubremetinium chloride (VIII) is reduced to two dihydrorubremetines (IX), both substances giving identical colour reactions and differing in stereochemistry at C*. These authors' observations on the oxidation products of emetine differ from those reported by Hazlett and McEwen.[21] A preliminary account of the synthesis of (±)-" c-noremetine " (VII; R = H) has

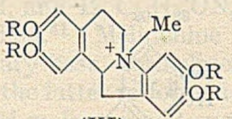
---

[14] A. R. Pinder, *J.*, 1952, 2236. [15] K. Gorter, *Rec. Trav. chim.*, 1911, **30**, 161.
[16] W. F. Cockburn and L. Marion, *Canad. J. Chem.*, 1952, **30**, 92.
[17] F. Galinovsky, O. Vogl, and W. Moroz, *Monatsh.*, 1952, **83**, 242.
[18] R. H. F. Manske, *J. Amer. Chem. Soc.*, 1952, **74**, 2864.
[19] Cf. *Ann. Reports*, 1949, **46**, 202.
[20] H. T. Openshaw and H. C. S. Wood, *J.*, 1952, 391.
[21] R. N. Hazlett and W. E. McEwen, *J. Amer. Chem. Soc.*, 1951, **73**, 2578.

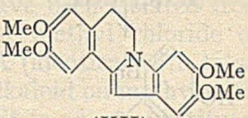
appeared.[22] Oxidation of laudanosoline (X) yields dehydrolaudanosoline (XI; R = H) which is methylated to (XI; R = Me).[23,24] A new alkaloid, $C_{20}H_{24}O_4NI$, related to dehydrolaudanosoline, has been isolated[25] from the bark of *Cryptocarya bowiei* (Hook), Druce, of Northern Queensland. The substance contains three methoxyl groups and yields a monomethyl ether. The latter, on treatment with alkali, gave an optically active methine (A); Hofmann degradation of A led to an optically inactive methine (B) identical with the compound from (XI; R = Me).[23,24] Pyrolysis of the *O*-methyl alkaloid chloride gave the known[23] indole (XII). Bark from Southern Queensland contained an alkaloid, $C_{19}H_{20}O_4NI$, probably of this type, but containing one methylenedioxy-group and one methoxyl group.



(X)



(XI)



(XII)

*Morphine.* The synthesis of morphine has been announced.[26] (±)-β-Δ⁶-Dihydrodeoxycodeine methyl ether (XIII)[27] was resolved, the (+)-form being identical with the substance obtained from natural sources. Hydration of (XIII) with dilute sulphuric acid gave β-dihydrothebainol methyl ether (XIV; R = Me); alkaline demethylation then yielded β-dihydrothebainol (XIV; R = H) which was oxidized to β-dihydrothebainone (XV). Bromination (2 mols.) of this, followed by treatment with 2 : 4-dinitrophenylhydrazine, gave a 2 : 4-dinitrophenylhydrazone (XVI), identical with the product obtained from thebainone (XVII) or β-thebainone (XVII; $C_{(14)}$-epimer) by treatment with 2 : 4-dinitrophenylhydrazine followed by bromination. This reaction involves epimerisation at $C_{(14)}$ of the β-series (*trans* ⟶ *cis*), leading to the natural configuration at $C_{(14)}$ (B–C *cis*). Cleavage of (XVI) with acetone produced 1-bromothebainone which was then reduced to dihydrothebainone (XVIII). Bromination (3 mols.) of (XVIII), followed by treatment with 2 : 4-dinitrophenylhydrazine, gave a small yield of 1-bromocodeinone 2 : 4-dinitrophenylhydrazone (XIX) which was cleaved by acetone to 1-bromocodeinone; the latter was reduced to codeine (XX; R = Me) which had previously been demethylated to morphine (XX; R = H).[28] The biogenesis[29] and the absolute stereochemical configuration[30] of morphine have been discussed. Evidence has been obtained that the ethanamine chain and the $C_{(6)}$-hydroxyl group are *trans* in codeine.[31] An account of the reactions of phenyldihydrothebaine has been published.[32]

---

[22] M. Pailer and H. Strohmayer, *Monatsh.*, 1951, **82**, 1125; 1952, **83**, 1198; cf. M. Pailer, K. Schneglberger, and W. Reifschneider, *ibid.*, 1952, **83**, 513.

[23] R. Robinson and S. Sugasawa, *J.*, 1932, 789.

[24] C. Schöpf and K. Thierfelder, *Annalen*, 1932, **497**, 22.

[25] J. Ewing, G. K. Hughes, E. Ritchie, and W. C. Taylor, *Nature*, 1952, **169**, 618.

[26] M. Gates and G. Tschudi, *J. Amer. Chem. Soc.*, 1952, **74**, 1109.

[27] *Idem*, *ibid.*, 1950, **72**, 4839.

[28] H. Rapoport, C. H. Lovell, and B. M. Tolbert, *ibid.*, 1951, **73**, 5900.

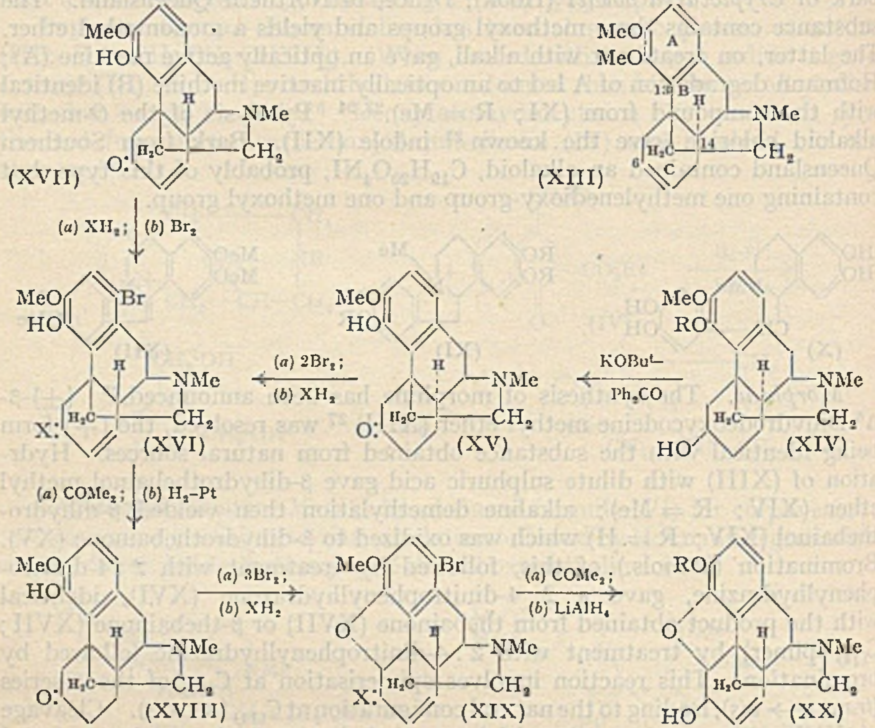
[29] C. Schöpf, *Naturwiss.*, 1952, **39**, 241.

[30] I. R. C. Bick, *Nature*, 1952, **169**, 755.

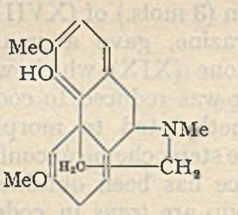
[31] H. Rapoport and G. B. Payne, *J. Amer. Chem. Soc.*, 1952, **74**, 2630.

[32] K. W. Bentley and (Sir) R. Robinson, *J.*, 1952, 947; cf. ref. 2 and L. F. Fieser and M. Fieser, " Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, 1949, p. 19.

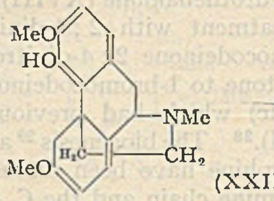
Reduction of thebaine by sodium in liquid ammonia gives dihydrothebaine-$\phi$ (XXI) (phenolic dihydrothebaine) ;[33] this structure is preferred to (XXII) as a result of a study of ultra-violet and infra-red spectra[34] and because it does not add dienophiles.[33] Formula (XXII) is that of the β-dihydrothebaine prepared by Karrer and Schmid.[35] The isomerism of the thebainones has



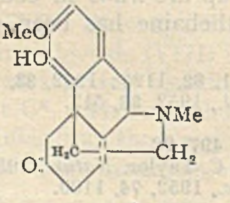
[X = 2 : 4 : 1-$(NO_2)_2C_6H_3\cdot NH\cdot N$]



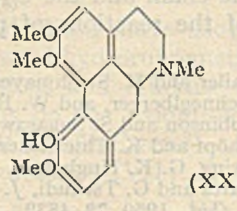
(XXI)



(XXII)



(XXIII)



(XXIV)

---

[33] K. W. Bentley, (Sir) R. Robinson, and A. E. Wain, *J.*, 1952, 958.

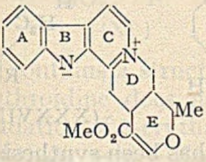
[34] G. Stork, *J. Amer. Chem. Soc.*, 1952, 74, 768.

[35] P. Karrer and H. Schmid, *Helv. Chim. Acta*, 1950, 33, 863.

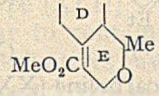
been studied, their nomenclature revised, and structures allotted on the basis of their ultra-violet and infra-red spectra. A fourth thebainone, thebainone-B (XXIII), has been obtained by hydrolysis of dihydrothebainone-$\phi$ (XXI).[36]

**Aporphine Group.**—The structure suggested for artabotrine [37] is incorrect, the substance is identical with *iso*corydine (XXIV).[38]

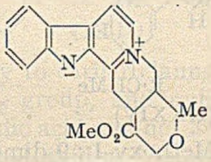
**Indole Group.**—Alstonine (ref. 1, p. 233) has now been isolated from various species of *Rauwolfia*; [39] structure (XXV) is preferred to (XXVI) on the basis of the infra-red spectrum. Serpentine (ref. 1, p. 233) has been found to contain a *C*-methyl group and is now formulated as (XXVII), a dihydro-derivative of alstonine (XXV).[40] Two new quaternary salts, melinonine A, $C_{22}H_{27}O_3N_2Cl$, and B, $C_{20}H_{29}ON_2Cl$, have been isolated from *Strychnos melinoniana* Baillon.[41] Melinonine A lost methyl chloride on being heated, giving a tertiary base, normelinonine A (identical with tetrahydroalstonine, XXVIII); the latter re-formed the alkaloid on methylation. The ultra-violet spectrum of melinonine B suggests it is an αβ-substituted indole. It is suggested that δ-yohimbine and mayumbine are stereoisomers of tetrahydroalstonine (XXVIII).[42] Hydrogenation of sempervirine (XXIX) gave (±)-*allo*yohimbane (XXX) which was resolved *via* the tartrate [43] and found to be identical with the product obtained by Wolff–Kishner reduction of *allo*yohimbone (corynanthidone).[44] Corynantheine (XXXI) appears always to be admixed with dihydrocorynantheine (XXXII),[45] and this explains the results obtained by various workers: [46] (XXXI) gives formaldehyde on ozonolysis, and (XXXII) gives acetic acid on Kuhn–Roth oxidation. Lithium aluminium hydride reduction of dihydrocorynantheine



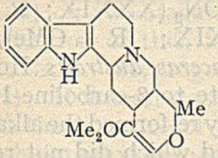
(XXV)



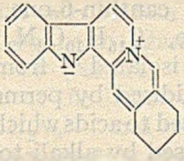
(XXVI)



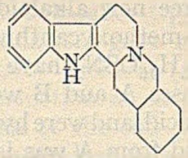
(XXVII)



(XXVIII)



(XXIX)



(XXX)

---

[36] K. W. Bentley and A. E. Wain, *J.*, 1952, 967.

[37] G. Barger and L. J. Sargent, *J.*, 1939, 991.

[38] E. Schlittler and H. U. Huber, *Helv. Chim. Acta*, 1952, 35, 111.

[39] E. Schlittler, H. Schwarz, and F. Bader, *ibid.*, p. 271.

[40] F. Bader and H. Schwarz, *ibid.*, p. 1594.

[41] E. Schlittler and J. Hohl, *ibid.*, p. 29.

[42] R. Goutarel and A. Le Hir, *Bull. Soc. chim.*, 1951, 18, 909; M. M. Janot, R. Goutarel, and J. Massonneau, *Compt. rend.*, 1952, 234, 850.

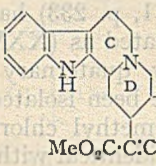
[43] A. Le Hir, R. Goutarel, and M. M. Janot, *ibid.*, 1952, 235, 63; *Bull. Soc. chim.*, 1952, 19, 1091.

[44] A. Le Hir, *Compt. rend.*, 1952, 234, 2613.

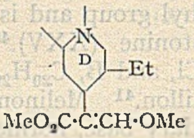
[45] P. Karrer, R. Schwyzer, and A. Flam, *Helv. Chim. Acta*, 1952, 35, 851.

[46] Ref. 1, p. 232; cf. M. M. Janot and R. Goutarel, *Compt. rend.*, 1952, 234, 1562.

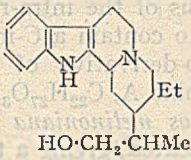
followed by catalytic hydrogenation gave tetrahydrodemethoxycorynantheine alcohol (XXXIII). Dehydrogenation of the last with selenium gave alstyrine (XXXIV; R = H) and a small quantity of methylalstyrine (XXXIV; R = Me); however, palladium dehydrogenation afforded flavocorynanthyrine (XXXV).[45, 47] Similarly, yohimbyl alcohol (XXXVI) with selenium gives a little yobyrine (XXXVII; R = H) and mainly methylyobyrine (XXXVII; R = Me), but use of palladium leads only to yobyrine (XXXVII; R = H).[48]



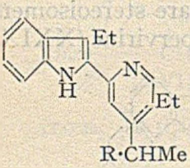
(XXXI)



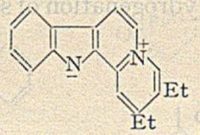
(XXXII)



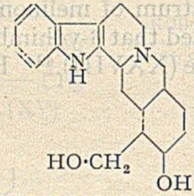
(XXXIII)



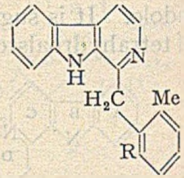
(XXXIV)



(XXXV)



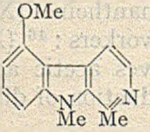
(XXXVI)



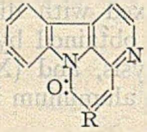
(XXXVII)

5-Methoxy-1 : 9-dimethyl-β-carboline (XXXVIII) has been synthesised[49] and shown to be identical with a degradation product of mitragynine.[50]

Three new alkaloids, (A) canthin-6-one, $C_{14}H_8ON_2$ (XXXIX; R = H), (B) 5-methoxycanthin-6-one, $C_{15}H_{10}O_2N_2$ (XXXIX; R = OMe), and (C) $C_{15}H_{10}OSN_2$ have been isolated[51] from *Pentaceras australis* Hook. f. The bases A and B were oxidised by permanganate to β-carboline-1-carboxylic acid, and were hydrolysed to acids which readily re-formed the alkaloids; the acid from A was isomerised by alkali to an acid which did not re-form the lactam ring; both isomers gave the same dihydro-derivative on reduction. The position of the methoxyl group in B was established by the reaction of the demethylated substance (XXXIX; R = OH) with *o*-phenylenediamine.[52] This ring system has not been previously observed in Nature.



(XXXVIII)



(XXXIX)

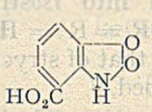
*Gelsemine.* Application of the Hofmann degradation to gelsemine (ref. 1, p. 234) is complicated by the fact that $\overset{+}{\geqslant}$NMe(*b*) alkylates CO·NH(*a*),

---

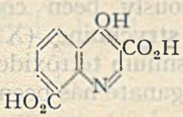
[47] R. Schwyzer, *Helv. Chim. Acta*, 1952, 35, 867.
[48] P. Karrer, R. Schwyzer, A. Flam, and R. Saemann, *ibid.*, p. 865.
[49] J. W. Cook, J. D. Loudon, and P. McCloskey, *J.*, 1952, 3904.
[50] H. R. Ing and C. G. Raison, *J.*, 1939, 986.
[51] H. F. Haynes, E. R. Nelson, and J. R. Price, *Austral. J. Sci. Res.*, 1952, 5, *A*, 387.
[52] E. R. Nelson and J. R. Price, *ibid.*, p. 563.

giving CO·NMe(*a*); for example, the substance described as *N*-demethylgelsemine[53] is actually *N*(*a*)-methylgelsemine. It is reduced by lithium aluminium hydride to deoxydihydro-*N*(*a*)-methylgelsemine. The latter is also obtained from deoxydihydrogelsemine by formylation, followed by lithium aluminium hydride reduction.[54] Heating gelsemine with tetramethylammonium hydroxide yields *N*(*a*)-methylgelsemine.[55]

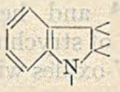
β-*Erythroidine.* None of the structures suggested for β-erythroidine (ref. 1, p. 230) has been accepted by Boekelheide and his colleagues.[56] These workers find that *apo*-β-erythroidine, $C_{15}H_{15}O_2N$, is readily dehydrogenated to dehydro*apo*-β-erythroidine, $C_{15}H_{13}O_2N$; the latter is a lactone, giving an indole colour reaction (Ehrlich). Alkaline permanganate oxidises dehydro-*apo*-β-erythroidine to 2-amino*iso*phthalic acid, isatin-7-carboxylic acid (XL), and 4-hydroxyquinoline-3 : 8-dicarboxylic acid (XLI), the last not giving 2-amino*iso*phthalic acid on oxidation. Similar oxidation of *apo*-β-erythroidine afforded (XL) and (XLI). These observations indicate that *apo*-β-erythroidine contains a structure of type (XLII). Contrary to earlier claims, *apo*-β-erythroidine does not appear to contain a $:CH_2$ group, and oxidative degradation of β-erythroidine derivatives gave phthalic acid and not 3-methoxyphthalic acid. Hofmann degradation of *apo*-β-erythroidine[57] shows the presence of $(\cdot CH_2\cdot CH_2\cdot)_2N-$. De-*N*-methyldihydro-β-erythroidinol (XLIII; R = OH) on two-stage Hofmann degradation gave a substance $C_{15}H_{18}O_2$, and reduction of this, followed by permanganate oxidation, gave *o*-ethylbenzoic acid. Hydrogenolysis of (XLIII; R = OH) yielded (XLIII; R = H); Hofmann degradation of the latter with reduction at each stage showed the presence of $(\cdot CH_2\cdot CH_2\cdot)_2N\cdot$, and ozonolysis of the end product gave ethyl methyl ketone. A consideration of these results lead to structure (XLIV) for β-erythroidine, and (XLV) for *apo*-β-erythroidine.



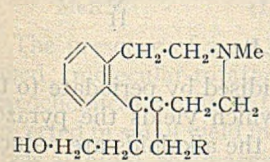
(XL)



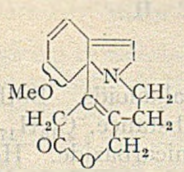
(XLI)



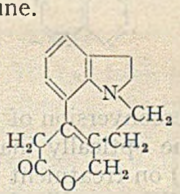
(XLII)



(XLIII)



(XLIV)



(XLV)

*Strychnos* **Alkaloids.**—The long suspected relation between α-colubrine (XLXVI; R = H, R′ = OMe), β-colubrine (XLVI; R = OMe, R′ = H), and strychnine (XLVI; R = R′ = H) has been established.[58] Lithium alu-

---

[53] R. Goutarel, M. M. Janot, V. Prelog, and R. P. A. Sneeden, *Helv. Chim. Acta*, 1951, **34**, 1962.

[54] T. Habgood, L. Marion, and H. Schwarz, *ibid.*, 1952, **35**, 638.

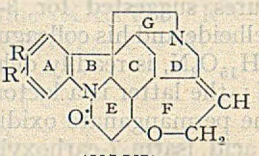
[55] V. Prelog, J. B. Patrick, and B. Witkop, *ibid.*, p. 640.

[56] M. F. Grundon and V. Boekelheide, *J. Amer. Chem. Soc.*, 1952, **74**, 2637.

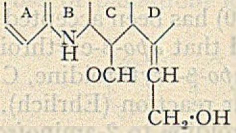
[57] V. Boekelheide, M. F. Grundon, and J. Weinstock, *ibid.*, p. 1866.

[58] S. P. Findlay, *ibid.*, 1951, **73**, 3008.

minium hydride reduction of the colubrines gave the corresponding colubridines which were then oxidised to 2 : 3-diketonucidine, the oxidation product of strychnidine.[59] A new alkaloid, novacine (*N*-methyl-*sec.*-*pseudo*brucine), has been isolated from *Strychnos nux-vomica* seeds.[60] Boit has continued his degradative studies on *pseudo*brucine.[61] Phenols have been found to form solid complexes with certain strychnine derivatives.[62] The

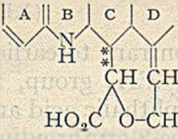


(XLVI)

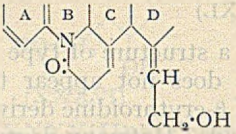


(XLVII)

Wieland–Gumlich aldehyde (XLVII) has been condensed with malonic acid, forming *iso*strychnic acid (XLVIII ; inversion at C* relative to strychnine).[63] *iso*Strychnic acid had previously been converted into *iso*strychnine-I (XLIX),[64] and hence into strychnine (XLVI ; R = R′ = H).[65] The oxidation of strychnine with osmium tetroxide,[66] and that of strychnine and brucine *N*-oxides with permanganate has been described.[67]

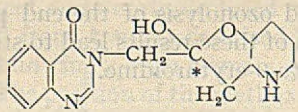


(XLVIII)

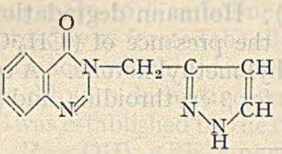


(XLIX)

**Quinazolone Group.**[68]—Koepfli, Brockman, and Moffat [69] consider febrifugine and *iso*febrifugine, $C_{16}H_{19}O_3N_3$, to be isomers of (L), the semiketal of (LII), differing in stereochemistry at C*. This explains the ready



(L)



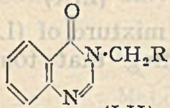
(LI)

interconversion of the two alkaloids. Both are oxidised by periodate to the same optically inactive substance, $C_{16}H_{17}O_3N_3$, which yields the pyrazole (LI) on treatment with semicarbazide. However, the alkaloids are reduced to different dihydro-derivatives, and febrifugine forms carbonyl derivatives

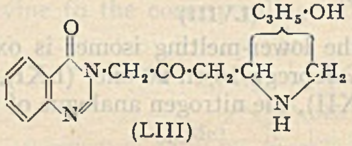
---

[59] H. Leuchs and H. S. Overberg, *Ber.*, 1931, **64**, 1009.
[60] W. F. Martin, H. R. Bentley, J. A. Henry, and F. S. Spring, *J.*, 1952, 3603.
[61] H. G. Boit, *Chem. Ber.*, 1952, **85**, 19, 106.
[62] J. T. Edward and (Sir) R. Robinson, *J.*, 1952, 1080.
[63] (Sir) R. Robinson and J. E. Saxton, *J.*, 1952, 982.
[64] H. G. Boit, *Ber.*, 1951, **84**, 16.
[65] V. Prelog, J. Battegay, and W. I. Taylor, *Helv. Chim. Acta*, 1948, **31**, 2244.
[66] A. Kogure and M. Kotake, *J. Inst. Polytech. Osaka City Univ.*, 1951, sec. C2, 39 (*Chem. Abs.*, 1952, **46**, 6131).
[67] K. Hirayama, *ibid.*, p. 45.
[68] Cf. *Ann. Reports*, 1949, **46**, 210.
[69] J. B. Koepfli, J. A. Brockman, and J. Moffat, *J. Amer. Chem. Soc.*, 1950, **72**, 3323.

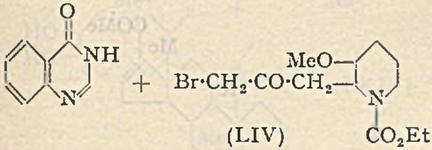
whilst *iso*febrifugine does not.[70] Febrifugine has also been isolated from hydrangea leaves.[71] Permanganate oxidation gave 3-carboxymethyl-4-quinazolone (LII; R = $CO_2H$), zinc dust distillation afforded the ketone (LII; R = Ac), and the alkaloid contained a carbonyl group, a hydroxyl group, and a *sec.*-amino-group, indicating a structure of type (LIII).[72] The racemic form of the alkaloid (LV) has been synthesised by treating ethyl 2-3′-bromoacetonyl-3-methoxypiperidine-1-carboxylate (LIV) with quinazol-4-one and then removing the protecting groups.[73]



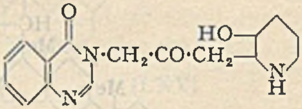
(LII)



(LIII)

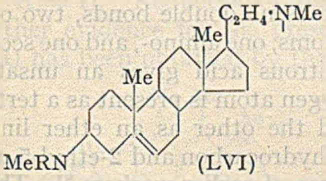


(LIV)

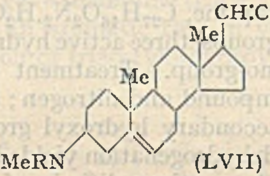


(LV)

**Steroid Alkaloids.**—A 3β-dimethylaminopregn-5-ene structure (LVI; R = Me) has been suggested for conessine.[74] This is in agreement with the optical rotation, ultra-violet, and infra-red spectral data. Degradation of conessine by von Braun's method affords *iso*conessimine (LVI; R = H).[75] Hofmann degradation of the *N*-acetyl derivative (LVI; R = Ac), followed by Emde reduction, gave (LVII; R = Ac) identical with the substance prepared by reaction of 3β-toluene-*p*-sulphonyloxypregna-5 : 20-diene with methylamine followed by acetylation of the resulting amine (LVII; R = H).



(LVI)



(LVII)

The presence of a *sec.*-amino-group in solasodine (LVIII) has been confirmed; molecular-rotation differences indicate that solasodine has the same stereochemical configuration as cholesterol; *N*-nitrososolasodine has been converted in small yield into diosgenin (LIX), confirming structure (LVIII).[76] A new alkaloid, solamargine, has been isolated [77] from *Solanum marginatum*; complete hydrolysis gave rhamnose, glucose, and solasodine (LVIII); partial hydrolysis yielded solasodine β-glucoside.

Tomatidine yields a diacetyl derivative (m. p. 194°) containing >NAc,

---

[70] J. B. Koepfli, J. F. Mead, and J. A. Brockman, *J. Amer. Chem. Soc.*, 1949, **71**, 1048.

[71] F. Ablondi, S. Gordon, J. Morton, and J. H. Williams, *J. Org. Chem.*, 1952, **17**, 14.

[72] B. L. Hutchings, S. Gordon, F. Ablondi, C. F. Wolf, and J. H. Williams, *ibid.*, p. 19.

[73] B. R. Baker, R. E. Schaub, F. J. McEvoy, and J. H. Williams, *ibid.*, p. 133.

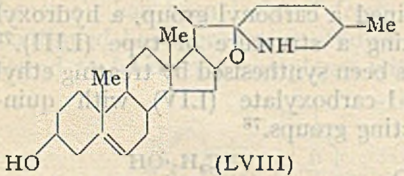
[74] R. D. Haworth, J. McKenna, R. G. Powell, and H. G. Whitfield, *Chem. and Ind.*, 1952, 215.

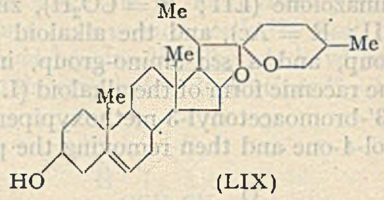
[75] S. Siddiqui, *Proc. Indian Acad. Sci.*, 1936, 3, *A*, 249, 257.

[76] L. H. Briggs and T. O'Shea, *J.*, 1952, 1654.

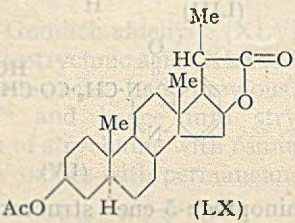
[77] L. H. Briggs, E. G. Brooker, W. E. Harvey, and A. D. Odell, *ibid.*, p. 3587.

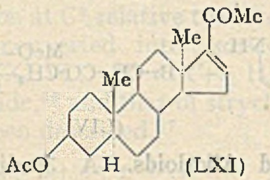
which is isomerised by light to a compound (m. p. 92°) containing –NHAc. The former product is oxidised by chromic acid to 3-acetyltigogenin lactone

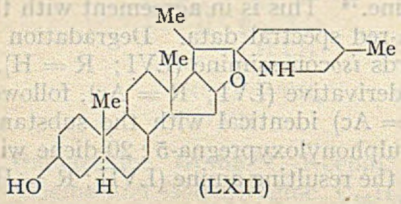

(LVIII)

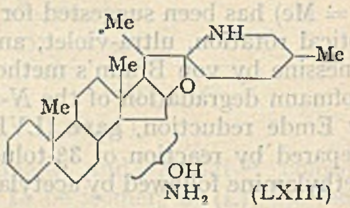

(LIX)

(LX);[78] the lower-melting isomer is oxidised to a mixture of (LX) and 3β-acetoxy*allo*pregn-16-en-20-one (LXI),[78, 79] suggesting that tomatidine may be (LXII), the nitrogen analogue of tigogenin.[78]

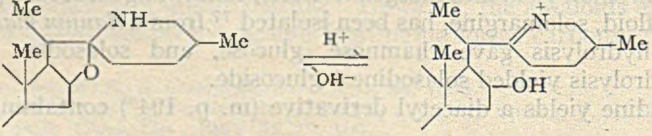

(LX)


(LXI)


(LXII)


(LXIII)

Solanocapsine, $C_{27}H_{46}O_2N_2,H_2O$, contains no double bonds, two or three *C*-methyl groups, three active hydrogen atoms, one amino-, and one secondary cyclic imino-group. Treatment with nitrous acid gives an unsaturated nitroso-compound and nitrogen; one oxygen atom is present as a tertiary or hindered secondary hydroxyl group, and the other as an ether linkage.[80] Selenium dehydrogenation yielded Diels' hydrocarbon and 2-ethyl-5-methylpyridine, observations differing from those of earlier workers.[81] These reactions lead to a formula of type (LXIII; stereochemistry unknown). Infrared spectral studies indicate that salt formation by this type of structure involves opening of the ether ring.



Careful hydrolysis of cevadine gives cevagenine and angelic acid; similarly veratridine gives veratric acid and cevagenine.[82] Further action of

---

[78] R. Kuhn and I. Löw, *Chem. Ber.*, 1952, 85, 416.

[79] Y. Sato, A. Katz, and E. Mosettig, *J. Amer. Chem. Soc.*, 1952, 74, 538.

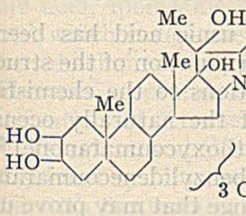
[80] E. Schlittler and H. Uehlinger, *Helv. Chim. Acta*, 1952, 35, 2034, 2608.

[81] G. Barger and H. L. Fraenkel-Conrat, *J.*, 1936, 1537.

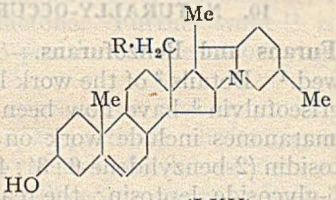
[82] A. Stoll and E. Seebeck, *Helv. Chim. Acta*, 1952, 35, 1270, 1942; cf. N. Elming, C. Vogel, O. Jeger, and V. Prelog, *ibid.*, p. 2541.

alkali isomerises cevagenine to the known cevine. Hence cevagenine is the true alkamine; its infra-red spectrum is similar to that of the alkaloids and shows the presence of a carbonyl group. This group is absent in cevine. Reduction of cevadine produces two dihydrocevadines; both these yield cevagenine on hydrolysis, but one gives (+)-α-methylbutyric acid and the other the (—)-isomer. Cevagenine contains a keto-group and seven hydroxyl groups; a consideration of its reactions lead to a formula of type (LXIV).

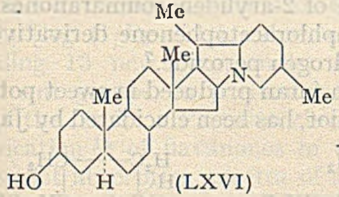
The skeleton of *iso*rubijervine (LXV; R = OH) has been established by the oxidation of dihydro*iso*rubijervine to the corresponding aldehyde and reduction of the latter to solanidan-3β-ol (LXVI),[83] and also by reaction of the toluene-*p*-sulphonic ester of *iso*rubijervine with potassium iodide to give (LXV; R = I). Reduction of this iodide gave solanidine (LXV; R = H).[84]



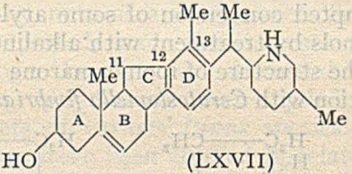
(LXIV)



(LXV)

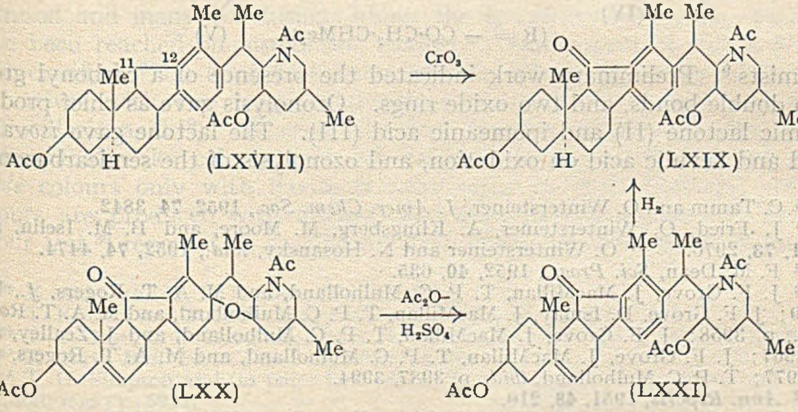


(LXVI)



(LXVII)

Further evidence for the presence of an aromatic ring in veratramine (LXVII) has been obtained by the nitration of triacetyldihydroveratramine



(LXVIII); the resulting nitro-compound was reduced to a diazotisable amine. *N*-Acetylveratramine has been oxidised to an αβ-unsaturated

---

[83] D. Burn and W. Rigby, *Chem. and Ind.*, 1952, 668.
[84] S. W. Pelletier and W. A. Jacobs, *J. Amer. Chem. Soc.*, 1952, 74, 4218.

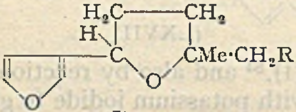
ketone, indicating that ring B is not aromatic.[85] Triacetyldihydroveratramine (LXVIII) has been oxidised by chromic acid to a ketone (LXIX) whose chemical and spectral properties indicate a carbonyl group at $C_{(11)}$. *ON*-Diacetyljervine (LXX) is converted on acetolysis into a triacetate having an indanone structure (LXXI).[86] This has now been reduced to (LXIX), identical with the product from veratramine, establishing the relation between veratramine and jervine.[87]

A. S. B.

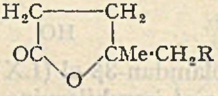
## 10. NATURALLY-OCCURRING OXYGEN RING COMPOUNDS.

**Furans and Benzofurans.**—The chemistry of usnic acid has been reviewed.[1] Details [2] of the work leading to the determination of the structure of griseofulvin [3] have now been given. Contributions to the chemistry of coumaranones include work on the synthesis [4] of the naturally occurring leptosidin (2-benzylidene-6 : 3′ : 4′-trihydroxy-7-methoxycoumaranone) [5] and its 6-glycoside, leptosin; the rearrangement [6] of 2-benzylidenecoumaranones under weakly alkaline conditions to flavones, a change that may prove useful in flavone synthesis; and the formation of 2-arylidenecoumaranones in the attempted conversion of some arylidenephloracetophenone derivatives into flavonols by treatment with alkaline hydrogen peroxide.[7]

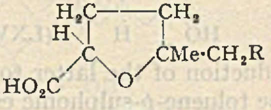
The structure of ipomeamarone (I),[8] a furan produced in sweet potato by infection with *Ceratostomella fimbriata* Elliot, has been elucidated by Japanese chemists.[9] Preliminary work indicated the presence of a carbonyl group, two double bonds, and two oxide rings. Ozonolysis gave as chief products ipomic lactone (II) and ipomeanic acid (III). The lactone gave *iso*valeric acid and lævulic acid on oxidation, and ozonolysis of the semicarbazone of



(I)



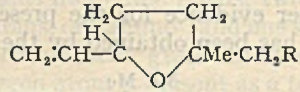
(II)



(III)

$MeO_2C{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CHR$

(IV)



$(R = -CO{\cdot}CH_2{\cdot}CHMe_2)$

(V)

---

[85] C. Tamm and O. Wintersteiner, *J. Amer. Chem. Soc.*, 1952, **74**, 3842.

[86] J. Fried, O. Wintersteiner, A. Klingsberg, M. Moore, and B. M. Iselin, *ibid.*, 1951, **73**, 2970.

[87] O. Wintersteiner and N. Hosansky, *ibid.*, 1952, **74**, 4474.

[1] F. M. Dean, *Sci. Progr.*, 1952, **40**, 635.

[2] J. F. Grove, J. MacMillan, T. P. C. Mulholland, and M. A. T. Rogers, *J.*, 1952, 3949; J. F. Grove, D. Ismay, J. MacMillan, T. P. C. Mulholland, and M. A. T. Rogers, *ibid.*, p. 3958; J. F. Grove, J. MacMillan, T. P. C. Mulholland, and J. Zealley, *ibid.*, p. 3967; J. F. Grove, J. MacMillan, T. P. C. Mulholland, and M. A. T. Rogers, *ibid.*, p. 3977; T. P. C. Mulholland, *ibid.*, p. 3987, 3994.

[3] *Ann. Reports*, 1951, **48**, 210.

[4] T. A. Geissman and W. Mojé, *J. Amer. Chem. Soc.*, 1951, **73**, 5765.

[5] T. A. Geissman and C. D. Heaton, *ibid.*, 1943, **65**, 677.

[6] D. M. Fitzgerald, E. M. Philbin, and T. S. Wheeler, *Chem. and Ind.*, 1952, 130.

[7] H. Ozawa and M. Kawanishi, *J. Pharm. Soc. Japan*, 1951, **71**, 1186.

[8] I. Oze and M. Hiura, *Ann. Rep. Jap. Veget. Path.*, 1939, **9**, 123.

[9] T. Kubota and T. Matsuura, *Proc. Japan Acad.*, 1952, **8**, 44, 83, 198.

the compound (IV) obtained by dehydration of the methyl ester formed on ring-opening of the lactone gave chiefly methyl lævulate and *iso*butylglyoxal semicarbazone. The structure (IV) of the keto-acid, thus deduced, was confirmed by synthesis, and the point of attachment of the carboxyl group in (III) was proved by degradation to the lactone (II). The furan structure of the remaining $C_{(4)}$ moiety was shown by colour tests, the formation of Diels–Alder adducts, and by a degradation[10] typical of $\alpha\alpha'$-unsubstituted furans, in which the adduct with acetylenedicarboxylic ester was partially reduced and heated, giving furan-3 : 4-dicarboxylic ester and an olefin (V). The olefin, on oxidative decomposition of its ozonide, gave formic acid, ipomeanic acid, and ipomic lactone. Further work[11] is described which independently confirmed the position of the carbonyl group in the side chain of ipomeamarone.

**Flavones.**—Several useful papers have appeared on the separation and identification of flavone derivatives by paper partition chromatography. Gage, Douglass, and Wender[12] give the $R_F$ values of 38 flavone derivatives in 11 solvent systems and also the colours produced on paper by each compound with 8 sprays in both visible and ultra-violet light. Paris[13] gives $R_F$ values in various solvents of 41 flavone derivatives. In two papers[14] the $R_M$ [log $(1/R_F - 1)$] values of many natural and synthetic flavones (including 13 new compounds) are reported, and the interactions of substituent groups, in particular hydrogen bonding, are discussed in the light of the results. Partition chromatography has also been applied to the identification[15] of flavanones in extracts of various *Pinus* species. The ultra-violet absorption spectra of flavones have been studied in relation to their structure by Briggs and Locker[16] who also discuss the effects of structure on the acidity and basicity of flavones. The determination of the ultra-violet absorption spectra of substances, including flavones, *iso*flavones, and coumarins, present as spots on paper after chromatography has been investigated[17] as an analytical method.

The literature concerning colour reactions of flavones is notoriously confused and many conclusions about the specificity of certain reactions have been reached on insufficient evidence. One aspect of this field has been clarified[18] by an investigation of the colours given by 57 flavone derivatives with two reagents (magnesium–hydrochloric acid and zinc–hydrochloric acid[19]). Whereas the first reagent appears to give stable anthocyanidin-like colours with all flavone derivatives, the second gives *stable* colours only with flavonols substituted in the 3-position; fading colours are produced with flavones and 3-hydroxyflavanones. A further colour test,[20] reported as specific for flavanones, depends on the formation

[10] K. Alder and H. F. Rickert, *Ber.*, 1937, **70**, 1354.
[11] T. Kubota and T. Matsuura, *J. Chem. Soc. Japan*, 1952, **73**, 530.
[12] T. B. Gage, C. D. Douglass, and S. H. Wender, *Analyt. Chem.*, 1951, **23**, 1582.
[13] R. Paris, *Bull. Soc. Chim. biol.*, 1952, **34**, 767.
[14] T. H. Simpson and (in part) L. Garden, *J.*, 1952, 4638; B. L. Shaw and T. H. Simpson, *ibid.*, p. 5027.
[15] G. Lindstedt and H. Misiorny, *Acta Chem. Scand.*, 1952, **6**, 744.
[16] L. H. Briggs and R. H. Locker, *J.*, 1951, 3136.
[17] A. E. Bradfield and A. E. Flood, *J.*, 1952, 4740.
[18] M. Shimizu, *J. Pharm. Soc. Japan*, 1951, **71**, 1329; 1952, **72**, 338.
[19] J. C. Pew, *J. Amer. Chem. Soc.*, 1948, **70**, 3031.
[20] S. Shibata and A. Kasahara, *J. Pharm. Soc. Japan*, 1952, **72**, 1386.

of a blue fluorescent spot (ultra-violet light) when the compound, on paper, is sprayed with magnesium acetate.

Experiments on the isolation, identification, and synthesis of flavones continue. New flavone derivatives isolated include ayanin [21] from the timber of *Distemonanthus Benthamianus*, shown by degradation and synthesis to be 3 : 7 : 4′-trimethylquercetin; 3-*O*-rhamnoglucosidylkæmpferol [22] from the leaves of *Hyptis capitata* and *Dryopteris oligophlebia*; rhoifolin (7-*O*-rhamnoglucosidylapigenin) from both the Japanese wax tree [23] (*Rhus succedenia*) and the peel of the ripe fruit of Japanese varieties of *Citrus aurantium* [24] where it is accompanied by naringin (the peel of European varieties of this plant contains only hesperidin [25]); a new glycoside of genkwanin from the bark of the Japanese cherry; [26] and astilbin (a rhamnoside of 3 : 5 : 6 : 3′ : 4′-pentahydroxyflavanone) from *Astilbe Thurbergii* [27] which also contains quercetin and the *iso*coumarin, bergenin. The substance aromadendrin, long known to occur in the kinos of many *Eucalyptus* species, has been identified [28] as dihydrokæmpferol which is also identical with katuranin.[29] In the light of new evidence the structure of meliternatin has been modified.[30]

Several known flavones have been isolated from new sources, including quercetin and its 3-glucoside (by the use of ion-exchange resins) from grapes [31] and black currants,[32] and from a variety of *Rosa polyantha*; [33] rutin from date-palm pollen [34] and the leaves of *Grevillea robusta*; [35] and naringenin from the timber of *Ferreirea spectabilis*.[36]

Synthetic investigations in the field include the synthesis of 5 : 4′-dimethoxyfurano(3″ : 2″-6 : 7)flavone and 7 : 4′-dimethoxyfurano(2″ : 3″-5 : 6) flavone,[37] possibly isomeric with, but shown not to be identical with, gingketin.[38] During experiments on the solubilising of flavones with boric acid [39] an observation has been made which may prove useful in the synthesis of partially methylated compounds. In the presence of borate, diazomethane fails to methylate not only the 5-hydroxyl, but also vicinal hydroxyl, groups; rutin can thus be methylated to the 7-methyl ether, and quercetin to the 3 : 7-dimethyl ether. Addition of boric acid also improves the reduction [40] of flavonols to hydroxyflavanones by dithionite.[19]

***iso*Flavones.**—A new *iso*flavone, muningin (6 : 4′-dihydroxy-5 : 7-di-

---

[21] F. E. King, T. J. King, and K. Sellars, *J.*, 1952, 92.

[22] K. Kobayashi, *J. Pharm. Soc. Japan*, 1952, **72**, 1; K. Kobayashi and K. Hayashi, *ibid.*, p. 3.

[23] S. Hattori and H. Matsuda, *Arch. Biochem.*, 1952, **37**, 85.

[24] S. Hattori, M. Shimokoriyama, and M. Kanao, *J. Amer. Chem. Soc.*, 1952, **74**, 3614.

[25] F. Kolle and K. E. Gloppe, *Pharm. Zentralh.*, 1936, **77**, 421.

[26] T. Ohta, *J. Pharm. Soc. Japan*, 1952, **73**, 456.

[27] H. Shimada, T. Sawada, and S. Fukuda, *ibid.*, p. 578.

[28] W. E. Hillis, *Austral. J. Sci. Res.*, 1952, **5**, 379.

[29] H. Voda, B. Fukushima, and T. Kondô, *J. Agric. Soc. Japan*, 1943, **19**, 467.

[30] L. H. Briggs and R. H. Locker, *J.*, 1951, 3131.

[31] B. L. Williams and S. H. Wender, *J. Amer. Chem. Soc.*, 1952, **74**, 4372.

[32] B. L. Williams, C. H. Ice, and S. H. Wender, *ibid.*, p. 4566.

[33] T. Ohta and T. Myazaki, *J. Pharm. Soc. Japan*, 1951, **71**, 1281.

[34] M. S. El Ridi, L. A. Strait, and M. H. Aboul Wafa, *Arch. Biochem.*, 1952, **39**, 317.

[35] K. Kobayashi, *J. Pharm. Soc. Japan*, 1951, **71**, 1493.

[36] F. E. King, M. F. Grundon, and K. G. Neill, *J.*, 1952, 4580.

[37] A. Kogure, *J. Chem. Soc. Japan*, 1952, **73**, 271, 308.

[38] W. Baker and W. H. C. Simmonds, *J.*, 1940, 1370.

[39] M. Shimizu *et al.*, *J. Pharm. Soc. Japan*, 1951, **71**, 875 *et seq.*

[40] M. Shimizu and T. Yoshikawa, *ibid.*, 1952, **72**, 331.

methoxy*iso*flavone) has been isolated[41] from the heartwood of *Pterocarpus angolensis* which also contains a small amount of prunetin.[42] Formononetin and genistein have been isolated from subterranean clover,[43] and genistein has been shown to be œstrogenic. Two independent groups of workers have isolated simple dihydro*iso*flavones, previously known in Nature only as complex derivatives, from natural sources. Indian workers on the constituents of *Prunus puddum*, known to contain prunetin as well as genkwanin and sakuranetin,[44] have isolated two new substances,[45] the glycoside padmakastin and its aglycone padmakastein. The latter was identified as dihydroprunetin (2 : 3-dihydro-5 : 4′-dihydroxy-7-methoxy*iso*flavone) by synthesis and by dehydrogenation to prunetin derivatives (by the action of selenium dioxide on the acetate). British workers[36] isolated from *Ferreirea spectabilis*, in addition to biochanin-A (4-methylgenistein) and naringenin, two compounds ferreirin and homoferreirin. Dehydrogenation (palladised charcoal), oxidation, and synthesis of the fully methylated derivatives established both compounds as derivatives of 5 : 7 : 2′ : 4′-tetrahydroxy*iso*flavanone; investigation of the ethyl ethers established the structures[46] of the natural compounds as, respectively, 5 : 7 : 2′-trihydroxy-4′-methoxy- and 5 : 7-dihydroxy-2′ : 4′-dimethoxy-*iso*flavanone.

A new synthetic route to *iso*flavones has been developed[47] which is particularly useful for the direct preparation of hydroxylated derivatives. The appropriate deoxybenzoin is treated, in pyridine, with ethoxalyl chloride, giving the 2-carbethoxy*iso*flavone, readily hydrolysed and decarboxylated under mild conditions. By this method biochanin-A, genistein, *ψ*-baptigenin, and 5 : 7 : 2′-trihydroxy*iso*flavone[48] have been made. The last was not identical with an aglycone from a soya-bean glycoside which had been allotted this structure.[49] The synthesis[42] from biochanin-A of 7 : 4′-dihydroxy-5-methoxy*iso*flavone, the so-called prunusetin[44] from *Prunus puddum*, does not give the substance described as occurring naturally, which was probably impure prunetin. The method of nuclear oxidation with persulphate, well known in the flavone field, has been successfully applied to several *iso*flavones.[50]

**Miscellaneous Benzopyrones and Coumarins.**—The first natural naphthopyrone, eleutherinol, has been found[51] in *Eleuthera bulbosa*;[52] only 500 mg. were obtained but the structure has been unambiguously established as (VI). Analysis, colour tests, the formation of a piperonylidene derivative of the dimethyl ether, and alkaline degradation [which gave acetone, acetic acid, a trihydroxy-ketone (VII ; R = Ac, R′ = H), and a small amount of a trihydroxy-compound (VII ; R = R′ = H)] indicated that the substance

---

[41] F. E. King, T. J. King, and A. J. Warwick, *J.*, 1952, 96.

[42] F. E. King and L. Jurd, *J.*, 1952, 3211.

[43] R. B. Bradbury and D. E. White, *J.*, 1951, 3447.

[44] D. Chakravarti and C. Bhar, *J. Indian Chem. Soc.*, 1945, **22**, 301.

[45] N. Narasimhachari and T. R. Seshadri, *Proc. Indian Acad. Sci.*, 1952, **35**, *A*, 202.

[46] F. E. King and K. G. Neill, *J.*, 1952, 4752.

[47] W. Baker and W. D. Ollis, *Nature*, 1952, **169**, 706.

[48] W. Baker, J. H. Harborne, and W. D. Ollis, *Chem. and Ind.*, 1952, 1058.

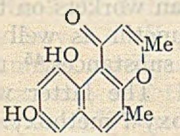
[49] K. Okano and I. Beppu, *J. Agric. Chem. Soc. Japan*, 1939, **15**, 645.

[50] N. Narasimhachari, L. R. Row, and T. R. Seshadri, *Proc. Indian Acad. Sci.*, 1952, **35**, *A*, 46.

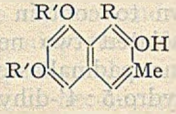
[51] A. Ebnöther, Th. M. Meijer, and H. Schmid, *Helv. Chim. Acta*, 1952, **35**, 910.

[52] Cf. *Ann. Reports*, 1950, **47**, 226.

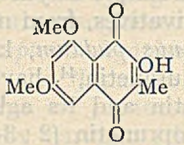
was a dihydroxy-2-methylchromone with one further methyl group (Kuhn-Roth). Alkaline degradation of dimethyleleutherinol gave the corresponding derivatives (VII; R = Ac, R′ = Me, and R = H, R′ = Me); oxidation of the former gave 3 : 5-dimethoxyphthalic anhydride, and of the latter



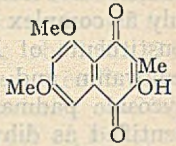
(VI)



(VII)



(VIII)



(IX)

(lead tetra-acetate) gave a mixture of a 2-hydroxy-dimethoxy-methyl-1 : 4-naphthaquinone and the corresponding dimethoxy-methyl-1 : 2-naphthaquinone. The data thus obtained did not distinguish between the two structures (VIII) and (IX) for the 1 : 4-quinone, but an unambiguous synthesis [53] of both quinones identified the degradation product as (VIII), and the structure (VI) for eleutherinol followed. Some analogous naphthopyrones have been synthesised by standard methods.[54]

Several papers concerning the chemistry of khellin and its analogues have appeared; visnagin has been converted into the more physiologically active khellin by a process which makes use of nuclear oxidation with persulphate; [55] khellol [56] and a visnagin isomer [5-methoxy-2-methylfurano(2′ : 3′-7 : 8)(2 : 3-benzopyrone)] [57] have been prepared by standard methods.

Work on natural coumarins has been largely confined to the analytical field. Paper chromatographic studies of coumarins have been published by two schools.[58, 59] Spectral studies are represented by a paper [60] on the variation of fluorescence spectrum with pH of 59 coumarin derivatives, and a variety of coumarins and furanocoumarins have been investigated polarographically.[61]

**Lactones and Lactols.**—A series of closely argued papers [62] on the structure of picrotoxin has appeared but the investigations described are not yet sufficiently complete to allow final conclusions to be reached. Further details [63] have now appeared concerning the synthesis of picrotoxadiene and its production from picrotoxinin.[64] The lignan arctigenin (β-3 : 4-dimethoxybenzyl-α-4-hydroxy-3-methoxybenzylbutyrolactone) [65] has been synthesised.[66]

---

[53] H. Schmid and M. Burger, *Helv. Chim. Acta*, 1952, **35**, 928.

[54] H. Schmid and H. Seiler, *ibid.*, p. 1990.

[55] S. K. Mukherjee and T. R. Seshadri, *Proc. Indian Acad. Sci.*, 1952, **35**, *A*, 323.

[56] T. A. Geissman and J. W. Bolger, *J. Amer. Chem. Soc.*, 1951, **73**, 5875.

[57] G. H. Phillips, A. Robertson, and W. B. Whalley, *J.*, 1952, 4951.

[58] K. Riedl and N. Neugebauer, *Monatsh.*, 1952, **83**, 1083.

[59] A. B. Svendsen, *Pharm. Acta Helv.*, 1952, **27**, 44.

[60] R. H. Goodwin and F. Kavanagh, *Arch. Biochem.*, 1952, **36**, 442.

[61] R. Patzak and L. Neugebauer, *Sitzungber. Akad. Wiss. Wien*, 1952, **161**, 776.

[62] J. C. Benstead, H. V. Brewerton, J. R. Fletcher, M. Martin-Smith, S. N. Slater, and A. T. Wilson, *J.*, 1952, 1042; S. N. Slater and A. T. Wilson, *ibid.*, p. 1597; J. C. Benstead, R. Gee, R. B. Johns, M. Martin-Smith, and S. N. Slater, *ibid.*, p. 2292.

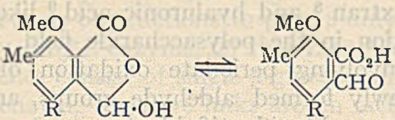
[63] H. Conroy, *J. Amer. Chem. Soc.*, 1952, **74**, 491, 3047.

[64] Cf. *Ann. Reports*, 1951, **48**, 211.

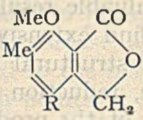
[65] R. D. Haworth and W. Kelly, *J.*, 1936, 998.

[66] T. Ozawa, *J. Pharm. Soc. Japan*, 1952, **72**, 285, 551.

Gladiolic acid, a metabolic product of *Penicillium gladioli*, has been shown [67] to have the tautomeric structure (X; R = CHO). The presence of a formyl group was proved by the formation of carbonyl derivatives and



(X)



(XI)

by the existence of reducing properties which disappeared on mild oxidation during which a new carboxyl group appeared. The $O_6$ product so obtained had two carboxyl groups and one methoxy-group, and showed both carbonyl and hydroxyl properties, which are best explained by assuming a tautomeric system as shown. Rearrangement under alkaline conditions to give a carboxy-lactone (XI; R = $CO_2H$) was best explained by an *ortho*-arrangement of formyl and lactol grouping, and vigorous oxidation gave 4-methoxybenzene-1 : 2 : 3 : 5-tetracarboxylic acid (structure by synthesis). The final orientation of the substituents followed from detailed arguments for which the original paper should be consulted; they depend chiefly on the interpretation of infra-red spectra and the isolation [68] from the phthalide (XI; R = Me), obtained by Clemmensen reduction of gladiolic acid, of 2 : 4 : 5-trimethylphenol.

T. J. K.

## 11. MACROMOLECULES.

During 1952, workers engaged in the study of macromolecules mourned the deaths of C. S. Hudson and K. H. Meyer, whose researches laid the foundations of so much of the work reported below.

### Polysaccharides.

It is the turn of polysaccharides to receive the main emphasis in a year which, in addition to furnishing its full quota of studies on new and rare polysaccharides, has seen some readjustments in widely accepted concepts of the structures of certain " simple " and well-known polysaccharides, such as starch, glycogen, and dextran. Structural studies have been facilitated by the continued use of chromatographic techniques for the fractionation of mixtures of oligosaccharides on filter paper, on charcoal columns,[1-3] and, as their acetates, on columns of " Silene EF." [4] It has been shown that care must be exercised in interpreting paper chromatograms of sugar solutions containing ammonium salts, or other nitrogenous compounds, because glycosylamines formed, in certain circumstances, on the paper itself may produce extra spots.[5] Studies of filter-paper ionophoresis of sugars in borate buffers have demonstrated that this new method is potentially very

---

[67] J. F. Grove, *Biochem. J.*, 1952, 50, 648.
[68] H. Raistrick and D. J. Ross, *ibid.*, p. 635.
[1] R. L. Whistler and Chen-Chuan Tu, *J. Amer. Chem. Soc.*, 1952, 74, 3609.
[2] S. Peat, W. J. Whelan, and G. J. Thomas, *J.*, 1952, 4546.
[3] S. A. Barker, E. J. Bourne, G. T. Bruce, and M. Stacey, *Chem. and Ind.*, 1952, 1156.
[4] M. L. Wolfrom and J. C. Dacons, *J. Amer. Chem. Soc.*, 1952, 74, 5331.
[5] R. J. Bayly, E. J. Bourne, and M. Stacey, *Nature*, 1952, **169**, 876.

valuable for characterisations;[6] there is no doubt that it will shortly be widely used to unravel the complexities of polysaccharide structures, as also will electrokinetic ultra-filtration analysis.[7] Infra-red absorption, having yielded valuable results with dextran[8] and hyaluronic acid,[9] likewise will probably find extensive application in the polysaccharide field. A useful method of structural analysis, involving periodate oxidation of a polysaccharide, reduction of the newly formed aldehyde groups, and acidic hydrolysis of the product to give readily identifiable fragments, has been reported.[10]

**Starch and Glycogen.**—Maple-sapwood starch has been shown, by potentiometric titration with iodine, to contain *ca.* 19% of amylose.[11] Hydrolysis of the trimethyl ether gave 2 : 3 : 4 : 6-tetramethyl and 2 : 3 : 6-trimethyl glucose (3·3—3·4 and 92—93%, respectively), together with dimethyl glucoses (4—5%), a result which indicated that the principal glucosidic linkages involved positions 1 and 4, and that the average chain length of the amylopectin fraction was 26 glucose units. A somewhat lower figure (22 units) was derived from a determination of the formic acid liberated during oxidation of the starch with periodate. The presence of xylose in the starch was attributed to an associated xylan.[11] Nuclear-substituted tricarbanilates of maize starch, amylose, and amylopectin have been prepared by treatment of the polysaccharides, in pyridine, with derivatives of phenyl *iso*cyanate.[12] The greatly differing optical rotations and melting points of the *ortho*-substituted products, as compared with the *meta*- and *para*-isomers, were consistent with their different intramolecular bondings. Alkaline ferricyanide, in the presence of cyanide, has been used for measurement of molecular weights of amylodextrins and other substances of the starch type.[13] Determinations of the molecular weight of an amylopectin acetate, by osmotic and light-scattering methods, have given approximate values of $6 \times 10^6$ and $400 \times 10^6$, respectively, the former being a number-average and the latter a weight-average.[14] The swelling of starch granules, caused by the sorption of water vapour,[15] and the effect of temperature and aggregation on the absorption spectrum of the amylose–iodine complex,[16] have been studied.

Important advances have been made concerning the finer structures of the starch components. A detailed account has been given of the properties of Z-enzyme, which occurs in impure samples of soya-bean β-amylase.[17] Whereas the purified soya-bean β-amylase, like the crystalline β-amylase from sweet potatoes, effects only a 70% conversion of potato amylose into maltose (and not *ca.* 100%, as was believed previously), in the presence of

---

[6] A. B. Foster, *Chem. and Ind.*, 1952, 828; R. Consden and W. M. Stanier, *Nature*, 1952, **169**, 783.

[7] D. L. Mould and R. L. M. Synge, *Biochem. J.*, 1951, **50**, xi.

[8] S. C. Burket and E. H. Melvin, *Science*, 1952, **115**, 516.

[9] S. F. D. Orr, R. J. C. Harris, and B. Sylvén, *Nature*, 1952, **169**, 544.

[10] M. Abdel-Akher, J. K. Hamilton, R. Montgomery, and F. Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 4970.

[11] C. E. Ballou and E. G. V. Percival, *J.*, 1952, 1054.

[12] I. A. Wolff, P. R. Watson, and C. E. Rist, *J. Amer. Chem. Soc.*, 1952, **74**, 3061, 3064.

[13] S. Nussenbaum and W. Z. Hassid, *Analyt. Chem.*, 1952, **24**, 501.

[14] B. H. Zimm and C. D. Thurmond, *J. Amer. Chem. Soc.*, 1952, **74**, 1111.

[15] N. N. Hellman, T. F. Boesch, and E. T. Melvin, *ibid.*, p. 348.

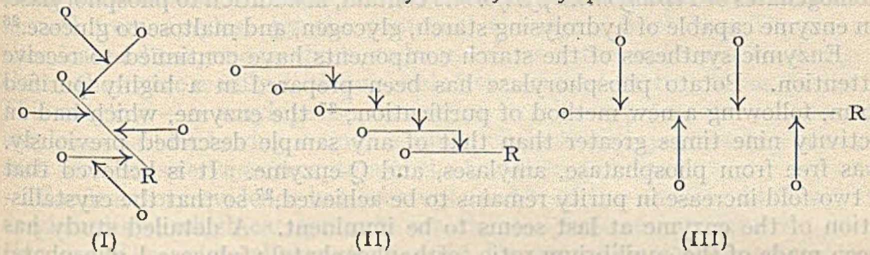
[16] J. F. Foster and E. F. Paschall, *ibid.*, p. 2105.

[17] S. Peat, S. J. Pirt, and W. J. Whelan, *J.*, 1952, 705, 714; S. Peat, G. J. Thomas, and W. J. Whelan, *ibid.*, p. 722.

Z-enzyme an almost complete conversion into the disaccharide results. The amyloses of sago, tapioca, and maize behave similarly.[17] It was concluded (*a*) that some degree of branching occurs in amyloses, and that the branches, which serve as obstructions to pure β-amylase (and also to phosphorylase), are removed by Z-enzyme, (*b*) that Z-enzyme is a β-glucosidase, and (*c*) that the branches consist of single β-glucose units attached to the main chain.[17] If the Z-enzyme-sensitive links are, in fact, at branch points, it seems that the enzyme responsible for their synthesis still remains to be found. Alternatively, the anomalous links may not be branches, but may occur at the non-reducing ends of 30% of the amylose molecules, and may result from imperfections in the synthesis by phosphorylase. Branching in amylose has been postulated also on the basis of the rates of sugar production with amylo-glucosidase and with β-amylase;[18] it appears that potato amylose has 1—2, and tapioca amylose 2—3, branches per molecule.

Evidence that amylopectin and glycogen have structures similar to that (I) suggested by Meyer, rather than the simpler " laminated " formula (II) due to Haworth, or the " comb-like " structure (III) proposed by Freudenberg, has been obtained by two methods [2, 19] (cf. ref. 20). In the first, the polysaccharides were treated with salivary α-amylase and then with R-enzyme (which hydrolyses the 1 : 6-α-branch linkages), and the resulting mixtures of linear saccharides were analysed on charcoal columns. From the analytical figures, it was deduced that multiple branching occurred in the polysaccharide structures.[19, 21] The second method entailed a similar analysis of the amylosaccharides formed when the β-limit dextrin from amylopectin was treated with R-enzyme.[2]

*Possible structural formulæ for amylopectin.*



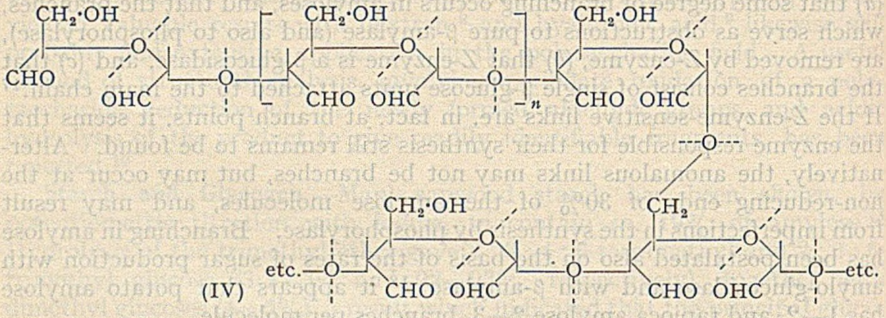
(I) (II) (III)

o = Non-reducing chain end, ↓ = α-1 : 6-Link, R = Free reducing chain end.

A new procedure for the determination of polysaccharide structures has been illustrated by its application to amylopectin.[10] Periodate-oxidised amylopectin (IV) was hydrogenated and hydrolysed, and the resulting mixture was analysed for glycerol and erythritol. Since the former arises only from the non-reducing terminal units, and the latter from the remaining units, the molar ratio glycerol : erythritol is related to the chain length of the polysaccharide. In addition, about 0·5% of the sugar units resisted periodate, and gave glucose on hydrolysis, from which it was concluded [10] that some 1 : 3-linkages occur in amylopectin. Glycogen (1%), amylose

[18] R. W. Kerr and F. C. Cleveland, *J. Amer. Chem. Soc.*, 1952, **74**, 4036.
[19] W. J. Whelan and P. J. P. Roberts, *Nature*, 1952, **170**, 748.
[20] G. T. Cori and J. Larner, *J. Biol. Chem.*, 1951, **188**, 17.
[21] P. J. P. Roberts and W. J. Whelan, *Biochem. J.*, 1952, **51**, xviii.

(0·2—0·5%), and cellulose (0·1—0·2%) likewise contain periodate-resistant units.[10]


(IV)

Other studies have been devoted to the determination and purification of amylases. An improved method has been developed for the preparation of hog pancreatic amylase.[22] Adsorption indicators have been used for the determination of β-amylase activity.[23] Earlier reports that indole derivatives, and other plant hormones, inhibit human α-amylase have been disproved.[24] Crystalline malt β-amylase is a very soluble albumin, which can be stored in the cold for long periods without loss of activity; it is totally and irreversibly destroyed by the salts of heavy metals, but is relatively stable to low pH; its isoelectric point is at pH 6·1, and it displays its optimum activity at pH 5·2.[25] An interesting observation is that cell-free homogenates of *Tetrahymena pyriformis* contain, in addition to phosphorylase, an enzyme capable of hydrolysing starch, glycogen, and maltose to glucose.[26]

Enzymic syntheses of the starch components have continued to receive attention. Potato phosphorylase has been prepared in a highly purified form, following a new method of purification; [27] the enzyme, which had an activity nine times greater than that of any sample described previously, was free from phosphatase, amylases, and Q-enzyme. It is believed that a two-fold increase in purity remains to be achieved,[27] so that the crystallisation of the enzyme at last seems to be imminent. A detailed study has been made of the equilibrium ratio [orthophosphate] : [glucose-1 phosphate] established by potato phosphorylase, and the effect of $Mg^{++}$ ions on this ratio has been explained in equations relating it to the concentration of $Mg^{++}$ ion, and to the dissociation constants of magnesium complexes with orthophosphoric and glucose-1 phosphoric acids.[28] Magnesium ions are believed to have little effect on the ratio under physiological conditions. The second dissociation constant of glucose-1 phosphoric acid has been redetermined as $3{\cdot}09 \times 10^{-7}$ at 30°.[28] The free-energy change, at 30°, of the reaction glucose-1 phosphate $\longrightarrow$ acid orthophosphate + polysaccharide is −1460 cal.[28] Additional support for the current theory that potato

---

[22] M. L. Caldwell, M. Adams, J. T. Kung, and G. C. Toralballa, *J. Amer. Chem. Soc.*, 1952, 74, 4033. [23] B. Carroll and J. W. Van Dyk, *Science*, 1952, 116, 168.

[24] E. H. Fischer and J. Fellig, *ibid.*, 1952, 115, 684.

[25] A. Piguet and E. H. Fischer, *Helv. Chim. Acta*, 1952, 35, 257.

[26] J. F. Ryley, *Biochem. J.*, 1952, 52, 483.

[27] G. A. Gilbert and A. D. Patrick, *ibid.*, 1952, 51, 186.

[28] W. E. Trevelyan, P. F. E. Mann, and J. S. Harrison, *Arch. Biochem.*, 1952, 39, 419, 440.

phosphorylase functions by lengthening the chains of all primer molecules simultaneously, and not by converting one primer molecule into amyloes before attacking another, has resulted from measurements of the spectra of the iodine stains of the products formed when different proportions of glucose-1 phosphate and primer molecules are employed, and also from electrokinetic ultra-filtration analysis of the products.[29] Chromatographic analysis of the non-protein fraction of crystalline muscle phosphorylase has revealed uridylic acid, cystine, and (probably) 2-methyl-1 : 4-naphthaquinone;[30] the cystine was isolated in sufficient quantity to suggest that cysteine may constitute an end group of the protein molecule, and serve as a connecting link with the prosthetic group.[30] The crystalline enzyme is inhibited significantly by D-glucose, and by α-methyl- and α-phenyl-D-glucopyranoside, but not by a variety of other sugars, including β-methylglucoside and β-D-glucose-1 phosphate.[31]

Details have been given of the preparation and properties of crystalline potato Q-enzyme.[32] (Q-enzyme converts the slightly branched amylose component of starch into the highly branched amylopectin structure.) Like earlier, less pure, samples of the enzyme, the crystalline enzyme is rapidly inactivated in solution at 30°; it is more stable in the presence of starch.[32] In support of the hypothesis that Q-enzyme is a transglucosylase, it has been shown by two independent groups of workers [33, 34] that the potato enzyme cannot utilise amylose-type molecules as substrates unless they contain more than *ca.* 42 glucose units. For the synthesis of starch from acetate, *Polytomella coeca* utilises *inter alia* a phosphorylase and a Q-enzyme, these being very similar in their actions to the potato enzymes.[35] Products formed from amylose by the protozoal Q-enzyme have been shown, by chemical and enzymic methods, to be members of the amylopectin–glycogen class; they were readily distinguishable from amylose–fatty acid complexes.[36] This amylose ⟶ amylopectin conversion is more rapid in the presence of amylosaccharides having a small average chain length, presumably because such molecules serve as receptors of the transferred chains.

Confirmatory evidence has been obtained [37] of the presence in *E. coli* of amylomaltase, which catalyses the reaction : $n$ maltose $\rightleftharpoons$ $(\text{glucose})_n + n$ glucose. The extra-cellular saccharides, formed when washed cells of the organism were incubated with maltose in the presence of iodoacetate, were fractionated on a charcoal column into glucose, unchanged maltose, and the lower members of the homologous series of 1 : 4-α-glucosans.[37] Improved conditions for the production of Schardinger dextrinogenase by *B. macerans* [38] have facilitated the preparation of an enzyme sample which behaves as essentially one component in solubility tests, in electrophoretic analysis, and in the ultra-centrifuge.[39]

---

[29] J. M. Bailey and W. J. Whelan, *Biochem. J.*, 1952, **51**, xxxiii.
[30] M. V. Buell, *Fed. Proc.*, 1952, **11**, 192.
[31] P. N. Campbell, N. H. Creasey, and C. W. Parr, *Biochem. J.*, 1952, **52**, 448.
[32] G. A. Gilbert and A. D. Patrick, *ibid.*, 1952, **51**, 181.
[33] S. Nussenbaum and W. Z. Hassid, *J. Biol. Chem.*, 1952, **196**, 785.
[34] J. M. Bailey, S. Peat, and W. J. Whelan, *Biochem. J.*, 1952, **51**, xxxiv.
[35] A. Bebbington, E. J. Bourne, M. Stacey, and I. A. Wilkinson, *J.*, 1952, 240.
[36] A. Bebbington, E. J. Bourne, and I. A. Wilkinson, *ibid.*, p. 246.
[37] S. A. Barker and E. J. Bourne, *ibid.*, p. 209.
[38] S. Schwimmer and J. A. Garibaldi, *Cereal Chem.*, 1952, **29**, 108.
[39] S. Schwimmer, *Fed. Proc.*, 1952, **11**, 283.

Interest has been focussed on glycogen in papers additional to those mentioned above. A polysaccharide synthesised by *Tetrahymena pyriformis* has been proved to be a glycogen, having a molecular weight of $9{\cdot}8 \times 10^6$ (light-scattering method) and an average chain length of 13 glucose residues.[40] The molecular weights of other glycogens have been determined [41] by a light-scattering method as $3—15 \times 10^6$ (cf. ref. 14). Maltulose has been found in the saccharides resulting from the action of salivary α-amylase on a glycogen obtained from the livers of pregnant rabbits.[42] This important observation raises the question of the possible occurrence of fructose in other glycogens, and perhaps in starches. By periodate oxidation, and determination of the liberated formic acid, chain lengths of 13 units were found for cat-liver and fœtal-sheep-liver glycogens, while three samples of glycogen from *Mytilus edulis* had chain lengths of 5, 12, and 17.[43] The structures of these and other glycogens were discussed in the light of their behaviour during β-amylolysis.[43, 44]

The liver " branching factor," freed from α-amylase, has been shown to convert amylopectin into a polysaccharide giving a reddish-brown, rather than a purple, iodine stain ; it was believed that the reaction entailed branching of the outer chains of amylopectin.[45] As confirmation of this, a synthetic polysaccharide, prepared from glycogen by lengthening the outer chains by means of phosphorylase and [$^{14}$C] glucose-1 phosphate, was treated with the " branching factor," and the product was proved by an enzymic method to possess radioactivity at the new branch points. The liver enzyme, which functions in the absence of added phosphate, probably detaches a short chain of glucose residues by scission of a 1 : 4-link and attaches the chain, as a branch, through a 1 : 6-link ; [45] this mechanism is similar to that established for Q-enzyme. The syntheses of glycogen and other carbohydrates during fermentation of glucose by baker's yeast have been studied and discussed in terms of the enzymic processes of fermentation.[46]

**Cellulose.**—A polysaccharide from *Posidonia australis*, previously the subject of conflicting reports, is now known to be a cellulose ; when methylated and hydrolysed, it gives 2 : 3 : 6-trimethyl glucose almost exclusively.[47] An important recent contribution to cellulose chemistry is the isolation of cellodextrins containing 2—7 glucose residues ; [4] this notable achievement was accomplished by fractionating, on a column of " Silene EF," the dextrin acetates produced by acetolysis of cellulose, and then deacetylating them. It seems certain that studies of these cellodextrins will lead to a better understanding of the properties of cellulose. It has been demonstrated that a certain amount of re-esterification occurs during the hydrolysis of cellulose acetate with aqueous acetic acid,[48] and that the heterogeneous hydrolysis of highly methylated cotton cellulose causes scission in the non-crystalline regions, followed by more rapid destruction of the smaller fragments.[49]

[40] D. J. Manners and J. F. Ryley, *Biochem. J.*, 1952, **52**, 480.

[41] B. S. Harrap and D. J. Manners, *Nature*, 1952, **170**, 419.

[42] S. Peat, P. J. P. Roberts, and W. J. Whelan, *Biochem. J.*, 1952, **51**, xvii.

[43] D. J. Bell and D. J. Manners, *J.*, 1952, 3641.

[44] D. J. Manners, *Biochem. J.*, 1952, **51**, xxx.

[45] J. Larner and G. T. Cori, *Fed. Proc.*, 1952, **11**, 245.

[46] W. E. Trevelyan, J. N. Gammon, E. H. Wiggins, and J. S. Harrison, *Biochem. J.*, 1952, **50**, 303.

[47] D. J. Bell, *J.*, 1952, 3649.

[48] C. J. Malm, L. J. Tanghe, B. C. Laird, and G. D. Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 4105.

[49] R. E. Reeves, B. J. Barrett, and L. W. Mazzeno, *ibid.*, p. 4491.

Other papers have dealt with the molecular dimensions of cellulose tributyrate and trioctanoate,[50] the alcoholysis of cellulose and its derivatives with 2-methoxyethanol,[51] and the oxidation of hydrocellulose with hypoiodite.[52]

*Limnoria lignorum*, a marine wood-boring isopod, has been found to secrete a cellulase which converts cellulose into reducing substances; [53] earlier work had failed to detect this enzyme. The cellulase of *Myrothecium verrucaria* is stimulated by proteins.[54] An investigation of the relation between the action of brown rot fungi, cellulose degradation, and lignin composition in bagasse has been made.[55] An observation which may be of fundamental importance with regard to the enzymic synthesis of cellulose is that an enzyme from *Neisseria meningitidis* catalyses the reversible reaction : maltose + phosphate $\rightleftharpoons$ β-D-glucose-1 phosphate + glucose.[56] This transition from the α- to the β-series may well be the key to the synthesis of β-glucose polymers.

**Dextran.**—The common tacit assumption that the branches of all dextrans involve positions 1 and 4 has been proved to be invalid by several independent groups of workers. Periodate oxidations of the dextrans from *Leuconostoc mesenteroides* NRRL B-742 and NRRL B-512 have shown the presence of periodate-resistant units, which yield glucose on hydrolysis.[10, 57] It was suggested that these units carried branches at position 3, or positions 2 and 4. Similar observations have since been made on other dextrans.[58] In such cases there are anomalous optical rotations and infra-red spectra.[8, 57, 58] A full structural analysis of a *Betacoccus arabinosaceous* dextran (used in Britain for the production of a blood plasma substitute) has revealed that the branches are attached at position 3 almost exclusively.[3] Methylation and end-group assay gave 2 : 3 : 4 : 6-tetramethyl, 2 : 3 : 4-trimethyl, and 2 : 4-dimethyl glucose, in proportions corresponding to an average chain length of *ca.* 6 glucose residues. Partial acidic hydrolysis of the dextran and fractionation of the resulting oligosaccharides on a charcoal column yielded, *inter alia*, *iso*maltose and 3-glucosyl glucose; there were periodate-resistant units giving glucose on hydrolysis.[3] An added complication is that some dextrans can be separated, by graded precipitation with ethanol, into fractions with no 1 : 3-branches and with an increased proportion of such branches.[57, 58] In the thermal degradation of dextran, there is a notable absence of reducing oligosaccharides when oxygen is excluded.[59] The toxicity and blood anticoagulant properties of dextran sulphates have been examined over a range of molecular weights and sulphate contents.[60]

The optimum conditions for the production of dextran sucrase by *Leuconostoc mesenteroides* NRRL B-512 have been ascertained; [61] from

[50] L. Mandelkern and P. J. Flory, *J. Amer. Chem. Soc.*, 1952, **74**, 2517.
[51] M. G. Blair, *ibid.*, p. 3411.
[52] M. G. Blair and R. E. Reeves, *ibid.*, p. 2622.
[53] D. L. Ray and J. R. Julian, *Nature*, 1952, **169**, 32.
[54] D. R. Whitaker, *Science*, 1952, **116**, 90.
[55] G. de Stevens and F. F. Nord, *J. Amer. Chem. Soc.*, 1952, **74**, 3326.
[56] C. Fitting and M. Doudoroff, *J. Biol. Chem.*, 1952, **199**, 153.
[57] R. Lohmar, *J. Amer. Chem. Soc.*, 1952, **74**, 4974.
[58] A. Jeanes and C. A. Wilham, *ibid.*, p. 5339.
[59] M. Stacey and F. G. Pautard, *Chem. and Ind.*, 1952, 1058.
[60] C. R. Ricketts, *Biochem. J.*, 1952, **51**, 129.
[61] H. J. Koepsell and H. M. Tsuchiya, *J. Bact.*, 1952, **63**, 293.

sucrose the culture filtrates produce small amounts of levan, in addition to dextran. High sucrose levels in the culture medium lead to viscous cultures, from which the separation of the cells is difficult.[61] It has been claimed [62] that a new disaccharide, leucrose [5-D-(glucopyranosyl)-D-fructopyranose], " plays a role in the polymerisation process "; this hypothesis is at variance with the accepted mechanism of dextran synthesis, and, if substantiated, would cast doubt on current concepts of the formation of other polysaccharides from sucrose. Perhaps the disaccharide arises in a side reaction involving the transfer of a glucose residue to fructopyranose, instead of to a growing dextran molecule. Cell-free culture filtrates of certain bacteria from the human intestine,[63] and of an *Aspergillus* strain isolated from soil,[64] display dextranase activity, inasmuch as they decrease the average molecular weights of dextrans (to *ca.* 75,000 in the latter case) without liberating significant quantities of reducing sugar.

**1 : 3-Linked Glucosans.**—It appears that 1 : 3-linked glucosans occur more widely in Nature than has been believed hitherto; studies of three of them have been reported this year. Confirmation that laminarin is composed of β-glucopyranose units, mutually linked through positions 1 and 3, was obtained when it was proved that the disaccharide (laminaribiose), to which it gives rise when partially hydrolysed with acid, is identical with a synthetic specimen of 3-β-D-glucopyranosyl-D-glucopyranose.[65] The synthesis was accomplished by condensing 2 : 3 : 4 : 6-tetra-acetyl glucosyl bromide with 1 : 2-5 : 6-di*iso*propylidene glucofuranose, and then removing the protecting substituents.[65] The flesh of the bracket fungus, *Polyporus betulinus*, when methylated and hydrolysed, has given 2 : 3 : 4 : 6-tetramethyl, 2 : 4 : 6-trimethyl, 4 : 6-dimethyl, and a monomethyl glucose, in the molar ratio 1 : 13 : 4 : 1, and would thus seem to contain a highly branched 1 : 3-glucosan.[66] An interesting polysaccharide (" mycodextran ") separates when hot-water extracts of *Aspergillus niger* 152, grown on a sucrose medium, are cooled; [67] it has $[\alpha]_D$ +283° in alkali, an unusually high figure.[68] Chemical analyses of the products of partial hydrolysis of the polysaccharide, and of the methyl glucoses formed by hydrolysis of its trimethyl ether, have shown " mycodextran " to be a glucosan containing 1 : 3-α- and 1 : 4-α-linkages in approximately equal amount.[68]

**Galactans and Galactomannans.**—Methylation of the galactan of beef lung has indicated that a main chain of 1 : 6-D-galactopyranose units carries a single D-galactopyranose residue, as a branch, at position 3 of every alternate unit; in addition, there is one titratable acid function, probably carboxyl, per 35—40 sugar residues.[69]

A structure has been proposed for guaran on the basis of enzymic [70] and acidic hydrolyses; [71] the former gave Gal 1α—6 Man (0·5%) and Man 1β—4 Man 1β—4 Man (7·5%), and the latter, Gal 1α—6 Man 1β—4 Man (3%) (where Gal and Man are galactopyranose and mannopyranose residues,

---

[62] F. H. Stodola, H. J. Koepsell, and E. S. Sharpe, *J. Amer. Chem. Soc.*, 1952, **74**, 3202.
[63] E. J. Hehre and T. W. Sery, *J. Bact.*, 1952, **63**, 424.
[64] V. Whiteside-Carlson and W. W. Carlson, *Science*, 1952, **115**, 43.
[65] P. Bächli and E. G. V. Percival, *J.*, 1952, 1243.
[66] R. B. Duff, *ibid.*, p. 2592.
[67] J. L. Yuill, *Chem. and Ind.*, 1952, 755.
[68] S. A. Barker, E. J. Bourne, and M. Stacey, *ibid.*, p. 756.
[69] M. L. Wolfrom, G. Sutherland, and M. Schlamowitz, *J. Amer. Chem. Soc.*, 1952, **74**, 4883.
[70] R. L. Whistler and C. G. Smith, *ibid.*, p. 3795.
[71] R. L. Whistler and D. F. Durso, *ibid.*, p. 5140.

respectively). It was concluded that guaran consists of a chain of 1 : 4-linked β-D-mannopyranose units, with an α-D-galactopyranosyl group at position 6 of every other (average) mannose residue of the chain. The galactomannans of lucerne and clover seed resemble guaran in that they are highly branched, and contain D-galactopyranose end-groups united to chains of 1 : 4(or 1 : 6)-linked D-mannose residues (probably in the pyranose form).[72] A similar structure has been assigned to the galactomannan of fenugreek seed, but in this case the galactose : mannose ratio is appreciably higher (5 : 6), as also is the degree of branching.[73] 2-Cyanoethyl ethers have been prepared from guaran with acrylonitrile, and have been hydrolysed with alkali to the corresponding 2-carboxyethyl ethers.[74]

**Fructosans.**—A polysaccharide from elecampane has been proved to be of the inulin class by hydrolysis of its methyl ether to 1 : 3 : 4 : 6-tetramethyl, 3 : 4 : 6-trimethyl, and a dimethyl fructose (molar ratio, 1 : 32·7 : 1·5).[75] Polysaccharides from leaf cocksfoot and Italian rye grass have been classified as levans, because their methyl ethers yield 1 : 3 : 4 : 6-tetramethyl, 1 : 3 : 4-trimethyl, and a dimethyl fructose (molar ratios, 1 : 12 : 2 and 1 : 11 : 1, respectively).[75] It is interesting, in view of the enzymic studies reported below, that each of these three polysaccharides contained *ca.* 3% of glucose residues. However, the glucose did not appear to be present as non-reducing end-groups (as it is in the inulin of dahlia tubers),[76] because it was isolated during the end-group assays principally as trimethyl glucose.[75]

Studies of transfructosidases have extended the work of Bacon and Edelman,[77] and Blanchard and Albon;[78] they provide possible routes to the synthesis of inulin and levan. " Difco " invertase solution catalyses the conversion of sucrose into a reducing disaccharide, two trisaccharides, and a tetrasaccharide, all containing fructose unit(s) linked to a single glucose residue.[79] β-Methylfructofuranoside has been prepared from sucrose and 25% methanol with yeast invertase.[80] With an enzyme from *Aspergillus oryzae*, sucrose has been converted into a trisaccharide containing one glucose and two fructose units, and a tetrasaccharide composed of one glucose and three fructose residues.[81] All of these reactions conform with the equation :

$$\text{Sucrose} + \text{HOR} \rightleftharpoons \text{Fructosyl–O–R} + \text{Glucose}$$

where ROH is sucrose, glucose, methanol, or a growing oligosaccharide chain with a non-reducing terminal fructofuranose group. A related phenomenon appears to be responsible for the occurrence, in barley leaves and stems, of glucose, fructose, sucrose, and at least four higher oligosaccharides with decreasing glucose : fructose ratios.[82]

**Xylan.**—A valuable contribution to the chemistry of xylan has been

---

[72] P. Andrews, L. Hough, and J. K. N. Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 4029.
[73] *Idem, J.*, 1952, 2744.
[74] O. A. Moe, S. E. Miller, and M. I. Buckley, *J. Amer. Chem. Soc.*, 1952, **74**, 1325.
[75] D. J. Bell and A. Palmer, *J.*, 1952, 3763.
[76] E. L. Hirst, D. I. McGilvray, and E. G. V. Percival, *J.*, 1950, 1297.
[77] J. S. D. Bacon and J. Edelman, *Arch. Biochem.*, 1950, **28**, 467.
[78] P. H. Blanchard and N. Albon, *ibid.*, 1950, **29**, 220.
[79] L. M. White and G. E. Secor, *ibid.*, 1952, **36**, 490.
[80] J. S. D. Bacon, *Biochem. J.*, 1952, **50**, xviii.
[81] J. H. Pazur, *Fed. Proc.*, 1952, **11**, 267; *J. Biol. Chem.*, 1952, **199**, 217.
[82] H. K. Porter and J. Edelman, *Biochem. J.*, 1952, **50**, xxxiii.

made by Whistler and his colleagues, who separated, on charcoal columns, the oligosaccharides resulting from partial acidic hydrolysis of the polysaccharide.[1, 83] They isolated a series of five oligosaccharides, all crystalline, extending from the dimer to the hexamer, and obtained evidence that all were composed of unbranched chains of 1 : 4-linked β-D-xylopyranose units; each of them gave a crystalline β-acetate.

**Hemicelluloses.**—European beech hemicellulose A gives xylose and a uronic acid (not glucuronic acid) when hydrolysed; the pentosan and uronic acid anhydride contents are 81·4 and 10·4%, respectively.[84] Hydrolysis of extractive-free aspen sawdust yields L-rhamnose, L-arabinose, D-xylose, D-galactose, xylobiose, xylotriose, 4-methyl D-glucuronic acid, D-galacturonic acid, 2-α-(4-methyl-D-glucuronosyl)-α-D-xylose, and several unidentified acidic fractions of higher molecular weight.[85] The uronic acid anhydride and pentosan contents of hemicellulose fractions of hays and straws have been compared for different plant families and for members of the same families.[86]

**Pectic Substances, Gums, and Mucilages.**—Chromatographic methods are assisting the elucidation of enzyme actions on pectic substances.[87-89] With their aid crystalline mono-, di-, and tri-galacturonic acids have been isolated from the products of polygalacturonase action on pectic acid.[87, 88] *Byssochlamys fulva* has been shown to produce a pectin esterase and a polygalacturonase.[90] This year has revealed that the problems to be faced in studies of the enzymic degradation of pectic materials are even more complex than had been realised previously, as the following four examples show. First, a pectin depolymerase of *Neurospora crassa* differs from others reported earlier in that it yields lower polyuronides, rather than galacturonic acid, as end products, and also in that it degrades pectin without preliminary demethylation.[91] Secondly, *Aspergillus foetidus* utilises at least two enzymes to effect the conversion of pectic acid into galacturonic acid; one produces di- and tri-uronides, which serve as substrates for the other.[89] Thirdly, a polymethylgalacturonase from commercial "hydralase," which attacks pectin more rapidly than pectic acid, cannot hydrolyse more than 26% of the available uronide bonds of the pectin.[92] Fourthly, Schubert [93] claims to have shown with certainty the presence of at least four different polygalacturonases in extracts of a single culture of *Aspergillus niger*.

The monomethyl aldobiuronic acid which, together with 4-methyl D-glucuronic acid, results from controlled hydrolysis of mesquite gum,[94] is now known to be 6-β-(4-methyl D-glucuronosyl) D-galactopyranose.[95] Acidic hydrolysis of *Khaya grandifolia* gum gives galactose and a degraded

---

[83] R. L. Whistler, J. Bachrach, and Chen-Chuan Tu, *J. Amer. Chem. Soc.*, 1952, **74**, 3059; R. L. Whistler and Chen-Chuan Tu, *ibid.*, p. 4334.

[84] I. R. C. McDonald, *J.*, 1952, 3183.

[85] J. K. N. Jones and L. E. Wise, *ibid.*, pp. 2750, 3389.

[86] C. A. Flanders, *Arch. Biochem.*, 1952, **36**, 421, 425.

[87] H. J. Phaff and B. S. Luh, *ibid.*, p. 231.

[88] H. Altermatt and H. Deuel, *Helv. Chim. Acta*, 1952, **35**, 1422.

[89] A. Ayres, J. Dingle, A. Phipps, W. W. Reid, and G. L. Solomons, *Nature*, 1952, **170**, 834.

[90] W. W. Reid, *Biochem. J.*, 1952, **50**, 289.

[91] E. Roboz, R. W. Barratt, and E. L. Tatum, *J. Biol. Chem.*, 1952, **195**, 459.

[92] C. G. Seegmiller and E. F. Jansen, *ibid.*, p. 327.

[93] E. Schubert, *Nature*, 1952, **169**, 931.

[94] F. Smith, *J.*, 1951, 2646.

[95] M. Abdel-Akher, F. Smith, and D. Spriestersbach, *J.*, 1952, 3637.

polysaccharide containing galactose, rhamnose, and galacturonic acid units; *Anogeissus schimperi* gum yields arabinose, galactose, and a degraded polysaccharide containing arabinose, galactose, and glucuronic acid residues.[96] A polysaccharide of *Lupinus termis* seeds consists of D-galactose, L-arabinose, and galacturonic acid residues.[97]

**Hyaluronic Acid.**—Methods for the isolation of hyaluronic acid with trichloroacetic acid,[98] and for the determination of hyaluronidase activity [99] have been reported. The polysaccharide has been obtained from the callus tissue of healing rabbit fractures.[100] Attempts have been made to find the best method for the isolation, without degradation, of the protein–hyaluronic acid complex of ox sinovial fluid.[101] About 93% of the complex was accounted for in terms of *N*-acetylglucosamine, glucuronic acid, protein, and ash; its particle weight is *ca.* $10^7$. Methylation and methanolysis of hyaluronic acid have been studied.[102] The crystalline disaccharide, prepared previously from hyaluronic acid,[103] has been shown to be 3-β-D-glucopyruronosyl-D-glucosamine by its conversion into 2-β-D-glucopyranosyl-D-arabinose, which has been obtained also from laminaribiose.[104] Infra-red spectroscopy has confirmed the presence in hyaluronic acid of free carboxyl groups and monosubstituted amides; none of the hydroxyl groups is acetylated.[9] Purified testicular hyaluronidase converts the polysaccharide into a mixture of oligosaccharides, but the crude testicular extract gives glucuronic acid and *N*-acetylglucosamine.[105] A trisaccharide constituent of the oligosaccharide mixture, when treated with glucosaminidase, affords *N*-acetylglucosamine and a glucuronosyl-*N*-acetylglucosamine.[105] Tracer experiments suggest that the glucosamine moiety of the polysaccharide arises from glucose during biosynthesis.[106]

**Other Polysaccharides.**—Alginates have been examined with respect to viscosity [107] and electrolyte absorption.[108] It has been confirmed that their main structural feature is a chain of 1 : 4-linked β-D-mannuronic acid residues.[109] A useful method developed for fractionation of the cell carbohydrates of yeast is applicable to as little as 10 mg. of material.[110] The occurrence of L-fucose, rhamnose, and methylated carbohydrates in soil has been reported.[111] It is interesting that, whereas L-arabinose had been found previously in polysaccharides only in the furanose form, independent researches have now revealed the presence of the pyranose form in larch ε-galactan,[112] and in sapote gum.[113] An electrophoretically pure non-

---

[96] R. J. McIlroy, *J.*, 1952, 1918. [97] W. Tadros and M. Kamel, *ibid.*, p. 4532.

[98] W. E. Jancsik and E. Kaiser, *Nature*, 1952, **169**, 114.

[99] R. L. Greif, *J. Biol. Chem.*, 1952, **194**, 619; J. G. Bachtold and L. P. Gebhardt, *ibid.*, p. 635.

[100] P. H. Maurer and S. S. Hudack, *Arch. Biochem.*, 1952, **38**, 49.

[101] A. G. Ogston and J. E. Stanier, *Biochem. J.*, 1952, **52**, 149.

[102] R. W. Jeanloz, *J. Biol. Chem.*, 1952, **197**, 141; *Helv. Chim. Acta*, 1952, **35**, 262.

[103] M. M. Rapport, B. Weissmann, F. Linker, and K. Meyer, *Nature*, 1951, **168**, 996.

[104] B. Weissmann and K. Meyer, *J. Amer. Chem. Soc.*, 1952, **74**, 4729.

[105] A. Linker and K. Meyer, *Fed. Proc.*, 1952, **11**, 249.

[106] S. Roseman *et al.*, *ibid.*, p. 276.

[107] M. L. R. Harkness and A. Wassermann, *J.*, 1952, 497.

[108] I. L. Mongar and A. Wassermann, *ibid.*, pp. 492, 500, 510.

[109] S. K. Chanda, E. L. Hirst, E. G. V. Percival, and A. G. Ross, *ibid.*, p. 1833.

[110] W. E. Trevelyan and J. S. Harrison, *Biochem. J.*, 1952, **50**, 298.

[111] R. B. Duff, *Chem. and Ind.*, 1952, 1104; *J. Sci. Food Agric.*, 1952, **3**, 140.

[112] J. K. N. Jones, *Chem. and Ind.*, 1952, 954.

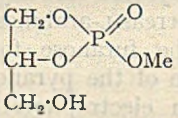
[113] E. V. White, *J. Amer. Chem. Soc.*, 1952, **74**, 3966.

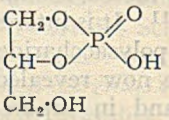
reducing oligosaccharide from the cell wall of *Corynebacterium diphtheriae* appears to contain two D-galactose residues, one of D-mannose, and three of D-arabinose, but the molecular weight of such a molecule is only *ca.* 75% of that actually found.[114] Polysaccharides isolated from three fresh-water algæ, *Nitella, Oscillatoria,* and *Nostoc,* were, respectively, a cellulose-like polyglucosan, a polyglucosan of the amylopectin class, and a mucilaginous acidic polysaccharide containing at least six different monosaccharide units.[115] Chondrosine, the component disaccharide of chondroitin sulphuric acid, has been characterised as 4-β(?)-[2-amino-2-deoxy-D-galactopyranosyl] D-glucuronic acid; [116] in the heteropolymer, which is very probably linear, one sulphate acid ester group and the glycosidic attachment of the adjacent D-glucuronic acid unit are yet to be assigned between positions 3, 4, and 6 of each chondrosamine residue.[116]

### Nucleic acids.

This year has been an important one in the development of nucleic acid chemistry, mainly as a result of contributions by Brown and Todd, and by Markham and Smith. The former workers [117] showed that phosphorylation of 5′-trityl adenosine with dibenzyl chlorophosphonate (phosphorochloridate), followed by removal of the protecting groups, yielded two adenylic acids, seemingly identical with the isomeric adenylic acids *a* and *b* derived from ribonucleic acids; evidence was presented for their formulation as adenosine-2′ and adenosine-3′ phosphate, although not necessarily respectively. Their interconversion under acidic conditions into an equilibrium mixture of the two was explained by ready phosphoryl migration *via* an intermediate cyclic ortho-structure; there was no rearrangement under alkaline conditions. In these respects, there is a close parallel with the behaviour of glycerol monophosphates.[117] On the other hand, it was recalled that glycerol α-(methyl hydrogen phosphate) and triesters of phosphoric acid are unstable to alkali; in the former case, the reaction probably proceeds *via* the neutral cyclic triester (V), which is hydrolysed immediately to methanol and the cyclic

(V)





(VI)

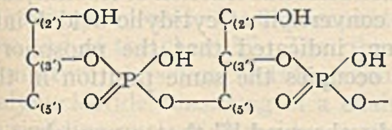
phosphate (VI), and this, in turn, gives glycerol α- and β-phosphate.[117] Dialkyl phosphates, devoid of a hydroxyl function in proximity to the phosphoryl group, are stable to alkali. For these and other reasons, a simple straight-chain polynucleotide sequence was represented as (VII), in which the individual nucleoside residues are shown briefly as $C_{(2')}$–$C_{(3')}$–$C_{(5')}$; alkaline degradation was regarded as proceeding through an intermediate (VIII), followed by ready fission of the triester groups *exclusively* at the P–O–$C_{(5')}$ linkage, to give eventually a mixture of nucleoside-2′ and -3′ phosphates.[117] In addition to structure (VII), in which the polymeric linkage is shown joining the 3′- and 5′-positions, other structures with

---

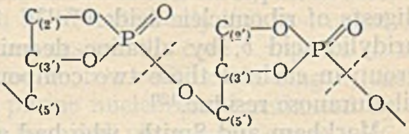
[114] E. S. Holdsworth, *Biochim. Biophys. Acta,* 1952, 8, 110; 1952, 9, 19; T. J. Bowen, *ibid.*, p. 29. [115] L. Hough, J. K. N. Jones, and W. H. Wadman, *J.*, 1952, 3393.

[116] M. L. Wolfrom, R. K. Madison, and M. J. Cron, *J. Amer. Chem. Soc.*, 1952, 74, 1491. [117] D. M. Brown and A. R. Todd, *J.*, 1952, 44, 52.

$C_{(2')}$–$C_{(5)}$ or $C_{(2')}$–$C_{(3')}$ links, or mixed $C_{(2)}$–$C_{(2')}$ and $C_{(3')}$–$C_{(3')}$ units in sequence would all show alkali lability. A $C_{(5')}$–$C_{(5'}$ linkage, however, cannot occur anywhere in the molecule as this would be stable to alkali and would lead to the appearance of dinucleotides in ribonucleic acid hydrolysates.[117] Reasons were given for believing that $C_{(5')}$ is involved in the main internucleotide linkage of both ribonucleic and deoxyribonucleic acids, thus restricting the choice of linkage to $C_{(2')}$–$C_{(5')}$ and $C_{(3')}$–$C_{(5')}$. Since deoxyribonucleic acids cannot be of the former type, it was regarded as advantageous, at the moment, to represent the " backbone " of ribonucleic acids as (VII). Deoxyribonucleic acids are not degraded to small molecules by mild treatment with alkali because the essential formation of a cyclic structure is precluded.[117]

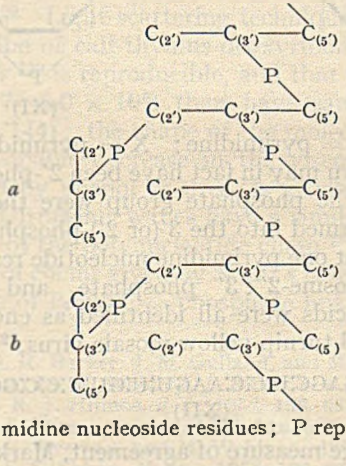


(VII)



(VIII)

Brown and Todd [117] pointed out that, although deoxyribonucleic acids appear to be largely straight-chain polynucleotides, ribonucleic acids probably have a branched-chain structure. They considered the known production of large amounts of pyrimidine nucleotides during ribonuclease treatment of ribonucleic acids to suggest that these nucleotides are derived from short side chains, which occur at frequent intervals and probably for the most part contain only one nucleoside residue. Accordingly, they envisaged a possible general structure for ribonucleic acid as (IX), an extension of (VII).



(IX) *a* and *b* are pyrimidine nucleoside residues ; P represents a phosphate group.

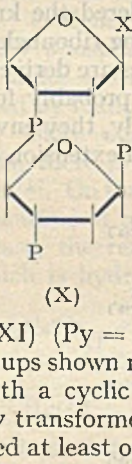
Further experimental support for the above concepts of the architecture of the ribonucleic acid molecule was obtained subsequently. The cyclic 2′ : 3′-phosphates of adenosine, cytidine, and uridine were prepared [118] from the corresponding 2′- and 3′-phosphates, by the widely applicable esteri-

---

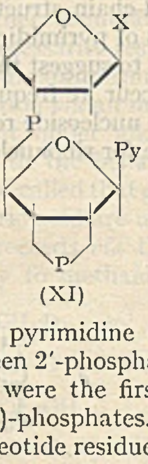
[118] D. M. Brown, D. I. Magrath, and A. R. Todd, *J.*, 1952, 2708.

fication process promoted by trifluoroacetic anhydride.[119] With acid or alkali, the cyclic esters gave mixtures of the *a* and *b* nucleotides.[118] Ribonuclease converted cytidine-2′ : 3′-phosphate into cytidylic acid *b*, and uridine-2′ : 3′ phosphate into uridylic acid *b*, but it had no action on adenosine-2′ : 3′ phosphate;[120] these observations accord well with the fact that there is little or no purine nucleotide in the mononucleotide fraction of ribonuclease digests of ribonucleic acids.[120, 121] The conversion of cytidylic acid *b* into uridylic acid *b*, by alkaline deamination, indicated that the phosphoryl group in each of these two compounds occupies the same position in the ribofuranose residue.[120]

Markham and Smith, who had already observed[122] that a new class of nucleotide appears during the digestion of ribonucleic acid with ribonuclease, have extended their studies[123] and have provided excellent confirmation of part of the theory of Brown and Todd.[117] They have shown[123] that the new class of nucleotide is, in fact, composed of nucleoside-2′ : 3′ phosphates, which are formed also by mild alkaline hydrolysis of ribonucleic acid, and have confirmed that the cyclic phosphates of pyrimidine, but not of purine, nucleosides are substrates for ribonuclease. In a more detailed analysis, based on chromatography and paper electrophoresis, methods were given for the isolation of fifteen of the smaller products formed from ribonucleic acid by ribonuclease.[123] The general structure of the dinucleotides was



(X)



(XI)

either (X) or (XI) (Py = pyrimidine; X = pyrimidine or purine); the 3′-phosphate groups shown may in fact have been 2′-phosphate groups. The dinucleotides with a cyclic phosphate group were the first liberated, and were then slowly transformed into the 3′(or 2′)-phosphates. The trinucleotides all contained at least one pyrimidine nucleotide residue.[123] Adenosine-2′ : 3′ phosphate, guanosine-2′ : 3′ phosphate, and adenylic, guanylic, cytidylic, and uridylic acids were all identified as end-groups in the ribonucleic acids of yeast and turnip yellow mosaic virus.[123]

AC:U:C:U:C:C:AGAGC:U:C:C:AAGU:U:GU:U:C:C:GC:C:U:AGC:A

(XII)

In spite of such a large measure of agreement, Markham and Smith were not able to accept the branched structure (IX) advanced by Brown and Todd for ribonucleic acid. They believed the acid to be composed of a mixture

---

[119] E. J. Bourne, M. Stacey, J. C. Tatlow, and J. M. Tedder, *J.*, 1949, 2976.
[120] D. M. Brown, C. A. Dekker, and A. R. Todd, *J.*, 1952, 2715.
[121] R. Markham and J. D. Smith, *Nature*, 1951, **168**, 406.
[122] *Idem, Research*, 1951, **4**, 344. [123] *Idem, Biochem. J.*, 1952, **52**, 552, 558, 565.

of many kinds of comparatively short chains, with the general features of (XII) in which A, G, C, and U represent adenylic, guanylic, cytidylic, and uridylic acid residues, respectively, each nucleoside being joined at position-2′ (or -3′) through a phosphate ester link to the adjacent residue on the right-hand side, and at position-5′ through a similar link to its neighbour on the left; the bonds which are broken by ribonuclease are shown as colons. A purine nucleoside-2′ : 3′ phosphate can be liberated only if it is situated at one end of the chain.[123] The ribonuclease-resistant " core " appears to be a mixture of polynucleotides about three to five residues in length, each polynucleotide consisting of a chain of purine nucleotides terminated by a pyrimidine nucleotide residue, with the terminal phosphoryl group on $C_{(2')}$ or $C_{(3')}$. The failure of this " core " to dialyse through Cellophane is due apparently largely to its charge, rather than to its molecular size [123] (see also ref. 127). Methylation evidence has been claimed to demonstrate that yeast ribonucleic acid possesses internucleotide linkages between ribose and phosphoryl residues, and also that there is a high degree of branching, due to triply phosphorylated ribose units.[124] Several dinucleotides have been isolated in an analytically pure state from acid-treated yeast ribonucleic acid.[125] Studies have been made of the splitting of purine ribosides by both a hydrolytic and a phosphorolytic system found in autolysates of dried baker's yeast.[126] A promising method for the degradation of ribonucleic acid, catalysed by methoxide ion, has been announced.[126a]

Deoxyribonucleic acids have continued to receive considerable attention. Samples derived from animal, plant, and bacterial sources have been analysed carefully,[127, 128] as also have the enzyme-resistant " cores " produced therefrom by deoxyribonuclease; [127] a new pyrimidine base, 5-hydroxymethylcytosine, is present in bacteriophage nucleic acids.[128] The deoxypentose-nucleic acids from three different strains of *E. coli* possess unusual purine and pyrimidine contents.[129] Light-scattering techniques have revealed that the method for the isolation of calf-thymus deoxyribonucleic acid developed by Schwander and Signer [130] is reproducible, and that the product has a higher molecular weight ($6{\cdot}7$—$8{\cdot}0 \times 10^6$) than have samples prepared in other ways [131] (see also ref. 144); the shape of the molecule is greatly dependent on pH.[131] The irreversible decrease in the viscosity of deoxyribonucleic acid solutions, caused by phenol or urea, is attributed to the breakage of hydrogen bonds.[132] Ultrasonic waves have a similar effect, but in addition there is some scission of the polynucleotide chain.[133] Dilute acid and alkali increase the intensity of colour given by Schiff's reagent; this might possibly be due to the rupture of labile $C_{(1')}$–phosphate links.[134] Under mild acidic

---

[124] A. S. Anderson, G. R. Barker, J. M. Gulland, and M. V. Lock, *J.*, 1952, 369.
[125] R. B. Merrifield and D. W. Woolley, *J. Biol. Chem.*, 1952, **197**, 521.
[126] L. A. Heppel and R. J. Hilmoe, *ibid.*, 1952, **198**, 683.
[126a] D. Lipkin and J. S. Dixon, *Science*, 1952, **116**, 525.
[127] S. G. Laland, W. G. Overend, and M. Webb, *J.*, 1952, 3224.
[128] G. R. Wyatt and S. S. Cohen, *Nature*, 1952, **170**, 846, 1072.
[129] B. Gandelman, S. Zamenhof, and E. Chargaff, *Biochim. Biophys. Acta*, 1952, **9**, 399.
[130] H. Schwander and R. Signer, *Helv. Chim. Acta*, 1950, **33**, 1521.
[131] M. E. Reichmann, R. Varin, and P. Doty, *J. Amer. Chem. Soc.*, 1952, **74**, 3203; P. Doty and B. H. Bunce, *ibid.*, p. 5029.
[132] B. E. Conway and J. A. V. Butler, *J.*, 1952, 3075.
[133] S. G. Laland, W. G. Overend, and M. Stacey, *ibid.*, p. 303.
[134] W. A. Lee and A. R. Peacocke, *ibid.*, p. 130.

conditions purines can be removed quantitatively from calf-thymus deoxyribonucleic acid, without completely destroying the original highly polymerised structure and without changing the distribution of the pyrimidine nucleotides.[135]

The nucleotides and dinucleotides resulting from deoxyribonuclease action on the deoxyribonucleic acids of calf thymus,[136] wheat embryo,[137] and herring sperm [137, 138] have been examined; in one case 5′-deoxycytidylic acid was identified in the digest.[139] An ion-exchange chromatographic procedure, suitable for use on a large scale, has been described for the separation of deoxyribonucleosides.[138] Earlier assumptions that sodium arsenate, sodium citrate, and sodium borate (known inhibitors of pancreatic deoxyribonuclease) inhibit intra-cellular deoxypentosenucleases of mammalian tissues have been shown to be invalid.[140]

It has been demonstrated, by indirect methods, that enzyme preparations from *Lactobacillus helveticus*, *Lactobacillus delbrueckii*, and *Thermobacterium acidophilus* R. 26 catalyse the transfer of the deoxyribose residue from one purine or pyrimidine to another.[141] These enzyme(s) are trans-*N*-glycosidases; they are unable to utilise either deoxyribose or deoxyribose-1 phosphate.[141] Among other topics studied are (*a*) the binding of sodium chloride [142] and mercuric chloride [143] with calf-thymus deoxypentosenucleate, and (*b*) the spectrophotometry of this nucleic acid,[144] and of natural and synthetic pyrimidine ribo- and deoxyribo-nucleosides,[145] as a function of pH.

### Proteins.

Since the chemistry of proteins was covered very fully in the *Annual Reports* for 1951, only brief reference to the subject will be made this year. The formidable task of condensing such a vast field into so small a space can best be accomplished by drawing attention to useful reviews of current researches; five such reviews, published during 1952, give a fairly comprehensive picture of the present position. Writing from the viewpoint of the organic chemist, Khorana [146] has surveyed structural investigations, and chemical methods of synthesis of polypeptides and proteins. Edsall [147] has provided a concise account of a Royal Society Discussion, in which the main emphasis was on the contributions of *X*-ray and infra-red techniques to the problem of the structural pattern of the polypeptide chains in proteins. Particular attention was paid to synthetic poly-$\gamma$-methyl L-glutamate fibres, and it was concluded [147] that, although further work is certainly needed, the balance of evidence on these synthetic polypeptides seems to be in favour of the $\alpha$-helix. In a survey of recent developments in the separations of proteins and enzymes by paper chromatography, Boman [148] laid stress on the

---

[135] C. Tamm, M. E. Hodes, and E. Chargaff, *J. Biol. Chem.*, 1952, **195**, 49.

[136] R. L. Sinsheimer and J. F. Koerner, *J. Amer. Chem. Soc.*, 1952, **74**, 283.

[137] J. D. Smith and R. Markham, *Nature*, 1952, **170**, 120; *Biochim. Biophys. Acta*, 1952, **8**, 350. [138] W. Andersen, C. A. Dekker, and A. R. Todd, *J.*, 1952, 2721.

[139] J. L. Potter, K. D. Brown, and M. Laskowski, *Biochim. Biophys. Acta*, 1952, **9**, 150. [140] M. Webb, *Nature*, 1952, **169**, 417.

[141] W. S. Macnutt, *Biochem. J.*, 1952, **50**, 384.

[142] J. Shack, R. J. Jenkins, and J. M. Thompsett, *J. Biol. Chem.*, 1952, **198**, 85.

[143] S. Katz, *J. Amer. Chem. Soc.*, 1952, **74**, 2238.

[144] J. Shack and J. M. Thompsett, *J. Biol. Chem.*, 1952, **197**, 17; G. Frick, *Biochim. Biophys. Acta*, 1952, **8**, 625. [145] D. Shugar and J. J. Fox, *ibid.*, 1952, **9**, 199, 369.

[146] H. G. Khorana, *Quart. Reviews*, 1952, **6**, 340.

[147] J. T. Edsall, *Nature*, 1952, **170**, 53. [148] H. G. Boman, *ibid.*, p. 703.

phenomenon of "double-fronting." An interesting discussion[149] of the physical chemistry of proteins ranged over such topics as the globular–fibrous protein transformation, zone electrophoresis in filter-paper, mechanisms of muscular action, the conversion of fibrinogen into fibrin, mucoproteins, nucleoproteins, antigen–antibody reactions, and protein interactions with heavy metals, alkaline earths, heparin, and other organic molecules. The biogenesis of proteins was the subject of a symposium in Paris.[150]

E. J. B.

A. S. Bailey.
E. J. Bourne.
J. W. Cornforth.
T. G. Halsall.
T. J. King.
J. F. W. McOmie.
R. A. Raphael.
J. Walker.
W. A. Waters.
B. C. L. Weedon.

---

[149] The Physical Chemistry of Proteins, *Discuss. Faraday Soc.*, 1952.

[150] Symposium on the Biogenesis of Proteins, 2nd Internat. Congr. Biochem., Paris, 1952.

# BIOCHEMISTRY

## 1. INTRODUCTION.

THE present report forms the third of the series since the commencement of the new attempt to report on " larger fields of biochemistry." The Second International Congress of Biochemistry, held in Paris in July, 1952, was considered to be a great success.

E. B.

## 2. BACTERIAL NUTRITION.

Micro-organisms, because of their widely differing nutritional requirements, have proved valuable tools in the elucidation of biosynthetical pathways and the metabolic functions of B-group vitamins. This Report has been written from this point of view, though it is obviously limited, since a discussion of bacterial nutrition in its widest sense would include all substances and environmental conditions influencing bacterial growth. Some recently published reviews and books dealing with aspects of the field are given in ref. 1.

Methods of approach to problems of biosynthesis and metabolic function have been discussed by Woods,[2] who stresses the importance of nutritional investigations; these may guide the planning of further experiments (*e.g.*, with cell suspensions and enzyme preparations) likely to provide more direct information. Induced biochemical mutant strains of bacteria are now widely used to investigate mechanisms of biosynthesis. The penicillin technique [3] for the isolation of such strains has contributed greatly to the development of this field; it has been improved recently by Adelberg and Myers.[4]

**Nature and Function of the Vitamin B Group Complex.**—It may now be accepted as a working hypothesis that B-group vitamins function catalytically in cell metabolism as components of coenzymes. An outstanding recent advance in this field has been in the clarification of the nature and function of the protogen–lipoic acid group of factors, which can now be included in the vitamin-B complex.

*Protogen, lipoic acid, and pyruvate-oxidation factors.* Early work on these factors developed independently along three lines. Substances were found in yeast extract which (*a*) replaced acetate for growth of some lactobacilli (" acetate-replacing factor "),[5] (*b*) promoted pyruvate oxidation by cell suspensions of *Streptococcus faecalis* 10 Cl grown in a semi-synthetic

---

[1] H. C. Lichstein, *Ann. Rev. Microbiol.*, 1952, **6**, 1; J. L. Stokes, *ibid.*, p. 29; E. C. Barton-Wright, " The Microbiological Assay of the Vitamin B Complex and Amino-acids," Pitman and Sons Ltd., London, 1952; F. A. Robinson, " The Vitamin B Complex," Chapman and Hall Ltd., London, 1951; C. H. Werkman and P. W. Wilson (editors), " Bacterial Physiology," Academic Press, New York, 1951; D. W. Woolley, " A Study of Antimetabolites," Chapman and Hall Ltd., London, 1952.

[2] D. D. Woods, *Bull. World Hlth. Org.*, 1952, **6**, 35.

[3] B. D. Davis, *Experientia*, 1950, **6**, 41.

[4] E. A. Adelberg and J. W. Myers, *Fed. Proc.*, 1952, **11**, 179.

[5] B. M. Guirard, E. E. Snell, and R. J. Williams, *Arch. Biochem.*, 1946, **9**, 381.

medium ("pyruvate-oxidation factor"),[6] and (*c*) were growth factors for *Tetrahymena geleii* and an unidentified *Corynebacterium sp.* ("protogen").[7] Snell and Broquist [8] found preparations of these factors to be interchangeable in the different test systems and suggested that they were closely related; subsequent work has confirmed this view. There is now strong evidence that *Butyribacterium rettgeri* factor [9] also belongs to this group.

These substances have all been found to exist in natural materials in several biologically active but chromatographically distinct forms.[9–13] One of the acetate-replacing factors from liver has been obtained crystalline (α-lipoic acid) [12] and simultaneously, protogen-B was isolated from the same source as the crystalline benzylthiuronium salt.[13] Highly purified concentrates of α-lipoic acid and of protogen-B each contained another active principle, named β-lipoic acid and protogen-A, respectively.[14, 15] As purification proceeded these were transformed into the factors finally isolated. The chemical properties of α-lipoic acid and protogen-B suggest that both are derived from a dimercapto-*n*-octanoic acid.[14–16] The Lederle workers [17] find (±)-5 : 8-dimercapto-octanoic acid ("thioctic acid") and (±)-6 : 8-dimercapto-octanoic acid ("6-thioctic acid") to have the biological activity of protogen-B in a number of test systems (acetate replacement, pyruvate oxidation, and growth-promoting activity for *Corynebacterium sp.* and *T. geleii*); 6-thioctic acid is 100—1000 times more active than 5-thioctic acid. A synthetic preparation with properties similar to those of α-lipoic acid has also been obtained; it is suggested, on the basis of experiments with the synthetic substance and α-lipoic acid, that the latter is one of the optical isomers of the cyclic disulphide derived from 5 : 8-dimercapto-octanoic acid.[18] The present chemical data are insufficient to permit assignment of definite structures to α-lipoic acid and protogen-B. The relationship of these compounds to the other biologically active, natural substances is also not yet clear.

Factors of this group act at very low concentration in promoting bacterial

---

[6] D. J. O'Kane and I. C. Gunsalus, *J. Bact.*, 1948, **56**, 499.

[7] E. L. R. Stokstad, C. E. Hoffmann, M. A. Regan, D. Fordham, and T. H. Jukes, *Arch. Biochem.*, 1949, **20**, 75; E. L. R. Stokstad, C. E. Hoffmann, and M. Belt, *Proc. Soc. Exp. Biol. N.Y.*, 1950, **74**, 571.

[8] E. E. Snell and H. P. Broquist, *Arch. Biochem.*, 1949, **23**, 326.

[9] L. Kline and H. A. Barker, *J. Bact.*, 1950, **60**, 349; L. Kline, L. Pine, I. C. Gunsalus, and H. A. Barker, *ibid.*, 1952, **64**, 467.

[10] L. J. Reed, B. G. De Busk, P. M. Johnston, and M. E. Getzendaner, *J. Biol. Chem.*, 1951, **192**, 851; L. J. Reed, M. E. Getzendaner, B. G. De Busk, and P. M. Johnston, *ibid.*, p. 859.

[11] I. C. Gunsalus, L. Struglia, and D. J. O'Kane, *ibid.*, 1952, **194**, 859.

[12] L. J. Reed, B. G. De Busk, I. C. Gunsalus, and C. S. Hornberger, Jnr., *Science*, 1951, **114**, 93.

[13] E. L. Patterson, J. A. Brockman, Jnr., F. P. Day, J. V. Pierce, M. E. Macchi, C. E. Hoffmann, C. T. O. Fong, E. L. R. Stokstad, and T. H. Jukes, *J. Amer. Chem. Soc.*, 1951, **73**, 5919.

[14] L. J. Reed, B. G. De Busk, I. C. Gunsalus, and G. H. F. Schnakenberg, *ibid.*, p. 5920.

[15] J. A. Brockman, Jnr., E. L. R. Stokstad, E. L. Patterson, J. V. Pierce, M. Macchi, and F. P. Day, *ibid.*, 1952, **74**, 1868.

[16] L. J. Reed, Q. F. Soper, G. H. F. Schnakenberg, S. F. Kern, H. Boaz, and I. C. Gunsalus, *ibid.*, p. 2383.

[17] M. W. Bullock, J. A. Brockman, Jnr., E. L. Patterson, J. V. Pierce, and E. L. R. Stokstad, *ibid.*, p. 1868, 3455.

[18] C. S. Hornberger, Jnr., R. F. Heitmiller, I. C. Gunsalus, G. H. F. Schnakenberg, and L. J. Reed, *ibid.*, p. 2382.

growth. Other compounds besides acetate have been found to replace them for different organisms. These include malate, succinate, hydrogen carbonate (a strain of *Strep. faecalis*) [19] and sorbitan mono-oleate (*Streptococcus cremoris*).[20] A mutant strain of *Bacterium coli* normally requiring a higher form of α-lipoic acid (see below) grows in its absence provided that acetate, citrate, and succinate are all present in the medium.[21] It appears, therefore, that acetate and di- and tri-carboxylic acids are direct or indirect products of reactions requiring factors of this group as coenzymes. Experiments with deficient cell suspensions and enzyme preparations promise to provide information about the mechanisms of these reactions. Using these methods of approach, Reed and De Busk [21] find that α-lipoic acid functions in the oxidative decarboxylation of pyruvate and α-ketoglutarate in the form of a lipoic acid–thiamine pyrophosphate coenzyme. A mutant strain of *Bact. coli* was isolated which requires for growth "lipothiamide" (prepared by heating α-lipoic acid and thiamine together *in vacuo*); α-lipoic acid is not utilised. Lipothiamide is also essential for the oxidation of pyruvate and α-ketoglutarate by deficient cell suspensions of this organism; with cell-free extracts, lipothiamide pyrophosphate is needed. Lipothiamide and its phosphorylated derivatives appear to be identical with bound forms of α-lipoic acid present in extracts of natural materials.

*Pantothenic acid.* Many organisms utilise pantoic acid or β-alanine for growth in place of pantothenic acid, suggesting that these compounds are intermediates in the formation of the vitamin. Synthesis of the vitamin from β-alanine and pantoic acid has also been observed in cell extracts of *Bact. coli*.[22] Preparations from a mutant strain of this organism, which requires pantothenic acid only when grown at >30°, also form this substance from its precursors, but the enzyme system is much more heat-labile than that from the parent strain.[23]

The synthesis of coenzyme A (the coenzyme form of pantothenic acid) from pantothenic acid may occur through the intermediate formation of pantetheine (α-pantothenoylaminoethanethiol) (I) or its corresponding

$$HO\cdot CH_2\cdot CMe_2\cdot CH(OH)\cdot CO\cdot NH\cdot [CH_2]_2\cdot CO\cdot NH\cdot [CH_2]_2\cdot SH \quad (I)$$

disulphide, pantethine.[24] Pantethine has the same activity as highly purified concentrates of *Lactobacillus bulgaricus* factor for growth of that and related organisms. Pantothenic acid also promotes growth of these organisms but is active at high concentrations only.[25,26] The several chromatographically distinct forms of *Lb. bulgaricus* factor found in extracts of natural materials are probably mixed disulphides formed between pantetheine and other thiols.[27,28]

---

[19] V. L. Lytle, S. M. Zulick, and D. J. O'Kane, *J. Biol. Chem.*, 1951, **189**, 551.

[20] V. L. Lytle and D. J. O'Kane, *J. Bact.*, 1951, **61**, 240.

[21] L. J. Reed and B. G. de Busk, *J. Amer. Chem. Soc.*, 1952, **74**, 3457, 3964, 4727; *Idem*, *J. Biol. Chem.*, 1952, **199**, 873, 881. [22] W. K. Maas, *J. Biol. Chem.*, 1952, **198**, 23.

[23] W. K. Maas and B. D. Davis, *Proc. Nat. Acad. Sci. Wash.*, 1952, **38**, 785.

[24] E. E. Snell, G. M. Brown, V. J. Peters, J. A. Craig, E. L. Wittle, J. A. Moore, V. M. McGlohan, and O. D. Bird, *J. Amer. Chem. Soc.*, 1950, **72**, 5349.

[25] G. M. Brown, J. A. Craig, and E. E. Snell, *Arch. Biochem.*, 1950, **27**, 473; R. A. McRorie, P. M. Masley, and W. L. Williams, *ibid.*, p. 471; R. A. McRorie and W. L. Williams, *J. Bact.*, 1951, **61**, 737. [26] J. A. Craig and E. E. Snell, *ibid.*, p. 283.

[27] G. M. Brown and E. E. Snell, *J. Biol. Chem.*, 1952, **198**, 375.

[28] J. C. Vitucci, N. Bohonos, O. P. Wieland, D. V. Lefemine, and B. L. Hutchings, *Arch. Biochem.*, 1951, **34**, 409.

The importance of coenzyme A in reactions involving transfer of acetyl groups and also in other systems had been fully reviewed by Lipmann, Ochoa, and others.[29,30]

*Pyridoxine and derivatives* (*vitamin-$B_6$ group*). Snell[31] has discussed some of the recent work concerning the function and mechanism of action of these factors in the amino-acid metabolism of micro-organisms. Vitamin $B_6$ is concerned in the synthesis of many amino-acids. Thus, in the presence of vitamin $B_6$, *Lactobacillus arabinosus* no longer requires lysine, serine, alanine, histidine, threonine, or cystine for growth;[32,33] with both vitamin $B_6$ and carbon dioxide present it can also dispense with phenylalanine, tyrosine, arginine, and aspartic acid.[32] The stage at which vitamin $B_6$ acts in the synthesis of these amino-acids was not shown by these experiments. In *Leuconostoc mesenteroides*, however, it is involved in the conversion of glycine into serine; it is essential for growth when high concentrations of glycine replace serine.[34] Pyridoxal is also needed for serine synthesis from glycine and formate by cell suspensions of *Strep. faecalis*.[34] Vitamin $B_6$ is required for growth of *Lb. arabinosus* and *Strep. faecalis* when α-keto-acid analogues are substituted for the corresponding amino-acids.[35] These experiments indicate that transamination reactions (requiring pyridoxal phosphate as co-factor) are responsible for the formation of amino-acids from the α-keto-acids. The latter may not, however, be normal intermediates in the synthesis of all the amino-acids in whose formation vitamin $B_6$ is implicated, and the factor may well play a part at some stage other than transamination. Pyridoxal phosphate is, for instance, a coenzyme for the system which condenses indole and serine to give tryptophan in enzyme preparations from *Neurospora*.[36]

D-Alanine becomes essential for growth of *Strep. faecalis* and *Lactobacillus casei* in media devoid of vitamin $B_6$, suggesting that the latter is needed for the synthesis of the D-amino-acid.[37] Subsequent work with enzyme preparations has confirmed this; L-alanine is converted into the D-form by a racemase requiring pyridoxal phosphate for activation.[38] Many D-amino-acids are utilised for growth of *Lb. arabinosus* in place of the L-isomers, provided that vitamin $B_6$ is present in the medium.[39,40] It appears that the co-racemase function of the factor also accounts for these observations.

*Biotin*. This compound occurs, mainly in bound forms, in many natural products.[41] Recently the isolation, identification, and chemical synthesis of

---

[29] "Symposium sur le Cycle Tricarboxylique," Second Int. Congr. Biochem., Paris, 1952.

[30] S. Ochoa and J. R. Stern, *Ann. Rev. Biochem.*, 1952, **21**, 547; A. D. Welch and C. A. Nichol, *ibid.*, p. 633.

[31] E. E. Snell, "Symposium sur le Métabolisme Microbien," p. 47, Second Int. Congr. Biochem., Paris, 1952.

[32] C. M. Lyman, O. Moseley, S. Wood, B. Butler, and F. Hale, *J. Biol. Chem.*, 1947, **167**, 177. [33] J. L. Stokes and M. Gunness, *Science*, 1945, **101**, 43.

[34] J. Lascelles and D. D. Woods, *Nature*, 1950, **166**, 649.

[35] J. T. Holden, R. B. Wildman, and E. E. Snell, *J. Biol. Chem.*, 1951, **191**, 559.

[36] W. W. Umbreit, W. A. Wood, and I. C. Gunsalus, *ibid.*, 1946, **165**, 731; C. Yanofsky, *ibid.*, 1952, **194**, 279.

[37] J. T. Holden, C. Furman, and E. E. Snell, *ibid.*, 1949, **178**, 789; J. T. Holden and E. E. Snell, *ibid.*, p. 799.

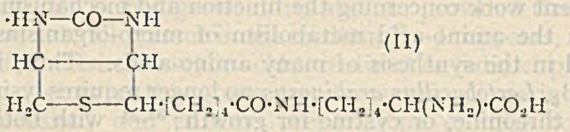
[38] W. A. Wood and I. C. Gunsalus, *ibid.*, 1951, **190**, 403.

[39] C. M. Lyman and K. A. Kuiken, *Fed. Proc.*, 1948, **7**, 170.

[40] M. N. Camien and M. S. Dunn, *J. Biol. Chem.*, 1950, **182**, 119.

[41] R. C. Thompson, R. E. Eakin, and R. J. Williams, *Science*, 1941, **94**, 589.

one of these complexes, biocytin, has been described;[42,43] it was obtained from yeast and identified as ε-*N*-biotyl-lysine (II). The synthetic compound has the same biological activity as the crystalline natural material. Biocytin is not attacked by proteolytic enzymes, such as papain and trypsin, and strong acids or alkalis are needed to liberate biotin. It is, however, as active as biotin itself for growth of many organisms (*e.g.*, *Lb. casei*), but is inactive for *Lb. arabinosus*, *Ln. mesenteroides*, and *Penicillium chrysogenum*. Like biotin, it overcomes competitively inhibition of growth of *Lb. casei* by homobiotin. Biocytin also behaves similarly to biotin in reactivating aspartic acid deaminase in " aged " cells suspensions of *Proteus vulgaris*, but does not appear to be identical with Lichstein's " biotin coenzyme " since it does not replace preparations of this substance in the aspartic acid deaminase system of *Bacterium cadaveris*.[44]



$$\begin{array}{l} \cdot HN-CO-NH \\ \quad\ |\qquad\qquad | \\ \ HC\text{------}CH \\ \quad\ |\qquad\qquad | \\ H_2C-S-CH\cdot[CH_2]_4\cdot CO\cdot NH\cdot[CH_2]_4\cdot CH(NH_2)\cdot CO_2H \end{array} \qquad (II)$$

Pimelic acid replaces biotin for growth of *Corynebacterium diphtheriae*[45] and is presumably a precursor in this organism. Evidence that it is also a precursor in *Bacillus tenuis* and other organisms has come from work with growth-inhibitory analogues of pimelic acid; inhibition by these compounds is overcome competitively by pimelic acid whereas, in the presence of biotin, growth is insensitive to the analogues.[46]

The function of biotin in cell metabolism is not clear; Lichstein[47] has reviewed some aspects of this problem. Research with bacteria has pointed to its possible role in carboxylation reactions and in the synthesis of oleic acid. Thus, growth of *Lb. arabinosus* (and other lactobacilli) occurs in the absence of biotin provided that aspartic acid and oleic acid (together with Tween-40 or -80 to detoxify the fatty acid) are present in the medium.[48,49] Growth under these conditions is stimulated by carbon dioxide, but in the presence of biotin either aspartic acid or carbon dioxide is stimulatory. Biotin does not however appear to be involved in aspartic acid formation in *Clostridium butyricum* and *Lactobacillus fermenti*; oleic acid alone promotes growth in the absence of the vitamin, and under these conditions the organisms synthesise aspartic acid.[49] Blanchard *et al.*[50] have suggested that biotin is concerned in the formation of enzymes required in carboxylation reactions rather than as a co-factor in these systems; this conclusion was based on experiments with the " malic enzyme " system from *Lb. arabinosus*, which

---

[42] L. D. Wright, E. L. Cresson, H. R. Skeggs, T. R. Wood, R. L. Peck, D. E. Wolf, and K. Folkers, *J. Amer. Chem. Soc.*, 1950, **72**, 1048.

[43] *Idem, ibid.*, 1952, **74**, 1996; R. L. Peck, D. E. Wolf, and K. Folkers, *ibid.*, p. 1999; D. E. Wolf, J. Valiant, R. L. Peck, and K. Folkers, *ivid.*, p. 2002; L. D. Wright, E. L. Cresson, K. V. Liebert, and H. R. Skeggs, *ibid.*, p. 2004.

[44] H. C. Lichstein, J. F. Christman, and W. L. Boyd, *J. Bact.*, 1950, **59**, 113; H. C. Lichstein, *ibid.*, 1950, **60**, 485.

[45] J. H. Mueller, *J. Biol. Chem.*, 1937, **119**, 121; V. Du Vigneaud, K. Dittmer, E. Hague, and B. Long, *Science*, 1942, **96**, 186.

[46] D. W. Woolley, *J. Biol. Chem.*, 1950, **183**, 495.

[47] H. C. Lichstein, *Vitamins and Hormones*, 1951, **9**, 27.

[48] R. L. Potter and C. A. Elvehjem, *J. Biol. Chem.*, 1948, **172**, 531.

[49] H. P. Broquist and E. E. Snell, *ibid.*, 1951, **188**, 431.

[50] M. L. Blanchard, S. Korkes, A. del Campillo, and S. Ochoa, *ibid.*, 1950, **187**, 875.

catalyses the reversible decarboxylation of malic acid to pyruvic acid and carbon dioxide.

It may be significant that traces of biotin have been found in cells of *Lb. arabinosus, Cl. butyricum,*[49] *Lb. casei,*[51] and *Clostridium perfringens*[52] grown in the complete absence of the factor.

*Factors of the folic acid group.* This group includes *p*-aminobenzoic acid, pteroylglutamic acid, and *Leuconostoc citrovorum* factor. Aspects of the subject have been reviewed recently by Woods,[2, 53] Welch and Nichol,[30] and Shive.[54]

Investigations of the requirement of different organisms for factors of the folic acid group have shown that *p*-aminobenzoic acid is converted into a higher form closely related to, though not necessarily identical with *Ln. citrovorum* factor; there is strong evidence that sulphonamides inhibit bacterial growth by preventing competitively the utilisation of *p*-aminobenzoic acid in this way.[55] Some organisms (*e.g.*, *Lb. casei* and *Strep. faecalis*) are unable to grow on *p*-aminobenzoic acid but respond to either pteroylglutamic acid or *Ln. citrovorum* factor, while *Ln. citrovorum* utilises the latter substance only. The status of pteroylglutamic acid as a normal intermediate in the conversion of *p*-aminobenzoic acid into higher forms is, however, very doubtful.[2]

The outstanding recent advance in this field has been the identification of *Ln. citrovorum* factor as a formyltetrahydropteroylglutamic acid; synthetic *Ln. citrovorum* factor (leucovorin[56] or folinic acid-SF[57]) is 5-formyl-5 : 6 : 7 : 8-tetrahydropteroylglutamic acid (cf. *Ann. Reports*, 1951, **48**, 227), and full details of its synthesis have now been published.[58] Leucovorin has only one half the activity of the natural factor (isolated as the crystalline barium salt from liver) for growth of *Ln. citrovorum.*[59] It is also less active than pteroylglutamic acid as a growth factor for *Lb. casei* and *Strep. faecalis* whereas the natural substance has the same potency.[60, 61] The fact that the synthetic compound is a mixture of the (+):L- and the (−):L-isomer probably accounts for these differences. The calcium salts of the isomers have been separated, and the (−)L-form shown to have the same activity as natural *citrovorum* factor and to be twice as active as the (+):L-isomer.[62]

That *Ln. citrovorum* factor is more closely related than pteroylglutamic acid to the coenzyme form of folic acid is suggested also by the greater activity

---

[51] E. A. Andrews and V. R. Williams, *I. Boil, Chem.*, 1951, **193**, 11.

[52] E. Rosenwasser and M. J. Boyd, *Fed. Proc.*, 1952, **11**, 277.

[53] D. D. Woods, " Symposium sur le Métabolisme Microbien," p. 86, Second Int. Congr. Biochem., Paris, 1952.

[54] W. Shive, *Vitamins and Hormones*, 1951, **9**, 75; *Ann. Rev. Microbiol.*, 1952, **6**, 437.

[55] R. H. Nimmo-Smith, J. Lascelles, and D. D. Woods, *Brit. J. Exp. Path.*, 1948, **29**, 264; J. Lascelles and D. D. Woods, *ibid.*, 1952, **33**, 288.

[56] J. Brockman, Jnr., B. Roth, H. P. Broquist, M. E. Hultquist, J. M. Smith, Jnr., M. J. Fahrenbach, D. B. Cosulich, R. P. Parker, E. L. R. Stokstad, and T. H. Jukes, *J. Amer. Chem. Soc.*, 1950, **72**, 4325.

[57] E. H. Flynn, T. J. Bond, T. J. Bardos, and W. Shive, *ibid.*, 1951, **73**, 1979; A. Pohland, E. H. Flynn, R. G. Jones, and W. Shive, *ibid.*, p. 3247.

[58] B. Roth, M. E. Hultquist, M. J. Fahrenbach, D. B. Cosulich, H. P. Broquist, J. A. Brockman, Jnr., J. M. Smith, Jnr., R. P. Parker, E. L. R. Stokstad, and T. H. Jukes, *ibid.*, 1952, **74**, 3247. [59] J. C. Keresztesy and M. Silverman, *ibid.*, 1951, **73**, 5510.

[60] H. E. Sauberlich, *J. Biol. Chem.*, 1952, **195**, 337.

[61] O. P. Wieland, B. L. Hutchings, and J. H. Willams, *Arch. Biochem.*, 1952, **40**, 205.

[62] D. B. Cosulich, J. M. Smith, Jnr., and H. P. Broquist, *J. Amer. Chem. Soc.*, 1952, **74**, 4215.

of leucovorin and the natural factor in overcoming inhibition of growth of *Strep. faecalis* by 4-aminopteroylglutamic acid (aminopterin).[60, 63] Like pteroylglutamic acid, leucovorin is a competitive antagonist of the analogue.

With one exception, leucovorin has so far been found inactive in replacing *p*-aminobenzoic acid for growth of organisms requiring that compound. *Ln. mesenteroides*, however, utilises it in place of *p*-aminobenzoic acid, whereas pteroylglutamic acid is inactive.[64] Possibly, *Ln. citrovorum* factor may be converted into a still more complex form before it functions in cell metabolism.

Recently, strains of *Strep. faecalis* and *Ln. citrovorum* have been described, whose growth is insensitive to inhibition by 4-amino- and 4-amino-10-methylpteroylglutamic acid (amethopterin).[65] The resistant strain of *Strep. faecalis* utilises the analogues in place of pteroylglutamic acid, but the variant strain of *Ln. citrovorum* does not respond to the analogues instead of leucovorin.

Factors of the folic acid group may be concerned as cofactors in reactions involving transfer of a one-carbon unit. They are involved in the synthesis of methionine, serine, histidine, and possibly other amino-acids, as well as in the formation of purines and thymine.[2, 30, 53, 54] The initial information concerning the function of these factors was provided by investigations of the substances able to replace them for growth of micro-organisms. For instance, the importance of *Ln. citrovorum* factor in the conversion of glycine into serine is shown by the requirement of *Ln. mesenteroides* for leucovorin when high concentrations of glycine replace serine for growth; under these conditions, *p*-aminobenzoic acid is utilised instead of leucovorin only if incubation is in an atmosphere enriched with carbon dioxide.[34, 64] In *Torula cremoris* inhibition of growth by aminopterin is overcome competitively by concentrates of *Ln. citrovorum* factor; in the absence of the latter inhibition is overcome non-competitively by a mixture of methionine, purines, and histidine.[66] The requirement of mutant strains of *Saccharomyces cerevisiæ* for *p*-aminobenzoic acid is abolished by similar mixtures.[67, 68]

The precise stage in the various syntheses at which folic acid acts has not always been clearly shown by growth experiments. For methionine and serine, more direct evidence has come from work with deficient cell suspensions. Thus, *p*-aminobenzoic acid is needed for the conversion of homocysteine into methionine by cell suspensions of *Bact. coli* deficient in that factor; the β-carbon atom of serine may serve as a source of the one-carbon residue needed in this reaction.[69] Deficient cell suspensions of *Strep. faecalis* form serine from glycine and formate provided that pteroylglutamic acid or leucovorin is present.[34] It is probable that folic acid is concerned in the formation of the amidine carbon in the glyoxaline ring of histidine; this has been found by isotopic techniques to arise from formate in yeast.[70] In purine synthesis factors of the folic acid group are very probably needed for the formation of the 2- and the 8-carbon atom of the nucleus.[54] The factors are involved in the utilisation of 4-aminoglyoxaline-5-carboxyamide, a possible precursor of

---

[63] H. P. Broquist, E. L. R. Stokstad, and T. H. Jukes, *Fed. Proc.*, 1951, **10**, 167.

[64] J. Lascelles, M. J. Cross, and D. D. Woods, *Biochem. J.*, 1951, **49**, lxvi.

[65] J. H. Burchenal, G. B. Waring, and D. J. Hutchison, *Proc. Soc. Exp. Biol. N.Y.*, 1951, **78**, 311; D. J. Hutchison and J. H. Burchenal, *ibid.*, 1952, **80**, 516.

[66] H. P. Broquist, *Fed. Proc.*, 1952, **11**, 191.

[67] N. S. Cutts and C. Rainbow, *J. Gen. Microbiol.*, 1950, **4**, 150.

[68] S. Pomper, *J. Bact.*, 1952, **64**, 353.

[69] F. Gibson and D. D. Woods, *Biochem. J.*, 1952, **51**, v.

[70] L. Levy and M. J. Coon, *J. Biol. Chem.*, 1951, **192**, 807.

purines, since the amine accumulates in cultures of *Bact. coli* when the effective concentration of *p*-aminobenzoic acid is limited by sulphonamides;[71] it is also found in cultures of mutant strains of *Bact. coli* requiring *p*-aminobenzoic acid, when that compound is supplied in suboptimal concentration.[72]

*Vitamin* $B_{12}$. The chemistry and function of this vitamin have been reviewed recently by Jukes and Stokstad;[73] little is known about its biosynthesis. Vitamin $B_{12}$ contains a 5 : 6-dimethylbenziminazole moiety whereas *pseudo*vitamin $B_{12}$ contains adenine instead.[74] Nevertheless, both factors are equally active in promoting growth of mutant strains of *Bact. coli* and both exert the same sparing effect on the requirement of other mutant strains for *p*-aminobenzoic acid.[75] Thus, the suggestion that the latter compound is a precursor of the benziminazole portion of vitamin $B_{12}$ seems untenable.[76] There is evidence that 4 : 5-dimethylphenylene-1 : 2-diamine may serve as a precursor of this residue in some organisms. This is based mainly upon the action of 4 : 5-dimethylphenylene-1 : 2-diamine in overcoming competitively growth inhibition by 4 : 5-dichlorophenylene-1 : 2-diamine.[77] The dichloro-analogue inhibits growth only of those organisms which do not require vitamin $B_{12}$; addition of that factor does not however overcome the inhibition. In *Lactobacillus lactis* Dorner, which requires vitamin $B_{12}$ for growth, 5 : 6-dimethylbenziminazole and 4 : 5-dimethylphenylene-1 : 2-diamine are inhibitory.[78]

Nutritional investigations with bacteria have suggested that vitamin $B_{12}$ is concerned in the conversion of homocysteine into methionine. Mutant strains of *Bact. coli*, needing vitamin $B_{12}$ for growth, respond also to methionine but not to homocysteine.[79] Dubnoff [80] has claimed, however, that such mutants do respond to homocysteine (but not homocystine) when grown anærobically, and suggests that one of the functions of vitamin $B_{12}$ in methionine synthesis is to keep homocysteine in the reduced state. The suggestions from growth experiments of the role of vitamin $B_{12}$ in methionine formation have been followed by more direct experiments with deficient cell suspensions of $B_{12}$-requiring strains of *Bact. coli*; the factor is essential for the formation of the amino-acid from homocysteine (cf. p. 258).[69]

Vitamin $B_{12}$ also appears to be concerned in the formation of nucleosides. Purine deoxyribosides or thymidine abolish the requirement of many lactobacilli (*e.g.*, *Lb. leichmannii*) for vitamin $B_{12}$; in its presence the organisms can utilise free purines, suggesting that vitamin $B_{12}$ is needed for their conversion into deoxyribosides.[81] Cell extracts of some of these lactobacilli contain enzymes catalysing the transfer of the deoxyribosyl group from nucleosides to free purines or pyrimidines.[82] Such reactions probably account for the equal ability of different deoxyribosides to abolish the need for vitamin $B_{12}$.

[71] W. Shive, W. W. Ackermann, M. Gordon, M. E. Getzendaner, and R. E. Eakin, *J. Amer. Chem. Soc.*, 1947, **69**, 725.

[72] J. S. Gots and E. C. Chu, *J. Bact.*, 1952, **64**, 537.

[73] T. H. Jukes and E. L. R. Stokstad, *Vitamins and Hormones*, 1951, **9**, 1.

[74] H. W. Dion, D. G. Calkins, and J. J. Pfiffner, *J. Amer. Chem. Soc.*, 1952, **74**, 1108.

[75] B. D. Davis, *J. Bact.*, 1952, **64**, 432.

[76] *Idem*, *ibid.*, 1951, **62**, 221.

[77] D. W. Woolley, *J. Exp. Med.*, 1951, **93**, 13.

[78] D. Hendlin and M. H. Soars, *J. Bact.*, 1951, **62**, 633.

[79] B. D. Davis and E. S. Mingioli, *ibid.*, 1950, **60**, 17.

[80] J. W. Dubnoff, *Arch. Biochem.*, 1952, **37**, 37.

[81] E. Kitay, W. S. McNutt, and E. E. Snell, *J. Bact.*, 1950, **59**, 727; E. Kitay and E. E. Snell, *ibid.*, 1950, **60**, 49.

[82] W. S. McNutt, *Biochem. J.*, 1952, **50**, 384.

*Higher forms of B-group vitamins.* Some organisms fail at a stage in the conversion of a free B-group vitamin into its coenzyme form and consequently require the latter or a precursor (more complex than the free vitamin) for growth. Examples of these are shown in the Table. Such observations may provide clues to the intermediates in the synthesis of coenzyme forms from the free vitamins. With most organisms so far studied, however, the more complex forms of these compounds are less active or are inactive in promoting growth in place of the free factors. For example, coenzyme A does not replace pantothenic acid for growth of many yeasts and lactobacilli, and it has only slight activity for one strain of *Lb. acidophilus* which responds to pantothine; the latter compound is less active than pantothenic acid as a growth factor for some lactobacilli and inactive in strains of yeast.[26] Coenzyme A, however, promotes more rapid growth of *Acetobacter suboxydans* than pantothenic acid.[83] Satisfactory explanations are yet to be found to account for the differences among bacteria with respect to their ability to respond to higher forms of the vitamins.

*Organisms requiring higher forms of B-group vitamins.*

| Free factor | Higher form | Organisms requiring higher form | Reference |
|---|---|---|---|
| Nicotinic acid ... | Di- or tri-phosphopyridine nucleotide | *Haemophilus para-influenzæ* | *a* |
| Thiamine ......... | Thiamine pyrophosphate | *Haem. piscium* | *b* |
| | | *Neisseria gonorrhoeæ* | *c* |
| Pantothenic acid | Pantethine | *Lb. bulgaricus* and related organisms | 26 |
| Vitamin $B_6$ ...... | Pyridoxal or pyridoxamine phosphates | *Lb. lactis* Dorner | *d* |
| | | *Lb. helveticus* and related organisms | *e* |
| | | *Ln. mesenteroides* | *f* |
| α-Lipoic acid ... | Lipothiamide pyrophosphate | *Bact. coli* (mutant) | 21 |

(*a*) A. Lwoff and M. Lwoff, *Proc. Roy. Soc.*, 1937, *B*, **122**, 352. (*b*) P. J. Griffin, *Arch. Biochem.*, 1951, **30**, 100. (*c*) C. E. Lankford and P. K. Skaggs, *ibid.*, 1946, **9**, 265. (*d*) D. Hendlin, M. C. Caswell, V. J. Peters, and T. R. Wood, *J. Biol. Chem.*, 1950, **186**, 647. (*e*) W. S. McNutt and E. E. Snell, *ibid.*, 1950, **182**, 557. (*f*) V. H. Cheldelin, A. P. Nygaard, H. A. Kornberg, and R. J. Williams, *J. Bact.*, 1951, **62**, 134.

**Amino-acids and Peptides.**—Nutritional research with micro-organisms, particularly with induced mutant strains, has thrown light upon the intermediates in the synthesis of many amino-acids.

*Aromatic amino-acids.* Davis [84, 85] has provided strong evidence that shikimic acid (V) is an intermediate in the synthesis of the aromatic metabolites, tryptophan, tyrosine, phenylalanine, *p*-aminobenzoic acid, and *p*-hydroxybenzoic acid. Quintuple mutant strains of *Bact. coli* were isolated which respond to a mixture of those compounds or to shikimic acid alone. Other strains, unable to utilise shikimic acid, accumulate it in the culture fluid. Further work along these lines has shown that 5-dehydroquinic acid (III) and 5-dehydroshikimic acid (IV) may be precursors of shikimic acid.[84] The suggested intermediates still contain the ring structure which may arise directly from glucose; labelled shikimic acid is formed by a

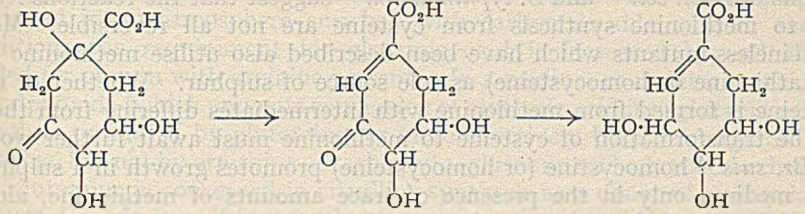
---

[83] G. D. Novelli, R. M. Flynn, and F. Lipmann, *J. Biol. Chem.*, 1949, **177**, 493.

[84] B. D. Davis, " Symposium sur le Métabolisme Microbien," p. 32, Second Int. Congr. Biochem., Paris, 1952; *J. Bact.*, 1952, **64**, 729, 749.

[85] *Idem*, *J. Biol. Chem.*, 1951, **191**, 315.

quintuple mutant strain of *Bact. coli* grown with [1-$^{14}$C]glucose.[86] Isotopically labelled acetate, formate, or carbon dioxide are not incorporated.



(III) (IV) (V)

The aromatic amino-acids may also arise from a common precursor in *Lb. arabinosus.*[87] Strains which grow in the absence of tyrosine give rise to variants which have also lost their requirement for phenylalanine. Such variants readily become independent of tryptophan, whereas cultures of the parent organism (requiring all three amino-acids) do not show this tendency.

*Lysine.* Studies with mutant strains of *Bact. coli* have suggested that αα′-diaminopimelic acid is an intermediate in lysine synthesis.[88] Some lysineless-mutants accumulate diaminopimelic acid, which replaces lysine for growth of other strains. Cell suspensions of mutants, which utilise this compound for growth, contain diaminopimelic acid decarboxylase and can thus convert the precursor into lysine (in turn degraded by lysine decarboxylase to cadaverine and carbon dioxide). Wild type strains of *Bact. coli* also contain this enzyme. On the other hand, cell suspensions of mutant strains, unable to utilise diaminopimelic acid for growth, are also unable to decarboxylate it; this suggests that their failure to synthesise lysine is due to the absence or inactivity of the decarboxylase. In *Neurospora*, α-aminoadipic acid is probably an intermediate in lysine synthesis.[89] This compound is not utilised by lysineless-mutants of *Bact. coli*, nor is diaminopimelic acid utilised by *Neurospora* mutants. This suggests that the pathways of lysine synthesis in *Bact. coli* and *Neurospora* may differ.

*Sulphur-containing amino-acids.* The synthesis of methionine with intermediate formation of cysteine, cystathionine (formed by condensation of homoserine and cysteine), and homocysteine has been well established by nutritional studies with mutant strains of *Neurospora*,[90] *Bact. coli*,[91] and *Bacillus subtilis*.[92] Similarly, methionine formation by the pathogens, *Salmonella typhimurium*,[93] *Brucella suis*,[94] and *Pasteurella pestis*,[95] appears to involve the same intermediates. The last-named organism normally needs both cysteine (replaced by thiosulphate, sulphite, or sulphide) and methionine for growth; cystathionine or homocystine replaces methionine.

---

[86] H. Shigeura and D. B. Sprinson, *Fed. Proc.*, 1952, **11**, 286.

[87] D. E. Atkinson and S. W. Fox, *Arch. Biochem.*, 1951, **31**, 212.

[88] D. L. Dewey and E. Work, *Nature*, 1952, **169**, 533; B. D. Davis, *ibid.*, p. 534.

[89] H. K. Mitchell and M. B. Houlahan, *J. Biol. Chem.*, 1948, **174**, 883.

[90] H. J. Teas, N. H. Horowitz, and M. Fling, *ibid.*, 1948, **172**, 651.

[91] J. O. Lampen, R. R. Roepke, and M. J. Jones, *Arch. Biochem.*, 1947, **13**, 55.

[92] H. J. Teas, *J. Bact.*, 1950, **59**, 93.

[93] H. H. Plough, H. Y. Miller, and M. E. Berry, *Proc. Nat. Acad. Sci.*, 1951, **37**, 640.

[94] L. J Rode, C. E. Lankford, and V. T. Schuhardt, *J. Bact.*, 1951, **62**, 571; C. E. Lankford, L. J. Rode, and V. T. Schuhardt, *Proc. Soc. Exp. Biol. N.Y.*, 1952, **80**, 727.

[95] E. Englesberg, *J. Bact.*, 1952, **63**, 675.

A mutant strain is able, however, to utilise cysteine, though not methionine, as sole source of sulphur. These results and similar findings with mutant strains of *Bact. coli* [96] and *S. typhimurium* [93] suggest that the reactions leading to methionine synthesis from cysteine are not all reversible. Most cysteineless-mutants which have been described also utilise methionine (or cystathionine or homocysteine) as sole source of sulphur. Whether or not cysteine is formed from methionine with intermediates differing from those in the transformation of cysteine to methionine must await further work. In *Br. suis* [94] homocystine (or homocysteine) promotes growth in a sulphur-free medium only in the presence of trace amounts of methionine, alone insufficient to give measurable growth. Some commercial samples of homocystine contain sufficient methionine to give this effect, the cause of which is unknown.

iso*Leucine and valine.* The properties of mutant strains of *Neurospora, Bact. coli, B. subtilis,* and *S. typhimurium* have indicated that αβ-dihydroxy-β-methylvaleric acid and αβ-dihydroxy-β-methylbutyric acid, as well as the corresponding α-keto-acids, are precursors of *iso*leucine and valine, respectively.[97] The dihydroxy-acids accumulate in cultures of a strain of *Neurospora* needing both amino-acids for growth.[98] They are utilised by some strains of *Bact. coli* responding to *iso*leucine and valine, as are the corresponding α-keto-acids, whereas with other strains only the keto-acids replace the amino-acids for growth.[97, 99] Another strain of *Bact. coli* which has an absolute requirement for *iso*leucine and a partial one for valine (evident only under semi-aerobic conditions) accumulates the keto-acid analogues of both *iso*leucine and valine.[99] The results suggest that *iso*leucine and valine are formed as follows:

Precursors → dihydroxy-acid analogues → keto-acid analogues → *iso*leucine, valine.

The immediate precursors of the carbon chains of these amino-acids are not known, though work with mutants has suggested that D-threonine and α-amino- and α-keto-butyric acids may serve.[97, 99] Experiments with isotopically labelled acetate have shown that this compound is a precursor in *Neurospora.*[100] The inhibitory inter-relationships of *iso*leucine and valine are discussed elsewhere.

*Proline.* Vogel and Davis,[101] working with mutant strains of *Bact. coli* requiring proline, have shown that the amino-acid may be formed from glutamic acid with intermediate formation of glutamic acid γ-semialdehyde. This compound is accumulated by one such mutant and is utilised by another strain, which also responds to either proline or glutamic acid. Glutamic acid is also a precursor of proline in *Penicillium.*[102]

*Ornithine, citrulline, and arginine.* The synthesis of arginine from glutamic acid with intermediate formation of ornithine and citrulline has been

---

[96] S. Simmonds, *J. Biol. Chem.*, 1948, **174**, 717.

[97] E. A. Adelberg, *J. Bact.*, 1951, **61**, 365; H. E. Umbarger and E. A. Adelberg, *J. Biol. Chem.*, 1951, **192**, 883.

[98] E. A. Adelberg and E. L. Tatum, *Arch. Biochem.*, 1950, **29**, 235; E. A. Adelberg, D. M. Bonner, and E. L. Tatum, *J. Biol. Chem.*, 1951, **190**, 837.

[99] H. E. Umbarger and J. H. Mueller, *ibid.*, 1951, **189**, 277; H. E. Umbarger and B. Magasanik, *ibid.*, p. 287.

[100] E. L. Tatum and E. A. Adelberg, *J. Biol. Chem.*, 1951, **190**, 843.

[101] H. J. Vogel and B. D. Davis, *J. Amer. Chem. Soc.*, 1952, **74**, 109.

[102] D. Bonner, *Cold Spring Harbor Symp. Quant. Biol.*, 1946, **11**, 14.

established by work with mutant strains of *Neurospora* [103] and *Penicillium*.[102] Evidence for a similar mechanism in *Lb. arabinosus* has been obtained by Hood and Lyman.[104] This organism grows in the absence of arginine if incubated in an atmosphere enriched with carbon dioxide. Under these conditions the requirement for glutamic acid is increased beyond that needed for growth with arginine present. In a medium containing methionine sulphoxide (which prevents conversion of glutamic acid into glutamine [105]) growth is promoted by glutamine, or more effectively by either arginine or citrulline, but not by ornithine or carbamyl-L-glutamic acid. It was concluded that glutamine is concerned in citrulline synthesis as a donor of ammonia.

*Peptides.* It is well known that many organisms grow more rapidly on media containing partial hydrolysates of proteins than on free amino-acids. Woolley has shown that peptides are largely responsible for the activity of "strepogenin" concentrates (prepared from partially hydrolyzed proteins) in stimulating growth of *Lb. casei* and other organisms.[106] In most cases studied synthetic di- and tri-peptides are less active than the free amino-acids in promoting growth, and their activity seems to be due to hydrolysis to their component amino-acids.[107] Marshall and Woods [108] have found, however, that L-tyrosyl-L-tryptophan and L-tryptophanyl-L-phenylalanine are more active than tryptophan in overcoming inhibition of growth of *Strep. faecalis* and *Staphylococcus aureus* by 4-methyltryptophan. In the presence of the dipeptides, growth is insensitive to the inhibitor, whereas tryptophan acts competitively in overcoming the inhibition. Tyrosine and phenylalanine are also competitive antagonists though less active than tryptophan. In the absence of the inhibitor the peptides have the same growth-promoting activity as the free amino-acids. One interpretation of these results is that phenylalanine and tyrosine are concerned in the utilisation of tryptophan; these reactions are inhibited by 4-methyltryptophan which competes with tryptophan. Growth inhibition by β-2-thienylalanine is also overcome competitively by tyrosine, phenylalanine, or tryptophan (though less active), suggesting that this analogue inhibits similar reactions. Tyrosine peptides are more active than free tyrosine in promoting growth of *Strep. faecalis* in media containing vitamin $B_6$.[109] Without this factor (the medium contained D-alanine and all the necessary amino-acids except tyrosine) L-leucyl-L-tyrosine has the same activity as tyrosine. The experimental evidence indicates that tyrosine decarboxylase, active only in cells grown with vitamin $B_6$, decomposes free tyrosine, but does not attack tyrosine produced by hydrolysis of the peptides.

*Glutamine and asparagine.* Glutamine plays an important role in bacterial metabolism (reviewed by Waelsch [110]) and is essential for growth of haemolytic streptococci.[111] It is a non-competitive antagonist of many

---

[103] A. M. Srb and N. H. Horowitz, *J. Biol. Chem.*, 1944, **154**, 129.
[104] D. W. Hood and C. M. Lyman, *ibid.*, 1950, **185**, 39.
[105] H. Waelsch, P. Owades, H. K. Miller, and E. Borek, *ibid.*, 1946, **166**, 273.
[106] H. Sprince and D. W. Woolley, *J. Amer. Chem. Soc.*, 1945, **67**, 1734; D. W. Woolley, *J. Biol. Chem.*, 1948, **172**, 71.
[107] J. S. Fruton and S. Simmonds, *Cold Spring Harbor Symp. Quant. Biol.*, 1949, **14**, 55.
[108] J. H. Marshall and D. D. Woods, *Biochem. J.*, 1952, **51**, ii.
[109] H. Kihara, O. A. Klatt, and E. E. Snell, *J. Biol. Chem.*, 1952, **197**, 801.
[110] H. Waelsch, *Adv. Enzymology*, 1952, **13**, 237.
[111] H. McIlwain, P. Fildes, G. P. Gladstone, and B. C. J. G. Knight, *Biochem. J.*, 1939, **33**, 223.

inhibitory analogues of glutamic acid.[105,112] Its function is unknown though it may play a part in citrulline synthesis.[104] In *Lb. arabinosus* glutamine is more active than glutamic acid in the early stages of growth; the dipeptides, glutaminylglycine and glycylglutamic acid, have the same activity as glutamine.[113] On the other hand, asparagine is much less active than aspartic acid for this organism (grown in the absence of carbon dioxide) and for *Ln. mesenteroides*, but the glycine dipeptides of asparagine have activity almost equal to that of aspartic acid. The peptides are more readily deaminated by cell suspensions than the free amide, suggesting that they may give rise to aspartic acid by deamination followed by hydrolysis.[114]

**Nucleic Acid Derivatives.**—Research with micro-organisms has also provided information on the mechanism of synthesis of purines and pyrimidines and their utilisation (see review by Christman [115]).

*Purines.* The observation that 4-aminoglyoxaline-5-carboxyamide accumulates in bacterial cultures when the availability of *p*-aminobenzoic acid is limited (see p. 258; refs. 71 and 72) first indicated that it might be a precursor of purines. It also accumulates in cultures of a purineless-strain of *Bact. coli*, and replaces purines (though it is less active) for growth of another mutant strain.[116] Glycine stimulates production of the amine.[71,72] This amino-acid, formate, and carbon dioxide have been found by isotopic techniques to be precursors of purines in yeast,[117] and *Bact. coli* [118] and *Bacterium prodigiosum*,[119] as in animals.[120]

*Pyrimidines.* That orotic acid (4-carboxyuracil) is closely related to an intermediate in pyrimidine synthesis is suggested by its activity in replacing uracil for growth of mutant strains of *Neurospora*.[121,122] It is also accumulated by other pyrimidineless-mutants of this organism, but there is evidence that it is not a normal intermediate in *Neurospora*.[122] Orotic acid is essential for growth of a strain of *Lb. bulgaricus*; [123] ureidosuccinic acid replaces it (though at a higher concentration), and may be a precursor.[124] Uracil is not utilised for growth of this organism; nevertheless isotopically labelled orotic acid and ureidosuccinic acid are both incorporated into the uracil of the cell nucleic acids.[125] Clarification of the role of orotic acid in pyrimidine metabolism must await more detailed knowledge of the mechanism of incorporation of the free bases into nucleic acids, if indeed the free bases are intermediates.

*Nucleosides and nucleotides.* Some micro-organisms are unable to utilise free purine or pyrimidine bases and require nucleosides or nucleotides for

---

[112] P. Ayengar and E. Roberts, *Proc. Soc. Exp. Biol. N.Y.*, 1952, **79**, 476.

[113] H. K. Miller and H. Waelsch, *Arch. Biochem.*, 1952, **35**, 184.

[114] *Idem, Nature*, 1952, **169**, 30. [115] A. A. Christman, *Physiol. Rev.*, 1952, **32**, 303.

[116] J. Gots, *Arch. Biochem.*, 1950, **29**, 222.

[117] M. Edmonds, A. M. Delluva, and D. W. Wilson, *J. Biol. Chem.*, 1952, **197**, 251.

[118] A. L. Koch, F. W. Putnam, and E. A. Evans, Jnr., *ibid.*, p. 105.

[119] D. J. McLean and E. F. Purdie, *ibid.*, p. 539.

[120] G. R. Greenberg, *ibid.*, 1951, **190**, 611.

[121] H. S. Loring and J. G. Pierce, *ibid.*, 1944, **153**, 61.

[122] H. K. Mitchell, M. B. Houlahan, and J. F. Nyc, *ibid.*, 1948, **172**, 525.

[123] L. D. Wright, J. W. Huff, H. R. Skeggs, K. A. Valentik, and D. K. Bosshardt, *J. Amer. Chem. Soc.*, 1950, **72**, 2312; O. P. Wieland, J. Avener, E. M. Boggiano, N. Bohonos, B. L. Hutchings, and J. H. Williams, *J. Biol. Chem.*, 1950, **186**, 737.

[124] D. S. Spicer, K. V. Liebert, L. D. Wright, and J. W. Huff, *Proc. Soc. Exp. Biol. N.Y.*, 1952, **79**, 587.

[125] L. D. Wright, C. S. Miller, H. R. Skeggs, J. W. Huff, L. L. Weed, and D. W. Wilson, *J. Amer. Chem. Soc.*, 1951, **73**, 1898.

growth, suggesting that these are intermediates in the synthesis of nucleic acids (see also p. 259; ref. 81). *Lb. gayonii*, for instance, requires adenylic, guanylic, uridylic, or cytidylic acid; guanosine (the only nucleoside tested) is inactive.[126] Recently, a strain of *Strep. faecalis* has been described which needs a pyrimidine nucleoside or nucleotide for rapid growth; uridine is the most active of the compounds tested, whereas purine nucleosides and nucleotides are inactive.[127] Uridine is also more active than uracil in promoting growth of a mutant strain of *Neurospora*.[121] Merrifield and Woolley [128] have evidence that *Lb. helveticus* may incorporate uracil directly into a dinucleotide without intermediate formation of a mononucleoside or nucleotide. Certain dinucleotides (isolated from acid-hydrolysates of yeast nucleic acid) and their dephosphorylated derivatives replace uracil for growth of this organism, whereas pyrimidine and purine mononucleotides and nucleosides are inactive. The smallest unit common to the active compounds is cytidine-5′ phosphate diesterified at the 3′(or 2′)-position of another nucleoside; similar derivatives of uridylic acid were not tested.

**Inhibitory Interrelationships of Growth Factors.**—Many examples are known of antagonism between essential metabolites, particularly between amino-acids of similar structure where competition for an enzyme may occur.[129] Another type of inhibition, observed frequently in research with biochemical mutants, may occur when an intermediate in the synthesis of one essential metabolite may prevent the utilisation of a precursor of another metabolite. An inhibition of this type has been shown to account for the requirement of a mutant strain of *Bact. coli* for both *iso*leucine and valine.[99] This strain cannot form *iso*leucine from its α-keto-acid analogue, α-keto-β-methylvaleric acid; this compound accumulates and inhibits the conversion of the corresponding analogue of valine (α-keto-β-methylbutyric acid) into valine. In mutants of *Neurospora* with the same double requirement for *iso*leucine and valine, the dihydroxy-acid analogue of *iso*leucine accumulates (not the keto-acid analogue as postulated by Bonner [130]) and inhibits utilisation of the corresponding analogue of valine.[97] An interesting example of antagonism has been described by Kihara *et al.*[131] They found that alanylpeptides are responsible for the activity of enzymic digests of casein in replacing vitamin $B_6$ for growth of *Lb. casei*; a number of synthetic L-alanylpeptides have the same effect as the digests. For replacement, D-alanine has also to be added to the medium, and this compound inhibits utilisation of L-alanine, but not that of the L-alanylpeptides. The peptides appear, therefore, to be required for growth in the absence of vitamin $B_6$ because utilisation of free L-alanine is prevented by D-alanine, present in excess under the experimental conditions.

Another example of antagonism has been shown by Rabinowitz and Snell [132] with *Saccharomyces carlsbergensis*. This organism grows in the

---

[126] B. L. Hutchings, N. H. Sloane, and E. Boggiano, *J. Biol. Chem.*, 1946, **162**, 737.
[127] H. A. Hoffmann and P. L. Paveck, *J. Amer. Chem. Soc.*, 1952, **74**, 344.
[128] R. B. Merrifield and D. W. Woolley, *J. Biol. Chem.*, 1952, **197**, 521.
[129] E. L. Tatum, *Fed. Proc.*, 1949, **8**, 511.
[130] D. Bonner, *J. Biol. Chem.*, 1946, **166**, 545.
[131] H. Kihara, W. G. McCullough, and E. E. Snell, *ibid.*, 1952, **197**, 783; H. Kihara and E. E. Snell, *ibid.*, p. 791.
[132] J. C. Rabinowitz and E. E. Snell, *Arch. Biochem.*, 1951, **33**, 472.

absence of both vitamin $B_6$ and thiamine; in a medium containing thiamine, however, pyridoxine (or derivatives) becomes essential for growth. The reason for this is not known.

**General.**—Substances which do not come under the above headings, but which have been found to be growth factors for some micro-organisms include *p*-hydroxybenzoic acid, putrescine, and " coprogen." *p*-Hydroxybenzoic acid is a component of a mixture of aromatic compounds needed for growth of mutant strains of *Bact. coli.*[84, 85] Its effect on growth is most marked in media containing aspartic acid. It also overcomes inhibition of growth of *Bact. coli* by high concentrations of *p*-aminobenzoic acid.[133] Replacement experiments have suggested that *p*-hydroxybenzoic acid is concerned at a stage in the conversion of cysteine into methionine and in lysine synthesis.[84] Putrescine is essential for growth of *Haemophilus parainfluenzæ*; its function is unknown.[134] A crystalline compound (" coprogen ") isolated from dung, is needed for growth of *Pilobolus spp.* High concentrations of haemin replace this substance, which contains iron and may possibly be a precursor of iron porphyrins.[135] A similar compound, active for *Pilobolus*, has been obtained from the cells of a rust fungus when grown under conditions which result in a high production of cytochrome *c*.[136]

J. L.

## 3. VITAMINS.

**Nomenclature.**—The Commission for the Reform of Nomenclature in Biological Chemistry of the International Union of Pure and Applied Chemistry has adopted the following names :[1]

| Present name | Name adopted |
|---|---|
| Vitamin $D_2$ or calciferol | Ergocalciferol |
| Vitamin $D_3$ | Cholecalciferol |
| Vitamins E | α-, β-, and γ-Tocopherol |
| Vitamin $B_1$, aneurin, or thiamine | Thiamine |
| Vitamin $B_2$, or riboflavin | Riboflavin |
| Vitamin PP, niacinamide, or nicotinamide | Nicotinamide |
| Vitamins possessed of $B_{12}$ activity | Cobalamin (collective name) |
| Vitamin $B_{12}$ | Cyanocobalamin |
| Vitamin $B_{12b}$ | Hydroxocobalamin |
| Vitamin $B_{12c}$ | Nitrosocobalamin * |
| Vitamin C or ascorbic acid | Ascorbic acid |

* This name will probably need altering to Nitritocobalamin; cf. Lester-Smith, *Biochem. J.*, 1952, **50**, xxxvi.—ED.

The names panthothenic acid, biotin, *p*-aminobenzoic acid, and choline remain unchanged.

Names of other vitamins are under discussion.

**Fat-soluble Vitamins.**—Because of limitations of space, attention is limited to the fat-soluble vitamins, with the exception of vitamin A, which has recently been reported on.[1a]

**Vitamins D.**—*Standards and assay.* A new international standard has

---

[133] B. D. Davis, *J. Exp. Med.*, 1951, **94**, 243.

[134] E. J. Herbst and E. E. Snell, *J. Biol. Chem.*, 1949, **181**, 47.

[135] C. W. Hesseltine, C. Pidacks, A. R. Whitehill, N. Bohonos, B. L. Hutchings, and J. H. Williams, *J. Amer. Chem. Soc.*, 1952, **74**, 1362.

[136] J. B. Neilands, *ibid.*, p. 4846.

[1] *Biochem. J.*, 1952, **52**, 1; *J.*, 1951, 3526.

[1a] R. A. Morton, *Ann. Reports*, 1949, **56**, 244.

been adopted, in which the international unit is 0·025 μg. of crystalline cholecalciferol.[2] This has the advantage over the League of Nations standard based on ergocalciferol that cholecalciferol is identical with the natural vitamin and is equipotent in mammals and birds.

An enormous effort has been made to improve methods of assay, and to date the most useful methods remain biological rather than chemical. Rat growth on Steenbock and Black's rachitogenic diet can be improved by the addition of 0·5% of lysine.[3] The A.O.A.C. basal rachitogenic diet for chicks does not appear to be susceptible to much improvement.[4] The use of the chick toe-ash rather than the tibia-ash has been advocated as an assay criterion.[5] The B.S.I. curative test has been compared with, and found superior to, the A.O.A.C. preventive test.[6] New bioassays suggested include the uptake of injected $^{32}$P by the paws of rats,[7] and the level of chick-plasma alkaline phosphatase.[8] A microbiological assay for pure ergocalciferol and cholecalciferol has been described.[9]

Among the physicochemical methods investigated are the colorations with antimony trichloride,[10,11] dichlorohydrin,[12,13] and iodine trichloride,[14] a modified Pettenkofer's reaction,[15] and the " carbenium salts." [16] The absorption spectra of the vitamins D have been investigated as a method of assay.[11,17] In order to remove interfering substances chemical separation [13] and chromatographic fractionation [11,14,18] have been used.

*Chemistry.* Syntheses of 7-dehydrocholesterol,[19] and the preparation and separation of a complex of cholecalciferol and cholesterol which is reputed [20] more stable during processing have been described; biologically active alkyl ethers of the vitamins D have been prepared from metallic vitamin derivatives.[21] Pro-ergocalciferol [22] has been isolated as a dinitro-

---

[2] " Expert Committee on Biological Standardization. Rept. Sub-Committee on Fat-soluble vitamins," W.H.O. Tech. Rept. Ser. No. 3, 1950, Geneva.

[3] P. S. Francis, *J. Assoc. Off. Agric. Chem.*, 1947, **30**, 364.

[4] C. I. Bliss, *ibid.*, 1946, **29**, 396; B. B. Migicovsky and A. R. G. Emslie, *Arch. Biochem.*, 1947, **13**, 175, 185.

[5] C. I. Bliss, *Poultry Sci.*, 1945, **24**, 534; C. I. Bliss and G. H. Kennedy, *J. Assoc. Off. Agric. Chem.*, 1950, **33**, 860.

[6] J. A. Campbell and A. R. G. Emslie, *Poultry Sci.*, 1947, **26**, 255.

[7] R. H. Synder, H. J. Eisner, and H. Steenbock, *J. Nutrit.*, 1951, **45**, 305.

[8] I. Motzok, *Biochem. J.*, 1950, **47**, 196. [9] E. Kodicek, *ibid.*, 1950, **46**, xiv.

[10] F. W. Lamb, A. Mueller, and G. W. Beach, *Ind. Eng. Chem. Anal.*, 1946, **18**, 187; A. Mueller, *ibid.*, p. 214.

[11] D. T. Ewing, M. J. Powell, R. A. Brown, and A. D. Emmett, *Analyt. Chem.*, 1948, **20**, 317; J. B. de Witt and M. X. Sullivan, *Ind. Eng. Chem. Anal.*, 1946, **18**, 117; I. N. Garkina and V. N. Bukin, *Biokhim.*, 1951, **16**, 176.

[12] A. E. Sobel, A. M. Mayer, and B. Kramer, *Ind. Eng. Chem. Anal.*, 1945, **17**, 160; J. A. Campbell, *Analyt. Chem.*, 1948, **20**, 766.

[13] E. V. Rouir and G. Pirlot, *Bull. Soc. Chim. biol.*, 1947, **29**, 1005.

[14] J. Green, *Biochem. J.*, 1951, **49**, 36, 45, 54; 1952, **51**, 144.

[15] V. Villar Palasí, *Nature*, 1947, **160**, 88.

[16] H. Schaltegger, *Helv. Chim. Acta*, 1946, **29**, 285.

[17] W. Huber, G. W. Ewing, and J. Kriger, *J. Amer. Chem. Soc.*, 1945, **67**, 609; G. Pirlot, *Analyt. Chem. Acta*, 1948, **2**, 744.

[18] A. Fujita and M. Aoyama, *J. Biochem., Japan*, 1950, **37**, 113; H. E. Cox, *Analyst* 1950, **75**, 521.

[19] J. A. K. Buisman, W. Stevens, and J. v. d. Vliet, *Rec. Trav. chim.*, 1947, **66**, 83; A. E. Bide, H. B. Henbest, E. R. H. Jones, R. W. Peevers, and P. A. Wilkinson, *J.*, 1948, 1783; J. Redel and B. Gauthier, *Bull. Soc. chim.*, 1948, 607.

[20] J. Waddell and W. W. Waessner, U.S.P. 2,410,254/1946.

[21] N. A. Milas, U.S.P. 2,410,893/1946.

[22] L. Velluz and G. Amiard, *Compt. rend.*, 1949, **228**, 692, 853, 1037.

benzoate which differs from that of ergocalciferol in its crystalline form, optical rotation, and extinction at 265 mμ; it is unstable to heat and is converted into ergocalciferol at temperatures such as are reached when solutions of irradiated ergosterol are concentrated. Ergocalciferol is, however, the predominating isomer at equilibrium. A new provitamin D, norcholesta-5 : 7-dien-3β-ol,[23] has been described; unlike other such substances it possesses a saturated unbranched side-chain. *X*-Ray analysis[24] of ergocalciferol indicates that $C_{(5)}$, $C_{(6)}$, $C_{(7)}$, and $C_{(8)}$ lie in a straight chain. Infra-red spectra[25] indicate a *trans*-configuration of the $C_{(22)}$–$C_{(23)}$ double bond in ergocalciferol, ergosterol, ergosteryl acetate, stigmasterol, and stigmasteryl acetate.

*Physiology.* Very little progress has been made in determining the exact mode of action of the vitamins D. That vitamin D increases the absorption of calcium and phosphorus from the gut has been shown by a number of workers; in man by balance experiments[26] an increased absorption of all kinds of phosphorus with a concomitant increased retention of calcium is found on administration of vitamin D. The absorption of calcium from isolated loops of intestine during 24 hours is greater in rats given vitamin D than in controls, and absorption appears more rapid in the upper part of the small intestine than in the lower part.[27] The vitamins D appear to enhance the absorption of phosphorus from the gut when the latter is present as phytin,[26, 28, 29] though it had no effect on the phytase activity of the gut[28] and could not increase the absorption of phytate phosphorus as much as that of the inorganic element.[29] It is concluded that the best method of combating a high level of phytate in the diet is by administration of calcium as well as vitamin D.[29] The use of $^{45}$Ca and $^{32}$P as tracers has also failed to yield much information about the mode of action of vitamins D. There are considerable difficulties with these techniques in that these elements appear to exchange very rapidly with the bone salt which makes interpretation of results hazardous. Vitamin D increases the absorption and skeletal deposition of $^{45}$Ca and $^{89}$Sr[30] in rats weaned on to a rachitogenic diet for 15—20 days. The rate of turnover of $^{45}$Ca in bone is increased by vitamin D as is the absorption from the small intestine,[31] absorption being demonstrated from both proximal and distal parts. In chicks more $^{45}$Ca was incorporated in bone with vitamin D when the element was fed but no difference was found when it was injected.[32]

In vitamin D deficiency, the crystal structure of bone is reported to be disoriented as shown by *X*-ray studies;[33] on the other hand the mechanical and structural properties of bone in rats on rachitogenic diets are reported to

---

[23] C. G. Alberti, B. Camerino, L. Mamoli, *Helv. Chim. Acta*, 1949, **32**, 2038; 1950, **33**, 229.

[24] D. Crowfoot and J. D. Dunitz, *Nature*, 1948, **162**, 608.

[25] J. H. Turnbull, D. H. Whiffen, and W. Wilson, *Chem. and Ind.*, 1950, **33**, 626.

[26] K. Wang, S. H. Liu, H. I. Chu, T. F. Yü, H. C. Chao, and H. C. Hsu, *Chinese Med. J. Wash.*, 1944, **62**, 1.

[27] R. Nicolaysen, *Acta physiol. Scand.*, 1951, **22**, 260.

[28] R. R. Spitzer, G. Maruyama, L. Michaud, and P. H. Phillips, *J. Nutrit.*, 1948, **35**, 185.

[29] Sir E. Mellanby, *J. Physiol.*, 1949, **109**, 488.

[30] D. M. Greenberg, *J. Biol. Chem.*, 1945, **157**, 99.

[31] H. E. Harrison and H. C. Harrison, *J. Biol. Chem.*, 1951, **188**, 83; 1950, **185**, 857.

[32] B. B. Migicovsky and A. R. G. Emslie, *Arch. Biochem.*, 1949, **20**, 325; 1950, **28**, 324.

[33] C. I. Reed and B. P. Reed, *Amer. J. Physiol.*, 1945, **143**, 413.

be normal except that the strength is low.[34] The local effect of ergocalciferol on bone has been investigated by implantation of pellets of the vitamin on pieces of parietal bone grafted intracerebrally in mice. After 14 days there is diffuse re-absorption of bone. Ergosterol, cholesterol, and œstradiol were inactive.[35] Vitamin D is reported to improve healing of experimental fractures.[36]

A possible site of conversion of cholesterol into procholecalciferol is the gut. It is reported that in the lining of the small intestine of the guinea pig, the rat, and the ox there is a sterol having an ultra-violet absorption spectrum characteristic of the pro-cholecalciferols. In the guinea pig it is concentrated in the mucosa and lamina propria of the duodenum. It persisted after 24 hours' fasting and 2 weeks on a diet of low sterol content. On administration of cholesterol, spectroscopically free from pro-cholecalciferol, the amount of the provitamin in the gut wall at first increased, later returning to normal while the amount in the liver increased. It is concluded that 7-dehydrocholesterol may be formed in the gut by dehydrogenation of cholesterol.[37]

*Rickets.* There was no evidence of an increase in rickets in Great Britain during the last war. The incidence of rickets was reduced with longer breast-feeding. The percentage of children with radiological rickets who had at some time received cod-liver oil was however high.[38] The occurrence of rickets in more than half of a group of 118 premature infants leads to the suggestion that human milk cannot satisfy the phosphorus requirement,[39] rickets not being prevented by vitamins D alone. The use of the serum alkaline phosphatase level as a diagnostic criterion for rickets is suggested.[40] The prophylaxis of rickets requires more vitamin D than had been thought. Study of the prevention of radiological rickets in infants suggests an intake of 1500—3000 i.u. per day;[41] from data on the maximal absorption of calcium and phosphorus from the gut an intake of 250—300 i.u. per day[42] appears to be adequate. It is also suggested that ergocalciferol is only half as potent in infants as cholecalciferol, in terms of international units.[43] Massive dosage of vitamin D has been used successfully in prophylaxis of rickets;[42, 44] the preferred dose is 600,000 i.u. (15 mg.), the protection lasting for 4—6 months. No toxic effects were noted.

The use of vitamin D in massive doses in the treatment of cutaneous tuberculosis has been popular in recent years,[45] but doubt has been

---

[34] G. H. Bell, J. W. Chambers, and I. M. Dawson, *J. Physiol.*, 1947, **106**, 286.

[35] N. A. Barnicot, *J. Anat.*, 1951, **85**, 120.

[36] D. H. Copp and D. M. Greenberg, *J. Nutrit.*, 1945, **29**, 261; M. Mourgue, *J. Physiol. path. gen.*, 1939—1940, **37**, 1269.

[37] M. Scott, J. Glover, and R. A. Morton, *Nature*, 1949, **163**, 530; M. Glover, J. Glover, and R. A. Morton, *Biochem. J.*, 1952, **51**, 1.

[38] Brit. Pediatric Assoc. "The Incidence of Rickets in War-Time," Min. of Health Rep. Pub. Hlth. and Med. Subjects, No. 92, 1944, H.M.S.O., London.

[39] G. V. Sydow, *Acta Pædiat.*, 1946, **33**, Suppl. 2, p. 1; 1948, **35**, Suppl. 1, p. 169.

[40] J. D. Barnes, R. Munks, and M. Kaucher, *J. Pediat.*, 1944, **24**, 159; Y. Raoul and A. Vinet, *Bull. Soc. Chim. biol.*, 1941, **23**, 205.

[41] D. Krestin, *Arch. Dis. Childhood*, 1945, **20**, 28.

[42] R. Houet, *Ann. Pediat.*, 1946, **167**, 225. [43] *Idem, ibid.*, 1949, **172**, 28.

[44] D. Krestin, *Lancet*, 1945, I, 781; T. Johnsson, *Acta Pædiat.*, 1944—1945, **32**, 473; G. Klackenberg, *ibid.*, p. 508.

[45] J. Charpy, *Brit. J. Derm. Syph.*, 1948, **60**, 121; S. Lanholt, *ibid.*, p. 132.; G. B. Dowling, S. Gauvain, and D. E. Macrae, *Brit. Med. J.*, 1948, I, 430.

expressed as to its superiority over ultra-violet light treatment.[46] The use of such massive dosages has led to reports of many cases of vitamin D intoxication.[47]

**Vitamins E.**—A fourth tocopherol, δ-tocopherol, has been described;[48] it is more resistant to oxidation than the other tocopherols, but biologically it has only 1/100th of the activity (+)-α-tocopherol. The coumarin analogue of α-tocopherol has been synthesised; it has only 1/20th of the biopotency of α-tocopherol.[49] A reversible-oxidation product of α-tocopherol, containing one more oxygen atom and which is probably an epoxide, has been isolated.[50] The dependence of biological activity on structure has been stressed; almost all compounds showing vitamin-E activity in the rat-sterility test being chroman derivatives, the requisite substituents are (*a*) one or more alkyl groups on the carbocyclic ring, (*b*) a free or esterified hydroxyl at $C_{(5)}$, and (*c*) a short and a long side-chain at $C_{(2)}$.[51] Analytical methods have been improved;[52] a scheme for the analysis of individual tocopherols in mixtures of the four forms has been devised.[53]

*Physiology.* While we do not yet know how the tocopherols function in the body the idea that there is a dual role *in vivo*, a specific vitamin-like function and a secondary antioxidant action,[54] is still useful. A third pharmacological role may be of importance when large doses are given. The role of tocopherols in the nutrition of farm animals has been reviewed.[54a]

*Antioxidant activity.* The commercial use of tocopherols in the stabilisation of fats has been summarised.[55] The protective action of tocopherols against the hæmolysis of erythrocytes by alloxan or dialuric acid[56] can be considered as an antioxidant effect. The protective action of α-tocopherol against *X*-ray mortality is attributed to the inhibition of peroxide formation in fats.[57] From histochemical studies it is suggested that the yellow-brown pigment occurring in granules in the fat cells of rats deficient in vitamin E represents, at least partly, the oxidation of highly unsaturated fatty acids beyond the peroxide stage.[58] The increased liver storage of vitamin A caused by feeding tocopherols to chicks on a diet containing cod-liver oil could also be obtained by feeding methylene blue.[59]

*Relation to enzyme systems.* The enzymic oxidation of linoleic acid by

---

[46] J. T. Ingram and S. T. Anning, *Brit. J. Derm. Syph.*, 1948, **60**, 159; J. Dawson, *ibid.*, p. 164.

[47] T. S. Danowski, A. M. Winkler, and J. P. Peters, *Ann. Intern. Med.*, 1945, **23**, 22; G. W. Covey and H. H. Whitlock, *ibid.*, 1946, **25**, 508; J. M. Bauer and R. H. Freyberg, *J. Amer. Med. Assoc.*, 1946, **130**, 1208; H. Bell, *Brit. Med. J.*, 1949, I, 139.

[48] M. H. Stern, C. D. Robeson, L. Weisler, and J. G. Baxter, *J. Amer. Chem. Soc.*, 1947, **69**, 869.

[49] L. I. Smith and G. A. Boyack, *ibid.*, 1948, **70**, 2690.

[50] P. D. Boyer, M. Rabinovitz, and E. Liebe *Ann. N.Y. Acad. Sci.*, 1949—1950, **52**, 188.

[51] *Idem, J. Biol. Chem.*, 1951, **192**, 95.

[52] H. W. Rawlings, N. H. Kuhrt, and J. G. Baxter, *J. Amer. Oil Chem. Soc.*, 1948, **25**, 24; R. W. Swick and C. A. Baumann, *Analyt. Chem.*, 1952, **24**, 758; M. L. Quaife and P. L. Harris, *ibid.*, 1948, **20**, 1221.

[53] M. L. Quaife, *J. Biol. Chem.*, 1948, **175**, 605; F. Brown, *Biochem. J.*, 1952, **51**, 237.

[54] K. C. D. Hickman and P. L. Harris, *Adv. Enzymology*, 1946, **6**, 469.

[54a] K. L. Blaxted and F. Brown, *Nutrit. Abs. Reviews*, 1952, **22**, 1.

[55] W. O. Lundberg, " A Survey of the Present Knowledge, Researches and Practices in the U.S. Concerning the Stabilization of Fats," No. 20 (The Hormel Institute of the Univ. of Minnesota, Minneapolis, Minn., 1947).

[56] C. S. Rose and P. György, *J. Nutrit.*, 1949, **39**, 529; *Amer. J. Physiol.*, 1952, **168**, 414.

[57] A. Herve and Z. M. Bacq, *Compt. rend. Soc. Biol.*, 1949, **143**, 1158.

[58] H. Granados and H. Dam, *Acta Path. Microbiol. Scand.*, 1950, **27**, 591.

[59] H. Dam, I. Prange, and E. Sondergaard, *Experientia*, 1951, **7**, 184.

crystalline lipoxidase is inhibited by tocopherols,[60] this is a selective inhibition in that the desired oxidation is permitted but the undesired autoxidation of linoleic peroxides is prevented.[61] Plasma lipase and cholinesterase are reduced in tocopherol deficiency,[62] as is muscle adenosinetriphosphatase activity in some species.[63] Tocopheryl phosphates have been shown to inhibit a number of enzyme systems *in vitro,* diphosphopyridine nucleotidase,[64] succinic oxidase,[65] and muscle acid phosphatase.[63] The possibility that these actions of tocopheryl phosphates are due to some non-specific detergent action must be remembered.[66]

*Fertility.* No difference is found in the blood tocopherol level in normal, pregnant, or aborting women,[67] or in normal and sterile men [71] though this is disputed.[74] Lesions of the reproductive system in male rabbits are shown in tocopherol deficiency,[68] while increased work intensifies the degeneration of the testes in deficient male rats [69] though there is no decrease in androgen production.[70] Reports at a conference on human infertility were contradictory concerning the value of tocopherol therapy.[72] Tocopherols are necessary for successful implantation of the fertilised ovum in rats, though less is required than for gestation to proceed to term.[73]

*Liver degeneration.* α-Tocopherol protects rats on a low-protein diet against carbon tetrachloride poisoning; this effect is duplicated by increasing the protein intake or by giving methionine.[75] Massive liver necrosis in rats on a diet low in low sulphur-containing amino-acid is prevented by tocopherol.[76] A similar effect is found in rats fed a semisynthetic diet containing a British baker's yeast as the sole source of protein.[77] The protective effect of methionine on sodium selenate liver damage is only evident when tocopherol is present.[78] From a study of the protective action of tocopherol and methionine on liver necrosis in rats caused by feeding raw soyabean meal as the sole source of protein it was concluded that methionine gave better protection than tocopherol, the action of the former being specific while the latter acts non-specifically.[79]

---

[60] S. Bergström and R. T. Holman, *Nature*, 1948, **161**, 55.

[61] K. C. D. Hickman, *Arch. Biochem.*, 1948, **17**, 360; H. O. Kunkel, *ibid.*, 1951, **30**, 306, 317.

[62] W. Hess and G. Viollier, *Helv. Chim. Acta*, 1948, **31**, 381.

[63] J. P. Hummel, *J. Biol. Chem.*, 1948, **172**, 421; M. M. Corey and D. D. Dziewiatkowski, *ibid.*, 1949, **179**, 119.

[64] W. M. Govier and N. S. Jetter, *Science*, 1948, **107**, 146.

[65] S. R. Ames and H. A. Risley, *Ann. N.Y. Acad. Sci.*, 1949—1950, **52**, 149.

[66] M. Rabinowitz and P. D. Boyer, *J. Biol. Chem.*, 1950, **183**, 111.

[67] K. Faaborg-Andersen, *Nord. Med.*, 1946, **32**, 2401.

[68] M. L. Chevrel and M. Cormier, *Compt. rend.*, 1948, **226**, 2013.

[69] E. Kokas, B. Gorka, and A. Hesz, *Z. Vitamin-, Hormon- u. Fermentforsch.*, 1947—1948, **1**, 466.

[70] J. R. Valle and L. C. U. Junqueira, *Endrocrinol.*, 1947, **40**, 316.

[71] E. C. Jungck, W. O. Maddock, J. T. Van Bruggen, and C. G. Heller *Fed. Proc.*, 1947, **6**, 139.

[72] Family Planning Assoc. Conf. on Infertility, *Lancet*, 1948, II, 542.

[73] H. Kaunitz, C. A. Slanetz, and R. E. Johnson, *J. Nutrit.*, 1948, **36**, 331; R. J. Blandau, H. Kaunitz, and C. A. Slanetz, *ibid.*, 1949, **38**, 97.

[74] G. Athanassiu, *Med. Monatsschr.*, 1948, **2**, 186.

[75] E. L. Hove, *Arch. Biochem.*, 1948, **17**, 467; M. V. R. Rao, *Nature*, 1948, **161**, 446; A. Neuberger and T. A. Webster, *Biochem. J.*, 1947, **41**, 449.

[76] O. Lindan and H. P. Himsworth, *Brit. J. Exp. Path.*, 1950, **31**, 651; M. Goettsch, *J. Nutrit.*, 1951, **44**, 443.

[77] P. György, C. S. Rose, R. M. Tomarelli, and H. Goldblatt, *ibid.*, 1950, **41**, 265.

[78] E. A. Sellers, R. W. You, and C. C. Lucas, *Proc. Soc. Exp. Biol. N.Y.*, 1950, **75**, 118

[79] A. Matet, J. Matet, and O. Friedenson, *Compt. rend. Soc. Biol.*, 1949, **143**, 235.

The relative potencies of various tocopherols in protecting rats against massive hepatic necrosis have been studied; α-tocopherol is active while γ- and δ-tocopherols are inactive, β-tocopherol was not studied.[79a]

*Muscular dystrophy.* A detailed study of the muscles of rabbits on a diet deficient in vitamin E has been reported. The optical behaviour of fibres which have not yet grossly degenerated resembles that of normal fibres from which actomyosin has been removed; there is a loss of bi-refringent material,[79b] and the appearance of the actin G under the electron microscope is altered.[79c] The amount of both actomyosin and myosin which can be extracted from dystrophic muscles is reduced, the myosin even disappearing.[79d]

*Medicine.* Tocopherols in massive doses have been used in the treatment of a large number of morbid conditions with claims of success; these include anginal pain and cardiac failure,[80] acute nephritis,[81] Dupuytren's contracture,[82] Peyronie's disease,[83] disease characterised by collagen degeneration,[84] obliterative vascular disease,[85] and diabetes.[86] Time alone will show how many of these claims are justified and how many are on a par with the rash assertions with which the history of the vitamins in therapeutics is full.

**Vitamin K.**—*Chemistry and assay.* Menadione (2-methyl-1 : 4-naphthaquinone) is unstable in dilute solution on exposure to radiation at 366 mμ; it may be protected, however, by small amounts of chloride or bromide ions.[87] Methods of conversion of common carbohydrates into menadione and the incorporation of isotopic carbon at various positions are described.[88] The fate of such labelled menadione in dogs has been investigated;[87a] most of the administered dose was excreted in the urine, only traces being found in the blood, liver, and lungs. Various compounds related to menadione have been made including 4-amino-2-methyl-1-naphthol hydrochloride, "$K_5$,"[89] 1 : 4-diamino-2-methylnaphthalene dihydrochloride, "$K_6$,"[90] 4-amino-3-methyl-1-naphthol hydrochloride, "$K_7$."[91] Colorimetric estimations of vitamin K with 2 : 4-dinitrophenylhydrazine,[92] polarographic estimation of menadione,[93] and a spectrophotometric estimation of menadione by using the absorption at 430 mμ[94] have been described. A simple diet deficient in

---

[79a] G. Selzer, R. G. F. Parker, D. McKenzie, and G. C. Linder, *Brit. J. Exp. Path.*, 1951, **32**, 493.

[79b] M. Aloisi, A. Ascenzi, and E. Bonetti, *J. Path. Bact.*, 1952, **64**, 321.

[79c] *Idem, Experientia*, 1952, **8**, 266. [79d] *Idem, ibid.*, p. 69.

[80] A. B. Vogelsang, E. V. Shute, and W. E. Shute, *Med. Record*, 1947, **160**, 21, 91, 163, 230, 279. [81] W. E. Shute, *Urol. Cutaneous Reviews*, 1946, **50**, 679.

[82] C. L. Steinberg, *N.Y. State J. Med.*, 1947, **47**, 1679.

[83] W. W. Scott and P. L. Scardino, *Southern Med. J.*, 1948, **41**, 173.

[84] J. F. Burgess, *Lancet*, 1948, II, 215.

[85] E. V. Shute, *Ann. N.Y. Acad. Sci.*, 1949—1950, **52**, 358; A. M. Boyd, A. Hall Ratcliffe, G. W. H. James, and R. P. Jepson, *Lancet*, 1949, II, 132.

[86] A. Vogelsang, *Ann. N.Y. Acad. Sci.*, 1949—1950, **52**, 406.

[87] R. H. Davis, A. L. Mathis, D. R. Howton, H. Schneiderman, and J. F. Mead. *J. Biol. Chem.*, 1949, **179**, 383.

[87a] P. F. Solvonuk, L. B. Jaques, J. E. Leddy, L. W. Trevoy, and J. W. T. Spinks, *Proc. Soc. Exp. Biol. N.Y.*, 1952, **79**, 597.

[88] P. P. T. Sah, *Z. Vitamin-, Hormon- u. Fermentforsch.*, 1949—1950, **3**, 40.

[89] F. N.-H. Chang, J. F. Oneto, and P. P. T. Sah, *ibid.*, p. 61; P. P. T. Sah and T. C. Daniels, *ibid.*, p. 81. [90] P. P. T. Sah, G. Subbaraju, and T. C. Daniels, *ibid.*, p. 87.

[91] P. P. T. Sah, *ibid.*, p. 324.

[92] D. V. S. Reddy and V. Srinivasan, *Current Sci.*, 1948, **17**, 22; E. E. v. Koestveld, *Rec. Trav. chim.*, 1950, **69**, 1217. [93] H. Onrust and B. Wöstmann, *ibid.*, p. 1207.

[94] Pereira Forjaz, *Anais Azevedos*, 1950, **2**, 278.

vitamin K which regularly produces marked hypoprothrombinæmia in chicks has been devised.[95] The determination of vitamin K by the curative method in chicks has been simplified; a single dose of the test substance is given and the effect on the prothrombin time 20—22 hours later is determined.[96]

*Blood Coagulation.* Vitamin K and menadione both counteract the hypoprothrombinæmic action of dicoumarin and are equipotent in this respect; [95] the equipotency is, however, disputed.[104] The exact mechanism of the anti-vitamin K action of dicoumarin and other substances has been studied by several investigators. Dam [97] has pointed out that, in the plasma of dicoumarol-poisoned chicks and chicks deficient in vitamin K, in addition to a lack of prothrombin there are two other common factors: (*a*) the $\delta$-factor,[98] which is absent from vitamin K-deficient plasma but present in dicoumarol-poisoned plasma which, when added to the former, stimulated coagulation; and (*b*) the $\kappa$-factor,[99] which is absent in dicoumerol-poisoned plasma but present in vitamin K-deficient plasma which, when added to the former, also stimulates coagulation. The $\delta$- and the $\kappa$-factor may be inactivated by two entities partially separable from normal blood.[100] From various considerations it is supposed that vitamin K is not part of the prothrombin molecule but is concerned in the mechanism of prothrombin production. It is suggested that vitamin K serves as the prosthetic group which complements the apo enzyme AE, to form the active synthesising enzyme, AEK.[101] It is claimed that dicoumerol decreases both prothrombin and accelerator globulin, vitamin K being able to restore the former, but not the latter.[102] The structural requirement for anti-vitamin K activity is a 3-hydroxy-1 : 4-naphthaquinone substituted at $C_{(2)}$, the nature of the substituent being important, one condition being that it contains a hydrocarbon chain of at least six carbon atoms.[103]

The hypoprothrombinæmia occurring in hypervitaminosis A can be prevented by giving vitamin K, but the other effects are in no way affected.[105] Hypoprothrombinæmia from liver injury such as that caused by injection of pyramidone is relieved by vitamin K [106] but this effect is not obtained in cancer of the liver.[107] Vitamin K is still considered of value in prevention of hæmorrhagic manifestations in new-born infants.[108] The value of administering 10 mg. of synthetic vitamin K (tetrasodium 2-methyl-1 : 4-naphthaquinone diphosphate) before labour is established in a trial with 20,000 mothers (half this number being controls), the incidence of malæna and hæmatemesis in the offspring being much reduced.[109]

**Miscellaneous Fat-soluble Factors.**—*Essential fatty acids.* The necessity

---

[95] A. J. Quick and M. Stefanini, *J. Biol. Chem.*, 1948, **175**, 945.

[96] H. Dam, I. Kruse, and E. Søndergaard, *Acta Physiol. Scand.*, 1951, **22**, 238.

[97] H. Dam and E. Søndergaard, *Biochem. et Biophys. Acta*, 1948, **2**, 409.

[98] Ø. Sørbye, I. Kruse, and H. Dam, *Acta Chem. Scand.*, 1950, **4**, 831.

[99] *Idem, ibid.*, p. 549. [100] *Idem, ibid.*, 1951, **5**, 487.

[101] A. J. Quick and G. E. Collentine, *Amer. J. Physiol.*, 1951, **164**, 716.

[102] K. Felix, I. Pendl, P. Pin, and L. Roka, *Z. physiol. Chem.*, 1949, **284**, 185.

[103] C. Mentzer, *Bull Soc. Chim. biol.*, 1948, **30**, 872; C. C. Smith, *Proc. Soc. Exp. Biol. N.Y.*, 1950, **73**, 562.

[104] R. Miller, W. P. Harvey, and C. A. Finch, *New Engl. J. Med.*, 1950, **242**, 211.

[105] S. E. Walker, R. Eylenburg, and T. Moore, *Biochem. J.*, 1947, **41**, 575.

[106] J. E. Galimard, *Bull. Soc. Chim. biol.*, 1947, **29**, 641.

[107] W. Begtrup, *Acta Med. Scand.*, 1947—1948, **129**, 33.

[108] H. N. Sanford, M. Kostalik, and B. Blackmore, *Amer. J. Dis. Children*, 1949, **78**, 686. [109] H. Dyggve, Trans. 5th Intern. Congr. Pediat., New York, 1947.

for linoleic and linolenic acid in the diet of various species has been investigated. Linoleic acid is necessary for the emergence and development of the moth Ephestia, but some moths can synthesise this nutrient.[110] Rats on fat-deficient diets do not grow more rapidly when given pituitary-growth hormone. Hormone with linoleate gave better growth than linoleate alone;[111] male rats require 50 mg. of linoleic acid daily, females 10—20 mg. Linolenic acid at the same level was poor in growth-promotion but when fed with linoleate in sub-optimum amounts it was much more efficient.[112] Chicks on fat-free diets fail to grow at the same rate as chicks receiving supplementary linoleic acid;[113] they can convert dienoic acids into tetraenoic and pentaenoic acids, and trienoic acids into hexaenoic and other polyenoic acids.[114] The laying hen can probably synthesise small amounts of linoleic acid, and it is interesting that egg production and hatchability remain normal with hens fed on the fat-free diet.[115] The follicular hyperkeratosis in man, normally associated with vitamin-A deficiency, can be cured by fats containing polyunsaturated fatty acids.[116]

The distribution of unsaturated fatty acids has been studied in horse, beef and mutton,[118] rats,[117] guinea pigs,[119] dogs,[120] and milk.[120a] The fatty acid requirements of bacteria have been studied.[121]

Linoleic acid has been synthesised by the partial hydrogenation of the corresponding β-diacetylenic acid which is, however, difficult to obtain in good yield.[122]

*Guinea-pig anti-stiffness factor.* This crystalline factor, isolated from cane-sugar juice,[123] continues to receive considerable attention. Many sterols have been tested,[124] but only ergostanyl acetate is active. Deficiency is thought to lead to a disturbance in the phosphate distribution in muscle;[125] deafness and disorganisation of the ear are associated phenomena.[126] The results, and particularly the lack of a good method of assay have been criticised.[127]

*Anti-gizzard-ulcer factor.* This factor, which was reported as occurring

---

[110] G. Fraenkel and M. Blewett, *Biochem. J.*, 1947, **41**, 475.

[111] H. Deuel, Jr., S. M. Greenberg, C. E. Calbert, E. E. Savage, and T. Fukui, *J. Nutrit.*, 1950, **40**, 351.

[112] S. M. Greenberg, C. E. Calbert, E. E. Savage, and H. J. Deuel, Jr., *ibid.*, 1950, **41**, 473.

[113] R. Reiser, *ibid.*, 1950, **42**, 319.

[114] *Idem, ibid.*, p. 325.

[115] *Idem, ibid.*, 1951, **44**, 159.

[116] P. S. Menon, P. G. Tulpule, and V. N. Patwardhan, *Indian J. Med. Res.*, 1950, **38**, 173.

[117] C. Widmer, Jr., and R. T. Holman, *Arch. Biochem.*, 1950, **25**, 1.

[118] F. B. Shorland, *Nature*, 1950, **165**, 766.

[119] A. Chevallier, C. Burg, M. Lagoutière, and R. Schneider, *Compt. rend. Soc. Biol.*, 1949, **143**, 1380.

[120] H. F. Wiese, R. T. Holman, and A. E. Hansen, *Fed. Proc.*, 1950, **9**, 374.

[120a] P. S. Schaffer and G. E. Holm, *J. Dairy Sci.*, 1950, **33**, 865.

[121] M. R. Pollock, G. A. Howard, and B. W. Boughton, *Biochem. J.*, 1949, **45**, 417; J. B. Hassinen, G. T. Durbin, and F. W. Bernhart, *Arch. Biochem.*, 1950, **25**, 91.

[122] R. A. Raphael and F. Sondheimer, *Nature*, 1950, **165**, 235.

[123] W. J. van Wagtendonk and R. Wulzen, *J. Biol. Chem.*, 1946, **164**, 597.

[124] J. J. Oleson, E. C. van Donk, S. Bernstein, L. Dorfman, and Y. Subarrow, *ibid.*, 1947, **171**, 1.

[125] W. J. van Wagtendonk, *ibid.*, 1947, **167**, 219; W. J. van Wagtendonk and A. M. Freed, *ibid.*, p. 225.

[126] H. Krueger, R. Wulzen, and P. Leveque, *Abs. Comm. 18th Intern. Physiol. Congr.*, 1950, p. 316.

[127] W. Dasler, *Chicago Med. Sch. Quart.*, 1950, **11**, 70; W. Dasler and C. D. Bauer, *Proc. Soc. Exp. Biol. N.Y.*, 1949, **70**, 134.

in the saponifiable sterol fraction of fats and designated vitamin U,[128] has been the cause of considerable confusion. Highly unsaturated fatty acids of hog-liver fat exert a marked effect against gizzard ulcers,[129] as does arachidonic acid.[130] That the factor may not be fat-soluble is shown by the facts that cyanocobalamin partially prevents chick-gizzard ulcers,[131] and both ether-extracts of calves brain and water-extracts of the ether-extracted brain are active.[132] Both extracts together exert a greater effect than either separately, and cyanocobalamin can replace the aqueous extract. Thus, this gizzard ulcer is probably caused by an interplay of deficiencies of several factors, some of which are fat soluble. There is a corresponding problem with stomach ulcers in rats.[133]

S. P. D.

## 4. PHOSPHATE METABOLISM.

Abbreviations used are: ATP = adenosine triphosphate; ADP = adenosine diphosphate; AMP = adenylic acid; CoI, CoII, CoA = Coenzyme I, Coenzyme II, Coenzyme A; diNP = dinitrophenol.

In this Report, since it is impossible to cover all aspects of the subject, first place has been given to the part played by phosphate in the storage and transfer of energy. It is interesting that, though the energy-rich phosphate bond still keeps its place as providing the most important known mechanism for storage of readily available energy, the metabolic importance of an energy-rich bond not involving phosphate, the acylmercaptide bond, has recently come to light. The transfer of a component of the acylmercaptide compound, together with energy, can take place without the intervention of phosphate, although phosphate may act as an acceptor. In this connection also the discussion by Woolley [1] is of great interest, on the free energy to be derived from the reduction of quaternary ammonium and sulphonium ions, and the possible biological rôle of such ions.

**Oxidative Phosphorylation.**—*The phosphorus : oxygen ratio.* In 1948, Green, Loomis, and Auerbach [1a] started the series of studies on cyclophorase, which showed that this preparation of washed tissue particles can catalyse all the oxidations of the tricarboxylic acid cycle, as well as oxidise many amino- and fatty acids.[2] Cross, Taggart, Covo, and Green [3] studied phosphate esterification with this preparation, and found that usually more than two atoms of phosphorus were esterified for every atom of oxygen absorbed, thus confirming the earlier values with cruder preparations, where a large allowance had been necessary for phosphatase activity (see, *e.g.*, Ochoa [4]). By 1948 the work of Hogeboom, Schneider, and Pallade [5] had made possible the isolation, by differential centrifugation of tissue homogenates in hyper-

[128] G. Chesney, *Arch. Intern. Med.*, 1942, **70**, 532.
[129] H. Dam, *Acta Physiol. Scand.*, 1946, **12**, 189.
[130] H. Dam and H. L. Segal, *ibid.*, 1945, **10**, 295.
[131] C. W. Mushett and W. H. Ott, *Poultry Sci.*, 1949, **28**, 850.
[132] H. Dam, B. Noer, and E. Søndergaard, *Acta Physiol. Scand.*, 1950, **21**, 315.
[133] E. L. Hove and P. L. Harris, *J. Nutrit.*, 1950, **40**, 177; G. Chesney, *J. Amer. Dietet. Assoc.*, 1950, **26**, 668.
[1] D. W. Woolley, *Nature*, 1953, **171**, 323.
[1a] D. E. Green, W. F. Loomis, and V. H. Auerbach, *J. Biol. Chem.*, 1948, **172**, 389.
[2] D. E. Green, *Biol. Reviews*, 1951, **26**, 410.
[3] R. J. Cross, J. V. Taggart, G. A. Covo, and D. E. Green, *J. Biol. Chem.*, 1948, **177**, 655.
[4] S. Ochoa, *ibid.*, 1941, **138**, 751; 1943, **151**, 493; 1944, **155**, 87.
[5] G. H. Hoogeboom, W. C. Schneider, and G. E. Pallade, *ibid.*, 1948, **172**, 619.

tonic sucrose solution, of the large cell granules or mitochondria, in a morphological state apparently identical with that *in vivo*. It was soon found that this mitochondrial fraction was the main site of cell oxidations and showed a higher phosphorus : oxygen ratio than other cell constituents.[6] Harman and co-workers [7] showed that the activity of cyclophorase depended on the number and integrity of the mitochondria.

With the use of these intact, isolated mitochondria, many interesting relationships have come to light. Thus, Kielley and Kielley [8] have shown that ageing of the preparations by maintaining them for some time under various conditions without substrate before the experiment, causes a tenfold increase in adenosine triphosphatase activity on addition of ATP. At the same time the content in ATP and ADP falls and inorganic phosphorus is lost into the medium. This rise in adenosine triphosphatase activity must be an important factor in causing the low phosphorus : oxygen ratios so often encountered with mitochrondria preparations, but probably there are more subtle aspects also. Thus, it is suggested that a certain level of internal ADP (to act as phosphate acceptor) is necessary for initiating the phosphorylation process; and that continual resynthesis of essential co-factors may go on, so that any period during which internal ATP is absent and during which degradation products of such factors might leak away, would have irreversible deleterious results. Hunter and Hixon's work [9] had earlier shown the importance of experimentation at a low temperature (15°) to obtain high phosphorus : oxygen ratios.

The influence of phosphorus acceptors on oxidation rate is very clearly seen with the intact mitochondria.[6, 10] Lardy and Wellman [10] found very low oxygen uptake with rat-liver mitochondria, prepared in isotonic sucrose solution and fortified with ATP, magnesium, and phosphate; the rates were greatly enhanced by addition of phosphorus acceptors.

Some complicated questions of permeability of the intact mitochondria, and of the accessibility of their enzyme systems, have been discussed by Lehninger.[11]

*The evidence for phosphorylation accompanying hydrogen transport.* From energy considerations and from analogy with glyceraldehyde dehydrogenation during glycolysis, we should expect only one phosphorus atom to be esterified for every pair of hydrogen atoms removed from the substrate; whereas an average of three is found for the passage of pyruvate through the tricarboxylic acid cycle to carbon dioxide and water.[3, 4] This means that the later stages of hydrogen transport (or at any rate some of them), through flavin and cytochrome C to oxygen, must be involved. The latest assessments [12] of the free energy of the energy-rich phosphate bond give values between about 12,000 cal. per mole for the pyrophosphate bond in ATP, and about 15,000 cal. per mole for the phospho-enolic bond in phosphopyruvate. The free energy likely to be available at the different stages may be gauged

---

[6] A. L. Lehninger and E. P. Kennedy, *J. Biol. Chem.*, 1949, **179**, 957; V. R. Potter, G. G. Lyle, and W. C. Schneider, *ibid.*, 1950, **190**, 293.

[7] J. W. Harman, *Exp. Cell. Res.*, 1950, **1**, 382, 394; J. W. Harman and M. Feigelson, *ibid.*, 1952, **3**, 47, 509.

[8] W. W. Kielley and R. K. Kielley, *J. Biol. Chem.*, 1951, **191**, 485.

[9] F. E. Hunter and W. S. Hixon, *ibid.*, 1949, **181**, 73.

[10] H. A. Lardy and H. Wellman, *ibid.*, 1952, **195**, 215.

[11] A. L. Lehninger, in " Phosphorus Metabolism," Johns Hopkins Press, Baltimore, 1951, p. 344.

[12] P. Oesper, *ibid.*, p. 523.

from the charts given by Dixon;[13] the values per two hydrogen atoms at pH 7·0 are approximately 12,000 cals. between the CoI stage and the flavoprotein stage; 14,000 between the latter and the cytochrome C system; and 24,000 between this last system and oxygen at one atmosphere.[cf. 13a]

Only two steps in the tricarboxylic acid cycle have been studied individually. The oxidation of α-ketoglutarate to succinate and carbon dioxide was found by Hunter and Hixon[9] to give a phosphorus : oxygen ratio of 3 or more (probably 4) in conditions where about 75% of the succinate could be recovered after the oxidation. The same workers also examined the oxidation of succinate to fumarate practically as a single step (under their conditions, fumarate was being oxidised at only one-fifth of the rate for the succinate). Here, as well as in experiments of Cross *et al.*[3] and of Lehninger and Smith,[14] experimental phosphorus : oxygen values of 1·4—1·7, indicated a true ratio of 2. The oxidation of succinate does not pass through CoI or CoII, and the low phosphorus : oxygen ratios are probably to be explained by the availability of only the stages from cytochrome C onwards.

With regard to the remaining oxidations in the tricarboxylic acid cycle, the case of pyruvate is considered below. The oxidation of *iso*citrate to oxalosuccinate, and of malate to oxaloacetate has not been investigated as isolated steps, and it is not possible to say definitely whether phosphorylation is connected with these substrate stages. From the probable position of their equilbria on the rH scale,[15] this seems unlikely.

We may now consider the direct evidence for esterification at various stages of the hydrogen-transport chain. In experiments with washed liver-particles, Lehninger[16] showed that the anaerobic oxidation–reduction between β-hydroxybutyrate and oxaloacetate is not accompanied by phosphate esterification, as indeed is to be expected from the position of its equilibrium on the electrode-potential scale. However, when conditions were aerobic, incorporation of $^{32}$P into ATP was found to be coupled with the oxidation, and Lehninger and Smith, using high concentrations of ADP or AMP as acceptor, found phosphorus : oxygen ratios higher than 2. Since acetoacetate was not further oxidised and since the substrate stage alone did not lead to phosphate uptake, this esterification must be coupled with the later stages of electron transfer. Lehninger[17] was later successful in showing that the oxidation of high concentrations of reduced CoI could give a ratio of nearly 2.

The question of phosphorus esterification associated with transport of hydrogen between reduced CoI and cytochrome C has been studied by Friedkin and Lehninger,[18] using large amounts of cytochrome C as hydrogen acceptor, but without success; Slater,[19] using α-ketoglutarate oxidation by heart mitochondria, compared phosphorus : oxygen ratios with either cytochrome C in high concentration or oxygen as the final hydrogen acceptor, and found no difference. Too much weight must not be laid on such negative results, since they probably mean that experimental difficulties (such as

[13] M. Dixon, " Multi-enzyme Systems," University Press, Cambridge, 1948, pp. 65, 73, 87.

[13a] A. W. D. Avison and J. D. Hawkins, *Quart. Reviews*, 1951, **5**, 171; S. Ochoa and J. R. Stern, *Ann. Rev. Biochem.*, 1952, **21**, 547.

[14] A. L. Lehninger and S. W. Smith, *J. Biol. Chem.*, 1949, **181**, 415.

[15] M. Dixon, " Multi-enzyme Systems," University Press, Cambridge, 1948, p. 28.

[16] A. L. Lehninger, *J. Biol. Chem.*, 1949, **178**, 625. [17] *Idem, ibid.*, 1951, **190**, 345.

[18] M. Friedkin and A. L. Lehninger, *ibid.*, 1949, **178**, 611.

[19] E. C. Slater, *Nature*, 1950, **166**, 982.

the lability of the individual esterification mechanisms or limitations due to permeability barriers in the mitochondria) have not yet been overcome. Judah [20] seems to have had some success in showing esterification associated with the oxidation of reduced cytochrome C, by using a liver-mitochondrial system in which ascorbic acid provided continual reduction of cytochrome C. Control experiments showed that the dehydroascorbic acid was not further oxidised.

*Mechanism of phosphate uptake.* A good deal of information has recently been gained on the mechanism of phosphate uptake at the substrate stage in the tricarboxylic acid cycle.

Lipmann [21] had shown that the primary product of oxidation of pyruvate by extracts of *B. Delbruckii* was acetyl phosphate. However, efforts to bring about synthesis of citrate in animal tissues by means of acetyl phosphate and oxaloacetate failed, although synthesis was obtained either during oxidation of pyruvate or fatty acids or in the presence of acetate and ATP.[22] Light was first thrown on the nature of "active acetate" as acetyl-coenzyme A by the work of Stadtman and his collaborators. Stadtman [23] prepared from extracts of *Cl. Kluyveri* an enzyme, phosphotransacetylase, which could make available the acetyl group of acetyl phosphate for condensations, *e.g.*, citrate formation in presence of the condensing enzyme from liver. Phosphotransacetylase is CoA dependent, and further work [24] indicated that the reaction catalysed is :

$$\text{acetyl phosphate} + \text{CoA} \rightleftharpoons \text{acetyl–CoA} + \text{phosphate}$$

Lynen, Reichert, and Rueff [25] had meanwhile isolated acetyl–CoA, and this was shown by Stern, Shapiro, Stadtman, and Ochoa [26] to react, in presence of the crystalline condensing enzyme, to give citrate. Stadtman [27] also isolated the acetyl–CoA formed by phosphotransacetylase action.

Lipmann and his colleagues [28] have recently studied the mechanism of the reaction whereby acetyl–CoA is formed in yeast and pigeon-liver preparations, in presence of ATP, CoA, and acetate, although acetyl phosphate is unavailing. Lynen, Reichert, and Rueff [25] had suggested that CoA is phosphorylated by ATP, with formation of an energy-rich bond, and that the phosphate can then exchange for acetyl, acetyl–CoA resulting :

$$\text{ATP} + \text{CoA} \longrightarrow \text{CoA–phosphate} + \text{ADP}$$
$$\text{CoA} + \text{acetate} \longrightarrow \text{acetyl–CoA} + \text{phosphate}$$

However, Lipmann's investigation showed that the final form of the ATP is AMP + pyrophosphate ; and further that, while pyrophosphate can displace acetyl from acetyl–CoA, inorganic phosphate cannot do so. It was concluded that the reactions were :

$$\text{ATP} + \text{CoA} \rightleftharpoons \text{AMP} + \text{CoA-pyrophosphate}$$
$$\text{CoA–pyrophosphate} + \text{acetate} \rightleftharpoons \text{acetyl–CoA} + \text{pyrophosphate}$$

---

[20] J. D. Judah, *Biochem. J.*, 1951, **49**, 27. [21] F. Lipmann, *J. Biol. Chem.*, 1944, **155**, 55.

[22] J. R. Stern and S. Ochoa, *ibid.*, 1949, **179**, 491.

[23] E. R. Stadtman, *Fed. Proc.*, 1950, **9**, 233.

[24] E. R. Stadtman, G. D. Novelli, and F. Lipmann, *J. Biol. Chem.*, 1951, **191**, 365; E. R. Stadtman, *ibid.*, 1952, **196**, 527.

[25] F. Lynen, R. Reichert, and L. Rueff, *Ann. Chem.*, 1951, **574**, 1.

[26] J. R. Stern, B. Shapiro, E. R. Stadtman, and S. Ochoa, *J. Biol. Chem.*, 1951, **193**, 703.

[27] E. R. Stadtman, *ibid.*, 1952, **195**, 535.

[28] F. Lipmann, M. E. Jones, and S. Black, "Symposium sur le Cycle Tricarboxylique," Second Int. Congr. Biochem, Paris, 1952, p. 55.

The same reactions are catalysed by a soluble enzyme from pig's heart.[29]

Partially purified, soluble systems have been isolated[30] from *E. coli* and from heart, which catalysed the oxidation of pyruvate in presence of both CoI and CoA. With catalytic amounts of CoA, the reaction only proceeded if an acetyl acceptor was present, together with the appropriate acetylating enzyme. The supply of CoI could be kept up by coupling reaction with lactic dehydrogenase:

$$\text{Pyruvate} + \text{CoI} + \text{CoA} \rightleftharpoons \text{acetyl–CoA} + CO_2 + \text{CoI–}H_2$$

Schweet, Fuld, Cheslock, and Paul,[31] using a soluble preparation from pigeon-breast muscle, came to similar conclusions. Littlefield and Sanadi,[32] using large amounts of CoA, have recently been able to show stoicheiometric relations between the disappearance of pyruvate and CoA–SH groups (see below) and the appearance of active acetate (by the hydroxamic reaction) and reduced CoI. These findings explain how the free energy of pyruvate oxidation is used in the tricarboxylic acid cycle for the synthesis of citrate from pyruvate and oxaloacetate. No examination of phosphate uptake associated with pyruvate oxidation has been described, but it seems likely that the acetyl–CoA might, under some conditions, undergo pyrophosphorolysis or phosphorolysis.

The esterification of phosphate accompanying the oxidation of α-ketoglutarate to succinate and carbon dioxide has been studied by Kaufman,[33] by using a soluble enzyme preparation from heart. This catalyses the dismutation of α-ketoglutarate to glutamate and succinate, in the presence of ammonium ions. If phosphate acceptors are added, phosphate is esterified. The following formulation seems to fit the facts:

$$\alpha\text{-ketoglutarate} + \text{CoI} + \text{CoA} \rightleftharpoons \text{succinyl–CoA} + CO_2 + \text{CoI–}H_2$$
$$\alpha\text{-ketoglutarate} + NH_4 + \text{CoI–}H_2 \rightleftharpoons \text{glutamate} + \text{CoI}$$
$$\text{succinyl–CoA} + H_2O \rightleftharpoons \text{succinate} + \text{CoA}$$
$$\text{succinyl–CoA} + \text{ADP} + H_3PO_4 \rightleftharpoons \text{succinate} + \text{ATP} + \text{CoA}$$

Although this is not actually suggested by Kaufman, it seems likely that the last reaction is:

$$\text{succinyl–CoA} + H_3PO_4 \rightleftharpoons \text{succinate} + \text{CoA–phosphate}$$
$$\text{CoA–phosphate} + \text{ADP} \rightleftharpoons \text{ATP} + \text{CoA}$$

It is significant that, in contrast to the system with acetate studied by Lipmann *et al.*,[28] this could catalyse the liberation of inorganic phosphate from ATP in presence of succinate and CoA. Acetyl–CoA could not react with ADP and phosphoric acid in this system. Succinyl–CoA has been isolated by Sanadi and Littlefield.[34] Ochoa[35] has reported that, by further ammonium sulphate fractionation of Kaufman's heart preparation, two protein fractions were obtained, one of which catalysed oxidation of α-keto-

---

[29] Quoted by D. E. Green, *Science*, 1952, **115**, 661.

[30] S. Korkes, A. del Campillo, I. C. Gunsalus, and S. Ochoa, *J. Biol. Chem.*, 1951, **193**, 721; S. Korkes, A. del Campillo, and S. Ochoa, *ibid.*, 1952, **195**, 541.

[31] R. S. Schweet, M. Fuld, K. Cheslock, and M. H. Paul, in "Phosphorus Metabolism," Johns Hopkins Press, Baltimore, 1951, p. 246.

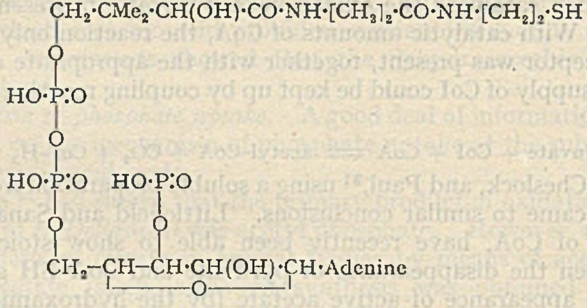
[32] J. W. Littlefield and D. R. Sanadi, *J. Biol. Chem.*, 1952, **199**, 65.

[33] S. Kaufman, in "Phosphorus Metabolism," Johns Hopkins Press, Baltimore, 1951, p. 370. [34] D. R. Sanadi and J. W. Littlefield, *Science*, 1952, **116**, 327.

[35] S. Ochoa, "Symposium sur le Cycle Tricarboxylique," Second Int. Congr. Biochem., Paris, 1952, p. 73.

glutaric acid without coupled phosphorylation. Addition of the second fraction (completely inactive in absence of the first) caused phosphorylation.

*Co-enzyme A.* Recent work[36] points to the formula :



Lynen, Reichert, and Rueff[25] showed that reaction of acyl groups with CoA takes place through the thiol group of the pantothenic acid :

$$\text{CoA–SH} + \text{AcR} \longrightarrow \text{CoA–SAc} + \text{RH}$$

During the previous discussion it has been assumed that the acylthio-bond is energy-rich, since the acetylations and the pyrophosphorylation which it is known to implement, as well as the phosphorylations which seem to depend upon it, are reactions requiring energy provision. The free energy of its rupture has been assessed by Stern, Ochoa, and Lynen.[37] They measured the equilibrium constant of the reaction :

$$\text{CoA–SAc} + \text{malate} + \text{CoI} + H_2O \rightleftharpoons \text{CoA–SH} + \text{citrate} + \text{CoI–H}_2$$

and from this, together with that of the reaction catalysed by malic dehydrogenase at the same pH, calculated that the free energy of the acylthio-bond is of the order of 12,000 cals./mole.

*Reversibility.* The reversibility which is such a marked feature of the series of reactions participating in hydrogen transfer and phosphorus uptake means that any accumulation of intermediates will hold up the whole course. This is probably the reason for the stimulating effect upon oxygen uptake of the presence of phosphate acceptors, and, as we shall see, of uncoupling agents. The need for inorganic phosphate, which is often observed in oxidation systems, may arise from the need for regeneration of intermediates: *e.g.*, of CoA by phosphorolysis of acyl–CoA, followed by transfer of the phosphate group from the CoA–phosphate to an adenylic acceptor. This must remain at present a matter of speculation, since so far CoA–phosphate has not been isolated, and the enzymes concerned in the suggested transfers have not been identified. The need for some mechanism to bring about rapid splitting of acyl–CoA compounds is shown by the work of Gergely, Hele, and Ramakrishnan.[38] Using purified α-ketoglutarate oxidase, they showed that the oxidation only proceeds in presence of catalytic amounts of CoA if another enzyme, succinyl–CoA deacylase, is provided. This enzyme brings about the reaction

$$\text{Succinyl–CoA} + H_2O \longrightarrow \text{succinate} + \text{CoA}$$

---

[36] J. Baddiley and E. M. Thain, *J.*, 1951, 2253; J. D. Gregory, G. D. Novelli, and F. Lipmann, *J. Amer. Chem. Soc.*, 1952, 74, 854.

[37] J. R. Stern, S. Ochoa, and F. Lynen, *Fed. Proc.*, 1952, 11, 293.

[38] J. Gergeley, M. P. Hele, and C. V. Ramakrishnan, *J. Biol. Chem.*, 1952, 198, 323.

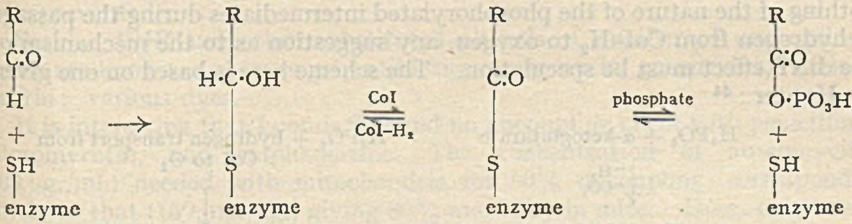
and evidence was obtained for a similar enzyme acting upon acetyl–CoA. The activity of such enzymes could, of course, speed up oxidations, but would involve dissipation of the energy of the acylthio-bond.

**Esterification of Phosphate during Oxidation of Glyceraldehyde Phosphate.**—It will be noticed that in the conceptions of phosphate uptake described above, no phosphorylation of the substrate is postulated, as it was in Warburg and Christian's theory with regard to the esterification accompanying the oxidation of glyceraldehyde phosphate during glycolysis. It is of great interest, therefore, to find that a new view of the action of glyceraldehyde phosphate dehydrogenase has emerged, in which phosphate uptake is a post-oxidation stage.

Krimsky and Racker [39] have recently obtained evidence that crystalline glyceraldehyde phosphate dehydrogenase contains glutathione as a firmly bound prosthetic group. Racker and Krimsky [40] then showed that oxidation of aldehydes proceeds in two stages : first the aldehyde reacts with the thiol group of the enzyme and is oxidised to a thiol ester; and only later does phosphorolysis take place with removal of the acyl group to phosphate. The evidence for the first step may be summarised as follows : (1) formation of a thiol ester when the reaction was carried out in the presence of glutathione and the absence of phosphate; (2) the power of the reaction to provide acyl groups for acylation of, *e.g.*, sulphanilamide in presence of the appropriate additional enzyme system; and (3) release of acyl groups from the washed denatured enzyme into solution with hydroxylamine. The evidence for the second step depends on a study of the back reaction : in the presence of arsenate the enzyme liberated inorganic phosphate from diphosphoglycerate, even though there was no hydrogen donor present and no CoI reduction; and even though iodoacetate was present to inhibit any oxidation or reduction. It will be seen that this arsenolysis is incompatible with the old formulation of the reaction series :

$$\text{glyceraldehyde} + \text{phosphate} \rightleftharpoons \text{glyceraldehyde diphosphate} \rightleftharpoons \text{diphosphoglyceric acid}$$

Racker and Krimsky suggest :



A similar conclusion was reached by Holzer and Holzer,[41] who found that crystalline triose phosphate dehydrogenase can be protected from iodoacetate inhibition by previous addition of its substrate. They showed the dissociation constants of the enzyme–substrate complex to be in the ratio, 500 : 1, for glyceraldehyde and glyceraldehyde phosphate; and the amounts of the two substrates which had to be added to obtain protection bore roughly this same relation—300 : 1. They concluded that the aldehydes combine with

---

[39] I. Krimsky and E. Racker, *J. Biol. Chem.*, 1952, **198**, 721.

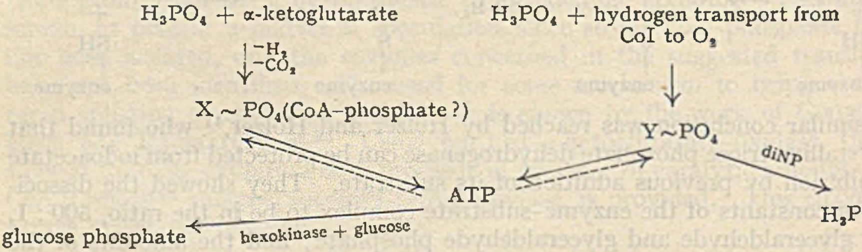
[40] E. Racker and I. Krimsky, *ibid.*, p. 731.

[41] H. Holzer and E. Holzer, *Z. Physiol. Chem.*, 1952, **291**, 67.

the enzyme by means of the same group as the iodoacetate, *i.e.*, through the thiol group. These facts are suggestive but not conclusive.

**Uncoupling of Oxidation and Phosphorylation.**—Many reagents can be used to dissociate phosphorylation from oxidation and an intensive study has been made recently of some, *e.g.*, dinitrophenol (diNP). It has long been known that this substance, while stimulating metabolism, can prevent many sorts of anabolic process—growth, differentiation, nitrogen and phosphate assimilation, etc. Ronzoni and Ehrenfest,[42] using intact frog muscle, seem to have been the first to show that the increased metabolism was associated not, as might be expected, with increased phosphocreatine synthesis, but with a very marked breakdown. Then Loomis and Lipmann,[43] using washed kidney particles, found that the increased oxygen-uptake in presence of diNP was accompanied by inhibition of phosphate esterification, and that the rate of oxidation became independent of added phosphate. The most likely explanation is that in its presence a small amount of residual inorganic phosphate in the homogenate can be used over and over again, presumably on account of very rapid release of inorganic phosphate from phosphorylated intermediates. Indeed, Judah [20] has shown, by exhaustive washing of liver mitochondria (which did not damage their powers of oxidative phosphorylation under appropriate conditions) that with less than about M/1000-phosphate, little or no stimulating effect of diNP on oxidation is seen.

This uncoupling effect seems to have no connection with phosphorylation at the substrate level, but only with that accompanying the later hydrogen-transport stages. Thus, both Hunter [44] and Judah [20] have observed that diNP has little effect on the phosphorus : oxygen ratio of the anaerobic dismutation of α-ketoglutarate in presence of mitochondria; and Greville and Rowsell [45] found no effect on phosphate uptake during the oxidation–reduction between glyceraldehyde phosphate and pyruvate, by extract of muscle acetone powder. DiNP reduces the phosphorus esterification connected with α-ketoglutarate oxidation to one quarter; while with β-hydroxybutyrate oxidation (where no phosphate uptake is associated with the substrate level) diNP abolishes the whole phosphate uptake. As we know nothing of the nature of the phosphorylated intermediates during the passage of hydrogen from CoI–$H_2$ to oxygen, any suggestion as to the mechanism of the diNP effect must be speculation. The scheme here is based on one given by Hunter : [44]



---

[42] E. Ronzoni and E. Ehrenfest, *J. Biol. Chem.*, 1936, **115**, 749.
[43] W. F. Loomis and F. Lipmann, *ibid.*, 1948, **173**, 807.
[44] F. E. Hunter, in " Phosphorus Metabolism," Johns Hopkins Press, Baltimore, 1951, p. 297.
[45] G. D. Greville and E. V. Rowsell, unpublished results.

Hunter points out that, since the energy of the phosphate link in the hypothetical $Y–PO_4$ compound is probably of the same order as that of the pyrophosphate link in ATP, one would expect the reaction between the two compounds to be reversible. If this is the case, ATP from any source would run a risk of dephosphorylation by means of the diNP leak. Whether or not this dephosphorylation happened would depend on the relative rate of phosphate transfer to acceptors other than the compound Y, and on the rate of $Y–PO_4$ dephosphorylation. From all the considerations which have been put forward above, we should expect that only the oxidised form of the compound Y would be capable of accepting phosphate in high-energy bonding, and the energy, of course, would be dissipated on dephosphorylation. The scheme given might thus explain the greatly increased dephosphorylation of ATP in presence of diNP by mitochondria [44] and by minced muscle [46] as long as oxygen were available; this dephosphorylation is in contrast to the lack of effect of diNP on partly purified potato apyrase and the comparatively small effect on myosin.[46a] It might also account for Ronzoni and Ehrenfest's observations [42] of the uncoupling of phosphorylation with intact frog muscle even under anaerobic conditions with greatly accelerated lactic acid formation, since here oxygen may not have been completely excluded. It would not explain the finding by Hunter that diNP exerts its effect of increasing the apparent adenosine triphosphatase activity of mitochondria even in strict anaerobiosis. Lynen and Koenigsberger [47] have found with yeast suspensions that, in aerobic conditions, disappearance of inorganic phosphate is prevented by diNP., while anaerobically phosphorylation continues unchanged. Aerobic fermentation becomes marked in presence of diNP and these workers regard this as strong support for their conception that lack of inorganic phosphate (which would reduce the activity of triose phosphate dehydrogenase) is the cause of the diminished carbohydrate utilisation seen in the Pasteur effect. They bring forward some further interesting anomalies in diNP effects—the facts that although the energy-providing phosphorylation in fermentation is not interrupted, yet anaerobic synthesis of glycogen and also of enzyme proteins during adaptation seem to be prevented.

Besides diNP and other substituted phenols, a number of uncoupling agents are known, *e.g.*, amongst antibiotics, aureomycin, gramicidin; azide; atebrin; various dyes.

It is interesting that Loomis [48] found no uncoupling effect with penicillin, chloromycetin, and sulphadiazine. The concentration of aureomycin (200 μg./ml.) needed with mitochondria for 80% uncoupling, corresponds closely to that (150 mg./kg.) giving 80% mortality in mice. Doses only one-hundredth of this are needed with bacteria to bring about other toxic effects (inhibition of protein synthesis [48a]) so that it seems likely that the uncoupling effect is related, not to the chemotherapeutic action but to the toxicity to the host.

Loomis and Lipmann,[49] using kidney homogenates, report that azide

[46] H. A. Lardy, unpublished results, mentioned in H. A. Lardy and C. A. Elvejhem, *Ann. Rev. Biochem.*, 1945, 14, 1.

[46a] H. L. Webster, personal communication.

[47] F. Lynen and R. Koenigsberger, *Ann. Chem.*, 1951, 573, 60.

[48] W. F. Loomis, *Science*, 1950, 111, 474.

[48a] E. F. Gale and J. P. Folkes, *Biochem. J.*, 1953, 53, 493.

[49] W. F. Loomis and F. Lipmann, *J. Biol. Chem.*, 1949, 179, 403.

cannot "replace" phosphate but can partially "replace" adenylic acid. They suggest that azide acts upon the stage of phosphorus transfer from primarily formed phosphate ($Y-PO_4$ above?) to adenylic compounds. Spiegelman, Kamen, and Sussman [50] found dissociation of phosphorylation from oxidation–reduction in anaerobic fermentation with yeast suspensions; and from the azide effects in presence of other inhibitors, they suggest that the azide, under the influence of phosphoglycerate phosphokinase, can accept phosphate from diphosphoglycerate, with formation of an unstable compound which releases inorganic phosphate. It is not clear why, with such a system, azide should not show some phosphate "replacement." Spiegelman *et al.* found no uncoupling effect in Lebedew yeast extracts, nor could Judah [20] find any effect with anaerobic dismutation of α-ketoglutarate.

Judah and Williams-Ashman [51] list a number of dyes, notably phenosafranine, Janus green, Brilliant cresyl blue, which increase the oxygen uptake in absence of added phosphate and greatly decrease the phosphorus : oxygen ratio. The dyes may act as supplementary electron carriers, and in so doing may by-pass reactions connected with phosphorylation.

**Hormonal Effects.**—*Thyroxine.* The stimulation of metabolic rate by thyroxine suggests comparison with the increased metabolism found with such drugs as diNP, and many workers have wondered whether uncoupling played a part in thyroxine effects. The position at present is rather confused, as the results from different laboratories have been conflicting, but possible reasons for the disagreements begin to emerge. Lardy and Feldott [52] found that thyroxine added *in vitro* had no effect on phosphorus : oxygen ratios of fresh mitochondria by using the Krebs cycle; however, it and its biologically active analogues did inhibit the one-step oxidation of glutamate to succinate and the associated phosphorus : oxygen ratio was affected more than proportionately. Liver tissue of hyperthyroid rats (fed on thyroid for at least two weeks) had lower phosphorus : oxygen ratios; nevertheless owing to the greatly stimulated metabolism, the actual amount of phosphate esterification was greater. Lipmann [53] reported no difference in phosphorus : oxygen ratios between tissues of thyroxine-injected and normal rats. There was, however, an interesting effect of the thyroxine. There had been found [54] with mitochondrial preparations from liver of normal animals a greatly enhanced oxygen-uptake as the result of addition of phosphate acceptors; in similar preparations from thyroxine-injected animals, the oxygen uptake was already high, and there was no phosphate-acceptor effect. Since the phosphorus : oxygen ratio was not changed, this seems to indicate that under certain conditions, thyroxine can cause more effective transphosphorylation.

Martius and Hess [55] found depression of phosphate-uptake *in vitro*, but only if the mitochondria were treated with thyroxine ($3 \times 10^{-6}$—$5 \times 10^{-5}$M) for 30 minutes at 0° before measurements; very small thyroxine concentrations had the opposite effect, stimulating phosphate uptake. They found

---

[50] S. Spiegelman, M. D. Kamen, and M. Sussman, *Arch. Biochem.*, 1948, 18, 409.

[51] J. D. Judah and H. G. Williams-Ashman, *Biochem. J.*, 1951, 48, 33.

[52] H. A. Lardy and G. Feldott, *Ann. N.Y. Acad. Sci.*, 1951, 54, 531.

[53] C. H. Dutoit, F. L. Hoch, E. Wright, and F. Lipmann, Abstracts, Second Int. Congr. Biochem., Paris, 1952, p. 50.

[54] H. Niemeyer, R. K. Crane, E. P. Kennedy, and F. Lipmann, *Fed. Proc.*, 1951, 10, 229.

[55] C. Martius and B. Hess, *Arch. Biochem. Biophys.*, 1951, 33, 486.

lower phosphate uptake than normal if animals were previously injected with thyroxine (4—12 mg. over 24—72 hours), but here there was a marked seasonal variation.

Thyroxine also affects some phosphokinases. Askonas [56] found creatine phosphokinase to be 80% inhibited *in vitro* by $10^{-4}$ M-thyroxine ; with a single large injection there was 25% inhibition when the crude muscle extract was tested some hours later. Crude muscle extracts from thyroid-injected rats show much enhanced hexokinase activity.[57]

An effect of insulin has also been recorded which seems to be on oxidative phosphorylation.[58] In liver homogenates carrying on oxidation of $\alpha$-ketoglutarate with phosphorylation under sub-optimal conditions (*e.g.*, with high adenosine triphosphatase content of the system) insulin had a significant effect in increasing phosphorylation without increasing oxidation. This effect cannot be through an inhibition of adenosine triphosphatase activity.[59] Foa *et al.*,[60] using a suspension of washed liver particles from normal and alloxan-diabetic rats, with glutamate as substrate for oxidation, found that insulin addition brings about an increase in the degree of phosphorylation of thiamine in the diabetic preparations, but not in the normal. Goranson and Erulkar,[61] with heart and brain homogenates, found the aerobic phosphorylation of creatine during succinate and malate oxidation was significantly less than normal in preparations from alloxan-diabetic rats, although the oxygen uptake was unchanged. Injection of insulin restored the phosphocreatine synthesis to normal without affecting the oxygen uptake. Insulin added *in vitro* could also increase synthesis.

A similar action of insulin in increasing ATP-provision could, of course, explain its well-known effect of increasing glucose uptake *in vitro* by diaphragm. Krahl [62] has summarised the evidence that there is rather an effect here directly upon glucokinase. He emphasises that the value for the easily hydrolysable phosphorus of ATP is the same (about 18 mg.-%) for diabetic and normal diaphragms in aerobic conditions; and Walaas and Walaas [63] found that even under strictly anaerobic conditions, when this value had fallen to 2—3 mg.-%, insulin caused a significant increase in glucose uptake. It would seem therefore that ATP provision is not a limiting factor.

The main identified effect of adrenaline injection seems to be acceleration of formation of active from inactive phosphorylase.[64] But it is well known also to have an inhibitory effect on glucose utilisation, and the work of Cohen and Needham [65] with crude muscle extracts from injected animals, suggests that some interference with ATP resynthesis is concerned here. They found no diminution in hexokinase activity.

**Utilisation of Phosphate Bond Energy.**—We will consider first some cases of synthesis where we have at least a little insight into the mechanism of the reactions.

[56] B. A. Askonas, *Nature*, 1951, **167**, 933.
[57] R. H. Smith and H. G. Williams-Ashman, *Acta Biochim. Biophys.*, 1951, **7**, 295.
[58] B. D. Polis, E. Polis, M. Kerrigan, and L. Jedeikin, *Arch. Biochem.*, 1949, **23**, 505.
[59] R. H. Broh-Kahn, P. Foldes, and I. A. Mirsky, *ibid.*, 1950, **26**, 460.
[60] P. P. Foa, H. R. Weinstein, J. A. Smith, and M. Greenberg, *ibid.*, 1952, **40**, 323.
[61] E. S. Goranson and S. D. Erulkar, *ibid.*, 1949, **24**, 40.
[62] M. Krahl, *Ann. N.Y. Acad. Sci.*, 1951, **54**, 649.
[63] E. Walaas and O. Walaas, *J. Biol. Chem.*, 1952, **195**, 367.
[64] E. W. Sutherland, *Ann. N.Y. Acad. Sci.*, 1951, **54**, 693.
[65] J. A. Cohen and D. M. Needham, *Acta Biochem. Biophys.*, 1950—1951, **6**, 141.

In the case of the formation of the ·CO·NH· bond in the synthesis of hippuric acid, from benzoate and glycine, CoA as well as ATP is needed. Cohen and McGilvery [66] showed that *N*-phosphoglycine cannot replace glycine, and Chantrenne [67] that benzoyl phosphate cannot replace benzoate. There is no detailed evidence, but it seems likely that CoA–phosphate is first formed and then benzoyl–CoA; in fact, that this synthesis involves a reversal of the sort of process suggested for ATP formation during oxidation of α-ketoglutarate. A rather similar train of events is indicated by the considerations put forward by Green [68] on the well-known sparking phenomenon preliminary to the oxidation of fatty acids by mitochondria. He and his collaborators have studied fatty acid oxidation in soluble extracts of pig heart and the steps seem to be:

$$\text{ATP} + \text{CoA} \longrightarrow \text{CoA–phosphate (or –pyrophosphate)} + \text{ADP}$$

$$\text{CoA–phosphate} + \text{fatty acid} \longrightarrow \text{(fatty) acyl–CoA}$$

$$\text{(fatty) acyl–CoA} \longrightarrow \beta\text{-ketoacyl–CoA}$$

$$\beta\text{-ketoacyl–CoA} \longrightarrow \text{acyl–CoA (with 2 carbon atoms less)} + \text{acetyl–CoA}$$

Another mechanism for synthesis of the ·CO·NH· bond has been studied independently by Speck [69] and by Elliott [70] in the formation of glutamine from glutamate and ammonia. Partially purified, soluble preparations from acetone-dried liver and brain were mainly used, and the dependence of the synthesis upon stoicheiometric dephosphorylation of ATP was shown. It has not so far been possible to isolate any phosphorylated intermediate compound, or to show that more than one enzyme is concerned. The synthesis of glutathione has been studied by Bloch [71] and his collaborators by using extracts of acetone-dried pigeon liver and glycine and glutamic acids with labelled carbon or nitrogen atoms. At least two enzymes are concerned, one in the formation of glutamylcysteine, the other in the reaction of this compound with glycine; ATP is essential in both cases. The enzyme system concerned in the latter reaction has been considerably purified, and it has been shown that stoicheiometric amounts of phosphate are set free from ATP during the synthesis.

There are now strong indications that phosphorylation plays an essential part at three stages in the ornithine cycle of urea formation. Grisolia and Cohen [72] have shown that the reaction:

$$\text{ornithine} + CO_2 + NH_3 \xrightarrow{\text{ATP}\ \ Mg^{++}} \text{citrulline}$$

proceeds in three steps:

$$\text{glutamate} + CO_2 + NH_3 \xrightarrow{\text{ATP}} \text{carbamoylglutamate} \quad . \quad . \quad (1)$$

$$\text{carbamoylglutamate} + CO_2 + NH_3 \xrightarrow{\text{ATP}} \text{intermediate} \quad . \quad . \quad (2a)$$

$$\text{intermediate} + \text{ornithine} \longrightarrow \text{citrulline} + \text{carbamoylglutamate} \quad . \quad (2b)$$

The last two enzyme systems have been partially separated, and can be studied separately, since (2*b*) only comes into play if ornithine is added. In

---

[66] P. P. Cohen and R. W. McGilvery, *J. Biol. Chem.*, 1947, **171**, 121.

[67] H. Chantrenne, *ibid.*, 1951, **189**, 227.

[68] D. E. Green, *Science*, 1952, **115**, 661.

[69] J. F. Speck, *J. Biol. Chem.*, 1949, **179**, 1405.

[70] W. H. Elliott, *Biochem. J.*, 1951, **49**, 106.

[71] K. Bloch, *J. Biol. Chem.*, 1949, **179**, 1245; R. B. Johnston and K. Bloch, *ibid.*, 1951, **188**, 221; J. E. Snoke and K. Bloch, *ibid.*, 1952, **199**, 407; K. Bloch, J. Snoke, and S. Yanari, "Symposium sur la Biogénèse des Protéines," Second Int. Congr. Biochem., Paris, 1952, p. 32.

[72] S. Grisolia and P. P. Cohen, *J. Biol. Chem.*, 1951, **191**, 189; 1952, **198**, 561.

absence of ornithine, the accumulation in (2*a*) of an activated compound can be demonstrated, which can be estimated by its power to react with ornithine. The incorporation of carbon dioxide and ammonia in (2*a*) is proportional to the carbamoylglutamate added; and with all constituents present, the inorganic phosphate set free is proportional to the citrulline formed. There is some evidence that the intermediate formed in (2*a*) is a phosphorylated compound. Under certain conditions, inorganic phosphorus is not set free in (2*a*); then (*a*) this mixture can be deproteinised, and by addition of system (2*b*) + ornithine, liberation of inorganic phosphorus as well as citrulline formation is obtained; (*b*) if the incubation mixture (2*a*) is heated, there is an increase in inorganic phosphate, and it can be shown that the increase runs parallel to a decrease in the power of the system to react with ornithine. The formation of arginine from citrulline has been shown by Ratner and her collaborators [73] to involve at least three enzymes, which have been partially purified by alcoholic fractionation of extract of acetone liver powder. The steps studied are :

$$\text{citrulline} + \text{aspartate} + \text{ATP} \longrightarrow \text{intermedate} + \text{ADP} + \text{phosphate}$$
$$\text{intermediate} + H_2O \longrightarrow \text{arginine} + \text{malate}$$

There is evidence that the first reaction involves two enzymes : upon fractionation of the system, a fraction was obtained which had little activity unless supplemented with a protein fraction from yeast (itself having no condensing activity). It seems likely that there is phosphorylation of the citrulline before the condensation, but no phosphorylated intermediate has yet been detected. Possibly the equilibrium conditions are such that significant amounts cannot accumulate, and the dephosphorylation of the ATP only goes on at a perceptible rate when dephosphorylation of the intermediate occurs on condensation. The ratio of 1·4—1·8 moles of ATP dephosphorylated per mole of citrulline used suggests that phosphorylation outstrips condensation and that some breakdown of the phosphorylated intermediate can go on by phosphatase activity.

A case of synthesis in which until recently it was believed that phosphorus bond energy was used, is trans-methylation to nicotinamide or guanidinoacetic acid with methionine as the donor.[74] This transfer took place in a soluble enzyme system but only in the presence of ATP, and methionine addition increased inorganic phosphorus formation from ATP. The formation of an intermediate labile phosphorylated compound had not been shown, but an active " methionine," free from phosphorus, accumulated on incubation of methionine with partially purified enzyme preparations. This substance could methylate nicotinamide, in absence of high-energy phosphate, when a preparation containing methylkinase (not yet purified) was added. Cantoni [74a] has now shown that active methionine is probably :

$$\text{Adenine–}\underbrace{\text{CH·CH(OH)·CH(OH)·CH}}_{\text{O}}\text{·CH}_2\text{·}\overset{+}{\text{S}}\text{Me·CH}_2\text{·CH}_2\text{·CH(NH}_2\text{)·CO}_2^-$$

---

[73] S. Ratner and A. Pappas, *J. Biol. Chem.*, 1949, **179**, 1183, 1199; S. Ratner and B. Petrack, *ibid.*, 1951, **191**, 693; S. Ratner, in " Phosphorus Metabolism," Johns Hopkins Press, Baltimore, 1951, p. 601.

[74] G. L. Cantoni, *ibid.*, p. 641; *J. Biol. Chem.*, 1951, **189**, 203, 745.

[74a] G. L. Cantoni, *J. Amer. Chem. Soc.*, 1952, **74**, 2942.

and can be considered as a product of methionine and the adenosine portion of ATP. The sulphur of the methionine acquires an additional covalent bond; and it seems likely (see also Woolley [1]) that the reduction of this sulphonium compound, when the methyl group is removed and the valency falls to 2, provides the free energy for the methylation of the acceptor.

From the work of Vogt [75] on the isolated perfused adrenal gland, it seems that secretion of the adrenal cortical hormones must depend on a continuous synthetic process, since stores of active hormone in the gland are very small. Her finding that the amounts secreted can be temporarily increased by addition of ATP or phosphocreatine to the perfusing fluid shows that these compounds can supply readily available energy.

We may turn now to more complicated physiological processes where there is evidence of participation of phosphate in the energy-providing metabolism. Little will be said of muscle contraction, since three reviews [76] have appeared on this subject during 1952. It may be mentioned that further interesting studies of the adenosine triphosphatase activity of myosin and actomyosin have been made.[77, 78] The increase in adenosine triphosphatase activity obtained by pre-treatment of the myosin with calcium ions, mentioned by Mommaerts,[79] may prove important, though the increase in activity found in these preliminary experiments does not seem great enough to suggest that here is the entire explanation of the discrepancy between rate of adenosine triphosphatase activity *in vitro* and the rate to be presumed *in vivo* if all the energy of contraction is supplied through ATP breakdown. Other cases where movement seems to depend on ATP provision have been described. Thus Mann [80] found with spermatozoa that decrease in ATP content, whether the conditions are aerobic or anaerobic, coincides with loss of motility; and Goldacre and Lorch [81] found that injection of 1% of the sodium salt into amœbæ led to a several-fold increase in speed of streaming.

McElroy [82] has reviewed our knowledge of the mechanism of bioluminescence in the firefly. In the presence of the purified enzyme, luciferase, there are needed for the emission of light the oxidisable substrate luciferin, oxygen, magnesium, cobalt, or manganese ions, and ATP. The emission of light quickly fails and it is clear that ATP has become the limiting factor, since only by addition of this constituent can renewed output be obtained. Nevertheless the greater part of the ATP originally added can be shown still to be present, for example, by reaction with glucose in presence of hexokinase. It seems that it undergoes some complexing reaction with the luciferase–

---

[75] M. Vogt, *J. Physiol.*, 1951, **113**, 129.

[76] H. H. Weber and H. Portzehl, *Adv. Protein Chem.*, 1952, **7**, 162; M. Dubuisson, *Ann. Rev. Biochem.*, 1952, **21**, 387; D. M. Needham, *Adv. Enzymology*, 1952, **13**, 151. See also A. Szent-Gyorgyi, "Chemistry of Muscular Contraction," Acad. Press, Inc., 2nd edn., New York, 1951; and W. F. H. M. Mommaerts, in "Phosphorus Metabolism," Johns Hopkins Press, Baltimore, 1951, p. 551.

[77] W Hasselbach, *Z. Naturforsch.*, 1952, **7**, *B*, 163, 338.

[78] L. Ouellet, K. J. Laidler, and M. F. Morales, *Arch. Biochem. Biophys.*, 1952, **39**, 37.

[79] W. H. F. M. Mommaerts, in "Phosphorus Metabolism," Johns Hopkins Press, Baltimore, 1951, p. 518.

[80] T. Mann, *Biochem. J.*, 1945, **39**, 451.

[81] R. J. Goldacre and I. J. Lorch, *Nature*, 1950, **166**, 497.

[82] W. D. McElroy, in "Phosphorus Metabolism," Johns Hopkins Press, Baltimore, 1951, p. 585.

luciferin–oxygen system, after which it becomes unavailable for the light-producing process. The light-emitting system may be an intermediate in this complexing reaction. It is interesting that pyrophosphate and triphosphate, quite inactive if replacing ATP in the original system, cause light-emission if added after the ATP has become inaccessible. This is interpretated as due to displacement of the ATP from the complex. Recently, Strehler and Totter [83] have succeeded in maintaining luminescence with little decay for several minutes, by using arsenate or phosphate buffers at concentrations of 0·02M or more. These substances thus seem to prevent the disappearance of ATP by complexing, although their addition will not stimulate light emission once it has fallen off.

Dixon [13] has outlined a general mechanism whereby chemical energy could be utilised in the passage of substances into cells against an osmotic gradient. This depends upon the substance in question undergoing a chemical reaction on the inner side of the cell membrane; and further (in order that the absorption may proceed practically to completion) upon the reaction being one with the equilibrium far to one side, *i.e.*, proceeding with liberation of free energy. With regard to absorption of sugars from the intestine, Hele [84] has recently shown a close correlation between the relative rates of absorption *in vivo* of different hexoses and the rates of phosphorylation *in vitro* by hexokinase preparations from the intestinal mucosa. Dratz and Handler,[85] however, using injection of $^{32}$P-labelled phosphate, could not find in renal tubules any indication that either glucose-1 phosphate or -6 phosphate mediated the absorption of sugar. From *in vitro* studies on erythrocytes with $^{32}$P-labelled phosphate, Gourley [86] has brought forward evidence consistent with the view that inorganic phosphate is incorporated into ATP at the cell membrane before entering the cell. It is possible that some also enters by diffusion. Sacks [87] came to rather similar conclusions on examining the acid-soluble phosphate fractions of liver after injection of $^{32}$P-labelled phosphate; but here the impossibility of assessing the true intracellular inorganic phosphate causes difficulties of interpretation. Presumably in these cases the irreversible reaction would be the subsequent dephosphorylation of the ATP. Gourley has shown with red blood cells that glucose is necessary for phosphate uptake, and he, as well as Kamen and Spiegelman [88] with fermenting yeast and Hotchkiss [89] with respiring staphylococci, found that poisons preventing phosphate esterification also prevented phosphorus absorption. There is evidence, depending on the use of uncoupling agents, that interference with oxidative phosphorylation prevents absorption of such substances as phenol-red, aminohippuric acid, etc., in kidney tubules; [90] and also prevents the active transport of water, which, it is suggested, is responsible for the maintenance of normal volume and intracellular hypertonicity of kidney slices.[91] In such cases the mechanism of utilisation of

---

[83] B. L. Strehler and J. R. Totter, *Arch. Biochem. Biophys.*, 1952, **40**, 28.
[84] M. P. Hele, *Nature*, 1950, **166**, 786, 1018.
[85] A. F. Dratz and P. Handler, *J. Biol. Chem.*, 1952, **197**, 419.
[86] D. R. H. Gourley, *Arch. Biochem. Biophys.*, 1952, **40**, 1, 13.
[87] J. Sacks, *Arch. Biochem.*, 1951, **30**, 423.
[88] M. D. Kamen and S. Spiegelman, *Symp. Quant. Biol.*, 1948, **13**, 151.
[89] R. D. Hotchkiss, *Fed. Proc.*, 1947, **6**, 263.
[90] R. P. Forster and J. V. Taggart, *J. Cell. Comp. Physiol.*, 1950, **36**, 251.
[91] J. R. Robinson, *Nature*, 1950, **166**, 989.

phosphorus bond energy remains obscure. Davies and Krebs [92] have outlined a tentative hypothesis directed towards explaining this utilisation in the secretion of hydrochloric acid by the oxyntic cells of the stomach; and in maintaining the concentration of potassium ions against a gradient in nervous tissue.

**Phosphate Transfer catalysed by Alkaline and Acid Phosphatases.**—Meyerhof and Green [93] have extended the work on phosphate transfer by means of phosphatase activity. Using alkaline intestinal phosphatase, in conditions of high inorganic phosphate concentration where synthetic action of the enzyme could go on, they showed that this synthetic action was greatly increased if phosphate donors were also added. Morton [94] has recently purified alkaline phosphatase from intestine and from milk, obtaining them essentially homogeneous electrophoretically. It has thus been possible to show definitely for the first time that the phosphate transfer is carried out by the hydrolytic enzyme. In Morton's experiments the initial rates of phosphatase and of phosphate-transferring activity were measured; he found the percentage transfer to be constant for a given donor, under varying conditions, *e.g.*, of pH and donor concentration; it increased up to a maximum with increasing acceptor concentration. The percentage transfer was unrelated to the energy content of the phosphate bond of the donor. This view is also expressed by Green and Meyerhof,[95] though their earlier results had led them to think that energy relations played an important rôle. The physiological significance of this method of phosphate transfer is still uncertain especially as the concentration of acceptor needed, at any rate to show measurable effects *in vitro*, is very high, *viz.*, 1—2 M. Ross *et al.*[96] have shown that the optimum pH falls with falling substrate concentration, and this has been confirmed by Morton. It seems possible that conditions might arise in the cell under which phosphorylation by this mechanism might spare energy, for example phosphorylation of glucose by hexose diphosphate. Danielli [97] has suggested that the alkaline phosphatases may have their main function in providing energy by phosphate transfer for changes in shape of contractile protein systems and that *in vivo* their phosphatase activity may be negligible: he instances the cytological distribution of the enzyme in support of this view. Morton's results suggest, however, a fundamental difference between the phosphatases and the phosphokinases, in that with the former water is activated and acts as an acceptor competing with the organic acceptors.

**Pentose Metabolism and the Alternative Path of Glucose Oxidation.**—Work on the CoII specific oxidation of glucose-6 phosphate has continued actively, with animal tissues [98] and bacteria and yeast.[99,100] Using purified phosphogluconate dehydrogenase, Horecker and Smyrniotis [100] have shown

---

[92] R. E. Davies and H. A. Krebs, *Biochem. Soc. Symp.*, 1952, **8**, 77.

[93] O. Meyerhof and H. Green, *ibid.*, 1950, **183**, 377.

[94] R. A. Morton, *Nature*, 1950, **166**, 1092; Abstracts, Second Int. Congr. Biochem., Paris, 1952, p. 262.

[95] H. Green and O. Meyerhof, *J. Biol. Chem.*, 1952, **197**, 347.

[96] M. H. Ross, J. O. Ely, and J. G. Archer, *ibid.*, 1951, **192**, 561.

[97] J. F. Danielli, *Nature*, 1951, **166**, 464.

[98] F. Dickens and G. E. Glock, *Biochem. J.*, 1951, **50**, 81; G. E. Glock, *ibid.*, 1952, **52**, 575; J. E. Seegmiller and B. L. Horecker, *J. Biol. Chem.*, 1952, **194**, 261.

[99] D. M. B. Scott and S. S. Cohen, *ibid.*, 1951, **188**, 509; *J. Comp. Cell. Physiol.*, 1951, **38**, Suppl. 1, 173.

[100] B. L. Horecker and P. Z. Smyrniotis, *J. Biol. Chem.*, 1951, **193**, 371; B. L. Horecker, P. Z. Smyrniotis, and J. E. Seegmiller, *ibid.*, p. 383.

that ribulose phosphate is an intermediate in the formation of ribose phosphate. Scott and Cohen[99] describe the formation of an unknown ester, suspected to be an enediol pentose phosphate, during pentose formation by this pathway in yeast. Glock,[98] using liver preparations, has carried further the examination of the fate of the ribose-5 phosphate. Anaerobically, 75% of the ribose carbon appears as glucose-6 phosphate; it seems likely that there is a split to triose phosphate and glycollaldehyde (by an aldolase distinct from muscle aldolase) followed by condensation to hexose monophosphate; more carbon than that contained in the triose phosphate appears in the hexose. No free glycollaldehyde was formed. Aerobically the course of events seems to be similar, followed by oxidation of the glucose-6 phosphate.

These findings have interesting similarities with those of Dische[101] on the fate of ribose-5 phosphate in human red blood cells. Here 75% of the ribose disappearing was found as hexose-6 phosphate and fructose diphosphate. Hough and Jones[102] have discussed the metabolism of pentoses. They obtained xylulose phosphate from glycollaldehyde and triose phosphate in presence of pea-seed aldolase. Horecker and Smyrniotis[103] describe the synthesis of sedoheptulose from pentose phosphate with crystalline muscle aldolase, together with pentose-splitting enzyme from rat liver.

Oxidation of glucose-6 phosphate by this path proceeds in the absence of inorganic phosphate, and there is no evidence so far that the free energy of the oxidations (of glucose-6 phosphate to phosphogluconate, and of the latter to ribulose phosphate possibly through 2-keto-6-phosphogluconate) is conserved or utilised. Its biological significance seems most likely to be in the provision of essential ribose phosphate. This question has been considered by Cohen.[104]

D. M. N.

## 5. THE THYROID HORMONE.

Since the last report by F. G. Young in 1944, others have dealt adequately with the general physiology of the gland,[1,2] the biosynthesis of the hormone,[1,3] the metabolism of iodine,[3,4] antithyroid substances,[5] the mode of action of thyroid hormone,[6] and the experimental[4,7] and clinical[8] use of

---

[101] Z. Dische, in "Phosphorus Metabolism," Johns Hopkins Press, Baltimore, 1951, p. 171.

[102] L. Hough and J. K. N. Jones, *Nature*, 1951, **167**, 180; *J.*, 1952, 4047.

[103] B. L. Horecker and P. Z. Smyrniotis, *J. Amer. Chem. Soc.*, 1952, **74**, 2123.

[104] S. S. Cohen, *J. Biol. Chem.*, 1951, **189**, 617; in "Phosphorus Metabolism," Johns Hopkins Press, Baltimore, 1951, p. 148.

[1] A. Albert, *Ann. Rev. Physiol.*, 1952, **14**, 481.

[2] J. Kühnau, W. Grab, C. Martius, and B. Hess, *Arch. exp. Path. Pharmak.*, 1952, **216**, 1; Sir C. R. Harington, *Endocrinol.*, 1951, **49**, 401; J. Roche and R. Michel, *Adv. Protein Chem.*, 1951, **6**, 253; W. T. Salter, "The Hormones: Physiology, Chemistry and Applications," Eds. G. Pincus and K. V. Thimann, Academic Press, Inc., New York, 1950, p. 181; C. Niemann, *Fortschr. Chem. org. Naturstoffe*, 1950, **7**, 167; "Transactions of the American Goiter Association," C. C. Thomas, Springfield, Ill., U.S.A.

[3] R. Michel, "Symposium sur les Hormones Protéiques," Second Int. Congr. Biochem., Paris, 1952, p. 75.

[4] C. P. Leblond, *J. Amer. Pharm. Assoc.*, 1951, **40**, 595.

[5] R. Pitt-Rivers, *Physiol. Rev.*, 1950, **30**, 194; A. Lawson and C. Rimington, *Ann. Reports*, 1947, **44**, 247.

[6] S. B. Barker, *Physiol. Rev.*, 1951, **31**, 205.

[7] J. Gross and R. Pitt-Rivers, *Brit. Med. Bull.*, 1952, **8**, 136.

[8] N. B. Myant, *ibid.*, p. 141; E. J. Wayne, A. G. MacGregor, and G. W. Blomfield, *ibid.*, p. 148; R. Paterson, H. C. Warrington, and C. W. Gilbert, *ibid.*, p. 154; E. E. Pochin, *Lancet*, 1950, II, 41, 84.

$^{131}$I. This Report will therefore be restricted to recent work concerning the nature of the thyroid hormone, a new synthesis of thyroxine, and the study of thyroxine antagonists.

**Nature of the Hormone.**—It is in this field that the most striking developments have occurred. Despite the impressive evidence that the circulating hormone consists essentially of free thyroxine in loose association with protein,[9] difficulties have been experienced by various workers in expressing the metabolic activity of thyroid preparations in terms of thyroxine content.[10] The probable explanation of these discrepancies is provided by recent discoveries made possible by the development of paper and column chromatography and paper electrophoresis in conjunction with autoradiography, $^{131}$I being used as a labelling agent.

It has been established that, although thyroxine and di-iodotyrosine make up the major part of the organic iodine in the thyroid gland, monoiodotyrosine is also present.[11–15] Several workers have also reported the presence of small amounts of a number of other unidentified iodine compounds.[12, 14] In the plasma the main iodine-containing constituents demonstrated were thyroxine and iodide with small amounts of unidentified material, but earlier reports [16] of the presence of di-iodotyrosine have not been substantiated.[4, 15] Roche, Michel, Michel, and Lissitzky [13] introduced a fresh approach by showing that mono- and di-iodotyrosine were deiodinated by a specific enzyme [3] whose presence they demonstrated in thyroid slices and, in smaller amount, in slices of liver, kidney, and intestine. Thyroxine was found to be resistant to this deiodination, an observation which appears to explain its preponderance in the blood.[9] The association of circulating thyroxine with a human-serum constituent having an electrophoretic mobility at pH 8·5 similar to that of $\alpha_1$-globulin was demonstrated by Gordon, Gross, O'Connor, and Pitt-Rivers.[17]

Subsequently Gross and Pitt-Rivers [18] announced the identification as 3 : 5 : 3′-tri-iodo-L-thyronine of their " unknown I " component,[19] previously isolated from the plasma of patients under treatment with therapeutic doses of $^{131}$I. This implies that the substance in thyroid-gland extracts known as " compound I" [14] must also have been tri-iodothyronine.[7] Almost simultaneously, Roche, Lissitzky, and Michel [20] described the preparation of

---

[9] C. R. Harington, *Proc. Roy. Soc.*, 1944, *B*, **152**, 223; A. Taurog and I. L. Chaikoff, *J. Biol. Chem.*, 1948, **176**, 639; J. C. Laidlaw, *Nature*, 1949, **164**, 927; C. P. Leblond and J. Gross, *J. Clin. Endocrinol.*, 1949, **9**, 171; A. Taurog, I. L. Chaikoff, and W. Tong, *J. Biol. Chem.*, 1950, **184**, 99; L. N. Rosenberg, *J. Clin. Invest.*, 1951, **30**, 1; A. Lachaze and O. Thibault, *Bull. Soc. Chim. biol.*, 1951, **33**, 1458.

[10] C. R. Harington, " The Thyroid Gland," Oxford Univ. Press, London, 1933; J. H. Means, J. Lerman, and W. T. Salter, *J. Clin. Invest.*, 1933, **12**, 683; A. E. Meyer and A. Wertz, *Endocrinol.*, 1939, **24**, 683; E. Frieden and R. J. Winzler, *ibid.*, 1948, **43**, 40.

[11] K. Fink and R. M. Fink, *Science*, 1948, **108**, 358; A. Taurog, W. Tong, and I. L. Chaikoff, *J. Biol. Chem.*, 1950, **184**, 83; J. Roche, G. H. Deltour, S. Lissitzky, and R. Michel, *Compt. rend. Soc. Biol.*, 1950, **144**, 1321; J. Gross, C. P. Leblond, A. E. Franklin, and J. H. Quastel, *Science*, 1950, **111**, 605.

[12] G. H. Tishkoff, R. Bennett, V. Bennett, and L. L. Miller, *ibid.*, 1949, **110**, 452.

[13] J. Roche, R. Michel, O. Michel, and S. Lissitzky, *Compt. rend. Soc. Biol.*, 1951, **145**, 288.

[14] J. Gross and C. P. Leblond, *Proc. Soc. Exp. Biol. N.Y.*, 1951, **76**, 686.

[15] *Idem, Endocrinol.*, 1951, **48**, 714.

[16] V. Treverrow, *J. Biol. Chem.*, 1939, **127**, 737.

[17] A. H. Gordon, J. Gross, D. O'Connor, and R. Pitt-Rivers, *Nature*, 1952, **169**, 19.

[18] J. Gross and R. Pitt-Rivers, *Lancet*, 1952, I, 439.

[19] *Idem, ibid.*, 1951, II, 766.

[20] J. Roche, S. Lissitzky, and R. Michel, *Compt. rend.*, 1952, **234**, 997.

tri-iodothyronine by the iodination of the di-iodo-derivative, followed by chromatographic separation from thyroxine. Later tri-iodothyronine was shown by Gross and Pitt-Rivers to be several times more active than thyroxine, both by the goitre-prevention method in rats [21] and by the dose required to relieve myxœdematous manifestations in two hypothyroid patients.[22] It was suggested that tri-iodothyronine is the active form of the thyroid hormone and that thyroxine requires conversion into the tri-iodo-compound before becoming physiologically active.[21] Some confirmation of the physiological role of tri-iodothyronine has also been obtained from the study of anti-thyroxine compounds,[23] which apparently act by inhibiting deiodination processes (see below). The fact that thyroxine is antagonised by these compounds, while tri-iodothyronine is not, fits in well with this new hypothesis.

Gross and Pitt-Rivers appear to have made a noteworthy advance by drawing attention to the importance of tri-iodothyronine. At present the site and mode of its production are uncertain. It might arise by the combination of mono- and di-iodotyrosine in the thyroid [3] by a process analogous to that suggested by Harington and Barger [24] for the production of thyroxine. Alternatively, it could be produced by the deiodination of thyroxine, a process well known to occur from older work [25] and from the newer and more specific methods employing $^{131}$I-labelled material.[14, 15, 26, 27] The conversion of thyroxine into tri-iodothyronine has not been unequivocally demonstrated, although Gross and Leblond's experiments [14, 15] have been subsequently interpreted by Gross and Pitt-Rivers [21] as a probable indication of this process. In this study [14] tri-iodothyronine was found in the plasma and excreta of both intact and thyroidectomised rats treated with radioactive thyroxine. If tri-iodothyronine is indeed the active form of the hormone then extrathyroidal sites of production must be at least as important in deiodination as the thyroid, since thyroidectomised animals respond to thyroxine and to anti-thyroxine compounds. It is therefore still possible that thyroxine is the main secretion of the thyroid, and is converted into tri-iodothyronine in other tissues. This hypothesis is consistent with most of the facts now known, but awaits more detailed investigation.

**Anti-thyroxine Compounds.**—Following Woolley's pioneer work [28] on the inhibitory effects of certain ethers of *N*-acetyldi-iodotyrosine on tadpole metamorphosis, attempts have been made to produce compounds effective in antagonising the peripheral actions of thyroxine. Harington [29] discussed the question and showed that the thio-ether analogue of thyroxine had

---

[21] J. Gross and R. Pitt-Rivers, *Lancet*, 1952, I, 593.

[22] *Idem, ibid.*, 1952, I, 1044.

[23] N. F. Maclagan, W. E. Sprott, and J. H. Wilkinson, *ibid.*, 1952, II, 915.

[24] C. R. Harington and G. Barger, *Biochem. J.*, 1927, **21**, 169.

[25] A. W. Elmer, "Iodine Metabolism and Thyroid Function," Oxford Univ. Press, London, 1938.

[26] F. Joliot, R. Courrier, A. Horeau, and P. Süe, *Compt. rend.* 1944, **218**, 769; *Compt. rend. Soc. Biol.*, 1944, **138**, 325; A. Horeau and P. Süe, *Bull. Soc. Chim. biol.*, 1945, **27**, 483. F. Joliot, *Proc. Roy. Soc.*, 1945, *A*, **184**, 1; N. B. Myant and E. E. Pochin, *Clin. Sci.*, 1950, **9**, 421; J. Gross and S. Schwartz, *Cancer Res.*, 1951, **11**, 614.

[27] J. C. Clayton, A. A. Free, J. E. Page, G. F. Somers, and E. A. Woollett, *Biochem. J.*, 1950, **46**, 598.

[28] D. W. Woolley, *J. Biol. Chem.*, 1946, **164**, 11.

[29] Sir C. R. Harington, *Biochem. J.*, 1948, **43**, 434.

thyroxine-like properties and was not inhibitory. Tetrabromothyronine was administered to patients with thyrotoxicosis, but the results were indefinite.[30] The range of compounds active in the tadpole test was considerably extended by Frieden and Winzler.[31,32] One of their most effective compounds, 4-benzyloxy-3 : 5-di-iodobenzoic acid,[32] was shown by Maclagan, Sheahan, and Wilkinson [33] to be active in depressing the metabolism of intact thyroxine-treated mice, by using a simplified method of measuring oxygen consumption.[34] Later, a number of alkyl [35] and hydroxyalkyl [36] esters of 4-hydroxy-3 : 5-di-iodobenzoic acid, several ethers of this acid and their esters,[37] and some derivatives of 4-hydroxy-3 : 5-di-iodobenzaldehyde [38] were shown to be active. The most active inhibitors observed during this study were *n*-butyl (BHDB),[35] 2-hydroxyethyl and 2- and 3-hydroxypropyl [36] 4-hydroxy-3 : 5-di-iodobenzoates. Evidence, based upon a study of the physicochemical properties of a series of these esters, has been presented in support of the view that the inhibiting reaction is the same for all these compounds and that differences in potency are caused by variations in distribution and cell penetration.[39]

Barker and his co-workers found that BHDB was active in thyroidectomised rats maintained on thyroxine.[40] The same group reported that certain iodophenoxyacetic acids [41] exhibited anti-thyroxine effects: the 2 : 4-di-iodo-derivative was the most effective, but the 2-, 3-, and 4-iodo-compounds were also active. A somewhat different approach was that of Cortell,[42] who found that 2′ : 6′-di-iodothyronine [43] exerted some anti-thyroxine effect when tested by the goitre-prevention method. This compound, however, proved almost inactive by the mouse oxygen-consumption method.[44]

The nature of the biological effects produced by this class of compound has not been completely elucidated, but in addition to those mentioned above, BHDB has been shown to inhibit the uptake of $^{131}$I by the thyroid gland in rats [45] and mice,[46] an effect which appears unlikely to be due to liberation of iodide. Some workers have found it to increase the growth rate of thyroxine-treated rats [47] but others reported either no effect [45] or a reduction of growth rate.[48] The raised metabolism following administration

---

[30] J. Lerman and Sir C. R. Harington, *J. Clin. Endocrinol.*, 1949, **9**, 1099.

[31] E. Frieden and R. J. Winzler, *J. Biol. Chem.*, 1948, **176**, 155.

[32] *Idem, ibid.*, 1949, **179**, 423.

[33] N. F. Maclagan, M. M. Sheahan, and J. H. Wilkinson, *Nature*, 1949, **164**, 699.

[34] N. F. Maclagan and M. M. Sheahan, *J. Endocrinol.*, 1950, **6**, 456.

[35] M. M. Sheahan, J. H. Wilkinson, and N. F. Maclagan, *Biochem. J.*, 1951, **48**, 188.

[36] J. H. Wilkinson, W. E. Sprott, and N. F. Maclagan, *ibid.*, 1953, in the press.

[37] J. H. Wilkinson, M. M. Sheahan, and N. F. Maclagan, *ibid.*, 1951, **49**, 710.

[38] *Idem, ibid.*, p. 714.

[39] J. H. Wilkinson and N. F. Maclagan, Abstracts, Second Int. Congr. Biochem., Paris, 1952, p. 69; J. H. Wilkinson, *Biochem. J.*, 1953, in the press.

[40] S. B. Barker, H. B. Dirks, Jr., W. R. Garlick, and H. M. Klitgaard, *Proc. Soc. Exp. Biol., N.Y.* 1951, **78**, 840.

[41] S. B. Barker, C. E. Kiely, Jr., H. B. Dirks, Jr., H. M. Klitgaard, S. C. Wang, and S. Wawzonek, *J. Pharmacol.*, 1950, **99**, 202; *Endocrinol.*, 1951, **48**, 70.

[42] R. E. Cortell, *J. Clin. Endocrinol.*, 1949, **9**, 955.

[43] C. Niemann and G. E. McCasland, *J. Amer. Chem. Soc.*, 1944, **66**, 1870; J. H. Barnes, R. C. Cookson, G. T. Dickson, J. Elks, and V. D. Poole, *J.*, 1953, in the press.

[44] N. F. Maclagan and M. M. Sheahan, unpublished.

[45] M. Lawson and C. E. Searle, *J. Endocrinol.*, 1952, **8**, 32.

[46] M. K. Brayne and N. F. Maclagan, *ibid.*, in the press.

[47] H. M. Sharp and W. F. J. Cuthbertson, *ibid.*, 1951, **7**, xxxviii.

[48] N. F. Maclagan and W. E. Sprott, unpublished.

of dinitro-*o*-cresol was inhibited.[49] It did not antagonise the anti-goitrogenic effects of thyroxine and was not itself goitrogenic,[49] thus differing profoundly from antithyroid drugs of the thiouracil type. A clinical trial in thyrotoxicosis has so far proved disappointing. Fraser and Maclagan [50] used BHDB in doses up to 3 g. *per diem* in ten cases and, although some improvement in symptoms was noted, the effects were indecisive. They may have been due to liberation of inorganic iodide, which is difficult to demonstrate in the urine in these circumstances.[51] It appeared that this compound was too toxic to be used in doses large enough to produce genuine anti-thyroxine effects.

Of the several hundred compounds tested, those which exhibited anti-thyroxine activity, with few exceptions, contained 2 : 6-di-iodophenoxy- or 4 : 6-di-iodophenoxy-groups in their molecules.[6,35] It has been postulated that these groups enable the inhibitor to displace thyroxine from an enzyme surface,[35] but the fact that certain monoiodo-compounds are also active [23, 40] suggests that even simpler structures may be capable of similar interference. This view has been extended by the observation that BHDB actually enhanced the metabolic effects of tri-iodothyronine,[23] the exact opposite of the results obtained with thyroxine. A similar increase was obtained with *n*-butyl 4-hydroxy-3-iodobenzoate. These results, in conjunction with the work on tri-iodothyronine reviewed above, strongly suggest that these inhibitory compounds act by interfering with deiodination, leading to antagonism in the case of thyroxine and to diminished destruction in the case of tri-iodothyronine. If this explanation is correct, the term "anti-thyroxine compound" is still appropriate, since interference occurs with the preliminary deiodination of thyroxine which is probably essential for its physiological action.

**New Synthesis of Thyroxine.**—An important new route to thyroxine, the first alternative to that of Harington and Barger,[24] has been described by Hems *et al.*[52–58] The original synthesis depended upon the reaction of 3 : 4 : 5-tri-iodonitrobenzene with *p*-methoxyphenol to give the diphenyl ether (I), from the aromatic nitro-group of which the L-alanine side-chain had to be built up by a somewhat laborious process. This difficulty has been overcome by the new process, which is based on two new methods of preparing 2 : 6-dinitrodiphenyl ethers.[53]

The first of these involves the conversion, by means of phosphoryl chloride and a tertiary base,[59] *e.g.*, diethylaniline or pyridine, of a suitably substituted 2 : 6-dinitrophenol into the corresponding chloronitrobenzene. The pyridinium quaternary salt (II) of this reacts with a variety of substituted phenols in pyridine to give high yields of the corresponding diphenyl ethers. The latter may also be obtained easily from the benzene- or toluene-*p*-

---

[49] N. F. Maclagan, W. E. Sprott, and J. H. Wilkinson, Abstracts, Second Int. Congr. Biochem., Paris, 1952, p. 58.

[50] T. Russell Fraser and N. F. Maclagan, *J. Endocrin.*, in the press.

[51] N. F. Maclagan and J. H. Wilkinson, *Nature*, 1951, **168**, 251.

[52] E. T. Borrows, J. C. Clayton, and B. A. Hems, *J.*, 1949, S185.

[53] E. T. Borrows, J. C. Clayton, B. A. Hems, and A. G. Long, *J.*, 1949, S190.

[54] E. T. Borrows, J. C. Clayton, and B. A. Hems, *J.*, 1949, S199.

[55] E. T. Borrows, B. A. Hems, and J. E. Page, *J.*, 1949, S204.

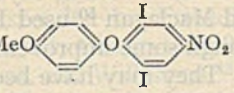
[56] J. R. Chalmers, G. T. Dickson, J. Elks, and B. A. Hems, *J.*, 1949, 3424.

[57] J. C. Clayton and B. A. Hems, *J.*, 1950, 840.

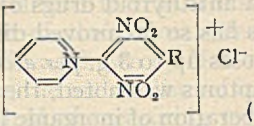
[58] J. H. Barnes, E. T. Borrows, J. Elks, B. A. Hems, and A. G. Long, *J.*, 1950, 2824.

[59] J. Baddiley and A. Topham, *J.*, 1944, 678.

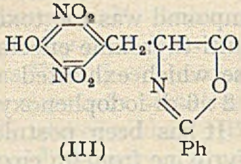
sulphonate [53] of the 2 : 6-dinitrophenol by treating the pyridinium quaternary salt [60] with a phenol.



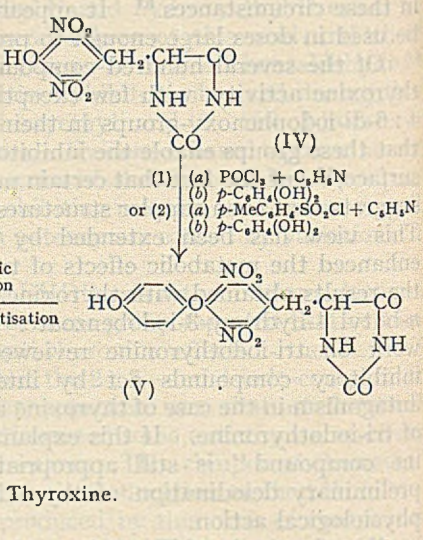
(I)



(II)



(III)



In the thyroxine synthesis the $C_{(4)}$-substituent of the 2 : 6-dinitrophenol may be one of several groups capable of easy transformation into the alanine side-chain, *e.g.*, formyl, the oxazolone derived from alanine (in III), or the corresponding hydantoin (IV). Catalytic hydrogenation of the dinitrodiphenyl ether (V), followed by tetrazotisation with nitrosylsulphuric acid under anhydrous conditions [52, 54] and reaction with iodide, gave the di-iodo-compound (VI). Alkaline hydrolysis converted this into 3 : 5-di-iodothyronine (VII) which, on treatment with iodine in ammoniacal solution,[24] gave DL-thyroxine. The explosion hazard which results from the presence of nitrogen iodide during the final stage has been obviated by the replacement of the ammonia by an organic base,[57] *e.g.*, aqueous ethylamine.

Chalmers *et al.*,[56] in applying this route to the synthesis of L-thyroxine from L-tyrosine, found that appreciable racemisation occurred when the alanine side-chain was protected by conversion into the hydantoin ring. The desired product, however, was obtained in an overall yield of 26%, without loss of optical activity, when the amino- and carboxy-groups were protected by acetylation and esterification, respectively.

A similar process was used by Elks and Waller [61] for the synthesis of D-thyroxine from 3 : 5-dinitro-D-tyrosine. The D-isomer had previously been prepared in small amounts by Harington,[62] who iodinated the 3 : 5-di-iodo-

---

[60] W. Borsche and E. Feske, *Ber.*, 1927, 60, 157.
[61] J. Elks and G. J. Waller, *J.*, 1952, 2366.
[62] C. R. Harington, *Biochem. J.*, 1928, 22, 1429.

D-thyronine obtained by resolution of the synthetic racemic compound, and by Pitt-Rivers and Lerman,[63] by the inversion of L-tyrosine, followed by iodination and mild oxidation of the resulting 3 : 5-di-iodo-D-tyrosine with hydrogen peroxide. The 3 : 5-dinitro-D-tyrosine used in the new process [61] was obtained by the reaction of the L-isomer with nitrosyl bromide to give L-α-bromo-β-(4-hydroxy-3 : 5-dinitrophenyl)propionic acid which underwent inversion on subsequent treatment with ammonia.

N. F. M.
J. H. W.

E. BOYLAND.
S. P. DATTA.
J. LASCELLES.
N. F. MACLAGAN.
D. M. NEEDHAM.
J. H. WILKINSON.

---

[63] R. Pitt-Rivers and J. Lerman, *J. Endocrinol.*, 1948, 5, 223.

# ANALYTICAL CHEMISTRY.

## I. INTRODUCTION.

ANALYSIS is " the separation, the identification or the determination of the concentration of part or all of the constituents or components of a sample." This dispassionate statement, one of the definitions recently recommended by the Committee on Nomenclature, Division of Analytical Chemistry of the American Chemical Society,[1] is one to which no one could take serious exception. It is bald, but in a definition there is no room for imagination. An article of faith, as distinct from a definition, has also, however, recently been forthcoming.[2] " Analysis, qualitative and quantitative, is the basis of the technique of chemical operations. No synthesis can be accounted complete until the synthesised product has been analysed, its component parts established and determined. In fact, chemistry is founded, is based, on analysis. The theories of the thinkers are proved or disproved by analysis ; the guesses of the inspired can only become certainties through the manipulation of the analyst." Up to this point the definitive essence parallels precisely enough with the previous quotation, and the addenda are the logical consequences of serious thinking about the place and scope of this branch of chemistry.

It would not, however, be right to end the quotation at this point, since the sequel contains more than the germ of a truth. It continues : " But analysis is not a separate discipline, although from the importance it has attained . . . it might be assumed it were an end in itself. Although analysis is but an aspect of chemical technique, the analyst himself has almost become such a specialist that he may be divorced from the genuine trend of chemical development and become immersed in the study of the break-down of compounds or of the determination of ' pointers ' to the composition of natural or of manufactured compounds. And so it is that one of the dangers . . . is that workers lose their love of chemistry, and, instead, take to themselves analysis."

This divorce from the genuine trend of chemical development, a very real danger in any branch of chemistry, is perhaps particularly so in analytical chemistry, and is always to be seen in any close survey of the literature. Specific aspects of it will appear later in this Report. On the general issue, however, it behoves anyone presenting advances in analytical chemistry to consider how best his work can serve the general body of chemistry. The subject may range over the vast field from the most specialised of applied analyses to fundamental problems whose spheres of influence are obviously large though their boundaries may not be clearly discernible. The *ad hoc* work of the industrial analyst may be of no interest to the vast mass of analytical chemists, much less to the body of chemists in general. On the other hand it might well have within it an idea which, more widely known

---

[1] L. T. Hallett *et al.*, *Analyt. Chem.*, 1952, **24**, 1348.
[2] L. H. Lampitt, *Analyst*, 1952, **77**, 564.

and applied, could revolutionise some branch of chemistry. One must, then, take note of those apparently minor papers which " analytical intuition " or one's own interest suggests might be of interest to one's chemical colleagues. One must do this, moreover, always unpleasantly aware of the unreliability of intuition's aid. Who would have been inspired by a paper describing physicochemical studies on chlorophyll in 1906 [3] or one on the manipulation of small precipitates in 1909 [4] to forecast that these were seeds which would produce, in 1923 and in 1952, Nobel prizes awarded for distinction in the field of analytical chemistry?

At the same time the Reporter must select from the extensive series of papers dealing specifically with analytical chemistry—certainly more than 4000 per annum—those which will present a starting point for any analyst wishing to follow up any particular section. His selection must in addition represent fairly the distribution of work throughout the past year. In this way chemists whose main interests are other than analytical may be able to note activities and to judge trends.

His selection, however, must always be personal, and it can never be highly critical. It is possible to refute or to support a theory. But analytical chemistry is *in excelsis* that branch of the science where the proof lies at the bench. A method may sound promising, or novel, but until one has tried it one can rarely say more than this about it.

With all this the Reporter's work is not finished. There is still that " trend of *chemical* development " and the action and reaction between it and the field of analytical chemistry. Just as the chemist benefits from the work of the analyst in all fields, the analyst must benefit from the work of the chemist in all fields. The necessity for fundamental research in analytical chemistry was stressed in this Report last year. The fundamental work may, however, be of two kinds—that done by analytical chemists within their own field, usually easy to recognise; and that done by other workers, who have no knowledge that they are increasing (and perhaps, indeed, no desire to increase) the resources of the analyst. Assessment of such work must again, of necessity, be largely by intuition and personal interest, but now additionally hampered by the fact that one is working outside one's specialist field.

Indeed, the selection on this last basis must almost be random. The most obvious fundamental development in which the analytical chemist must interest himself at the present time is that dealing with the structures of organometallic compounds. Both within and without the analytical field this branch has been increasingly active during the past few years and a valuable survey of this field is now available.[4a] In the long term the major part of the work must fit together to form a pattern. At the present time, since little assembly and less pattern can be said to exist, it can only be hoped that a few of the more critical pieces near the centre can be indicated.

None of these major aims of the Reporter will be satisfactorily achieved; but the Report may, in spite of this, attain a final form which will please some of the people some of the time.

---

[3] M. Tswett, *Ber. deut. bot. Ges.*, 1906, 24, 316.

[4] F. Emich and J. Donau, *Monatsh.*, 1909, 30, 745.

[4a] A. E. Martell and M. Calvin, " Chemistry of the Metal Chelate Compounds," New York, 1952.

In Great Britain, in 1952, much interest was centred in the International Congress held in Oxford in September, and now fully documented,[5] and in the smaller, but still quite important Symposium in Birmingham which followed the Congress, and which is, as yet, only reported in abstract form.[6] From the former of these we have freely and gratefully used one of the Congress lectures to illustrate our opening remarks. Individual papers will be reported in their appropriate places.

The remaining two Congress lectures may be mentioned here as expressing clearly two topical aspects of analytical chemistry. R. H. Müller,[7] in dealing with research in analytical instrumentation, was mainly concerned with future trends. He maintained that analytical chemists have not yet made anything like full use of the resources of the science of instrumentation, although he claimed that the use of instruments is widespread and " already dominates many types of analysis." The use of the term " dominates " is, one would hope, ill-founded, and is, perhaps, a slip, since the speaker went on to point out that the analyst could, and more and more should, relegate his instrumental problems to the specialist, but that only the analyst could determine the problems.

The other Congress speaker, C. J. van Nieuwenburg,[8] was concerned with the place of " classical " methods in analytical chemistry. The growth of instrumental methods has given rise in some quarters to the belief that classical methods are a dying species. This he regards as completely unfounded. That the two opposite types of solution to analytical problems are not opposed types, but are capable of being employed together, was his principal theme. The variety of weapons available has been increased rather than altered. His conclusions are strikingly similar to those of Müller when one considers the different terms of reference. He holds that instrumentation and organisation " will not be any use unless there are leading men who understand the whole job. Maybe the old classical methods will disappear some day, although I do not think that day is very near. But the old classical knowledge of analytical chemistry will remain. In the long run brains will count."

The practice of analytical chemistry has been discussed on other occasions. It is significant that similar conclusions regarding the need for integration of instrumental and classical methods, rather than a complete replacement of classical by instrumental methods, is explicitly emphasised from the pedagogic point of view [9] as well as implicitly from that of the professional practitioner.[10] In the latter case we are reminded that the practising analytical chemist is called upon to apply " a knowledge not only of his background in the field of analytical chemistry, but the broadest background of chemical subjects that he can command, and to strive for a solution by the application of known methods, principles and procedures *in new patterns.*" Much of the research in analytical chemistry today is concerned, not with the provision of new principles and methods, but with the summation of knowledge in a new way.

[5] *Analyst*, 1952, 77, 557 ff.
[6] *Ind. Chem. Chem. Manuf.*, 1952, 28, 487.
[7] *Analyst*, 1952, 77, 557.
[8] *Ibid.*, p. 573.
[9] P. W. West, *J. Chem. Educ.*, 1952, 29, 222.
[10] S. E. Q. Ashley, *Analyt. Chem.*, 1952, 24, 1690.

## 2. GENERAL.

In the Progress Report of the Committee on Nomenclature already referred to,[1] specific definitions are put forward as recommendations, but the Report is not regarded as final. A number of the definitions are not novel, but it is useful to have them in compact form. The term "volumetric," it is recommended, should refer to measurement by volume, and is not to be regarded as synonymous with "titrimetric," which is measurement by titration. This is a view that will be welcomed by many analysts, although it will require constant caution to prevent falling into the older usage. Definitions are proposed, based on sample size, for the prefixes macro-, semimicro-, micro-, and ultramicro-, and this is more likely to be a subject for future debate.

It is somewhat unexpected, in view of the distinction that some workers have stressed in the past between "iodimetry" and "iodometry," to find that "iodometry" is defined as the measurement of concentration by titration with a standard solution of iodine; but measurement of concentration by titration with a standard solution of thiosulphate is denoted by the term "thiosulphatimetry." There seems to be no reason for the divergent treatment of the two terms, and one wonders on what basis the Committee will discriminate between the various forms that have been proposed from time to time for the performance of titrations by measurement of conductance.

The definitions so far proposed are limited in number, and many terms have yet to be considered.

A more detailed Report on proposed terms and definitions in applied spectroscopy has also been published.[11] In the Report, in addition to proposals, a group of general principles of nomenclature-standardisation is stated, and there is also included a list of terms about which no decision has yet been reached.

The preparation of sodium chloride suitable for use as a primary analytical standard has been described.[12] Acetylsalicylic acid [13] and sulphamic acid [14] have been proposed as primary standards in alkalimetry. The former has the advantage that its purity can be checked, after titration, by hydrolysis with excess alkali to salicylic acid, and back titration, which should indicate the consumption of a further equivalent of alkali. The latter reagent is known to hydrolyse slowly, a slight but appreciable test for sulphate being obtained after six days storage of the solution. The hydrolysis is to bisulphate, however, and the replaceable hydrogen of the sulphamic acid ought merely to be substituted by the replaceable hydrogen of the bisulphate. In consequence there should be no alteration in the normality towards alkali; no appreciable change in normality was found, on test, after 213 days. The advantages claimed for the reagent are its ready solubility in water; the fact that it is an acid only slightly weaker than the mineral acids so that it can be titrated readily by using indicators whose working range is pH 4—9; and the ease of obtaining and maintaining it in a high

[11] H. K. Hughes *et al.*, *Analyt. Chem.*, 1952, **24**, 1349.

[12] L. Meites, *J. Chem. Educ.*, 1952, **29**, 74.

[13] F. Burriel, F. Pino, and M. D. Vinuesa, *Afinidad*, 1950, **27**, 337.

[14] W. F. Wagner, W. F. Wuellner, and C. E. Feiler, *Analyt. Chem.*, 1952, **24**, 1491.

state of purity. In addition, since practically all its salts are soluble, there is little danger of interference with the titration through formation of precipitates. Its only notable drawback is its low molecular weight.

Calcium acid malate hexahydrate has been recommended [15] as a standard for alkalimetry and for the calibration of pH meters. In addition it proves useful as a standard for calcium titrations—a field which has extended considerably in recent years (p. 305). With a very high equivalent weight of 207, it possesses all other desirable qualifications of such a standard except that it cannot be dried at 100°. However, it is non-hygroscopic, and any trace of adsorbed moisture, which is not a likely feature, can be removed by aspiration of dry air over the solid. The same solid may be used indirectly as a standard for acidimetry by ignition to the oxide, solution of this in excess of acid, and back titration with alkali.

Statistical aspects of analytical chemistry have been discussed by a number of authors.[16] Methods for approximating to the standard deviation have been proposed and applied to practical examples.[17] The reconciliation of scientific and statistical hypotheses, in the special case of radiochemistry, has been considered.[18]

H. Ballczo [19] has pointed out some of the ways in which errors in titrimetric analysis, particularly with dilute solutions, may be reduced by attention to calibration of apparatus and to temperature corrections. The special case of the double titration has been included in this treatment. The possible sources of error inherent in weighing techniques have been discussed by M. J. Marteret.[20] The titrimetric error arising from adsorption of silver ions on glass has been studied by a radioactive indicator method.[21]

The importance of training students of chemistry to appreciate sources of error has been pointed out,[22] and a suitable course outlined which includes such procedures as the determination of uncertainty in analytical results. It has also been stressed [23] that in addition to operational error there may, in such conditions, also be instructional error, which may exist even if students obtain the correct result. The consequences of this, methods of appreciating its existence, and methods of reducing it have been outlined.

Tables have been issued for use in the calibration of graduated glassware [24] and specifications have been drawn up for one-mark graduated flasks [25] and automatic microchemical burettes.[26]

The field of inorganic microchemistry has been reviewed,[27] and semi-micro-techniques for titrimetric analysis, employing sealed vessels of the pharmaceutical-serum type, and hypodermic syringes, with measurements carried out by weighing rather than by volume, have been described.[28]

---

[15] A. C. Shead, *Analyt. Chem.*, 1952, **24**, 1451.

[16] R. J. Hader and W. J. Youden, *ibid.*, p. 120; W. J. Youden, *Analyst*, 1952, **77**, 874; G. E. P. Box, *ibid.*, p. 879; E. G. Gracheva, *J. Anal. Chem.*, *U.S.S.R.*, 1952, **7**, 48; J. M. Pertierra, *Inform. Quim. analit.*, 1952, **6**, 117.

[17] B. Woolf, *Nature*, 1952, **170**, 631; H. de Miranda, *Chem. Weekblad*, 1951, **47**, 1046.

[18] L. Martin, *Analyst*, 1952, **77**, 892.

[19] *Z. anal. Chem.*, 1952, **134**, 321.

[20] *Chim. analyt.*, 1952, **34**, 149.

[21] H. M. Hershenson and L. B. Rogers, *Analyt. Chem.*, 1952, **24**, 219.

[22] W. R. Carmody, *J. Chem. Educ.*, 1952, **29**, 349.

[23] W. J. Blaedel, J. H. Jefferson, and H. T. Knight, *ibid.*, p. 480.

[24] B.S.I. Specif., 1952, No. 1797.

[25] *Ibid.*, No. 1792.

[26] *Ibid.*, No. 1428, Pt. D1.

[27] P. W. West, *Analyt. Chem.*, 1952, **24**, 76.

[28] D. M. Smith, J. Mitchell, and A. M. Billmeyer, *ibid.*, p. 1847.

A general review of ultramicro-quantitative analytical methods has been given,[29] and micro-manipulators [30, 31] and other apparatus [31, 32] designed for work on the microgram scale have been described.

**Reagents.**—In the field of reagents there has been much work of direct use to the analytical chemist, and probably even more that is likely to be of future importance to him. A. E. Martell[33] has discussed some of the ways in which aqueous metal ions are affected by complex formation, with particular reference to the formation of chelate compounds. Such properties as solubility, electrical conductance, interaction with hydrogen ions, absorption spectra, oxidation potentials and, above all, stabilities as measured by the equilibrium constants of the formation reactions, are all fundamental properties which are of value in the investigation of the formation of complexes. Such study must lead to the development of new and valuable applications of complex formation. New analytical reagents utilising unusual oxidation states have been reviewed.[34]

Many investigations of the structures of complexes have been reported, both by analytical chemists and by those outside the field of analytical chemistry, and it is difficult to determine which of these will, in the long term, have most significance. In this connection earlier comments regarding the tendency of the analytical chemist to fall behind the general stream of development have considerable force. It is unfortunate that in many of the studies which have been made on organometallic compounds, and, indeed in the general literature of analytical chemistry, there is a tendency to cling to conceptions which are, as far as the general theory of chemistry is concerned, out-of-date and by now almost meaningless. Thus the classification of such complexes which was current some time ago, and which was never anything more than an *ad hoc* classification, into groups such as " penetration," and " inner-complex " compounds, still persists in many of the publications, although modern ideas on the structures and binding forces of molecules, atoms, and ions permit us at least to discard this for something more in keeping with the times. Such terms still appear too frequently. In at least one recent publication valencies were referred to as " principal " and " auxiliary," which might almost be said to smack of the phlogiston era. If analytical chemists are to make satisfactory contributions to the theoretical side of this topic, they must familiarise themselves with modern ideas on bond structure, and they can, with profit, read some of the publications referred to in this section. Many of these, which have no direct or immediate bearing on practical problems of analytical chemistry, seem to contribute significantly to the theory of complex-formation, and thus to have an ultimate value for the man at the bench.

It is, perhaps, going to the other extreme to refer, as some authors do, to compounds such as calcium oxalate and calcium acetate under the classification of complexes. While it is true that an extreme current view is to regard any anion derived from more than one atom as a complex ion, the term " complex " loses much of its significance, in the analytical sense at least, and probably also in a wider field, if some sort of division is not indicated

---

[29] A. E. Sobel and A. Hanok, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 51.

[30] T. Brindle and C. L. Wilson, *ibid.*, p. 310.

[31] M. C. Alvarez Querol, *ibid.*, p. 117.

[32] A. Lazarow, *J. Lab. Clin. Med.*, 1951, **38**, 660.

[33] *J. Chem. Educ.*, 1952, **29**, 270.

[34] M. Kapel, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 466.

between these structures and the more complicated ones which are normally classed as complexes. It may be that the distinction will be supplied by the increasing use of the term " chelates."

There is now available an excellent account [4a] of methods of study in this field, and of the results which these methods have so far given. An order of stability for metal complexes has been reported, and generally speaking, this seems to agree among the various groups of complexes between the metallic ions and a variety of organic compounds.[35] The studies also support the greater stability of five- than of six-membered chelates. It is found that zinc, nickel, and cobalt(II) co-ordinate with three molecules of tropolone to form singly charged ions, while the corresponding copper(II), beryllium, and lead complexes contain only two organic molecules and are neutral.

The co-ordination chemistry of the transition metals has been studied,[36] and magnetic data for many of these compounds have been related to valency, structure, and bond type, with particular reference to the ionic or covalent nature of the linking. From a more strictly analytical point of view H. M. Irving and R. J. P. Williams [37] have considered a number of the factors controlling the action of organic reagents. The stabilities of the complexes have been considered in relation to their solubilities, the nature of the metallic ion, the nature and the acid dissociation constant of the reagent, and the pH at which the complex exists. Particular attention is paid to the specificity of reagents.

H. Freiser [38] discusses stability in relation to analytical use for a wide range of metal-chelate compounds, and brings home clearly the enormous extent of the field which has to be examined before any comprehensive theory can be advanced, and the complexity of the factors involved, such as steric hindrance and solubility. In this paper particular examples used for illustrative purposes are 2-*o*-hydroxyphenylbenzoxazole as a reagent for cadmium, 2-*o*-hydroxyphenylbenzothiazole for copper or cadmium, and 2-*o*-hydroxyphenylbenziminazole for mercuric mercury.

Probably the reagent which has received most analytical attention throughout the past year is ethylenediaminetetra-acetic acid. Uses for this reagent were reviewed in last year's Report,[39] but many extensions of existing uses and many new uses have since been developed. The uses of this reagent and of the related nitrilotriacetic acid have been reviewed from a practical point of view [40] and theoretical aspects of its application have been discussed.[41]

E. M. Diskant [42] claims that in order to overcome the instability of the indicator Eriochrome Black T [or sodium 1-(1-hydroxy-2-naphthylazo)-5-nitro-2-naphthol-4-sulphonic acid] it may be made up in diethanolamine or triethanolamine solution, which will remain stable for at least seven months. It should be stored in such a way that the solution is protected from atmo-

---

[35] B. E. Bryant, W. C. Fernelius, and B. E. Douglas, *Nature*, 1952, **170**, 247.

[36] F. H. Burstall and R. S. Nyholm, *J.*, 1952, 2906, 3570; R. S. Nyholm and A. G. Sharpe, *ibid.*, p. 3579. [37] *Analyst*, 1952, 77, 813.

[38] *Ibid.*, p. 830. [39] *Ann. Reports*, 1951, 48, 311.

[40] M. O. Lawson, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 512, 559; G. C. Krijn, *Chem. Weekblad*, 1952, **48**, 165; H. Flaschka, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 38.

[41] G. Schwarzenbach, *Analyt. Chim. Acta*, 1952, **7**, 141.

[42] *Analyt. Chem.*, 1952, **24**, 1856.

spheric moisture, but need not be protected from light or from alterations of atmospheric temperature. Several variants of methods for determination of calcium- and total-hardness of water have been proposed,[43] and in one case copper and iron are first removed by addition of cyanide and passage through an anion-exchange resin column.[44] The reagent has been widely applied to the determination of calcium [45] and magnesium [46] in biological fluids, and of these elements in other materials such as limestones.[47] The effect of varying the concentration of potassium chloride in the calcium determination has been examined.[48] Direct or indirect titration methods for a number of other elements have been proposed. Phosphate is determined by precipitation as magnesium ammonium phosphate and subsequent determination of the magnesium.[49] Barium [50] and zinc [51] may be titrated directly. Sodium may be estimated through zinc after precipitation as sodium zinc uranyl acetate.[52] Nickel, first precipitated by dimethylglyoxime, may be titrated directly.[53] When a solution of a silver salt is allowed to react with ammoniacal nickel cyanide solution, an equivalent amount of nickel ion is set free which may be titrated, thus giving a measure of the silver.[54, 55] This, in turn, may be used to determine halide after precipitation as silver halide. This determination may be used in coloured or cloudy solutions where the classical methods for halide are unsatisfactory. Thallium may be titrated directly with a solution of the magnesium complex.[56] Lead may be titrated directly, either alone [57] or in the presence of copper,[58] which latter may be masked by cyanide and then subsequently estimated by a total titration in absence of cyanide.

Apart from its uses as a titrimetric reagent, ethylenediaminetetra-acetic acid has been used to prevent interference in the estimation of sulphate,[59] nitrate,[60] beryllium,[61, 62] and iron.[63] It has been recommended for the

---

[43] J. E. Houlihan, *Analyst*, 1952, **77**, 158; R. Sijderius, *Chem. Weekblad*, 1952, **48**, 378; W. Fivian and M. Moser, *Sugar Ind. Abstr.*, 1951, **13**, 131.

[44] J. W. McCoy, *Analyt. Chim. Acta*, 1952, **6**, 259.

[45] A. C. Mason, *Analyst*, 1952, **77**, 529; H. Lempfrid and J. Stürmer, *Klin. Wochenschr.*, 1952, **30**, 227; H. Neilsen, *Nord. Med.*, 1952, **48**, 1059; H. Flaschka and A. Holasek, *Z. physiol. Chem.*, 1951, **288**, 244.

[46] A. Holasek and H. Flaschka, *ibid.*, 1952, **290**, 57; E. S. Buckley, J. C. Gibson, and T. R. Bortolotti, *J. Lab. Clin. Med.*, 1951, **38**, 751; A. H. Holtz, *Chem. Weekblad*, 1951, **47**, 907; A. E. Sobel and A. Hanok, *Proc. Soc. Exp. Biol., N.Y.*, 1951, **77**, 737; Kuang Lu Cheng and R. H. Bray, *Soil Sci.*, 1951, **72**, 449.

[47] J. J. Banewicz and C. T. Kenner, *Analyt. Chem.*, 1952, **24**, 1186; Kuang Lu Cheng, T. Kurtz, and R. H. Bray, *ibid.*, p. 1640; J. Banks, *Analyst*, 1952, **77**, 484; L. E. Smith, *Pulp and Paper*, 1952, **26**, No. 5, 86, 88; K. E. Langford, *Electroplating*, 1952, **5**, No. 2, 41.

[48] F. F. Carini and A. E. Martell, *J. Amer. Chem. Soc.*, 1952, **74**, 5744.

[49] H. Flaschka and A. Holasek, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 101; F. Huditz, H. Flaschka, and I. Petzold, *Z. anal. Chem.*, 1952, **135**, 333.

[50] T. J. Manns, M. U. Reschovsky, and A. J. Certa, *Analyt. Chem.*, 1952, **24**, 908.

[51] E. W. Debney, *Nature*, 1952, **169**, 1104.

[52] H. Flaschka, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 391.

[53] W. F. Harris and T. R. Sweet, *Analyt. Chem.*, 1952, **24**, 1062.

[54] H. Flaschka, *Mikrochem. Mikrochim. Acta*, 1952, **40**, 21.

[55] H. Flaschka and F. Huditz, *Z. anal. Chem.*, 1952, **137**, 104.

[56] H. Flaschka, *Mikrochem. Mikrochim. Acta*, 1952, **40**, 42. [57] *Idem, ibid.*, **39**, 315.

[58] H. Flaschka and F. Huditz, *Z. anal. Chem.*, 1952, **137**, 172.

[59] D. Gibbons, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 487.

[60] F. L. Hahn, *Analyt. Chim. Acta*, 1952, **7**, 68.

[61] J. Huré, M. Kremer, and F. le Berquier, *ibid.*, p. 37; R. G. Smith, A. J. Boyle, W. G. Fredrick, and B. Zak, *Analyt. Chem.*, 1952, **24**, 406; P. I. Brewer, *Analyst*, 1952, **77**, 539.

[62] J. A. Adam, E. Booth, and J. D. H. Strickland, *Analyt. Chim. Acta*, 1952, **6**, 462.

[63] R. L. Morris, *Analyt. Chem.*, 1952, **24**, 1374.

colorimetric determination of cobalt.[64] The complexes with europium [65] and with thorium and uranyl ions [66] have been examined. R. C. Vickery [67, 68] has investigated the stability constants of metallic ions with this reagent, with particular reference to their use in ion-exchange methods for separating the lanthanons. He has shown that the elution series for complexes of bivalent metals is affected by the presence or absence of tervalent metal complexes. He has also achieved a good separation of praseodymium from neodymium by addition of manganese to act as a separating element. For the most efficient separation, low concentration of the reagent together with a low flow rate, a high pH value, and an exchange resin in the ammonium form are recommended. Finally, H. Flaschka [69] has investigated the effect of the presence of ethylenediaminetetra-acetic acid on the behaviour of thioacetamide as an alternative precipitant to hydrogen sulphide, and has described the behaviour of a wide range of cations in acid, neutral, and alkaline solution towards the combined reagents.

While discussing this reagent it is perhaps pertinent to introduce a more general note. In the literature the range of synonyms for ethylenediaminetetra-acetic acid is bewildering—EDTA, ED, enta, Complexone (together with its derivative Complexometric titration), Versene, Versenate, and Trilon B all have considerable currency. For an internal report such names may have their advantage, but it is doubtful if the space saved in a printed paper is sufficient to offset the confusion which must exist. No doubt the tendency to apply shortened names to organic reagents became popular with " oxine," though this has little advantage over 8-hydroxyquinoline or 8-quinolinol, either of which is unequivocal. It was not altogether to be expected by those who incautiously lent " oxine " currency that we should ultimately be assailed by ferroin, cuproin, neo-cuproin, tiron, magneson-I, and magneson-II, to choose only a few of those which spring immediately to mind. None of these names gives any clue to the nature of the reagent, and they are not altogether to be trusted as a guide to use. It is true that the nomenclature of organic reagents must cause dismay to those analytical chemists who make use of these reagents, and an easy solution of the problem is not to be expected. But strenuous efforts are being made to standardise the nomenclature in other branches of chemistry, and the conclusion has regretfully been reached that many of the trivial names of the nineteenth century must be retained though they are misleading in the light of systematic nomenclature. It seems a pity, therefore, that the field of analytical chemistry bids fair to provide a further problem for committees on nomenclature by the lavish use of trivial names which may or may not have gained general acceptance.

In a comprehensive study of the complexes of copper with 1 : 10-phenanthroline and its methyl derivatives [70] the range of pH which permits of their formation, and their stabilities have been examined. The structures have been related to such properties as absorption spectra, and use has been made of this in predictions for some of the methyl derivatives. Similar studies

---

[64] M. Jean, *Analyt. Chim. Acta*, 1952, **6**, 278.
[65] E. I. Onstott, *J. Amer. Chem. Soc.*, 1952, **74**, 3773.
[66] M. J. Cabell, *Analyst*, 1952, **77**, 859.
[67] *Nature*, 1952, **170**, 665. [68] *J.*, 1952, 4357.
[69] *Z. anal. Chem.*, 1952, **137**, 107.
[70] W. H. McCurdy and G. F. Smith, *Analyst*, 1952, **77**, 846.

have been made for the 1 : 10-phenanthroline complexes with iron(II),[71] iron(III),[72] and zinc.[73] Investigations on various oximes and dioximes have been reported.[74] Measurements of the stabilities of complexes of 8-hydroxyquinoline and related compounds [75] confirm the greater stability of 5-membered chelate rings mentioned above, and also indicate an order of stability for the bivalent metals Cu > Ni > Co > Zn > Pb > Cd > Mn > Mg which is in general agreement with other investigations. It has been shown that 8-hydroxyquinaldine may be quantitatively brominated,[76] and a number of quantitative precipitations with this reagent, notably of indium, uranyl, scandium, lead, and thorium, have been described.

On the assumption that an indophenol of 8-hydroxyquinoline should possess both the redox-indicating properties of indophenols and a precipitating power related to the parent compound, a number of indophenols of this compound and its derivatives have been prepared.[77] Most of these products were unstable. However,, 2-methylindo-8-hydroxyquinoline, prepared by the action of hydroxylamine in an alkaline oxidising medium on 8-hydroxy-2-methylquinoline, gives precipitates at pH 5 with certain cations, and at pH 12 with a wider range of ions. Aluminium is not precipitated.

Work on the stabilities of metal chelates of iminodiacetic acid and iminodipropionic acid and their derivatives [78] suggests an order corresponding to that quoted above, but with lead and cobalt interchanged, and again supports the greater stability of 5-membered chelates. The analytical behaviour as precipitants of thiourea [79] and of 4- and 5-phenyl-substituted 1 : 2-dimercapto-3-thiones [80] has been reported. Ammonium thiocarbamate has been recommended [81] as an alternative to hydrogen sulphide for the precipitation of sulphides. An extensive investigation of disubstituted dithiocarbamates [82] has shown that many metallic ions may be precipitated as stable crystalline compounds which frequently have characteristic colours, generally brighter than those of the corresponding sulphides. The extractability of these metal dithiocarbamates has been investigated.

The separation from bivalent cations of iron, aluminium, and manganese as hydroxides may be carried out [83] by aminomercuric chloride, $NH_2 \cdot HgCl$, prepared *in situ* through successive additions of mercuric chloride, ammonium chloride, and ammonia. Consideration of the " weighting " effect as applied to benzidine, its homologues, and related compounds indicate that 4 : 4′-diaminotolane is likely to form a sulphate of low solubility.[84] This compound has been examined, and found to have the

---

[71] W. W. Brandt and D. K. Gullstrom, *J. Amer. Chem. Soc.*, 1952, 74, 3532.

[72] A. E. Harvey and D. L. Manning, *ibid.*, p. 4744.

[73] J. M. Kruse and W. W. Brandt, *Analyt. Chem.*, 1952, 24, 1306.

[74] C. V. Banks and A. B. Carlson, *Analyt. Chim. Acta*, 1952, 7, 291; R. Pallaud, *Chim. analyt.*, 1951, 33, 239, 343.

[75] W. D. Johnston and H. Freiser, *J. Amer. Chem. Soc.*, 1952, 74, 5239.

[76] J. P. Phillips, J. F. Emery, and H. P. Price, *Analyt. Chem.*, 1952, 24, 1033.

[77] J. P. Phillips, J. F. Emery, and Q. Fernando, *J. Amer. Chem. Soc.*, 1952, 74, 5542.

[78] S. Chaberek and A. E. Martell, *ibid.*, p. 5052; S. Chaberek, R. C. Courtney, and A. E. Martell, *ibid.*, p. 5057.

[79] K. B. Yatsimirsky and A. A. Astasheva, *J. Anal. Chem., U.S.S.R.*, 1952, 7, 43.

[80] M. G. Voronkov and F. P. Tsiper, *ibid.*, 1951, 6, 331.

[81] E. Wiberg and R. Bauer, *Angew. Chem.*, 1952, 64, 270.

[82] H. Malissa and F. F. Miller, *Mikrochem. Mikrochim. Acta*, 1952, 40, 63.

[83] S. K. Šušić and N. V. Njegovan, *Analyt. Chim. Acta*, 1952, 7, 304.

[84] M. Kapel, *Ind. Chem. Chem. Manuf.*, 1952, 28, 490.

lowest solubility recorded for an amine sulphate. The stabilities of a range of alkaline-earth compounds have been discussed theoretically.[85]

General methods for the estimation of magnesium in calcium metal [86] and of zinc in zinc–cadmium mixtures [87] have been critically examined. D. C. Atkins and C. S. Garner [88] have divided chelate compounds of zinc into two classes, " fused-ring " compounds where isotopic exchange with radioactive zinc takes place very slowly if at all, and " non-fused-ring " complexes where this exchange is very rapid. The structures and properties of salicylideneamine [89] and *N*-alkylethylenediamine [90] complexes of copper and nickel have been described. An order of stability for amino-acid complexes of copper has been related to the structures of the amino-acids.[91] Silver has been shown to form several types of complex ion with triethylenetetramine.[92] The complexes formed by chromium and gallium with iodine have been studied,[93] and the bearing of these on other halide complexes and on general bond-type theory is indicated.

In a general article B. J. Lerner, C. S. Grove and R. S. Casey [94] point out that much of the knowledge required for a complete explanation of the " complex " chemistry of iron—knowledge of all forces operating at molecular level and a valid all-inclusive theory of valency—is still not available. Such factors as solvation, magnetic susceptibility, electron transfer, the effect of pH, and the relation of colour to structure are discussed. Complexes of cobalt with salicylaldehyde, its derivatives and related compounds [95] and with the unusual sexadentate sulphur-containing $\alpha\omega$-diamines [96] have been described. Organometallic compounds of cobalt,[97] nickel,[97, 98] chromium,[99] uranium,[100] and zirconium [101] have been investigated. Formulæ have been proposed for a number of the ions formed by zirconium in mineral acid solutions.[102] The reactions of some thiosemicarbazides with ruthenium have been examined.[103]

## 3. INORGANIC QUALITATIVE ANALYSIS.

In a scheme for the separation and recognition of the more familiar cations, J. Galmés [104] recommends removal of the alkaline-earth metals together with the usual chloride group by following the addition of hydrochloric acid with ethanol and sodium sulphate. After removal of the acid-insoluble sulphides, the cations normally precipitated as hydroxides and as

[85] R. J. P. Williams, *J.*, 1952, 3770.

[86] S. Abbey, *Chem. Canad.*, 1951, **3**, No. 10, 53.

[87] W. Scheller and W. D. Treadwell, *Helv. Chim. Acta*, 1952, **35**, 754.

[88] *J. Amer. Chem. Soc.*, 1952, **74**, 3527.

[89] A. P. Terentev and E. G. Rukhadze, *J. Anal. Chem.*, *U.S.S.R.*, 1951, **6**, 303; A. P. Terentev, E. G. Rukhadze, and Z. A. Fadeeva, *ibid.*, 1952, **7**, 120.

[90] F. Basolo and R. K. Murmann, *J. Amer. Chem. Soc.*, 1952, **74**, 5243.

[91] N. C. Li and E. Doody, *ibid.*, p. 4184.

[92] H. B. Jonassen and P. C. Yates, *ibid.*, p. 3388.

[93] A. S. Wilson and H. Taube, *ibid.*, p. 3509.

[94] *J. Chem. Educ.*, 1952, **29**, 438. [95] B. West, *J.*, 1952, 3115, 3123.

[96] F. P. Dwyer, N. S. Gill, E. C. Gyarfas, and F. Lions, *J. Amer. Chem. Soc.*, 1952, **74**, 4188. [97] C. F. Callis, N. C. Neilsen, and J. C. Bailar, *ibid.*, p. 3461.

[98] L. Sacconi, *ibid.*, p. 4503. [99] W. R. King and C. S. Garner, *ibid.*, p. 5534.

[100] J. T. Barr and C. A. Horton, *ibid.*, p. 4430.

[101] H. B. Jonassen and W. R. de Monsabert, *ibid.*, p. 5298.

[102] B. A. J. Lister and L. A. McDonald, *J.*, 1952, 4315.

[103] R. P. Yaffe and A. F. Voigt, *J. Amer. Chem. Soc.*, 1952, **74**, 5043.

[104] *Afinidad*, 1951, **28**, 154.

sulphides in alkaline solution are precipitated by solid sodium carbonate. The unsatisfactory separation of the alkali-insoluble sulphides from the hydroxides may be overcome, it is claimed,[105] by the application of selective spot tests without reliance on separation methods. An alternative scheme [106] removes the chlorides in the usual manner, followed by tin and antimony, which are separated by evaporation with nitric acid. The insoluble sulphates and the insoluble hydroxides constitute the two major succeeding groups. Potassium xanthate is recommended [107] as a satisfactory alternative to hydrogen sulphide, being used to precipitate a large group of elements, including a number of the less familiar ones, after removal of the insoluble chlorides and sulphates. The xanthate group is then subdivided by treatment with alkali hydroxide, which produces a group of soluble and a group of insoluble sulphides.

A method has been described [108] for the preparation of the titanium reagent recommended for the removal of phosphate in the orthodox schematic method of analysis. Alternative procedures have been proposed for the treatment of the sulphides of the copper group [109] and the nickel group,[110] and of the alkali-metal group.[111]

J. Gillis [112] has discussed a number of aspects of theoretical and practical importance regarding the "sensitivity" of a reaction. The general field of spot reactions has been reviewed,[113] particularly with reference to specificity.

Among tests for the identification of individual ions a method has been outlined for the removal of interferences before detecting chloride by silver nitrate.[114] A bismuth mercaptoglyoxaline gives a red complex with iodide which is specific for this ion.[115] Nitrate may be removed and identified as volatile methyl nitrite.[116] Sulphur in any form is reduced to hydrogen sulphide which gives a red colour with a molybdate–thiocyanate solution.[117] Thiocyanate is extracted and identified by a ferric chloride–aluminium chloride reagent.[118] Azo-dyes based on pyrocatechol and hæmatoxylin are sensitive colour reagents for boric acid.[119] A range of specific reagents for germanium has been critically examined, and their behaviours described.[120] R. J. Winterton [121] has investigated claims for sodium cobaltithiosulphate, sodium calcium ferrocyanide, and sodium uranyl chromate as

[105] A. Okač and M. Bezdek, *Publ. Fac. Sci. Univ. Masaryk*, 1950, No. 3, 9.

[106] F. Bianchi, *Monit. Farm. Terap.*, 1952, 58, 139.

[107] L. R. Chaves Lavin, *Inform. Quim. anal.*, 1951, 5, 62.

[108] A. J. Nutten and W. I. Stephen, *Analyt. Chim. Acta*, 1952, 7, 31.

[109] M. S. Jovanovič and B. M. Jovanovič, *Bull. Soc. chim. Belgrade*, 1951, 16, 167.

[110] E. G. Maleeva, *J. Anal. Chem., U.S.S.R.*, 1951, 6, 383.

[111] A. Casini, *Ann. Chim. Roma*, 1952, 42, 317.

[112] *Mikrochem. Mikrochim. Acta*, 1951, 38, 381; *J. Chem. Educ.*, 1952, 29, 170; *Ind. Chem. Chem. Manuf.*, 1952, 28, 488.

[113] F. Feigl, *Mikrochem. Mikrochim. Acta*, 1952, 39, 368; P. W. West, *Analyst*, 1952, 77, 611.

[114] C. Mahr and W. Brömer, *Z. anal. Chem.*., 1952, 135, 107.

[115] R. A. McAllister, *Nature*, 1952, 169, 708.

[116] C. Franzke and K. Romminger, *Z. anal. Chem.*, 1952, 136, 1.

[117] L. P. Pepkowitz and E. L. Shirley, *Nuclear Sci. Abstr.*, 1952 6. 15.

[118] L. Mennucci, *Rev. Fac. Cienc. quim., La Plata*, 1947, 22, 7.

[119] I. M. Korenman and F. R. Sheyanova, *J. Anal. Chem., U.S.S.R.*, 1952, 7, 128.

[120] P. Bévillard, *Mikrochem. Mikrochim. Acta*, 1952, 39, 209; A. Tchakirian and P. Bévillard, *Compt. rend.*, 1951, 233, 256, 1033.

[121] *Ind. Chem. Chem. Manuf.*, 1952, 28, 492.

precipitants for potassium. None of these has proved as sensitive as sodium cobaltinitrite, although the first may be used to detect rubidium in the absence of potassium, and the first and last may prove useful as tests for potassium in the presence of ammonium, as no precipitate is given by the latter ion.

A spot procedure for the detection of zinc using potassium ferrocyanide,[122] and methods for the recognition of cadmium after precipitation as an ammonium iodide complex [123] and of mercury as red cuprous mercuric iodide [124] have been described. Alizarin-blue, which contains the active groups of both alizarin and 8-hydroxyquinoline, may be used for the detection of traces of copper,[125] although the general behaviour of the individual reagents has largely been lost by combining the two structures. Aluminium, bismuth, iron, and titanium are precipitated by diphenyl phosphate.[126] Manganese gives a green colour with triethanolamine in the presence of alkali hydroxide,[127] and is satisfactorily detected in field tests on minerals by 8-hydroxyquinoline.[128] The zinc 1 : 10-phenanthroline complex mentioned earlier [73] may be used to provide a sensitive test for ferricyanide in the presence of ferrocyanide. F. Buscaróns and J. Artigas [129] recommend 2-mercaptoacetamido-4-nitrophenol as a reagent for cobalt. Gossypol forms a red complex with molybdenum.[130] It is claimed [131] that the interference of fluorides in the detection of molybdenum by orthodox reagents is not so marked as has previously been reported, and that detection is still possible in the presence of 100 times its concentration of fluoride as sodium fluoride. A photochemical reaction of tungsten in the presence of hydrochloric acid and ethanol is stated [132] to be suitable for the detection of a few μg. of this element. Tungsten may also be detected in ores by 8-hydroxyquinoline.[133] The test for antimony with rhodamine-B may be made specific for this element, and will enable 0·2 μg. to be detected.[134]

On the assumption that the mandelic acid group, $\cdot CH(OH) \cdot CO_2H$, should be generally sensitive for zirconium, R. E. Oesper, R. A. Dunleavy, and J. J. Klingenberg [135] prepared *m*-2-hydroxynaphthylazomandelic acid so as to introduce a coloured centre into the reagent. As expected, this forms a coloured precipitate with zirconium, but the precipitate has the same colour as the reagent. It may be used, however, semi-quantitatively by the confined spot-test technique.

Colour reactions between finely divided solids have been discussed [136] as a basis for qualitative analysis, and a number of highly sensitive tests have been described which may be applied directly to minerals.

---

[122] A. Lewandowski, *Roczn. Chem.*, 1952, **26**, 8.

[123] A. A. Komarovskaya, *J. Gen. Chem.*, *U.S.S.R.*, 1949, **19**, 1459.

[124] E. Van Dalen and B. Van't Riet, *Analyt. Chim. Acta*, 1952, **6**, 101.

[125] F. Feigl, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 487.

[126] F. Knotz, *Anal. real Soc. esp. Fis. Quim.*, 1952, **48**, *B*, 564.

[127] E. Jaffe, *Ann. Chim. Roma*, 1951, **41**, 397.

[128] A. de Sousa, *Analyt. Chim. Acta*, 1952, **7**, 393.

[129] *Anal. real Soc. esp. Fis. Quim.*, 1952, **48**, *B*, 140.

[130] A. Vioque-Pizarro, *Analyt. Chim. Acta*, 1952, **6**, 105.

[131] F. Bermejo Martinez, A. Prieto Bouza, and J. Flores de Ligondés, *Anal. real Soc. esp. Fis. Quim.*, 1951, **47**, *B*, 523.

[132] A. de Sousa, *Analyt. Chim. Acta*, 1952, **7**, 24.

[133] *Idem*, *Mikrochem. Mikrochim. Acta*, 1952, **40**, 104.

[134] P. W. West and W. C. Hamilton, *Analyt. Chem.*, 1952, **24**, 1025.

[135] *Ibid.*, p. 1492.

[136] P. M. Isakov, *J. Anal. Chem.*, *U.S.S.R.*, 1951, **6**, 281.

## 4. INORGANIC GRAVIMETRIC ANALYSIS

Five types of weighing vessel have been specified for microchemical analysis.[137] W. H. Bromund and A. A. Benedetti-Pichler [138] have described the use of an assay balance for the gravimetric analysis of milligram samples with use of microchemical equipment. A quartz microbalance for the determination of magnetic susceptibility on milligram samples has been described [139] and its performance investigated.

The ageing of crystalline precipitates has been considered from the theoretical standpoint by I. M. Kolthoff,[140] and factors influencing both physical and chemical ageing have been discussed. It has been suggested that some form of numerical indications of the analytical characteristics of a precipitate such as " coefficient of filtration," " rate of sedimentation," [141] and " nucleation potential " [142] should be available. Such values would be a valuable guide to the analytical behaviour of precipitates. They might permit a more fundamental approach to precipitation problems, and they would help in the development of new or the improvement of existing methods.

**Precipitation in Homogeneous Solution.**—The method by which the precipitating agent is produced slowly throughout the body of the solution, so that uniform precipitating conditions are achieved, continues to be extended. A review of existing methods has been made.[143] Calcium may be determined in the presence of magnesium by using the hydolysis of methyl oxalate.[144] Barium has been precipitated by the hydrolysis of sulphamic acid.[145] Praseodymium has been separated from lanthanum by the fractional precipitation of the carbonates from trichloroacetic acid solution.[146] Thorium is gradually precipitated by ammonium picrate or by 2 : 4-dinitrophenol,[147] and lead is satisfactorily precipitated as phosphate in a solution whose pH is altered gradually by the hydrolysis of urea.[148]

*Methods of analysis.* Recent gravimetric methods of analysis have been reviewed.[149] C. Duval [150] has collated earlier work, using the thermobalance. From a study of the thermolysis curves, nitron, cinchonamine, and di-1-methylnaphthylamine are recommended [151] as gravimetric reagents for nitrate; no reagent tested was found to be suitable for the determination of nitrite, hyponitrite, or azide. R. C. Brasted [152] has described an indirect gravimetric determination of nitrite through the loss in weight from gas evolution with sulphamic acid. Optimum conditions have been proposed [153] for the determination of phosphorus as ammonium phosphomolybdate,

---

[137] B.S.I. Specif., 1952, No. 1428, Pt. H1.

[138] *Mikrochem. Mikrochim. Acta*, 1951, 38, 505.

[139] F. Blaha, *ibid.*, 1952, 39, 339. [140] *Analyst*, 1952, 77, 1000.

[141] A. V. Nikolaev and M. P. Elentukh, *J. Anal. Chem.*, *U.S.S.R.*, 1952, 7, 21.

[142] R. A. Johnson, *Ind. Chem. Chem. Manuf.*, 1952, 28, 489.

[143] L. Gordon, *Analyt. Chem.*, 1952, 24, 459.

[144] L. Gordon and A. F. Wroczynski, *ibid.*, p. 896.

[145] W. F. Wagner and J. A. Wuellner, *ibid.*, p. 1031.

[146] L. L. Quill and M. L. Salutsky, *ibid.*, p. 1453.

[147] C. L. Rao, M. Venkataramaniah, and B. S. V. R. Rao, *J. Indian Chem. Soc.*, 1951, 28, 515. [148] Shu-Chuan Liang and Kuo-I Lu, *Analyt. Chim. Acta*, 1952, 7, 451.

[149] F. E. Beamish and W. A. E. McBryde, *Analyt. Chem.*, 1952, 24, 95.

[150] *Chim. anal.*, 1952, 34, 55.

[151] C. Duval and N. D. Xuong, *Analyt. Chim. Acta*, 1952, 6, 245.

[152] *Analyt. Chem.*, 1952, 24, 1111.

[153] A. Bacon and H. C. Davis, *Metal Abstr.*, 1952, 19, 734.

either in simple phosphate solutions or in the presence of iron or chromium, and for the determination of sulphate as barium sulphate in the presence of iron.[154] Following a study of five co-ordination compounds of cobalt, octa-ammino-μ-amino-μ-nitrodicobaltic nitrite has been proposed [59, 155] as a gravimetric reagent for sulphate. Although the precipitate is more soluble than barium sulphate, it is little affected by foreign ion adsorption. In particular, nitrate does not interfere. Germanium may be estimated by 3 : 4-dihydroxyazobenzene.[156]

Critical examination of the precipitation of potassium with sodium cobaltinitrite [157] has confirmed the unsuitability of this reagent for the gravimetric determination of potassium, even under the most stringent empirical conditions, because of variability in the structure of the precipitate and co-precipitation of reagent. If this reagent is used, some indirect method of determination, such as that based on a colorimetric cobalt determination, must be utilised. The gravimetric determination of potassium as potassium tetraphenylboron, $K[B(C_6H_5)_4]$,[158] is claimed to be rapid and free from error. A method has been described for the separation of rubidium and cæsium in large amounts of sodium and potassium chlorides.[159] The precipitation of beryllium and its determination as pyrophosphate have been critically examined, and suitable procedures have been selected.[160]

J. L. Walter and H. Freiser [161] have found 2-*o*-hydroxyphenylbenzoxazole, one of the reagents which they investigated from the structural point of view,[38] suitable as a gravimetric reagent for cadmium. Only nickel and cobalt interfere seriously, and copper interference can be avoided. Microgram amounts of mercury in the mercurous form have been determined gravimetrically as the chloride with a coefficient of variation of ±1%.[162] Investigations with the thermobalance have indicated some twenty gravimetric methods which are suitable for the determination of copper, with the conditions which are appropriate for drying the precipitates.[163] Copper may be determined gravimetrically as cuprous thiocyanate by using ferrous ammonium sulphate as reducing agent,[164] or as sulphide by using the ammonium or sodium salt of trithiocarbonic acid as precipitant.[165] Precipitation of copper with 5 : 6-benzoquinaldinic acid has been described.[166] Silver has been determined gravimetrically on the microgram scale as the chloride,[162] and gold may be precipitated by morpholine oxalate.[167]

Aluminium can be precipitated quantitatively as the hydroxide by using pyridine.[168] Interference by iron in the precipitation with ammonium

---

[154] N. Gandolfo, *R. C. Ist. sup. Sanit.*, 1951, **14**, 654.

[155] R. Belcher and D. Gibbons, *J.*, 1952, 4216.

[156] A. Tchakirian and P. Bévillard, *Compt. rend.*, 1951, **233**, 1112.

[157] D. Bourdon, *Chim. anal.*, 1950, **32**, 273; J. W. Robinson, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 491.

[158] H. Flaschka, *Z. anal. Chem.*, 1952, **136**, 99; H. W. Spier, *Biochem. Z.*, 1952, **322**, 467.

[159] D. Meier and W. D. Treadwell, *Helv. Chim. Acta*, 1951, **34**, 805.

[160] R. Airoldi, *Ann. Chim. appl. Roma*, 1951, **41**, 478.

[161] *Nuclear Sci. Abstr.*, 1952, **6**, 212; *Analyt. Chem.*, 1952, **24**, 984.

[162] H. M. El-Badry and C. L. Wilson, *Analyst*, 1952, **77**, 596.

[163] Y. Marin and C. Duval, *Analyt. Chim. Acta*, 1952, **6**, 47.

[164] R. Belcher and T. S. West, *ibid.*, p. 337.

[165] E. Gagliardi and W. Pilz, *Monatsh.*, 1952, **83**, 54.

[166] A. K. Majumdar and A. K. Mallick, *J. Indian Chem. Soc.*, 1952, **29**, 255.

[167] L. S. Malowan, *Rev. Soc. venezol. Quim.*, 1951, **5**, No. 23, 23.

[168] E. Peltenburg, *Rev. Fac. Cienc. quim.*, *La Plata*, 1947, **22**, 175.

hydroxide may be prevented by complexing with thioglycollic acid.[169] The micro-determination of aluminium with 8-hydroxyquinoline has been modified.[170] Lanthanons may be precipitated by ammonium sebacate.[171]

From thermolytic examination, tetraphenylarsonium perrhenate is stated to be the most satisfactory weighing form for rhenium.[172] Iron and chromium may be precipitated as the hydroxides with pyridine,[168] and cobalt as the double mercuric thiocyanate.[173] Molybdenum may be separated from interfering elements by a preliminary precipitation with α-benzoin oxime followed by conversion into sulphide.[174] The sulphide may also be obtained by precipitation with sodium trithiocarbonate.[175] A method for volatilisation of tin as stannic iodide permits estimation of this element in bronzes.[176] Lead has been determined with phenylarsonic acid [177] and on the microgram scale as sulphate.[162]

For the quantitative precipitation of zirconium, benzilic acid,[178] cinnamic acid,[179] and salicylic and phenoxyacetic acids [180] have all been found satisfactory. Quantitative precipitants proposed for thorium include camphoric,[181] anisic,[182] succinic,[183] adipic,[183] benzoic,[171, 184] and *m*-tolyloxyacetic acids,[185] ammonium furoate,[186] sodium sulphanilate,[186] and cinnamic acid.[187]

Antimony may be precipitated as the sulphide by sodium trithiocarbonate [188] or as a cobalt complex with bisethylenediaminocobaltic chloride.[189] Vanadium may be precipitated with diantipyrylphenylmethane and ignited to the pentoxide.[190] The temperatures of decomposition of a number of niobium complexes have been recorded.[191] Separation of the tannin complexes of niobium and tantalum may be achieved in aqueous ammonium oxalate solution.[192] From temperatures of decomposition, precipitation of tantalum by tartaric acid is indicated as the most satisfactory of the current methods.[193]

---

[169] R. A. Hummel and E. B. Sandell, *Analyt. Chim. Acta*, 1952, **7**, 308.

[170] M. C. Alvarez Querol, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 121.

[171] G. B. Wengert, R. C. Walker, M. F. Loucks, and V. A. Stenger, *Analyt. Chem.*, 1952, **24**, 1636.

[172] S. Tribalat and C. Duval, *Analyt. Chim. Acta*, 1952, **6**, 138.

[173] F. Sierra and F. Cárceles, *Anal. real Soc. esp. Fís. Quím.*, 1951, **47**, *B*, 811.

[174] *J. Iron Steel Inst.*, 1952, **171**, 75.

[175] E. Gagliardi and W. Pilz, *Z. anal. Chem.*, 1952, **136**, 103.

[176] J. Besson and R. Budenz, *Chim. anal.*, 1952, **34**, 163.

[177] A. K. Majumdar and R. N. S. Sarma, *J. Indian Chem. Soc.*, 1951, **28**, 654.

[178] M. Venkataramaniah and B. S. V. R. Rao, *ibid.*, p. 257.

[179] C. Venkateswarlu and B. S. V. R. Rao, *ibid.*, p. 354.

[180] T. V. Sastry and B. S. V. R. Rao, *ibid.*, p. 530.

[181] D. S. N. Murty and B. S. V. R. Rao, *ibid.*, p. 218.

[182] K. V. S. Krishnamurty and B. S. V. R. Rao, *ibid.*, p. 261; *Rec. Trav. chim.*, 1951, **70**, 421.

[183] T. V. S. Suryanarayana and B. S. V. R. Rao, *J. Indian Chem. Soc.*, 1951, **28**, 511.

[184] M. Venkataramaniah, C. L. Rao, and B. S. V. R. Rao, *Analyst*, 1952, **77**, 103; *J. Sci. Ind. Res., India.*, 1951, **10**, *B*, 254.

[185] M. Venkataramaniah, B. S. V. R. Rao, and C. L. Rao, *Analyt. Chem.*, 1952, **24**, 747.

[186] O. Lakshminarayana and B. S. V. R. Rao, *J. Indian. Chem. Soc.*, 1951, **28**, 551.

[187] K. V. S. Krishnamurty and C. Venkateswarlu, *Rec. Trav. chim.*, 1952, **71**, 668.

[188] E. Gagliardi and W. Pilz, *Z. anal. Chem.*, 1952, **136**, 344.

[189] D. Gibbons, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 487.

[190] S. I. Gusev, R. G. Beyles, and E. V. Sokolova, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 43.

[191] U. M. Doan and C. Duval, *Analyt. Chim. Acta*, 1952, **6**, 81.

[192] N. H. Bailey, *S. Afr. Ind. Chem.*, 1951, **5**, 235.

[193] U. M. Doan and C. Duval, *Analyt. Chim. Acta*, 1952, **6**, 135.

Precipitation of platinum by thioformamide is stated [194] to be more satisfactory than precipitation by hydrogen sulphide, and reduction of precipitated ammonium hexachloroplatinate by zinc is recommended in preference to the more usual methods.[195] Errors in the assay of iridium [196] and of osmium [197, 198] have been investigated, and precipitation of osmium by "thionalide" followed by ignition in hydrogen to the metal is recommended. Palladium may be precipitated as the sulphide by thioformamide [199] or as a complex with 1 : 10-phenanthroline.[200] The latter precipitate or the precipitate with 8-hydroxyquinoline is recommended as weighing form on the basis of thermolysis curves.[201]

## 5. INORGANIC TITRIMETRIC ANALYSIS.

Recent advances in titrimetric analysis are presented in the new edition of a standard work [202] and in a review.[203] A titration bench with built-in lighting and stirring apparatus has been described.[204] Reductors and reductor methods have been reviewed [205] and new or improved reductor methods have been proposed.[206] A study by potentiometric methods of some of the reactions of bromide–bromate and iodide–iodate systems has been reported.[207] An extensive correspondence on the standardisation of iodine solutions by sodium thiosulphate has stressed the inadvisability of alkaline stabilisers for standard thiosulphate solutions, and the necessity for acid conditions in the titration.[208] A comprehensive review of the titrimetric uses of cerium(IV) solutions has been made.[209] L. S. Theobald and J. P. Stern [210] have recommended methods for preparing standard solutions of aluminium and zinc.[210] The stability of aqueous potassium ferrate solutions to light, temperature, and varying conditions of alkalinity and concentration has been examined.[211] Chloramine-T has been recommended as a more economical titrimetric reagent than iodine.[212] The use of standard stannous chloride,[213] potassium metaperiodate,[214] and manganese(III) [215]

---

[194] E. Gagliardi and R. Pietsch, *Monatsh.*, 1951, **82**, 656.

[195] A. P. Blackmore, M. A. Marks, R. R. Barefoot, and F. E. Beamish, *Analyt. Chem.*, 1952, **24**, 1815. [196] R. R. Barefoot and F. E. Beamish, *ibid.*, p. 840.

[197] W. J. Allan and F. E. Beamish, *ibid.*, p. 1608.

[198] *Idem, ibid.*, p. 1567. [199] E. Gagliardi and R. Pietsch, *Monatsh.*, 1951, **82**, 432.

[200] D. E. Ryan, *Analyst*, 1952, **77**, 46.

[201] P. Champ, P. Fauconnier, and C. Duval, *Analyt. Chim. Acta*, 1952, **6**, 250.

[202] "Neuere massanalytische Methoden," Ed. W. Böttger, 3rd edtn., Stuttgart, 1951.

[203] C. S. Rodden and C. G. Goldbeck, *Analyt. Chem.*, 1952, **24**, 102.

[204] W. Schöniger, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 456.

[205] W. I. Stephen, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 13, 55, 107.

[206] C. W. Sill and H. E. Peterson, *U.S. Bur. Min.*, 1952, Rep. Invest. 4882; *Analyt. Chem.*, 1952, **24**, 1175; J. M. Thompson, *ibid.*, 1632; E. R. Riegel and R. D. Schwartz, *ibid.*, p. 1803; J. A. Rahm, *ibid.*, p. 1832; C. C. Miller and R. A. Chalmers, *Analyst*, 1952, **77**, 2; P. Wehber and H. Hahn, *Z. anal. Chem.*, 1952, **136**, 321, 325; M. I. Kriventsov, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 384; E. Gagliardi and W. Pilz, *Monatsh.*, 1951, **82**, 1012.

[207] H. T. S. Britton, R. E. Cockaday, and J. K. Foreman, *J.*, 1952, 3877; H. T. S. Britton and H. G. Britton, *ibid.*, pp. 3879, 3887, 3892.

[208] R. Rands, *Chem. and Ind.*, 1952, 1001; J. J. Lamond, *ibid.*, p. 1128; A. I. Vogel, *ibid.*, p. 1177; T. A. H. Peacocke, *ibid.*, p. 1245.

[209] P. Young, *Analyt. Chem.*, 1952, **24**, 152.

[210] *Analyst*, 1952, **77**, 99.

[211] W. F. Wagner, J. R. Gump, and E. N. Hart, *Analyt. Chem.*, 1952, **24**, 1497.

[212] W. Poethke and F. Wolf, *Z. anorg. Chem.*, 1952, **268**, 244.

[213] Z. G. Szabó and E. Sugár, *Analyt. Chim. Acta.*, 1952, **6**, 293.

[214] B. Singh and A. Singh, *J. Indian Chem. Soc.*, 1952, **29**, 34.

[215] R. Belcher and T. S. West, *Analyt. Chim. Acta*, 1952, **6**, 322.

solutions as general titrimetric reagents has been described. R. H. Müller and A. M. Vogel[216] have recommended an instrument with temperature-compensation for the standardisation of titrimetric solutions by conductance measurements.

**Methods of Analysis.**—From a critical examination of methods for the estimation of hypochlorite, A. Lassieur and D. Jouslin[217] recommend titration with standard arsenious oxide solution using an internal indicator. Bromide ion may be oxidised to bromate by chlorine[218] or by hypochlorite[219] before iodometric determination. Iodide may be accurately titrated by permanganate,[220] and fluoride by zirconium solution.[221] Ammonia may be precipitated by Nessler's reagent, and the precipitate reduced to mercury, which is then treated with iodate-iodide and the liberated iodine estimated by thiosulphate.[222] Treatment of hydroxylamine with excess of cerium(IV) solution enables the compound to be determined by back titration with standard arsenic solution.[223] The estimation of nitrate by the method of Z. G. Szabó and L. Bartha[224] has been modified and converted to the micro-scale.[225] Azide may be determined by reduction to give an ammonia–nitrogen mixture in which the ammonia is estimated.[226]

The bromate titration of arsenic(III) has been studied,[227] and it is stated that significant errors occur except when the end-point acidity is maintained within the range 1·2—3·5N. Ozone may be determined iodometrically,[228] and peroxide by titration with permanganate.[229] Sulphite is oxidised to sulphate by hypochlorite, the excess of hypochlorite being estimated by an iodide–thiosulphate titration.[230] G. Denk[231] has shown that a direct alkalimetric titration for alkaline-earth metals is possible, and that this may in turn be applied to the indirect determination of sulphate. Titrimetric methods have been described for selenium[232, 233] and tellurium.[233, 234] A method for alkali carbonate and bicarbonate in the presence of each other utilises titration with standard barium chloride and back titration, after addition of excess of acid, with carbonate-free sodium hydroxide.[235] Cyanide may be titrated with standard nickel solution, murexide being used as indicator.[236]

The estimation of potassium as the tetraphenylboron compound[158] may

[216] *Analyt. Chem.*, 1952, **24**, 1590.

[217] A. Lassieur and D. Jouslin, *Chim. anal.*, 1951, **33**, 45.

[218] Z. G. Szabó and L. Csányi, *Analyt. Chim. Acta*, 1952, **6**, 208.

[219] M. R. Block, S. Kertes, and I. Schnerts, *Bull. Res. Council Israel*, 1952, **1**, No. 4, 82.

[220] S. A. Celsi and M. A. Copello, *Monit. Farm.*, 1951, **57**, 158.

[221] H. v. Zeppelin and J. Fuchs, *Angew. Chem.*, 1952, **64**, 223.

[222] H. Lestra and G. Roux, *Compt. rend.*, 1951, **233**, 1453.

[223] S. R. Cooper and J. B. Morris, *Analyt. Chem.*, 1952, **24**, 1360.

[224] *Ann. Reports*, 1951, **48**, 323.

[225] Z. G. Szabó and L. Bartha, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 413.

[226] L. P. Pepkowitz, *Analyt. Chem.*, 1952, **24**, 900.

[227] D. J. Kew, M. D. Amos, and M. C. Greaves, *Analyst*, 1952, **77**, 488.

[228] C. M. Birdsall, A. C. Jenkins, and E. Spadinger, *Analyt. Chem.*, 1952, **24**, 662.

[229] J. Mattner, *Z. anal. Chem.*, 1952, **135**, 415.

[230] B. L. Dunicz and T. Rosenquist, *Analyt. Chem.*, 1952, **24**, 404.

[231] *Z. anal. Chem.*, 1952, **137**, 99.

[232] G. S. Deshmukh and B. R. Sant, *Analyst*, 1952, **77**, 272.

[233] K. Geiersberger and A. Durst, *Z. anal. Chem.*, 1952, **135**, 11; K. Geiersberger, *ibid.*, pp. 15, 18.

[234] R. A. Johnson and D. R. Fredrickson, *Analyt. Chem.*, 1952, **24**, 866.

[235] D. Köszegi and E. Salgó, *Z. anal. Chem.*, 1952, **137**, 22.

[236] F. Huditz and H. Flaschka, *ibid.*, **136**, 185.

be completed titrimetrically instead of gravimetrically, an argentometric titration in acetone solution being used.[237] Interference from iron, aluminium, and chromium is masked by fluoride. The direct alkalimetric estimation of alkaline-earth metals [231] is possible in hot solution, with sodium carbonate, thymol-blue being used as indicator. Beryllium solutions may be titrated directly with barium hydroxide to a phenolphthalein end-point, or may be estimated by precipitating the hydroxide, treating this with potassium fluoride, and titrating the liberated alkali with standard acid.[238] Cadmium and zinc may be indirectly estimated with alkali, making use of the fact that the hydroxides or basic carbonates, when dissolved in sodium thiosulphate, liberate an equivalent amount of acid.[239] The salts of cadmium with strong acids may be titrated directly against sodium hydroxide to a cresolphthalein end-point.[240]

The effect of nitric acid on the iodometric determination of copper may be eliminated almost completely by addition of sufficient solid sulphamic acid to retain crystals in the solution throughout the titration.[241] L. Meites claims [242] that comparison shows that addition of sufficient excess of potassium iodide to retain cuprous iodide in solution is more satisfactory than the more usual method by which the iodide is precipitated. The increase in cost is held to be offset by the greater speed and accuracy attained. Gold may be titrated by using " dithizone," and interference from other metals can be overcome.[243] Alkaline aluminate solutions may be estimated by a double titration with standard acid and standard potassium fluoride solution.[244] The iodometric determination of copper described by R. O. Brasted [241] may be extended to deal simultaneously with the estimation of iron also present in the solution. The titration of iron with permanganate on the micro-scale has been found to be more satisfactory after reduction with stannous chloride than after use of the silver reductor.[245] Conditions for the iodometric determination of iron(III) have been established.[246] Ferrocyanide has been determined in the presence of cyanide by titration with cerium(IV),[247] and ferricyanide can first be reduced by metallic mercury and then titrated in the same way [248] since the presence of cyanide, or alternatively of thiocyanate, enhances the reducing power of the mercury. The same effect can be utilised in the reduction of iron(III), and appears to have some advantages over the use of amalgam reductors. Precipitated nickel dimethylglyoxime may be dissolved in acid, treated with excess of vanadate solution, and back titrated with iron(II) solution, phenylanthranilic acid being used as indicator.[249] Nickel may also be oxidised by persulphate, and the resulting compound estimated iodometrically.[250] Chromium(III) oxid-

---

[237] W. Rüdorff and H. Zannier, *Z. anal. Chem.*, 1952, **137**, 1.
[238] V. K. Zolutukhin, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 246.
[239] M. M. Tillu, *Analyt. Chem.*, 1952, **24**, 1495.
[240] G. Denk, *Z. anal. Chem.*, 1952, **136**, 336.
[241] R. O. Brasted, *Analyt. Chem.*, 1952, **24**, 1040. [242] *Ibid.*, p. 1618.
[243] L. Erdey and G. Rady, *Z. anal. Chem.*, 1952, **135**, 1.
[244] M. Beck and Z. G. Szabó, *Analyt. Chim. Acta*, 1952, **6**, 316.
[245] M. C. Alvarez Querol, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 126; F. de A. Bosch Ariño and M. C. Alvarez Querol, *Anal. real Soc. esp. Fís. Quím.*, 1952, **48**, *B*, 267.
[246] L. J. White, *Coke and Gas*, 1952, **14**, 285.
[247] F. Burriel Martí, F. Lucena-Conde, and S. Bolle, *Analyt. Chim. Acta*, 1952, **7**, 302.
[248] F. Burriel Martí, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 487.
[249] V. S. Syrokomsky and S. M. Gubelbank, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 207.
[250] E. S. Tomula, O. Juutinen, and P. Tanskanen, *Z. anal. Chem.*, 1952, **135**, 265.

ation by mixed perchloric–sulphuric acids is more complete in the presence of silver nitrate,[251] and the resulting chromium(VI) may then be estimated iodometrically without interference from precipitated silver iodide.

The iodometric determination of tin has been reviewed, and a procedure recommended.[252] Bronzes may be dissolved in acid and reduced by antimony powder, thus enabling the copper to be precipitated as cuprous thiocyanate before iodometric determination of tin(II).[253] Tin salts, when treated with sodium tartrate, liberate hydrogen ions which may then be estimated by titration to a phenolphthalein end-point.[254] Thorium may be precipitated as molybdate [255] and the molybdate reduced and titrated, or by selenious acid in the presence of ethanol [256] followed by an iodine–thiosulphate titration. Thorium may also be titrated directly against standard oxalic acid, alizarin-S being used as an internal indicator.[257] A direct titration of vanadate solution using standard silver nitrate is possible, with an alcoholic gallic acid test-paper as indicator.[258] Preliminary treatment and titration conditions for the estimation of vanadium in steels,[259] ferrovanadium,[260] and uranium [261] have been described.

**Indicators and Related Topics.**—R. G. Bates [262] has discussed the definition of pH and the uncertainty in the value as measured, relating this to the necessity for a more precise definition of the conditions of measurement than is usually given. Methods have been described for the calculation of the pH of solutions.[263] The desirable characteristics of an indicator have been discussed in terms of colour theory, and such processes as the screening of indicators have been examined in the light of ideal behaviour.[264] Colorimetric methods for the determination of pH have been described and discussed.[265]

A method for stabilising litmus solutions over a period of a year has been described.[266] *p*-Ethoxychrysoidine adsorbed on silver iodide has been recommended as an acid–base indicator.[267] The behaviour of a range of indicators with various compounds in chlorobenzene and other non-aqueous solvents has been examined.[268]

Investigation of a wide range of protective colloids for the retention of silver chloride in suspension, with dichlorofluorescein solution as indicator, has shown the best to be polyethylene glycol 400, a condensation product of ethylene oxide.[269] The protective colloids usually recommended—dextrin

---

[251] S. Lynn and D. M. Mason, *Analyt. Chem.*, 1952, **24**, 1855.
[252] A. Doadrio, *Inform. Quim. anal.*, 1952, **6**, 79.
[253] M. L. Malaprade, *Bull. Soc. chim.*, 1951, **18**, 739.
[254] V. K. Zolutukhin, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 300.
[255] C. V. Banks, *Iowa State Coll. J. Sci.*, 1951, **25**, 145.
[256] G. S. Desmukh and L. K. Swamy, *Analyt. Chem.*, 1952, **24**, 218.
[257] P. Venkateswarlu and A. N. Ramanathan, *Current Sci.*, 1952, **21**, 45.
[258] M. Nivoli, *Ann. Chim., Roma*, 1952, **42**, 370.
[259] Methods of Analysis Committee, *J. Iron Steel Inst.*, 1952, **171**, 81.
[260] *Idem, ibid.*, **170**, 343.
[261] S. H. Simonsen, *Analyt. Chim. Acta*, 1952, **7**, 33. [262] *Analyst.*, 1952, **77**, 653.
[263] J. Eeckhout, *Analyt. Chim. Acta*, 1952, **7**, 203; A. J. McBay, *J. Chem. Educ.*, 1952, **29**, 526. [264] J. King, *Analyst*, 1952, **77**, 742.
[265] T. B. Smith, C. A. White, P. Woodward, and P. A. H. Wyatt, *J.*, 1952, 3848; R. H. M. Simon, *Analyt. Chem.*, 1952, **24**, 1215.
[266] L. W. Cumming, *J. Pharm. Pharmacol.*, 1952, **4**, 324.
[267] E. Schulek and E. Pungor, *Analyt. Chim. Acta*, 1952, **7**, 446.
[268] R. V. Rice, S. Zuffanti, and W. F. Luder, *Analyt. Chem.*, 1952, **24**, 1022.
[269] R. B. Dean, W. C. Wiser, G. E. Martin, and D. W. Barnum, *ibid.*, p. 1638.

or gum arabic—may affect the end point significantly. Acid-violet 4BL [270] and acid-red 6B [271] have been recommended as indicators for silver titrations. The systems iron(III) with benzidine, tolidine, and *o*-dianisidine have been found satisfactory for the argentometric titration of bromides and iodides at great dilution [272] and for mercurous titration of chloride.[273]

Naphthidinesulphonic acid [274, 275] and 3 : 3′-dimethylnaphthidinesulphonic acid [274] have been recommended for a range of oxidation–reduction titrations, and their oxidation potentials have been established. Rhodamine-B has been proposed as a fluorescent indicator in iodometric titrations with coloured solutions,[276] although in straightforward titrations sodium starch glycollate is to be preferred to any other indicator examined.

Diphenylcarbazone screened with bromophenol-blue, which also permits adjustment of pH,[277] or with a nickel solution,[278] has been recommended as an indicator in mercuric titrations of chloride. Alternatively, the chloride may be treated with silver solution and mercuric solution, and diphenylcarbazone is used to indicate the end-point.[279] Conditions are described for the titration of zinc with ferrocyanide, diphenylthiocarbazone being used as indicator.[280]

## 6. CLASSICAL ORGANIC ANALYSIS.

**General.**—General microchemical methods,[281] volumetric methods in organic analysis,[282] the determination of metals in organic compounds,[283] and the determination of organic functional groups [284] have been reviewed. The use of derivative melting points [285] and general precautions to be taken in the small-scale preparation of derivatives [286] have been discussed.

**Qualitative.**—Methods have been proposed for the identification of amides and nitriles,[287] carbonyl compounds,[288] acids,[289] hydroxyquinones,[290] and steroids.[291]

**Quantitative.**—H. Goldberger and M. Pöhm [292] have described the weighing of hygroscopic liquid samples for combustion analysis. Stainless

---

[270] W. H. Weihe, *Klin. Wochenschr.*, 1952, **30**, 85.

[271] G. Mannelli and M. L. Rossi, *Analyt. Chim. Acta*, 1952, **6**, 333.

[272] F. Sierra and J. Hernández Cañavate, *Anal. real Soc. esp. Fís. Quím.*, 1952, **48**, *B*, 451, 457.

[273] F. Sierra and J. A. Sánchez Fernández, *ibid.*, p. 339.

[274] R. Belcher, A. J. Nutten, and W. I. Stephen, *J.*, 1952, 1269, 3857.

[275] G. W. C. Milner, *Analyt. Chim. Acta*, 1952, **6**, 226.

[276] L. Deibner, *Chim. anal.*, 1951, **33**, 207.

[277] G. B. Smit, *Analyt. Chim. Acta*, 1952, **7**, 330.

[278] J. S. Parsons and J. H. Yoe, *ibid.*, **6**, 217.

[279] J. Rodolfo Bayer, *Anal. Asoc. Quím. Argentina*, 1951, **39**, (193), 131.

[280] J. P. Mehlig and A. P. Guill, *Analyt. Chem.*, 1951, **23**, 1876.

[281] C. O. Willits and C. L. Ogg, *ibid.*, p. 70.

[282] W. T. Smith and R. E. Buckles, *ibid.*, p. 108.

[283] R. Belcher, D. Gibbons, and A. Sykes, *Mikrochem. Mikrochim. Acta*, 1952, **40**, 76.

[284] A. J. Nutten, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 273, 321; H. Lieb, *Chimia*, 1952, **6**, 34.

[285] M. Brandstätter and H. Thaler, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 358.

[286] N. D. Cheronis and A. Vavoulis, *ibid.*, p. 428.

[287] S. Soloway and A. Lipschitz, *Analyt. Chem.*, 1952, **24**, 898.

[288] L. Rosenthaler, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 360; C. Neuberg, A. Grauer, and B. V. Pisha, *Analyt. Chim. Acta*, 1952, **7**, 238; J. J. Ritter and M. J. Lover, *J. Amer. Chem. Soc.*, 1952, **74**, 5576; G. Uttolino and M. Valente, *Boll. Soc. ital. Biol. sper.*, 1951, **27**, 446.

[289] P. Clarke, *Chem. and Ind.*, 1952, 450.

[290] J. R. Anderson, K. G. O'Brien, and F. H. Reuter, *Analyt. Chim. Acta*, 1952, **7**, 226.

[291] H. Tauber, *Analyt. Chem.*, 1952, **24**, 1494.

[292] *Mikrochem. Mikrochim. Acta*, 1952, **39**, 73.

steel has been proposed [293] as a material suitable for making absorption tubes for semi-micro carbon–hydrogen determination. A. A. Sirotenko [294] reports that potassium persulphate should be mixed with the sample in carbon–hydrogen determinations on compounds containing alkali metals, in order to prevent the formation of stable alkali carbonates, and magnesium oxide pellets have been used [295] to retain silicon tetrafluoride and other objectionable combustion products from fluorine-containing compounds. Standard methods for carbon–hydrogen combustion have been modified by a number of workers.[296]

A furnace for use in the direct determination of oxygen has been described,[297] and detailed accounts of the method have been given.[298] The importance of proper preparation of the iodine pentoxide used for conversion of carbon monoxide into carbon dioxide in this determination has been stressed.[298, 299]

Specifications have been drawn up for apparatus for the combustion determination of halogens and sulphur.[300] Modifications of the standard combustion method for sulphur and halogens have been proposed.[301] A rapid combustion method for these elements, using apparatus which follows the general design of the rapid combustion method for carbon and hydrogen,[302] has been described.[303] A modified combustion method suitable for very small amounts of sulphur has been proposed.[304] The reactions resulting in the formation of silver sulphate in the sulphur determination [305] and those taking place in the decomposition of organic compounds with potassium [306] have been examined. Decomposition with magnesium has been recommended for compounds containing sulphur and nitrogen.[307] Wet oxidation methods for sulphur compounds have been proposed, using potassium chromate in phosphoric acid [308] or a nitric acid–hydrochloric acid mixture in the presence of sodium chloride with selenious acid as catalyst.[309]

Specifications have been given for the apparatus for determination of nitrogen by combustion,[310] and modifications of the Dumas method have

[293] J. A. Kuck and M. Arnold, *Mikrochem. Mikrochim. Acta*, 1951, 38, 521.

[294] *Ibid.*, 1952, 40, 30.

[295] W. H. Throckmorton and G. H. Hutton, *Analyt. Chem.*, 1952, 24, 2003.

[296] S. S. Israelstam, *Analyt. Chem.*, 1952, 24, 1207; O. G. Backeberg and S. S. Israelstam, *ibid.*, p. 1209; G. De Vries and E. van Dalen, *Analyt. Chim. Acta*, 1952, 7, 274; G. Kainz, *Mikrochem. Mikrochim. Acta*, 1952, 39, 166; G. Mangeney, *Bull. Soc. chim.*, 1951, 4, 809; V. A. Klimova and M. O. Korshun, *J. Anal. Chem., U.S.S.R.*, 1951, 6, 230; M. O. Korshun, *ibid.*, 1952, 7, 96; M. O. Korshun and N. S. Sheveleva, *ibid.*, p. 104.

[297] A. Steyermark, M. J. McNally, W. A. Wiseman, R. Nivens, and F. P. Biava, *Analyt. Chem.*, 1952, 24, 589.

[298] J. Unterzaucher, *Analyst*, 1952, 77, 584; *Ind. Chem. Chem. Manuf.*, 1952, 28, 492.

[299] E. G. Adams and N. T. Simmons, *J. Appl. Chem.*, 1951, Suppl. 1, S 20.

[300] B.S.I. Specif., 1952, No. 1428, Pt. A3.

[301] E. D. Peters, G. C. Rounds, and E. J. Agazzi, *Analyt. Chem.*, 1952, 24, 710; O. E. Sundberg and G. L. Royer, *ibid.*, p. 907; G. W. Perold, *S. Afr. Ind. Chem.*, 1951, 5, 135.

[302] R. Belcher and G. Ingram, *Analyt. Chim. Acta*, 1950, 4, 118.

[303] *Idem, ibid.*, 1952, 7, 319.

[304] F. Grassner, *Z. anal. Chem.*, 1952, 135, 186.

[305] M. O. Korshun, *J. Anal. Chem., U.S.S.R.*, 1952, 7, 101.

[306] G. Kainz and A. Resch, *Mikrochem. Mikrochim. Acta*, 1952, 39, 75.

[307] P. N. Fedoseev and N. P. Ivashova, *J. Anal. Chem., U.S.S.R.*, 1952, 7, 112, 116.

[308] D. Köszegi and J. Barcsay, *Z. anal. Chem.*, 1952, 135, 349.

[309] A. Steinbergs, *J. Aust. Inst. Agric. Sci.*, 1951, 17, 3, 155.

[310] B.S.I. Specif., 1952, No. 1428, Pt. A2.

been proposed.[311] The reactions taking place in the Dumas method have been discussed in some detail[312] and means of avoiding errors have been suggested.[313]

W. Kirsten[314] has described apparatus for the Kjeldahl method for nitrogen, and catalysts for the digestion process have been examined.[315] Reduction before digestion may be achieved by zinc and methanol[316] or thiosalicylic acid.[317] In describing a diffusion microgram method for nitrogen, B. W. Grunbaum, F. L. Schaffer, and P. L. Kirk[318] point out that, in spite of the mass of empirical information about the Kjeldahl digestion process, little fundamental information regarding it is available. Their experiments show that digestion in a sealed tube without a catalyst is quite satisfactory provided that the temperature is not allowed to rise above 450°, at which temperature the sulphuric acid begins to oxidise the ammonia with consequent loss. A diffusion method is also proposed by D. Seligson and H. Seligson.[319] M. Marzadro[320] shows how it is possible, by utilising the selective action of the Kjeldahl method together with the Dumas method, to distinguish between nuclear and extra-nuclear nitrogen in heterocyclic compounds.

The determination of phosphorus after decomposition in the Parr bomb has been described.[321] Halogens have been determined by combustion,[322] by potassium fusion,[323] by peroxide decomposition,[324] and by a modification of Vieböck's method.[325] Acid chlorides have been estimated by argentometric titration in acetone solution,[326] aliphatic halogens on aromatic side-chains by hydrolysis with alkali in ethylene glycol solution,[327] and halogen compounds have been reduced by hydrogen with a nickel catalyst in an aqueous-ethanolic alkalisolution.[328]

The reaction velocities of organic halides with amines have been claimed to have diagnostic value in the identification and determination of mono-halides and in the identification of more complex substances.[329] Iodine may be determined by reduction with zinc powder in sodium hydroxide solution, followed by titrimetric determination of the iodide.[330] The lead

---

[311] W. C. Alford, *Analyt. Chem.*, 1952, **24**, 881; H. Swift and E. S. Morton, *Analyst*, 1952, **77**, 392; H. Gysel, *Helv. Chim. Acta*, 1952, **35**, 802; W. Schöniger, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 229.

[312] Sheau-Shya Kao and W. C. Woodland, *ibid.*, 1951, **38**, 309; W. Kirsten, *ibid.*, 1952, **39**, 389.

[313] *Idem, ibid.*, p. 245; H. A. Pagel and I. J. Oita, *Analyt. Chem.*, 1952, **24**, 756.

[314] *Ibid.*, p. 1078.

[315] A. Mallol, *Anal. real Soc. esp. Fis. Quim.*, 1951, **47**, *B*, 659; S. Dahl and R. Oehler, *J. Amer. Leather Chem. Assoc.*, 1951, **46**, 317; G. Middleton and R. E. Stuckey, *J. Pharm. Pharmacol.*, 1951, **3**, 829; G. N. Badami and J. W. Whitaker, *Fuel, London*, 1951, **30**, 211.

[316] V. B. Fish, *Analyt. Chem.*, 1952, **24**, 760.

[317] P. McCutchan and W. F. Roth, *ibid.*, p. 369.

[318] *Ibid.*, p. 1487. [319] *J. Lab. Clin. Med.*, 1951, **38**, 324.

[320] *R. C. Ist. sup. Sanit.*, 1951, **14**, 668; *Mikrochem. Mikrochim. Acta*, 1951, **38**, 372.

[321] W. Perkow and H. Koddesbusch, *Z. anal. Chem.*, 1952, **136**, 189.

[322] W. Kirsten and I. Alperowicz, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 234.

[323] G. Kainz and A. Resch, *ibid.*, p. 1.

[324] *Idem, ibid.*, p. 292. [325] A. J. Nutten, *ibid.*, p. 355.

[326] D. Klamann, *Monatsh.*, 1952, **83**, 719.

[327] F. Buscarons and P. Mir, *Analyt. Chim. Acta*, 1952, **7**, 185.

[328] A. K. Ruzhentseva and V. V. Kolpakova, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 223.

[329] G. Salomon, *Analyst*, 1952, **77**, 1017.

[330] C. W. Ballard and S. Spice, *J. Pharm. Pharmacol.*, 1952, **4**, 322.

chlorofluoride method for the determination of fluorine has been adapted to provide a Volhard titration finish.[331]

Oxalic acid may be titrated with permanganate at room temperature in the presence of ferric alum.[332] Tartaric acid has been determined by treatment with excess of standard sodium vanadate solution and back titration with standard iron(II) solution.[333] A method has been described which is suitable for the simultaneous determination of aldehydes, ketones, and compounds such as acetals,[334] and methods for carbonyl compounds have been critically examined.[335] The necessity for close tolerances on the standard glass joints in methoxyl apparatus has been stressed.[336] A modification has been proposed for the van Slyke apparatus for determining amino-groups in which carbon dioxide is used as a sweeping gas.[337] Methods for the determination of reactive hydrogen have been reviewed.[338]

A method of titration referred to as " solubilisation titration " has been proposed for the analysis of binary mixtures which are not readily analysed by other methods.[339] This is based on phase changes in the presence of aqueous solutions of substances such as Teepol. Thus a hexane–octan-1-ol mixture is titrated with hexane–Teepol–water either to the point where a clear isotropic mixture results or where an aqueous phase just begins to deposit. These phase changes are readily detected, and provide precise end-points.

## 7. INSTRUMENTAL METHODS.

In a new edition of their book, H. H. Willard, L. L. Merritt, and J. A. Dean [340] present an up-to-date account of the more important branches of instrumental analysis, with full working descriptions of simple apparatus for applying the methods. The single drawback, for British users of the book, is that commercial models of apparatus described are of American origin, but this does not prevent the book from being a very valuable laboratory adjunct. Other reviews of instrumental operations in analytical chemistry, with special reference to automatic operations [341] and to work in the organic field,[342] have appeared. In the paper already referred to [7] R. H. Müller illustrates possible future developments by reference to some very recent types of apparatus and the requirements which led to their construction.

**Electroanalysis.**—Recent developments have been reviewed.[343] An indirect method for the determination of mixed halides has been devised [344] which is based on precipitation of the silver halides, solution of these in

---

[331] R. Belcher, E. F. Caldas, and S. J. Clark, *Analyst*, 1952, **77**, 602.

[332] G. E. Mapstone and J. W. Smith, *Chem. and Ind.*, 1952, 856.

[333] G. G. Rao and H. Sankegowda, *Current Sci.*, 1952, **21**, 188.

[334] R. H. Buchanan, *Austr. J. Appl. Sci.*, 1951, **2**, 276.

[335] J. J. Perret, *Helv. Chim. Acta*, 1951, **34**, 1531.

[336] R. L. Huang and F. Morsingh, *Analyt. Chem.*, 1952, **24**, 1359; C. A. Redfarn and D. R. Newton, *Chem. and Ind.*, 1952, 404, 857; R. G. Stuart, *ibid.*, p. 520; W. McCorkindale and A. C. Syme, *ibid.*, p. 758; G. Weston, *ibid.*, p. 1059.

[337] A. S. Hussey and J. E. Maurer, *Analyt. Chem.*, 1952, **24**, 1642.

[338] F. D. Olleman, *ibid.*, p. 1425.

[339] E. C. Lumb and P. A. Winsor, *Analyst*, 1952, **77**, 1012.

[340] " Instrumental Methods of Analysis," 2nd edtn., New York, 1951.

[341] G. D. Patterson and G. Mellon, *Analyt. Chem.*, 1952, **24**, 131.

[342] R. L. Peck and P. H. Gale, *ibid.*, p. 116.

[343] S. E. Q. Ashley, *ibid.*, p. 91. [344] R. Fort, *Chim. analyt.*, 1952, **34**, 143.

cyanide solution, and electrochemical deposition of the silver. Electrodeposition methods have been described for the determination of copper in ferrotitanium,[345] and of copper and silver in alloys containing the two metals.[346] Manganese can be deposited on a mercury cathode from aqueous solution and thus estimated.[347] Plutonium can be electrodeposited on platinum.[348]

Controlled potential analysis has been applied to copper-base alloys[349] and to mixtures of copper, bismuth, lead, and tin.[350] Internal electrolysis has been used for the determination of copper in steel.[351]

**Coulometry and Related Methods.**—In a general consideration of the application of polarisation curves to electrochemical processes, the use of these curves and other factors in deducing conditions for coulometric and potentiometric analysis is discussed.[352] P. Delahay[353] has dealt with the relation between equilibrium potentials and the irreversibility of electrode processed in relation to coulometric titrations. Coulometric methods have been developed for cerium(IV), dichromate, permanganate, and vanadium(V),[354] iron(II) and arsenic(III),[355] silver,[356] thallium(I),[357] manganese,[358] and uranium.[359] Titanium(IV) chloride has been recommended as an intermediate in coulometric titrations which provides a more powerful couple than those hitherto reported, and hence permits the method to be more widely applied.[360] Inner electrolysis has been applied on a time basis to the titration of manganese and other elements.[361] Low concentrations of oxygen have been measured by the capacity of a cell in which the gas surrounds a platinum electrode to form one of the units.[362]

**Polarography.**—Probably the most significant contribution to this branch is the new edition of the standard work by I. M. Kolthoff and J. J. Lingane,[363] which is approximately doubled in size. Polarography has been reviewed,[364] and in a review of the polarography of organic compounds J. E. Page[365] gives an excellent introduction to general aspects of the subject. Theoretical aspects of polarographic currents have been discussed.[366] The application of square-wave polarography to the detection

---

[345] L. Bonnafous, *Chim. analyt.*, 1952, **34**, 176.

[346] H. Diehl and J. P. Butler, *Analyst*, 1952, **77**, 268.

[347] B. McDuffie and L. S. Hazlegrove, *Analyt. Chem.*, 1952, **24**, 826.

[348] H. W. Miller and R. J. Brouns, *ibid.*, p. 536.

[349] G. W. C. Milner and R. N. Whittem, *Analyst*, 1952, **77**, 11.

[350] J. J. Lingane and S. L. Jones, *Analyt. Chem.*, 1952, **24**, 1798.

[351] D. L. Carpenter and A. D. Hopkins, *Analyst*, 1952, **77**, 86.

[352] R. Gauguin, G. Charlot, and J. Coursier, *Analyt. Chim. Acta*, 1952, **7**, 172; R. Gauguin, G. Charlot, C. Bertin, and J. Badoz, *ibid.*, p. 360; R. Gauguin and G. Charlot, *ibid.*, p. 408; R. Gauguin, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 487.

[353] *Analyt. Chim. Acta*, 1952, **6**, 542. [354] L. Meites, *Analyt. Chem.*, 1952, **24**, 1057.

[355] W. M. MacNevin and B. B. Baker, *ibid.*, p. 986.

[356] S. S. Lord, R. C. O'Neill, and L. B. Rogers, *ibid.*, p. 209.

[357] R. P. Buck, P. S. Farrington, and E. H. Swift, *ibid.*, 1195.

[358] W. D. Cooke, C. N. Reilley, and N. H. Furman, *ibid.*, p. 205.

[359] N. H. Furman, C. E. Bricker, and R. V. Dilts, *Nuclear Sci. Abstr.*, 1952, **6**, 179.

[360] P. Arthur and J. F. Donahue, *Analyt. Chem.*, 1952, **24**, 1612.

[361] A. Schleicher, *Z. anal. Chem.*, 1952, **136**, 330; W. Oelsen, H. Haase, and G. Graue, *Angew. Chem.*, 1952, **64**, 76.

[362] P. Hersch, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 488.

[363] " Polarography," 2nd edtn., New York and London, 1952.

[364] J. A. Lewis, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 531.

[365] *Quart. Reviews*, 1952, **6**, 262.

[366] P. Delahay and G. L. Stiehl, *J. Amer. Chem. Soc.*, 1952, **74**, 3500; P. Delahay, *ibid.*, p. 3506; P. Delahay and T. J. Adams, *ibid.*, p. 5740; S. L. Miller, *ibid.*, p. 4130.

and determination of very low concentrations of ions, of the order of $10^{-7}$ to $10^{-9}$M, has been described.[367] W. Furness[368] has discussed the desirability of more precise measurement of the diffusion current and potential of the dropping-mercury electrode, and has suggested methods by which this may be achieved. Recording apparatus suitable for polarography has been described.[369] J. Heyrovsky[370] has instanced advantages of using a cathode-ray oscilloscope for qualitative analysis by means of potential–time curves. A rotating mercury electrode which combines advantages of the dropping-mercury and of the rotating-platinum electrode, though with certain consequent disadvantages, is stated[371] to be applicable to the analysis of materials at very low concentrations. A method of differential polarography using a single dropping electrode has been proposed.[372]

Individual polarographic methods have been proposed for the determination of fluoride by complexing with aluminium and estimation of the excess of aluminium,[373] of sulphate by conversion into cadmium sulphide and determination of cadmium,[374] of tetrathionate,[375] of potassium by precipitation with excess of dipicrylamine,[376] of germanium,[377] of copper-base alloys,[378] of trace elements in lead[379] and in oils,[380] of copper by excess of quinaldinic acid,[381] of silver,[382] of indium,[383] of iron,[384] of chromium,[385] of molybdenum,[386] and of titanium.[387]

Recent developments in organic polarography have been reviewed,[365, 388] and polarographic methods of determination have been proposed for acraldehyde,[389] formaldehyde,[390] and glucose.[391] Polarographic studies have been made of some heterocyclic nitrogen compounds[392] and some dyes.[393] G. E. O. Proske[394] has proposed the use of certain wetting agents such as the dialkyl sodium sulphosuccinates, which have little effect on polarographic waves, for the solubilisation of organic compounds which are insoluble in water, thus enabling polarographic determinations to be carried

[367] G. C. Barker and I. L. Jenkins, *Analyst*, 1952, **77**, 685. [368] *Ibid.*, pp. 246, 345.

[369] E. B. Thomàs and R. J. Nook, *J. Chem. Educ.*, 1952, **29**, 414; M. T. Kelley and H. H. Miller, *Nuclear Sci. Abstr.*, 1952, **6**, 148; *Analyt. Chem.*, 1952, **24**, 1895.

[370] *Ind. Chem. Chem. Manuf.*, 1952, **28**, 489.

[371] T. S. Lee, *J. Amer. Chem. Soc.*, 1952, **74**, 5001.

[372] M. Ishibashi and T. Fuginaga, *Bull. Chem. Soc. Japan*, 1952, **25**, 68.

[373] B. J. MacNulty, G. F. Reynolds, and E. A. Terry, *Nature*, 1952, **169**, 888.

[374] A. D. Horton and P. F. Thomason, *Analyt. Chem.*, 1951, **23**, 1859.

[375] W. Furness and W. C. Davies, *Analyst*, 1952, **77**, 697.

[376] D. Monnier and Z. Besso, *Analyt. Chim. Acta*, 1952, **7**, 380.

[377] D. Cozzi and S. Vivarelli, *Mikrochem. Mikrochim. Acta*, 1952, **40**, 1.

[378] W. E. Allsopp and T. E. Arthur, *Analyt. Chem.*, 1951, **23**, 1883.

[379] F. Burriel Martí and J. F. Sáiz del Río, *Anal. real Soc. esp. Fís. Quím.*, 1951, **47**, *B*, 803.

[380] O. I. Milner, J. R. Glass, J. P. Kirchner, and A. N. Yurick, *Analyt. Chem.*, 1952, **24**, 1728.

[381] P. E. Wenger, D. Monnier, and L. Epars, *Helv. Chim. Acta*, 1952, **35**, 561.

[382] G. C. B. Cave and D. N. Hume, *Analyt. Chem.*, 1952, **24**, 588.

[383] G. Rienäcker and E. Hoschek, *Z. anorg. Chem.*, 1952, **268**, 260.

[384] L. Meites, *Analyt. Chem.*, 1952, **24**, 1374.

[385] E. C. Mills and S. E. Hermon, *Metallurgia*, 1951, **44**, 327.

[386] M. G. Johnson and R. J. Robinson, *Analyt. Chem.*, 1952, **24**, 366.

[387] R. P. Graham and A. Hitchen, *Analyst*, 1952, **77**, 533.

[388] S. Wawzonek, *Analyt. Chem.*, 1952, **24**, 32.

[389] A. S. Kirillova and I. A. Korshunov, *J. Anal. Chem.*, *U.S.S.R.*, 1951, **6**, 257.

[390] A. S. Bogorad and S. N. Aleksandrov, *ibid.*, p. 276.

[391] R. N. Adams, C. N. Reilley, and N. H. Furman, *Analyt. Chem.*, 1952, **24**, 1200.

[392] R. C. Kaye and H. I. Stonehill, *J.*, 1952, 3240.

[393] *Idem, ibid.*, pp. 3231, 3244. [394] *Analyt. Chem.*, 1952, **24**, 1834.

out. A polarographic study of certain metal salts and a number of acid chlorides in non-aqueous solution has been carried out, and the difficulties normally encountered in such work have been discussed.[395]

**Amperometric Titrations.**—Recent work has been reviewed.[396] Methods have been proposed for the determination of fluoride through a decrease in the diffusion current from an aluminium–organic complex,[397] for the determination of iodine,[398] of potassium with sodium dipicrylaminate,[399] and of zinc with potassium ferrocyanide.[400]

**Potentiometric Titrations.**—The mechanism of the dead-stop end-point has been discussed,[401] and it has been shown that the method ought to be applicable to any oxidation–reduction system by choosing suitable conditions. G. Gran [402] has described a method, applicable to all types of potentiometric titrations, by which end-points which are not normally well-defined may be represented precisely by transforming the curves into intersecting straight lines. E. Bishop [403] has proposed the use of " indicator-reference " electrodes, thus simplifying the apparatus in potentiometric titrations, and has extended the method to deal with non-aqueous as well as aqueous solutions.

Peroxides have been determined iodometrically.[404] Small amounts of chloride have been estimated by making use of two half-cells which differ only in the chloride content due to the unknown [405] or by precipitating the chloride with iodide as carrier, the iodide being removed before titration.[406] The errors involved in the potentiometric titration of mixtures of halides with silver nitrate have been studied.[407] Methods have been proposed for the argentometric titration of mixtures of bromides and thiocyanates,[408] for the mercurimetric titration of bromide,[409] for the cerimetric titration of hypophosphate,[410] for the estimation of phosphate by precipitation as zinc phosphate and titration of the acid liberated,[411] of thiocyanate using a silver thiocyanate electrode,[412] of rubidium and cæsium as chlorides argentometrically,[159] of magnesium by addition of excess of fluoride and titration of the excess with ferric chloride,[413] of cadmium by applying an empirical factor in the bromate–bromide titration of 2-*o*-hydroxyphenylbenzoxazole,[161, 414] of copper in the presence of oxidising anions iodometrically,[415] of

---

[395] P. Arthur and H. Lyons, *ibid.*, p. 1422.

[396] H. A. Laitinen, *ibid.*, p. 46; T. D. Parks, *Analyt. Chim. Acta*, 1952, **6**, 553.

[397] C. R. Castor and J. H. Saylor, *Analyt. Chem.*, 1952, **24**, 1369.

[398] H. P. Kramer, W. A. Moore, and D. G. Ballinger, *ibid.*, p. 1892.

[399] Y. Yasumori, *Bull. Chem. Soc. Japan*, 1951, **24**, 107.

[400] A. L. Woodson, B. H. Johnson, and S. R. Cooper, *Analyt. Chem.*, 1952, **24**, 1198.

[401] K. G. Stone and H. G. Scholten, *ibid.*, p. 671; J. E. B. Randles, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 490.

[402] *Analyst*, 1952, **77**, 661. [403] *Ibid.*, p. 672.

[404] E. W. Abrahamson and H. Linschitz, *Analyt. Chem.*, 1952, **24**, 1355.

[405] W. J. Blaedel, W. B. Lewis, and J. W. Thomas, *ibid.*, p. 509.

[406] G. S. Spicer and J. D. H. Strickland, *Analyt. Chim. Acta*, 1952, **6**, 493.

[407] H. Chateau and J. Pouradier, *Compt. rend.*, 1952, **234**, 623.

[408] C. Léon, *ibid.*, 1951, **233**, 170.

[409] F. Sierra and O. Carpena, *Anal. real Soc. esp. Fis. Quim.*, 1951, **47**, *B*, 527.

[410] T. Moeller and G. H. Quinty, *Analyt. Chem.*, 1952, **24**, 1354.

[411] R. N. Bell, A. R. Wreath, and W. T. Curless, *ibid.*, p. 1997.

[412] R. N. Parida, S. Aditya, and B. Prasad, *J. Indian Chem. Soc.*, 1952, **29**, 377.

[413] W. Mannchen, *Metal Abstr.*, 1952, **19**, 795.

[414] J. L. Walter and H. Freiser, *Analyt. Chem.*, 1952, **24**, 1985.

[415] J. Bernal Nievas and L. Serrano Berges, *Anal. real Soc. esp. Fis. Quim.*, 1951, **47**, *B*, 601.

manganese, chromium, and vanadium in steels,[416] of chromium and iron in chromite ores,[417] of iron(III) by titration with mercurous solution,[418] of tungsten with chromous chloride,[419] of uranium cerimetrically,[420] and of thorium as molybdate.[255]

**Conductance Methods.**—In the last few years methods have been proposed for high-frequency titrations in addition to the normal methods for conductimetric titrations; and high-frequency conductance measurements are being used in ways other than titrimetric for analytical purposes. A simple apparatus for conductimetric titration has been described.[421] A conductimetric titration method has been proposed for the determination of free acid in the presence of hydrolysable salts, and is applicable both to very small aliquots of solution and to solutions of low concentration, so that it is recommended for the titration of highly radioactive solutions.[422] The sulphate titration with barium solution has been studied, and it is pointed out [423] that the conductimetric end-point and the true equivalence-point are not necessarily coincident, the former being affected by composition and concentration of the solution. Such divergence should be taken into account in precise work. Potassium perchlorate titrations are suitable for conductance measurements.[424] A method is described by which calcium and strontium occurring together may be determined by conductance measurement, without titration.[425] R. P. Taylor and N. H. Furman [426] have reported favourably on the possibility of using direct rather than alternating current for conductance measurements, and have devised an apparatus which does not require either the specialised or inconvenient equipment necessary for alternating-current measurements. The accuracy and precision of this apparatus, as applied to several different conductimetric determinations, compare favourably with those of the more normal methods.

Theoretical and practical aspects of chemical analysis by high-frequency conductance measurements have been discussed.[427] P. W. West has described an apparatus suitable for both titrimetric and concentration determinations,[428] and simple apparatus which could be set up and maintained in the ordinary laboratory has also been described.[429] The high-frequency titration of sulphates [430] and of calcium [431] has been reported.

**Colorimetry and Absorptiometry.**—A new edition of a standard work has appeared.[432] General colorimetric methods have been reviewed.[433] A

[416] F. Burriel Martí and R. Suárez Acosta, *Inform. Quím. anal.*, 1951, **5**, 159; P. Enghag, *J. Iron Steel Inst.*, 1952, **171**, 443.

[417] D. Zivanović, *Bull. Soc. chim. Belgrade*, 1951, **16**, 151.

[418] R. Belcher and T. S. West, *Analyt. Chim. Acta*, 1952, **7**, 470.

[419] S. E. S. El Wakkad and H. A. M. Rizk, *Analyst*, 1952, **77**, 161.

[420] R. B. Hahn and M. T. Kelley, *Nuclear Sci. Abstr.*, 1952, **6**, 211.

[421] R. Weiner and L. Koller, *Z. anal.* Chem., 1952, **136**, 241.

[422] L. P. Pepkowitz, W. W. Sabot, and D. Dutina, *Analyt. Chem.*, 1952, **24**, 1956.

[423] D. Lydersen and O. Gjems, *Z. anal. Chem.*, 1952, **137**, 189.

[424] R. Weiner and L. Koller, *ibid.*, p. 246.

[425] G. O. Assarsson and A. Balder, *Analyt. Chem.*, 1952, **24**, 1679.

[426] *Ibid.*, p. 1931.

[427] W. J. Blaedel, T. S. Burkhalter, D. G. Flom, G. Hare, and F. W. Jensen, *ibid.*, p 198; J. L. Hall, *ibid.*, p. 1236; W. J. Blaedel, H. V. Malmstadt, D. L. Petitjean, and W. K. Anderson, *ibid.*, p. 1240. [428] *Ind. Chem. Chem. Manuf.*, 1952, **28**, 492.

[429] J. L. Hall, *Analyt. Chem.*, 1952, **24**, 1244.

[430] O. I. Milner, *ibid.*, p. 1247. [431] S. Musha, *Sci. Rep. Tôhoku*, 1951, *A*, **3**, 55.

[432] B. Lange, " Kolorimetrische Analyse," 4th edtn., Weinheim, 1952.

[433] M. G. Mellon, *Analyt. Chem.*, 1952, **24**, 924; E. Geffroy, *Chim. analyt.*, 1952, **34**, 119.

capillary colorimeter for very small amounts of material[434] and a photoelectric comparator have been described.[435] Means of improving precision have been suggested,[436] and the fallacy of assuming that addition of a known amount of constituent to a trace sample will improve the precision by bringing the final amount out of the region of high relative analysis error has been pointed out.[437] Methods of dealing with two-component colour systems[438] and with turbid solutions[439] have been discussed. Filters for the mercury lines have been described,[440] and alkaline potassium chromate has been recommended as a transmittancy standard for work in the ultraviolet.[441]

Absorptiometric methods of analysis have been put forward for alloys[442] and for trace metals in petroleum fractions.[443] Individual analytical methods have been described for fluoride by its bleaching effect on various lakes,[444] for hydrazine by *p*-dimethylaminobenzaldehyde,[445] for high nitrate content by phenoldisulphonic acid,[446] for phosphorus as molybdate[447, 448] or as vanadate–molybdate,[449] for arsenic as molybdate.[450, 451]

Oxygen in metallic tin is estimated by removing the metal with mercury and estimating the tin in the residual oxide by phosphomolybdate,[452] and gaseous oxygen is determined by the colour given with alkaline pyrogallol.[453] Metal sulphide sols have been examined for the estimation of sulphur, and a method for preparing a satisfactory bismuth sulphide sol is given.[454] Sulphur may also be estimated by conversion into methylene-blue[455] or into Lauth's violet.[456] Colorimetric procedures have been described for selenium and tellurium,[233] for cyanide by reduction of sodium picrate,[457] and for boron by 1 : 1-dianthraquinoylamine,[458] quinalizarin,[459] or pentamethylquer-

---

[434] G. Gorbach, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 204.

[435] T. F. Stanton, *Fuel, London*, 1951, **30**, 208.

[436] F. F. Pollak and J. W. Nicholas, *Metallurgia*, 1951, **44**, 319.

[437] W. A. E. MacBryde, *Analyt. Chem.*, 1952, **24**, 1639.

[438] E. Allen and E. M. Hammaker, *ibid.*, p. 1295; R. G. Milkey, *ibid.*, p. 1675.

[439] J. Fog, *Analyst*, 1952, **77**, 454.

[440] J. W. Nicholas and F. F. Pollak, *Analyst*, 1952, **77**, 49; J. Chance, E. Guillemot, J. Lenoble, and G. Tendron, *Compt. rend.*, 1951, **233**, 35.

[441] G. K. Haupt, *J. Opt. Soc. Amer.*, 1952, **42**, 441.

[442] G. W. C. Milner and W. R. Nall, *Analyt. Chim. Acta*, 1952, **6**, 420; M. Jean, *ibid.*, **7**, 338.

[443] J. H. Karchmer and E. L. Gunn, *Analyt. Chem.*, 1952, **24**, 1733.

[444] A. D. Horton, P. F. Thomason, and F. J. Miller, *ibid.*, p. 548; M. J. Price and O. J. Walker, *ibid.*, p. 1593; H. E. Bumsted and J. C. Wells, *ibid.*, p. 1595.

[445] G. W. Watt and J. D. Chrisp, *ibid.*, p. 2006.

[446] J. M. Komarmy, W. J. Broach, and M. K. Testerman, *Analyt. Chim. Acta*, 1952, **7**, 349.

[447] G. R. Nakamura, *Analyt. Chem.*, 1952, **24**, 1372.

[448] W. Teichert, *J. Iron Steel Inst.*, 1952, **170**, 181.

[449] S. Gericke and B. Kurmies, *Z. anal. Chem.*, 1952, **137**, 15.

[450] J. C. Bartlet, M. Wood, and R. A. Chapman, *Analyt. Chem.*, 1952, **24**, 1821; C. Wadelin and M. G. Mellon, *Analyst*, 1952, **77**, 708; Y. Kakita, *Sci. Rep. Tôhoku*, 1951, **3**, *A*, 698.

[451] W. C. Coppins and J. W. Price, *Metallurgia*, 1952, **46**, 52.

[452] L. Silverman, *Nuclear Sci. Abstr.*, 1952, **6**, 145.

[453] C. H. Blachly and R. R. Miller, *Anal. Chem.*, 1952, **24**, 1819.

[454] E. Treiber, H. Koren, and W. Gierlinger, *Mikrochem. Mikrochim. Acta*, 1952, **40**, 32.

[455] M. S. Budd and H. A. Bewick, *Analyt. Chem.*, 1952, **24**, 1536.

[456] D. S. C. Polson and J. D. H. Strickland, *Analyt. Chim. Acta*, 1952, **6**, 452.

[457] F. B. Fisher and J. S. Brown, *Analyt. Chem.*, 1952, **24**, 1440.

[458] D. A. Brewster, *ibid.*, 1951, **23**, 1809.

[459] D. MacDougall and D. A. Biggs, *ibid.*, 1952, **24**, 566.

cetin.[460] Silicon may be determined as silicomolybdate,[461, 462] and germanium with quinalizarin.[463]

Methods for the determination of potassium have been reviewed,[464] and methods based on chloroplatinate [465] and silver cobaltinitrite [466] have been described. Methods for the determination of sodium have been reviewed.[467] Colorimetric methods for calcium using murexide,[468] chloranilic acid,[469, 470] or the reaction of oxalate with diphenylamine to give aniline-blue [471] have been examined. Methods for beryllium use aluminon,[472] acetylacetone,[62] or morin.[473] Magnesium has been estimated by using Eriochrome-cyanine-R (Solochrome-cyanine-RS),[474] Titan-yellow,[474, 475] 3-hydroxy-1-*p*-nitrophenyl-3-phenyltriazen,[476] 8-hydroxyquinoline,[477] or the complex formed by 8-hydroxyquinoline and iron.[478] Zinc has been determined by *o*-[α-(2-hydroxy-5-sulphophenylazo)benzylidenehydrazino]benzoic acid.[479] For cadmium [480] and mercury [481] diphenylthiocarbazone has been used. Mercury has also been determined by its effect on the colour of ferric thiocyanate solution.[482]

Copper has been estimated as tartrate,[483] by diethyldithiocarbamate,[484] by rubeanic acid,[485] and by bis*cyclo*hexanone oxalyldihydrazone; [486] silver by *p*-dimethylaminobenzylidenerhodanine; [487] gold by diphenylamine [488] or by diphenylthiocarbazone; [243] aluminium by Eriochrome-cyanine-R,[489] by 8-hydroxyquinoline,[490, 491] or by aluminon; [492] manganese as per-

[460] M. K. Urs and K. Neelakantam, *J. Sci. Ind. Res., India*, 1952, **11**, *B*, 259.

[461] J. R. Boyd, *Analyt. Chem.*, 1952, **24**, 805.

[462] A. B. Carlson and C. V. Banks, *ibid.*, p. 472.

[463] C. K. N. Nair and J. Gupta, *J. Sci. Ind. Res., India*, 1951, **10**, *B*, 300; 1952, **11**, *B*, 274.

[464] T. S. West, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 158.

[465] R. E. Eckel, *J. Biol. Chem.*, 1952, **195**, 191.

[466] E. M. Chenery, *Analyst*, 1952, **77**, 102.

[467] T. S. West, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 225.

[468] H. Ostertag and É. Rinck, *Compt. rend.*, 1951, **232**, 629; *Chim. analyt.*, 1952, **34**, 108; J. Raaflaub, *Z. physiol. Chem.*, 1951, **288**, 228.

[469] F. Koroleff, *Suomen Kem.*, 1951, **60**, 56.

[470] R. F. U. Frost-Jones and J. T. Yardley, *Analyst*, 1952, **77**, 468.

[471] J. de la Rubia Pacheco and F. Blasco López-Rubio, *Inform. Quím. analít.*, 1952, **6**, 40.

[472] C. L. Luke and M. E. Campbell, *Analyt. Chem.*, 1952, **24**, 1056.

[473] T. Y. Toribara and P. S. Chen, *ibid.*, p. 539.

[474] A. Bacon, *Metallurgia*, 1951, **44**, 207.

[475] O. Glemser and W. Dautzenberg, *Z. anal. Chem.*, 1952, **136**, 254; A. C. Mason, A.R.E. Malling Res. Sta., 1951, 126.

[476] K. N. Pochinok and V. Y. Pochinok, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 288.

[477] J. Davidson, *Analyst*, 1952, **77**, 263.

[478] R. Bittel, *Ann. nat. Inst. rech. Agron.*, 1951, **1**, *A*, 144.

[479] J. H. Yoe and R. M. Rush, *Analyt. Chim. Acta*, 1952, **6**, 526.

[480] L. Silverman and K. Trego, *Analyst*, 1952, **77**, 143.

[481] D. J. S. Gray, *ibid.*, p. 436.

[482] R. O. Brumblay, *Analyt. Chem.*, 1952, **24**, 905.

[483] M. Bobtelsky and C. Heitner, *Bull. Soc. chim.*, 1951, **18**, 502.

[484] J. L. Hague, E. D. Brown, and H. A. Bright, *J. Res. Nat. Bur. Stand.*, 1951, **47**, 380; C. A. Noll and L. D. Betz, *Analyt. Chem.*, 1952, **24**, 1894.

[485] A. Lemoine, *Analyt. Chim. Acta*, 1952, **6**, 528; W. L. Miller, M. Acampora, and G. Norwitz, *Metal Abstr.*, 1952, **19**, 856.

[486] C. U. Wetlesen and G. Gran, *Svensk Papperstidning*, 1952, **55**, 212.

[487] G. C. B. Cave and D. N. Hume, *Analyt. Chem.*, 1952, **24**, 1503; E. B. Sandell and J. J. Neumayer, *ibid.*, 1951, **23**, 1863.

[488] P. A. Heredia and J. C. Cuezzo, *Monit. Farm.*, 1951, **57**, 361.

[489] L. C. Ikenberry and A. Thomas, *Analyt. Chem.*, 1951, **23**, 1806; A. Bacon, *Analyst*, 1952, **77**, 90.

[490] W. Sprain and C. V. Banks, *Analyt. Chim. Acta*, 1952, **6**, 363.

[491] O. A. Kenyon and H. A. Bewick, *Analyt. Chem.*, 1952, **24**, 1826.

[492] C. L. Luke and K. C. Braun, *ibid.*, p. 1120; C. L. Luke, *ibid.*, p. 1122.

manganate,[461, 493, 494, 495] or through permanganate by the starch–iodide blue;[448] and rhenium as tetraphenylarsonium perrhenate.[496]

Iron has been estimated as acetate[497] or thiocyanate,[495, 498, 499] or by 8-hydroxyquinoline,[500] thioglycollic acid,[493] 1 : 10-phenanthroline,[380, 490, 501] 4 : 7-diphenyl-1 : 10-phenanthroline,[502] or 1 : 2-dihydroxybenzene-3 : 5-disulphonic acid;[503] cobalt as tartrate[483] or thiocyanate,[504] or by nitroso-R salt,[504, 505] diphenylthiocarbazone,[506] peroxide–bicarbonate treatment,[507] *iso*nitrosomalonylguanidine,[64] ethylenediaminetetra-acetic acid,[64] or 4-nitro-2-mercaptoacetamidophenol;[129] nickel as tartrate[483] or with dimethylglyoxime;[380, 493, 508] chromium as dichromate[509] or with diphenylcarbazide;[510] molybdenum by thiocyanate,[511, 515] protocatechualdehyde,[512] or 1 : 2-dihydroxybenzene-3 : 5-disulphonic acid;[513] tungsten by treatment with thiocyanate and stannous chloride;[514] uranium by thiocyanate[516] or by resacetophenone;[517] tin by 4-methyl-1 : 2-dimercaptobenzene (toluenedithiol) stabilised by Teepol;[518] lead by diphenylthiocarbazone;[519] titanium as pertitanate[498] or by thymol,[520] 1 : 2-dihydroxybenzene-3 : 5-disulphonic acid,[503] or chromotropic acid;[521] zirconium by precipitation as phosphate and conversion into phosphomolybdate,[522] by alizarin-S,[523] or by chloranilic acid;[470] thorium by *o*-arsenophenylazo-2-naphthol-3 : 6-disulphonic acid;[524] antimony as the iodoantimonite complex,[451] by

[493] G. W. C. Milner and H. Groom, *Metallurgia*, 1951, **44**, 271.

[494] B.S.I. Specif., 1951, No. 1121, Pt. 23.

[495] N. M. Silverstone and D. W. D. Showell, *Metal Ind.*, 1952, **80**, 467.

[496] S. Tribalat, I. Pamm, and M. L. Jungfleisch, *Analyt. Chim. Acta*, 1952, **6**, 142.

[497] W. Reiss, J. F. Hazel, and W. M. McNabb, *Analyt. Chem.*, 1952, **24**, 1646.

[498] H. Seiser, *Ber. deut. keram. Ges.*, 1951, **28**, 699.

[499] W. Teichert, *J. Iron Steel Inst.*, 1952, **170**, 181.

[500] A. G. Hamlin, *J. Text. Inst.*, 1952, **43**, T, 234.

[501] A. Gottlieb, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 176.

[502] G. F. Smith, W. H. McCurdy, and H. Diehl, *Analyst*, 1952, **77**, 418.

[503] R. H. Beaumont, *Nuclear Sci. Abstr.*, 1952, **6**, 212.

[504] W. A. C. Campen and H. Geerling, *Chem. Weekblad*, 1952, **78**, 193.

[505] W. Stross and G. Stross, *Metallurgia*, 1952, **45**, 315.

[506] J. Mermillod, *Metal Abstr.*, 1951, **19**, 215.

[507] G. Telep and D. F. Boltz, *Analyt. Chem.*, 1952, **24**, 945.

[508] J. Haslam, F. R. Russell, and N. T. Wilkinson, *Analyst*, 1952, **77**, 464; V. T. Chuyko, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 297.

[509] E. Asmus, *Z. anal. Chem.*, 1952, **135**, 179.

[510] B.S.I. Specif., 1952, No. 1121, Pt. 24; Methods of Analysis Committee, *J. Iron Steel Inst.*, 1952, **170**, 268; H. J. Cahnmann and R. Bisen, *Analyt. Chem.*, 1952, **24**, 1341; B. E. Saltzman, *ibid.*, p. 1016.

[511] R. B. Henrickson and E. B. Sandell, *Analyt. Chim. Acta*, 1952, **7**, 57; P. Karsten and J. H. C. van Mourik, *Rec. Trav. chim.*, 1952, **71**, 302.

[512] M. Y. Shapiro, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 371.

[513] J. H. Yoe and F. Will, *Analyt. Chim. Acta*, 1952, **6**, 450.

[514] G. Gran, *Svensk Papperstidning*, 1951, **54**, 764.

[515] F. Jungblut, *Chim. analyt.*, 1951, **33**, 248.

[516] C. E. Crouthamel and C. E. Johnson, *Analyt. Chem.*, 1952, **24**, 1780.

[517] M. K. Urs and K. Neelakantam, *J. Sci. Ind. Res., India*, 1952, **11**, *B*, 79.

[518] F. R. Williams and J. Whitehead, *J. Appl. Chem.*, 1952, **2**, 213.

[519] F. Neuwirth, *J. Iron Steel Inst.*, 1952, **170**, 310.

[520] J. V. Griel and R. J. Robinson, *Analyt. Chem.*, 1951, **23**, 1871.

[521] T. C. J. Ovenston, C. A. Parker, and C. G. Hatchard, *Analyt. Chim. Acta*, 1952, **6**, 7; R. Rosotte and E. Jaudon, *ibid.*, p. 149.

[522] E. W. Kiefer and D. F. Boltz, *Analyt. Chem.*, 1952, **24**, 542.

[523] G. B. Wengert, *ibid.*, p. 1449; A. Mayer and G. Bradshaw, *Analyst*, 1952, **77**, 476.

[524] *Idem, ibid.*, p. 154; A. E. Taylor and R. T. Dillon, *Analyt. Chem.*, 1952, **24**, 1624; R. Kronstadt and A. R. Eberle, *Nuclear Sci. Abstr.*, 1952, **6**, 179.

methyl-violet,[525] or by triphenylmethylarsonium iodide;[526] bismuth by thiourea,[527] cupferron,[528] or diallyldithiocarbamidohydrazine;[529] vanadium as vanadyl ion,[530] by catalytic liberation of iodine,[531] as the complex phosphotungstic acid,[380] or with benzhydroxamic acid;[532] niobium as thiocyanate[533] or as perniobic acid;[534] osmium by thiourea;[197] ruthenium by *p*-nitrosodimethylaniline;[535] rhodium by the blue complex formed with hypochlorite;[536] and palladium with β-furfuraldoxime[537] or phenylthiourea.[538]

From the large number of colorimetric methods for organic compounds the following may be mentioned: determination of methanol by Schiff's reagent;[539] of acetic acid[540] and glycerol[541] by reduction of dichromate; of nitroparaffins by decomposition, and combination of the resulting nitrous acid with resorcinol;[542] of amides through the reaction of the derived hydroxamic acids with ferric chloride.[543] The system dichromate–chromium(III) has been studied with a view to its use for the colorimetric determination of sulphite[544] and of organic compounds,[541, 545] and it has been found to be very sensitive, particularly if absorptiometric measurements are carried out in the ultra-violet region. A similar indirect method for organic compounds depends on treatment by standard oxidising agents followed by an oxidisable dye. The amount of oxidising agent used, and hence of organic compound, is determined by colorimetry of the residual dye.[546]

Photometric titrations have been proposed for bromide–bromate reactions,[547] using the absorption of the tribromide ion to indicate the end-point, and absorptiometric methods have also been used to follow the titration of arsenic by cerium(IV).[548] Luminol has been proposed as a chemiluminescent indicator to enable detection of the end-point photometrically in acid–base titrations of highly opaque solutions;[549] for example, by using this method it was possible to determine the end-point of the titration of a solution containing Indian ink.

---

[525] M. Jean, *Analyt. Chim. Acta*, 1952, **7**, 462.

[526] B. Figgis and N. A. Gibson, *ibid.*, p. 313.

[527] B. B. Bendigo, R. K. Bell, and H. A. Bright, *J. Res. Nat. Bur. Stand.*, 1951, **47**, 252; C. J. Hall, *Analyst*, 1952, **77**, 318.

[528] H. Bode and G. Henrich, *Z. anal. Chem.*, 1952, **135**, 98.

[529] J. Gupta and K. P. S. Sarma, *J. Indian Chem. Soc.*, 1951, **28**, 89.

[530] R. Santini, J. F. Hazel, and W. M. McNabb, *Analyt. Chim. Acta*, 1952, **6**, 368.

[531] T. Shiokava, *Sci. Rep. Tôhoku*, 1950, **2**, *A*, 613.

[532] A. K. Das Gupta and M. M. Singh, *J. Sci. Ind. Res., India*, 1952, **11**, *B*, 268.

[533] H. Freund and A. E. Levitt, *Analyt. Chem.*, 1951, **23**, 1813; A. B. H. Lauw-Zecha, S. S. Lord, and D. N. Hume, *ibid.*, 1952, **24**, 1169.

[534] G. Telep and D. F. Boltz, *ibid.*, p. 163.

[535] J. E. Currah, A. Fischel, W. A. E. McBryde, and F. E. Beamish, *ibid.*, p. 1980.

[536] G. H. Ayres and F. Young, *ibid.*, p. 165. [537] E. W. Rice, *ibid.*, p. 1995.

[538] G. H. Ayres and B. L. Tuffly, *ibid.*, p. 949.

[539] J. F. Guymon, *J. Ass. Off. Agric. Chem.*, 1951, **34**, 310.

[540] E. Ciaranfi and A. Fonnesu, *Biochem. J.*, 1952, **50**, 698.

[541] D. T. Englis and L. A. Wollerman, *Analyt. Chem.*, 1952, **24**, 1983.

[542] L. R. Jones and J. A. Riddick, *ibid.*, p. 1533.

[543] F. Bergmann, *ibid.*, p. 1367.

[544] S. Sussman and I. L. Portnoy, *ibid.*, p. 1652.

[545] M. J. Cardone and J. Compton, *ibid.*, p. 1903.

[546] H. T. Gordon, *ibid.*, 1951, **23**, 1853.

[547] P. B. Sweetser and C. E. Bricker, *ibid.*, 1952, **24**, 1107.

[548] *Idem*, *ibid.*, p. 409.

[549] F. Kenney and R. B. Kurtz, *ibid.*, p. 1218.

**Nephelometry.**—Chloride has been determined in titanium sponge by precipitation as silver chloride followed by conversion into a silver sulphide sol.[550] Zinc may be precipitated in a form suitable for nephelometric estimation by 8-hydroxyquinoline,[551] and tin(IV) by precipitation with 4-hydroxy-3-nitrobenzenearsonic acid.[552] A nephelometric titration has been devised from the estimation of very small amounts of halides based on the colour change at the end-point of the sol formed with silver nitrate.[553]

**Fluorimetry.**—Fluorimetric analysis has been reviewed.[554] Fluorescent tests have been described for hydrazine,[555] aluminium,[556] lead,[557] and 8-hydroxyquinoline and its derivatives.[558]

Quantitative methods depending on fluorescence have been proposed for fluoride,[559] beryllium,[560] and uranium.[561]

**Emission Spectrography.**—Advances in instruments and in analytical methods have been reviewed.[562] R. C. Hughes has described a method of applying powdered samples to graphite electrodes in a reproducible manner.[563] The line-width method of quantitative analysis has been applied to plant products so as to produce reproducible results over a wide range of concentrations.[564] Methods of concentrating [565] and analysing [566] trace elements have been described, and spectroscopic analysis has been applied to small amounts of impurities in tungsten,[567] of metals in cracking catalysts [568] and in oils,[569] and to the analysis of coppers and brasses,[570] of lanthanon mixtures [571] and of mixtures of the platinum metals.[572]

For individual elements spectrographic methods have been recommended for the determination of lithium and sodium,[573] rubidium,[574] lithium,[575] iron,[576] lead,[577] and tantalum and niobium.[578] A spectrographic study has

---

[550] M. Codell and J. J. Mikla, *Analyt. Chem.*, 1952, **24**, 1972.

[551] L. Bertiaux, *Chim. analyt.*, 1951, **33**, 59.

[552] P. Karsten, H. L. Kies, and J. J. Walraven, *Analyt. Chim. Acta*, 1952, **7**, 355.

[553] M. Hasselmann and G. Laustriat, *Compt. rend.*, 1952, **234**, 625.

[554] C. E. White, *Analyt. Chem.*, 1952, **24**, 85; C. E. White *et al.*, *ibid.*, p. 1965.

[555] F. Feigl and W. A. Mannheimer, *Mikrochem. Mikrochim. Acta*, 1952, **40**, 50.

[556] F. Feigl and G. B. Heisig, *J. Chem. Educ.*, 1952, **29**, 192.

[557] S. Šlijivić, *Bull. Soc. chim. Belgrade*, 1951, **16**, 147.

[558] F. Feigl, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 404.

[559] H. H. Willard and C. A. Horton, *Analyt. Chem.*, 1952, **24**, 862.

[560] H. A. Laitinen and P. Kivalo, *Nuclear Sci. Abstr.*, 1952, **6**, 69; *Analyt. Chem.*, 1952, **24**, 1467.

[561] M. D. Yeaman, *Nuclear Sci. Abstr.*, 1952, **6**, 104; N. S. Guttag and F. S. Grimaldi, *ibid.*, p. 145; M. Nakanishi, *Bull. Chem. Soc. Japan*, 1951, **24**, 33, 36.

[562] W. F. Meggers, *Analyt. Chem.*, 1952, **24**, 23; R. L. Mitchell, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 491; J. K. Hurwitz, *J. Opt. Soc. Amer.*, 1952, **42**, 484.

[563] *Analyt. Chem.*, 1952, **24**, 1406.

[564] R. T. O'Connor and D. C. Heinzelman, *ibid.*, p. 1667.

[565] G. Gorbach and F. Pohl, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 328.

[566] *Idem, ibid.*, p. 335; S. Wilska, *Acta Chem. Scand.*, 1951, **5**, 1368.

[567] C. H. R. Gentry and G. P. Mitchell, *Metallurgia*, 1952, **46**, 47.

[568] J. P. Pagliassotti and F. W. Porsche, *Analyt. Chem.*, 1952, **24**, 1403.

[569] A. J. Ham, J. Noar, and J. G. Reynolds, *Analyst*, 1952, **77**, 766.

[570] F. V. Schatz, *J. Inst. Met.*, 1951, **80**, 77.

[571] J. A. Norris and C. E. Pepper, *Analyt. Chem.*, 1952, **24**, 1399.

[572] G. H. Ayres and E. W. Berg, *ibid.*, p. 465; H. Oberländer, *Metal Abstr.*, 1952, **19**, 403; J. E. Hawley, W. J. Wark, C. L. Lewis, and W. L. Ott, *ibid.*, p. 856.

[573] A. B. Chandler, *Brit. Ceram. Abstr.*, 1952, 107 A.

[574] A. Halperin and S. Samursky, *J. Opt. Soc. Amer.*, 1952, **42**, 475.

[575] G. I. Stukenbroeker, D. D. Smith, G. K. Werner, and J. R. McNally, *ibid.*, p. 383.

[576] J. E. Barney and W. A. Kimball, *Analyt. Chem.*, 1952, **24**, 1548.

[577] V. Brustier, P. Cornec, and H. Triché, *Compt. rend.*, 1952, **234**, 2367.

[578] W. J. Poehlman and R. E. Sarnowski, *J. Opt. Soc. Amer.*, 1952, **42**, 489.

been made of the co-precipitation of vanadium with the hydroxides of tervalent metals.[579]

Improved flame photometers have been described,[580, 581] and an improved method for the flame analysis of plant ash has been devised.[582] Individual flame photometric methods have been proposed for the elements boron,[583] lithium,[584] sodium,[585, 586, 587] potassium,[585, 586] rubidium,[588] and calcium,[586, 589] G. C. Collins and H. Polkinhorne [581] have studied the effect of anions on the flame-photometric determination of sodium and potassium.

An emission spectrographic method has been proposed for the determination of halogen compounds.[590] In this, the emission spectrum excited by a high-frequency electrodeless discharge has been used. Little work seems to have been done along these lines, and with modern apparatus it would seem to the Reporter feasible to assume that the characteristic high-frequency spectra of many organic compounds, first studied many years ago from a theoretical point of view,[591] ought to be capable of considerable analytical application.

**Absorption Spectra.**—Analytical applications of absorption spectra in the visible and ultra-violet regions have been reviewed.[592, 593] An electrodeless hydrogen discharge tube as a source of ultra-violet continuum has been described.[594] The absorption spectra of substances may be measured as reflection spectra, and this has been utilised to identify materials on an adsorption column.[595]

Infra-red spectroscopy has also been reviewed.[592, 596] A differential method of analysis depending on the comparison of known and unknown samples has been discussed theoretically, and possible sources of error have been examined.[597] A simple infra-red absorption cell has been described.[598] A. E. Martin [599] has pointed out the potential value of a comprehensive catalogue of infra-red spectra of organic compounds, and the ease with which this could be obtained, in a fairly complete form, within a reasonably short time, if workers were to co-operate in providing data according to a scheme which he outlines. Infra-red absorption studies of aromatic hydro-

---

[579] F. Burriel Martí, E. Fernández Caldas, and J. Ramírez Muños, *Anal. real Soc. esp. Fís. Quím.*, 1952, **48**, *B*, 59.

[580] J. U. White, *Analyt. Chem.*, 1952, **24**, **394**; C. A. Dubbs, *ibid.*, p. 1654; L. Leyton, *Biochem J.*, 1952, **50**, Proc., xl. [581] *Analyst*, 1952, **77**, 430.

[582] F. H. Vanstone, A.R.E. Malling Res. Sta., 1951, 122.

[583] C. E. Bricker, W. A. Dippel, and N. H. Furman, *Nuclear Sci. Abstr.*, 1952, **6**, 212.

[584] L. H. Kalenowski and S. M. Runke, *U.S. Bur. Mines*, 1952, Rep. Invest., 4863.

[585] L. I. Obolenskaya, *Soils and Fert.*, 1951, **14**, 449.

[586] R. Herrmann, *Z. ges. exp. Med.*, 1952, **118**, 187.

[587] S. B. Knight and M. H. Peterson, *Analyt. Chem.*, 1952, **24**, 1514.

[588] H. E. Freytag, *Z. anal. Chem.*, 1952, **136**, 161.

[589] H. J. Hübener, *Z. physiol. Chem.*, 1952, **289**, 188.

[590] R. E. Keller and L. Smith, *Analyt. Chem.*, 1952, **24**, 796.

[591] A. W. Stewart and C. L. Wilson, "Recent Advances in Physical and Inorganic Chemistry," 7th edtn., London, 1944, p. 452.

[592] O. D. Shreve, *Analyt. Chem.*, 1952, **24**, 1693.

[593] M. G. Mellon, *ibid.*, p. 2; E. J. Rosenbaum, *ibid.*, p. 14.

[594] G. H. Dieke and S. P. Cunningham, *J. Opt. Soc. Amer.*, 1952, **42**, 187.

[595] F. Pruckner, M. van der Schulenberg, and G. Schwuttke, *Naturwiss.*, 1951, **38**, 45.

[596] R. C. Gore, *Analyt. Chem.*, 1952, **24**, 8; N. Sheppard, *Analyst*, 1952, **77**, 732; R. C. Lord, R. S. McDonald, and F. A. Miller, *J. Opt. Soc. Amer.*, 1952, **42**, 149; A. E. Martin, *Indust. Chem. Chem. Manuf.*, 1952, **28**, 243.

[597] D. Z. Robinson, *Analyt. Chem.*, 1952, **24**, 619.

[598] K. S. Tetlow, *J. Sci. Instr.*, 1951, **28**, 322. [599] *Nature*, 1952, **170**, 20.

carbons,[600] barbiturate derivatives,[601] alkaloids,[602] and polymer degradation products [603] have been reported.

F. A. Miller and C. H. Wilkins [604] have discussed the use of infra-red absorption spectra in the identification of inorganic polyatomic ions. Pointing out that no systematic study has, up to the present, been made of these spectra, and that little up-to-date information is available, they present, both graphically and in tabular form, the spectra of about 160 inorganic compounds which can be used, in conjunction with other methods of analysis, to provide useful information about the composition of inorganic materials. The principal drawback to more extended use of the method is the necessity for determining the spectra from samples in powder form.

**Chemical Microscopy.**—Hot-stages for work with the microscope have been described [605] and a method has been outlined for the determination of boiling points and boiling ranges using such a hot-stage.[606] The use of mixed melting points for the construction of phase diagrams has been discussed,[607] and a method has been described by which the techniques applicable in such studies may be used for purification.[608] Fusion methods accompanied by crystallographic examination have been compared with the methods used for phase studies,[609] and the former have been extended to the inorganic field by an examination of the fusion behaviour of a wide range of inorganic compounds with 8-hydroxyquinoline.[610]

A simple method has been described for determining the optic axial angle of crystals,[611] and crystallographic data have been presented for lanthanum oxalate decahydrate,[612] ethylenedinitramine,[613] 2 : 4 : 6 : 2′ : 4′ : 6′-hexanitrodiphenylamine,[614] *N*-acetyl-*N*′-phenylhydrazine,[615] phthalic anhydride,[616] dibenzyl succinate,[617] *s*-diphenylcarbazide,[618] $\text{L}_s$-threonine,[619] pseudotropine,[620] (±)-mandelic acid,[621] 2 : 4-dinitrophenol,[622] and 4 : 6-dinitroresorcinol.[623]

Nicotine thiocyanate has been found [624] to give crystalline precipitates which are suitable for identification under the microscope with a number of cations. Crystal tests have been proposed for nitrate and nitrite using *p*-aminophenylmercuric acetate,[625] and for cobalt using potassium tri-

---

[600] R. B. Williams, S. H. Hastings, and J. A. Anderson, *Analyt. Chem.*, 1952, **24**. 1911.

[601] C. J. Umberger and G. Adams, *ibid.*, p. 1309.

[602] G. Papineau-Couture and R. A. Burley, *ibid.*, p. 1918.

[603] B. C. Achhammer, *ibid.*, p. 1925. [604] *Ibid.*, p. 1253.

[605] E. G. Steward, *J. Sci. Instr.*, 1952, **29**, 214; W. Kofler, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 84; F. Hippenmeyer, *ibid.*, p. 409.

[606] J. S. Wiberley, R. K. Siegfriedt, and A. A. Benedetti-Pichler, *ibid.*, 1951, **38**, 471.

[607] L. Kofler, *Z. anal. Chem.*, 1951, **133**, 27.

[608] R. Fischer, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 342.

[609] W. C. McCrone, *ibid.*, p. 476.

[610] P. W. West and L. Granatelli, *Analyt. Chem.*, 1952, **24**, 870.

[611] A. J. Pollard, L. I. Braddock, and M. L. Willard, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 192. [612] V. Gilpin and W. C. McCrone, *Analyt. Chem.*, 1952, **24**, 225.

[613] W. C. McCrone, *ibid.*, p. 421. [614] *Idem*, *ibid.*, p. 592.

[615] M. B. Williams and W. P. Van Meter, *ibid.*, p. 762.

[616] M. B. Williams, W. P. Van Meter, and W. C. McCrone, *ibid.*, p. 911.

[617] J. Krc, *ibid.*, p. 1070.

[618] M. B. Williams, W. P. Van Meter, and R. J. Robinson, *ibid.*, p. 1220.

[619] R. L. Clarke and J. Krc, *ibid.*, p. 1378. [620] *Idem*, *ibid.*, p. 1516.

[621] H. A. Rose, *ibid.*, p. 1680. [622] W. C. McCrone and J. Krc, *ibid.*, p. 1863.

[623] W. C. McCrone and I. Corvin, *ibid.*, p. 2008.

[624] S. E. Burkat, E. N. Skrynnik, and S. S. Yaroslavskaya, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 325. [625] I. M. Korenman and A. A. Belyakov, *ibid.*, 1952, **7**, 52.

oxalatoferrate.[626] Zirconium and hafnium may be distinguished by the proper application of the crystal test using quinoline and ammonium thiocyanate.[627]

**Miscellaneous Instrumental Methods.**—*X*-Ray methods have been reviewed.[628] *X*-Ray spectra have been used for the quantitative analysis of minerals,[629] and powder patterns have been used for the identification of molybdenum and tungsten oxides.[630]

The application of the mass spectrometer to analytical problems has been reviewed [631] and a simple pen recorder has been described.[632] The mass spectrometer has been applied to the analysis of hydrocarbons.[633] An extension of the use of the instrument for the analysis of non-volatile materials, by examination of pyrolysis products obtained under controlled conditions, has been recommended.[634] Various modes of pyrolysis have been investigated, and the method may be used, either for direct identification in the simpler cases, or for identification by comparison with known samples in the case of more complex materials.

## 8. PHYSICAL SEPARATION METHODS.

H. H. Strain and G. W. Murphy [635] have reviewed what they term "chromatography and analogous differential migration methods," and a number of other reviews of these methods have also appeared.[636]

Any survey of this field leads to the conclusion that it will be many years before any coherent overall picture of the methods and their potentialities can be presented. The confusion in terminology which already exists seems to become greater with the passage of time and with the formation of new sub-divisions, some of these unfortunately with rather slight justification. Among relatively new terms which have to be fitted into the complete picture are "gradient elution analysis," [637] "ionography," [638] "papyrography," [639] "ultra-violet papyrography," [640] even "ultra-micro-papyrography" [641] (achieving a double distinction in that paper is not used in the separation, which is achieved by means of cotton thread), "electrokinetic ultrafiltration," [642] "electrophoresis-convection," [643] and "chromathermography." [644]

[626] J. C. Ryan, L. K. Yanowski, and M. Cefola, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 466.

[627] C. J. van Nieuwenburg and J. W. L. van Ligten, *Analyt. Chim. Acta*, 1952, **7**, 390.

[628] H. A. Liebhafsky, *Analyt. Chem.*, 1952, **24**, 16; H. S. Kaufman and I. Fankuchen, *ibid.*, p. 20.

[629] G. Talvenheimo and J. L. White, *ibid.*, p. 1784; M. Tournay, *Compt. rend.*, 1952, **234**, 2527.

[630] A. Magnéli, G. Anderson, B. Blomberg, and L. Kihlborg, *Analyt. Chem.*, 1952, **24**, 1998. [631] V. H. Dibeler and J. A. Hipple, *ibid.*, p. 27.

[632] K. K. Jensen, W. E. Bell, and F. E. Blacet, *ibid.*, p. 1614.

[633] H. Sobcov, *ibid.*, pp. 1386, 1908; I. W. Kinney and G. L. Cook, *ibid.*, p. 1391.

[634] P. D. Zemany, *ibid.*, p. 1709. [635] *Ibid.*, p. 50.

[636] A. Tiselius, *Endeavour*, 1952, **11**, 5; G. B. Marini-Bettolo, *Chim. e Ind.*, 1952, **34**, 269; Anon., *Chem. Eng. News*, 1952, **30**, 4244.

[637] R. J. P. Williams, *Analyst*, 1952, **77**, 905.

[638] H. J. McDonald, *J. Chem. Educ.*, 1952, **29**, 428.

[639] M. R. Nayar and V. K. M. Rao, *J. Sci. Ind. Res., India*, 1952, **11**, *B*, 78.

[640] Y. Hashimoto and I. Mori, *Nature*, 1952, **170**, 1024.

[641] D. S. Venkatesh and M. Sreenivasaya, *Current Sci.*, 1951, **20**, 156.

[642] D. L. Mould and R. L. M. Synge, *Analyst*, 1952, **77**, 964.

[643] D. M. Tennent and M. Kniazuk, *Analyt. Chem.*, 1952, **24**, 1661.

[644] A. A. Zhukhovitsky, O. V. Zolotareva, N. A. Sokolov, and N. M. Turkeltaub, *Compt. rend. Acad. Sci., U.R.S.S.*, 1951, **77**, 435.

This multiplication of terminology is objectionable, merely on the grounds stated earlier (p. 306). It is additionally objectionable here on two counts: it increases the confusion regarding the causes of such separations, and it makes more difficult the recognition of really novel techniques. "Chromatographic analysis" has been soberly defined [1] as the "analysis of a solution by the use of solid sorbents such as paper or alumina, to separate substances in solution by selective sorption." This definition tallies closely enough with the terminology of H. H. Strain and G. W. Murphy [635] to merit acceptance. However, it does not seem to be sufficiently all-embracing for the enthusiast, who continues to present us with other definitions which are not so readily defensible. Thus T. I. Williams and H. Weil,[645] while admitting that "so many processes are now *by common consent* accepted as forms of chromatography that an unequivocal definition of the word in its present chemical sense presents difficulties," have proposed that it be defined as "those processes which allow the resolution of mixtures by effecting separation of some or all of their components in concentration zones or in phases different from those in which they are originally present, irrespective of the nature of the force or forces causing the substance to move from one phase to another." They claim that this definition embraces not only the various forms of chromatography hitherto achieved, but also all forms which have been postulated as theoretical possibilities. It does this, of course, but it surely includes also such analytical operations as precipitation and steam-distillation; and in any case, common consent without critical discussion is no ground for attempting to make "chromatography" the touchstone-term for every new device, whatever its merits and whatever its mechanism.

To provide a definition that does not define is only to add further confusion to an already overcrowded pattern. The word "chromatography" has, at the present time, become one of the magic words—in the same class as "resonance" in the nineteen-thirties. The illusion exists that to give a process a name explains the process; and this in turn may lead to misinterpretation of the causes which are operating in any separation, and to the conclusion that new causes have been observed when in fact they do not exist.

Some of the dangers in this state of affairs seem likely to arise, for example, from the increased use of impregnated papers which has been reported recently. Papers impregnated with alumina,[646] borate,[647] and various other inorganic salts,[648] glycerol and various glycols,[646, 649] silicones,[650] phenylcellosolve,[651] toluene-*p*-sulphonate,[652] and stearatochromic chloride [653] have all been used. It is almost impossible, in some of these cases, to determine on the published information and in view of the little that is known about the simpler separations, the mechanism by which the separations are taking place.

[645] *Nature*, 1952, **170**, 503.
[646] I. E. Bush, *Nature*, 1950, **166**, 445; *Biochem. J.*, 1952, **50**, 370.
[647] C. A. Wachtmeister, *Acta Chem. Scand.*, 1951, **5**, 976.
[648] M. Lederer, *Analyt. Chim. Acta*, 1952, **7**, 458.
[649] R. J. Boscott, *Biochem. J.*, 1951, **48**, Proc. xlvii; A. Zaffaroni, R. B. Burton, and E. H. Keutmann, *Science*, 1950, **111**, 6; *J. Biol. Chem.*, 1951, **188**, 763.
[650] T. H. Kritchevsky and A. Tiselius, *Science*, 1951, **114**, 299.
[651] R. Neher and A. Wettstein, *Helv. Chim. Acta*, 1952, **35**, 276.
[652] R. J. Boscott, *Chem. and Ind.*, 1952, 472.
[653] D. Kritchevsky and M. R. Kirk, *J. Amer. Chem. Soc.*, 1952, **74**, 4484.

That considerable caution must be used is stressed by the ease with which artefacts may appear in separations which are apparently quite straightforward, as has been pointed out by a number of authors.[654] Even such simple operations as acid-washing of paper [655] may produce a radical change in mechanism, while insufficient attention to water-content [656] will certainly do so, and can lead to the anomalous result that a column of material such as hydrated magnesium silicate is condemned because of variation in water content on the one hand,[657] and is recommended for *adsorption* chromatography, using elution by ethyl acetate *saturated with water*, on the other; [658] or that " single-phase chromatography " of inorganic ions,[659] or even " salting-out chromatography," [660] may be regarded as advances on partition chromatographic methods when they are in fact probably largely the result of separative forces recognised before the introduction of partition methods, such as ion exchange, or even simple adsorption.

Finally, resolution of substances by complex liquid mixtures such as progressively changing mixtures of chloroform, *n*-amyl alcohol, and *tert*.-amyl alcohol,[661] while probably empirically satisfactory, can nevertheless only make theoretical interpretation of these separations more difficult. In view of difficulties of this nature, it is only possible here to refer to isolated instances of methods which appear to be practically useful, and to pay inadequate attention to theoretical considerations other than those which make a very simple approach to small sections of the larger problem. It must also be stressed that the allocation to separate types which is made here must, of necessity, be somewhat arbitrary since the mechanisms are not always evident.

**Adsorption Chromatography.**—A number of less usual, sparingly soluble, inorganic compounds have been investigated in respect of their adsorption properties,[662] and it has been found that when both natural and synthetic sources are available the natural product has a higher adsorptive capacity. A range of reagents for use in the detection of colourless zones in the separation of a wide range of organic compounds has been tabulated, together with useful information about their application.[663] Various other methods, many of them instrumental, have been proposed for the detection of zones or fractions.[664]

Inorganic chromatographic separations (as distinct from partition separations) have been discussed theoretically,[665] and have been applied to the separation and identification of the more familiar cations [666] and

---

[654] E. L. Smith, *Nature*, 1952, **169**, 60; T. C. J. Ovenston, *ibid*., p. 924; J. D. Acland, *ibid*., **170**, 32; H. G. Boman, *ibid*., p. 703.

[655] S. Burrows, F. S. M. Grylls, and J. S. Harrison, *ibid*., p. 800.

[656] A. Sibatani and M. Fukuda, *J. Biochem. Tokyo*, 1951, **38**, 181.

[657] M. L. Wolfrom, A. Thompson, T. T. Galkowski, and E. J. Quinn, *Analyt. Chem*., 1952, **24**, 1670. [658] C. H. Ice and S. H. Wender, *ibid*., p. 1616.

[659] B. Milićević, *Bull. Soc. chim. Belgrade*, 1952, **16**, 101.

[660] L. Hagdahl and A. Tiselius, *Nature*, 1952, **170**, 799.

[661] L. M. Marshall, K. O. Donaldson, and F. Friedberg, *Analyt. Chem*., 1952, **24**, 328, 773.

[662] D. J. O'Connor and F. Bryant, *Nature*, 1952, **170**, 84.

[663] A. L. LeRosen, R. T. Moravek, and J. K. Carlton, *Analyt. Chem*., 1952, **24**, 1335.

[664] P. H. Monaghan, P. B. Moseley, T. S. Burkhalter, and O. A. Nance, *ibid*., p. 193; R. A. Glenn, J. S. Wolfarth, and C. W. DeWalt, *ibid*., p. 1138; J. M. Miller and J. G. Kirchner, *ibid*., p. 1480; H. Hoyer, *Kolloid Z*., 1952, **127**, 166.

[665] M. Tanaka and M. Shibata, *Bull. Tokyo Inst. Technol*., 1951, *B*, **1**, 11.

[666] H. H. Fillinger and L. A. Trafton, *J. Chem. Educ*., 1952, **29**, 285.

anions[667] and to the detection or determination of strontium,[668] zinc in cadmium,[669] and copper in zinc.[670] Further work has been carried out on the separation of metal-chelates, the separation of 8-hydroxyquinoline complexes having been studied,[671] and separation of cobalt by 2-nitroso-1-naphthol[672] and further investigations of the separation of alkaline-earth and alkali cations by violuric acid[673] having been reported.

" Gas chromatography " of volatile organic mixtures, using displacement chromatography from charcoal columns, has been recommended[674] as a valuable method, capable of high accuracy and of considerable further development.

**Ion Exchange.**—The principles and the application of ion exchange to analytical problems have been extensively reviewed,[675] and it is clear that these extend far beyond the simple possibilities of separations by columnar or analogous means. Chromatography of amino-acids has been carried out on oxidised cellulose, and study has shown[676] that the process taking place is probably an ion-exchange process, the movement of individual acids being related to the carboxyl content of the cellulose. Ion-exchange processes have been used to remove or concentrate ions in water,[677] to separate ordinary[678] or radioactive[679] halogens, to separate calcium prior to phosphate determination,[680] to separate arsenic from iron,[681] to remove interferences prior to sulphate determination[682] or boron determination,[683] to separate aluminium, iron, and manganese as chloro-complexes,[684] to separate thorium and lanthanum,[685] to separate molybdenum from rhenium[686] or from other heavy metals,[687] and to separate vanadium from phosphoric acid solutions.[688]

An interesting development is the increasing application of ion-exchange columns for the production of standard solutions, and 0·1N-[689] and 0·001N-alkali hydroxide[690] free from carbonate have been prepared in this fashion from alkali chloride. The exchange is stoicheiometric, and the column will

[667] Y. Oka and A. Murata, *Sci. Rep. Tôhoku*, 1951, *A*, **3**, 82.

[668] H. Ballczo and H. Muthenthaller, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 152.

[669] Y. Oka and A. Murata, *Sci. Rep. Tôhoku*, 1951, *A*, **3**, 711.

[670] *Idem*, *ibid.*, p. 707.

[671] L. B. Hilliard and H. Freiser, *Analyt. Chem.*, 1952, **24**, 752.

[672] R. O. Bach and A. A. Garmendia, *Anal. Asoc. Quim. Argentina*, 1951, **39**, 11.

[673] H. Seiler, E. Sorkin, and H. Erlenmeyer, *Helv. Chim. Acta*, 1952, **35**, 120.

[674] J. Griffiths, D. James, and C. Phillips, *Analyst*, 1952, **77**, 897.

[675] E. R. Tompkins, *ibid.*, p. 970; R. Kunin, *Analyt. Chem.*, 1952, **24**, 64; Anon., *Nature*, 1952, **170**, 150; G. Dickel and K. Titzmann, *Angew. Chem.*, 1951, **63**, 450.

[676] T. Wieland and A. Berg, *ibid.*, 1952, **64**, 418.

[677] H. Ballczo and G. Mondl, *Mikrochem. Mikrochim. Acta*, 1952, **39**, 247; S. Sussman and I. L. Portnoy, *Analyt. Chem.*, 1952, **24**, 1644.

[678] W. Riemann and S. Lindenbaum, *ibid.*, p. 1199.

[679] E. Berne, *Acta Chem. Scand.*, 1951, **5**, 1260.

[680] B. H. Kindt, E. W. Balis, and H. A. Liebhafsky, *Analyt. Chem.*, 1952, **24**, 1501.

[681] Y. Yoshino, *Bull. Chem. Soc. Japan*, 1951, **24**, 39.

[682] H. Frey, *Analyt. Chim. Acta*, 1952, **6**, 126.

[683] J. R. Martin and J. R. Hayes, *Analyt. Chem.*, 1952, **24**, 182; G. Brunisholtz and J. Bonnet, *Helv. Chim. Acta*, 1951, **34**, 2074.

[684] E. Blasius and M. Negwer, *Naturwiss.*, 1952, **39**, 257.

[685] P. Radhakrishna, *Analyt. Chim. Acta*, 1952, **6**, 351.

[686] S. A. Fisher and V. W. Meloche, *Analyt. Chem.*, 1952, **24**, 1100.

[687] R. Klement, *Z. anal. Chem.*, 1952, **136**, 17.

[688] J. E. Salmon and H. R. Tietze, *J.*, 1952, 2324.

[689] J. Steinbach and H. Freiser, *Analyt. Chem.*, 1952, **24**, 1027.

[690] B. W. Grunbaum, W. Schöniger, and P. L. Kirk, *ibid.*, p. 1857.

deliver accurately standardised alkali without attention over a period of many months. C. Calmon[691] has proposed the use of the volume-change characteristics of an ion-exchange resin for quantitative analysis, either on a large scale, where the volume occupied in a column is measured, or on a small scale, where the change in volume of a single bead of resin is measured under the microscope. The amount of swelling or shrinkage is related to the structure of the resin, to the cation being exchanged, and to the concentration of the exchanging solution.[692]

In the organic field, separations of aldehydes and ketones from acids[693] and of amino-acids[694] and nitrogenous plant extracts[695] have been reported.

**Extraction.**—Solvent-extraction methods have been reviewed,[696] and a radio-tracer study has been made of the solvent extraction of the halides of gallium, indium, and thallium[697] from which it is possible to recommend an extraction of indium as iodide for separation from other elements. Lead iodide may be extracted by methyl *iso*propyl ketone,[698] bismuth iodide by *iso*butyl methyl ketone,[699] and copper by organic solutions containing organic acids.[700] Apparatus for countercurrent extraction,[701] and a simple apparatus for continuous extraction[702] have been described. In quantitative analysis, extraction procedures have been used in the removal of iron(III) by extraction with *n*-butyl phosphate prior to aluminium determination,[703] in the estimation of zinc in soils by diphenylthiocarbazone,[704] and in the extraction by ethyl methyl ketone of niobium and tantalum from uranium alloys as the fluorides, prior to determination.[705]

**Partition Chromatrography.**—As in recent years, the individual publications on partition chromatography probably outnumber those in any other comparable branch of analytical chemistry. Two books have been published which deal extensively with existing literature,[706] and the methods have been reviewed elsewhere.[707] Several investigations of factors affecting partition separations have been reported,[708] the most fundamental probably being those of H. G. Cassidy,[709] who has analysed the factors into three main groups, not, of course, mutually exclusive, affecting flow, $R_F$ values,

---

[691] *Analyt. Chem.*, 1952, **24**, 1456.

[692] K. W. Pepper, D. Reichenberg, and D. K. Hale, *J.*, 1952, 3129.

[693] G. Gabrielson and O. Samuelson, *Acta Chem. Scand.*, 1952, **6**, 729, 738.

[694] C. H. W. Hirs, S. Moore, and W. H. Stein, *J. Biol. Chem.*, 1952, **195**, 669.

[695] S. M. Partridge, *Analyst*, 1952, **77**, 955.

[696] L. C. Craig, *Analyt. Chem.*, 1952, **24**, 66; D. Pillon, *Bull. Soc. chim.*, 1952, **19**, D 1.

[697] H. M. Irving and F. J. C. Rossotti, *Analyst*, 1952, **77**, 801.

[698] P. W. West and J. K. Carlton, *Analyt. Chim. Acta*, 1952, **6**, 406.

[699] P. W. West, P. Senise, and J. K. Carlton, *ibid.*, p. 488.

[700] P. W. West, T. G. Lyons, and J. K. Carlton, *ibid.*, p. 400.

[701] F. C. Hickey, *Analyt. Chem.*, 1952, **24**, 1993; R. Spence and R. J. W. Streeton, *Analyst*, 1952, **77**, 578.

[702] W. W. Meinke and R. E. Anderson, *Analyt. Chem.*, 1952, **24**, 708.

[703] M. Aven and H. Freiser, *Analyt. Chim. Acta*, 1952, **6**, 412.

[704] E. Shaw and L. A. Dean, *Soil Sci.*, 1952, **73**, 341.

[705] G. W. C. Milner and A. J. Wood, Atomic Energy Res. Establ., 1952, C/R 895.

[706] R. J. Block, R. LeStrange, and G. Zweig, " Paper Chromatography : A Laboratory Manual," New York and London, 1952; J. N. Balston and B. E. Talbot, " Guide to Filter Paper and Cellulose Powder Chromatography," London, 1952.

[707] P. von Tavel, *Chimia*, 1951, **5**, 256; R. Signer, *ibid.*, p. 245

[708] G. N. Kowkabany and H. G. Cassidy, *Analyt. Chem.*, 1952, **24**, 643; A. Lacourt, G. Sommereyns, and G. Wantier, *Analyst*, 1952, **77**, 943; C. N. Trumbore and H. E. Rogers, *J. Chem. Educ.*, 1952, **29**, 404; G. Heinrich, *Naturwiss.*, 1952, **39**, 257.

[709] *Analyt. Chem.*, 1952, **24**, 1415.

and zone-definition respectively, and has considered some of these factors in more detail. Instrumental methods have been recommended for controlling separations,[710] and numerous devices of apparatus, application of reagent, choice of support for the stationary phase, and detection of zones have been reported.[711] It has been shown that the measurement of spot areas [712] or the excision of spots and elution for quantitative analysis [713] may be considerably simplified either by direct analysis on the cut paper [714] or by cutting out the spots and weighing directly.[715] In the latter case the result is more closely related to the concentration than the actual spot area, probably because of compensation for errors arising from varying paper thickness.

In the organic field alcohols,[716] the 2 : 4-dinitrophenylhydrazones of aldehydes and ketones,[717] acids,[718] amines,[719] azo-dyes derived from arylamines,[720] phenols,[721] sugars and related compounds [722, 723] and amino-acids and related compounds [723, 724] are among the long list of substances that have been separated.

Because of the considerable use of benzidine in the detection of zones, its behaviour with a wide range of materials, including inorganic salts, has been studied.[725] The halides from halogen compounds, after sodium fusion, have been separated.[726] Separations of a number of mixtures of inorganic

---

[710] D. C. Müller, *Analyst*, 1952, **77**, 933.

[711] P. Meredith and H. G. Sammons, *ibid.*, p. 416; L. A. Boggs, *Analyt. Chem.*, 1952, **24**, 1673; L. A. Boggs, L. S. Cuendet, M. Dubois, and F. Smith, *ibid.*, p. 1148; D. F. Meigh, *Nature*, 1952, **169**, 706; U. S. von Euler, *ibid.*, **170**, 664; A. Grieg, *ibid.*, p. 845; G. Zimmermann and K. Nehring, *Angew. Chem.*, 1951, **63**, 556; J. G. Marchal and T. Mittwer, *Proc. K. Ned. Akad. Wet.*, 1951, **54**, c 4, 391; S. Berlingozzi and G. Serchi, *Sper. Sez. Chim. biol.*, 1952, **3**, 1.

[712] J. A. Brown and M. M. Marsh, *Analyt. Chem.*, 1952, **24**, 1952.

[713] T. Kariyone and S. Shimizu, *Nature*, 1952, **170**, 422.

[714] B. Levin and V. G. Oberholzer, *ibid.*, p. 123.

[715] J. H. Freeman, *Analyt. Chem.*, 1952, **24**, 2001.

[716] A. C. Neish, *Canad. J. Chem.*, 1951, **29**, 552.

[717] D. F. Meigh, *Nature*, 1952, **170**, 579.

[718] F. W. Denison and E. F. Phares, *Analyt. Chem.*, 1952, **24**, 1628; T. L. Parkinson, *Analyst*, 1952, **77**, 438; V. K. M. Rao, *J. Sci. Ind. Res., India*, 1952, **11**, *B*, 277; S. S. Phatak, A. P. Mahadevan, and V. D. Patwardhan, *Current Sci.*, 1952, **21**, 162.

[719] W. Baker, J. B. Harborne, and W. D. Ollis, *J.*, 1952, 3215; J. M. Bremner and R. H. Kenten, *Biochem. J.*, 1951, **49**, 651; A. Wickström and B. Salvesen, *J. Pharm. Pharmacol.*, 1952, **4**, 631; R. Schwyzer, *Acta Chem. Scand.*, 1952, **6**, 219.

[720] M. Zalokar, *J. Amer. Chem. Soc.*, 1952, **74**, 4213.

[721] Wen-Hua Chang, R. L. Hossfeld, and W. M. Sandstrom, *ibid.*, p. 5766; G. M. Barton, R. S. Evans, and J. A. F. Gardner, *Nature*, 1952, **170**, 249; S. A. Ashmore and H. Savage, *Analyst*, 1952, **77**, 439.

[722] J. L. Buchan and R. I. Savage, *ibid.*, p. 401; N. Albon and D. Gross, *ibid.*, p. 410; J. T. Edward and D. M. Waldron, *J.*, 1952, 3631; R. J. Dimler, W. C. Schaeffer, C. S. Wise, and C. E. Rist, *Analyt. Chem.*, 1952, **24**, 1411; L. Sattler, *ibid.*, p. 1862; R. J. Bayley, E. J. Bourne, and M. Stacey, *Nature*, 1952, **169**, 876; P. S. Rao and R. M. Beri, *Proc. Indian Acad. Sci.*, 1951, **28**, *A*, 368; A. Yoda, *Sugar Ind. Abstr.*, 1952, **14**, 116; J. Saarnio, E. Niskasaari, and C. Gustafsson, *Suomen Kem.*, 1952, **25**, *B*, 25; J. Opieńska-Blauth, E. Drozdowski, and M. Kański, *Ann. Univ. M. Curie-Sklowdowska*, 1951, **6**, D, 27.

[723] L. F. Wiggins and J. H. Williams, *Nature*, 1952, **170**, 279; R. Radhakrishnamurty and P. S. Sarma, *J. Sci. Ind. Res., India*, 1952, **11**, *B*, 279.

[724] C. Klatzkin, *Nature*, 1952, **169**, 422; H. N. Rydon and P. W. G. Smith, *ibid.*, p. 922; K. V. Giri and N. A. N. Rao, *ibid.*, p. 923; A. C. Hulme and W. Arthington, *ibid.*, **170**, 659; A. R. Kemble and H. T. Macpherson, *ibid.*, p. 664; K. V. Giri, A. N. Radhakrishnan, and S. V. Vaidyanathan, *Analyt. Chem.*, 1952, **24**, 1677; E. F. Wellington, *Canad. J. Chem.*, 1952, **30**, 581.

[725] H. Miller and D. M. Kraemer, *Analyt. Chem.*, 1952, **24**, 1371.

[726] T. Ando and S. Ishii, *Bull. Chem. Soc. Japan*, 1952, **25**, 106.

ions have been reported.[727] More limited separations have been described for phosphates,[728] alkali metals,[729, 730] alkaline-earth metals,[730] zinc,[731] bismuth,[732] uranium,[733, 734] thorium,[734, 735] niobium and tantalum,[736] and zirconium and hafnium.[737]

On theoretical considerations, partition methods have been extended to partition between gas–liquid phases, and some separations based on this theory, such as the separation of volatile fatty acids, are described.[738]

**Ionophoresis and Electrophoresis.**—The methods of "electrochromatography" have been reviewed,[739] and apparatus for carrying out ionophoretic or electrophoretic separations in filter-paper has been described.[740] G. Manecke [741] has described the application of ionophoretic separations to mixtures of ions on ion-exchange columns. Copper has been separated and determined on paper by ionophoretic methods.[742] The methods normally applied in this field have utilised low voltages to achieve separations. Flavonoids and sugars have been separated by using high constant voltages of the order of 100—1000 volts.[743]

## 9. MISCELLANEOUS.

**Radiochemical Analysis.**—An excellent account of the basis and experimental aspects of radiochemical analysis has appeared in book form,[744] and there have been other reviews of the subject [745] from the analytical standpoint. The precision counting of α-particles has been discussed [746] and a method of apportioning radioactivity between radioactive parents and

---

[727] J. G. Surak and D. P. Schlueter, *J. Chem. Educ.*, 1952, **29**, 144; H. H. Fillinger and L. A. Trafton, *ibid.*, p. 285; F. H. Pollard and J. F. W. McOmie, *Endeavour*, 1951, **10**, 213; G. Venturello and A. M. Ghe, *Analyt. Chim. Acta*, 1952, **7**, 261, 268; A. Lacourt, G. Sommereyns, and J. Soete, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 348; A. Lacourt, G. Sommereyns, and M. Claret, *ibid.*, p. 444; A. Lacourt, G. Sommereyns, and G. Wantier, *ibid.*, 1952, **39**, 396; A. Lacourt, G. Sommereyns, J. Hoffmann, A. Stadler, and G. Wantier, *Compt. rend.*, 1952, **234**, 2365.

[728] J. P. Ebel and Y. Volmar, *ibid.*, 1951, **233**, 415; T. Ando, J. Ito, S. Ishi, and T. Soda, *Bull. Chem. Soc. Japan*, 1952, **25**, 78.

[729] D. P. Burma, *Analyst*, 1952, **77**, 382.

[730] H. Erlenmeyer, H. von Hahn, and E. Sorkin, *Helv. Chim. Acta*, 1951, **34**, 1419.

[731] W. Hermanowicz and C. Sikorowska, *Przm. Chem.*, 1952, **8**, 238.

[732] M. M. Singh and J. Gupta, *J. Sci. Ind. Res., India*, 1951, **10**, *B*, 289.

[733] W. Ryan and A. F. Williams, *Analyst*, 1952, **77**, 293.

[734] A. F. Williams, *ibid.*, p. 297.

[735] N. F. Kember, *ibid.*, p. 78; G. W. J. Kingsbury and R. B. F. Temple, *ibid.*, p. 307.

[736] F. H. Burstall and A. F. Williams, *ibid.*, p. 983; F. H. Burstall, P. Swain, A. F. Williams, and G. A. Wood, *J.*, 1952, 1497; A. F. Williams, *ibid.*, p. 3155; R. A. Mercer and A. F. Williams, *ibid.*, p. 3399.

[737] N. F. Kember and R. A. Wells, *Chem. and Ind.*, 1952, 1129.

[738] A. T. James and A. J. P. Martin, *Biochem. J.*, 1952, **50**, 679; *Analyst*, 1952, **77**, 915.

[739] H. H. Strain, *Analyt. Chem.*, 1952, **24**, 356; M. Lederer and F. L. Ward, *Analyt. Chim. Acta*, 1952, **6**, 355.

[740] T. R. Sato, W. P. Norris, and H. H. Strain, *Analyt. Chem.*, 1952, **24**, 776; A. Tiselius, *J. Gen. Physiol.*, 1951, **35**, 89; R. Consden and W. M. Stanier, *Nature*, 1952, **169**, 783; **170**, 1069; A. B. Foster, *Chem. and Ind.*, 1952, 1050; I. Brattsten and A. Nilsson, *Arkiv Kemi*, 1951, **3**, 337.

[741] G. Manecke, *Naturwiss.*, 1952, **39**, 62.

[742] J. R. A. Anderson and M. Lederer, *Analyt. Chim. Acta*, 1952, **6**, 472.

[743] Y. Hashimoto, I. Mori, and M. Kimura, *Nature*, 1952, **170**, 975.

[744] G. B. Cook and J. F. Duncan, "Modern Radiochemical Practice," Oxford, 1952.

[745] J. E. Hudgens, *Analyt. Chem.*, 1952, **24**, 1704; M. P. Süe, *Bull. Soc. chim.*, 1951, **18**, D 9.

[746] R. Hurst and G. R. Hall, *Analyst*, 1952, **77**, 790.

daughters has been described.[747] Radio-tracers have been used for chromatographic separations.[748] Some reactions of thiosulphate and tetrathionate have been studied by tracer methods.[749] Precautions necessary for reproducible results in the elementary analysis of organic compounds containing radio-tracers have been described.[750] Radioactivity measurements have been employed for the determination of potassium,[751, 752] rubidium,[752] chromium, vanadium, and molybdenum,[753] astatine,[754] francium,[755] and americium.[756] Radioactive iron has been separated from biological materials by precipitation with cupferron and subsequent extraction.[757]

**Radioactivation.**—This important new technique for the determination, particularly, of microgram or sub-microgram amounts of materials, has been considerably extended in its application. Conditions have been described for the determination of copper in luminescent solids,[758] uranium in rocks and minerals,[759] indium,[760] arsenic,[761] antimony,[762] and trace elements in high-purity aluminium [763] and in high-purity magnesium.[764]

**Non-radioactive Tracers.**—Methods for the determination of deuterium have been discussed.[765] Methods have been described for the isolation of hydrogen before isotopic assay,[766] and for the determination of oxygen in organic compounds [767] and of hydrate-water.[768] Combined chemical analysis and tracer assay in organic analysis has been discussed, and rapid and accurate methods making use of simple interlocked chemical and tracer procedures have been described.[769]

**Gas Analysis.**—The use of a simple apparatus for the detection of a wide range of gases has been described,[770] and sensitivities for the reactions are quoted. A simple manometric gas-analysis apparatus for general quantitative work,[771] and the analysis of gas mixtures containing oxides of nitrogen [772] have been described. A method of analysis depending on desorption

---

[747] H. W. Kirby, *Analyt. Chem.*, 1952, **24**, 1678.

[748] O. G. Lion, E. A. Peterson, and D. M. Greenberg, *ibid.*, p. 920; F. P. W. Winteringham, A. Harrison, and R. G. Bridges, *Analyst*, 1952, **77**, 19; E. L. Smith and D. Allison, *ibid.*, p. 29.

[749] H. B. v. d. Heijde and A. H. W. Aten, *J. Amer. Chem. Soc.*, 1952, **74**, 3706.

[750] E. A. Evans and J. L. Huston, *Analyt. Chem.*, 1952, **24**, 1482.

[751] O. Gübeli and K. Stammbach, *Helv. Chim. Acta*, 1951, **34**, 1245.

[752] *Idem*, *ibid.*, p. 1253.

[753] J. Govaerts and C. Barcia Goyanes, *Analyt. Chim. Acta*, 1952, **6**, 121.

[754] A. H. W. Aten, T. Doorgeest, U. Hollstein, and H. P. Moeken, *Analyst*, 1952, **77**, 774.

[755] E. K. Hyde, *J. Amer. Chem. Soc.*, 1952, **74**, 4181.

[756] H. W. Miller, *Nuclear Sci. Abstr.*, 1952, **6**, 15.

[757] R. E. Peterson, *Analyt. Chem.*, 1952, **24**, 1850.

[758] E. Grillot, *Compt. rend.*, 1952, **234**, 1775.

[759] A. A. Smales, *Analyst*, 1952, **77**, 778.

[760] J. E. Hudgens and L. C. Nelson, *Analyt. Chem.*, 1952, **24**, 1472.

[761] A. A. Smales and B. D. Pate, *ibid.*, p. 717; *Analyst*, 1952, **77**, 188, 196.

[762] J. E. Hudgens and P. J. Call, *Analyt. Chem.*, 1952, **24**, 171.

[763] P. Albert, M. Caron, and G. Chaudron, *Compt. rend.*, 1951, **233**, 1108.

[764] G. J. Atchison and W. H. Beamer, *Analyt. Chem.*, 1952, **24**, 1812.

[765] M. E. Reinders, *Chem. Weekblad*, 1951, **47**, 785.

[766] J. Bigeleisen, M. L. Perlman, and H. C. Prosser, *Analyt. Chem.*, 1952, **24**, 1356.

[767] A. V. Grosse and A. D. Kirshenbaum, *ibid.*, p. 584; A. D. Kirshenbaum, A. G. Streng, and A. V. Grosse, *ibid.*, p. 1361.

[768] H. J. Morowitz and H. P. Broida, *ibid.*, p. 1657.

[769] R. C. Anderson, Y. Delabarre, and A. A. Bothner-by, *ibid.*, p. 1298.

[770] H. Malissa, A. Musil, and R. Kreibich, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 385, 403.

[771] J. N. Pitts, D. D. DeFord, and G. W. Recktenwald, *Analyt. Chem.*, 1952, **24**, 1566.

[772] C. L. Johnson, *ibid.*, p. 1572; G. Meyer and P. Voogel, *Rec. Trav. chim.*, 1951, **70**, 833.

followed by heat-conductivity measurements has been proposed.[773] Indirect analysis of mixtures by the measurement of the gas evolved by a suitable reaction has been recommended.[774] Ethylenediamine is stated to be a readily purified absorbent for carbon dioxide,[775] possessing the advantage that it is easily separated from its carbonate by vacuum distillation.

**Moisture Determination.**—A micro-method for the determination of hydrate-water in minerals has been described.[776] The preparation and use of the Karl Fischer reagent has been discussed in detail,[777] and its use in the presence of ferric salts [778] and with a dead-stop end-point apparatus [779] has been described. A solution of bromine and sulphur dioxide in chloroform has been recommended [780] as being more satisfactory in some determinations than the Karl Fischer reagent. Water in alcohols has been determined by using high-frequency oscillators,[781] and this method is reported to give particularly good results in the system ethanol–water.

**Operations in Non-aqueous Solvents.**—Acid–base [782] and general [783] titrations in non-aqueous solvents have been reviewed. Apart from investigations noted elsewhere in this Report, the titration of ammonium and amine salts of mineral acids,[784] and of a range of sodium and other metal salts [785] and of amines [786] has been described. The electrochemical potentials of a number of inorganic and organic redox systems in pyridine have been determined.[787] It has been shown that by using a glass electrode acid–base titrations in this solvent might also be possible. Ionophoretic separation of dye mixtures in non-aqueous solvents has been achieved.[788]

**Sedimentation Analysis.**—Lead has been determined by centrifuging lead sulphate,[789] and the zinc–1 : 10-phenanthroline reaction already mentioned [73] has been used in a sedimentation determination of vanadium.

**Catalysed Reactions.**—Both qualitative and quantitative methods based on catalysed reactions, in addition to those mentioned elsewhere in this Report, have been proposed. Cobalt may be detected by a catalysed oxidation of manganese(II) to manganese(IV).[790] The reducing power of the mercurous ion is enhanced in the presence of thiocyanate, so that it can be detected by its ability to reduce iron(III) to iron(II) (cf. p. 316).[791] Copper may be used for the catalytic reduction of nitrate to ammonia for quantitative determination.[792] Various catalysts have been employed in the iodometric

[773] H. Wirth, *Mikrochem. Mikrochim. Acta*, 1952, **40**, 15.

[774] N. I. Pyshkin and O. M. Lukin, *J. Anal. Chem., U.S.S.R.*, 1951, **6**, 261.

[775] R. W. Swick, D. L. Buchanan, and A. Nakao, *Analyt. Chem.*, 1952, **24**, 2000.

[776] E. B. Sandell, *Mikrochem. Mikrochim. Acta*, 1951, **38**, 487.

[777] E. Eberius, *Z. anal. Chem.*, 1952, **137**, 81.

[778] A. H. Laurene, *Analyt. Chem.*, 1952, **24**, 1496.

[779] W. A. Frediniani, *ibid.*, p. 1126.

[780] T. S. West, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 491.

[781] P. W. West, P. Senise, and T. S. Burkhalter, *Analyt. Chem.*, 1952, **24**, 1250.

[782] J. A. Riddick, *ibid.*, p. 41.

[783] J. A. Riddick, J. S. Fritz, M. M. Davis, E. F. Hillenbrand, and P. C. Markunas, *ibid.*, p. 310; T. S. West, *Ind. Chem. Chem. Manuf.*, 1952, **28**, 368, 415.

[784] J. S. Fritz, *Analyt. Chem.*, 1952, **24**, 306.

[785] C. W. Pifer and E. G. Wollish, *ibid.*, p. 519.

[786] R. J. Keen and J. S. Fritz, *ibid.*, p. 564.

[787] A. K. Gupta, *J.*, 1952, 3473, 3479.

[788] M. H. Paul and E. L. Durrum, *J. Amer. Chem. Soc.*, 1952, **74**, 4721.

[789] R. C. Jarnagin, J. T. Jones, O. L. Willbanks, and C. T. Kenner, *Analyt. Chem.*, 1952, **24**, 1115. [790] P. W. West and L. A. Longacre, *Analyt. Chim. Acta*, 1952, **6**, 485.

[791] F. Lucena Conde, *Mikrochem. Mikrochim. Acta*, 1952, **40**, 8.

[792] Z. G. Szabó and L. G. Bartha, *Analyt. Chim. Acta*, 1952, **6**, 416.

determination of persulphate.[793] Copper in sub-microgram amounts may be determined by its catalytic effect on resorcinol oxidation,[794] silver by a similar effect on the persulphate oxidation of manganese(II),[795] and iron by its catalytic effect, when co-precipitated with a cobalt–copper hydroxide carrier, on the decomposition of hydrogen peroxide.[796] The reduction of palladium in the presence of selenium by hydrazine sulphate has been utilised for the determination of palladium.[797]

**Miscellaneous Methods.**—There are several methods which cannot properly be classified under any heading, but which seem to present distinct possibilities to the analyst. H. M. Powell [798] has shown that clathrate-formation may be used in the resolution of optical isomers, and a somewhat similar operation, the formation of urea and thiourea adducts,[799] has also been found to encourage separation. The use of specific adsorbents, first suggested by L. Pauling,[800] has been investigated, and some success has been achieved with these.[801] There is some indication of a relation between the structure of the substance adsorbed and specificity, but the results are not nearly extensive enough to allow any precise deductions to be made regarding this. Finally, D. J. D. Nicholas has shown [802] that by altering the amount of trace metal in a nutrient on which a fungus is growing, the amount of the metal may be assessed by growth of the fungus, over a range from zero content to sufficiency level.

Cecil L. Wilson.

---

[793] Z. G. Szabó, L. Csanyi, and H. Galiba, *Z. anal. Chem.*, 1952, **135**, 269.

[794] R. H. Lambert, *Analyt. Chem.*, 1952, **24**, 868.

[795] A. L. Underwood, A. M. Burrill, and L. B. Rogers, *ibid.*, p. 1597.

[796] A. Krause, *Roczn. Chem.*, 1952, **26**, 3:

[797] F. Pino Perez and F. Burriel Martí, *Anal. real Soc. esp. Fís. Quím.*, 1951, **47**, *B*, 653, 657.

[798] *Nature*, 1952, **170**, 155.

[799] W. Schlenk, *Analyst*, 1952, **77**, 867.

[800] *Chem. Eng. News*, 1949, **27**, 913.

[801] F. H. Dickey, *Proc. Nat. Acad. Sci.*, 1949, **35**, 229; U. Curti and U. Colombo, *J. Amer. Chem. Soc.*, 1952, **74**, 3961; S. A. Bernhard, *ibid.*, p. 4946.

[802] *Analyst*, 1952, **77**, 629.

# CRYSTALLOGRAPHY.

## 1. CRYSTAL GROWTH.

THE remarkable outburst of interest in the mechanism of crystal growth appears to have been stimulated by the recognition that all crystals are imperfect and that dislocations can be self-perpetuating. In addition, the recent development of multiple-beam interferometry as a tool [1, 2, 3] should be mentioned.. Since the Faraday Discussion in 1949 something like 100 papers have appeared reporting observations relevant to the dislocation mechanism, or developing the mathematical theory of imperfect crystal growth. So striking are the results found, in certain cases at least, that there cannot now be any doubt of the important part played by screw dislocations in crystal growth, in these instances even if not more generally.

Theoretical physicists have developed the theory of the perfect crystal and, in particular, of the nucleation of new phases.[4, 5] This led to the predictions, (1) that, given nucleation, growth rate should be proportional to supersaturation, a relation which was found to hold rather well experimentally, and (2) that growth-rate, as determined by the rate of formation of fresh 2-dimensional nuclei on existing crystal faces, should be excessively small for the principle faces of a perfect crystal, unless supersaturation were as high as, say, 50%. At 1% supersaturation, the rate of growth should be about $10^{1000}$ times less than at 50%. Burton has remarked that this must be one of the largest known discrepancies between theory and experiment! It was recognised very early that the observed rate of growth of real crystals must be connected with their lattice imperfections but as late as 1949 there was no clear conception of how the theory should be modified. Crystal imperfections were by no means the central concern for the Faraday Discussion. It is to Frank [6] that the credit is due for pointing out that a screw-dislocation can be self-perpetuating, and that the classical conceptions of the critical nuclear size, etc., when applied to a growth step of this kind, predict a spiral-shaped growing edge, in agreement with certain well-known features of some crystal surfaces. The self-perpetuating step allows growth of the crystal to proceed without fresh nucleation, as the continual winding upon itself of an infinite single layer of unit elements, thus avoiding altogether the need for fresh nucleation of successive layers, and explaining the observed rate of growth of crystals in a most elegant fashion. Burton, Cabrera, Frank,[7, 8, 9, 10] and others have been developing the theory of dislocations very considerably. The dislocation translation (Burgers' vector [11]) may be either the unit cell

---

[1] S. Tolansky and M. Omar, *Nature*, 1952, **170**, 81.

[2] S. Tolansky, *Z. Elektrochem.*, 1952, **56**, 263.

[3] *Idem, Nature*, 1952, **169**, 445.

[4] I. N. Stransky and R. Kaischew, *Physikal. Z.*, 1935, **36**, 393.

[5] R. Becker and W. Doering, *Ann. Physik*, 1935, **24**, 719; W. K. Burton and N. Cabrera, *Discuss. Faraday Soc.*, 1949, **5**, 33, 40.

[6] F. C. Frank, *ibid.*, p. 48.

[7] W. K. Burton, N. Cabrera, and F. C. Frank, *Nature*, 1949, **163**, 398.

[8] *Idem, Phil. Trans.*, 1951, **243**, *A*, 299; F. R. N. Nabarro, *Adv. Physics*, 1952, **1**, 271.

[9] F. C. Frank, *Phil. Mag.*, 1951, **42**, 809; *Adv. Physics*, 1952, **1**, 91.

[10] *Idem, Acta Cryst.*, 1951, **4**, 497; *Z. Elektrochem.*, 1952, **56**, 429.

[11] J. M. Burgers, *Proc. K. Ned. Akad. Wet.*, 1939, **42**, 293.

translation or some simple multiple thereof; screw dislocation may be right- or left-handed and, if several are present on one face (densities up to $10^4$ dislocations per mm.$^2$ have been observed), they will give characteristic and easily recognisable patterns on the surface. The new concepts have been applied to explain polytypism [12] and twin-formation.[13]

What makes the Frank mechanism so convincing is the striking confirmation it has received from the study of crystal surfaces. The range of crystals on which markings consistent with Frank's theory have been observed includes graphite,[14] corundum,[15] hæmatite,[16] pyrites,[17] beryl,[18] quartz,[19] apatite,[20] mica,[21] and cadmium iodide; [22] also, amongst the metals, Au,[23] Mg,[24] Cd,[24] and Ti.[25] $AlB_2$[26] gives evidence of screw dislocations in the centre of the crystals, since the action of acid is to create a hole at this point; most elegant of all, and incidentally the only organic compounds represented in this list, the hydrocarbons $C_{36}H_{74}$ [27] and $C_{100}H_{202}$,[28] examined in the electron microscope by Dawson and Vand, show well-marked spirals of unimolecular step height.

It is certainly too early to form any proper assessment of the generality of the screw-dislocation mechanism in crystal growth. From the observations so far available, it would seem to be more important in minerals, simple inorganic salts, and elements. The spreading of layers outwards over the surface of a growing crystal has, of course, been observed in many instances, inorganic and organic, particularly by Bunn,[29] but, as a general rule, spiral patterns are not seen. Electron micrographs confirm the existence of layers on protein crystal faces (*e.g.*, the Rothamsted necrosis protein [30]) but show neither spirals nor the hole at the site of the dislocation itself, which in the case of protein crystals was predicted to be of the order of 100 mμ.[31] The necessity for some form of 2-dimensional nucleation is clear; but that it is always a screw dislocation cannot be said to have been proved. Dawson and Vand have shown (for $C_{100}H_{202}$) [28] that twinning can give rise to an indestructible step resulting in unimpeded growth in one direction. Perhaps many other such mechanisms remain to be found. Possibly, too, the role of impurities may have to be taken more into account.

---

[12] F. C. Frank, *Phil. Mag.*, 1951, **42**, 1014; V. Vand, *Nature*, 1951, **168**, 783; *Phil. Mag.*, 1951, **42**, 1384; G. Honjo, S. Miyake, and T. Tomita, *Acta Cryst.*, 1950, **3**, 396; see also L. S. Ramsdell and J. Kohn, *ibid.*, 1951, **4**, 75, 111.

[13] A. H. Cottrell, and B. A. Bilby, *Phil. Mag.*, 1951, **42**, 573.

[14] F. H. Horn, *Nature*, 1952, **170**, 581.

[15] A. R. Verma, *ibid.*, 1951, **167**, 939; **168**, 430, 783; *Z. Elektrochem.*, 1952, **56**, 268; *Phil. Mag.*, 1951, **42**, 1005; 1952, **43**, 441; S. Amelinckx, *Nature*, 1951, **168**, 431; H. E. Buckley, *Z. Elecktrochem.*, 1952, **56**, 275.

[16] A. R. Verma, *Nature*, 1952, **169**, 540.

[17] A. F. Seager, *ibid.*, **170**, 425.

[18] L. J. Griffin, *Phil. Mag.*, 1951, **42**, 775, 1337; **43**, 827.

[19] C. S. Brown, R. C. Kell, L. A. Thomas, N. Wooster, and W. A. Wooster, *Nature*, 1951, **167**, 940; G. van Praagh and B. T. M. Willis, *ibid.*, 1952, **169**, 623; B. T. M. Willis, *ibid.*, **170**, 115.

[20] S. Amelinckx, *ibid.*, **169**, 841; **170**, 760.

[21] *Idem*, *ibid.*, **169**, 580.

[22] A. J. Forty, *Phil. Mag.*, 1951, **42**, 670; 1952, **43**, 72, 377.

[23] S. Amelinckx, *ibid.*, p. 562; S. Amelinckx, C. C. Grosjean, and W. Dekeyser, *Compt. rend.*, 1952, **234**, 113.

[24] A. J. Forty, *Phil. Mag.*, 1952, **43**, 481, 949.

[25] M. A. Steinberg, *Nature*, 1952, **170**, 1119.

[26] F. H. Horn, E. F. Fullam, and J. S. Kasper, *ibid.*, **169**, 927.

[27] I. M. Dawson and V. Vand, *ibid.*, 1951, **167**, 476; *Proc. Roy. Soc.*, 1951, *A*, **206**, 555.

[28] I. M. Dawson, *ibid.*, 1952, *A*, **214**, 72.

[29] C. W. Bunn, *Discuss. Faraday Soc.*, 1949, **5**, 119.

[30] R. W. G. Wyckoff, *Acta Cryst.*, 1948, **1**, 292 (Fig. 7).

[31] F. C. Frank, *ibid.*, 1951, **4**, 497.

The case of $CdI_2$ is instructive. Initial crystallisation proceeds at first with great rapidity, excessively thin platelets being formed; growth then slows down, the plates begin to thicken, and it is only then that terraced steps, etc., begin to appear on the (0001) faces. $CdI_2$ affords some of the most beautiful examples of spiral growth patterns. But if screw dislocations account only for the second phase of its growth, what shall we postulate for the first? Buckley in particular has expressed scepticism in this connection.[32]

Another line of evidence which must in due course be brought to bear on the subject is the mosaic-block theory of crystal texture, strongly supported by the intensities of $X$-ray reflections.[33] Light-scattering indicates an average grain diameter of about 2000 Å for NaCl.[34] It is clear that before more can be said about the growth of crystals in general, very much more experimental work will have to be done.

There is more work on related aspects of crystal growth much harder to summarise. In this report only the briefest indication can be given of the main directions of such endeavours—the alterations of crystal form by the presence of impurites, dyes,[35] etc.; oriented overgrowths;[36] and the study by interferometry of cleavage surfaces.[37]

J. H. R.

## 2. THE TECHNIQUE OF STRUCTURE ANALYSIS.

Since 1949 when this subject was last reviewed considerable attention has been given to the development of methods for the determination of crystal structures directly from diffraction data. Trial and error methods have been used for many years with great success and there is no doubt that in the hands of a capable investigator, and especially when used in conjunction with molecular transforms, they can be very powerful. They have recently been strongly implemented (at least in 2-dimensional cases) by the further development of optical methods utilising the correspondence between the diffraction of $X$-rays and the diffraction of light. Lipson and his collaborators have pointed out that the original fly's eye procedure may be greatly simplified by the use of masks containing only a few, instead of several hundred, unit cells.[38] The revised procedure is not only faster and more convenient but also, in some respects, more useful, since the pattern can conveniently be compared with the molecular transform also obtained optically on the same scale. Positive and negative regions of the transforms may be distinguished by inserting a " pseudoatom " at a centre of symmetry. It is evident that some otherwise laborious aspects of trial analysis may be greatly eased by use of optical methods, and applications to the solution of

---

[32] H. E. Buckley, *Proc. Phys. Soc.*, 1952, *B*, **65**, 578; *Z. Elektrochem.*, 1952, **56**, 275.

[33] See, however, A. J. C. Wilson, *Acta Cryst.*, 1952, **5**, 318.

[34] R. Fürth and S. P. F. Humphreys-Owen, *Nature*, 1951, **167**, 715.

[35] J. Whetstone, *ibid.*, **168**, 663; H. E. Buckley, *Mem. Manchester Lit. Phil. Soc.*, 1950—1951, **92**, 77; H. Seifert, *Z. Elektrochem.*, 1952, **56**, 331.

[36] L. G. Schulz, *Acta Cryst.*, 1951, **4**, 483; 1952, **5**, 130, 264; D. W. Pashley, *ibid.*, p. 850; *Proc. Phys. Soc.*, 1952, *A*, **65**, 33; J. Willems, *Z. Elektrochem.*, 1952, **56**, 345; A. Neuhaus, *ibid.*, p. 453; E. Stanley, *Research*, 1951, **4**, 293; A. A. Fuller, *Nature*, 1951, **168**, 471; D. M. Evans and H. Wilman, *Acta Cryst.*, 1952, **5**, 731.

[37] S. Amelinckx, *Phil. Mag.*, 1951, **42**, 342.

[38] H. Lipson and C. A. Taylor, *Acta Cryst.*, 1951, **4**, 485; A. W. Hanson and H. Lipson, *ibid.*, 1952, **5**, 145.

several structural problems have been described.[39] Optical methods have also been applied to the summation of Fourier series.[40] It is clear, however, that, for complex crystals where the steric arrangement of the atoms is not even approximately known, trial methods may become impossible, and it is evidently desirable to have more direct routes to the solution of such structures.

Buerger [41] has described certain formal relations between the idealised electron density and the corresponding Patterson function. Regarding both maps as being composed of sets of points, the *fundamental* set and the *vector* set, he has given systematic methods of obtaining the former from the latter. Since the Patterson map can always be obtained directly from diffraction data this is equivalent to a proof that, in principle at least, the crystal structure may be solved directly from such data. The difficulty is that in practical cases the density of peaks in the Patterson map may be so great and the degree of resolution so small (for $X$-ray wave-lengths in common use) that the individual elements of the vector set are not separately recognisable. The function may, of course, be sharpened by the use of suitable modification functions but only at the cost of introducing spurious detail. Nevertheless, some degree of sharpening is certainly useful and a number of fairly complex crystal structures have been solved by the systematic interpretation of the sharpened 3-dimensional Patterson function; a detailed description of such an analysis has been given for hydroxy-L-proline.[42]

Provided that some of the atoms in the structure can be located, several methods of determining the positions of the other atoms are available. One of these (the "heavy atom" method) based on Fourier synthesis with coefficients $F_o$ and phase angles $\alpha_c$, is well known and has been of great importance in solving some very complex structures. Luzzati [43] has given a useful critical examination of the method and has shown that its power is greatly increased by the presence of a centre of symmetry. Other methods based on the systematic analysis of the Patterson function have now been proposed for such cases. Beevers and Robertson have described the "vector convergence diagram" [44] and have applied it with success to the strychnine hydrobromide structure.[45] The method involves a summation of superimposed Patterson functions, appropriately weighted if necessary, with their origin displaced to the known atomic positions; it is usually applied graphically but it may easily be shown that this process is equivalent to calculating the Fourier series with coefficients $F_o{}^2F_o$ and with phase angles $\alpha_c$. Buerger [46] has made use of a *product* function and a *minimum* function in place of the previous summation over Pattersons' and it is claimed that the minimum function provides the best convergence to the electron density. Other forms of Fourier coefficients have been proposed [47]

---

[39] A. W. Hanson, C. A. Taylor, and H. Lipson, *Nature*, 1952, **169**, 1086; C. A. Taylor, *ibid.*, p. 1087.

[40] A. W. Hanson, C. A. Taylor, and H. Lipson, *ibid.*, 1951, **168**, 160; A. W. Hanson and H. Lipson, *Acta Cryst.*, 1952, **5**, 362.

[41] M. J. Buerger, *ibid.*, 1950, **3**, 87.

[42] J. Donohue and K. N. Trueblood, *ibid.*, 1952, **5**, 414.

[43] V. Luzzati, *ibid.*, in the press.

[44] C. A. Beevers and J. H. Robertson, *ibid.*, 1950, **3**, 164.

[45] J. H. Robertson and C. A. Beevers, *ibid.*, 1951, **4**, 270.

[46] M. J. Buerger, *ibid.*, p. 531.

[47] D. McLauchlan, *Proc. Nat. Acad. Sci.*, 1951, **37**, 115; I. D. Thomas and D. McLauchlan, *Acta Cryst.*, 1952, **5**, 301; D. Rogers, *Research*, 1951, **4**, 295.

but, in the Reporters' view, it remains to be shown that any of the methods discussed above are superior to the original heavy-atom method.

A great deal of interest has centred on direct methods in which the problem is handled in transform space rather than in crystal space. The approximate structure can be recognised from a Fourier series containing comparatively few strong terms, provided that the correct phase angles (or signs) can be assigned to these, and the problem becomes one of devising means of fixing or of limiting the possible phase relations amongst the strongest terms. The Harker–Kasper (H–K) inequalities,[48] derived by application of Schwartz's inequality to the structure factor expression, have not only been of some practical importance, but have also provided the stimulus for further theoretical development. Karle and Hauptmann [49, 50] have shown that inequality relations result from the conditions that the electron density be everywhere positive and have given a general formula for deriving all such relations. No symmetry properties are required but they may readily be introduced to give the H–K inequalities as special cases. It is shown [50, 51] that if the *U*'s (unitary structure factors) rather than the *F*'s are considered, then some of the inequalities reduce to equalities, special cases of which have been reported previously.[52] A method of deriving the H–K inequalities for any space group has been described.[53] Additional phase limitations are imposed if the electron density is known over a portion of the unit cell [54] or if it is restricted to a maximum possible value; [55] no such limitations are imposed, however, by the condition that atoms must be separated by a certain minimum distance.[54] Some linear inequalties have been derived for centrosymmetric crystals; [56] these are not quite so restrictive [57] as the H–K inequalities (which involve quadratic relations) but they are easier to apply and may prove very useful. Methods for the systematic application of inequalities have been described [58] and they have been used to solve the crystal structures of oxalic acid dihydrate,[59] decaborane,[60] α- and β-selenium[61, 62] *p*-di-*tert.*-butylbenzene,[63] ethylenediamine sulphate,[56] and realgar.[64]

For the H–K inequality relation to produce definite restrictions on the signs, the *F* values involved must be greater than some minimum value. Their usefulness thus decreases as the unit of structure becomes larger until, at a certain stage, no limitations whatsoever are imposed.[65] In principle, high-order determinantal inequalities [51] could be used in such circumstances, but their practical application is likely to be rather difficult.

[48] D. Harker and J. S. Kasper, *Acta Cryst.*, 1948, **1**, 70.

[49] J. Karle and H. Hauptman, *ibid.*, 1950, **3**, 181.

[50] H. Hauptman and J. Karle, *Phys. Review*, 1950, **80**, 244.

[51] J. A. Goedkoop, *Acta Cryst.*, 1950, **3**, 374.

[52] K. Banerjee, *Proc. Roy. Soc.*, 1933, *A*, **141**, 188; M. J. Buerger, *Proc. Nat. Acad. Sci.*, 1948, **34**, 277. [53] C. H. MacGillavry, *Acta Cryst.*, 1950, **3**, 214.

[54] J. A. Goedkoop, C. H. MacGillavry, and R. Pepinsky, *ibid.*, 1951, **4**, 491.

[55] R. Pepinsky and C. H. MacGillavry, *ibid.*, p. 284.

[56] Y. Okaya and I. Nitta, *ibid.*, 1952, **5**, 564. [57] K. Sakurai, *ibid.*, p. 697.

[58] *Idem, ibid.*, p. 546; J. Gillis, *ibid.*, 1948, **1**, 174; E. Grison, *ibid.*, 1951, **4**, 489.

[59] J. Gillis, ref. 58.

[60] J. S. Kasper, C. M. Lucht, and D. Harker, *Acta Cryst.*, 1950, **3**, 436.

[61] R. D. Burbank, *ibid.*, 1951, **4**, 140. [62] *Idem, ibid.*, 1952, **5**, 236.

[63] B. S. Magdoff, *ibid.*, 1951, **4**, 176, 268.

[64] T. Ito, N. Morimoto, and R. Sadanaga, *ibid.*, 1952, **5**, 775.

[65] E. W. Hughes, *ibid.*, 1949, **2**, 34.

For a crystal composed of atoms whose atomic numbers do not differ too greatly, the electron density $\rho(\mathbf{x})$ and its square $\rho^2(\mathbf{x})$ have approximately the same form. Sayre [66] has shown that, as a consequence, $F(\mathbf{h})$ must equal its self-convolution $\Sigma_{\mathbf{p}}F(\mathbf{p})F(\mathbf{h}-\mathbf{p})$; the phase angles (or signs) must be such as to satisfy this set of equations. The equations hold in two dimensions provided that the atoms are well resolved and they have been applied to the [100] projection of hydroxy-L-proline. The equations imply a tendency for the sign of $F(\mathbf{h}+\mathbf{p})$ to be the same as that of $F(\mathbf{h})F(\mathbf{p})$. This result has also been derived by considering the extent to which a Fourier series containing only a few large terms can represent $\rho(\mathbf{x})$,[67] and also by a statistical argument.[68] The relation (1) $S(\mathbf{h}+\mathbf{p}) = S(\mathbf{h})S(\mathbf{p})$ which can be proved from inequalities to be true when the corresponding structure factors are sufficiently large, is thus *probably* true in other circumstances, as indeed is suggested by a simple trigonometric manipulation of the structure factor expression. When some signs can be obtained from inequalities, the probable validity of (1), especially when applied statistically,[68] provides a useful extension by which more signs may be discovered. The structures of glutamine [69] and of metaboric acid [68] have been solved by this method. It has been suggested that the statistical application of (1) may be valid even for structures containing up to 200 atoms in the unit cell but, from the Reporters' experience, this would appear to be a highly optimistic estimate.

A new approach to direct structure analysis has been introduced by Hauptman and Karle.[70] Each structure factor is regarded as a closed vector polygon; the magnitudes of the vectors ($f_i$) are known, but their orientations ($\phi_i$) are to be found. For each observation of $F(\mathbf{h})$, the application of the random-walk analysis leads to a distribution function for the $\phi_i$'s, and hence for the atomic co-ordinates. The strict coupling between the polygons is ignored and the individual distribution functions are multiplied together to yield a resultant probability distribution function for the co-ordinates. It remains to be seen whether this method, in its present form, will be of practical importance; the calculations are excessively lengthy and it is shown too that the final probability function is closely related to a " super-sharpened " Patterson, exp $[P(\mathbf{x})]$. The introduction of coupling between the vector polygons must necessarily strengthen the relations and we understand that this extension is being developed.

None of the methods so far described seems generally applicable to molecules of very high molecular weight. For these, rather specialised methods of restricted application are likely to be required. Vand [71] has described one such method for compounds containing structural periodicities, where the crystal unit cell may contain sub-cells. The structure may, in favourable cases, be inferred from the relations between the structure factors of the main cell and those of the sub-cell, as in the analysis of trilaurin.[72] Bragg and Perutz [73] have applied knowledge of the general shape of the hæmoglobin molecule to the absolute $F$ values at various shrinkage stages and are well on the way to a direct projection of the electron density.

---

[66] D. Sayre, *Acta Cryst.*, 1952, 5, 60.
[67] W. Cochran, *ibid.*, p. 65.
[68] W. H. Zachariasen, *ibid.*, p. 68.
[69] W. Cochran and B. R. Penfold, *ibid.*, p. 644.
[70] H. Hauptman and J. Karle, *ibid.*, p. 48.
[71] V. Vand, *ibid.*, 1951, 4, 104.
[72] V. Vand and I. P. Bell, *ibid.*, p. 465.
[73] Sir W. L. Bragg and M. F. Perutz, *Proc. Roy. Soc.*, 1952, *A*, 213, 425.

The statistical treatment of $X$-ray intensities is capable of yielding much information concerning crystal structures. One of the earliest applications gave an easy method of placing relative intensity measurements on an absolute scale.[74] A very important new development has been to provide an $X$-ray method of distinguishing between centrosymmetric and non-centrosymmetric crystals.[75] The method is quite simple and depends essentially on the different characteristics of the one- and two-dimensional Gaussian functions which describe the distribution of real and complex structure factors respectively. Centrosymmetric molecules arranged centrosymmetrically give a " hypercentric " distribution [76] distinguishable from the ordinary centric one. Other symmetry elements may also be recognised.[77] It is noteworthy that all of the 219 distinguishable space-groups may now be recognised from $X$-ray data.[77, 78]

We come now to the questions of determining the degree of reliability to be associated with a structure analysis at any given stage. Luzzati [79] has extended some earlier arguments of Wilson and others and has derived relations between the reliability index $R$ and the mean value of $\cos 2\pi(\Delta\mathbf{r}\,.\,\mathbf{s})$ where $\Delta\mathbf{r}$ is the error in an atomic co-ordinate and $\mathbf{s} = 2 \sin \theta/\lambda$. For the same degree of precision of the atomic co-ordinates, $R$ is lower in non-centrosymmetric than in centrosymmetric structures. It is shown that if the $\Delta\mathbf{r}$'s are normally distributed about zero, then $R$ plotted against $\sin \theta$ must lie on a family of curves corresponding to different values of $|\overline{\Delta\mathbf{r}}|$. This thus provides a much more delicate test for the approximate correctness of a structure than the value of $R$ itself, for, if the errors are not distributed normally, the proposed structure is incorrect, but it may nevertheless yield $R$ values as low as approximately correct, though unrefined, structures. Examples of structures which gave reasonably low $R$ values, but which had to be radically modified because they were found incapable of further refinement, are " *cis*-naphthodioxan " [80] (where an incorrect ring structure was first tested) and purpurogallin [81] (where one translational parameter of the molecule was wrongly estimated). It is possible that other examples are to be found in the literature.

The accuracy of the final co-ordinates obtainable by the Fourier and the least squares method has been discussed by Booth and by Cruickshank.[82] The relation between the two methods has been examined by the latter,[83] who finds an exact similarity between the equations for co-ordinate refinement. The convergence of the Fourier method has been discussed by Luzzati,[84] who confirms some of Cruickshank's conclusions. The principal results are as follows: (1) The same corrections (provided they are sufficiently small) are given by both methods. (2) Under identical conditions the final errors in atomic positions are twice as great for the non-centrosymmetric as for the

---

[74] A. J. C. Wilson, *Nature*, 1942, **150**, 152.

[75] *Idem*, *Acta Cryst.*, 1949, **2**, 318; E. R. Howells, D. C. Phillips, and D. Rogers, *ibid.*, 1950, **3**, 210.

[76] H. Lipson and M. M. Woolfson, *ibid.*, 1952, **5**, 680.

[77] D. Rogers, *ibid.*, 1950, **3**, 455.

[78] M. J. Buerger, *ibid.*, p. 465.

[79] V. Luzzati, *ibid.*, 1952, **5**, 802.

[80] S. Furberg and O. Hassel, *Acta Chem. Scand.*, 1950, **4**, 1584.

[81] J. D. Dunitz, *Nature*, 1952, **169**, 1087.

[82] A. D. Booth, *Proc. Roy. Soc.*, 1947, *A*, **188**, 77; *A*, **190**, 482, 490; *A*, **193**, 305; D. W. J. Cruickshank, *Acta Cryst.*, 1948, **1**, 92; 1949, **2**, 65.

[83] D. W. J. Cruickshank, *ibid.*, 1950, **3**, 10; 1952, **5**, 511.

[84] V. Luzzati, *ibid.*, 1951, **4** 367.

centrosymmetric case. Cochran [85] has given a detailed discussion of the $(F_o - F_c)$ synthesis. In the early stages, this type of synthesis may be valuable in indicating the need for structural revisions of a drastic character; Cochran has shown that it possesses a number of properties which make it useful for accurate structure analysis. One advantage of the method is that termination of series errors are largely eliminated; another is that temperature-factor parameters as well as atomic co-ordinates are refined. The method seems particularly useful for the unequivocal placing of hydrogen atoms, and for investigation of the fine detail of the electron distribution (*e.g.*, in bonds).

For very accurate results it is of course necessary to have data of the highest accuracy. With photographic recording and visual estimates it is difficult to obtain intensities more accurately than to within about 10%. Considerable advances have taken place in the techniques of using Geiger [86] and proportional [87] counters for the measurement of intensities. Absorption constitutes another serious source of error and methods of applying corrections have been described [88] although perhaps the best procedure is to eliminate such errors as far as possible by using either uniformly shaped or very small crystals where practicable. Indeed, experimental measurements of the electron distribution can only be regarded as meaningful provided that they include all the above precautions for ensuring the accuracy of the data, and have been carried out at sufficiently low temperatures.

J. D. D.

## 3. STRUCTURAL CHEMISTRY.

**Introduction.**—In this report, we have tried to cover three years of inorganic and two years of organic structure analyses by *X*-ray crystallographic methods. Metal and alloy structures have been omitted—it seemed preferable to leave them for a subsequent report than to deal with them inadequately in the space available this year. But limited space is a problem which future Reporters will have to face more and more in future years. *Acta Crystallographica* alone in 1948 contained 348 pages, which included 61 papers and 15 short communications; in 1952 the figures were 860, 150, and 67 respectively. Several factors seem to have contributed to this remarkable expansion.

The more widespread adoption of modern computing techniques has brought with it a corresponding increase in the use of three-dimensional methods. This is important for high-precision work but it also means that structures of very great complexity are now being attacked by *X*-ray methods. One molecule, whose structure is slowly being elucidated, contains about 100 atoms, and already more than ten three-dimensional Patterson and Fourier series have been computed in the course of this analysis alone; a few years ago the labour involved would have been considered prohibitive.

Structural problems concerning substances which are gaseous or liquid

---

[85] W. Cochran, *Acta. Cryst.*, 1951, 4, 408. [86] *Idem, ibid.*, 1950, 3, 268.

[87] A. R. Lang, *Nature*, 1951, 168, 907; *Proc. Phys. Soc.*, 1952, *A*, 65, 372; U. W. Arndt and D. P. Riley, *ibid.*, p. 74.

[88] R. G. Howells, *Acta Cryst.*, 1950, 3, 366; D. Grdenić, *ibid.*, 1952, 5, 283; H. T. Evans and M. G. Ekstein, *ibid.*, p. 540.

under ordinary conditions have also now been brought within the range of crystallographic analysis by recent advances in low-temperature techniques.[89] Phase transitions, residual entropy, and dielectric anomalies have already been extensively studied; hydrogen cyanide,[90] carbonyl chloride,[91] 1 : 2-dichloroethane,[92] methanol,[93, 94] *n*-propylammonium halides,[95] *cyclo*pentane,[96] *neo*hexane,[96] *neo*pentane,[97] and thiophen[98] are among the compounds examined and others will be discussed later in connection with aspects of molecular structure. Some points from the analysis of methanol illustrate the problems involved. The two independent investigations of the high-temperature modification, carried out within approximately the same temperature range, lead to different results. One,[93] based on single-crystal data, gives an orthorhombic cell in which the molecules are linked by infinite zig-zag chains of hydrogen bonds; the other,[94] based on powder data and therefore perhaps not completely reliable, leads to a hexagonal cell of a somewhat related structure. The situation is evidently more complex than had been thought and may be clarified by further *X*-ray work, especially as another transition point (at 156·3° K) has now been detected[99] in addition to the well-marked one at 159·2° K. Tauer and Lipscomb have also succeeded in interpreting the data for the low-temperature modification. The infinite zig-zags of hydrogen bonds are preserved, but they become somewhat more puckered. It is concluded that the residual entropy is zero, and that the dielectric anomaly is associated with puckering of the hydrogen-bond chains. Carbonyl chloride, at −160° C, is found to have a completely ordered structure, so that the residual entropy of 1·63 e.u. remains unexplained and presents an apparently very serious problem.

Neutron diffraction extends the range in other directions. Structural problems concerning the location of light, in the presence of heavy, atoms may now be attacked. The most extreme example of this kind, the structure of uranium hydride, $UH_3$, has already been solved.[100] The hydrogen atoms lie in distorted tetrahedra equidistant (at 2·32 Å) from four uranium atoms and not, as previously thought, between the pairs whose separation is 3·71 Å. Thorium and zirconium hydrides[101] have deformed fluorite structures with similarly large M–H distances, 2·41 Å. Earlier views on thorium carbide must be completely revised;[102] the cell is not tetragonal but monoclinic, the C–C distance is 1·5 Å, and the Th–C bonds seem to have considerable covalent character. In ammonium chloride (room temperature phase) the N–H bonds (1·03 Å) are directed towards

---

[89] S. C. Abrahams, R. L. Collin, W. N. Lipscomb, and T. B. Reed, *Rev. Sci. Instr.*, 1950, **21**, 396; H. S. Kaufman and I. Fankuchen, *ibid.*, p. 733; B. Post, R. S. Schwartz, and I. Fankuchen, *ibid.*, 1951, **22**, 218.

[90] W. J. Dulmage and W. N. Lipscomb, *Acta Cryst.*, 1951, **4**, 330.

[91] B. Zaslow, M. Atoji, and W. N. Lipscomb, *ibid.*, 1952, **5**, 833.

[92] M. E. Milberg and W. N. Lipscomb, *ibid.*, 1951, **4**, 369.

[93] K. J. Tauer and W. N. Lipscomb, *ibid.*, 1952, **5**, 606.

[94] B. Dreyfus-Alâin and J.-M. Dunoyer, *Compt. rend.*, 1952, **234**, 320; B. Dreyfus-Alain and R. Viallard, *ibid.*, p. 536.

[95] M. V. King and W. N. Lipscomb, *Acta Cryst.*, 1950, **3**, 222, 227.

[96] B. Post, R. S. Schwartz, and I. Fankuchen, *J. Amer. Chem. Soc.*, 1951, **73**, 5113.

[97] A. H. Mones and B. Post, *J. Chem. Phys.*, 1952, **20**, 755.

[98] S. C. Abrahams and W. N. Lipscomb, *Acta Cryst.*, 1952, **5**, 93.

[99] L. A. K. Staveley and M. A. P. Hogg, personal communication.

[100] R. E. Rundle, *J. Amer. Chem. Soc.*, 1951, **73**, 4172.

[101] R. E. Rundle, C. G. Shull, and E. O. Wollan, *Acta Cryst.*, 1952, **5**, 22.

[102] E. B. Hunt and R. E. Rundle, *J. Amer. Chem. Soc.*, 1951, **73**, 4777.

four of the surrounding chlorine ions, the two possible orientations being occupied at random.[103] In potassium hydrogen fluoride, the hydrogen atom is at the centre of the F–H–F bond.[104] Another type of result beyond the power of *X*-ray diffraction is the establishment of the relative positions of $Mg^{2+}$ and $Al^{3+}$ spinel as the *normal* rather than the *inverse* arrangement.[105]

Fairly accurate location of hydrogen atoms can also be given by *X*-ray analysis, if the data are sufficiently accurate and the other atoms present are not too heavy. Cochran [106] has provided an elegant demonstration that in the hydrogen bonds of salicylic acid the hydrogen atom is at nearly the normal covalent distance from one oxygen atom and that O–H···O is approximately collinear (Fig. 1). The whole question of hydrogen bonding in organic crystals has been discussed by Donohue [107] who has shown that strong hydrogen bonds are only formed when the H atom is approximately collinear with the bonded atoms; he estimates that symmetric O···O hydrogen bonds will occur only when the O···O distance is about 2·3 Å. In the several recent cases where a symmetric O···H···O bond appears to be demanded by the crystal symmetry, *e.g.*, in sodium sesquicarbonate dihydrate,[108] in potassium hydrogen bisphenylacetate,[109] and in potassium

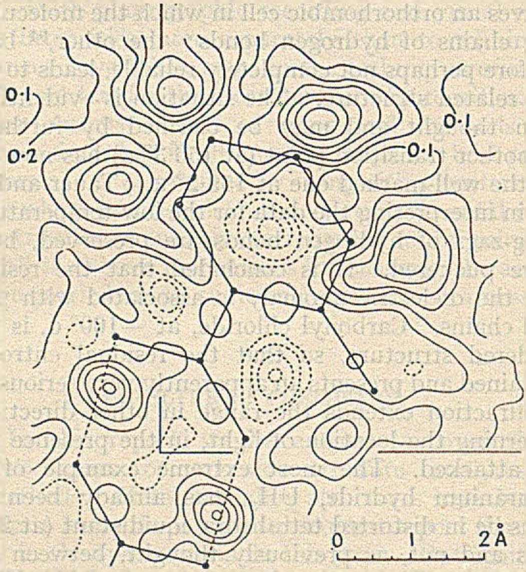


FIG. 1. ($F_o$ — $F_c$) *synthesis for salicylic acid projected on* (001). *The carbon and oxygen atoms have been "subtracted out." Hydrogen atoms and bonding electron density may be recognised in the residual function.*

---

[103] H. A. Levy and S. W. Peterson, *Phys. Rev.*, 1952, **86**, 766. See also G. H. Goldschmidt and D. G. Hurst, *ibid.*, p. 797.

[104] S. W. Peterson and H. A. Levy, *J. Chem. Phys.*, 1952, **20**, 704.

[105] G. E. Bacon, *Acta Cryst.*, 1952, **5**, 684.

[106] W. Cochran, *ibid.*, in the press.

[107] J. Donohue, *J. Phys. Chem.*, 1952, **56**, 502.

[108] C. J. Brown, H. S. Peiser, and A. Turner-Jones, *Acta Cryst.*, 1949, **2**, 167.

[109] J. C. Speakman, *J.*, 1949, 3357.

hydrogen bis-*p*-hydroxybenzoate hydrate,[110] the O–H···O distance is greater than 2·5 Å and Davies and Thomas have shown,[111] for the second example at least, that the spectroscopic data are in marked disagreement with the symmetric hypothesis. It seems likely that these bonds are not really symmetric, but rather, that the crystal symmetry arises as a result of randomness in the structure. Entropy measurements would be of considerable interest. In two cases, however, the possibility of a O···H···O bond cannot be excluded. In nickel dimethylglyoxime an O···O approach of 2·42 Å occurs and no absorption maxima corresponding to free O–H or normally bonded O–H···O are detected in the infra-red spectrum.[112] In maleic acid, an intramolecular O···O distance of 2·46 Å is observed; [113] here the bond distances in the carboxyl groups (Fig. 2) show fairly conclusively that the hydrogen atom is more firmly associated with one oxygen atom than the other. In the singly ionised maleate ion the negative charge should tend to be equally distributed between the two carboxyl groups and the proton should therefore adopt a more symmetric position. The infra-red absorption spectrum of potassium hydrogen maleate has been examined and no characteristic O–H···O bands seem to occur.[114]

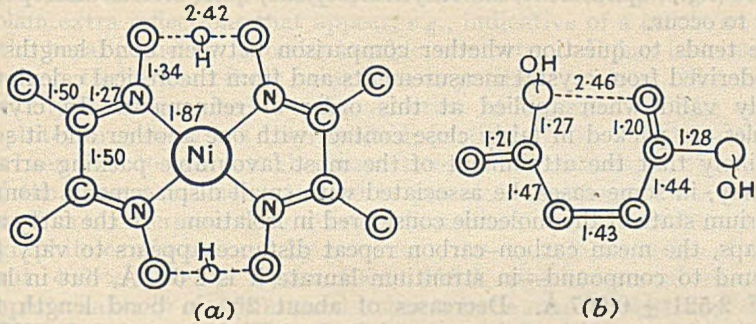


FIG. 2. *Interatomic distances* (*in* Å) *in* (a) *nickel dimethylglyoxime and* (b) *maleic acid.*

Together with the widening of the range of crystal analysis comes a significant increase in depth. It is only within the last few years that *all* the diffraction data available from a given crystal have been exploited to the full in the course of analysis. Urea, one of the first organic compounds to have been studied by *X*-ray methods, has been the subject of a recent reinvestigation; [115] the final molecular parameters and probable errors reported are: C–O, 1·262 ± 0·011 Å; C–N, 1·335 ± 0·009 Å; N–C–N, 118° ± 0·9°; N–C–O, 121° ± 0·45°. While probable errors close to the above have been claimed for many years, it may be useful to call attention to the length of the refinement process considered necessary for this simple structure in which only four parameters define the atomic positions. Of 120 reflections accessible with Cu-$K_\alpha$ radiation, the intensities of 111 could

---

[110] J. M. Skinner and J. C. Speakman, *J.*, 1951, 185.

[111] M. Davies and W. J. O. Thomas, *ibid.*, p. 2858.

[112] L. E. Godycki, R. E. Rundle, R. C. Voter, and C. V. Banks, *J. Chem. Phys.*, 1951, 19, 1205.

[113] M. Shahat, *Acta Cryst.*, 1952, 5, 763.

[114] H. M. E. Cardwell, J. D. Dunitz, and L. E. Orgel, unpublished.

[115] P. Vaughan and J. Donohue, *Acta Cryst.*, 1952, 5, 530.

be estimated, the remaining 9 being negligibly small. The final parameters were obtained after 12 Fourier sections and 2 least-square analyses in which hydrogen atom contributions and variation of the atomic form factors were both taken into account. In this report we shall mention about a dozen other analyses, many of them much more complex than this, for which similar calculations have been carried out.

Meanwhile theoretical chemists have been calculating bond lengths on the basis of various quantum-mechanical approximations, particularly for conjugated and aromatic molecules, and it is claimed [116] that, in favourable cases, they may be estimated to within 0·015 Å. We shall be discussing some of the results in later pages, noting here only that while in some cases (*e.g.*, anthracene) the agreement between observation and theory is good, in others (*e.g.*, naphthalene, dimethyltriacetylene) quite serious discrepancies appear to occur.

One tends to question whether comparison between bond lengths and angles derived from crystal measurements and from theoretical calculations is really valid when applied at this order of refinement. In crystals, molecules are packed in fairly close contact with one another and it seems quite likely that the attainment of the most favourable packing arrangement may, in some cases, be associated with small displacements from the equilibrium state of the molecule considered in isolation. In the fatty acids and soaps, the mean carbon–carbon repeat distance appears to vary from compound to compound—in strontium laurate it is 2·610 Å, but in lauric acid [117] 2·521 ± 0·007 Å. Decreases of about 2% in bond length from the gas to the crystal have been noted for hexamethylenetetramine [118] and for pentaborane.[119, 120] Such changes may well depend on the compression forces within the crystal. As yet, the nature and magnitudes of the intermolecular forces involved are not well understood but Löwdin's recent calculations [121] on lattice energies may point the way for future development.

**Elements.**—The analysis of solid chlorine provides a good example of the increased power of modern low-temperature techniques. The structure had been reported to contain a Cl–Cl bond of length only 1·82 Å, considerably shorter than the distance (2·01 Å) found in the gas by electron diffraction,[122] and also an unusually short intermolecular approach of 2·52 Å. With new single crystal data obtained at −160° c, Collin [123] has shown that the earlier results were incorrect; the structure is similar to that of bromine and iodine, with Cl–Cl 2·02 Å and Cl···Cl 3·34 Å.

The two monoclinic varieties of selenium have been studied. The more stable α-form is shown [61] to contain 8-membered puckered rings of symmetry $D_{4d}$ as in the rhombic sulphur $S_8$ molecule. The Se–Se distance is 2·34 Å, considerably longer than the 2·19 Å found in the gaseous $Se_2$ molecule [the corresponding distances for sulphur are 2·07 Å ($S_8$) and 1·89 Å ($S_2$)], and ∠Se–Se–Se is 105°. For the second, less stable, β-modification, Burbank [62]

---

[116] C. A. Coulson, *J. Phys. Chem.*, 1952, **56**, 311.

[117] V. Vand, W. M. Morley, and T. R. Lomer, *Acta Cryst.*, 1951, **4**, 324.

[118] P. A. Shaffer, *J. Amer. Chem. Soc.*, 1947, **69**, 1557.

[119] W. J. Dulmage and W. N. Lipscomb, *Acta Cryst.*, 1952, **5**, 260.

[120] K. Hedberg, M. E. Jones, and V. Schomaker, *J. Amer. Chem. Soc.*, 1951, **73**, 3538.

[121] P. O. Löwdin, *J. Chem. Phys.*, 1951, **19**, 1570, 1579.

[122] For a compilation of electron-diffraction results see P. W. Allen and L. E. Sutton, *Acta Cryst.*, 1950, **3**, 46.

[123] R. L. Collin, *Acta Cryst.*, 1952, **5**, 431.

proposed a molecule which may be described as an 8-membered ring in which one bond has been broken; we understand, however, that his data may be re-interpreted in terms of a normal 8-membered ring.[124] White phosphorus has a cubic cell containing 56 $P_4$ molecules but the complete structure has not yet been established.[125]

A good deal of attention has been given to graphite. Very careful measurements of the unit-cell size appeared to show a systematic decrease of *c* with increasing quality of crystallinity (size of crystallites, measured by line broadening).[126] It has now been established fairly definitely that the variation is only apparent, the observed spacing being the mean value of two inter-layer spacings, 3·35 Å for graphitic carbons and 3·44 Å for "non-graphitic carbons".[127, 128] The *a*-axis remains constant.[127] Various modifications of the graphite lattice have been put forward,[129] to explain extra reflections that appear, *e.g.*, indicative of a cell twice as large in the basal plane, or of orthorhombic symmetry. It has been suggested, however, that these effects arise from impurities; at least, the effects can certainly be reproduced by the addition of bromine.[130] The nature of graphites in general has been studied, particularly by Franklin,[128, 131] who has been able to estimate the proportions of the material in the crystalline and the non-crystalline state, and to postulate grouping of the crystallites, as well as to determine their average dimensions. The crystalline perfection of graphite can be reduced by grinding : the crystallite size is reduced from about 400 × 1200 to about 100 × 400 Å (thickness and diameter).[132] Graphite flakes in cast iron can be shown to be more perfect near their core than near their exterior.[133]

Of particular interest in the case of graphite is the evidence concerning the distortion of the outer electron shell of the carbon atom owing to bonding. Neutron diffraction intensities agree so well with calculated values that the Bernal structure is certainly correct, though deformation from strictly hexagonal symmetry is still a possibility.[134] $X$-Ray intensities do not agree so well. This is now clearly due to the $f$-curves used hitherto. But there can be no doubt as to the agreement of the observed data with McWeeny's new scattering function,[135] derived from Duncanson and Coulson's wave functions.[136] Strong support for the McWeeny curve is also given by Brill's results on diamond.[137] The graphite results point to the existence of about 0·08 electron in the region of each C–C bond.[134] Brill had earlier estimated 0·5—0·75 electron/bond for diamond. But the latest results of Cochran's very accurate work appear to confirm the lower value.[106]

For boron nitride, Hassel's long accepted structure,[138] though

[124] L. Pauling, personal communication.

[125] D. E. C. Corbridge and E. J. Lowe, *Nature*, 1952, **170**, 629.

[126] G. E. Bacon, *Acta Cryst.*, 1950, **3**, 137.

[127] *Idem, ibid.*, 1951, **4**, 558, 561.

[128] R. E. Franklin, *ibid.*, p. 253.

[129] G. E. Bacon, *ibid.*, 1950, **3**, 320; J. Hoerni and J. Weigle, *Nature*, 1949, **164**, 1088; J. S. Lukesh, *Phys. Reviews*, 1950, **80**, 226; 1951, **84**, 1068; *J. Chem. Phys.*, 1951, **19**, 383.

[130] J. S. Lukesh, *J. Chem. Phys.*, 1951, **19**, 1203.

[131] R. E. Franklin, *Acta Cryst.*, 1950, **3**, 107.

[132] G. E. Bacon, *ibid.*, 1952, **5**, 392.

[133] E. Matuyama, *Nature*, 1952, **170**, 1123.

[134] G. E. Bacon, *Acta Cryst.*, 1952, **5**, 492.

[135] R. McWeeny, *ibid.*, 1951, **4**, 513; 1952, **5**, 463.

[136] W. E. Duncanson and C. A. Coulson, *Proc. Roy. Soc. Edinburgh*, 1944, **62**, 37.

[137] R. Brill, *Acta Cryst.*, 1950, **3**, 333.

[138] O. Hassel, *Norsk. geol. Tidsskr.*, 1926, **9**, 266.

correct in outline, must be modified in favour of a pseudo-graphitic one.[139] Hexagonal networks of $B_3N_3$ rings (B–N, 1·45 Å) are stacked in direct register (B above N), not shifted laterally as in graphite. This stacking sequence is undoubtedly due to the polarity of the B–N bonds. An analysis of *BBB*-trichloroborazole,[140] $B_3N_3H_3Cl_3$, furnishes a fairly accurate value of the B–N distance, 1·41 Å, somewhat shorter than the value (1·44 Å) reported earlier for borazole itself.[122] Some striking similarities exist between these boron–nitrogen compounds and the isoelectronic carbon compounds (*e.g.*, the chemical behaviour of borazole and benzene) but on the other hand, $B_3N_3$ and graphite differ markedly both in electric properties and in colour. The electronic band structures of both graphite and boron nitride have been discussed.[141]

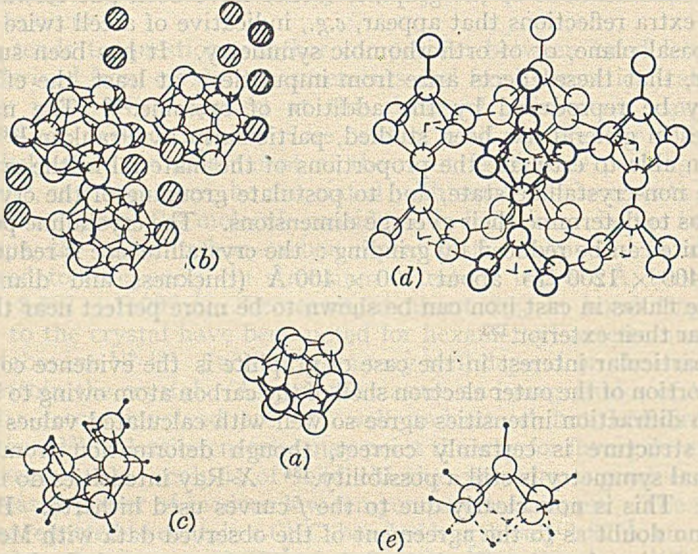


FIG. 3. *Arrangement of atoms in* (a) *elementary boron,* (b) *boron carbide,* (c) *decaborane,* (d) *calcium boride, and* (e) *pentaborane.*

A structure has at last been presented for elementary boron.[142] In the tetragonal unit cell 48 B atoms occur at the vertices of four nearly regular icosahedra which pack so that every atom forms 6 bonds in a pentagonal pyramid arrangement. Two extra atoms in special positions form tetrahedral bonds. The B–B distances are 1·75—1·80 Å, which agree well with distances found in boron hydrides and in the diborides of Al, Cr, Ti, Zr, Nb, Ta, and V, where the boron atoms form graphite-like nets.[143] The eicosohedral arrangement of boron atoms occurs also in boron carbide and (less two atoms) in decaborane. Some quite striking relations may now be recognised in several structures containing boron (Fig. 3). The structure of

---

[139] R. S. Pease, *Acta Cryst.*, 1952, **5**, 356.

[140] D. L. Coursen and J. L. Hoard, *J. Amer. Chem. Soc.*, 1952, **74**, 1742.

[141] C. A. Coulson and R. Taylor, *Proc. Phys. Soc.*, 1952, **64**, *A*, 815, 834.

[142] J. L. Hoard, S. Gellar, and R. E. Hughes, *J. Amer. Chem. Soc.*, 1951, **73**, 1892.

[143] J. T. Norton, H. Blumenthal, and S. J. Sindeband, *J. Metals*, 1949, **1**, *Trans. Sect.*, 749; R. Kiessling, *Acta Chem. Scand.*, 1949, **3**, 595.

stable pentaborane, which can now be regarded as firmly established,[119, 120] is clearly related to that of calcium boride. Boron and its compounds are continuing to supply theoretical chemistry with problems of a unique character; Longuet-Higgins [144] has discussed some of the electron-deficient compounds in terms of non-localised molecular orbitals and Hedberg [145] has given a detailed discussion of the bond lengths in the boron hydrides and related molecules.

The β-uranium structure has been solved.[146] It is tetragonal with two parallel but dissimilar planar sheets between which lie other atoms, bound, not to one another, but only to the sheets on either side. It is suggested that this relatively complex arrangement is stabilised by the presence of a nearly full Brillouin zone. Essentially the same structure is found in the σ-phase of the Fe–Cr,[147] Co–Cr,[148] and V–Ni [149] systems.

**Simple Inorganic Molecules.**—Low-temperature studies are reported for hydrazine [150] and for hydrogen peroxide,[151] two molecules important in any scheme of standard covalent radii. The *X*-ray results are 1·49 Å for O–O and 1·46 Å for N–N, in pleasing agreement with earlier values from spectroscopic and electron-diffraction evidence.[122] In hydrogen peroxide the arrangement of the hydrogen atoms, inferred from the intermolecular hydrogen bonding, is that predicted from theoretical considerations.[152] The hydrogen bonds form infinite helices round the $4_1$ screw axes of the crystal to give a rather compact structure (the density is 1·70 g. $cm.^{-3}$). In any one helix there are only two possible arrangements of hydrogen atoms and, since a given helix must retain the same arrangement throughout the crystal, no measurable residual entropy is to be expected at absolute zero. For hydrazine the possibility of residual entropy due to randomness of orientation in the solid has been suggested in view of the small discrepancy (0·44 e.u.) between the entropies calculated from calorimetric data and from structural parameters and spectroscopic assignments,[153] but here again the structure does not appear to permit the retention of any measurable entropy at low temperatures. Hydrogen bonds occur in infinite zig-zag chains in such a way as to suggest that the molecules must have either the $C_{2v}$ eclipsed or the $C_2$ semi-eclipsed configuration, instead of the staggered as usually assumed, and the same configuration must be retained throughout the length of the chains. Spectroscopic evidence, while not in serious disagreement with the eclipsed forms, has been interpreted as favouring the $C_2$ staggered configuration; [154] a *trans*($C_{2h}$)-configuration has also been suggested, on the basis of infra-red and Raman spectra, for the solid at —190°.[155] It is likely that there is only a small difference in stability between the various forms

---

[144] H. C. Longuet-Higgins, *J.*, in the press.

[145] K. Hedberg, *J. Amer. Chem. Soc.*, 1952, **74**, 3486.

[146] C. W. Tucker, *Acta Cryst.*, 1951, **4**, 425; 1952, **5**, 389, 395.

[147] B. G. Bergman and D. P. Shoemaker, *J. Chem. Phys.*, 1951, **19**, 515.

[148] D. J. Dickens, A. M. B. Douglas, and W. H. Taylor, *J. Iron Steel Inst.*, 1951, **167**, 27; J. S. Kasper, B. F. Decker, and J. R. Belanger, *J. Appl. Phys.*, 1951, **22**, 361.

[149] J. B. Pearson and J. W. Christian, *Acta Cryst.*, 1952, **5**, 157.

[150] R. L. Collin and W. N. Lipscomb, *ibid.*, 1951, **4**, 10.

[151] S. C. Abrahams, R. L. Collin, and W. N. Lipscomb, *ibid.*, p. 15.

[152] W. G. Penney and G. M. B. Sutherland, *Trans. Faraday Soc.*, 1934, **30**, 898.

[153] D. W. Scott, G. D. Oliver, M. E. Gross, W. N. Hubbard, and H. M. Huffman, *J. Amer. Chem. Soc.*, 1949, **71**, 2293.

[154] P. A. Giguere and E. A. Jones, *J. Chem. Phys.*, 1952, **20**, 136.

[155] E. L. Wagner and E. L. Bulgozdy, *ibid.*, 1951, **19**, 1210.

and that the eclipsed molecules are stabilised in the crystal by hydrogen bonds.

In hydrazine dihydrogen sulphate $(N_2H_6^{2+})(SO_4^{2-})$ [156] the hydrogen atoms have the staggered arrangement, as in the dihydrofluoride [157] and dihydrochloride.[158] In all three salts the $N_2H_6^{2+}$ ion shows a shortening of the N–N distance, from 1·47 to 1·40—1·42 Å. The value 1·45 Å has been reported for this distance in the $N_2H_5^+$ ion.[159] It has been suggested [157] that the shortening is caused by increased coulombic attraction between the extra formal charge on the nitrogen atoms and the charge of the surrounding electronic cloud, but this mechanism has been criticised [158] on the grounds that the expected degree of shortening would be much smaller than that actually observed. It is difficult to make a quantitative estimate of the effect; the coulomb attraction is increased but so is the internuclear repulsion, and it is certain that the latter will predominate for very large charges. Theoretical calculations do indicate that, in a hydrogen-like molecule, the internuclear distance is decreased as the positive charge on the nuclei increases from unity,[160] and ample spectroscopic evidence is available to show that the internuclear distance invariably decreases (and often by a considerable amount) in passing from a diatomic molecule to the corresponding isoelectronic positive ion, where the latter exists.[161] These comparisons are not strictly analogous to that between $N_2H_4$ and $N_2H_6^{++}$, but they appear to suggest that the formal charge effect may well be large enough to account for the observed shortening.[162]

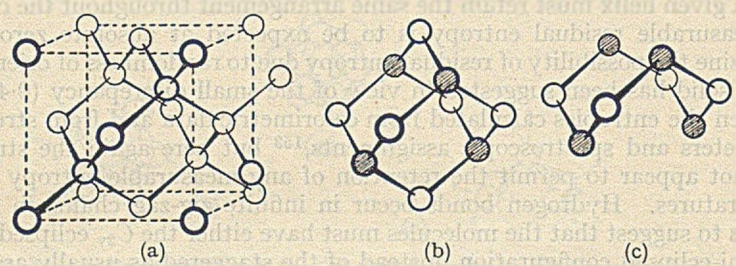


FIG. 4. *Arrangement of atoms in* (a) *diamond,* (b) "*cage*" *molecule,* e.g., $As_4S_6$, *and* (c) "*cradle*" *molecule,* e.g., $As_4S_4$. *Sulphur occupies the square positions in* $As_4S_4$ *but the tetrahedral positions in* $N_4S_4$.

Two very interesting molecular crystals, sulphur nitride [163] and realgar (arsenic sulphide),[64] whose structures have long defied analysis, have now been solved and found to be closely related. Both contain tetrameric "cradle"-shaped molecules (Fig. 4) as found by Lu and Donohue [164] for

---

[156] I. Nitta, K. Sakurai, and Y. Tomiie, *Acta Cryst.*, 1951, **4**, 289.

[157] M. L. Kronberg and D. Harker, *J. Chem. Phys.*, 1942, **10**, 309.

[158] J. Donohue and W. N. Lipscomb, *ibid.*, 1947, **15**, 115.

[159] K. Sakurai and Y. Tomiie, *Acta Cryst.*, 1952, **5**, 289, 293.

[160] T. L. Cottrell and L. E. Sutton, *Proc. Roy. Soc.*, 1951, *A*, **207**, 49.

[161] Compare, for example, internuclear distances for ground states of: LiH 1·595 Å with $(BeH)^+$ 1·312 Å; NaH 1·887 Å with $(MgH)^+$ 1·649 Å; BeH 1·343 Å with $(BH)^+$ 1·215 Å; $N_2$ 1·094 Å with $(NO)^+$ 1·066 Å; NO 1·151 Å with $(O_2)^+$ 1·123 Å: extracted from the compilation of G. Herzberg, "Spectra of Diatomic Molecules," Van Nostrand, 1950, pp. 501 *et seq.*

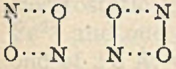
[162] See also L. Pauling, "Nature of the Chemical Bond," Cornell Univ. Press, 1940, p. 169. [163] D. Clark, *J.*, 1952, 1615.

[164] C. S. Lu and J. Donohue, *J. Amer. Chem. Soc.*, 1944, **66**, 818.

the vapour state. The bond distances, S–N 1·60, S–S 2·58 (in $N_4S_4$), and S–As 2·24, As–As 2·59 Å (in $As_4S_4$) agree fairly well with the electron diffraction results. The vapour of another arsenic sulphide, orpiment, contains " cage "-shaped $As_4S_6$ molecules.[164] It is worth remarking that the " cradle " molecule is derived from the " cage " by removal of two atoms at opposite vertices of an octahedron. The " cage " molecule is itself derived by isolating a portion of the diamond lattice, with distortion if necessary, and occurs in a wide variety of substances, adamantane ($C_{10}H_{16}$), hexamethylenetetramine ($C_{10}H_{12}N_4$), $P_4O_6$, $As_4O_6$, $As_4S_6$, and also in the $Al_4O_6$ molecules which have been shown to constitute the film on the surface of aluminium metal.[165a] The orpiment crystal does not contain discrete molecules.[64] Instead, we have superimposed layers of S-shaped chains in which each As is surrounded by three S atoms, each shared by two As atoms. The structure is nevertheless related geometrically to that of realgar, and also to that of claudetite, $As_2O_3$.[165b]

A single-crystal analysis of nickel carbonyl, $Ni(CO)_4$,[166] confirms that the molecule is tetrahedral with linear Ni–C–O ; the bond distances, Ni–C 1·84 and Ni–O 2·99 Å, agree well with the electron-diffraction results.[122]

**Oxides and Oxy-acids of the Non-metals and Related Compounds.**—Oxides and oxy-acids of nitrogen have received much attention. Nitric oxide crystals contain dimeric molecules $N_2O_2$, with N–O 1·10 and N···O 2·38 Å, rectangular in shape.[167] The electron densities are interpreted as supporting a random distribution of the two possible arrangements in agreement with the observed residual entropy of nearly $\frac{1}{2}R \ln 2$ per mole. A statistically arranged dimer with the short N–O groups parallel would also satisfy the data but one would hardly expect this arrangement to give even approximately rectangular molecules. It seems difficult to reconcile these results with the infra-red and Raman results which indicate the absence of a centre of symmetry.[168]



Nitrogen pentoxide has been examined at $-60^\circ$ and at $+20^\circ$ C ; apart from an expansion of the lattice the structure does not change within this temperature range ; [169] it is of an ionic type and may be represented as $[NO_2]^+[NO_3]^-$. The planar nitrate ions are arranged in sheets, 3·28 Å apart, and the nitronium ions are placed perpendicular to the sheets with their nitrogen atom in the plane of the sheet. The low-temperature analysis has been carried out with a high degree of accuracy, and the N–O distances are given as 1·154 and 1·243 Å in the positive and the negative ion respectively. The nitronium ion occurs also in nitronium perchlorate and in the crystalline solids isolated from nitric–sulphuric acid mixtures.[170]

Two independent refinements of Ziegler's early work [171] lead to widely differing results for the dimensions of the nitrite ion. Truter [172] has reported

---

[165a] H. G. F. Wilsdorf, *Nature*, 1951, **168**, 600.

[165b] K. A. Becker, K. Plieth, and I. N. Stransky, *Z. anorg. Chem.*, 1951, **266**, 293.

[166] J. Ladell, B. Post, and I. Fankuchen, *Acta Cryst.*, 1952, **5**, 795.

[167] W. J. Dulmage, E. A. Meyers, and W. N. Lipscomb, *J. Chem. Phys.*, 1951, **19**, 1432.

[168] A. L. Smith, W. E. Keller, and H. L. Jonston, *ibid.*, p. 189.

[169] E. Grison, K. Eriks, and J. L. de Vries, *Acta Cryst.*, 1950, **3**, 290.

[170] K. Eriks, Thesis, Amsterdam, 1952.

[171] G. E. Ziegler, *Phys. Review*, 1931, **38**, 1040.

[172] M. R. Truter, *Nature*, 1951, **168**, 344.

1·14 Å for N–O and 132° for ∠O–N–O, while Carpenter,[173] on the basis of a least-squares refinement, finds 1·23 Å and 116°. A high degree of accuracy is claimed for both analyses and it seems very difficult to reconcile the results. Carpenter's result is more likely on theoretical grounds since it gives a sensible sequence for the three molecules $NO_2^+$ (1·15 Å, 180°),[169] $NO_2$ (1·20 Å, 132°),[174] and $NO_2^-$ (1·23 Å, 116°). The nitronium ion with 16 valency electrons is expected to be linear and the bond angle should decrease from 180° as each extra electron is added,[175] with diminishing degree of N–O bonding.

In the gas phase, one bond in nitric acid is markedly longer than the others (N–OH, 1·41 Å; N–O, 1·22 Å) [122] but in condensed phases, where hydrogen bonding is possible, the proton becomes less firmly associated with any one oxygen atom and the distances tend to become more nearly equal. A very good example of this is found in the structure of ammonium trinitrate, $NH_4NO_3,2HNO_3$.[176] The two protons from the acid molecules are involved in hydrogen bonds to form a trimer diagramatically represented in Fig. 5. The bond distances are sufficiently accurate to indicate significant shortening of the N–OH distance in the acid molecules. It is also to be noted that the 3-fold symmetry of the nitrate ion is destroyed by the perturbation produced by the close approach of protons to two oxygen atoms but not to the third. Other interesting examples of the way in which nitric acid molecules may be linked are found in anhydrous nitric acid [177] (a very complex structure), in nitric acid monohydrate,[178] and in nitric acid trihydrate.[179]

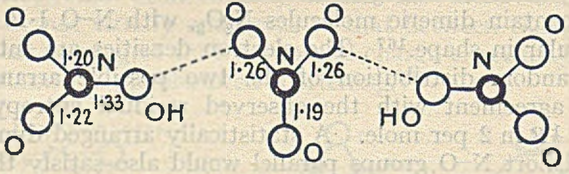


FIG. 5. *Trimer formed by two nitric acid molecules and one nitrate ion in* $NH_4NO_3,2HNO_3$.

**Borates and Silicates.**—A structure for boron trioxide, $B_2O_3$, has been derived from powder photographs.[180] The rather open 3-dimensional framework is built of distorted $BO_4$ tetrahedra with one B–O distance much longer (about 2·1 Å) than the other three (about 1·5 Å), an apparent compromise between trigonal and tetrahedral co-ordination. Cobalt [181] and magnesium [182] pyroborate, $M_2B_2O_5$, contain discrete $(B_2O_5)^{4-}$ ions, formed by two $BO_3$ triangles with one oxygen in common. $B_2O_5$ groups occur together with $BO_4$ tetrahedra in endless chains in metaboric acid, $HBO_2$.[68] Boron is triangularly co-ordinated also in the minerals warkwickite, ludwigite, and pinakiolite,[183] where the structural type is

---

[173] G. B. Carpenter, *Acta Cryst.*, 1952, 5, 132.

[174] S. Claesson, J. Donohue, and V. Schomaker, *J. Chem. Phys.*, 1948, 16, 207.

[175] A. D. Walsh, *Nature*, 1952, 170, 974.

[176] J. R. C. Duke and F. J. Llewellyn, *Acta Cryst.*, 1950, 3, 305.

[177] V. Luzzati, *ibid.*, 1951, 4, 120.

[178] *Idem, ibid.*, p. 239.

[179] *Idem, Compt. rend.*, 1951, 232, 1428.

[180] S. V. Berger, *Acta Cryst.*, 1952, 5, 389.

[181] *Idem, Acta Chem. Scand.*, 1950, 4, 1054.

[182] Y. Takéuchi, *Acta Cryst.*, 1952, 5, 574.

[183] Y. Takéuchi, T. Watanabé, and T. Ito, *ibid.*, 1950, 3, 98.

determined mainly by the packing of oxygen atoms in bands, boron cementing these bands together. One may compare the boroferrites.[184] Boron is tetrahedrally surrounded by four OH's, however, in teepleite, $2NaCl,Na_2B_2O_4,H_2O$,[185] and in bandylite, $CuCl_2,CuB_2O_4,4H_2O$ [185, 186] [where the Cu atoms are in planar 4-fold co-ordination, as in malachite $Cu_2(OH)_6CO_3$ [187] and basic copper nitrate, $Cu_4(OH)_6(NO_3)_2$].[188] In boracite, $ClMg_3B_7O_{13}$,[189] high- and low-temperature forms, boron is found in tetrahedra and in $BO_3$–O pyramids, the latter built on a nearly planar $BO_3$ triangle. The tetrahedra and pyramids share all their corners, so forming a rigid unbroken boron–oxygen network in which relatively large spaces are left for Mg and Cl ions.

Isolated $SiO_4$ groups exist in chloritoid, $(Fe,Mg)_2Al(OH)_4Al_2O_3(SiO_4)_2$,[190] where the arrangement is in layers similar to those in muscovite but without fusion of the $SiO_4$ groups into sheets. Like moscovite, this mineral contains an OH group; it was identified (by balancing the electrostatic valencies) but the position of the hydrogen atom was not inferred. Infinite chains of tetrahedra are found in sodium silicate, $Na_2SiO_3$,[191] where the structure is essentially similar to that of diopside. In the mineral axinite, $Ca_2Al_2(Fe,Mn)BO_3SiO_{12}OH$,[192] the $SiO_4$ tetrahedra associate into rings of $Si_4O_{12}$, similar to the $P_4O_{12}$ rings of the tetrametaphosphate ion.[193] This is the first time that independent $Si_4$ rings have been observed (in beryl, for example, they are fused with $Si_6O_{18}$ rings). The $BO_3$ groups are planar and symmetrical. The OH group identified by electrostatic considerations is situated almost equidistantly between the $Fe^{2+}$ and one $Al^{3+}$ ion. Its distances from four oxygen neighbours include one of 2·5 Å, while the others exceed 2·9 Å, from which the position of the hydrogen bond might well be deduced. But unfortunately the accuracy of atomic parameters is not sufficient to allow certainty in this: at least four other O–O distances are apparently below 2·5 Å. The $Si_6O_{18}$ ring is exemplified by tourmaline. The original note by Buerger and Hamburger, mentioned in 1949, has been followed by a full account of their analysis of this complex and beautiful structure.[194] In the meantime Japanese workers have given a detailed report of an independent analysis,[195] the first announcement of which was as early as 1947. There are no essential differences in the results obtained, although some atomic parameters differ by as much as 0·5 Å. Another very beautiful structure is that of milarite, $K_2Ca_4Be_4Al_2Si_{24}O_{60},H_2O$,[196] where double rings, $Si_{12}O_{30}$, have been found, formed by the fusion of six additional $SiO_4$ tetrahedra, by edges, to the $Si_6O_{18}$ ring. These rings are linked into three-dimensional framework by (Be,Si) atoms, with $K^+$ and $H_2O$ in the centres of the double rings, and $Ca^{2+}$ ions in the spaces between the rings. The peculiar optical properties of

---

[184] E. F. Bertaut, *Acta Cryst.*, 1950, **3**, 473.
[185] M. Fornaseri, *Ric. sci.*, 1951, **21**, 1192.
[186] R. L. Collin, *Acta Cryst.*, 1951, **4**, 204.
[187] A. F. Wells, *ibid.*, p. 200.
[188] W. Nowacki and R. Scheidegger, *Helv. Chim. Acta*, 1952, **35**, 375.
[189] T. Ito, N. Morimoto, and R. Sadanaga, *Acta Cryst.*, 1951, **4**, 310.
[190] G. W. Brindley and F. W. Harrison, *ibid.*, 1952, **5**, 698.
[191] A. Grund and M. M. Pizy, *ibid.*, p. 837.
[192] T. Ito and Y. Takéuchi, *ibid.*, p. 202.
[193] C. Romers, J. A. A. Ketelaar, and C. H. MacGillavry, *ibid.*, 1951, **4**, 114.
[194] G. Donnay and M. J. Buerger, *ibid.*, 1950, **3**, 379.
[195] T. Ito and R. Sadanaga, *ibid.*, 1951, **4**, 385.
[196] T. Ito, N. Morimoto, and R. Sadanaga, *ibid.*, 1952, **5**, 209.

this mineral were attributed to "incipient" twinning; but it is probable that this requires further investigation. A continuous layer structure is found in the mineral amesite, long thought to be a chlorite, but now clearly a kaolin-type crystal.[197]

Several calcium silicate minerals occurring in cement have been studied recently, with interesting results. Isolated $SiO_4$ tetrahedra are found in each case. The dicalcium compound,[198] $Ca_2SiO_4$ has $\alpha$, $\alpha'$, $\beta$, and $\gamma$ forms, in order of temperature stability. The second, stable at moderate temperatures, has a $\beta$-$K_2SO_4$ structure; the $\beta$-form is only slightly distorted from this. The $\gamma$-form, into which the $\beta$-crystal changes slowly, has an olivine structure. Tricalcium silicate [199] also has a number of distinct forms, but with more marked pseudo-hexagonal symmetry, rather more tendency to disorder and, relatively to the dicalcium salt, a somewhat more open structure which is thought to explain its much more rapid rate of hydration by water. The structures of two hydrates are reported. In $Ca_2SiO_4$ $\alpha$-hydrate,[200] the $SiO_4$ groups are arranged so as to accommodate one water molecule per formula unit. From consideration of the temperature required to dehydrate the crystal, the water is thought to be present as hydroxyl ion, with loss of a proton to an $SiO_4$ group. Unfortunately, owing to the limited data available, it is not possible to discuss the hydrogen bonding. Hydrogen bonding has been studied with great care, however, in the afwillite crystal, $Ca_3(SiO_3OH)_2 2H_2O$,[201] occurring in cement. The combined evidence of the electrostatic balance and inter-atomic distances establishes the presence of 6 hydrogen bonds, which fall strikingly into two groups, of mean length 2·52 and 2·72 Å. They are all situated near the plane across which cleavage is thought to occur.

Before leaving the silicates, mention should be made of the observation recently made, that, at a controlled temperature, acid will remove the Al atoms from tetrahedral and octahedral sites at quite different rates.[202] Also there is the important study of the laminated structure of certain silicate minerals, microclase,[203] anorthoclase,[203] and chrysotile,[204] where two different crystal structures have been found associated on a sub-microscopic scale. Stacking disorder, where successive layers suffer rotational and translational displacements, is very frequent among the silicates. The case of the chlorites has been given detailed attention.[205]

**Phosphates and Sulphates, etc.**—An interesting phosphate structure is that of tervalent cerium (and the rare earths La, Pr, Nd).[206] The hexagonal crystal has oxygen-lined channels containing zeolitic water. The open character of the structure is emphasised by the startling increase in density—25%—on passing to the monoclinic modification monazite. The hydrated iron phosphate minerals, vivianite [207] (and the isomorphous arsenate) and ludlamite,[208] have related structures in which $FeO_6$ octahedra, some sharing edges and corners, are linked by $PO_4$ groups into bands. These are held

---

[197] G. W. Brindley, B. M. Oughton, and R. F. Youell, *Acta Cryst.*, 1951, **4**, 552.

[198] C. M. Midgley, *ibid.*, 1952, **5**, 307.

[199] J. W. Jeffery, *ibid.*, p. 26.

[200] L. Heller, *ibid.*, p. 724.

[201] H. D. Megaw, *ibid.*, p. 477.

[202] G. W. Brindley and R. F. Youell, *ibid.*, 1951, **4**, 495.

[203] T. Ito and R. Sadanaga, *ibid.*, 1952, **5**, 441.

[204] E. J. W. Whittaker, *ibid.*, 1951, **4**, 187.

[205] G. W. Brindley, B. M. Oughton, and K. Robinson, *ibid.*, 1950, **3**, 408.

[206] R. C. L. Mooney, *ibid.*, p. 337.

[207] H. Mori and T. Ito, *ibid.*, p. 1.

[208] *Idem*, *ibid.*, 1951, **4**, 412.

together in vivianite only by hydrogen bonds between the water molecules, in ludlamite by the sharing of water molecules. A synthetic mineral, iron lazulite, $Fe_7(PO_4)_4(OH)_4$,[209] has a similar, though closer packed, arrangement. Potassium, ammonium, and cæsium hexafluorophosphates have an NaCl-type structure formed of $K^+$ and $(PF_6)^-$ ions.[210]

An interesting thiosulphate structure is that of sodium thiosulphate $Na_2S_2O_3,5H_2O$; sodium is surrounded by a distorted octahedron of water molecules and oxygen atoms, and columns of linked octahedra are held together laterally by the thiosulphate groups (which are approximately tetrahedral, S–S 1·97 Å).[211] It is instructive to compare the Na co-ordination in this salt and in $Na_3SbS_4,9H_2O$.[212]

Detailed analyses are reported for three sulphuric acid derivatives. In potassium sulphamate [213] the S–N distance, 1·60 Å, indicates considerable π-bonding corresponding to $H_2\overset{+}{N}{=}SO_3^{--}$. In potassium and ammonium dinitrososulphite S–N is 1·79 Å, exceptionally long even for a single bond (Tables of covalent radii give 1·74 Å). Within the planar $N_2O_2$ groups the bonds lengths are shortened, in fair agreement with results of molecular-orbital calculations. For sulphamic acid itself,[214] S–N is 1·73 and S–O 1·48 Å. Here, as expected from the high melting point, 206° c (cf. sulphuric acid 10°), the molecule is a zwitterion, $H_3\overset{+}{N}\cdot SO_3^-$. The S–O distance is rather longer than is usual in molecules of this type. This distance remains remarkably constant in systems involving *d* orbitals on the central sulphur atom (see ref. 213), a point which is emphasised by a recent low-temperature study of sulphur dioxide where the value 1·430 Å is found,[215] in perfect agreement with micro-wave and electron-diffraction results.

The Cl–O distance in systems involving *d* orbitals on the central atom likewise seems constant, 1·49 Å in $ClO_2$ [216] and 1·48 Å in $LiClO_4$,[217] the only cases for which accurate results are available. With selenium as central atom the corresponding distance varies much more. In selenic acid [218] and in $SeO_2$ vapour [122] it is 1·61 Å but in selenious acid [219] and in crystalline $SeO_2$ [220] the bonds are much longer, between 1·72 and 1·78 Å.

**Metallic Oxides and Related Compounds.**—In discussing these compounds, it is convenient to note the transition from low to high co-ordination number; in particular, from tetrahedral to octahedral environment of the metal atom.

Tetrahedral $CrO_4$ groups are found in chromium trioxide,[221] linked in chains by sharing of corners. The complex oxide, $Th(OH)_2CrO_4,H_2O$ [222] contains discrete $CrO_4$ tetrahedra situated between infinite zig-zag chains

[209] L. Katz and W. N. Lipscomb, *Acta Cryst.*, 1951, 4, 345.
[210] H. Bode and H. Clausen, *Z. anorg. Chem.*, 1951, 265, 229.
[211] P. G. Taylor and C. A. Beevers, *Acta Cryst.*, 1952, 5, 341.
[212] A. Grund and U. Preisinger, *ibid.*, 1950, 3, 363.
[213] G. A. Jeffrey and H. P. Stadler, *J.*, 1951, 1467.
[214] F. A. Kanda and A. J. King, *J. Amer. Chem. Soc.*, 1951, 73, 2315.
[215] B. Post, R. S. Schwartz, and I. Fankuchen, *Acta Cryst.*, 1952, 5, 372.
[216] J. D. Dunitz and K. Hedberg, *J. Amer. Chem. Soc.*, 1950, 72, 3108.
[217] R. E. Gluyas, 10th Ann. Pittsburgh Diffraction Conference, 1952.
[218] M. Bailey and A. F. Wells, *J.*, 1951, 968.
[219] *Idem, ibid.*, 1949, 1282.
[220] J. D. McCullough, *J. Amer. Chem. Soc.*, 1937, 59, 789.
[221] A. Byström and K. A. Wilhelmi, *Acta Chem. Scand.*, 1950, 4, 1131.
[222] G. Lundgren and L. G. Sillen, *Arkiv Kemi*, 1949, 1, 277.

of $Th(OH)_2$. [Similar chains occur in $Th(OH)_2SO_4$.[223]] The ferrate ion, $FeO_4^{2-}$, as found in $BaFeO_4$ etc.,[224] has almost the same dimensions as the $CrO_4$ group. The $CrO_3Cl^-$ ion is very similar too; [225] the Cr–Cl distance, 2·16 Å, incidentally, agrees with that in chromyl chloride.[122] In carnotite, $KUO_2VO_4(H_2O)_{1\cdot5}$, and the synthetic compound, $KUO_2VO_4$,[226] 2-dimensional sheets are formed by linear $UO_2^+$ groups and tetrahedral $VO_4^{2-}$ groups, with the $K^+$ ions and water of crystallisation between the layers.

Nickel complexes are commonly square coplanar; the $BaNiO_3$ structure provides a further example. In NiO,BaO, planar 4-fold co-ordination occurs, although the magnetic moment shows two unpaired electrons. A quite unusual planar 3-fold arrangement is shown by NiO,3BaO, however.[227]

An unusual formation with 5-fold co-ordination exists apparently in vanadium pentoxide, $V_2O_5$, where the octahedron of oxygen atoms around the vanadium is so much distorted (longest bond 2·81, others between 1·54 and 2·02 Å) that the group is virtually a trigonal bipyramid.[228] Tetrahedra occur, however, in heavy metal orthovanadates, $M_3VO_4$, such as the rare-earth salts (all of which are isomorphous) which have the zircon structure, with M in 8-fold co-ordination.[229]

As regards octahedral complexes, much attention has again been given to such structures as those built up by the oxides of Mo and W. A number of these, notably the near-trioxides $Mo_8O_{23}$ and $Mo_9O_{26}$, were described in the previous Report. (The structure of the trioxide itself, known since 1931, has been confirmed and refined.[230]) A still more complex oxide, $WO_{2\cdot90}$, has been examined,[231] as well as a mixed oxide $(Mo_{0\cdot85}W_{0\cdot15})O_{2\cdot90}$.[232] All these near-trioxides may be written as $M_nO_{3n-1}$. In this type of structure, octahedra are linked by corners infinitely in three dimensions (which would give the composition $MoO_3$) except that, in one direction, after every $n$ octahedra, edges are shared instead of corners, thus giving rise to the ratio of metal to oxygen, $n : 3n - 1$. The paramolybdate ion $[Mo(Mo_6O_{24})]^{6-}$, as it exists in the salt $(NH_4)_6Mo_7O_{24},4H_2O$, has been found [233] to be slightly different from the corresponding ion $Te(Mo_6O_{24})^{6-}$ whose structure, a regular hexagon of $MoO_6$ octahedra round the tellurium atom, was obtained by Evans.[234] In the homopolyacid anion, the 7 octahedra do not lie in a single plane; instead, three lie in a plane a little separated from that of the remaining four; this distortion gives the ion a greater compactness. The paratungstate ion, however, in the compound $5Na_2O,12WO_3,28H_2O$,[235] consists, not of 6, but of 12 tungsten atoms associated with 46 oxygens rather than the 41 needed to give the ion a charge equal and opposite to $10Na^+$. The tungsten atoms themselves appear

---

[223] G. Lundgren, *Arkiv Kemi*, 1951, **2**, 535.

[224] H. Krebs, *Z. anorg. Chem.*, 1950, **263**, 175.

[225] L. Helmholz and W. R. Foster, *J. Amer. Chem. Soc.*, 1950, **72**, 4971.

[226] P. Sundberg and L. G. Sillen, *Arkiv Kemi*, 1950, **1**, 337.

[227] J. J. Lander, *Acta Cryst.*, 1951, **4**, 148.

[228] A. Byström, K. A. Wilhelmi, and O. Brotzen, *Acta Chem. Scand.*, 1950, **4**, 1119.

[229] W. O. Milligan and L. W. Vernon, *J. Phys. Colloid Chem.*, 1952, **56**, 145.

[230] G. Anderson and A. Magnéli, *Acta Chem. Scand.*, 1950, **4**, 793.

[231] A. Magnéli, *Nature*, 1950, **165**, 356. [232] *Idem*, *Research*, 1952, **5**, 394.

[233] I. Lindquist, *Acta Cryst.*, 1950, **3**, 159; *Arkiv Kemi*, 1950, **2**, 325.

[234] H. T. Evans, *J. Amer. Chem. Soc.*, 1948, **70**, 1291.

[235] I. Lindquist, *Acta Cryst.*, 1952, **5**, 667.

to be grouped as a hollow cage; but the oxygen atoms of their octahedra are actually all in contact, in hexagonal close packing. Incidentally the disposition and function of the water molecules in these structures is still an open question. Another ion, $Mo_2O_7^{2-}$ (and the corresponding $W_2O_7^{2-}$), has been found to be an infinite chain made up of $MoO_4$ tetrahedra and $MoO_6$ octahedra.[236] $MoO_4$ (or $WO_4$) tetrahedra are not common, but do occur in such compounds as $M_2MoO_4$ where M = Ag, Na, $\frac{1}{2}$Ca, etc. A six-membered ring of $WO_6$ octahedra, is formed in the tungsten bronzes, $M_xWO_3$.[237] Continuous sheets of octahedra are found in yellow molybdic acid, $MoO_3,2H_2O$, the octahedra sharing corners in two directions to give the layers the composition $(MoO_4)_n$. The remaining oxygen atom must lie between the layers and the very interesting speculation has been advanced that, by analogy with $BaUO_4$, a doubly charged ion $H_4O^{2+}$ is present.[238]

In lithiophorite,[239] $MnO_6$ octahedra form sheets stacked alternately with sheets of $(Al,Li)(OH)_6^-$ octahedra. The layers are bound to one another by hydrogen bonds very much as in hydrargillite. A three-dimensional framework of continuous tubes is built up by $MnO_6$ octahedra in psilomelane, $(BaH_2O)_2Mn_5O_{10}$. The arrangement is reminiscent of the zeolites and, indeed, dehydration properties are closely similar.[240]

The co-ordination of titanium with oxygen, as illustrated by barium titanate, can vary enormously—from a perfect octahedron with all oxygen atoms shared, to a trigonal pyramid with no sharing of oxygen. Barium titanate has received much attention, owing to its very important ferroelectric properties. The structures of the cubic[241] and the tetragonal[242] forms have been examined—as also have the structures of the ferroelectric niobates and tantalates.[243] Twinning and polymorphism in these and other ferroelectrics has been discussed.[244] A comprehensive study of the origin of ferroelectricity in $BaTiO_3$ in particular, and covering $PbZnO_3$, $NaNbO_3$, $KNbO_3$, $NaTaO_3$, $KTaO_3$, $RbTaO_3$, and $WO_3$, has been made by Megaw.[245] There are also more complex titanates and niobates.[246]

Another structure determination from powder photography is that of $Na_xPt_3O_4$ ($x < 1$).[247] Pt atoms, in continuous rods, surrounded by oxygen in square array, form an infinite cubic stage structure, with the Na ions at the centre of each cubic hole, between 8 oxygen atoms. As to oxides of very low oxygen content, it has been found that those of the formula $M_3Ti_3O$, where the metal is Mn, Fe, Co, Ni, or Cu (but not V, Cr, or Zn), have the high-speed steel carbide structure, $Fe_3W_3C$, and show metallic properties.[248]

**Halide Structures.**—The fluorides present cases of very varying complexity. The simple hydrate, $KF,2H_2O$, consists of distorted octahedra about both $K^+$ and $F^-$ ions, and distorted tetrahedra of two positive and

---

[236] *Idem*, *Acta Chem. Scand.*, 1950, **4**, 1066.

[237] A. Magnéli, *Nature*, 1952, **169**, 791.

[238] I. Lindquist, *Acta Chem. Scand.*, 1951, **5**, 670.

[239] A. D. Wadsley, *Acta Cryst.*, 1952, **5**, 676.

[240] *Idem*, *Nature*, 1952, **170**, 973.

[241] J. W. Edwards, R. Speiser, and H. L. Johnston, *J. Amer. Chem. Soc.*, 1951, **73**, 2934.

[242] H. T. Evans, *Acta Cryst.*, 1951, **4**, 377.

[243] P. Vousden, *ibid.*, p. 68, 373, 545; 1952, **5**, 690; R. Pepinsky, *ibid.*, p. 288.

[244] E. A. Wood, *ibid.*, 1951, **4**, 353; R. G. Rhodes, *ibid.*, p. 105.

[245] H. D. Megaw, *ibid.*, 1952, **5**, 739.

[246] B. Aurivillius, *Arkiv Kemi*, 1950, **1**, 499; 1951, **2**, 519; 1951, **3**, 153.

[247] J. Waser and E. D. McClanahan, *J. Chem. Phys.*, 1951, **19**, 413; 1952, **20**, 199.

[248] N. Karlsson, *Nature*, 1951, **168**, 558.

two negative ions about the $H_2O$ molecules.[249] In $K_2TiF_6$, titanium is octahedrally surrounded by fluorine (Ti–F 1·91 Å) while the potassium has 12 fluorine neighbours.[250] Quite simple structures are also found for $MnF_2$,[251] $MoF_3$, and $TaF_3$.[252] In $VF_3$ [253] the structure may be regarded as built up of alternate planes of fluorine and vanadium atoms. In $CsSb_2F_7$,[254] however, the antimony is approximately tetrahedrally surrounded by fluorine (Sb–F 2·2 Å); two tetrahedra sharing corners form the anion $Sb_2F_7^-$. A more complex situation appears to exist in the salts $MSb_4F_{13}$ (M = K, Rb, Cs, $NH_4$, or Tl).[255] The Sb is linked to three F's by three short bonds (pyramidal, Sb–F, 2·0 Å) and then through three more fluorine atoms at about 3·0 Å to three other $SbF_4$ tetrahedra forming in this way a finite complex $Sb_4F_{13}^-$. Some double fluoride structures have been briefly surveyed and the relationships between them and oxide structures discussed.[256] The oxyfluoride of actinium has the fluorite structure; LaOF, YOF, and PuOF are closely related.[257]

Like potassium cuprochloride, the compounds $(NH_4)_2CuCl_3$, $(NH_4)_2CuBr_3$, and $K_2AgI_3$ have been found to be based on $MX_4$ tetrahedra sharing corners to form long chains of composition $MX_3$, with the positive ions situated between them.[258] Copper is tetrahedral also in $CsCuCl_4$.[259] Indium monobromide, InBr, has a rather unusual double-layer structure with one In–Br distance 2·80, and four others 3·29 Å, indicating considerable covalency.[260] InBr is isostructural with orthorhombic TlI, which is interesting, in view of the similar electronic configuration of indium and thallium. However, TlI can also crystallise with a CsCl- or NaCl-type structure.[261] Another markedly covalent halide is $ThBr_4$, with two Th–Br distances of 2·57 Å.[262] $NaAlCl_4$ forms an ionic lattice of $Na^+$ and $AlCl_4^-$ ions (Al–Cl 2·13 Å),[263] in marked contrast to the octahedral arrangement in aluminium chloride; presumably the strongly electro-positive sodium is responsible. The bridged structure for fused aluminium chloride, $Al_2Cl_6$, has been confirmed. For fused indium(III) iodide the *X*-ray analysis does not distinguish clearly between the monomeric and the dimeric form; fused tin(IV) iodide, as expected, contains monomeric tetrahedral molecules.[264]

In $K_4Ru_2Cl_{10}O,H_2O$, the anion is a double octahedron composed of two Ru atoms joined by O and surrounded each by five Cl atoms (Ru–O–Ru is linear).[265] The compounds $Co(NH_3)_6,TlCl_6$ and $Co(NH_3)_6,TlBr_6$ have a simple NaCl-type lattice, with Co and Tl surrounded by octahedra

---

[249] T. H. Anderson and E. C. Lingafelter, *Acta Cryst.*, 1951, **4**, 181.

[250] S. Siegel, *ibid.*, 1952, **5**, 683.

[251] M. Griffel and J. W. Stout, *J. Amer. Chem. Soc.*, 1950, **72**, 4351.

[252] V. Gutmann and K. H. Jack, *Acta Cryst.*, 1951, **4**, 244.

[253] *Idem, ibid.*, p. 246.

[254] A. Byström and K. A. Wilhelmi, *Arkiv Kemi*, 1951, **3**, 373.

[255] *Idem, ibid.*, p. 17.

[256] W. L. W. Ludekens and A. J. E. Welch, *Acta Cryst.*, 1952, **5**, 841.

[257] W. H. Zachariasen, *ibid.*, 1951, **4**, 231.

[258] C. Brink and H. A. S. Kroese, *ibid.*, 1952, **5**, 433; C. Brink and A. E. van Arkel, *ibid.*, p. 506. [259] L. Helmholz and R. F. Kruh, *J. Amer. Chem. Soc.*, 1952, **74**, 1176.

[260] N. C. Stephenson and D. P. Mellor, *Austral. J. Sci. Res.*, 1950, **3**, *A*, 581.

[261] L. G. Schulz, *Acta Cryst.*, 1951, **4**, 487. [262] R. W. M. D'Eye, *J.*, 1950, 2764.

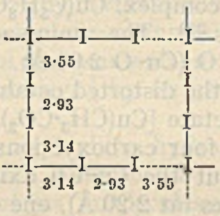
[263] N. C. Baenziger, *Acta Cryst.*, 1951, **4**, 216.

[264] R. L. Harris, R. E. Wood, and H. L. Ritter, *J. Amer. Chem. Soc.*, 1951, **73**, 3151; R. E. Wood and H. L. Ritter, *ibid.*, 1952, **74**, 1760, 1763.

[265] A. McL. Mathieson, D. P. Mellor, and N. C. Stephenson, *Acta Cryst.*, 1952, **5**, 185.

of ammonia and halogen respectively;[266] the bismuth compound, $Co(NH_3)_6,BiCl_6$, is isomorphous.[267] In the lead compound,[267] which is diamagnetic, the lead appears to exist in two valency states; $PbCl_6$ octahedra of differing dimensions are indicated by extra lines in the powder photographs. The structure of $K_2ReBr_6$ is of the $K_2PtCl_6$ type, as expected.[268] Other halide anions which have been studied by *X*-ray diffraction of their solutions include $PtCl_6$, $PtBr_6$, $Ta_6Br_{12}$, and $Ta_6Cl_{12}$.[269] Another bromide recently studied is $FeBr_2$.[270]

The mixed halide $PCl_6I$ has been shown to be tetrachlorophosphonium dichloroiodide, where the cation $[PCl_4]^+$ is tetrahedral and the anion $[Cl{-}I{-}Cl]^-$ is linear.[271] A series of polyiodide anions, $I_3^-$, $I_5^-$, $I_7^-$, and even $I_9^-$, may be obtained by dissolving iodine in aqueous potassium iodide. The $I_3^-$ ion has been found to be linear with I–I distances 2·82 and 3·10 Å [272] (cf. 2·67 Å in $I_2$). In $NMe_4I_5$ [273] we have two sets of almost square nets of iodine atoms (represented diagramatically below) separated by 4·3 Å. The cations are situated in the large empty spaces between the nets (see inset). The distances vary sufficiently so that discrete V-shaped $I_5^-$ ions may be recognised. It seems very probable that these complex ions arise from the polarisation of $I_2$ molecules by $I^-$ ions to give $I{-}I \cdots I^-$, $I{-}I \cdots I^- \cdots I{-}I$, etc. The high members are formed only with very large cations and it would be very interesting to know their structures.



(Bond lengths in Å.)

**Mercury Compounds.**—Several interesting compounds of mercury remain to be described. Aminomercuric chloride and bromide contain zig-zag chains $-Hg{-}NH_2^+{-}Hg-$, linear about Hg, tetrahedral about N, with the halide ions between the chains.[274] The structure of Millon's base, $Hg_2N{\cdot}OH,2H_2O$, must be rather similar, although here the $-Hg{-}N{-}Hg$ network is of the cristobalite type.[275] Cinnabar, HgS, has infinite spiral chains, $-Hg{-}S{-}Hg-$ with an angle of 105° at S, and the bonds nearly collinear at Hg (172°).[276]

**Chelate Compounds.**—Chromium has provided some rather interesting examples of chelate co-ordination in the oxalato-complexes. In $K_3[Cr(C_2O_4)_3)],3H_2O$, the chromium is surrounded octahedrally by the six oxygen atoms (Cr–O 1·90 Å) of the three oxalate groups, and the complex so

---

[266] T. Watanabé, M. Atoji, and C. Okazaki, *Acta Cryst.*, 1950, **3**, 405..

[267] M. Atoji and T. Watanabé, *J. Chem. Phys.*, 1952, **20**, 1045.

[268] D. H. Templeton and C. H. Dauben, *J. Amer. Chem. Soc.*, 1951, **73**, 4492.

[269] P. Vaughan, J. H. Sturdivant, and L. Pauling, *ibid.*, 1950, **72**, 5477.

[270] N. W. Gregory, *ibid.*, 1951, **73**, 472.

[271] W. F. Zelezny and N. C. Baenziger, *ibid.*, 1952, **74**, 6151.

[272] R. C. L. Mooney, *Z. Krist.*, 1935, **90**, 143.

[273] R. J. Hach and R. E. Rundle, *J. Amer. Chem. Soc.*, 1951, **73**, 4321.

[274] W. N. Lipscomb, *Acta Cryst.*, 1951, **4**, 266; L. Nijssen and W. N. Lipscomb, *ibid.*, 1952, **5**, 604. [275] W. N. Lipscomb, *ibid.*, 1951, **4**, 156.

[276] K. L. Aurivillius, *Acta Chem. Scand.*, 1950, **4**, 1413.

formed is packed by ionic and hydrogen bonding with the $K^+$ ions and the $H_2O$ molecules. The rubidium salt is isomorphous but not the ammonium salt, owing, probably, to the ability of $NH_4^+$ to form tetrahedrally directed hydrogen bonds resulting in a more open structure. In the red dioxalato-complex, *trans*-$K_2[Cr(C_2O_4)_2(H_2O)_2],3H_2O$, the two oxalate groups lie in a single plane and the two co-ordinated water molecules are above and below at slightly greater distances (Cr–O 1·92 for carboxyl oxygen, 2·02 Å for water).[277]

Copper is in roughly planar co-ordination with two molecules of ethylenediamine in the compound $Cu(en)_2,Hg(SCN)_4$; here the sulphur atoms are tetrahedrally arranged round the mercury but the ∠S–C–N reported differs from 180° by as much as 24°.[278] In copper[279] and nickel dimethylglyoxime[112] the entire molecule is planar with nitrogen in a square about the metal atom (Ni–N 1·87; Cu–N 1·92 Å). The nickel compound contains an unusually short O · · · O approach of 2·42 Å, and the possibility that the hydrogen bond might be symmetric has been discussed.

In the copper–DL-proline complex, $Cu(C_5H_8O_2O_2N)_2,2H_2O$, copper again forms square coplanar bonds.[280] The amino-acid molecules are attached by N (Cu–N 1·99 Å) and by O (Cu–O 2·03 Å). Two longer bonds, 2·52 Å, to water molecules complete the distorted octahedron so frequent in copper co-ordination. In cupric acetate $[Cu(CH_3{\cdot}CO_2)_2,H_2O]_2$, the two Cu atoms form a pair, bridged by the four carboxyl ions (Cu–O 1·97 Å), which are arranged symmetrically about the Cu–Cu axis. The octahedron is completed by two water molecules (at 2·20 Å), one on either side of the copper atom.[281] Particularly striking is the Cu–Cu distance, 2·64 Å, very close to that found in metallic copper (2·56 Å).

An organic base is involved in co-ordination, though not in chelation, in $MnCl_2,2(CH_2)_6N_4,2H_2O$.[282] The Mn, at a centre of symmetry on the common three-fold axis of the two hexamethylenetetramine molecules, is surrounded by two chlorine atoms (at 2·47 Å), two water molecules (at 2·00 Å) and two nitrogen atoms (at 2·40 Å). The bonding is $sp^3d^2$ and magnetic susceptibility measurements indicate five unpaired electrons. Hexamethylenetetramine forms complexes with a variety of simple salts; in $CaBr_2,2(CH_2)_6N_4,10H_2O$, however, the organic molecule is not involved in co-ordination round the calcium atom.[283]

**Molecular Compounds.**—A series of complete structure determinations of molecular compounds of boron trifluoride with ammonia, methylamine, trimethylamine, and methyl cyanide has been made and the results have been discussed in relation to the relative stabilities of the complexes.[284] The methyl cyanide compound is much less stable than the others, and in it

---

[277] J. H. van Niekerk and F. R. L. Schoening, *Acta Cryst.*, 1951, **4**, 35; 1952, **5**, 196, 475, 499. [278] H. Scouloudi and C. H. Carlisle, *Nature*, 1950, **166**, 357.

[279] E. Bua and G. Schiavinato, *Gazzetta*, 1951, **81**, 212, 847; S. Bezzi, E. Bua, and G. Schiavinato, *ibid.*, p. 856.

[280] A. McL. Mathieson and H. K. Welsh, *Acta Cryst.*, 1952, **5**, 599.

[281] J. N. van Niekerk and F. R. L. Schoening, *Nature*, 1953, **171**, 36.

[282] Y. C. Tang and J. H. Sturdivant, *Acta Cryst.*, 1952, **5**, 74.

[283] A. Addamiano and G. Giacomello, *Ric. sci.*, 1951, **21**, 2121.

[284] J. L. Hoard, S. Geller, and W. M. Cashin, *Acta Cryst.*, 1951, **4**, 396; S. Geller and J. L. Hoard, *ibid.*, p. 399; J. L. Hoard, S. Geller, and T. B. Owen, *ibid.*, p. 405; S. Geller and J. L. Hoard, *ibid.*, 1950, **3**, 121; J. L. Hoard, T. B. Owen, A. Buzzell, and O. N. Salmon, *ibid.*, p. 130.

(1) the B–N distance, 1·635 Å, is significantly longer than in the others (1·57—1·60 Å) and (2) the $BF_3$ molecule undergoes much less alteration in shape (compared with free $BF_3$). Preliminary data are also reported for methyl cyanide–$BCl_3$, methyl cyanide–$BBr_3$, trimethylamine–$BH_3$, and dimethylamine–$BF_3$.[285]

Clathrate compounds (complexes in which molecules of one kind form a framework within which molecules of a second kind are trapped) have continued to provide interesting results. The magnetic susceptibility of the oxygen–quinol complex has been measured and it is found that practically no magnetic interaction occurs between the oxygen molecules.[286] The dielectric properties of some quinol clathrates have been studied.[287] The existence of optically active clathrate-type frameworks [288a] has been utilised for the resolution of racemic mixtures of asymmetric molecules capable of entering the enclosures. *sec.*-Butyl bromide has been resolved by formation of its complex with trithymotide [288b] (here the exact nature of the enclosure is not yet known), and optically active derivatives of long-chain hydrocarbons have been resolved [289] by formation of complexes with urea and thiourea (here the void spaces are channels [290] rather than completely enclosed cages as in the quinol and ammonia–nickel cyanide [291] compounds). Resolutions have also been achieved by formation of addition compounds with *cyclo*dextrins.[292]

It now appears that the crystalline hydrates formed by many gases (Kr, $Cl_2$, $SO_2$, $H_2S$, $CH_3Cl$, etc.) constitute a further example of clathrate compounds in which the " inert gas " molecules are enclosed within polyhedra formed by the oxygen atoms of interlinked water molecules. Several alternative structures have been proposed [293] but we shall mention only one due to Pauling and Marsh who have obtained *X*-ray evidence for it in the case of chlorine hydrate. In the cubic cell 46 water molecules are arranged to form two pentagonal dodecahedra and six tetrakaidecahedra; for molecules as large as chlorine only the latter are occupied, to give the formula $6Cl_2,46H_2O$ or very nearly $Cl_2,8H_2O$.

**Organometallic Compounds.**—Dimethylberyllium has been examined by Snow and Rundle.[294] Linear chains $>Be(CH_3)_2{\cdot}Be(CH_3)_2{\cdot}Be<$ in which the $CH_3$ groups are tetrahedrally arranged about the Be atoms are found, showing the tendency of the metal atoms to use all their low-energy orbitals for bond formation even though combined with elements or groups containing no unshared pairs. A similar structure is found for beryllium dichloride.[295]

The very unusual " sandwich " structure (I), first suggested by Woodward

---

[285] S. Geller and O. N. Salmon, *Acta Cryst.*, 1951, **4**, 379; S. Geller, R. E. Hughes, and J. L. Hoard, *ibid.*, p. 380; S. Geller and M. E. Milberg, *ibid.*, p. 381.

[286] D. F. Evans and R. E. Richards, *Nature*, 1952, **170**, 246.

[287] J. S. Dryden and R. J. Meakins, *ibid.*, 1952, **169**, 324.

[288a] A. C. D. Newman and H. M. Powell, *J.*, 1952, 3747.

[288b] H. M. Powell, *Nature*, 1952, **170**, 155.

[289] W. Schlenk, Internat. Congr. Analyt. Chem., Oxford, 1952.

[290] *Idem, Annalen*, 1949, **565**, 204; A. E. Smith, *Acta Cryst.*, 1952, **5**, 224.

[291] J. H. Rayner and H. M. Powell, *J.*, 1952, 319.

[292] F. Cramer, *Angew. Chem.*, 1952, **64**, 136.

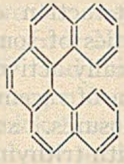
[293] L. Pauling and R. E. Marsh, *Proc. Nat. Acad. Sci.*, 1952, **20**, 112; M. von Stackleberg and H. R. Müller, *Naturwiss.*, 1951, **38**, 456; *J. Chem. Phys.*, 1951, **19**, 1319; W. F. Claussen, *ibid.*, pp. 259, 1425.

[294] A. I. Snow and R. E. Rundle, *Acta Cryst.*, 1951, **4**, 348.

[295] R. E. Rundle and P. H. Lewis, *J. Chem. Phys.*, 1952, **20**, 132.

*et al.*[296] for the remarkable new aromatic molecule di*cyclo*pentadienyliron (ferrocene) has been confirmed by *X*-ray analysis.[297] Accurate bond lengths are not yet available but the indications are C–C 1·4 and Fe–C 2·0 Å. Non-localised molecular orbitals give perhaps the best description of these molecules. It is not possible to write a simple 10-bonded structure for (I), but Dunitz and Orgel have shown that its stability can be attributed to bonding between an atomic *d* orbital of the iron atom and a molecular orbital associated with the *pair* of *cyclo*pentadienyl radicals.


(I)


(II)

**Hydrocarbons.**—Among the hydrocarbons we have three analyses of outstanding accuracy to report but, before proceeding to these, it is convenient to mention some other analyses which have been carried out with rather less attempt at precision. The structure of *p*-di-*tert.*-butylbenzene has been investigated in connection with a study of hyperconjugation; no marked shortening of the bonds connecting the phenyl with the attached groups is observed.[63] In 3 : 4-5 : 6-dibenzophenanthrene (II) steric considerations prevent the molecule from adopting a planar configuration; the individual rings are but little distorted.[298] In octamethylnaphthalene, mutual interference of the methyl groups, which lie alternately above and below the mean molecular plane, occurs; the ring system itself appears to be slightly distorted but the bond lengths are normal.[299]

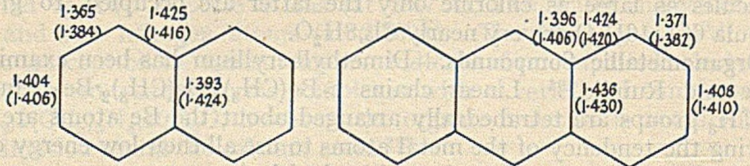


FIG. 6. *Interatomic distances (in Å) observed (and calculated) in naphthalene and anthracene.*

The 3-dimensional *X*-ray data for naphthalene and anthracene have now been corrected for termination-of-series errors.[300] The resultant changes in the bond lengths are not large, the maximum being 0·018 and the mean 0·006 Å. The new averaged lengths are given in Fig. 6 together with (in parentheses) results of the most recent calculations based on molecular

---

[296] G. Wilkinson, M. Rosenblum, M. C. Whiting, and R. B. Woodward, *J. Amer. Chem. Soc.*, 1952, **74**, 2125.

[297] E. O. Fischer and W. Pfab, *Z. Naturforsch.*, 1952, **7**, *B*, 377; P. F. Eiland and R. Pepinsky, *J. Amer. Chem. Soc.*, 1952, **74**, 4971; J. D. Dunitz and L. E. Orgel, *Nature*, 1953, **171**, 121.

[298] A. O. McIntosh, J. M. Robertson, and V. Vand, *Nature*, 1952, **169**, 322.

[299] J. M. Robertson, personal communication.

[300] F. R. Ahmed and D. W. J. Cruickshank, *Acta Cryst.*, 1952, **5**, 852.

orbital theory ;[301] for anthracene the agreement is good, but for naphthalene there are still significant discrepancies.

Jeffrey and Rollett[302] have taken full advantage of an opportunity for unusually accurate structure analyses in the case of dimethyltriacetylene (Fig. 7). The rod-shaped molecules lie on 3-fold axes, and the atomic positions are defined by only four parameters. In the calculations allowance has been made for termination-of-series corrections, free rotation of the methyl groups, thermal anisotropy, and for bonding-electron density. The final $R$ factor is 0·08 and the estimated standard deviation of the bond lengths is less than 0·01 Å. But here again marked discrepancies seem to exist between theory and the observed bond distances. One difficulty concerns the length of the triple bonds, which in conjugation should be greater than that of an isolated triple bond. In dimethyltriacetylene (and in other similar molecules) they are rather shorter than the acetylene value, 1·204 Å. It is possible, of course, that a smaller value than this should be adopted as standard triple bond because of the stretching effect of $\overset{+}{H}\,\overset{-}{C}{\equiv}\overset{-}{C}\,\overset{+}{H}$; Jeffrey and Rollett suggest 1·185 Å, but it can be estimated that, for stretching of 0·02 Å, the improbably large charge of about 0·4 electron per carbon atom would be required.

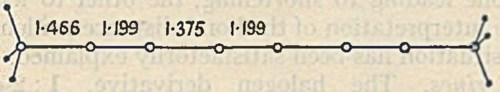


FIG. 7. *Interatomic distances (in Å) in dimethyltriacetylene.*

**Carbocyclic Compounds.**—*Small rings.* The results of structure analyses of small alicyclic rings are in some respects rather puzzling. Owen and Hoard[303] have determined the structure of octachloro*cyclo*butane and have shown that the ring is non-planar with markedly long C–C bonds. Non-planar ring systems are also found by electron diffraction in octafluoro*cyclo*butane[304] and in *cyclo*butane itself,[305] although in the latter a planar equilibrium configuration with large amplitude of out-of-plane bending is also compatible with the evidence. Planar, centrosymmetric, four-membered rings are found in tetraphenyl*cyclo*butane,[306] in dinaphthylene-*cyclo*butane,[307] and in dimethylketen dimer.[308, 299] In all these *cyclo*butane derivatives the ring C–C distances are 1·56—1·60 Å, *i.e.*, markedly longer than normal. The obvious interpretation of this elongation as being due to weaker bonding as a result of Baeyer strain is, however, quite unacceptable since, in 3-membered rings where the strain is much more severe, the ring-C–C distances are consistently shorter than normal. Coulson and Moffitt[309] have suggested that, since the bonding orbitals do not point in the bond directions, some degree of $\pi$–$\pi$ bonding must exist in addition to the usual

---

[301] C. A. Coulson, R. Daudel, and J. M. Robertson, *Proc. Roy. Soc.*, 1951, *A*, **207**, 306.
[302] G. A. Jeffrey and J. S. Rollett, *ibid.*, 1952, *A*, **213**, 86.
[303] T. B. Owen and J. L. Hoard, *Acta Cryst.*, 1951, **4**, 172.
[304] H. P. Lemaire and R. L. Livingston, *J. Amer. Chem. Soc.*, 1952, **74**, 5732.
[305] J. D. Dunitz and V. Schomaker, *J. Chem. Phys.*, 1952, **20**, 1703.
[306] J. D. Dunitz, *Acta Cryst.*, 1949, **2**, 1.
[307] J. D. Dunitz and L. Weissman, *ibid.*, p. 62.
[308] W. N. Lipscomb and V. Schomaker, *J. Chem. Phys.*, 1946, **14**, 475.
[309] C. A. Coulson and W. E. Moffitt, *Phil. Mag.*, 1949, **40**, 1.

σ–σ bonding, and that this might lead to bond shortening. Dunitz and Schomaker[305] have drawn attention to the fact that *cyclo*butane is thermochemically much more unstable than would be expected, and have tentatively ascribed this to repulsion of the non-bonded atoms (separated by only 2·2 Å), which may also result in elongation of the bonds. A combination of the two effects, one leading to shortening, the other to lengthening, might seem to offer one interpretation of the bond-distance evidence, but it cannot be said that the situation has been satisfactorily explained.

cyclo*Hexane rings*. The halogen derivative, 1 : 2-dibromo-4 : 5-dichloro*cyclo*hexane, has the configuration κκεε [310] and is isomorphous with the 1 : 2 : 4 : 5-tetrachloro- and -tetrabromo-compounds.[311] Of particular chemical interest is the fact that elimination of hydrogen chloride from δ-hexachloro*cyclo*hexane by alkali removes that chlorine atom which protrudes most directly from the ring, as shown by *X*-ray analysis of the resulting pentachloro*cyclo*hexene.[312] α-Phloroglucitol, a 1 : 3 : 5-hydroxy*cyclo*hexane with the configuration κκκ, gives a dihydrate and a diammoniate which are isomorphous.[313] The dihydrate of 1 : 3 : 5-triamino*cyclo*hexane has, it seems, the same structure also, so that, curiously enough, replacement of the O–H···O bonds, which hold the structure together, by bonds of the type N–H···O or O–H···N leaves the arrangement of the molecules unaffected. Naphthalene tetrachloride (a preliminary examination of which was made by W. H. Bragg as long ago as 1927) can be regarded as 1 : 2 : 3 : 4-tetrachloro-5 : 6-benzo*cyclo*hexene, in which the chlorine atoms have the configuration 1ε, 2κ, 3κ, 4ε.[314] Analyses of α- and β-1-chloromercuri-2-methoxy*cyclo*hexane have shown that, contrary to earlier opinions based on chemical evidence, the α-form has the *trans*-configuration, while the β-form is *cis*.[315]

*Seven-membered rings*. A well-resolved projection of the cupric tropolone structure provides confirmation [316] of the planar 7-membered ring system (III) which is supported also by electron-diffraction evidence.[317] The chemical structure of purpurogallin (IV) has also been confirmed.[318]

*Eight-membered rings*. Several papers pertaining to the structure of *cyclo*octatetraene have appeared. The $D_{2d}$ or "tub" model with unequal bond lengths is supported by two electron-diffraction studies of *cyclo*octatetraene itself,[319] by an *X*-ray analysis of the monocarboxylic acid,[320] and also by theoretical considerations,[321] in addition to the earlier

---

[310] The notation used is due to O. Hassel (*Tidsskr. Kjemi*, 1943, 5, 32); ε and κ correspond to the p (polar) and e (equatorial) of K. S. Pitzer and C. W. Beckett (*J. Amer. Chem. Soc.*, 1947, 69, 977). The co-existence of these two nomenclatures often leads to confusion.

[311] O. Bastiansen and O. Hassel, *Acta Chem. Scand.*, 1951, 5, 1404; O. Hassel and E. W. Lund, *ibid.*, 1952, 6, 238.

[312] R. A. Pasternak, *Acta Cryst.*, 1951, 4, 316.

[313] P. Anderson and O. Hassel, *Acta Chem. Scand.*, 1951, 5, 1349.

[314] M. A. Lasheen, *Acta Cryst.*, 1952, 5, 593.

[315] A. G. Brook and G. F. Wright, *ibid.*, 1951, 4, 50.

[316] J. M. Robertson, *J.*, 1951, 1222.

[317] E. Heilbronner and K. Hedberg, *J. Amer. Chem. Soc.*, 1951, 73, 1386.

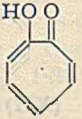
[318] J. D. Dunitz, *Nature*, 1952, 169, 1087.

[319] I. L. Karle, *J. Chem. Phys.*, 1952, 20, 65; K. Hedberg and V. Schomaker, 115th Amer. Chem. Soc. Meeting, San Francisco, 1949.

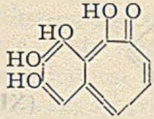
[320] D. P. Shoemaker, personal communication.

[321] W. B. Person, G. C. Pimentel, and K. S. Pitzer, *J. Amer. Chem. Soc.*, 1952, 74, 3437.

*X*-ray evidence.[322] The $D_4$ (crown) model and the $D_{4d}$ (tub with equal bonds) model have also been proposed [323] but the balance of the evidence seems to favour $D_{2d}$.



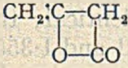
(III)



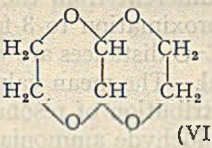
(IV)

**Heterocyclic Compounds.**—*Compounds containing oxygen.* A chemical problem has now been settled by a low-temperature *X*-ray analysis of diketen.[324] The arrangement of carbon and oxygen atoms corresponds to a β-lactone structure; the but-3-eno-β-lactone formula (V) is supported by the distribution of the bond lengths.

Structures assigned to two other molecules on chemical grounds must be altered in the light of *X*-ray evidence. The compound previously known as "*cis*-naphthodioxan" (VI) has been shown by Furberg and Hassel [325] to be di-1 : 3-dioxa*cyclo*pent-2-yl (VII). The molecule is centrosymmetric, the rings are non-planar (ascribed to mutual interference of neighbouring methylene groups), and the bond distances are quite normal (C–C 1·52; C–O 1·41 Å). Grdenić [326] has shown that the compound supposed to be 1-oxa-4-mercura*cyclo*hexane (VIII) has actually a structure corresponding to the 12-membered ring formula (IX). The angle C–Hg–C is close to 180°.

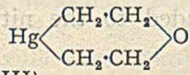


(V)

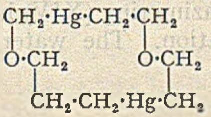


(VI)

(VII)



(VIII)



(IX)

*Compounds containing nitrogen.* A very careful refinement of the adenine hydrochloride structure has been undertaken by Cochran,[327] using the $(F_o - F_c)$ synthesis, and taking into account anisotropic temperature vibration for every atom. Geiger-counter intensity data were employed. The result, showing individual peaks for all the hydrogen atoms, allows unequivocal decision as to the particular tautomer present in the crystal (X), a conclusion reached independently by Donohue [107] by consideration of the hydrogen bonding. The structure of the hydrochloride of guanine, the other purine base occurring in nucleic acid, is closely related to that of the adenine salt,. despite the different symmetry of the crystals.[328] A

---

[322] H. Kaufman, I. Fankuchen, and H. Mark, *Nature*, 1948, **161**, 165.

[323] O. Bastiansen and O. Hassel, *Acta Chem. Scand.*, 1949, **3**, 209; B. D. Saksena and H. Narain, *Nature*, 1950, **165**, 723; E. R. Lippincott, R. C. Lord, and R. S. McDonald, *J. Amer. Chem. Soc.*, 1951, **73**, 3370.

[324] L. Katz and W. N. Lipscomb, *Acta Cryst.*, 1952, **5**, 313.

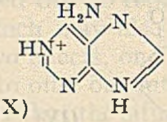
[325] S. Furberg and O. Hassel, *Acta Chem. Scand.*, 1950, **4**, 1584.

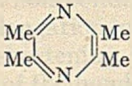
[326] D. Grdenić, *Acta Cryst.*, 1952, **5**, 367.

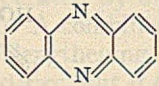
[327] W. Cochran, *ibid.*, 1951, **4**, 81. [328] J. M. Broomhead, *ibid.*, p. 92.

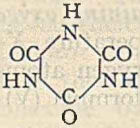
substituted pyrimidine, 5-bromo-2-metanilamidopyrimidine, an active antimalarial, has been studied, and the crystal structure reported.[329]

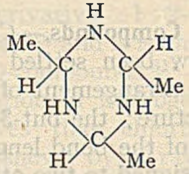
A 3-dimensional analysis for tetramethylpyrazine (XI) shows that the molecule is planar and centrosymmetric. Within the ring C–C is reported to be 1·44 and C–N 1·31 Å, and the external C–C bonds are 1·50 Å.[330] Presumably the π-electrons are concentrated more in the C–N bonds than in C–C because of the greater electronegativity of the nitrogen atoms. For phenazine (XII), a 2-dimensional study does not reveal such large differences in the bond lengths; C–N is given as 1·32—1·34 and C–C as 1·38—1·39 A.[331]


(X)

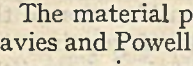

(XI)

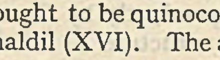

(XII)

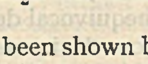

(XIII)


(XIV)

A preliminary announcement of a refinement of the cyanuric acid structure (XIII) has appeared.[332] In the earlier analysis one C–O bond length had been reported to be different from the other two but the new measurements show that the approximation to 3-fold molecular symmetry must be very close indeed. The C–O distances are virtually identical; those for C–N are also very nearly equal. The mean values are 1·21 and 1·355 Å, respectively, indicating some contribution of resonance structures in which NH is positively charged. In " aldehyde ammonia," according to Lund,[333] a reduced triazine ring (XIV) has the chair form, with the methyl groups in κκκ-configuration. The water, hydrogen-bonded to the nitrogen atoms, forms what are effectively puckered six-membered rings of $H_2O$ molecules (O···O 2·71 Å)—a striking and unusual arrangement.


(XV)


(XVI)


(XVII)

The material previously thought to be quinocol (XV) has been shown by Davies and Powell[334] to be quinaldil (XVI). The arrangement in the crystal is very curious, since the *cis*-configuration is adopted, and the molecules all point in the same direction to give a highly polar structure. The quinoline ring is coplanar with its neighbouring carbonyl group, and the molecule twists about the central C–C bond to achieve steric clearance.

---

[329] J. Singer and I. Fankuchen, *Acta Cryst.*, 1952, **5**, 99.

[330] D. T. Cromer, A. J. Ihde, and H. L. Ritter, *J. Amer. Chem. Soc.*, 1951, **73**, 5587.

[331] F. H. Herbstein and G. M. J. Schmidt, *Nature*, 1952, **169** 323.

[332] E. H. Wiebenga, *J. Amer. Chem. Soc.*, 1952, **74**, 6156.

[333] E. W. Lund, *Acta Chem. Scand.*, 1951, **5**, 678.

[334] D. R. Davies and H. M. Powell, *Nature*, 1951, **168**, 386.

*Compounds containing sulphur or selenium.* The structures of piazselenole, piazthiole, and benzofurazan (XVII; X = Se, S, and O respectively) have been determined.[335] The molecules are planar and appear to possess the expected symmetry. The distance N–X is given as 1·83, 1·60, and 1·20 Å respectively and N–C is close to 1·34 Å in all three compounds. The most interesting feature of the bond lengths, however, is the very short distance quoted for $C_{(1)}$–$C_{(2)}$ 1·30 Å and 1·29 Å in the selenium and the sulphur compound respectively. The other C–C distances are all greater than 1·4 Å. If these results are significant, they indicate almost complete double-bond fixation in the 1 : 2-position. It is noteworthy, though, that in a recent refinement of the structure of β-isoprene sulphone, termination-of-series errors alone were found to cause changes in the atomic co-ordinates of as much as 0·06 Å.[336]

Diselenan has been studied.[337] In the crystal the ring adopts the chair form; the angle C–Se–C is 99° and C–Se is found to be 2·01 Å, rather longer than the value (1·94 Å) based on Pauling's covalent radii. The expected value is found in diphenyl diselenide, where the planes of the phenyl groups are almost normal to one another.[338]

**Benzene Derivatives.**—*p*-Dichlorobenzene is isostructural with the dibromo-analogue; the crystal packing is of the parallel disc type.[339] In *p*-aminophenol,[340] a polar structure, the rings are packed in layers, and the plane of the rings is almost normal to the layer plane; three hydrogen bonds per molecule are formed. A three-dimensional analysis shows that the C–N bond distance is about 1·39 Å, shorter than normal; C–O is 1·47 Å, longer than in other phenols. In *m*-tolidine,[341] no hydrogen bonds are formed and the structure is very open. As in *m*-tolidine hydrochloride and 2 : 2′-dichlorobenzidine, the phenyl groups are nearly normal to one another; such molecules must be rather awkward for packing purposes. Like diphenyl itself, 4 : 4′-dihydroxydiphenyl must be planar, at least in the crystal where a molecular centre of symmetry is imposed.[342]

**Carboxylic Acids.**—The most common form of association in crystals of the monocarboxylic acids, dimerisation of type (*A*), is now found to occur in *p*-chlorobenzoic acid,[343] salicylic acid,[344] lauric acid,[117] "*iso*palmitic acid," [345] and *trans*-β-ionylidenecrotonic acid (related to vitamin A),[346] in addition to earlier examples. It is found also in potassium hydrogen carbonate, where pairs of bicarbonate ions are linked as in (*A*).[347] Formic acid, although it forms dimers in the gas phase,[122] is associated in the solid, to form infinite chains of type (*B*).[348] End-to-end bonding of type (*A*), is also usual for dicarboxylic acids, though here, by association at both ends, infinite chains

---

[335] V. Luzzati, *Acta Cryst.*, 1951, **4**, 193.

[336] G. A. Jeffrey, *ibid.*, p. 58.

[337] R. E. Marsh and J. D. McCullough, *J. Amer. Chem. Soc.*, 1951, **73**, 1106.

[338] R. E. Marsh, *Acta Cryst.*, 1952, **5**, 458.

[339] U. Croatto, S. Bezzi, and E. Bua, *ibid.*, p. 825.

[340] C. J. Brown, *ibid.*, 1951, **4**, 100.

[341] F. Fowweather, *ibid.*, 1952, **5**, 820.

[342] S. C. Wallwork and H. M. Powell, *Nature*, 1951, **167**, 1072.

[343] J. Toussaint, *Acta Cryst.*, 1951, **4**, 71.

[344] W. Cochran, *ibid.*, p. 376.

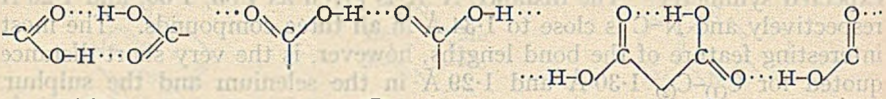
[345] E. Stenhagen, V. Vand, and A. Sim, *ibid.*, 1952, **5**, 695.

[346] C. H. MacGillavry, A. Kreuger, and E. L. Eichhorn, *Proc. K. Ned. Akad. Wet.*, 1951, **54**, 449.

[347] I. Nitta, Y. Tomiie, and C. H. Koo, *Acta Cryst.*, 1952, **5**, 292.

[348] F. Holtzberg, B. Post, and I. Fankuchen, *J. Chem. Phys.*, 1952, **20**, 198.

rather than dimers are formed. Type (*B*) occurs too, in α-oxalic acid, for example. Maleic acid [113] is an interesting case. One hydrogen atom forms a strong internal bond, so that, for intermolecular hydrogen bonding, we have two carboxyl groups but only one hydrogen atom per molecule. Once again we find infinite chains, but of type (*C*).



(*A*) (*B*) (*C*)

Careful re-investigations have been made of the structures of α-oxalic acid,[349] oxalic acid dihydrate,[350] and ammonium oxalate monohydrate.[351] The oxalic acid molecule is planar in both structures but the oxalate ion is non-planar, the angle between planes of opposite carboxyl ions being 28°. In none of these structures is the central C–C bond distance significantly different from 1·54 Å, so that the earlier interpretation of the evidence as favouring a somewhat contracted central bond in the dihydrate must now be discarded. As Jeffrey and Parry have indicated,[352] the absence of appreciable shortening is presumably due to removal of π-electrons from the central bond towards the more electronegative oxygen atoms. The relative stabilities of planar and non-planar forms of the molecules will therefore depend only to a minor degree on the π-conjugation; the formal charge distribution may be of greater importance.

**Amino-acids and Peptides.**—There is no doubt that the amount of precise structural information available for amino-acids and peptides is greater than for any other comparable class of molecules. The Pasadena group alone, in addition to providing several standard analyses, have contributed no less than 7 determinations (for urea,[115] L-threonine,[353] DL-alanine,[354] *N*-acetylglycine,[355] hydroxy-L-proline,[356] DL-serine,[357] glycyl-L-asparagine [358]) in which the full force of structure analysis has been brought to bear on three-dimensional data. Other structure studies, for DL-methionine,[359] glutamine,[360] and cysteinylglycine,[361] have also added to the evidence. The results are, of course, of particular importance in connection with the recent Pauling–Corey protein models, and we shall mention one or two points which seem especially interesting.

Two main features seem to emerge from these structures: (1) the invariable occurrence of zwitterions (acetylated glycine being an obvious exception) and (2) the tendency towards planar configurations. In the free

[349] E. G. Cox, M. W. Dougill, and G. A. Jeffrey, *J.*, 1952, 4854.
[350] F. R. Ahmed and D. W. J. Cruickshank, *Acta Cryst.*, in the press.
[351] G.A Jeffrey and G. S. Parry, *J.*, 1952, 4864.
[352] *Idem*, *Nature*, 1952, **169**, 1105.
[353] D. P. Shoemaker, J. Donohue, V. Schomaker, and R. B. Corey, *J. Amer. Chem. Soc.*, 1950, **72**, 2328. [354] J. Donohue, *ibid.*, p. 949.
[355] G. B. Carpenter and J. Donohue, *ibid.*, p. 2315.
[356] J. Donohue and K. N. Trueblood, *Acta Cryst.*, 1952, **5**, 419.
[357] D. P. Shoemaker, R. E. Barieau, J. Donohue, and C. S. Lu, 2nd Internat. Congr. Cryst., Stockholm, 1951.
[358] L. Katz, R. A. Pasternak, and R. B. Corey, *Nature*, 1952, **170**, 1066.
[359] A. McL. Mathieson, *Acta Cryst.*, 1952, **5**, 332.
[360] W. Cochran and B. R. Penfold, *ibid.*, p. 644.
[361] H. B. Dyer, *ibid.*, 1951, **4**, 42.

amino-acids one may distinguish two possible planar groupings. The carboxyl groups may lie coplanar with either the amino-group as in (*a*) (Fig. 8), or the β-carbon atom (*b*). Type (*a*), shown by hydroxy-L-prolone, acetylglycine, serine, glycylglycine, and nearly so by threonine, alanine, and glutamine, is clearly favoured by the opposite charges of the $NH_3^+$ and the carboxyl-oxygen atom. It does not occur, however, in α- or β-methionine or the peptide glycyl-L-asparagine, which show instead planarity of type (*b*). Both of these molecules contain carbon side chains and it seems possible that the preference for arrangement (*b*) may be associated with the tendency of carbon chains to adopt the planar zig-zag configuration, as, for example, in the long-chain hydrocarbons and decamethylenediamine.[362] In peptides, planarity is found for the five atoms of the peptide group, of the type (*c*). This planar configuration, expected theoretically and already found in *N*-acetylglycine and in β-glycylglycine, has been confirmed again by the analysis of glycyl-L-asparagine. Indeed, this molecule, lying almost exactly in two planes, simultaneously illustrated cases (*b*) and (*c*). The combination of planarity (*b*) and (*c*), if general in polypeptide structure, would impose a certain limitation on the mutual disposition of adjoining peptide groups, but more peptides must be studied before the importance of this can be properly assessed.

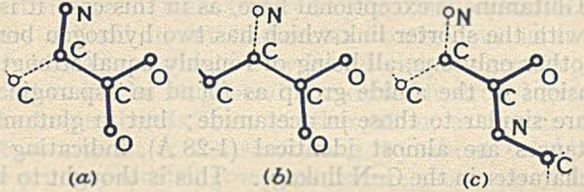


FIG. 8. *Planar groupings possible in amino-acids (a and b) and peptides (c).*

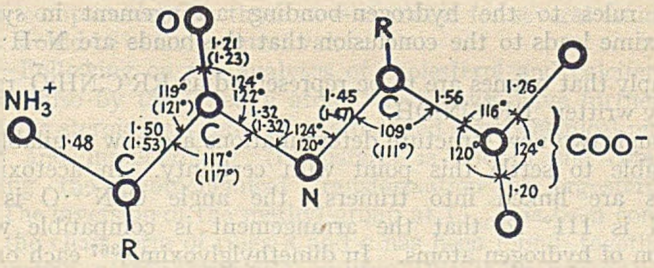


FIG. 9. *Some interatomic distances (in Å) and bond angles for glycyl-L-asparagine, with Corey–Donohue dimensions (in parentheses).*

Turning to finer details, it is gratifying that the evidence of the last two years leaves the Corey–Donohue model[363] substantially unchanged. In Fig. 9 it is compared with the results for glycyl-L-asparagine.

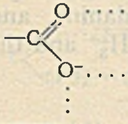
The variation of the C–O distances in the carboxyl ions is interesting.

---

[362] A. O. McIntosh and J. M. Robertson, *ibid.*, 1952, 5, 149.

[363] R. B. Corey and J. Donohue, *J. Amer. Chem. Soc.*, 1950, 72, 2899.

The isolated ion should be symmetrical; in different crystal environments, double-bond fixation in one or other C–O link is often present, to a greater or less degree, according to the symmetry of the hydrogen bonding with respect to the two oxygen atoms. Generally we find that the oxygen with the longer link forms two, and that with the shorter only one, hydrogen bond (XVIII). Glutamine is exceptional here, as in this case it is the oxygen with the shorter link which has two hydrogen bonds, and the other only one, all being of roughly equal strength.

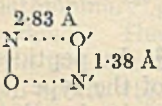


(XVIII)

The dimensions of the amide group as found in asparagine (C–O 1·22, C–N 1·38 Å) are similar to those in acetamide; but in glutamine the C–O and C–N distances are almost identical (1·28 Å), indicating considerable double-bond character in the C–N linkage. This is thought to be connected with the susceptibility of glutamine to hydrolysis or attack by nitrous acid. For asparagine, hydrolysis is slower and the amide group is not affected by nitrous acid. Incidentally, the petide analysis shows the asparagine residue to be an extended chain, and not cyclic as proposed recently,[364] notwithstanding the fact that the amide and carboxyl groups are still free to interact.

**Oximes.**—Pitt[365] has drawn attention to the fact that, while the hydrogen atoms could not be located with certainty, application of stereochemical rules to the hydrogen-bonding arrangement in *syn-p*-chlorobenzaldoxime leads to the conclusion that the bonds are N–H···O, which would imply that oximes are to be represented as $RR'C{:}\overset{+}{N}H{\cdot}\overset{-}{O}$, rather than, as usually written, $RR'C{:}N{\cdot}OH$.

Although two new structure determinations are now available, it is still not possible to settle this point with certainty. In acetoxime,[366] the molecules are linked into trimers; the angle O–N···O is 129° and N–O···N is 111° so that the arrangement is compatible with either disposition of hydrogen atoms. In dimethylglyoxime,[367] each oxime group is linked by hydrogen bonds to another related by a centre of symmetry. An obvious error occurs in the published paper where the angles N–O···N′ and O–N···O′ are both given as 75·9°. The centre of symmetry, however, requires that their sum be 180°. It would appear that N–O···N′ is indeed about 75°, so we assume for the present that the published value 75·9° refers to that angle and not to O–N···O′, which is therefore 104·1°. The arrangement is thus probably N–H···O′, in agreement with Pitt's suggestion and contrary to the usually accepted view. The dimethylglyoxime analysis has been carried out in considerable detail with the use of full 3-dimensional data. The refinement process was, however, effected by least-squares analysis only and it is to be regretted perhaps that the more orthodox Fourier method was not employed in this case since an $(F_o - F_c)$ synthesis might have provided a quite unambiguous determination of the positions of the hydrogen atoms.



In dimethylglyoxime (and acetoxime), C–N is given as 1·27 Å (1·29 Å),

---

[364] F. C. Steward and J. F. Thompson, *Nature*, 1952, **169**, 739.

[365] G. J. Pitt, *Ann. Reports*, 1950, **47**, 458.

[366] T. K. Bierlien and E. C. Lingafelter, *Acta Cryst.*, 1951, **4**, 450.

[367] L. L. Merritt and E. Lanterman, *ibid.*, 1952, **4**, 811.

N–O as 1·38 Å (1·36 Å), quite consistent with double and single bonds respectively. In dimethylglyoxime the central C–C bond is 1·44 Å, slightly shorter than the corresponding distance in buta-1 : 3-diene,[122] and about 0·1 Å shorter than in oxalic acid.[349]

**Carbohydrates.**—The crystal structure of α-D-glucose was reviewed in 1950 but a fuller publication [368] allows us to mention several finer points relating to the structure. Of the five hydrogen atoms available for hydrogen bonding, all are utilised in intermolecular bonds, four in inter-hydroxyl linkages, 2·70—2·78 Å, and one in a hydroxyl–ring-oxygen link, 2·86 Å. It may be noted that in the long bond the donor hydroxyl group does not itself accept hydrogen bonds from another atom, as in the other bonds. Another point of interest is the shortening, by about 0·1 Å, of the C–O distance in the primary alcohol group—a feature shown also in cytidine and connected possibly with the somewhat different chemical behaviour of the terminal $CH_2 \cdot OH$. The α-OH in the reducing group position exhibits a similar contraction. Unfortunately, the results for sucrose are not sufficiently accurate for a study of the details of bond distances, but the stereochemical configuration is given.[369] The general shape of the sucrose molecule in the sodium bromide compound is similar to that in sucrose itself, except that the molecule is rather more tightly curled, and one terminal hydroxyl group is differently oriented. More accurate analyses of the sugars, comparable with those now available for several amino-acids and peptides, would be of the greatest value.

**Steroids.**—Following on the analyses of cholesterol and calciferol, two more analyses, also by the " heavy atom " technique, have furthered our knowledge of the steroid field, providing a detailed stereochemical picture of lanostenol [370] and lumisterol.[371] (Lumisterol is one of the compounds formed during the photochemical transformation of ergosterol into calciferol.) The inversion of the methyl group at $C_{(10)}$ has been confirmed. In addition, the chair form of rings A and C has been found, together with the ε-configuration of the hydroxyl group. This is in agreement with recent infra-red studies.[372] In the case of lanostenol (dihydrolanosterol) chemical evidence was considerably confused as to the D-ring system and the point of attachment of the side chain. The *X*-ray evidence now shows ring D to be 5-membered, and the $C_8$ chain to be attached in such a way that the molecule does not fit the isoprene rule. The latter result would suggest that this and related triterpenes should really be considered as trimethylated steroids—a possibility emphasised by the co-existence of lanostenol and sterols such as ergosterol and cholesterol in Nature.

**Alkaloids.**—The simultaneous confirmation of the strychnine structure by the chemical work and by two independent groups of crystallographers was described in the 1950 report; fuller details of the analyses have now appeared.[373] A 2-dimensional analysis [374] of a colchicine adduct with $CH_2X_2$ ($X = Br$ or I) yields a projection which appears to confirm Dewar's

[368] T. R. R. McDonald and C. A. Beevers, *Acta Cryst.*, 1952, 4, 654.

[369] C. A. Beevers, T. R. R. McDonald, J. H. Robertson, and F. Stern, *ibid.*, p. 689.

[370] R. G. Curtis, J. Fridrichsons, and A. McL. Mathieson, *Nature*, 1952, **170**, 321.

[371] D. C. Hodgkin and D. Sayre, *J.*, 1952, 4561. [372] A. R. H. Cole, *ibid.*, p. 4969.

[373] J. H. Robertson and C. A. Beevers, *Acta Cryst.*, 1951, 4, 270; C. Bokhoven, J. C. Schoone, and J. M. Bijvoet, *ibid.*, p. 275.

[374] M. V. King, J. L. de Vries, and R. Pepinsky, *ibid.*, 1952, 5, 437.

ring structure[375] with the substituents placed according to Čech and Santavy.[376] The structure of ergine is confirmed, also by 2-dimensional analysis, but with much better resolution of the individual atoms.[377] The solution of the structure was obtained from a difference Patterson map, prepared from the isomorphous hydrochloride and hydrobromide.

**Antibiotics.**—A 3-dimensional analysis of chloramphenicol (and of bromamphenicol)[378] confirmed the chemical structure of this well-known antibiotic. The molecules adopt a curled configuration in the crystal, owing to a fairly strong intramolecular hydrogen bond between the two hydroxy-oxygen atoms. Attention is being given to terramycin and aureomycin, the close relation between this pair having been noted.[379] The crystal structure of potassium benzylpenicillin has been refined by a second 3-dimensional synthesis based on improved intensity data.[380] Kojic acid, a substance of mild bacteriostatic activity, has been studied, and its constitution confirmed.[381]

**Protein Structures.**—As a comprehensive and far-reaching review of this field was given last year, we propose to mention in only the briefest terms such developments as were not already covered in that report. *X*-Ray analysis is being applied to a variety of proteins: a " carbonmonoxyhæmoglobin ";[382] silk fibroin;[383] β-lactoglobulin[384] and actinomycin[385] (for the molecular weight); and others. Knowledge of the external form of the hæmoglobin molecule[386] is being applied to sign determination;[73] interpretation of the Patterson function is being continued.[387] Information of a general kind as to the arrangement of polypeptide chains in the crystal has been sought from 3-dimensional Patterson syntheses, notably for lysozyme hydrochloride[388] (using nearly 200 reflections) and for acid insulin sulphate[389] (where about 100 reflections were available).

Of very great interest is the continuing discussion concerned with the now well-known " 3·7 helix," the non-integral spiral structure proposed by Pauling and Corey for the polypeptide chain. Cochran, Crick, and Vand[390] have shown that the intensities of *X*-ray reflections given by poly-$\gamma$-methyl-L-glutamate are in remarkably close agreement with the intensity distribution predicted from the helix. The best agreements is obtained when the β-carbon atom is assumed to be in position 2.[391] This is true also of bovine

[375] M. J. S. Dewar, *Nature*, 1945, **155**, 141.

[376] J. Čech and F. Šantavy, *Coll. Trav. Chim. Tchecosl.*, 1949, **14**, 532.

[377] J. L. de Vries and R. Pepinsky, *Nature*, 1951, **168**, 432.

[378] J. D. Dunitz, *J. Amer. Chem. Soc.*, 1952, **74**, 995.

[379] J. D. Dunitz and J. H. Robertson, *ibid.*, p. 1108; R. Pepinsky and T. Watanabe, *Science*, 1952, **115**, 541.

[380] G. J. Pitt, *Acta Cryst.*, 1952, **5**, 770.

[381] H. A. McKinstry, P. F. Eiland, and R. Pepinsky, *ibid.*, p. 285.

[382] Y. C. Tang, *ibid.*, 1951, **4**, 564.

[383] F. Happey and A. J. Hyde, *Nature*, 1952, **169**, 921.

[384] I. M. Dawson and D. P. Riley, *ibid.*, 1951, **168**, 241.

[385] H. Sarlet, J. Toussaint, and H. Brasseur, *ibid.*, p. 469.

[386] Sir W. L. Bragg and M. F. Perutz, *Acta Cryst.*, 1952, **5**, 277, 323.

[387] Sir W. L. Bragg, E. R. Howells, and M. F. Perutz, *ibid.*, p. 136; F. H. C. Crick, *ibid.*, p. 381.

[388] R. B. Corey, J. Donohue, K. N. Trueblood, and K. J. Palmer, *ibid.*, p. 701.

[389] B. W. Low, *Nature*, 1952, **169**, 955.

[390] W. Cochran and F. H. C. Crick, *ibid.*, p. 234; W. Cochran, F. H. C. Crick, and V. Vand, *Acta Cryst.*, 1952, **5**, 581.

[391] H. L. Yakel, L. Pauling, and R. B. Corey, *Nature*, 1952, **169**, 920.

serum albumin, where the method of radial distribution curves was applied.[392] One rather important objection to the 3·7 spiral in poly-γ-methyl-L-glutamate, the density discrepancy,[393] seems to have been overcome by a new measurement of the unit-cell parameters.[391] Another apparent difficulty,[393] that the dichroism of the C=O absorption band is not as marked as that of N–H, may have been removed by calculations which show that the direction of the transition moment of the 1650-cm.$^{-1}$ band should be inclined by about 20° to the C–O direction, leading to a dichroic ratio comparable with that experimentally observed.[394] It has been suggested that a coiled coil is perhaps a general feature of polypeptide and protein structure, since helices inclined at about 18° should pack together more effectively; the meridian reflection at 5·2 Å given by α-keratin would be explained by this hypothesis.[395] A symposium on the structure of proteins was held at the Royal Society on May 1st, 1952,[396] and a Faraday Discussion on the biochemistry of proteins in August of the same year. Despite the baffling complexity of this field, substantial progress is undoubtedly being made.

We gratefully acknowledge assistance from Dr. B. Oughton, Mr. E. Wait, and Mrs. D. Crowfoot Hodgkin in the preparation of this report.

J. D. Dunitz.
J. H. Robertson.

---

[392] D. P. Riley and U. W. Arndt, *Nature*, 1952, **169**, 138.

[393] C. H. Bamford, L. Brown, A. Elliott, W. E. Hanby, and I. F. Trotter, *ibid.*, p. 357.

[394] R. D. B. Fraser and W. C. Price, *ibid.*, **170**, 490.

[395] F. H. C. Crick, *ibid.*, p. 882; L. Pauling and R. B. Corey, *ibid.*, 1953, **171**, 59.

[396] J. T. Edsall, *ibid.*, 1952, **170**, 53.