

COMPREHENSIVE BIOCHEMISTRY

EDITED BY
MARCEL FLORKIN
AND
ELMER H. STOTZ

VOLUME 9

PYRROLE PIGMENTS
ISOPRENOID COMPOUNDS
PHENOLIC PLANT CONSTITUENTS

COMPREHENSIVE BIOCHEMISTRY

EDITED BY

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PYRROLE PIGMENTS, ISOPRENOID COMPOUNDS

AND

PHENOLIC PLANT CONSTITUENTS



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GENERAL PREFACE

The Editors are keenly aware that the literature of Biochemistry is already very large, in fact so widespread that it is increasingly difficult to assemble the most pertinent material in a given area. Beyond the ordinary textbook the subject matter of the rapidly expanding knowledge of biochemistry is spread among innumerable journals, monographs, and series of reviews. The Editors believe that there is a real place for an advanced treatise in biochemistry which assembles the principal areas of the subject in a single set of books.

It would be ideal if an individual or small group of biochemists could produce such an advanced treatise, and within the time to keep reasonably abreast of rapid advances, but this is at least difficult if not impossible. Instead, the Editors with the advice of the Advisory Board, have assembled what they consider the best possible sequence of chapters written by competent authors; they must take the responsibility for inevitable gaps of subject matter and duplication which may result from this procedure.

Most evident to the modern biochemist, apart from the body of knowledge of the chemistry and metabolism of biological substances, is the extent to which he must draw from recent concepts of physical and organic chemistry, and in turn project into the vast field of biology. Thus in the organization of Comprehensive Biochemistry, the middle three sections, Chemistry of Biological Compounds, Biochemical Reaction Mechanisms, and Metabolism may be considered classical biochemistry, while the first and last sections provide selected material on the origins and projections of the subject.

It is hoped that sub-division of the sections into bound volumes will not only be convenient, but will find favour among students concerned with specialized areas, and will permit easier future revisions of the individual volumes. Toward the latter end particularly, the Editors will welcome all comments in their effort to produce a useful and efficient source of biochemical knowledge.

Liège/Rochester
July 1962

M. FLORKIN
E. H. STOTZ

PREFACE TO SECTION II

(VOLUMES 5-II)

Section II on the Chemistry of Biological Compounds deals with the organic and physical chemistry of the major organic constituents of living material. A general understanding of organic and physical chemistry is presumed, but the reader will find the special topics in Section I of value in the fuller understanding of several parts of Section II. The Editors have made special effort to include a sound treatment of the important biological high polymers, including sections on their shape and physical properties. A number of substances peculiar to plants, certain isoprenoids, flavonoids, tannins, lignins, and plant hormones, often omitted from textbooks of biochemistry, are included. Nevertheless, it is inevitable that some omissions, hopefully minor ones, have occurred. The only intentional omission is the chemistry of the coenzymes and certain components of biological oxidation, which will be covered in connection with their function in Section III.

The previous policy of dividing the section into smaller volumes has been continued, resulting in seven volumes for Section II. Two of the volumes each contain a complete area, namely Carbohydrates (Volume 5) and Sterols, Bile Acids and Steroids (Volume 10). Comments from readers will be appreciated by the Editors and be most helpful for possible future revisions.

Liège/Rochester
December 1962

M. FLORKIN
E. H. STOTZ

COMPREHENSIVE BIOCHEMISTRY

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Biochemical Reaction Mechanisms

Volume 12. *Enzymes - General Considerations*

- Chapter I. Introduction, historical, general concepts, isoenzymes by E. C. WEBB (Brisbane, Queensland)
- Chapter II. Equilibrium and thermodynamic considerations by R. WURMSER AND R. BANERJEE (Paris)
- Chapter III. Oxidation-reduction potentials by R. WURMSER AND R. BANERJEE (Paris)
- Chapter IV. Theories of enzyme catalysis by I. B. WILSON (New York)
- Chapter V. Enzyme kinetics (optimum pH, optimum temperature, activation energy) by E. A. DAWES (Glasgow)
- Chapter VI. Enzyme-substrate relations by J. M. Reiner (Atlanta, Ga.)
- Chapter VII. Chelation in relation to enzyme action by B. L. VALLEE (Boston, Mass.)
- Chapter VIII. Stereochemical considerations in enzyme reactions by H. HIRSCHMANN (Cleveland, Ohio)
- Chapter IX. Structure and function of an enzyme—ribonuclease by C. H. W. HIRS (New York)

Volume 13. *Classification of Enzymes*

- Enzyme Commission list and recommendations (revised and annotated by E. C. WEBB, Brisbane, Queensland)

Volume 14. *Biological Oxidations*

- Chapter I. Dehydrogenation (Chemistry of NAD, NADP, stereochemistry of hydrogen addition) by S. P. COLOWICK (Nashville, Tenn.)
- Chapter II. Pyruvate and α -ketoglutarate dehydrogenases
- (a) Thiamine pyrophosphate function by L. O. KRAMPITZ (Cleveland, Ohio)
 - (b) Lipoic acid function by L. J. REED (Austin, Texas)
- Chapter III. Succinate and related dehydrogenases by T. P. SINGER (Detroit, Mich.)
- Chapter IV. Flavoproteins in electron transport by Y. HATEFI (Iran)
- Chapter V. Cytochromes and cytochrome oxidase by K. OKUNUKI (Osaka)
- Chapter VI. Electron transport mechanisms by D. E. GREEN (Madison, Wisc.)
- Chapter VII. Oxidative phosphorylation by E. C. SLATER (Amsterdam)
- Chapter VIII. Photosynthetic phosphorylation by A. W. FRENKEL (Minneapolis, Minn.)
- Chapter IX. Oxygenases by L. L. INGRAHAM (Davis, Calif.)
- Chapter X. Peroxidases and catalase by A. S. BRILL (New Haven, Conn.)

Volume 15. *Group Transfer Reactions*

Chapter I. Methyl, hydroxyl and formyl transfer by G. L. CANTONI (Bethesda, Md.)

Chapter II. Transaldolase and transketolase by B. L. HORECKER (New York, N.Y.)

Chapter III. Transfer of acyl groups (CoA structure, function) by R. VAGELOS (Bethesda, Md.)

Chapter IV. Transfer of glycosyl groups (phosphorylases, UDP reactions) by L. GLASER (St. Louis, Minn.)

Chapter V. Amino group transfer (Pyridoxal function) by E. E. SNELL (Berkeley Calif.)

Chapter VI. Transfer of phosphate groups

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(b) Phosphomutases by C. F. CORI (St. Louis, Minn.)

Volume 16. *Hydrolytic Reactions; Isomerases*

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Chapter II. Phosphatases by R. K. MORTON (Loughborough, Great Britain)

Chapter III. Proteases and active centers

(a) Mechanism and active centers by L. A. CUNNINGHAM (Nashville, Tenn.)

(b) Activation of zymogen forms by H. NEURATH (Seattle)

Chapter IV. Chemistry and function of Vitamin B₁₂-coenzymes by H. WEISSBACH (Bethesda, Md.)

Chapter V. Carboxylases and the role of biotin by S. OCHOA (New York, N.Y.)

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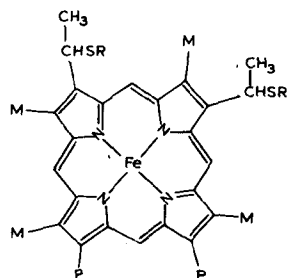
ERRATA

MARCEL FLORKIN AND ELMER H. STOTZ (Eds.), *Comprehensive Biochemistry*, Volume 9.

p. 13, line 3: read Ni, Co, Cu for Ni, Cd, Cu

p. 13, line 4: read Zn, Cd, Mg for Zn, Co, Mg

p. 19, the formula for Fig. 16, haem *c*, should be replaced by:



Volume 9

Part A

PYRROLE PIGMENTS

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Chapter I

Chemistry and Biochemistry of Porphyrins and Metalloporphyrins

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1. Introduction

The importance of the porphyrins in biochemistry is due mainly to the biological activities of the haemoproteins of which iron-porphyrin complexes form the prosthetic groups, to the photosynthetic activity of the related chlorophylls, and to the great advances in recent years in studies of the biosynthesis of porphyrins. Though some porphyrins and metalloporphyrins occur free in nature, they have no known metabolic functions in normal tissues.

It was not until the synthesis of protoporphyrin and its iron complex, haem, was achieved by Fischer and Zeile in 1929 that the basic structure of the porphin nucleus, as well as the structure of many porphyrins, was proven. The brilliant researches of Hans Fischer and his school in Munich, over the period 1910–1940, have provided an immense body of knowledge of pyrrole and porphyrin chemistry, most of which is summarized by Fischer and Orth¹. A comprehensive treatise on the more biological and biochemical aspects has been provided by Lemberg and Legge².

The biochemistry of porphyrins and their derivatives has had its richest period to date in the decade now closing. During the past ten or twelve years, many steps in the biosynthetic pathway to haem have been elucidated, many new techniques for biochemical analysis in the porphyrin field have been introduced, and the theoretical and physical chemistry of this class of compounds is now undergoing rapid development.

2. Occurrence

The important porphyrins occurring free (not complexed with metals) in nature are protoporphyrin and isomers I and III (see p. 5) of uro- and coproporphyrins. No other isomers are known to occur in nature. Relatively

minute amounts of these porphyrins occur normally in blood (copro- and protoporphyrins), urine (copro- and uroporphyrins) and faeces (coproporphyrin) and much larger amounts are found in certain pathological conditions³ (Table I). Proto- and deuteroporphyrins occur normally in the faeces of carnivores, following ingestion of blood or after intestinal haemorrhage, as the result of modification of protohaem by intestinal bacteria; the porphyrin phylloerythrin arises similarly from ingested chlorophyll in herbivores.

TABLE I
ORDER OF MAGNITUDE OF FREE PORPHYRIN CONTENT OF SOME TISSUES AND EXCRETA³

		Uro- porphyrin*	Copro- porphyrin*	Proto- porphyrin*
Normal human	blood ($\mu\text{g}/100$ ml red cells)		0.5	30
	faeces (mg/day)		0.5	0.6
	urine (mg/day)	0.02	0.1	
Acute porphyria (human)	faeces (mg/day)	2	3	
	urine (mg/day)	50	2	

* For structures, see Figs. 3-7 and Table II.

Free proto- and coproporphyrins occur in relatively large amounts in the root nodules of leguminous plants^{4,5} and in some higher plants¹, and traces of free uroporphyrin have been found in the epidermal cells adjacent to the stomatal guard-cells of leaves⁶. Protoporphyrin is excreted by the Harderian gland of the rat, and occurs in the pigmented areas of the egg shells of many species of birds. Uroporphyrin is found in the shells of molluscs. Porphyrins, usually coproporphyrin, are excreted into the growth medium by many microorganisms.

Uroporphyrin III occurs as its copper complex in very high concentration in the wing-feathers of *Turacus indicus*^{7,8}. Recent evidence⁹ suggests the presence of an Mn-porphyrin in blood.

The haems — the iron complexes of porphyrins — do not occur free in normal tissues, but form the prosthetic groups of the many important, biologically active haemoproteins. The known haem prosthetic groups are described in detail below.

3. General chemistry

(a) Structure

The parent nucleus of all the tetrapyrrole pigments is porphin (Fig. 1). Porphyrins are derivatives of porphin in which the β -carbon atoms 1 to 8