Book Reviews

Biological Chemistry

Biogenesis of Natural Compounds. Peter Bernfeld, Ed. Pergamon, London; Macmillan, New York, 1963. xiv + 930 pp. Illus. $28.

In *Science* [**144**, 634 (1964)] there appeared a hypothetical case history of a major work, a symposium volume written by a number of specialists under the editorship of a person charged with assembling and welding the constituent chapters into a coherent whole. The pitfalls attendant on such an operation are made abundantly clear, and the chances of producing a work of lasting significance are appropriately evaluated. That article is entirely pertinent to the present volume. *Biogenesis of Natural Compounds* consists of 18 chapters that deal with various classes of substances; presumably the chapters were written by authorities with ample backgrounds in the areas concerned. But, if one can judge by the voluminous literature citations, either this goal was not always achieved or some of the authors are unduly modest about citing their own work.

The book will be of primary interest to biologists and biological chemists; it contains relatively little that will appeal to organic chemists. Since the majority of the authors are biologists, this was probably unavoidable. In the excellent discussion of the interrelationships of various plant products, heavy emphasis is placed on use of isotopic labels and, to a lesser extent, on the use of microbial mutants in establishing pathways for the construction of the complex molecules. However, more discussion of the nonenzymatic, strictly organic chemistry of the types of precursor under consideration, with some interpretation of these relationships to the proposed biogenetic pathways, would have added much to the comprehensiveness of the volume. Typically, practically nothing is said about the extensive body of knowledge concerned with phenol oxidations, knowledge of which is a key to reaction types in understanding the origin and fate of many naturally occurring phenols and their derivatives. The excellent history of the problems and solutions of plant terpene biogenesis is written from the viewpoint of a biochemist and is little concerned with the examination of the very interesting chemistry and supporting evidence in terpene cyclizations.

In the chapter on alkaloid biogenesis, Leete, one of the few organic chemists actively working in this area, gives a straightforward account of studies and hypotheses that have been put forward in the past. However, there are some notable omissions, of which the most surprising is that of Leete's own work on the biogenesis of ajmaline, work that casts doubt on the shikimic acid route to ring E. Another striking omission is the failure to treat the rather extensive body of information on the origin and interrelationships of riboflavin.

Space does not permit detailed discussion of all the topics presented. Some chapters are mere compilations, with little attempt at critical discussion and appraisal. Others are good. With the exception of a few chapters, the literature is covered only through 1960, although some chapters have supplementary lists of references into 1962. Thus, even before publication, the volume is seriously out of date in many areas.

One particularly annoying facet is the very serious overduplication of material from chapter to chapter—in particular such repetition as the discussion of mevalonic acid and its incorporation into isoprenoid type compounds in the chapters on steroids, terpenes, carotenoids and vitamin A, lipids, and rubber. Similar overduplication is found in the chapters on purine and pyrimidine nucleotides and nucleic acids, and in those on the shikimic acid pathway for producing aromatic acids from nonaromatic precursors in the chapters on phenolic plant products, tannins, lignins, and amino acids. Although the duplication is admitted in the preface, more efficient editing would have removed this source of irritation and at the same time, provided an equally valuable but considerably smaller book.

The book is set in monotype and contains a number of errors, both typographical and otherwise. Despite its shortcomings, it constitutes a valuable compilation of references, but it seems hardly worth the price, particularly for the organic chemist interested in natural products.

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Research in Enzymology

The Enzymes. vol. 7, pt. A, *Oxidation and Reduction*. Nicotinamide nucleotide-linked enzymes; Flavin nucleotide-linked enzymes. Paul D. Boyer, Henry Lardy, and Karl Myrback, Eds. Academic Press, New York, ed. 2, 1963. xxii + 726 pp. Illus. $21.

The volumes in this series are written by leading workers in the field and contain comprehensive critical summaries of the present knowledge of enzymes, with emphasis on their chemistry and mechanism of action. This present volume maintains the high standards set in the preceding volumes of the series. It should be emphasized that these volumes have been much more completely revised than is usually the case with a second edition. The arrangement of subject matter and choice of authors is entirely new.

The contents of volume 7 are as follows: "L-glutamate dehydrogenases" (Carl Frieden); "Alcohol dehydrogenases" (Horst Sund and Hugo Theorell); "α-Glycerophosphate dehydrogenase" (Tadeusz Baranowski); "β-Hydroxyacyl CoA dehydrogenases" (Salih J. Wakil); "Isocitrate dehydrogenases" (Gerhard W. E. Plaut); "Lactate dehydrogenase" (George W. Schwert and Alfred D. Winer); "Malate dehydrogenases" (Ernest Kun); "Oxidation and reduction of nucleotide-linked sugars" (Jack L. Strominger, Reiji Okazaki, and Tuneko Okazaki); "Hydroxysteroid dehydrogenases" (Paul Talalay); "Aldehyde dehydrogenases" (William B. Jakoby); "D-Glucose 6-phosphate and 6-phosphogluconate dehydrogenases" (Ernst A. Noltmann and Stephen A. Kuby); "Glyceraldehyde 3-phosphate dehydrogenase" (Sidney F. Velick and Charles Furfine); "Lipoyl dehydrogenase" (Vincent Massey); "Pyruvate and α-ketoglutarate oxidation enzymes" (D. Rao Sanadi); "Flavoprotein dehydrogenases of the electron-transport chain: A survey" (Thomas P. Singer); "Succinate dehydrogenase" (Thomas P. Singer and Edna K. Kearney); "Acyl coenzyme A dehydrogenase" (Helmut Beinert); "Electron - transferring flavoprotein" (Helmut Beinert); "Old yellow enzyme" (Ake Akeson, Anders Ehrenberg, and Hugo Theorell); "The pyridine nucleotide-cytochrome c reductases" (Youssef Hatefi); "Quinone reductases" (Carl Martius); "Xanthine oxidase" (R. C. Bray); "Lactate dehydrogenases of yeast" (Agnar P. Nygaard); "Glucose oxidase" (Ronald Bentley); "Nitrate reductases" (Alvin Nason); and "Flavoprotein amino acid oxidases" (Alton Meister and Daniel Wellner).

It is not feasible here to review critically each of the articles in this volume. Instead, I will attempt to indicate the present status of the field and some of the concepts that have recently undergone change.

Despite the wealth of information presented here on the mechanisms of action of the enzymes, it is important to realize that many of the basic questions remain unsolved and will require more intensive study with the most modern tools of chemistry and physics. Although the use of kinetic and analytical methods has provided much information about binary, ternary, and quaternary complexes that involve enzyme, substrate, coenzyme, and activators or inhibitors, the structural features of an enzyme which account for its catalytic activity and specificity remain largely unknown.

Many of the earlier concepts of oxidation-reduction must be revised. The occurrence of metals in the enzymes that transfer hydrogen from substrate to the nicotinamide nucleotides was considered earlier (Vallee) to be a general phenomenon, but it now appears to be limited to certain dehydrogenases in which the metal plays a role in binding the nucleotide. Similarly, the metals in the flavoproteins were thought (Mahler) to be generally involved in 1-electron transfer from 2-electron donors, but it is now recognized that many flavoproteins can function without metal; the common occurrence of 2 moles of flavin per mole of enzyme (or of 1 flavin molecule with an adjacent disulfide group) is believed to allow 1-electron transfer to each flavin molecule from a 2-electron donor. However, the assumption of free radical formation, based on spectral changes during reduction of flavoproteins by substrates, is in many cases not confirmed by electron spin resonance measurements. This has led to the view that the spectral changes in these cases are due to complex formation between flavin and substrate rather than to free radical formation.

Until recently the pure flavoprotein enzymes that catalyze the reduction of cytochrome c by the reduced pyridine nucleotides, TPNH and DPNH, were considered responsible for these processes as they occur naturally during electron transport in the cell. However, the present view is that the "DPNH-cytochrome c reductase" is an artifact derived during the isolation of DPNH dehydrogenase, a flavoprotein that normally is involved in a complex which reduces coenzyme Q (ubiquinone). The coenzyme Q, in turn, is able to reduce cytochrome c in a reaction catalyzed by a second complex that contains cytochromes b and c_1. Thus, the isolated DPNH-cytochrome c reductase exhibits a "short-circuit" which apparently does not occur in vivo. The extent of the occurrence of this type of phenomenon has not been assessed. In fact, the question of the identity of the natural electron acceptors for most flavin-linked oxidations remains open.

Although vitamin K was formerly believed to play a role in electron transport and oxidative phosphorylation in mammalian mitochondria, it now appears to be involved in the spatial transfer of electrons from DPNH and TPNH in the cytoplasm to the mitochondria, by "shuttle" mechanisms that are analogous to those postulated for glycerophosphate dehydrogenase. Vitamin K retains its status, however, as a participant in oxidation phosphorylation in bacteria.

The view that steroid hormones promote transhydrogenation by undergoing alternate oxidation and reduction, challenged earlier by Villee, now appears firmly established by Talalay. There is no evidence, however, that the major transhydrogenation activity of tissues is mediated by steroid hormones.

The view that certain steroid hormones can act by causing dissociation of glutamic dehydrogenase into inactive subunits (Tomkins) requires modification, because it has been shown that the dissociated enzyme is active (Frieden). The dissociated form is apparently inactivated by steroids or other agents to yield an altered subunit which fails to aggregate.

The studies of glutamic dehydrogenase provide an excellent model for changes in enzyme structure resulting from the action of regulatory compounds at allosteric sites. Thus far, similar regulation of structure and activity of dehydrogenases has been seen with succinate dehydrogenase and isocitrate dehydrogenase.

The authors, editors, and publishers are to be congratulated on the excellence of the current series. We now look forward to a third edition in which the problem of the mechanism of enzyme action will be brought even nearer to solution by a more complete knowledge of the 3-dimensional enzyme structure at the active center.

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Chemical and Physical Aspects

The Chemistry of Imperfect Crystals. F. A. Kroger. North-Holland, Amsterdam; Interscience (Wiley), New York, 1964. xvi + 1039 pp. $33.

This book covers, in rather amazing detail, the subject of point defects in inorganic nonmetallic crystals, their formation, equilibrium condition, and effects. Despite the "chemistry" in its title, the book is as much or more concerned with physics, and it shows particular strength in the sections on the preparation of material, on theoretical aspects concerned with the equilibrium of impurities, on the effect of impurities on physical properties, and on the electrochemistry of impure materials.

The first of the three principal parts treats crystal growth and phase theory. The various methods of growth are described, and the limitations of the methods outlined. A table of substances and methods for growing them, complete with many references, is in-