

of activity for the Grignard reagent. The fact that a large amount of racemization was obtained suggests that racemization is occurring in the Grignard formation step.

Further work pertaining to the mechanism of

Grignard formation as well as to the optical stability of organometallics is now in progress.

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## BOOK REVIEWS

**Modern Probability Theory and its Applications.** By EMANUEL PARZEN, Associate Professor of Statistics, Stanford University. John Wiley and Sons, Inc., 440 Fourth Avenue, New York 16, N. Y. 1960. xv + 464 pp. 15.5 × 23.5 cm. Price, \$10.75.

The title of this book should perhaps be: Introduction to Probability Theory, since by mathematical standards it is a first undergraduate textbook. Content: Chapter I, Probability Theory as the Study of Mathematical Models of Random Phenomena; Chapter II, Basic Probability Theory; Chapter III, Independence and Dependence; Chapter IV, Numerical-Valued Random Phenomena; Chapter V, Mean and Variance of a Probability Law; Chapter VI, Normal, Poisson, and Related Probability Laws; Chapter VII, Random Variables, Chapter VIII, Expectation of a Random Variable; Chapter IX, Sums of Independent Random Variables; and Chapter X, Sequences of Random Variables.

The knowledge of Lebesgue integration is not assumed. Some theorems are stated without proof, the author usually pointing out this fact carefully. The book is written vividly, contains interesting bibliographical and historical remarks. Some points worth mentioning: Detailed treatment of elements of combinatorics in Chapters I-II; definition of conditional probability of an event given a random variable, without use of the Radon-Nikodym theorem, Chapter VII; an article on the measurement of the signal-to-noise ratio of a random variable, Chapter VIII; treatment of convergence in distribution by the method of characteristic functions, including in Chapter IX the proof of the inversion formulas for characteristic functions, in Chapter X the proof of the "continuity theorem of Probability Theory." A trivial flaw: the definition of a function, p. 269, is not correct.

In conclusion, it may be appropriate to compare this work with the classic treatise in the field, Feller's "Introduction to Probability Theory and Its Applications." At the price of limiting himself to the discrete case Feller achieves a mathematically admirable and completely self-contained treatment. The reviewer feels, however, that Parzen's book is to be preferred as an undergraduate textbook: it is considerably easier to understand and also treats the continuous case.

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**British Medical Bulletin.** Volume 16. Number 3. **Insulin.** F. G. YOUNG, Scientific Editor. Medical Department, The British Council, 65 Davies Street, London, W. 1, England. 1960. pp. 175-264. 22 × 28.5 cm. Price, \$3.25.

The issue "Insulin" of the British Medical Bulletin series is a worthy companion of its forerunners. In a group of 17 titles, the subject ranges from the chemical structure of insulin, its measurement in pancreatic extracts and in blood, the role of insulin (and hence the metabolic defects in diabetes) in carbohydrate, fat and protein metabolism, to more clinically oriented subjects including the chemistry and uses of synthetic hypoglycemic agents.

After a historical perspective and preview of the subject matter by the scientific editor, Charles H. Best describes in fine historical perspective his pioneer work with Banting on active insulin preparations, and his efforts to get on with

studies of the physiological effects of insulin in the face of pressing problems in the commercial production of the life-saving hormone. Supplementing a never-tiring description of his classical work on insulin structure, the article by F. Sanger is followed by an excellent treatment by Ieuan Harris on the structures of oxytocin, vasopressin, corticotropin and MSH with emphasis on the relation of structure and amino acid replacements to biological activity. Of theoretical interest but also of great practical import are the articles dealing with the measurement of insulin concentrations, the metabolic fate of insulin and the presence of insulin antagonists and antibodies in blood. These subjects comprise five articles by G. A. Stewart, A. J. Keeney, P. J. Randle and K. W. Taylor, J. Vallance-Owen, and P. H. Wright.

There follows a group of four articles concerned with the action of insulin on metabolism, particularly at the tissue and enzyme levels. In weighing many reports, R. B. Fisher is led toward the conclusion that the stimulation of carbohydrate metabolism is through the increased transport of glucose into the cell, while S. J. Folley and A. L. Greenbaum present the case for a possible primary role of insulin in the synthesis of fatty acids, and A. Korner and K. L. Manchester gather information which indicates a direct effect of insulin on the biosynthesis of protein. Finally P. J. Randle and F. G. Young provide a critical and provocative paper with a unifying concept of insulin action based on its effect on cell permeability, which may account in ways not entirely clear at the present time, for the apparent diversity of actions of insulin on metabolism.

The issue is concluded with articles by R. Fraser on the interplay of insulin with other hormones, by W. Oakley on the types of insulin available for clinical practice, and finally articles on the chemistry of the newer hypoglycemic agents (R. F. Mahler) and their clinical use (J. D. N. Nabarro).

In summary, "Insulin" provides a useful collection of concise, factual and well-documented articles of diverse nature, making it valuable for medical scientists as well as physicians.

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**The Biosynthesis and Secretion of Adrenocortical Steroids.** Biochemical Society Symposium No. 18 held at Senate House, University of London on 14 February, 1959. Organized by J. K. GRANT. Edited by F. CLARK and J. K. GRANT. Cambridge University Press, 32 East 57th Street, New York 22, N. Y. 1960. vii + 111 pp. 16 × 25.5 cm. Price, \$5.00.

An excellent section on laboratory technology as applied to the elucidation of new structures of adrenal and other steroids opens this symposium. The usefulness of micro techniques using several paper chromatographic systems in conjunction with the preparation of derivatives to eliminate "inimics" is stressed and practical examples of these are given.

Most significant findings (up to 1959) concerned with the biogenesis and control of secretion of adrenocortical steroids are reported. In conjunction with these subjects the symposium authors have given liberal play to their ideas and the possible without unbridling fancy at the expense of facts. Most importantly, attention is drawn to areas requiring re-

search. This is exemplified by the reports on the paucity of information as to whether there exists two pathways whereby corticosteroids are generated from a basic precursor such as acetate. Attention is drawn to the practical application of knowledge which until recently was of an academic nature (*e.g.*, steroid hydroxylation and functional zonation of the adrenal gland) for the purpose of diagnosing disease.

An excellent contribution on the morphology of the adrenal cortex draws attention to the necessity for close cooperation between clinicians, biochemists and pathologists if histochemical changes in the adrenal cortex are to be considered in terms of adrenal function.

The ubiquitous nature of the adrenal gland in terms of androgen, progesterone and estrogen production is amply demonstrated by physiological as well as chemical evidence. The problems of functional zonation whereby preferential steroid production proceeds within a histologically defined zone of the adrenal cortex and the site of production and the mechanisms involved in the release of the protein hormones responsible for the control of secretion of corticosteroids are very well reviewed.

In the light of recent publications the theory that the primary function of adrenocorticotropin (ACTH) is one which probably activates a mitochondrial enzyme complex will have to be modified. Recent evidence has substantiated the reports that ACTH also affects the rate of formation of the cofactor (TPNH) in the ox adrenal and probably can make available enzymatically a steroid precursor in the rat adrenal gland.

Misquotations are scarce and these in no way mar the good quality of the material presented at this symposium. The book is recommended for an up-to-date view of some problems involved in the study of the biogenesis and secretion of adrenocortical steroids.

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**Metabolic Pathways (Second Edition of Chemical Pathways of Metabolism).** Volume I. Edited by DAVID M. GREENBERG, Department of Biochemistry, School of Medicine, University of California, San Francisco, California. Academic Press, Inc., 111 Fifth Avenue, New York 3, N. Y. 1960. xv + 572 pp. 16 × 23.5 cm. Price, \$18.00.

This is Volume I of the second edition of a 2-volume work published in 1954 under the title "Chemical Pathways of Metabolism." Like its predecessor, Volume I is devoted to carbohydrates and lipids and Volume II (not yet published) will cover the nitrogen compounds.

The book opens with a chapter on free energy and entropy in metabolism by Pardee and Ingraham. This is an essentially non-mathematical introduction to the thermodynamics of metabolic reactions, written particularly for the biochemist lacking special training in this field and is designed to acquaint the reader with energetic aspects of the metabolic reactions discussed in subsequent chapters. The second chapter, entitled "The Mitochondrial System of Enzymes" is contributed by Green and Fleischer. It is a forceful delineation of the authors' views of the structure and function of this power plant of the cell, the mitochondrion. The remarkable achievement of dissecting this organelle, in which Green and his colleagues have played a leading role, is impressively presented with the aid of numerous excellent diagrams and electron photomicrographs. Green, with Gibson, is also the author of a chapter on fatty acid oxidation and synthesis, another field in which Green's group has made notable contributions.

Carbohydrate metabolism is covered by Axelrod in a scholarly and comprehensive fashion in two chapters, the first entitled "Glycolysis," the second cryptically labeled, "Other Pathways of Carbohydrate Metabolism." In view of the vastness of this subject, the author has used excellent judgment in selection of material and has happily produced a very well balanced coverage of this subject, though some phases, particularly those dealing with metabolism in individual animal tissues, are necessarily superficial.

This reviewer would like to carp a bit at this point about a biochemical sin—against logic and syntax—in the use of the term glycolysis, to designate one particular pathway of glucose metabolism, namely, that involving the symmetrical cleavage of fructose diphosphate to triose phosphate, with

ultimate formation of lactic acid or ethanol. The term "glycolysis" which simply means breakdown of glucose, came to be used synonymously with this particular metabolic pathway, because at the time it was the only one known. Unfortunately, this practice has persisted, despite the present recognition of numerous other pathways of sugar metabolism, and now biochemists have aggravated the error by designating these, as in the present volume, as "other pathways." To one who respects the meaning of words, this means that the "other pathways" of sugar breakdown, *i.e.*, glycolysis, are not glycolytic!

In a chapter by Krebs and Lowenstein, the history of the development of the tricarboxylic acid cycle, our present conceptions of the individual reactions involved, and its significance are discussed in masterly fashion.

A superb chapter by Hassid succinctly delineates the biosynthesis of complex saccharides, and Burns briefly covers the metabolism of ascorbic acid.

The remainder of the book is devoted to lipids, with chapters on phosphatides by Rossiter, on sterols by Tchen, on steroid hormones by Samuels, and carotenoids and Vitamin A by MacKinney.

In reading a book such as this, one cannot fail to be impressed with the unparalleled progress made in recent years in our knowledge of metabolic reactions. In the period since publication of the first volume, one can cite the outstanding discoveries of the Q coenzymes, the glyoxylate cycle, the carboxylation of ribulose diphosphate and its key role in photosynthesis, the role of sugar nucleotides in trans-glycosylation, the biosynthetic mechanisms of fatty acids and the phosphatides, and the well-nigh completion of the delineation of the intermediary steps in the biosynthesis of the sterol skeleton.

In any multiple-authored book, the reader expects to find some overlappings and some omissions, but examples of these are few and not very important in this volume. Uniformity in presentation has been achieved, obviously by careful editing, and clarity and readability are aided by a profusion of well-constructed diagrams. As a reference work, this and its companion volume on the nitrogen compounds should find a valued place in the library of chemists interested in biology and related sciences, and it should prove to be a valuable adjunct for supplementary reading in courses in biochemistry.

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**The Enzymes. Second Edition, Completely Revised.** Volume 2. Purine and Pyrimidine Nucleotides and Phosphagens. Prosthetic Groups and Cofactors (Part A). Edited by PAUL D. BOYER, Department of Physiological Chemistry, University of Minnesota, Minneapolis, Minnesota, HENRY LARBY, Institute for Enzyme Research, University of Wisconsin, Madison, Wisconsin, and KARL MYRBÄCK, Institute for Organic Chemistry and Biochemistry, University of Stockholm, Stockholm, Sweden. Academic Press Inc., 111 Fifth Avenue, New York 3, N. Y. 1960. xiii + 479 pp. 16 × 23.5 cm. Price, \$16.00.

The second edition of "The Enzymes," when completed, should constitute a major reference in biochemistry. The attainment of this objective seems secure if the quality of the first two volumes is maintained throughout the projected series. A great deal of the value of the completed work will depend upon the comprehensiveness and integration of the collected monographs.

The second volume deals with the chemistry of several compounds which have been designated as enzyme cofactors. The historical justification of this classification and its operational practicability are apparent, but as knowledge of mechanisms of enzyme reactions advances it seems less suitable. An example is seen in the treatment of nucleotides. Each chapter is written authoritatively and the quality is uniformly high. Yet, the subject of nucleotide participation in enzymic processes is more effectively and comprehensively presented by Strominger in his review article on the metabolism of mononucleotide anhydrides in *Physiological Reviews* (40, 55, (1960)). If the purpose of the present volume is to present chemical properties of nucleotides in relation to enzyme function, of those discussed (uridine nucleotide by