
 BOOK REVIEWS

The Biochemistry of Vitamin B₁₂. Biochemical Society Symposia No. 13. A Symposium held at The London School of Hygiene and Tropical Medicine on 19 February 1955. Organized and Edited by R. T. WILLIAMS. Cambridge University Press (American Branch), 32 East 57th Street, New York 22, N. Y. 1955. 123 pp. 16 × 25.5 cm. Price, \$3.75.

This booklet contains seven chapters which were organized and edited by R. T. Williams. The chapters correspond to lectures which constituted a symposium on "The Biochemistry of Vitamin B₁₂" held in London on February 19, 1955. The introduction is by Sir Alexander Todd. Some of the chapters contain information that was unpublished at the time of the Symposium, although each chapter is essentially a review of a given topic.

The subject is built around essentially two key chemical entities, vitamin B₁₂ and the intrinsic factor. Although these two entities are entirely different in chemical nature, they play a very significant joint role in "the transfer of one millionth gram of vitamin B₁₂ the distance of a small fraction of a millimeter across the intestinal mucosa and into the bloodstream (Castle)."

The isolation and chemical studies of vitamin B₁₂ were reviewed by E. Lester Smith in a series of well organized sub-topics. The time limitation of the lecture necessitated a considerable abbreviation of the substantial amount of literature material which falls under this heading. The discussion by Dorothy Hodgkin summarized the X-ray analysis of vitamin B₁₂, and the note added in proof contains a complete structural formulation. The subject of chemical and microbiological methods of measurement of vitamin B₁₂ and vitamin B₁₂-like compounds was reviewed by Coates and Ford.

The still expanding group of new cobalt complexes which are related to vitamin B₁₂ was recorded, classified and discussed in an effective style by S. K. Kon.

The two chapters on "The Function of Vitamin B₁₂ in Microorganisms" by Lascelles and Cross, and "The Function of Vitamin B₁₂ in Animal Metabolism" by Arnstein, are very good and readable.

"The Absorption and Excretion of Vitamin B₁₂ in Man" was surveyed by Mollin and Baker. These studies in man were extended and facilitated by the availability of radioactive vitamin B₁₂. The early work was done with vitamin B₁₂ labeled with Co⁶⁰. More recent studies were made with vitamin B₁₂ labeled with Co⁵⁶ (half-life 72 days) and Co⁵⁸ (half-life 72 days). Samples of radioactive vitamin B₁₂ with high specific activities of 12 and 13.5 mc./mg. have been made with Co⁵⁶ and Co⁵⁷ (Chapters I and IV).

Latner has reviewed the history, assay, purification and other related aspects of the intrinsic factor. In summarizing the chemical nature of the intrinsic factor, Latner considers that the mucoprotein nature is established. In reviewing the evidence on how the intrinsic factor is concerned with the absorption of vitamin B₁₂ across the intestine, Latner concludes in favor of the concept of catalyzed absorption.

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KARL FOLKERS

Vitamins and Hormones. Advances in Research and Applications. Volume XIII. Edited by ROBERT S. HARRIS, Professor of Biochemistry of Nutrition, Massachusetts Institute of Technology, Cambridge, Massachusetts, G. F. MARRIAN, Professor of Medical Chemistry, University of Edinburgh, Edinburgh, Scotland, and KENNETH V. THIMANN, Professor of Plant Physiology, Harvard University, Cambridge, Massachusetts. Academic Press, Inc., Publishers, 125 East 23rd Street, New York 10, N. Y. xi + 382 pp. 16.5 × 23.5 cm. Price, \$9.00.

Like its predecessors, this volume maintains the high standard of the series; it contains five articles on subjects relating to vitamins: "The Role of the Vitamin in Antibody Production," by Axelrod and Pruzansky, "The Biosynthesis

of Ascorbic Acid," by Mapson, "The Role of Vitamin B₁₂ in the Metabolism of Microorganisms," by Ford and Hutner, "The Chemotherapeutic Action of Vitamin B₁₂," by Ungley, and "Vitamin Requirements of Human Beings," by Pett; two articles dealing with other nutritional problems, "The Physiology and Biochemistry of the Essential Fatty Acids," by Deuel and Reiser, and "Parasitic Infections and Nutrition," by Smith; and two articles concerned with the mechanism of hormonal action, "Hormones and Mitotic Activity," by Bullough, and "Concerning Possible Mechanisms of Hormone Action," by Hechter. It is worthy of note that the two chapters on vitamin B₁₂, together with the one in the previous volume, furnish a thorough account of the chemistry, physiology and chemotherapeutics of this anti-pernicious anemia factor, cyanocobalamin.

It is now well-established that most vitamins act as coenzymes or co-factors in biocatalytic processes. On the other hand, little is known about the mechanism of hormonal action. It was therefore of special interest, particularly to the reviewer, to encounter the last two chapters in the present volume. Bullough, discussing the relationship of various hormones to mitosis, concluded that hormones exercise their effects on epidermal mitosis through their influence on the glucokinase system. In this connection, the author summarized data concerning the interaction between insulin and pituitary growth hormone with respect to mitotic activity in mouse ear epidermis. From the observation that, whereas insulin stimulates the development of mitotic activity, growth hormone acts as an inhibitor, questions arise about either the biological nature of the growth hormone or its function in connection with insulin. This furnishes just one example of the confusion which has arisen out of the terminology of the growth hormone, originally named on the basis of its most readily observable biological effect.

The last chapter, by O. Hechter, is perhaps the most stimulating and thoughtful essay ever to appear on the subject of the mechanisms of hormone action. The author points out that despite the spectacular progress in most spheres of the research on hormones, there is as yet no real understanding of the basic mechanisms of hormonal operation at a cellular level. He formulates two basic questions involving the modes of hormone action, which have yet to be elucidated, "How can trace amounts of hormone produce profound biological effects in target cells without contributing significant amounts of either energy or matter to the system?" and "How can the specificity of hormone action be accounted for?" After carefully reviewing the current concepts about hormone action and discussing the available data on the action of those three mammalian hormones, insulin, adrenaline and ACTH, on which the present knowledge seems the most advanced, he concludes that the hypothesis that emerges as possibly the most likely concept of hormone action is one which in essence had suggested itself to pioneer pharmacologists many years ago, namely, that hormones act by regulating permeability relationships between cells and metabolites. However, he emphasizes the very relevant point that, in view of the fact that diverse types of chemical structures can be subsumed under the present working definition of hormone, perhaps it is not reasonable to expect to uncover *only one* mode of action for all hormones. At any rate, as Hechter has very aptly said, "only when the 'fine details' of the cell mechanisms upon which a hormone primarily acts have been dissected, will it be possible to define hormone action in fundamental terms."

It is no small achievement on the part of the editors to have compiled a series that covers so well the current developments in these two rapidly-advancing fields of vitamins and hormones. In addition, they have contributed something more. In recent years there have appeared many series and review volumes recording the progress and listing the new accomplishments in various fields related to biochemistry—certainly no mean goal in itself, in view of the rapid acceleration of progress that has been observed in so many of these fields—and yet it is not so often that a volume such as this one appears, in which there is also a place for

provocative ideas, for speculations on the yet undeveloped aspects or concepts of a particular field or for the anticipation of possible future trends. It is to be hoped that the editors continue to solicit papers along these lines, and they are to be congratulated for their success with this volume.

HORMONE RESEARCH LABORATORY
AND DEPARTMENT OF BIOCHEMISTRY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

CHOH HAO LI

Physical Organic Chemistry. By JACK HINE, Professor of Chemistry, Georgia Institute of Technology. McGraw-Hill Book Company, Inc., 330 West 42nd Street, New York 36, New York. 1956. xiv + 497 pp. 16 × 23.5 cm. Price, \$9.00.

Any new book on physical organic chemistry will inevitably be compared with the two major modern classics of the field, Hammett and Ingold. In the reviewer's opinion, the present volume bears these comparisons very well indeed. While it may lack the authoritative and personal character of these works, it has an admirably critical and objective approach of its own. It is not surprising that this approach is most evident in treatments of fields in which the author has first-hand experience; rather it is gratifying that almost as high a standard is maintained throughout. One may disagree occasionally with a conclusion, but one can be sure that it was reached only after careful consideration of the evidence.

The book begins with a section entitled "Basic Principles" which includes discussions of molecular structure, acids and bases, and a brief chapter on kinetics. The major portion of the text is devoted to the different classes of polar reactions, among them being displacements, eliminations, additions, reactions of the carbonyl group, rearrangements and aromatic substitution. There is also a chapter on acid-base catalysis. A good deal of attention is given to linear free-energy relationships. The third section takes up the production of free radicals and their reactions. A final chapter on "four-center" reactions deals with processes such as the Claisen rearrangement and Diels-Alder additions.

So much work on reaction mechanisms has been done during the last ten years that writing a book of manageable size must involve a great deal of selection. It is therefore inevitable that any reader will find a pet topic or two given short shrift. Dr. Hine has nevertheless succeeded in covering most of the important aspects of the field. He achieves this in part by an emphasis on recent work at the expense of historical development. A count on Chapter 5 (Nucleophilic Displacements) revealed that about a third of the references were dated 1950 or later, and in some of the chapters the proportion is even higher. This emphasis enhances the immediate value of the book, but may cause it to date somewhat faster than one with a longer perspective. The chapter on carbonium-ion rearrangements, for example, gives the impression that bridged intermediates are of considerably greater importance than they now appear to be. In spite of its broad coverage the text is by no means superficial, one of its most valuable features from the pedagogical point of view being the detailed treatment given to certain selected reaction mechanisms.

Only a small number of typographical errors could be found and, with a very few exceptions, misleading or incorrect statements are absent. The claim on page 216 that "—the principle of microscopic reversibility requires that the dehydration of *t*-butyl alcohol by aqueous acid involve as its rate-controlling step the formation of the pi complex" overstates the case. The principle merely gives the *path* of the reverse reaction once that of the forward reaction is known. This still allows the rate-controlling step of the dehydration to be formation of the carbonium ion. One might wish that reaction rates had been more consistently discussed in terms of transition-state stabilities. The author is clearly aware of the implicit assumption involved in relating product stability to rate, since he points out on page 143 (and elsewhere as well) that "—it is the transition-state stability which is of fundamental importance." Later, however, he treats Saytzeff-type orientation in eliminations as a consequence of product stability, with only an oblique reference to the transition state later in the chapter. The distinction is one which the mature reader will

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