

Book Reviews

Progress in Drug Research. Volume 17. Edited by E. Jucker. Birkhäuser, Basel and Stuttgart. 1973. 532 pp. 17 × 24.5 cm. 192 SF.

Several of the nine chapters in this volume overlap. There are two chapters on drug metabolism (M. W. Anders, F. Kratz) and two on anthelmintic chemotherapy (R. B. Burrows, P. J. Islip) but the different approaches of the contributors to their topics have produced more complete pictures of the chemical and biological aspects of these fields. Chemotherapy also gets a good review in an authoritative chapter on the tetracyclines (J. J. Hlvka and J. H. Boothe). A chapter on prostaglandins (J. S. Bindra and R. Bindra) joins other reviews of this popular subject in other monographs. The history, structure elucidation, nomenclature, synthesis, and biochemical and biological activities of the prostaglandins are presented well, but a much-needed discussion of guidelines concerning structure-activity relationships of the natural prostaglandins and their now abundant synthetic analogs has been studiously avoided. An account of the electrophysiology of antiarrhythmic drugs (A. L. Bassett, A. L. Wit) and of the erythrocyte membrane as a model for targets of drug action (L. Bolis) makes interesting pharmacologic reading.

The chapter representing the most modern and comprehensive thinking in medicinal research is by J. A. Montgomery and R. F. Struck on the relationship of the metabolism of anticancer drugs to their activity. This review may serve as a model for similar surveys, and should remain a classic in this field, from a profound scientific, logistic, and linguistic point of view.

Just as one observes crowded audiences at review symposia, and can contrast them to the sparse attendance at general scientific sessions featuring short reports of individual progress, one feels great satisfaction at reading carefully prepared and well documented reviews. They reward the reader who has struggled through bulging library shelves and must draw his own conclusions from the primary literature. The series of monographs, *Progress in Drug Research*, has done much to unify our knowledge of medicinal science and has not settled for anything but high standards of reviewing.

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Fondamenti di Chimica Farmaceutica. Volume 4. By Carlo Runti. E. Lint, Trieste. 1973. 707 pp. 15 × 24 cm. 15,000 lire (ca. \$23).

The fourth volume is actually a supplement updating the contents of the original work published in 1969-1970 and reviewed in this Journal.

The style and format that so successfully characterized the first three volumes, namely great abundance of chemical formulas, tables, and superb bibliography at the end of each chapter, have been maintained. The first six chapters deal with nomenclature of drugs, stability (updating of literature only), extensive new data on structure-activity relationship, drug metabolism, mechanism of action, and drug design. Other chapters deal more specifically with radioisotopes, anti-infective drugs, antibiotics, and antiparasitic compounds.

The updating of the second volume includes CNS depressants, local anesthetics, curare-mimetics, CNS stimulants, autonomic drugs, and antihistamine and antiserotonin drugs. The third volume is here supplemented with recent data on cardiovascular drugs, drugs for G.I. disturbances, pulmonary drugs, dermatologicals, hematinics, anticoagulants, hypolipodemic and hypoglycemic compounds, vitamins, hormones, and alkaloids.

Professor Runti has to be congratulated again for his remarkably comprehensive and up-to-date treatise. Volume 4 is a must for the owners of his previous work and should be of interest to all who can read the original text or simply appreciate having in their offices or libraries the latest bibliography on recent drugs.

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Basic Principles in Nucleic Acid Chemistry. Volume 1. Edited by Paul O. P. Ts'o. Academic Press, New York, N. Y. 1974. ix + 636 pp. 15 × 23 cm.

This volume is the first in what is promised as a four-volume treatise on nucleic acid chemistry under the editorial supervision of Paul Ts'o, who is a recognized authority on the subject and has succeeded in assembling an outstanding team of collaborators for this obviously most ambitious undertaking. It is noteworthy that publication of the present volume coincides approximately with the centennial anniversary of the discovery by Friedrich Miescher, when he was working as a young investigator in the laboratory of the great German physiologist Hoppe-Seyler, of the nuclear substance "nuclein," which is known today as nucleohistone.

The opening chapter, aptly titled "In the Beginning" (the concluding chapter in the final volume, still in preparation, will be called "Without End"!) and prefaced with a quotation from the immortal *I Ching*, is a historic survey of the field and includes a very informative discussion of the complex role of nucleic acids in chemical and biological evolution, both past and future. This chapter, written by Ts'o himself, is breathtaking in scope and eloquence, to say the least. Apart from its excellent coverage of the postulated mechanism of formation of biomonomers and biopolymers in the prebiotic era and the eventual organization of these building blocks into the complex entity known as a "living cell," this chapter fearlessly comes to grips with such "heavy" subjects as the elegant mathematical work of Eigen and others on the evolution of autocatalytic information systems, and even the philosophic ideas of the social psychologist B. F. Skinner and the modern theologian Pierre Teilhard de Chardin on the future of the human species. With commendable optimism, Ts'o himself boldly envisions the ultimate appearance on this planet of a new form of Man called *Homo sapiens unitus*!

Chapter Two, entitled "Chemical Synthesis and Transformations of Nucleosides," is a comprehensive review by Goodman of the major developments that have occurred after about 1960 in the field of nucleoside synthesis. The chapter begins with a survey of the currently available methods of N-glycosidation using protected as well as unprotected sugars, a discussion of the stereochemical course of these reactions in the pyrimidine and purine nucleoside series, and a section on C-glycoside derivatives. This is followed by a review of various chemical transformations in the sugar moiety of nucleosides (e.g., neighboring-group reactions, substitutions, eliminations, and oxidations), then a survey of chemical reactions involving the heterocyclic moiety, and finally a discussion on cyclonucleosides. This chapter, written in a concise and most workmanlike manner, will be especially valuable to chemists engaged in the design and synthesis of fraudulent nucleoside analogs, an area of research which continues to enjoy widespread and well-deserved popularity.

Chapter Three, by J. A. McCloskey, deals with the mass spectrometric analysis of nucleosides and their derivatives and is a fine example of the effective presentation of technically difficult material to readers who may have limited prior knowledge of this subject. A helpful theoretical introduction is given, together with useful information on experimental technique and numerous illustrations of fragmentation patterns derivable from the spectra of various purine and pyrimidine bases, nucleosides, and nucleotides. The use of blocking groups such as trimethylsilyl to enhance volatility in the more polar nucleosides and nucleotides is also discussed in detail. Some of the spectra were obtained in the author's own laboratory and have not been published previously.

The fourth chapter, entitled "Excited States of Nucleic Acids," is a joint contribution by Gueron, Eisinger, and Lamola, who are known for their numerous fundamental investigations in this area. Their chapter includes basic as well as some highly technical material on the molecular orbital description of electronic excited states in nucleic acids and an extensive analysis of the fluorescence and phosphorescence emission spectra of these molecules. The types of complex information derivable from studies of the interaction of nucleosides and nucleotides in the presence of photoexcitation are considered in great detail, especially with respect to the interpretation of quenching phenomena, the identification of the preferred stereochemical conformation of nucleosides and nucleotides in solution, the structure and molecular interactions of various synthetic oligonucleotides, and finally the topo-

gy and the natural double-stranded helical DNA molecules of which the "nuclein" in chromosomes is in part composed.

In Chapter Five, Masamuchi Tsuboi presents a thorough discussion of the application of infrared and Raman spectroscopy to the study of nucleic acids and their constituents. Once again, the editor of this volume has done well in obtaining as a contributor someone who is an outstanding authority in his field. This is a short chapter, but the information which it imparts is clearly organized and the introduction includes some theoretical background to assist the uninitiated. Interpretations are given in detail for the various vibration modes in purine and pyrimidine nucleosides as well as nucleotides, and the effects of base-pair interaction, solvation, and other phenomena on the spectra of these molecules are expertly analyzed.

The concluding chapter, bearing the somewhat vague title, "Bases, Nucleosides, and Nucleotides," and written again by Ts'o, is in fact a useful compendium and interpretation of all the types of physicochemical properties known for these substances. There is some duplication of the material in Chapters 4 and 5 (and probably in some of the chapters in future volumes), but the overlap is not a serious detriment. Precise bond lengths and bond angles derived from crystal study are given, as well as tabulations of ionization constants, thermodynamic quantities for ionization, and dipole moments for the principal known bases and their derivatives. Extensive consideration is given to the important question of the extent of free rotation of the glycosidic linkage. The preference of different nucleosides and nucleotides for the syn or anti conformation is analyzed, especially with respect to the effect of the sugar moiety and the influence of diverse substituents on the heterocyclic moiety. Particularly detailed attention is directed to the use of nmr techniques, ORD-CD measurements, and X-ray crystallography for determining the sugar-base torsion angle. An extensive review is also given of the present state of knowledge concerning intermolecular hydrogen-bonded base pairs in aqueous as well as nonaqueous solution and in the crystal state.

In general, the writing in this volume is excellent, and there is a cohesive quality which could only have been achieved in such a multiauthored volume by the most diligent editorial review. Despite this, some lapses in proofreading occasionally caught this reviewer's eye. A number of scientific words are incorrectly spelled: "chiralty" on p 28, "onabain" and "coacerrate" (three times!) on p 32, "clinal" (twice!) on p 38, "*Byrophyta*" on p 40, and "orthofurmate" on p 114. Errors in structural formulas were also noted: compound 399a is named as an $O^6,5$ -anhydronucleoside on p 188 but the structure shown is that of an $O^{2,5}$ -anhydro derivative; an R group was omitted in structure 409 (p 191); and a double bond is missing in the *m/e* 69 fragment on p 264. Finally, on p 275 it is stated that C-C bonds are weaker than C-N

bonds (the opposite was undoubtedly intended by the author). Apart from these minor blemishes and a regrettable paucity of literature references after mid-1972, this reviewer finds every reason to conclude that this treatise clearly belongs on the shelf of every serious investigator in the field of nucleic acid chemistry.

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Antimalarial Agents. Chemistry and Pharmacology. Edited by Paul E. Thompson and Leslie M. Werbel. Academic Press, New York and London. 1972. xii + 395 pp. 23.4 × 16 cm. \$26.50.

The last few years have given us several books on malaria and its chemotherapeutic treatment, for example, "Chemotherapy and Drug Resistance in Malaria," by W. Peters (Academic Press, 1970); "Malaria" by R. M. Pinder [reviewed in *J. Med. Chem.*, 17, 149 (1974)]; and the present volume. All these books present a picture of the plasmodial life cycles and the biochemistry of the pathogens and of the emergence of drug-resistant strains. In Pinder's book a broad survey of the disease, the ecology of the plasmodia, economic and medical problems of malaria, and vector control with insecticides form prominent features. Thompson and Werbel's monograph emphasizes structure-activity relationships of every class of antimalarial drugs, synthetic schemes for major drug categories, and extensively documented sections on the pharmacology, metabolism, side actions, and actual clinical uses of the more important chemotherapeutic antimalarials. Written by a prominent protozoologist and an experienced medicinal chemist, the chemical, biochemical, and biological facets of each drug are so well interwoven that the dual authorship is barely discernible. Since both authors were interested in the clinical application of antimalarials, they steer the reader quickly to those aspects of each drug that supports chemotherapeutic utility. Thus, a combination of reading both the Thompson-Werbel and the Pinder volumes cannot help but draw a complete and in-depth picture of the whole field of malaria and the drugs to prevent, suppress, or cure it.

The text is written lucidly and is illustrated abundantly with formulas, figures, and tables. There are author and subject indexes. Printing and make-up of the book are good.

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