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Book Reviews

Insect Hormones and Bioanalogues. By K. Sláma, M. Romaňuk, and F. Šorm. Springer-Verlag, New York and Vienna. 1974. 477 pp. $45.90.

This important book includes a synthesis of insect endocrinology based on years of thinking about insect hormones by Karel Sláma of the Entomological Institute of the Czechoslovak Academy of Sciences. It is written in three sections: a survey of the neuroendocrine system in insects, a discussion of the chemistry and physiology of juvenoid compounds, and a similar, shorter discussion of ecdysoids. Sláma covers the biological material while the chemistry is described by Romaňuk and Šorm. The book ends with an appendix giving the effects of 353 juvenoids on a variety of insects in the laboratory. Much of this is previously unpublished material. This book should be a valuable reference for those considering the use of insect hormones as pesticides since, in addition to a comprehensive listing of bioanalogs, it also describes bioassays in detail.

Sláma's observations on insect endocrinology are clearly based on a vast amount of experience. He strongly emphasizes the point that the role of the juvenoids and ecdysoids in insect development is concerned with the expression of information already programmed at the cellular level and that these hormones serve chiefly to align the insect's developmental processes with the external environment. That is, that the ecdysoids and juvenoids are timing rather than scheduling devices.

In this respect it may be noted that in a recent paper [*J. Insect Physiol.*, 21, 921-955 (1975)] he attacks a popular concept, that the kind of morphogenesis which occurs in an insect depends primarily on the level of juvenile hormone at the time of a moult (a concept which would allow easy reversal of differentiation), and cites instead experiments which show that in insects, as in vertebrates, differentiation proceeds in the direction of progressive limitation of the options available to a cell.

Other valuable aspects of this book include Sláma's discussions of insect endocrinology in terms of a wide variety of insect types, a technique which separates the idiosyncratic results from general principals of insect physiology, and the extensive bibliographies which include European references often overlooked in American reviews.

Since this is a valuable (and expensive) book for workers in the field of insect hormones, it is unfortunate that the proofreading is sloppy and that ungrammatical phrases are allowed to mar an otherwise powerful exposition. Material discussed in this book covers papers published up to the year 1971 with additional references for 1972.

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Drug Disposition and Pharmacokinetics. By Steven H. Curry. Blackwell Scientific Publications, Oxford, London, Edinburgh, and Melbourne. 1975. 214 pp. 15.5 × 23 cm. $17.50.

This book summarizes much of the literature in the areas of drug metabolism and pharmacokinetics. It is intended to be useful to a diversified audience, from students to active researchers concerned with the rational investigation and application of drugs. The text discusses numerous aspects of drug disposition such as bioavailability, compartmental behavior, drug interactions, protein binding, and the factors which influence renal excretion. It has several worthwhile chapters describing the qualitative features of these and related topics. However, other characteristics of the book limit its utility. These include: (1) a style of referencing which makes it very difficult to locate sources of information; (2) a pharmacokinetics section which contains few detailed derivations and dwells upon the calculation of absorption rate constants while neglecting useful approaches to data analysis and blood level prediction such as superposition and clearance concepts; and (3) a chapter which summarizes metabolic reactions but does not identify the animal species in which the transformation was observed or state the relative importance of the pathway being discussed.

For these reasons, this book would seem to be a satisfactory guide to researchers who need to appreciate the qualitative aspects of pharmacokinetics and drug metabolism. Furthermore, it would be useful as a text in an introductory course in these fields. However, it seems to lack the quantitative detail and referencing necessary for use in more advanced courses. The book itself is reasonably free of typographical errors and the chapters are arranged in a logical fashion.

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Advances in Drug Research. Volume 9. Edited by N. J. Harper and A. B. Simmonds. Academic Press, London, New York, San Francisco. 1974. 142 pp. 23.5 × 15.5 cm. $12.25.

Six contributors, including R. Howe of the Imperial Chemical Industries, E. M. Jepson of the Central Middlesex Hospital, D. Kritchevsky of the Wistar Institute, J. R. Parrott of the Royal College, University of Strathclyde, E. M. V. Williams of the University of Oxford, and K. W. Walton of the University of Birmingham, have reviewed the physiological, pharmacological, and clinical aspects of ischemic heart disease in this volume. The first chapter (6 pp) by Jepson is concerned with the clinical management of the disease and involves a discussion of risk factors, clinical management of hyperlipoproteinemia, and preventive measures. Although most of the information found in this section is also available in greater detail in other works, this chapter represents a concise discussion of what is generally known about the management of a very complicated disease state.

The chapter by Howe on hypolipidemic agents (37 pp) follows. After a brief discussion concerning the significance of serum lipoproteins, the important clinically useful drugs as well as many of those having theoretical significance are discussed. Compounds are generally classified according to their "possible" modes of action and the enzyme systems which they are known to affect. This section is well referenced through 1971 and partially into 1972 but should not be considered as complete or exhaustive. Reasons why certain compounds did not become clinically useful are presented. Many of the interesting stereostructure-activity relationships are summarized. Since the more recent literature is not considered in this chapter, readers of this monograph would find it beneficial to reevaluate certain proposed mechanisms of action in light of more recent reports. Also, many of the results of the Coronary Drug Project Research Group are now available. This chapter could serve as an excellent starting point for investigators who previously have not worked in this area and are interested in the design and synthesis of antilipidemic drugs.

Next, Kritchevsky discusses various animal models for atherosclerosis (13 pp). Medicinal chemists will find the summary of various animal models, including dogs, rats, chickens, pigeons, pigs, rabbits, and primates, interesting and informative. When applicable, disadvantages to a particular model are described. Clearly, no animal model meets the needs of every objective. As Kritchevsky points out, "the search for a suitable animal model . . . continues;

the perfect model will be one ... that is readily adapted to the human". This section lists many references to the literature but does not include all references; other hyperlipidemic animal models may be found mainly in the more recent literature. Walton's section on hyperlipidemia and pathogenesis of atherosclerosis (13 pp) summarizes many relatively recent results concerning the significance of the various lipoproteins in atherosclerosis and the proposal that these proteins enter the arterial wall by an insudative process; they are selectively retained in the connective tissue by interaction with sulfated glycosaminoglycans.

The remainder of the monograph is concerned with a discussion by Williams on the electrophysiological basis for a rational approach to antidysrhythmic drug therapy (31 pp) and a chapter by Parrott on the pharmacological approaches to the therapy of angina (32 pp). Both sections are well referenced. The electrophysiological and pharmacological properties of the main classes of antidysrhythmic drugs and current theories of dysrhythmia are presented by Williams, whereas Parrott summarized pharmacological approaches to anginal therapy arising from hemodynamic changes and the effects of various drugs including a relatively large section on the pharmacology of nitroglycerin. Both chapters represent a rich source of biological material which should be of interest to the medicinal chemist concerned with drug design and synthesis.

Anyone interested in ischemic heart disease and research in this area will find this concisely written work well worth reading. It also will serve as a good source of lecture material for both undergraduate and graduate courses in pharmacology and medicinal chemistry.

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Advances in Cancer Research. Volume 20. Edited by George Klein and Sidney Weinhouse. Academic Press, New York, N.Y. 1974. ix + 378 pp. 16 × 23 cm. $29.50.

The twentieth volume in this highly respected series maintains the tradition of its predecessors in presenting timely and authoritative chapters on topics of importance in cancer research. Subjects are always chosen with care, and coverage of the literature is both critical and meticulous.

A glance at the contents page will quickly reveal that the major thrust of this particular volume is toward cancer immunology. The first chapter, by Rapin and Burger, deals with the properties of tumor cell membranes, especially in respect to their interaction with lectins such as concanavalin A and phytohemagglutinin. The mechanism of agglutination is discussed with great clarity, as are the possible relationships between agglutinability, the chemical composition of the cell membrane, and the tendency of a cell to undergo transformation. The second chapter, by Nossal, is a lucid account of the current state of knowledge concerning the immunologic tolerance induced in T lymphocytes and B lymphocytes by various kinds of antigens, including of course cell surface antigens associated with tumors. It is this tolerance phenomenon which seems to be primarily responsible for the collapse of host defenses in the face of malignant disease. As a complement to this discussion there is a separate chapter by Levy and Wheelock devoted exclusively to the role of macrophages and the reticuloendothelial system in tumor resistance. Taken together, these three chapters represent a fine introduction to a very complex subject.

The fourth chapter, by Sims and Grover, brings us up to date on the still extremely active field of polycyclic aromatic hydrocarbon carcinogenesis, especially in respect to the role of K-region and non-K-region epoxides. There is a particularly useful tabulation of some 20 hydrocarbons that have been studied in detail, with bountiful literature citations arranged according to the type of assay used to determine carcinogenicity. Methods currently available for the chemical synthesis of aryl hydrocarbon epoxides are surveyed, as are the chemical properties of these epoxides and the nature of their interaction with proteins and nucleic acids. The fifth chapter, by Bauer, an extremely technical one from the perspective of a medicinal chemist, deals with the morphology of C-type tumor viruses and with the antigens associated with these particles. The concluding chapter, by Haddow, is an addendum to an earlier review by the same author on the possible relationship between wound healing and neoplasia. Included in this addendum is a review of recent advances in the area of DNA repair mechanisms.

It is perhaps an ironic commentary on medicinal chemistry's contributions in the area of cancer research in recent years that, of the approximately 40 topics selected for review by the Editors of this series in Volumes 15–20, *only one has dealt with cancer chemotherapy*. This was a review of BCNU and other nitrosoureas written, already 5 years ago, by Carter and coworkers. Indeed, throughout the 25-year span of "Advances in Cancer Research", the number of chapters devoted to medicinal chemistry has been minuscule. One can only speculate sadly as to the reasons for this embarassing state of affairs.

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Progress in Chemical Toxicology. Volume 5. Edited by Abraham Stolman. Academic Press, New York, N.Y. 1974. xv + 389 pp. 16 × 23.5 cm. $39.50.

This volume is one in a continuing series covering recent developments in methods, techniques, and instrumentation for the toxicological analysis of drugs and poisons in humans and animals. This volume contains seven chapters of which the first chapter is titled "The Absorption, Distribution and Excretion of Drugs and Poisons and Their Metabolites". In chapter one, the author discusses quite extensively and in great detail the absorption, distribution, excretion, and metabolism of six classes of agents: volatile poisons, local anesthetics, stimulants (amphetamine type), hallucinogens (tryptamine type), narcotic analgesics, and marihuana in human subjects and animals. The second chapter deals with analyses of drugs in biological specimens. The author presents a relatively simple and rapid protocol for the isolation and identification of most of the commonly encountered basic, acidic, and neutral drugs which are routinely submitted for toxicological screens. The next chapter is concerned with the isolation and identification of phenothiazines from biological materials. As in chapter two, the author describes numerous procedures for the isolation and identification of various phenothiazine derivatives from serum, urine, and certain soft tissues (liver, brain, and kidney). The fourth chapter discusses the use of fluorescence in toxicology. A brief but descriptive introduction to the fundamentals and limitations of fluorescence analysis is given followed by numerous applications of spectrophotofluoremetry to toxicological determinations. The next chapter contains an interesting discussion of the toxicology of new synthetic organic polymers used in containers for food, pharmaceutical products, and drinking water. The final two chapters deal briefly with the applications of microcrystal tests for drugs and the use of polarography in toxicological analyses.

In general, this volume is well written and clear and each chapter is very well referenced giving the reader access to more detailed coverage of each topic. Probably the most glaring flaws in the book are the numerous errors in the chemical structures and the mislabeling of compounds throughout the volume. For example, on p 196, the author refers to *p*-hydroxybenzoic acid in the text while the structure of *m*-hydroxybenzoic acid is illustrated. This volume would have benefited greatly if a more thorough proofreading of the chemical structures had been made.

Although the book is not recommended for Everyperson, it compliments the series very nicely and is probably useful to many people in the field as a convenient reference book.

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Psychopharmacological Agents. Volume III. Edited by M. Gordon. Academic Press, New York, N.Y. 1974. xii + 403 pp. 16 × 23.5 cm. $28.50.

"Psychopharmacological Agents" is Volume 4 of the familiar "Medicinal Chemistry" monograph series. Volumes I (published in 1964) and II (1967) of "Psychopharmacological Agents" have been updated with this publication of Volume III, again edited by Maxwell Gordon. The need for this updating is obvious—there are hundreds of new reports to put in context. The recentness of the discussion varies from chapter to chapter but generally is surprisingly current. This must be attributed to the fact that the authors

themselves were making research contributions, or were aware of research in progress, as the book was being prepared.

The book is intended primarily for medicinal chemists and pharmacologists who are interested in the recent state of the development of psychopharmacological agents. Pharmacologists will probably not be disappointed by the coverage of the biological side of the structure–activity relationships. Clinicians interested in psychopharmacology will find in the book the pharmacological basis for clinical trial and the recent evaluation of agents, but it is not meant as a clinical handbook. Nor is it meant as an introduction to central nervous system pharmacology, but advanced students may find it useful. The extensive references at the end of each chapter increase the usefulness of the book; an index of all the authors referred to is at the end of the book, along with a thorough subject index.

The progressive development of drugs to specifically counter various diseases depends on progress in understanding mechanisms of action of drugs that have a proven value. So it is appropriate that this book largely deals with evidence and explanations of drug mechanisms.

Chapter 1 is a very concise introduction by the editor, which also briefly reviews several potential psychotherapeutic agents in odd chemical classes not covered in the other chapters.

The second chapter is titled "Biological Factors in the Affective Disorders and Schizophrenia". The authors (F. K. Goodwin and D. L. Murphy) have deliberately limited themselves to "the question of possible relationships between the neurotransmitter amines and abnormal mental functioning" because of the comprehensive data concerning the interactions between these transmitters and psychotropic drugs. Clinical considerations, such as the distinction between bipolar endogenous depression (i.e., with a prior history of mania) and unipolar endogenous depression, are used effectively by Goodwin and Murphy to interpret the biochemical and pharmacotherapeutic data. It is made clear that heterogeneity among individuals with the same psychiatric diagnosis may account for different responses to a drug.

Chapter 3 (by C. L. Zirkle and C. Kaiser) covers the tricyclic antipsychotic agents (phenothiazine and thioxanthene derivatives). This chapter and the one on the benzodiazepines (6) are the longest. Zirkle and Kaiser emphasize the observations and hypotheses that seem to help explain the therapeutic actions, but coverage is also given to those undesirable effects which may be relevant to an understanding of the biochemical mechanisms of therapeutic actions. Most space is devoted to reviewing the data on structure–activity relationships (though difficult to interpret at present) because structure–activity relationships may help increasingly in explaining biochemical mechanisms as the nature of the sites of action becomes more clearly defined.

The hypothesis that all of the tricyclic and the nontricyclic antipsychotics can interact with the same or very similar receptors is extended in chapter 4 ("Butyrophenones and Diphenylbutylpiperidines") by P. A. J. Janssen. Haloperidol and related butyrophenones were reviewed in Volume II of this series by Janssen, and the present chapter is very brief but is followed by a bibliography of about 875 new sources.

In chapter 5, M. Fink briefly discusses the hypothesis that acute drug-induced changes in scalp electroencephalogram (EEG) patterns are associated with specific behavioral changes in man. Applications of this association in classifying drugs and in measuring central nervous system bioavailability of different formulations of drugs are explained. The possibility of differences between normal and mentally ill persons' EEGs and differences between normal and mentally ill persons' responses to drugs are not discussed.

The benzodiazepines (chapter 6) are discussed by L. O. Randall, W. Schallek, L. H. Sternbach, and R. Y. Ning. The antianxiety "tranquilizers," chlordiazepoxide (Librium) and diazepam (Valium), are benzodiazepines. The wide use and the low toxicity of these drugs have led to the introduction of several new benzodiazepine derivatives for use as anxiolytics and hypnotics. This chapter is concerned with the syntheses of the biologically and clinically important members of this series; the potencies in various screening, toxicity, and clinical (antianxiety) tests; metabolism, distribution, and activity of metabolites; biochemical effects of benzodiazepines; behavioral and psycho- and neuropharmacology; and combined approaches to the study of these agents. Recent findings relevant to the anatomical sites and biochemical mechanisms of actions are emphasized. The abuse (or lack of abuse) of these drugs is not covered, and there is no chapter on barbiturates in this or the earlier volumes.

The final chapter covers the antidepressant drugs (by J. H. Biel and Barbara Bopp). The success of lithium in the treatment and prophylaxis of manic-depressive symptoms is viewed as one of several major recent advances in antidepressive therapy and understanding. Information from many sources—including psychiatry, endocrinology, biochemistry, and basic pharmacological research—points to possible improvement in the future therapy of the affective disorders. In order to take advantage of more selectively acting drugs and the potential prophylactic power of drugs, clinicians will have to use increasingly stringent and sophisticated diagnostic procedures.

In general, the failings and the newer problems in drug therapy of psychiatric disorders (such as the failure to discover agents with novel activity by the use of established pharmacological methods or hypotheses, the lack of understanding of the causes of mental illness, the lack of knowledge of the long-term effects of chronic drug administration, the lack of specificity and the very slow onset of therapeutic effects of many drug categories, etc.) are given fair coverage; good discussion is also given to the possible developments in the future. The critical nature of the commentary keeps the book from ever being tedious. In the longer chapters, thoughtful summaries and conclusions are consistently provided at appropriate points in the text.

The price of the book is reasonable, considering the care with which it was prepared and the good typography, structural drawings, and tables. In conclusion, this terse, well-written volume certainly appears to be authoritative, interesting, and useful for its intended interdisciplinary audience. Its value is not significantly diminished if one does not own the earlier volumes.

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Gas Chromotography–Mass Spectrometry in Neurobiology. Advances in Biochemical Psychopharmacology. Volume 7. Edited by E. Costa and B. Holmstedt. Raven Press, New York, N.Y. 1973. vii + 175 pp. 24.5 × 14 cm. $16.95.

The advent of the mass spectrometer as a detector for the gas chromatograph has permitted the accurate determination of a wide variety of chemical entities at levels (10^{-9}–10^{-12} mol) that previously had been accessible for only a limited number of specialized compounds. The editors of this volume have sought to describe the current state of this rapidly growing field. This effort has afforded a treatise that is of use to all scientists who are involved in the analysis of minute quantities of chemicals in all fields of chemistry and biology.

The first chapter provides a lucid account of the development of GC–MS analysis. This discussion stresses utility as well as practicality in using mass fragmentography as a research tool and in confirming other analytical methods. The second chapter describes the employment of chemical ionization in mass fragmentography. The author outlines some future possibilities for the development of new detector systems.

After these two introductory chapters the remainder of the book consists of examples drawn from recent work of the contributors. In most cases the details given are sufficient for the reader to evaluate how useful a method may be but will require a trip to the original publication for accurate reproduction of the methods.

Chapter 3 describes the use of multiple ion detection for determination of serotonin, methoxytryptamine, *n*-acetylserotonin, and melatonin after extraction from brain and pineal tissues. The following chapter deals with levels of hydroxynorephedrine in the brain after administration of amphetamine.

Chapter 5 describes the use of GC–MS and mass fragmentography to monitor the turnover of ^{18}O-labeled homovanillic acid in the brain. This elegant technique involves the in vivo production of ^{18}O-labeled catecholamines by means of placing animals in an atmosphere of $^{18}O_2$. The major limitation of this procedure is the expense of $^{18}O_2$. Chapter 6 discusses analysis of acetylcholine which was measured by demethylation with benzene thiolate and utilization of deuterium-labeled internal standards. The book then presents a general description of the use of isotopically labeled compounds as internal standards for the measurement of the corresponding unlabeled compound in biological media. This is followed by examples including amitriptyline measurements and levels of an active metabolite of propranolol in the brain. In an excellent chapter on perinatal pharmacology the authors describe how

the sensitivity of GC–MS and particularly selective ion monitoring permit measurement of drugs and metabolites in situations where only small samples are available. Studies with diphenylhydantoin, secobarbital, and phenobarbital were performed in the newborn.

Chapter 11 illustrates problems that arise when the compounds to be analyzed are unstable when subjected to gas chromatography. Acidity of the column packing and the nature of the solvent used can have pronounced effects on the sample. Morphine and codeine were analyzed using deuterated analogs as internal standards.

The last chapter illustrates the use of mass fragmentography for the determination of nortriptylene and its metabolites in man as well as the determination of the endogenous levels of 5-hydroxyindoleacetic acid, indoleacetic acid, and 3-methoxy-4-hydroxyphenylglycol in cerebral spinal fluid.

The book is concluded with a comprehensive list of references in mass fragmentography up to January 1973.

The rapid advances in the technology of GC–MS analytical application make the utility of this book primarily one of introduction to the field. The historical background and description of the basic techniques make this a useful book for those who are novitiates in the use of the mass spectrometer as a detector.

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Cell Cycle Controls. Edited by G. M. Padilla, I. L. Cameron, and Arthur Zimmerman with 41 contributors. Academic Press, New York, N.Y. 1974. x + 370 pp. 16 × 23 cm. $16.00.

This book provides an accurate description of the current state of knowledge in the field of cell cycle controls. It includes chapters by a number of well-known leaders of cell cycle research. It "should appeal to cellular, molecular, and developmental biologists as well as to many others in the life sciences. It is aimed not just at the specialist . . . but . . . to all those with a general interest in cellular control mechanisms."

Generally, this book reflects the primordial stage of research in this field which at present amounts to little more than crude observation of cell division patterns, timing, the isolation of ill-defined substances that appear to affect the mitotic rate, and crude biochemical studies of the division process. There are also some preliminary studies on the type of mechanism(s) that may regulate cell proliferation. Obviously, it will be some time before the field matures to adequate understanding of the molecular biology of cell cycle controls and its role in a number of diseases and, in particular, neoplastic growth. This book represents a sign post for the present position in this important field.

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The Red Blood Cell. Second Edition. Volume 1. Edited by Douglas MacN. Surgenor. Academic Press, New York, N.Y. 1974. xvi + 612 pp. $45.00.

This is an inclusive and well-organized text that would be extremely useful for those interested in erythrocyte (RBC), history, morphology, biochemistry, pathology, or preservation.

The book begins with a fascinating history of the RBC which traces the development of thought and function relating to this class of cells concisely with an inclusive list of many appropriate cross references. The role of early experimentation provides the reader with a unique insight into the development of current techniques of cell transfusion and preservation. Succeeding chapters discuss the primary development of RBC's and hemoglobin where the relationship of RBC development to the effect of erythropoietin and changes in hemoglobin synthesis is stressed. A chapter on the composition of normal human red blood cells includes an extensive table listing values, units, and reference sources for all known RBC enzymes, proteins, lipids, polysaccharides, nucleotides, and electrolytes. A description of various biosynthetic pathways for RBC lipids, their structural characteristics, and membrane localization is included. Significant changes in RBC associated lipids as related to certain liver and other disease states are discussed. The book also contains a chapter describing many current concepts of RBC morphology supplemented with superb electronmicrographs. The influence of cytoplasmic components on RBC structure is also described with specific emphasis on the alterations of the hemoglobin molecule and its effect on RBC morphology. Certain RBC diseases relating to differences in cell membrane structure are also described. Specifically the author stresses differences in surface determinants which alter membrane permeability. A chapter on the current biochemistry of RBC surfaces is included where the historical development of blood group substances is traced. Also the relative interaction of these RBC determinants is stressed. A section on RBC membrane associated components which are active in promoting blood clotting is included. This contains many historical references leading to the discovery of the role of RBC stroma in coagulation reactions. A chapter on general RBC metabolism describes all the major enzyme systems in RBC with particular emphasis on their role as causative agents in disease states. The final few chapters compare the various techniques useful for the preservation of RBC and their components.

In summary this book should be regarded as a major reference on the red blood cell for students, teachers, and researchers.

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Organophosphorus Pesticides: Organic and Biological Chemistry. By M. Eto. CRC Press, Cleveland, Ohio. 1974. 387 pp. 17.5 × 26 cm. $44.95.

This substantial book, with its 386 large pages and its 1097 references, provides an outstandingly useful review of the organophosphorus pesticides, which have in recent years become of even greater commercial importance and widespread use, because of the phasing out of chlorinated hydrocarbon insecticides. Some of the virtues of the present book are that it is both up to date (with numerous 1973 references) and goes conscientiously back into the earlier literature, without depending upon secondary reviews, as is so often the case.

Naturally, the strongest sections of the book deal with those aspects particularly associated with Professor Eto's own research, such as the neurotoxic action of organophosphates (i.e., the delayed neurotoxic effects), the relations between chemical structure and physiological activity, and the alkylating activity of the compounds. But all of the chemical portion of the book is outstandingly well written, and the discussions of topics such as pseudorotation and mass spectrometry and derivitization for chromatography are truly outstanding.

The biological aspects are very well treated, but it is here that the few substantive criticisms might be raised. The author perpetuates the exasperating nomenclature by which the cholinesterases are divided into "acetylcholinesterase" and "cholinesterase", instead of the more modern and logical division into "acetylcholinesterase" and "butyrylcholinesterase". The discussion on acetylcholine receptor is brief and not very informative. With respect to the spontaneous reactivation of acetylcholinesterase after inhibition by organophosphates, the fact that the insect enzyme shows a paradoxical failure to reactivate spontaneously has been missed. The comments upon neuromuscular transmission in insects do not accurately reflect the considerable weight of evidence which suggests that glutamate is the transmitter. But the sections dealing with metabolism are very strong indeed, and particularly it is refreshing to find appropriate emphasis given to the role of the mixed function oxidase system in metabolism of organophosphates. We have been all to bemused with the role of phosphatases and other hydrolases in degradation, and the mixed function oxidase may well prove to be the master system in the long run.

Turning to more general aspects, the general editor (Gunther Zweig) indicates that he has "endeavored to leave the text by Professor Eto in the original language and only to edit slightly". Consequently, it is a great pleasure to report that the book is eminently readable, written in a pleasant and straightforward style, without a trace of the awkard constructions and uncolloquial terminologies which are what one might reasonably expect from one for whom English is not his native language. It is a very valuable feature that structures have been used lavishly throughout, even though there is an inevitable repetition of the structures of the commonest compounds, and this adds greatly to the ease of reading of the text. Unfortunately there is a remarkable shortage of

graphical representation. Thus the discussion of structure–activity correlations, and the dependence of reaction rates upon time and concentration, would have been much improved if graphical materials had been added. For example, when dealing with the relations between structure and sensitivity to alkaline hydrolysis, the persuasiveness of a particular experimental claim is much modified by the excellence of the correlations observed, which can be estimated rapidly by the graphical presentations commonly provided in the original papers. This weakness is somewhat exacerbated by the fact that the author has often been rather reluctant to enter into truly critical evaluations of competing hypotheses and sometimes has a tendency to quote the author's own interpretations of his data, rather than examining them with a sceptical eye and indeed (when necessary) occasionally rejecting the conclusions of even the most distinguished authors.

But these minor criticisms should not obscure the fact that this is a contemporary, scholarly, readable, and comprehensive text, which will undoubtedly become the major reference source in this important area for many years to come.

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A Review of Cyclophosphamide. By Donald L. Hill. Charles C Thomas, Springfield, Ill. 1975. xi + 340 pp. $18.50.

This book reviews the literature pertaining to a single drug, one member of the large family of biological alkylating agents; thus, at first glance it might appear rather narrow in its range of readership appeal and interest. That this is not so is due to several reasons. First, cyclophosphamide is probably the most widely used antineoplastic drug today. Second, it is also a drug that has been the subject of some of the most thorough studies in recent years with respect to virtually all aspects of its chemical, pharmacologic, and therapeutic properties. Thus, cyclophosphamide may serve as a model for the complex interrelationships of the chemical and biological processes that are involved in the action of a pharmaceutical agent. Third, cyclophosphamide is a drug of particular interest to the medicinal chemist. It was originally designed, on a rational basis, to have *latent* alkylating activity which would be released by enzymatic activation in the tumor cells. As it turned out, cyclophosphamide is indeed a prodrug which undergoes enzymatic activation, but in the liver instead of the tumor tissues, and the mechanism of its activation as well as the structure of its "active form" is quite different from anything that could have been predicted when this agent was first synthesized. Nevertheless, this drug (to quote the author's double-negative conclusion) "has not been disappointing". This again shows that a "rational approach" in drug design may be quite successful even if some of the assumptions on which it is based turn out to be incorrect.

This is a very well written book. Although it is designed primarily as a reference work, the author succeeds in making it an enjoyable reading, mainly due to his clear-cut, well-balanced organization of the material. Chapter 1 provides a general introduction, and Chapter 10 contains the author's concluding remarks. Chapters 2–9 are restricted to the review of the cyclophosphamide literature, each chapter to a specific area, such as chemistry, metabolism, pharmacology, biochemical effects, hematology and immunological effects, toxicity, antitumor effects in experimental animals, and antitumor effects in humans. Each of these chapters is written as a separate entity, and the cited references are collected at the end of each chapter. Some of the literature reports, for example those pertaining to the exciting search for the "active form", are discussed in detail and, on occasion, generously illustrated with reproductions of graphs and even spectra. The clear and spacious printing of the text and, particularly, of the reaction schemes greatly adds to the readability of this book.

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Topics in Carbon-13 NMR Spectroscopy. Volume 1. Edited by George C. Levy. Wiley, New York, N.Y. 1974. x + 292 pp. 16 × 24 cm. $17.50.

According to the editor, this book "is intended to fill the gap between the current research literature and available carbon-13 NMR texts and reviews". The authors generally succeed in their objective. What makes the book particularly valuable is that it covers the literature during the years when carbon-13 NMR experienced a spectacular boom.

Each of the six chapters covered here is written by an expert. Physical chemical approaches to carbon-13 spectroscopy are generally emphasized. There is, however, a wealth of material that will interest the organic chemist. For a first volume the topics are well chosen. Carbon-13 chemical shifts are covered in the first two chapters. R. Ditchfield and P. D. Ellis discuss theoretical calculation of shifts and outline a successful method using ab initio MO theory. In the following chapter G. E. Maciel deals with empirical approaches to chemical shifts. Some substituent effects on carbon-13 chemical shifts are discussed together with the problems involved in their calculation.

The chemical applications of carbon-13 spin–lattice relaxation are treated very thoroughly in a chapter by J. R. Lyerla, Jr., and G. C. Levy. The use of carbon-13 chemical shifts and spin relaxation parameters has opened new horizons in the study of polymers. In a separate chapter J. Schaefer describes the opportunities and the problems. The advantages of high-field carbon-13 NMR, considerably fewer than those of proton NMR, are the subject of a chapter by F. A. L. Anet. The organic chemist studying reaction mechanisms, biosynthetic pathways, and the characterization of reactive intermediates will find J. B. Stother's chapter most informative. The author provides numerous examples from the recent literature and outlines the scope of this useful technique in organic chemistry.

All the chapters are written clearly. The beginner in carbon-13 research will find the chapter introductions very helpful. These are always accompanied with adequate experimental results.

The book is particularly recommended to the chemist who is acquainted with proton NMR and wants to know what is happening in the ever growing world of carbon-13.

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Membranes. Volume 2. Lipid Bilayers and Antibiotics. Edited by George Eisenman. Marcel Dekker, New York, N.Y. 1973. xiii + 542 pp. $38.00.

The preface of the book states that this series on membranes will . . . "provide a forum for the publication of significant creative advances and definitive syntheses bearing on the physics, chemistry, and biology of membranes". The editor and the chapter authors have maintained this standard in Volume 2, "Lipid Bilayers and Antibiotics".

The initial chapter by Lauger and Neumcke provides a theoretical treatment of ion transport through a continuous bilayer lipid membrane, focusing on the Nernst–Planck or Eyring rate-theory analysis of membrane conductance. The second chapter by Ciani, Eisenman, Laprade, and Szabo gives a theoretical analysis of ionic permeation in membranes mediated by neutral carriers, emphasizing several properties anticipated in the zero-current membrane conductance. These same authors, along with Krasne in chapter 3, summarize the experimentally observed effects of carriers on the electrical properties of bilayer lipid membranes and the molecular basis of ion selectivity and they have attempted to relate the experimentally observed events with the theoretical expectation (chapter 2). The remaining four chapters focus on specific areas: chapter 4 by Simon and Morf details the cation specificity of carrier antibiotics; chapter 5 by Finkelstein and Holz is a change of pace from the carrier mechanism and evaluates aqueous pores created in membranes by polyene antibiotics; chapter 6 by Bean promotes protein ion-conducting channels in membranes, and chapter 7 by Lev, Malev, and Osipov examines the electrochemical properties of thick membranes with macrocyclic antibiotics. These chapters are organized well and contain sufficient background information and details for relatively easy comprehension.

There is an author index at the end of the book. The cited references in this index are found at the end of each chapter without titles; the topics of these references may be inferred from the text. This reviewer enjoys crossword puzzles but not in this form, however. The subject index is insufficient for such an excellently written and composed book.

This reviewer would recommend this book highly for the serious student, the researcher, and the professor.

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Mass Spectrometry in Biochemistry and Medicine. Edited by A. Frigerio and N. Castagnoli. Raven Press, New York, N.Y. 1974. 389 pp. $35.00.

This book consists of a collection of papers presented at a 1973 symposium sponsored by the Mario Negri Institute in Milan, Italy. Typical of many books of this type, the bulk of the articles included in the collection has appeared in the scientific literature in some form or other, and the reader interested in only specific publications can locate them in the appropriate journals. Most of the papers are well referenced, but since few of them are of the review variety, the value of the articles and their references is mostly limited to the specific research problems investigated. In that respect, this book is strictly a publication of the proceedings of a meeting rather than a collection of comprehensive review articles as the title might imply. Nonetheless, the editors have brought together and under one cover material encompassing a reasonably wide range of applications of mass spectrometry in the biomedical field. Some of the subjects covered range from drug metabolism, metabolism of ingested pollutants, clinical chemistry, psychiatric research, studies on newborn infants, entomological applications, and others and include the mass spectrometric examination of a variety of compounds, among them catecholamines, steroids, amino acids, cannabinoids, and sugars. The recent surge of interest in selective ion recording (mass fragmentography) during GC–MS is reflected in the large number of monographs dealing with applications of this technique for both quantitative and qualitative purposes.

This book is not free of typographical errors and some grammatical errors do appear occasionally, without detracting, however, from the contents of the text. The editors have taken care to include a subject index which will be helpful to the reader. The type is large and clear and, with the exception of a few mass spectra, the figures are well reproduced. In general, this volume will serve as a useful reference in many laboratories involved in biomedical research. As indicated in the preface, it should indeed fulfill the very important function of pointing out the utility of mass spectrometry to biomedical researchers and stimulating its application to many other areas in biology and medicine.

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Narcotics and the Hypothalamus (Kroc Foundation Symposia, No. 2). Edited by Emery Zimmerman and Robert George. Raven Press, New York, N.Y. 1974. xiii + 272 pp. $18.95.

This is another in the veritable flood of books that are the minutes of, the results of, or inspired by the plethora of conferences, symposia, and meetings of one sort or another. All of them, including this particular volume, share common strengths and weaknesses. The major weakness is the variable character of the papers—the major strength is that the papers are usually, though not always, written by the people who are the recognized authorities in the particular field covered by the conference proceedings. This particular conference did assemble many of the leaders in the area of research on the interaction of the narcotic analgesics and the neuroendocrine system, particularly the hypothalamus. Most of the topics are covered adequately and some are handled extremely well, but there is really no unifying thread which ties the whole book together.

Despite this lack of cohesiveness, there are a number of chapters that do address themselves to the main theme of the conference and are quite good. Among these are the chapters by Lomax and by Kerr on the role of the hypothalamus in opiate action and abstinence. There are excellent papers by George and by de Wied and his colleagues on the effects of narcotic drugs on neuroendocrine control systems in addition to a solid contribution from E. Leong Way's laboratory on postulated neurobehavioral mechanisms in abstinence.

The paper by Zimmerman on the prepuberal effects of morphine is an excellent study of the interaction of morphine and the pituitary and the effect of morphine on growth. Above all there is a thought-provoking and incisive paper by Abraham Wikler discussing the not too apparent "glass eye booby trap" which many workers working to elucidate the site of action of drugs fall into. Wikler's paper, in my estimation, makes this volume worth having even if there were no others of any merit—which does not happen to be the case.

Many of the other papers, although excellent reviews of neuroendocrinological techniques, tissue culture studies, the blood brain barrier, etc., are only tangentially related to the topic of the conference. The chapter by Oldendorf, although not really related to the major thrust of the conference (at least as the original title would have one believe), is an excellent discussion of the interrelationship of blood-brain barrier penetration and chemical structure and raises the possibility that the action of morphine on the hypothalamus may in part be independent of the existence of the barrier. In many of the other studies, morphine is just one of a number of seemingly unrelated drugs that were thrown into the hopper; in others, the term "narcotic" is rather loosely defined to include ether, phenobarbital, and other centrally acting agents with mechanisms of action completely unrelated to the opiates and opioids. Despite this, this book should be of sufficient interest to investigators working with the narcotic analgesics to warrant its purchase at the relatively modest price asked for.

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Handbook of Radioactive Nuclides. Edited by Yen Wang. Chemical Rubber Publishing Company, Cleveland, Ohio. 1969. $31.50.

This is a reference volume which attempts to provide a convenient source of information on radioactive nuclides and their extremely varied uses. The book is divided into ten sections, covering nuclear physics, instrumentation, and dosimetry, as well as biochemical, medical, and industrial applications of radionuclides and ends with a substantial section on radiation protection. This volume is indeed extremely useful, often presenting topics in a very readable fashion.

The level of sophistication of the account varies considerably. An example is to contrast the chapters which introduce common detector types to the reader and that which discusses modulation transfer functions for radioisotope imaging systems. The latter chapter deals with its subject in a great deal of useful depth, whereas the former does little more than describe the common types of detectors, nevertheless adding six pages solely devoted to the detailed characteristics of different photomultiplier tubes. Another minor criticism is to ask why detector resolving times are dealt with twice in successive chapters, on the second occasion the resolving time (τ) being omitted from the denominator of the final equation, presumably by a printing error (p 103).

These criticisms, however, are a result of the problems involved in editing and publishing a book designed to cover a very extensive area of science and technology. Indeed, the editor in his preface specifically asks for modifications and additions to be suggested by his readers for incorporation in future editions. Many of the chapters and sections will be found to be informative and useful, particularly those on liquid scintillation techniques and the importance of radiation protection.

Although this book has been in print for several years, it still serves as a major reference text for physical and biologic data on the radionuclides. The chapters on applications of radioisotopes to diagnostic imaging in nuclear medicine are of limited usefulness, because of rapid technological advances in this area over the past 5 years. The reviewer would not recommend the book as an undergraduate or graduate text in nuclear chemistry, radiation physics, nuclear medicine, or other related fields. However, he strongly endorses the volume as a source book for atomic and nuclear data which would be a valuable asset in the radiation scientist's library.

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Specialist Periodical Reports. Alicyclic Chemistry. Volume 2. By W. Parker, Senior Reporter. Chemical Society, London. 1974. ix + 470 pp. 14 × 22 cm. £14.00 (Chemical Society members, £10.50).

The Specialist Periodical Reports of the Chemical Society offer an excellent summary of the significant papers during the year on specific topics. The second volume of *Alicyclic Chemistry* is no exception, for it provides a comprehensive review of the carbocyclic chemistry of 1972. The value of this compilation would have been greatly enhanced if a subject index could have been provided, however.

The information is presented according to ring size (3–4, reported by H. Maskill; 5–6, reported by D. G. Morris; medium and large, reported by M. S. Baird; and bridged, reported by J. M. Mellor). The synthesis of 3–4-membered rings and their reactions are emphasized in the first chapter while the discussion of the larger rings is concerned largely with stereochemical, particularly conformational, and mechanistic properties of the ring systems. The short section on reactions of six-membered rings is oriented toward stereochemical considerations, while some significant synthetic improvements in five-membered ring chemistry are included.

The chapters on "Medium and Larger-ring Compounds" and "Bridged Carbocyclics" provide a good balance of discussion of structure, physical properties, syntheses, and reactions of these interesting compounds. Both chapters contain sections about chemical and physical properties of the important organometallic derivatives of the unsaturated members of these series.

The variety of unusual structures and reactions abstracted from more than 1800 references gives a book which will be essential for the library of organic chemists interested in carbocyclic compounds and will be an interesting source of data for other practitioners of organic chemistry. The "Annual Reports" style of writing makes the reading more than casual; however, this volume will prove to be a valuable source of information about conformational and related stereochemical studies, a variety of unusual reactions, and improved synthetic methods such as 1,3-cyclopentadione (p 235), cyclopropanation (pp 23–24), ring expansion by two carbons (pp 261–262), and twistene (p 358).

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