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Additions and Corrections

1977, Volume 20

C. Robin Ganellin: Relative Concentrations of Zwitterionic and Uncharged Species in Catecholamines and the Effect of N-Substituents.

Page 580. Corrected values for Table I are given (only those columns where errors occurred are shown).

pH 7.4		pH 8.4			
Z^+	Z^-	Z^+	$Z^\pm$	Z^0	Z^-
95.5	0.02	67.3	20.3	11.2	1.2
96.1	0.008	70.6	23.4	5.4	0.6
96.6	0.005	73.9	21.1	4.5	0.4
96.4	0.006	72.6	22.2	4.7	0.4
96.3	0.004	72.2	24.1	3.4	0.3

Walter J. Gensler,* C. D. Murthy, and Marion H. Trammell: Nonenolizable Podophyllotoxin Derivatives.

Page 635. For contributing authors, C. D. Murthy should be C. A. Murthy.

James L. Kelley,* Carl A. Miller, and Helen L. White: Inhibition of Histidine Decarboxylase. Derivatives of Histidine.

Page 509. In column 1 the equation should read

$$\%\, I = \left[1 - \frac{\text{CPM (+ inhibitor)}}{\text{CPM (- inhibitor)}}\right] \times 100$$

George E. Wright* and Neal C. Brown: Inhibitors of *Bacillus subtilis* DNA Polymerase III. Structure–Activity Relationships of 6-(Phenylhydrazino)uracils.

Page 1182. In Table I the following footnote should be added to compounds **1**, **10**, **25–28**, and **32**: these azo compounds are completely reduced to hydrazinouracils under assay conditions (see Experimental Section). Also, compound **27** should have substituents 3′-Br-4′-OH.

Book Reviews

Antihypertensive Drugs with a Central Action. Progress in Pharmacology. Volume 1. No. 1. By P. A. vanZwieten. Gustav Fischer Verlag, Stuttgart. 1975. 17 × 24 cm. 63 pp. $16.40.

This small volume presents a concise overview of the pharmacology of centrally acting antihypertensive agents.

After a brief outline of the physiology of regulation of arterial blood pressure and the etiology of hypertension, the mode of action of each of the commonly recognized classes of antihypertensive agents is discussed.

The experimental procedures used to study the central actions of antihypertensive agents are reviewed and their physiological and pharmacological basis is explained in the second chapter.

The chapter headed "Antihypertensive agents with a central action; structure–activity relationship" does not undertake an in-depth review of the medicinal chemical literature; only six structures related to clonidine are mentioned. Other centrally acting agents discussed are methyl-Dopa, a heterogeneous group including reserpine, cocaine, amphetamine, tricyclic antidepressants, and MAO inhibitors that act indirectly through their various effects on central norepinephrine levels, and the more recently discovered benzodioxanyl-2-hydroxyethylpiperidine derivatives related to pimozide.

The chapter on mechanism of action is very well written and provides an extensively documented "guided tour" through the pharmacological literature describing the multiple factors that have been implicated in explaining the actions, both central and peripheral, of clonidine and methyl-Dopa.

Subsequent chapters discuss drugs that influence brain norepinephrine, the comparison between central and peripheral α-adrenergic receptors, evidence pro and con for the central antihypertensive action(s) of β-adrenergic blocking agents, and the clinical utilization of centrally acting antihypertensive drugs.

This book should be helpful to all medicinal chemists interested in antihypertensive research. It presents a concise overview that will be useful to the nonexpert. Chemists more familiar with the field will find this volume valuable for the perspective it gives to the complex interactions of this heterogeneous group of antihypertensive agents with the various physiological mechanisms that regulate blood pressure.

The bibliography is extensive. It is to be hoped that this valuable work will be kept up to date with timely revisions or supplements.

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Prolactin 1976. By D. F. Horrobin. Eden Press, Montreal. 1976. 208 pp. 15.5 × 21.5 cm. $20.00.

The present volume is the fourth book on human and mammalian prolactin that the author has written in the past 4 years. The author's first book, "Prolactin Physiology and Clinical Significance", published in 1973, is a review of the research on prolactin up until the end of 1972. Each succeeding year the author has written a review of the new material which has appeared each year since the first book. "Prolactin 1976" is intended to review all of the new material published in 1975. The "Index Medicus" was used as a primary source of the papers reviewed in this book.

The review covers new developments in several aspects of prolactin physiology including isolation, assays, control of secretion, effects of drugs, receptors, effects on reproduction and

lactation, and prolactin–thyroid interrelationships. In addition to reviewing new information on well-known aspects of prolactin physiology, a few chapters are devoted to areas such as immunology, cardiovascular system, calcium metabolism, and adrenal cortex where the relationship of prolactin to these systems is unclear and controversial. A chapter on prolactin in clinical medicine lists several different disease states where prolactin may play a role. About 18 disease states are listed; however, the evidence for participation of prolactin in some of them is rather tenuous.

The author merits our commendation for a thorough and stimulating presentation of progress in this burgeoning field of endocrinology. This book would prove to be a very valuable aid to someone contemplating entering into the field of prolactin physiology and pharmacology. Those active in the field should have this book available as a valuable resource.

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The Antigens. Volumes 1–3. Edited by Michael Sela. Academic Press, New York, N.Y. Volume 1: 1973, xiii + 573 pp, 23.5 × 15 cm, $35.00. Volume 2: 1974, 568 pp, 23.5 × 15 cm, $35.00. Volume 3: 1975, 624 pp, 23.5 × 15 cm, $46.50.

These three volumes of chapters by distinguished authors are intended to initiate a comprehensive treatise focusing primarily on the chemistry and biology of antigens but also covering related areas of immunology. The notion of antigens will include macromolecules, viruses, bacteria, fungi, cells, and tissues. Each chapter is supposed to provide not only in-depth analysis of the current status and recent developments of its subject but also a historical perspective. The first two volumes are devoted to macromolecules as antigens and to immunoglobulins. The third volume is concerned with more complex antigens and with antibodies. The wide variety of chapter topics indicates that a broad spectrum of immunological or even immunologically related topics will be included in this series.

Volume I. In the first chapter, "Nucleic Acid Antigens", B. David Stollar discusses immunogenicity, hapten functions, and serologic reactions of nucleic acids including systemic lupus erythematosus. The various types of studies and assays involving antibodies to nucleic acids also are discussed. The chapter "Immunochemistry of Enzymes" by Ruth Arnon reviews the efforts to elucidate structural and functional features of enzymes through the use of antibodies to these enzymes. Included are the effects of antibodies on enzyme activity, the antigenic similarity of enzymes from different species, and the antigenic similarity of alternate forms of enzymes like proenzymes, apoenzymes, and isoenzymes. The chapter "Structure of Immunoglobulins" by Joseph A. Gally covers the various levels and types of structural features of antibodies and also includes sections on nomenclature, combining sites, genetic markers, and origins of immunoglobulin diversity. In the next chapter, "Immunoglobulin Allotypes", Rose Mage, Rose Lieberman, Michael Potter, and William D. Terry review allotypic forms of rabbit, mouse, and human immunoglobulins. The chapters "The Evolution of Proteins" by Norman Arnheim and "Phylogeny of Immunoglobulins" by R. T. Kubo, B. Zimmerman, and H. M. Grey define the usefulness and approaches involved in studies of the structural homologies between corresponding proteins between different species. The former chapter summarizes the general state of the art, while the latter focuses on immunoglobulins. The last chapter, "Chemistry and Biology of Immunoglobulin E", by Kimishige Ishizaka is concerned with the unique structural and functional features of IgE and how the latter derive from the former.

Volume II. In the first chapter, "Protein Antigens: The Molecular Basis of Antigenicity and Immunogenicity", Michael J. Crumpton distinguishes between antigenicity ("the capacity to interact with antibody") and immunogenicity ("the capacity of a protein to stimulate antibody production") and then discusses the molecular basis of antigenicity and immunogenicity. Most of the chapter is devoted to the former topics and emphasizes antigenic determinants. The second chapter, "Blood Group Antigens", is written by Sen-Itiroh Hakomori and Akira Kobota. Among the topics they have included are glycosphingolipid and glycoprotein antigens, immunogenetics and biosynthesis of ABH and Lewis antigens, and blood group substances in malignant cells and tissues. In the third chapter, "Low Molecular Weight Antigens", A. L. DeWeck discusses immunogenicity, elicitation of allergic reactions, tolerance, and research applications (for example, identification and properties of cellular receptors) of low molecular antigens, which are arbitrarily limited in this review to antigens of molecular weight less than 5000. A short chapter, "The Application of Antibody to the Measurement of Substances of Physiological and Pharmacological Interest", by Edgar Haber and Knud Poulsen, reviews the principles and practical aspects of immunoassays. Three substances with which the authors have worked, angiotensin, aldosterone, and digitalis glycosides, are presented as examples. A timely and comprehensive review on idiotypy is provided by Jacques Oudin in the chapter, "Idiotypy of Antibodies". Many aspects of the subject are covered, from the technical means of the study of idiotypy to the role of genetic factors. A comprehensive, long chapter "Immunoglobulin A", by J. F. Heremans discusses the distribution, isolation, properties, biosynthesis, function, and role in disease of IgA.

Volume III. Microbial polysaccharides are an important and interesting class of antigens for several reasons, as reviewed in the initial chapter, "Microbial Antigens", by Klaus Jann and Otto Westphal. For example, these antigens are resistant to excretion or metabolic degradation and have been found to be complementary to some of the myeloma proteins. Chapter 2, "Antigenic Determinants and Antibody Combining Sites", by Joel W. Goodman, provides a very general review of the basic concepts and major developments concerning the antigen-immune response relationship. Both humoral and cellular immune responses to antigenic determinants are discussed. The next chapter, "Lymphocyte Receptors for Antigens", by G. L. Ada and P. L. Ey attempts to answer the question: What are the lymphocyte receptors for antigen and how do they function? The last four chapters, "Allergens and Genetics of Allergy" by David G. Marsh, "A Biologic and Chemical Profile of Histocompatibility Antigens" by S. Ferrone, M. A. Pellegrino, and R. A. Reisfeld, "Antigens of the Mycoplasmatales and Chlamydiae" by George E. Kenny, and "Virus Infections and the Immune Responses They Elicit" by William H. Burns and Anthony C. Allison, all are concerned with more complex antigens of major biologic importance which have as yet to be fully defined at the molecular level.

Because of its attention to all of the various aspects of antigens, this series of volumes will be of value for workers in any of the disciplines concerned with immunology.

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Carbohydrate Chemistry. Volume 9. Specialist Periodical Reports. By J. S. Brimacombe, Senior Reporter. The Chemical Society, Burlington House, London. 1977. xii + 485 pp. 13.5 × 21.5 cm. $58.00.

This report reviews the 1975 literature in carbohydrate chemistry and enzymology. As with the other eight volumes in this series, an attempt has been made to provide a comprehensive rather than selective review of the literature in these areas. In all, 2759 references are cited.

For those unfamiliar with this series, the report is divided into two parts. Part I (Mono-, Di-, and Trisaccharides and their Derivatives, 28 chapters) reviews the chemistry of carbohydrates according to functional type, physical methods of structure determination, and methods of separation and analysis. Part II (Macromolecules, 8 chapters) reviews the literature of polysaccharides, glycoproteins, and glycolipids, whether from plant, algal, microbial, or animal origin, enzymes which utilize carbohydrates as substrates, and procedures for the synthesis and modification of polysaccharides, glycoproteins, and enzymes.

These reports continue to be thorough, well organized, and well written. Carefully chosen figures, structural formulas, and tables

provide concise summaries of the work cited. Because of space limitations, however, in-depth discussion is lacking.

In summary, the breadth of research reported in this volume makes it a very valuable reference for those in any area of research related to carbohydrates.

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Organic Chemistry of Drug Synthesis. By Daniel Lednicer and Lester A. Mitscher. Wiley, New York, N.Y. 1977. xvii + 471 pp. 15.5 × 23.0 cm. $22.50.

The absence of a book which adequately covers the chemical synthesis of compounds of medicinal interest has long represented a gap in the literary armament of the medicinal chemist. In this work, the authors attempt to fill this gap by covering most of the major classes of drugs by describing the syntheses of the more important and/or more chemically interesting members of each class. To do so in the space of 471 pages, they have eliminated virtually all of the pharmacology and much of the mechanistic detail involved with the syntheses and thereby have retained the basic synthetic information. The book has been divided essentially into two sections, the first section which treats the synthesis of aliphatic, alicyclic, and carbocyclic aromatic compounds and the second section which is devoted to the various classes of heterocyclic drugs.

The first section of the book is introduced by an example of systematic drug design, namely, the evolution of local anesthetics derived from the aminobenzoic acids and alkanolamines. Monocyclic alicyclic syntheses are the subjects of Chapter 3 and are primarily examples of the various prostaglandin syntheses. Chapter 4 contains the syntheses primarily of antihistaminic drugs based on benzyl- and benzhydrylamines and alcohols. CNS stimulants (the phenethyl- and phenylpropylamines) and anti-inflammatory drugs (the arylacetic and arylpropionic acids) comprise the major portion of the next two chapters. Chapters 7 and 9, which describe the syntheses of arylethylenes and polycyclic aromatic compounds, tend to overlap both in the synthetic content and in the pharmacological activity of the drugs. Because of the vast number of synthetic possibilities for drugs derived from monocyclic aromatic compounds, only the preparation of compounds in which the pharmacophore is directly attached to the benzene ring is reviewed in Chapter 8. The next two chapters are devoted to the syntheses of steroids and tetracyclines and are followed by a short chapter on miscellaneous acyclic compounds.

Heterocyclic drug syntheses comprise the second half of the book, beginning with Chapters 13 and 14 which are devoted to the syntheses of five- and six-membered heterocyclic drugs. This is followed by a chapter which covers the preparation of narcotic analgesic agonists and antagonists. Five- and six-membered heterocycles fused to one benzene ring are covered in Chapters 16 and 17 and include a wide variety of drug classes, such as the indole alkaloids, coumarins, and quinolines. Because of their clinical importance, benzodiazepines, phenothiazines, and β-lactam antibiotics are covered in individual chapters. Finally, the syntheses of additional heterocycles fused to two benzene rings and other miscellaneous heterocyclic compounds are cursorily described in two short sections, Chapters 20 and 22.

In addition to the normal index, a cross index of drugs and a short glossary of medical terminology are included at the end of the book. For an organic chemist who may not be familiar with the pharmacological activity or medicinal application of a drug, these two sections can prove quite helpful.

The concept of an organic chemistry book of drug synthesis is desirable but, in this case, its translation into reality has been somewhat less than perfect. The chemical structures are often difficult to read and are plagued by numerous errors, e.g., the absence of bonds, misplacement of bonds, pentavalent carbons, and other incorrect structural features, which indicate careless editing. The organization of the first half of the book appeared to be poorly structured with some well-knit chapters and some short, fragmented ones that could have been combined. The content of the chapters, except for Chapter 3 which has overlooked the many syhtheses of prostaglandin analogues and Chapter 22 which neglects the synthesis of the numerous purine analogues, is adequate and the references are also good. Because of its reasonable price and content, the book will make a significant contribution to the library of any organic or medicinal chemist, in spite of the uneven organization of the chapters and the numerous textual errors.

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Advances in Prostaglandin and Thromboxane Research. Volumes 1 and 2. Edited by Bengt Samuelsson and Rodolfo Paoletti. Raven Press, New York, N.Y. 1976. Volume 1: xvi + 506 pp, 15.5 × 23.0 cm, $37.50. Volume 2: xvi + 521 pp, 15.5 × 23.0 cm, $39.00. Two-volume set, $75.00.

These two volumes, which represent the bulk of the contributed papers and abstracts of the poster presentations from the May 1975 international conference on prostaglandins at Florence, Italy, initiate a new series of reviews in an area of intense chemical and biological research. Since the middle 1960's, when the naturally occurring prostanoids were first synthesized, the contributions to the field of prostaglandin research have increased dramatically such that a series which reviews advances in the field is a welcome addition.

In these volumes, the editors have subdivided the 102 full papers into a number of specific research interest sections. The sections that are found in Volume 1 include Biosynthesis and Metabolism, Assay Methods, Prostaglandin Synthetase Inhibitors, Prostaglandin Dehydrogenase, Chemistry, Receptors, Cyclic Nucleotides, Nervous System, Cardiovascular System, and Respiration. Volume 2 contains the sections on Gastrointestinal System, Reproductive Physiology I and II, Pregnancy Interruption, Platelets, and Inflammation, as well as the abstracts of the poster presentations.

The first six sections comprise the chemical and biochemical aspects of the prostaglandin research as presented at the conference. The biochemical transformations of the endoperoxides to either prostaglandins by the vessicular glands or to thromboxanes by platelets are well discussed by Hamburg. The section on assay methodology describes several mass spectral and radioimmunoassay techniques for the analysis of the products of prostaglandin biosynthesis and metabolism. Aspects of the inhibition of prostaglandin biosynthesis by aspirin-like drugs are examined in a series of eight papers. The section on prostaglandin dehydrogenase, the primary metabolic enzyme for deactivating prostaglandins, includes experimental studies both on the increased purification of the enzyme by affinity chromatography and on the kinetic characteristics of the enzyme obtained from different organs. The syntheses of endoperoxide analogues, of 13-dehydro derivatives, and of other prostaglandin analogues are described in the series of seven papers which comprise the section on chemistry. The portion on receptors includes seven articles describing recent studies which use natural prostaglandins and their synthetic analogues to characterize the prostaglandin receptors in the corpora lutea, thymocytes, skin, and transport mechanisms.

The remainder of Volume 1 consists of papers relating research in the different organ systems. The interactions between the cyclic nucleotides and prostaglandins are examined under various circumstances including estrogen stimulation, the effect of aspirin-like drugs, and the effect of opiates and neurohormones in neuroblastoma X glioma cells. The role of prostaglandins in the nervous system is the subject of eight articles which examine the biosynthesis of prostaglandins in brain tissue in response to endogenous neurotransmitters, endogenous and exogenous precursors, and aspirin-like drugs as well as the effect of prostaglandins upon adrenergic transmission. Studies on the cardiovascular and respiratory effects of prostaglandins are presented in the next two sections which are introduced by a short review by Weeks. Although most of the papers explore the effects of

the prostaglandins on the cardiovascular or pulmonary function, several short articles regarding the activity of thromboxanes and PG precursors are also of note.

Volume 2 begins with the section entitled "Gastrointestinal System" and which should also include a mention of the "Renal System" as well since half of the contributed papers refer directly to the effect of prostaglandins upon the kidneys. The antisecretory effect of prostaglandins and their synthetic analogues is the subject of excellent articles by Robert and Karim. Another very good sequence of papers follows and relates the interactions between prostaglandins and blood pressure regulation, especially the renin–angiotensin system. Reproductive physiology and pregnancy interruption comprise two sections of overlapping content. The first section examines the experimental work done in small animal systems, primarily the guinea pig, and describes the relationship between prostaglandin levels and luteolytic hormone activity. The second section is more clinically oriented and presents data regarding the effectiveness of the natural and synthetic prostaglandins for the termination of pregnancy. Although the section on platelets is short, it contains several fine papers by Samuelsson, Smith, and Salzman describing the relationship between prostaglandin, endoperoxide, and thromboxene biosynthesis and platelet adhesion. In addition, the effect of metal-chelating agents and phospholipase A_2 upon platelet aggregation is presented. The short section on inflammation, which is introduced by a concise review by Vane, presents research efforts which attempt to defne the factors involved in prostaglandin release during inflammation as well as the effects of antiinflammatory drugs upon the biosynthesis of prostaglandins. The remaining 200 pages contain the abstracts of over 300 poster presentations which are generally one paragraph summaries of the research presentation.

Overall, the material in the two volumes is well presented and it contains sufficient experimental and clinical detail as well as substantial referencing to provide a very good background for prostaglandin research. The tables and figures are clear and easy to understand and the text is quite free of errors. The price for the set of two volumes seems very reasonable when compared to the amount of information that is contained. If there is one disappointing feature, it is that the field has advanced so rapidly that the absence of biological data regarding the endoperoxide analogues, thromboxanes, and prostacyclins tends to make these volumes slightly out of date by the time they are published.

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Biochemistry of Photosynthesis. Second Edition. By Richard P. F. Gregory. Wiley, London. 1977. 15.5 × 23.5 cm. xiv + 221 pp. $17.95.

The appearance of a second edition of any book, especially in these days of market-conscious publishers, is in itself a testimontial to the success of the first edition published just 6 years ago. In the second edition, the author has retained the overall organization of the first edition and has updated the fascinating topic of photosynthesis by incorporating the significant advances made between publication of the two editions. The literature coverage is up until the end of 1975. Particularly noteworthy are the updating of the topics, carbon metabolism and photophosphorylation.

The book is divided into two parts of approximately equal length. The first part is written as a relatively uncritical introduction to photosynthesis and its intent is to provide the reader with a concise overview of the subject in the context of its most important components, each of which is treated in one of the five chapters which make up Part I. These are entitled: The context of photosynthesis, The absorption of light, Light energy into chemical energy, Electron transport, and The path of carbon.

In order to satisfy the more serious student of photosynthesis, the author expands upon each of the aspects of this process in Part II. Here, significant experiments which form the bases for current beliefs as well as those which support alternative hypotheses are described. This part is written in the style of a scientific review with specific references to original research papers.

It is difficult to ascertain the reading audience for whom the book was intended. On the one hand, the presentation of certain topics appears to be directed toward the uninitiated, e.g., the depiction of not one, but four "isopentenyl units" which are in fact drawn as isopentane skeletons (p 31) and the distinction between "oxidative" and "substrate-level" phosphorylation (p 158). On the other hand, redox potentials and electron transport fall short of providing the unfamilar reader with an adequate understanding of these topics.

This book is highly recommended for those who have a particular interest in photosynthesis, but it is not recommended as a supplemental textbook, nor is it recommended for mandatory supplemental reading in a general course in biochemistry or botany. The central and singular role played by photosynthesis as the source of all organic compounds on Earth, even those derived from fossil fuels, should not be disregarded. Most of us take photosynthesis for granted simply because it happens whether we like it or not, just as we take for granted the fact that the sun shines whether we like it or not. In the same light, I would not propose that every course in chemistry or physics deal with the reactions that generate solar energy upon which photosynthesis and all life depends.

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Organophosphorus Chemistry. Volume 8. Specialist Periodical Reports. By S. Trippett, Senior Reporter. The Chemical Society, London. 1977. 14.5 × 22.5 cm. ix + 289 pp. $44.00.

Research on organic compounds containing phosphorus was booming from mid-1975 to mid-1976. Progress in this area is reported in fascinating, if brief, detail in the Chemical Society's latest Specialist Report. The 12 chapters, by 11 expert reporters, cover "Phosphines and Phosphonium Salts", "Quinquecovalent Phosphorus Compounds", "Halogenophosphines", "Phosphine Oxides and Sulfides", "Tervalent Phosphorus Acids", "Quinquevalent Phosphorus Acids", "Phosphates and Phosphonates of Biochemical Interest", "Nucleotides and Nucleic Acids", Ylides and Related Compounds", "Phosphazenes", "Photochemical, Radical, and Deoxygenation Reactions", and "Physical Methods".

As always, the quality of the reporting varies from chapter to chapter in this multiauthored series, and one can cavil about the organization of the book and the individual chapters. Nonetheless, the overall quality of the reports is high, and the scope of the literature coverage is beyond that which would be possible for even the most indefatigable individual journal reader and note taker. Writing these brief summaries of often complex papers is more difficult than it may seem, and the reporters have done outstanding jobs of combining brevity with clarity. Errors are rare and seem to be intelligently concentrated in misspelling names of authors of references, where they will do more harm to the authors' egos than to the users of this book.

The absence of a subject index is undoubtedly the most serious deficiency in this otherwise outstanding volume and of the series as a whole. The dividing lines between chapters, as always in multiauthored works, are fuzzy, and many subjects are discussed in several separate chapters. Readers of this series can expect to spend a good deal of time searching the Table of Contents for clues to the locations of particular topics.

Another severe limitation to the usefulness of this book is its price—which is high despite the devaluation of the pound. This will not seriously affect those users who occasionally search the library copy for references to specific subjects. However, the price will clearly inhibit personal ownership by those who would like to have the book to thumb through at odd moments, looking for nuggets of information to inspire new research projects or provide unexpected clues to solve old ones. This book could be a mother lode of such nuggets, and it would be lovely if the price were such as to make it more accessible for individual purchase.

Of course, you do get a fine book for the price. It is well bound, on good paper, and should last in the library for generations. My own preference, however, would be for a more cheaply bound version, on paper susceptible to self-destruction after a few years, but available at a lower price.

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The Hydrophobic Fragmental Constant. By Roelof F. Rekker. Elsevier, Amsterdam. 1977. 17 × 25 cm. xiv + 389 pp. $39.95.

This work is the first in a series of monographs to be published on various aspects of biological activity in terms of structural features. The book is divided into two parts of five chapters each. An author index and compound index, but no topical index, are included.

The book describes the author's systematic development of a series of empirically derived numerical values weighting the contribution of molecular fragments to the partition coefficient. The first chapter is a practical review of several aspects of the partition coefficient including a detailed review of their experimental determination. Chapter 2 describes the method of calculating the partition coefficient with examples of some of the shortcomings. Chapter 3 describes, in considerable detail, the derivation of aliphatic and aromatic fragment contributions to the partition coefficient. This is accomplished by a well-documented series of regression analyses and statistical evaluations. Chapter 4 describes the unification of aliphatic and aromatic fragment values with further empirical terms. Chapter 5 illustrates some application of the fragment approach to a few specific physicochemical and biological problems.

The next three chapters describe the unification of several solvent-pair systems using empirically derived parameters. Chapter 9 is a brief but informative consideration of membranes and their absorption characteristics, within the framework of the fragment approach to partition coefficient prediction. Chapter 10 presents a few applications of fragment utilization in considering the partition coefficient of the drug series.

The appendix lists 69 fragment constants for octanol with additional values for other solvents plus a series of empirical constants to convert octanol fragment values to other solvent systems. The appendix is essential for utilization of this approach because of the large number of terms and relating factors.

The approach leads to improved prediction of partition coefficients relative to previous methods. Investigators working with property–activity relationships to study drug activity as well as membrane phenomena will find this work useful.

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Davidson's The Biochemistry of the Nucleic Acids. Eighth Edition. Revised by R. L. P. Adams, R. H. Burdon, A. M. Campbell, and R. M. S. Smellic. Academic Press, New York, N.Y. 1976. 14 × 21 cm. xii + 420 pp. $14.95.

"The Child's Guide to the Nucleic Acids", as it is known at the University of Glascow, was first published in 1950 and revised six times by the late J. N. Davidson, who died in 1972 shortly after the seventh edition was completed. This eighth edition was revised by four of Professor Davidson's colleagues in the Department of Biochemistry at Glascow. The character of the book has remained the same. In fact, large sections are essentially unchanged except for rearrangement of sequence, not always for the best in the opinion of this reviewer. Other parts of the book have been deleted or completely updated and drastically altered. For example, the small section on the regulation of protein synthesis in the chapter on the biological function of RNA in the seventh edition is now a separate chapter with more than half the reference quoted having appeared since the last edition. In contrast, the chapters on the biosynthesis of mononucleotides and catabolism of nucleic acids have been combined into one chapter (a distinct improvement) entitled "The Metabolism of Nucleotides", and this reviewer detected only two new references—both to the same review article. These differences simply reflect current activity in the two fields. Other changes are intermediate in scope—a section on plasmids has been added to the chapter on "Nucleic Acids in Viruses".

This book is still intended primarily as an introduction to nucleic acids for advanced undergraduates in biochemistry and for scientists who are not experts in the field. As such it is invaluable. One area of particular interest to the medicinal chemist—that of drug actions— receives, as it has in the past, rather superficial treatment. In a treatise of this breadth, such a shortcoming can be excused.

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Encyclopedia of the Alkaloids. Volumes 1 and 2. Edited by John S. Glasby. Plenum Press, New York, N.Y. 1975. 1423 pp. 15.5 × 23.5 cm. $85.00.

"The writer of dictionaries...is...exposed to censure without hope of praise...", alas! And with more sympathy than most for the arduous task of compiling a dictionary of alkaloid names (for the book is less than encyclopedic in scope), I have serious reservations about the book's usefulness to the scientists for whom it was written.

The names of many, certainly not all, of the known, named alkaloids are listed here alphabetically with their physical properties, structural formulas when known, and a brief description which includes plant source(s), selected derivatives, and key references to the original literature.

There are, in my view, a number of shortcomings in such a presentation: one must know *the* "accepted" (by whom?) name of an alkaloid in order to find the information relating to it; cross-referencing of names is exceedingly light. About 3000 names are listed; approximately 4000 had been recorded almost 10 years ago. Where are the rest? Alphabetical listing of acetyl, deoxy, homo, iso, methyl, etc., derivatives scatters close chemical relatives over two volumes and, perhaps worse, separates them from their botanical origins. It is not possible, for example, to ascertain the alkaloid composition of peyote (*Lophophora williamsii* not *Anhalonium lewinii*) without an extensive effort. The botanist and chemotaxonomist will miss a botanical entry into the system.

Botanical data are often a problem for the chemist and the present instance is no exception. The confusions between *Xanthoxylum* and *Zanthoxylum*, *Rauwolfia* and *Rauvolfia*, *Tricachna* and *Tricachne*, etc., are preserved here. Case endings of species names are often inconsistent with those of the genera: *Solanum tuberosa*, *Gleditsia triacanthus*, *Schizozygia caffaeoidea* and/or *caffaeoides*, etc. The alkaloid himgaline is reported present in *several* species of *Himantandra*; there are only two (and some botanists hold for one!) in the family.

Descriptions of individual compounds are often superfluous; having given the $[\alpha]_D$ of isoeburnamine as +, it seems unnecessary to take a line of type to describe it as a dextrorotatory alkaloid or to point out the presence of specific substituents on a basic skeleton when the clear, well-drawn structures indicate this. The risk of having the verbal description disagree with the structure as pictured is ever-present—as in the case of hernandaline! Most of the lengthier description of the well-known alkaloids such as quinine, morphine, mescaline, atropine, and the like is available elsewhere in greater detail. Lacking any mention of limits or specificity, one might question the inclusion of some of the older color tests for some of the alkaloids as well as some of the spotty reports of pharmacological activity, at least one of which, mitragynine, is not the most recent nor most complete.

Botanical sources sometimes include the plant family, others do not; sometimes authorities are given, sometimes not; some alkaloids which have a fairly wide distribution through the plant kingdom (nicotine, anonaine, caffeine) are mentioned with respect to only the most common source(s). Nor is it true, as claimed on the fly leaf, that "information on the multitude of plant bases has remained scattered in a wide range of scientific journals".

One is prepared to grant the first printing of a major effort of this type its fair proportion of typographical errors; the layout is most clear and the type face and the structures are easy to read; yet, in all, there is clearly a large amount of clean white page space which might have been put to better use for the price.

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Analytical Profiles of Drug Substances. Volume 5. Edited by K. Florey. Academic Press, New York, N.Y. 1976. 15.5 × 22 cm. xi + 560 pp. $22.50.

This now familiar series completes its fifth volume with a detailed description of the physical and chemical properties of 18 drugs representative of a number of drug classes. These include Bendroflumethiazide, Cephradine, Chloroquine Phosphate, Dapsone, Flucytosine, Glutethimide, Levodopa, Sodium Levothyroxine, Methotrexate, Methyclothiazide, Metronidazole, Nitrofurantoin, Piperazine Estrone Sulfate, Procarbazine Hydrochloride, Promethazine Hydrochloride, Rifampin, Sulfasalazine, and Testolactone. The articles in this volume give the impression of cleaner typing and/or offset reproduction, in either case a distinct improvement over some of the articles in earlier volumes. Users of Volumes 1–4 will appreciate a listing of additions and corrections—surprisingly few!—and a cumulative index covering all five.

Staff Review

Cyclic Nucleotides and the Regulation of Cell Growth. Edited by M. Abou-Sabé. Halsted Press, New York, N.Y. 1977. 16 × 24 cm. xiii + 295 pp. $20.00.

This book is a collection of papers presented at a conference held in 1976 to discuss the role of cyclic nucleotides in the regulation of growth in eukaryotic and prokaryotic cell systems. Many of the leading laboratories in these areas contributed to the volume. In general, the 14 chapters are well written and illustrated with figure legends providing adequate information for understanding and critically evaluating the data. A sizable number of references are included in most chapters.

The book is divided into five sections. The first three deal with the involvement of cyclic nucleotides in bacterial growth, the regulation of the cell cycle, and the regulation of cell proliferation. The remaining sections discuss cyclic nucleotide metabolism during growth of various cell types and possible mechanisms of growth regulation by the cyclic nucleotides. The book appears to contain a significant amount of new data, and a good deal of extrapolation, speculation, and model building is included in each chapter. I found this stimulating.

Especially interesting are the models proposed for glucose and catabolite repression in bacteria, the discussion of cAMP–calcium coupling as a control mechanism for cell proliferation, and the evidence suggesting that β-agonists and cholinergic agents might act through cyclic nucleotides to "recruit" uncommitted G_0 cells into the cell cycle. There is a thorough discussion of the cyclic nucleotides in synchronous cultures of Hela cells. cGMP is given adequate coverage. Characteristics of guanylate cyclases in normal tissues and hepatomosa are presented. The possibility that cellular events involving oxidation and reduction may control cGMP synthesis is fully discussed and documented.

The importance of protein kinase in mediating cAMP effects on cellular constituents is demonstrated by the use of mutant cells deficient in protein kinase. It is shown that protein kinase changes during the cell cycle and that the enzyme can translocate in the cell to reach critical sites of activity, i.e., the nucleus. The usefulness of flow cytometry for cell cycle studies is illustrated.

In summary, this is a worthwhile volume for the cell cycle and cyclic nucleotide researcher who is looking for a well assembled and written update which bridges these two areas. The book should also serve those outside the immediate area who desire an introduction to the rapidly proliferating area of the involvement of cyclic nucleotides in cell growth.

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Opiate Dependence. Progress in Pharmacology. Volume 1. Number 2. By K. Kuchinsky. Gustav Fischer Verlag, Stuttgart. 1977. 17 × 24 cm. 39 pp. $9.50.

Definitions of what constitutes a book do not remain constant. This slim paper-bound brochure looks more like a review journal than a book. Its purpose is laudable—to provide a current overview of a pharmacological topic of broad interest. The scope of this monograph is that of a chapter in a textbook or symposium volume. It does not aim for the comprehensive coverage that is characteristic of *Pharmacological Reviews*, although there are six and a half pages of references. The emphasis here is on hypotheses that seek to explain opiate dependence in terms of changes in protein turnover or neurohormone metabolism. There is also brief consideration of psychological models of drug dependence.

While Kuchinsky does mention narcotic receptors and enkephalins, this review covers most of the same ground as that surveyed by Clouet and Iwatsubo in *Annual Review of Pharmacology* 2 years ago (volume 15, 1975). There is no discussion of the exciting work on endorphins that has been appearing since the beginning of 1976 or of the pharmacological responses to enkephalins. It would be difficult to describe this survey as up-to-date. Rather, this issue might provide useful background reading for physicians, medical students, or undergraduates. However, such a nonspecialist audience would need prior exposure to the descriptive pharmacology of narcotic drugs and the nature of addiction. While these readers might find its conciseness and readability attractive, they may hesitate to pay 25 cents a page for a booklet that is already being out-distanced by rapidly moving new developments.

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Receptors and Recognition. Series A. Volume 2. Edited by P. Cuatrecasas and M. F. Greaves. Halsted Press, New York, N.Y. 1977. 16 × 24 cm. viii + 229 pp. $24.50.

My first reaction on looking at the Table of Contents was what possible thread could hold together chapters ranging in subject matter from molecular recognition by antibodies, to cell activation by calcium, to "cell traffic", to incompatibility in flowering plants, to catecholamine receptors? The editors foresaw this question and address it in their preface: "The individual chapters describe in clear terms, for the relative nonspecialist, the basic elements of recognition events in distinct biological systems of cellular interaction and regulation." They express the hope that the search for evolutionary links or common mechanisms will lead to a cross fertilization of concepts, ideas, and methodologies. To some extent, they may have succeeded. As a relative nonspecialist in this area, a pharmacologist né organic chemist, I found most of the chapters interesting, informative, and thought provoking. However, I am afraid that many medicinal chemists will find chapters such as the one on "Incompatibility in Flowering Plants" much too highly biological and too slightly chemical for their tastes. Do we read, do we buy, books because they will introduce us to foreign fields or because they will strengthen us in our current areas? I am afraid most of us choose the latter alternative.

There are several weaknesses in this volume as a book. Not only is the thread of unity precarious, but there is no index—an absolute requirement, at least in my opinion, for a reference book. Where there is redundancy, such as in coverage of Ca^{2+} ionophores in both the chapter on catecholamine receptors as well as in the chapter on calcium cell activation, there is no cross referencing; the authors do not seem to have been aware of the overlapping coverage.

The first chapter, on molecular recognition by antibodies, seems good at an advanced level but weak by reason of incorrect ov-

ersimplifications at a lower level: "Enzymes are designed to bind ligands and catalyze a chemical reaction..." (Have you designed a good enzyme lately?); "There is *no* similarity between an enzyme that acts on carbohydrates (e.g., lysozyme) and an enzyme that acts on polypeptides (e.g., trypsin)" (my italics). Would the author care for a list of 5, 10, ..., similarities? Both are proteins, both contain similar amino acids, both.... As a whole, the chapter badly needs editing—tenses, typos, etc.—but it would be worth the editing since substantively it is good; it covers the structural basis for molecular recognition by antibodies throughly and well.

Dr. Gomperts gives a good rationale for the current resurgence of interest in the role of calcium in biological processes: the advent of ionophores for calcium which allows us to confirm much of what had formerly been merely speculated as well as to extend our understanding of many control processes which depend on calcium. An interesting off-beat chapter by Dr. di Sonsa entitled "Cell Traffic" covers the flow of cells through blood and lymph circuits. The recognition aspect, which is really not the major focus, has to do with sequestering particular cells in these traffic patterns. The final chapter on "Catecholamine Receptors" can serve as a useful introduction and catalog of α- and β-adrenergic receptors. Like the other chapters in this volume, it is well referenced, with many citations to work in press or even in preparation.

It is hard to come to a conclusion in the review of a book which itself has no conclusion. If it is judged as an annual review, I could recommend it for those interested in the developing areas of receptors and recognition.

(This review was written by Dr. Usdin in his private capacity. No official support or endorsement by the NIMH is intended or should be inferred.)

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Drug Metabolism Concepts. ACS Symposium Series Number 44. Edited by Donald M. Jerina. American Chemical Society, Washington, D.C. 1977. ix + 196 pp. 15 × 23 cm. $15.50.

This volume contains carefully written and edited transcripts of lectures presented at an ACS symposium in Aug 1976. The areas selected for coverage are among the most active in chemical and mechanistic aspects of drug metabolism research, and chapters were prepared by leading figures in each field.

The chapters by Coon et al. and by Johnson and Muller-Eberhard deal with resolution of the hepatic monooxygenase system into its component parts and with the relative effect of various inducing agents on the constituents of the system. Emphasis in the Coon chapter is on his group's demonstration of the existence of multiple forms of cytochrome P-450 in rabbit liver microsomes, while Johnson and Muller-Eberhard describe fractionation of P-450 and association of various enzymatic activities with distinct forms of P-450. Trager approaches the enzyme multiplicity problem from a slightly different perspective. His work with product ratios in the several metabolic pathways available to (*R*)- and (*S*)-warfarin, and the effect of various inducers on these, leads to the conclusion that at least five different enzymes are involved in warfarin metabolism.

Two chapters are concerned with chemical aspects of carcinogenesis associated with metabolites of benzo[*a*]pyrene (BP). Levin et al. describe the work of the NIAMDD–Hoffman-La Roche group in metabolic studies on BP which led to the identification of diol epoxides as proximate carcinogenic metabolites. The chapter by Moore et al. is concerned with the interaction of the diol epoxides with synthetic and natural nucleoside polymers. These chapters provide a highly useful summary of work in this rapidly advancing field through mid-1976, but readers interested in the field's current status will have to consult more recent reports.

Estabrook has reviewed in a useful manner his work on mechanistic aspects of the monooxygenase system with particular reference to oxygen activation. Collman and Sorrell present a very provocative account of their work on synthetic models for the reaction stages of bacterial P-450, which confirms ligand assignments previously inferred from spectroscopic data for three active P-450 stages, as well as the inactive P-450–CO complex.

The work is rounded out with a chapter by Nelson et al. which presents the work of the NHLBI group on the relationship among reactive metabolite formation, covalent binding, and tissue injury in a group of drugs bearing aromatic heterocycles which apparently act via arene oxides and a group of materials containing a hydrazine moiety.

The book also incorporates a carefully prepared and useful index, as well as numerous references, and is highly recommended as an authoritative and informative summary of the topics presented.

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Receptors and Mechanism of Action of Steroid Hormones. Part II. Edited by George R. Pasqualini. Modern Pharmacology—Toxicology. Volume 8. Marcel Dekker, New York, N.Y., and Basel, Switzerland. 1977. ix + 425 pp. 16 × 23.5 cm. $39.75.

Part II of Receptors and Mechanism of Action of Steroid Hormones is a sequel to Part I [reviewed: *J. Med. Chem.*, **20**, 1230 (1977)]. It is difficult to understand why this monograph costs $10.00 more than the already expensive first part. Nonetheless, information provided represents an interesting summary of the literature (some referencing into 1976). Part II includes chapters 8–12. The inconsistency found in referencing is unfortunate; chapter 8 includes complete titles in references whereas the remaining chapters do not. Abridged chapter titles (authors) are 8, Glucocorticoid Receptors and Mechanisms (Munck and Leung); 9, Mineralocorticoid Receptors (Pasqualini and Sumida); 10, Aldosterone Mechanism of Action (Crabbé); 11, Steroid Receptors in Breast Cancer (Jensen and DeSombre); 12, Steroid Receptors in Brain, Hypothalamus, and Hypophysis (Kato). This work is concluded with a useful author index to cited articles and a subject index for both Parts I and II. As recommended by this reviewer for Part I, Part II also is recommended reading by virtually all biomedical investigators. Unfortunately, this monograph likely is too expensive for individual ownership. The chapters may serve as a source of undergraduate and graduate lecture material. Sufficient detail of experimental results is presented in all chapters, thus rendering this summary of value to investigators desiring to study this area in some depth.

Munck and Leung's introduction to chapter 8 provides an interesting interpretation of research direction in this area. The chapter also includes a rather complete summary of glucocorticoid target tissues. This referenced summary (Table 1, Chapter 8) should be very useful to many scientists. Table 1 is subsequently discussed in terms of established target tissues and known physiologic effects. Primary mechanisms and glucocorticoid receptors are discussed in some detail. Chapter 8 includes 516 references to the literature. Similarly, the chapter on mineralocorticoid receptors is extensive (278 references). Pasqualini and Sumida consider tissue uptake, autoradiographic studies, tissue binding, specific receptors, and mechanism of action of mineralocorticoids. In addition to considerable discussion and many tables of data, three rather comprehensive tables (Tables 11, 12, and 15; Chapter 9) summarize total binding of [^{3}H]-aldosterone by different tissues of toads, rats, guinea pigs, and humans, total binding of other corticoids and spironolactone in adult rat kidneys, fetal guinea pig kidneys, and toad bladders, and the effect of different steroids on nuclear [^{3}H]aldosterone–macromolecular complexes of adrenalectomized rat kidney. Details of experiments are presented and analyzed. The summary section includes a hypothetical model (Figure 8, Chapter 9) of the present concept of steroid hormone–macromolecular complexes. Jean Crabbé concludes the adrenocorticoid discussion with an emphasis on the aldosterone mechanism of action (Chapter 10) in the ventral skin and urinary bladder of frogs and toads. Animal model justification and specific experimental results are discussed. Like the preceding two chapters, this somewhat shorter chapter (230 references) contains much information and is interesting to read.

The final two chapters of this work [Chapters 11 (127 references) and 12 (275 references)] involve discussions of estrogens in breast cancer (Chapter 11) and estrogens, androgens, progesterone, and corticosteroid receptors in the central nervous system (Chapter 12). Chapter 11 summarizes the principal features of estrogen–receptor interactions in hormone-dependent tissues and tumors. Clinical application of these studies in predicting hormone dependency in human breast cancer is also discussed. Details of experimental results are presented in both chapters 11 and 12. Kato's final chapter is also excellent and includes a summary of experiments concerned with estradiol receptors in the hypothalmus and adenohypophysis, estradiol organ selectivity, possible physiologic roles and feedback mechanisms, androgen receptors in the hypothalmus (gonadotropin-inhibiting action), uptake and distribution into neural tissue, and metabolism in brain. Shorter discussions of corticoid and progesterone uptake by brain or hypophysis and preliminary receptor experiments are also found in Chapter 12. Chapters 11 and 12 conclude a generally well-written monograph which is interesting to read.

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