Book Reviews

Diuretics. Chemistry, Pharmacology, and Medicine. Edited by Edward J. Cragoe, Jr. Wiley, New York. 1983. 624 pp. 24 × 16 cm. ISBN 0-471-8366-6. $80.00.

This is a book of heroic ambition and proportions. It reports the published (and patent) work of the past 20 years on the synthesis of diuretic compounds. Perhaps 25 000 new structures are described in some 20 classes. Attempts are made to put either the lead, or most successful, compound of a series in its physiological (and when appropriate) medical context.

The editor, Dr. Edward J. Cragoe of Merck, was a disciple and associate of the revered James Sprague, a pioneer in sulfonamide chemistry in the great early days of bacterial chemotherapy and the dawn of diuretic research. But it was Richard Roblin, his friend, rival, and opposite number at the American Cyanamid Co., who made the brilliant leap from flask to clinic with the carbonic anhydrase inhibitors and provided the economic and scientific stimulus that led to chlorthiazide in the hands of Sprague, Novello, Bayer, and Baer at Merck.

Sprague's group, and later Hoechst and dozens of pharmaceutical companies in the United States, Europe, and Japan, have gone far beyond the sulfonamides in finding structures with diuretic activity. A reading of this book shows the enormous range and diversity of compounds that act on the kidney, all hidden from view before 1950!

Cragoe writes an inspired introductory chapter, giving some elements of the history of renal physiology and pharmacology, his view of the present and future, and suggesting how this subject may be extended to effects on electrolyte transport elsewhere, i.e., gut, lung, eye, gallbladder, and brain.

Chapter 2, by Edward H. Blaine (Merck), is a scholarly account of the "Basic Principles of Renal Physiology and Pharmacology", which will be most valuable to the medicinal chemist entering the field. Chapter 3 is the magnum opus, 150 pages and 722 references on sulfonamide diuretics by Richard C. Allen (Hoechst). This covers the range of carbonic anhydrase inhibitors, the "thiazide" family, and the "high ceiling" sulfonamides. The synthetic activity in the latter is astonishing, and the structure–action relations are complex beyond the worst (or best) dreams of Paul Ehrlich. There follow seven chapters, one by Robert L. Smith (Merck) and the rest by Dr. Cragoe, on widely different structures, including the pyrazines and bicyclic heterocycles, the prototypes of K^+-sparing diuretics. The great variety of chemical types that inhibit renal reabsorption of sodium invites speculation as to the nature of the receptor(s) that mediate such response, but surprisingly little progress has been made on the essential topic.

The final chapter is a diversion from the rest of the book, but a most scholarly and important contribution. Robert L. Smith has written on "Endogenous Agents Affecting Kidney Function". This includes antidiuretic hormone, the various prostaglandins, the angiotensin system, aldosterone, and the kinins. Chemistry, physiology, and relations to disease are discussed. Although this is not the major emphasis, drug development also enters this picture in intellectually exciting ways, i.e., angiotensin converting enzyme inhibitors and receptor-specific analogues of hormones. I know of no better introduction to this bewilderingly complex field, and it is to be hoped that it will not be lost in computers programmed to index this book only for "diuretics".

Since there are four authors involved, there is the expected divergence of style and emphasis. The remarkably comprehensive chapter on sulfonamide SAR contains but a few lines on hearing loss following furosemide. It is not correct to imply that it occurs only in "resistant cases". A brief discussion of effects on endocochleal potential and endolymph electrolytes would be welcome. Dangers of electrolyte depletion are minimized. I do not believe it is settled that prostaglandins mediate the effects of the thiazides. I write these comments rather unconfortably, in view of the enormous effort and major emphasis on the chemical structures.

With even more reluctance, I say something about renal carbonic anhydrase and its inhibitors. These appear prominently in Chapters 2 and 3 because of their historical and physiological importance, although they now lie off the main track of drug development. It is not correct to say that bicarbonate reabsorbed from luminal fluid is "not derived from the filtered bicarbonate". This may be a semantic point, but surely the filtered bicarbonate is in part protonated to form carbonic acid and in part reabsorbed as such. Another implication from page 27 and the figure thereon is that *all* filtered bicarbonate is reabsorbed under the influence of carbonic anhydrase. If this were true, inhibition of the enzyme would cause such massive urinary bicarbonate loss that such drugs would be lethal in a few hours. The fact is that in man only 20% of filtered bicarbonate is reabsorbed through the enzymic mechanism, with the remainder reabsorbed in its ionic form. An important theoretical and practical issue concerning these and certain (but not all) other diuretics is why there is not a continued renal effect when drugs are administered chronically. Since 1956 it has been clear that the factor that prevents continuing loss of electrolytes in chronic carbonic anhydrase inhibition is the metabolic acidosis that supervenes. That is why, for instance, patients with glaucoma are saved from HCO_3^- depletion and lethal acidosis. The idea given on page 42 (pre-1955) that the refractory state is due to "low plasma bicarbonate" is incorrect, since (for example) these drugs are fully active in compensated respiratory alkalosis. It is also stated on this page that "acetazolamide and related compounds are tightly bound to plasma proteins and find their way into the lumen by active secretion". This is true for acetazolamide in man but is not true for many drugs of this series, for example, methazolamide. It is misleading to imply that their action depends on active secretion. No notice is taken of the single drug of this class that is specific for the kidney. The structure of benzolamide is given on page 61, but there is nothing in the text that shows how different it is from other carbonic anhydrase inhibitors in its specific action on the kidney and exclusion (at the correct dose) from action at other sites. Finally, the action of these drugs does not involve stimulation of adenylcyclase, although there are papers claiming this.

Some notice might have been taken of important recent advances in renal physiology and anatomy, showing the very great degree of heterogeneity at different sites of the nephron and that even within the proximal tubule there are at least three distinct biochemical–physiological units.

These criticisms or emendations are made for the record and should in no way detract from the enormous value of this book. It must find its way into every medical and chemical library in the world and the shelves of everyone concerned with any aspect of this fascinating and still explosively developing subject. It will give pleasure as well as knowledge, because the authors have taken care to humanize and enliven their subject. This is an astonishing piece of virtue in view of the great amount of material covered and what must have been the temptation to catalog data rather than to treat it intelligently and critically.

Dr. Cragoe's idealism and love for his subject have been infectious and caught by his three colleagues to make one of the most memorable books in the history of pharmaceutical chemistry.

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A Textbook of Pharmaceutical Analysis. Third Edition. By Kenneth A. Connors. Wiley, New York. 1982. x + 664 pp. 16 × 23.5 cm. ISBN 0-471-09034-4. $55.00.

What can be said for this edition is that it meets, and perhaps exceeds, the standard of excellence set by the author in previous

editions. Coverage of the theory and methods of modern analysis is sufficiently broad to allow the individual instructor considerable latitude in emphasis. The book could serve as a basic text in analytical chemistry, pharmaceutical or not.

It is divided into six sections, with relative concentration on physical methods which are gradually replacing the older, more traditional procedures in the official compendia. Two sections, one on elemental analysis, the other on chemical reactions in analysis, e.g., derivatization, introduce the student to concepts and techniques usually associated with other courses in the chemical curriculum.

The only thing that might be said against it for general student use is the price.

Staff

Calcium Blockers. Mechanisms of Action and Clinical Applications. Edited by Stephen F. Flaim and Robert Zelis. Urban and Schwarzenberg, Baltimore. 1982. x + 303 pp. 18.5 × 26 cm. ISBN 0-8067-0611-2. $44.50.

The recent introduction of the calcium blockers diltiazem, nifedipine, and verapamil into clinical medicine in the United States has focused new attention on the cellular roles of calcium and the mechanisms of action of these agents. The therapeutic value of the calcium blockers, as these agents are collectively termed by the editors, for a variety of cardiovascular disorders is clearly established, and an extensive number of reports from both the basic research and clinical levels have appeared. As such, the stated intention of the editors is to provide a book that bridges the information gap between scientists engaged in fundamental studies of the calcium blockers and physicians who require more basic scientific or background information. The editors envision an audience composed of practicing physicians, physician–scientists, and basic science investigators, chiefly physiologists and pharmacologists.

The book is divided into three sections. In section I (basic physiology) it is clear that the calcium blockers achieve their effects by multiple mechanisms in cardiac muscle (chapters 1 and 2) and vascular smooth muscle (chapters 3–6). Two chapters are devoted to the involvement of calcium ions and the possible influence of calcium blockers in the function of pancreatic acinar cells (chapter 7) and in the cells of various endocrine glands (anterior and posterior pituitary and pancreas) and steroidogenic organs (adrenals, ovary, and testis) (chapter 8).

Section II (pharmacology) provides a review of the chemical structures, a limited summary of structure–activity relationships, and the biochemical pharmacology of the calcium blockers (chapter 9), as well as chapters on the comparative pharmacology of these agents in cardiac muscle (chapter 10) and vascular smooth muscle (chapter 11). The comparative effects of diltiazem, nifedipine, and verapamil on blood flow in various vascular beds based on literature reports and the results of Flaim's work with intact, unanesthetized animals are reviewed in chapter 13. A brief chapter describing the clinical pharmacokinetic properties and hemodynamic effects of verapamil, nifedipine, and diltiazem concludes this section (chapter 13).

In Section III (clinical applications) the role of coronary artery spasm in the myocardial ischemic syndrome (chapter 14) and the relative effectiveness of the calcium blockers in comparison with other agents, such as the nitrates and β-blockers for the management of anginas (variant, unstable), which are associated with coronary artery spasm, are reviewed (chapter 15). The efficacy of the calcium blockers in chronic stable angina (chapter 16), various cardiac arrhythmias (chapter 17), and other vascular disorders, including hypertension, hypertrophic cardiomyopathy, acute myocardial infarction, congestive heart failure, and pulmonary hypertension (chapter 18) is also presented.

The book appears to fulfill the editors' goal of bridging the gap between members of the intended audience. As this book is an excellent compilation of referenced information on the physiology, pharmacology, and clinical utility of calcium blockers, members of other scientific disciplines, including medicinal chemistry, should also find it very worthwhile. Although there are a few mistakes in the chemical structures and some of the structures and figures could be more aesthetically presented, the book is generally well written and error free. An extensive subject index is provided, and each chapter includes many recent as well as pertinent older literature citations.

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Handbook of Experimental Pharmacology. Volume 55/II. Psychotropic Agents. Part II. Anxiolytics, Gerontopsychopharmacological Agents, and Psychomotor Stimulants. Edited by F. Hoffmeister and G. Stille. Springer-Verlag, New York. 1981. xxvi + 778 pp. 17 × 25 cm. ISBN 10300-7. $199.00.

This new addition of the Handbook series is primarily devoted to the anxiolytics. This volume is organized into 16 chapters, each addressing some more narrowly defined aspects—chemistry, neuropharmacology, biochemical effects, and behavioral effects—of the three classes of drugs contained in the title. It represents critical analyses of the status of our knowledge in these areas by 26 distinguished investigators. The largest chapter, and perhaps the one of broadest interest (chapter 2), provides an exhaustive review of all pharmacological effects of benzodiazepines on neural and nonneural cells and tissues ever published; not surprisingly, it occupies 40% of this volume. No less important, the five chapters devoted to gerontopsychopharmacological agents provides a roadmap for new investigators entering this nascent subdiscipline. Issues related to the problems of appropriate animal models and the heterogeneity of this group of drugs are well discussed. It is unfortunate that the three chapters on stimulants were not included in a previous volume of this series devoted to their social use and abuse, for their therapeutic use is limited.

It is helpful that this volume is indexed both by subject and author cited. The individualistic perspectives of this collection of reviews should provide a well-spring of intellectual stimulation for investigators in these areas. Accordingly, this volume belongs on the shelf of both medicinal chemists and pharmacologists whose area of special interest is contained in this group of psychotropics. Based on past and present volumes, the Handbook series belongs in every biomedical science library.

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Inorganic Biochemistry. Volume 3. Specialist Periodical Reports. Edited by H. A. O. Hill. The Royal Society of Chemistry, London. Bartholomew Press, Dorking. 1982. xv + 397 pp. 14 × 22.5 cm. ISBN 0-85186-565-8. $114.00.

This book is a Specialist Periodical Report. Most of the chapters contain references to work published in 1979 only. The chapters on "Trace Elements in Animal Nutrition" and "Inorganic Elements in Biology and Medicine" contain additional references to background information published prior to 1979. There are also occasional references to literature published in 1980. The principal purpose of this book is to review the literature published in 1979.

This is a printed book with remarkably few errors: on page 42, CD_2Cl_2 is missing a subscript; an "a" in Na^+ is occasionally missing on pages 51, 52, and 54; and on page 93, third paragraph, line 7 should contain a period at the end of the sentence rather than a comma. In addition to being extremely well edited, this book has another nice feature in that the references cited on a page are listed at the bottom of the page. This exceptionally well-written and authoratative book is a credit to its contributors' efforts in presenting the existing state of the art. The contributors are to be commended for their labor in providing this rather remarkable overview pertaining to known metal-dependent enzymes and proteins.

C. A. McAuliffe presents "Inorganic Analogs of Biologic Molecules", an overview of complexes of amino acids, peptides, the binding of small molecules by transition-metal complexes,

non-heme iron complexes, copper proteins, nucleic acid constituent complexes, complexes of molybdenum and tungsten, macrocyclic complexes, complexes of platinum, and others.

M. N. Hughes presents recent information concerning storage, transport, and function of sodium, potassium, calcium, and magnesium. These group 1A and 2A elements are considered with regard to interactions with synthetic ionophore including crown ehters, cryptands, and noncyclic ethers. In addition, ionophore antibiotics, other ionophores, and model membrane systems; transport ATPases (Na^+,K^+-ATPases, Ca^{2+},Mg^{2+}-ATPases, and H^+,K^+-ATPase); and cations fluxes are all considered in detail. Cations of groups 1A and 2A are also reviewed as activators or inhibitors of enzymes. The roles of calcium in calcification mobilization and clotting mechanisms are also presented.

R. R. Crichton and J.-C. Mareschal present recent information concerning transport and storage of transition metals. Structural and functional aspects of iron storage and transport proteins, including ferritin and transferrin, are reviewed. The transport and storage of copper, in the form of ceruloplasmin, and its function with regard to copper-binding sites, primary structure, ferroxidase activity, and antioxidant activity are reviewed. Transport and storage of zinc is also presented from the point of view of storage in metallothioneins and its role in metabolism. Information pertaining to transport and storage of nickel, manganese, cobalt, vanadium, and the actinides is also included in this chapter.

M. Brunori, B. Giardina, and H. A. Kuiper reviewed recent publications concerning oxygen-transport proteins. Their are two classes of proteins presented. In the first class, hemoglobins, their structure and ligand character, their dynamic structural changes, and other aspects of their structure and reactivity are discussed. The second class of oxygen-transport protein presented is hemocyanins, the principal oxygen-transport protein of molluscs and arthropods. These are connidered in some detail with regard to their spectrophotometric, functional, and ion-binding properties, as well as new approaches to stereochemical modeling.

A. E. G. Cass reviewed the current literature with regard to oxidases and reductases: copper–zinc superoxide dismutase, the manganese and iron superoxide dismutases, the nonblue copper oxidases (dopamine β-hydroxylase, amine oxidase, benzylamine oxidase, galactose oxidase, and several tyrosinases), and the multicopper oxidases (laccase, ascorbate oxidase, and ceruloplasmin). Heme-containing oxidases and reductases and cytochromes P-450 from liver, adrenal, and other nonbacterial sources in addition to those from bacteria are also presented. Other hemoprotein oxidoreductases from plant and animal sources, including peeroxidases and catalases, are considered as well. The three remaining major categories considered in this chapter are the metallo-oxidoreductase of the respiratory chain, non-heme iron-containing oxidoreductases, and the molybdenum-containing oxidoreductases.

A. Galdes reviewed many papers pertaining to a large group of zinc metalloenzymes (carbonic anhydrase, carboxypeptidase, neutral proteases, amino peptidases, angiotensin-converting enzymes, collagenases, alcohol dehydrogenases, alkaline phosphatases, nucleotidyl polymerases, and nucleases). Recent literature pertaining to other zinc metalloenzymes (fructose 1,6-bisphosphatase, δ-aminolevulinate dehydratase, phospholipase C, inorganic pyrophosphatase, exonuclease, glyoxalase I, superoxide dismutase, pyruvate, carboxylase, dihydropyrimidine, amino hydrolase, creatinine, amino hydrolase, and amino acylase) is also reviewed.

A. R. McEuen outlined the recent literature with regard to manganese metalloenzymes (concanavalin A and related lectins, phosphoglycerate phosphomutase, manganese containing superoxide dismutase, nitrogenase-activating system, UDP-galactose:glycoprotein galactosyltransferase, UDP-glucose: galactosyl-hydroxylysyl-collagen glucosyltransferase, phosphoenolpyruvate carboxykinase and arginase) and manganese-activated enzymes [Mn^{2+}/Mg^{2+}-activated enzymes glutamine synthetase, ribulose, diphosphate carboxylase/oxygenase, β-galactosidase, adenylate cyclase, guanylate cyclase, cytidylate cyclase, phosphoprotein prosphatase, carbamoyl phophate synthetase, malic enzyme (NAD^+-linked), anthranilate synthetase–phosphoribosyltransferase enzyme complex, orotate phosphoribosyltransferase, isocitrate dehydrogenase (NADP dependent), Na^+,K^+-ATPase, citrate lyase, protein kinase (cAMP dependent), Mg^{2+}-dependent ATPase, RNA, and DNA polymerases as well as gluconolactonase, guanidinoacetate amidinohydrolase, phosphofructokinase, and creatinine amino hydrolase].

J. R. Arthur, I. Bremner, and J. K. Chesters surveyed the recent literature concerning the essentiality of metalloelements (Cr, Co, Cu, Mn, Mo, Ni, and Zn) and the nonmetalloelements (I, Se, and Si). The description of Wilson's disease as a form of Cu toxicity in man and genetically induced is inappropriate, since Cu intoxication in man does not produce Wilson's disease, which is an inherited genetic disease. Also, differentiation between Wilson's disease and other liver diseases that are characterized by high concentrations of Cu in the liver, due to an inability of the liver to perform its function as the principal excretory route for Cu is noo difficult. Bedlington terriers, which are genetically prone to chronic accumulation of Cu in their liver, are also readily distinguished from Wilson's disease, since they do not exhibit the other symptoms of Cu storage found in Wilson's disease.

N. J. Birch and P. J. Sadler reviewed recent reports of the use of inorganic elements in biology and medicine. Toxicology and biological environment are mentioned briefly. Lithium is considered in some detail with regard to intoxication, distribution in tissues, subcellular actions, its effect on membranes, and its effects in the kidney. In addition, new antitumor complexes containing Ti, Va, and Mo metallocenes, as well as the dialkyltin dihalides, are included. Information concerning Va as a natural regulator of ATPase is also presented. Recent information is presented with regard to the uptake and removal of iron and the changes in tissue iron associated with infection. Various aspects of copper and inflammation are presented with regard to therapy, including therapy with Cu–Zn superoxide dismutase, and copper complexes as anticonvulsant drugs. Information concerning zinc citrate complexes in milk and their possible roles in neonatal nutrition and the role of zinc as an antiviral agent is also included. Rhodium(II) carboxylates, gold(I) and gold(III) compounds, and the Pt(II) compounds are reviewed with regard to their development as antitumor agents. Gold(I) compounds are also considered with regard to their use as antiarthritic agents. The section on chrysotherapy mentions that Cu has long been implicated in the etiology of rheumatoid arthritis. This view is dated, since there is an abundance of evidence implicating a role for Cu complexes in the physiological response to overcoming arthritic diseases rather than an association with the pathogenesis of these disease.

This book is recommended to all medicinal chemists because many of the topics are intimately related to drug design, mechanism of action, and metabolism. The information provided is well worth the price.

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Methods in Enzymology. Volume 86. Prostaglandins and Arachidonate Metabolites. Edited by William E. M. Lands and William L. Smith. Academic Press, New York, London, Paris, San Diego, San Francisco, Sao Paulo, Sydney, Tokyo, and Toronto. 1982. xxv + 705 pp. 16 × 23.5 cm. ISBN 0-12-181986-8. $67.50.

This volume provides an up-to-date reference to a variety of methods used in the study of arachidonate metabolism. It includes not only the methods for studying the enzymes and metabolites in the cyclooxygenase pathway but also those recently described in the lipoxygenase pathway. The entire volume is divided into six sections. The first section deals with the purification and assay of enzymes involved in arachidonate metabolism with a small portion of the section on identification and assay of prostaglandin receptors. The second section is devoted to the production of antibodies against enzymes and arachidonate metabolites and their use in the development of sensitive immunoassays and in the immunocytochemical localization of antigens. The third section includes methods for preparing labeled and unlabeled arachidonate and its metabolites and analogues. The fourth section is concerned with the general separation procedures for arachi-

donate and its metabolites using thin-layer and high-pressure liquid chromatography. The fifth section deals with the preparation of deuterium- and ^{18}O-labeled metabolites and their use in quantitation by gas chromatography–mass spectrometry. The last section is a short section on bioassay methods.

This volume is a rather comprehensive coverage of chemical, biochemical, and immunochemical methods commonly used in prostaglandin and leucotriene research. Investigators will find it very useful in adapting those procedures to their research, since adequate experimental detail has been included. Although it appears that some methodologies are redundant, they are presented to the researchers as some useful alternative procedures to follow. Not only does this volume contain methods that were described in the original publications, but it includes many up-to-date procedures that have not been previously described. Many useful tables and figures are included for ready reference. Author and subject indexes are also comprehensive. This volume should prove of value to both the researcher entering the field of prostaglandin and leucotriene research and the established investigator familiar with many of the methods.

In summary, this volume is well-organized and represents the most up-to-date and comprehensive treatment of the methods used in this rapidly growing field of biomedical research. The editors should be commended for doing an excellent job in compiling this volume.

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Methods in Enzymology. Volume 87. Enzyme Kinetics and Mechanism. Part C. Intermediates, Stereochemistry and Rate Studies. Edited by Daniel L. Purich. Academic Press, New York, London, Paris, San Diego, San Francisco, Sao Paulo, Sydney, Tokyo, and Toronto. 1982. xxi + 830 pp. 16 × 23.5 cm. ISBN 0-12-181987-6. $74.50.

This volume is the third of a series of volumes dealing with enzyme kinetics and mechanism (two preceding ones on this subject are Volumes 63 and 64). The same editor extends the coverage by including the characterization of enzyme covalent intermediates (section I), the determination of enzyme stereochemistry (section II), the analysis of initial rate and inhibitor method (section III), and the use of isotopes as mechanistic probes (section IV). The first two sections are new additions to this series, whereas the last two sections are extensions of previously covered subjects in the first two volumes. Section I includes the detection, preparation, isolation, and characterization of several representative enzyme–substrate covalent intermediates. Section II is concerned with the synthesis, analysis, and application of chiral methyl groups and phosphorus centers. Extensive attention was placed on the determination of the stereochemical courses of a number of substitution reactions at phosphorus, catalyzed by nucleotidyltransferases, phosphotransferases, and phosphohydrolases. Section III deals with kinetics of branched reaction pathways, terreactant mechanisms, and other complex mechanisms. The use of pH, two-protonic-state electrophiles, and affinity labeling for studying mechanism and function of enzymes is also included. Section IV is devoted to the use of isotopes as mechanistic probes. Although this topic was discussed previously in Volume 64, this section extends its coverage to solvent isotope effects on enzyme systems, hydrogen isotope effects on initial rate, use of isotope effects to determine transition-state structure, and equilibrium exchange kinetics as a tool for the study of modifier action on regulatory enzymes.

This volume provides an excellent and contemporary addition to the general topic on enzyme kinetics and mechanism. It documents the contributions of many noted enzymologists and enzyme kineticists who have made recent progress in theories and techniques in this field. It also emphasizes practicalities in its review of recent advances in methodology. Excellent author and subject indexes are included. This volume, along with the two previous volumes, should be the key reference source for biochemists and bioorganic chemists interested in enzyme mechanisms and kinetics. Selective chapters in these three volumes can be also used as a text from which one can learn the fundamentals of enzyme kinetics and mechanisms.

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Methods in Enzymology. Volume 88. Biomembranes. Part I. Visual Pigments and Purple Membranes. II. Edited by Lester Packer. Academic Press, New York, London, Toronto, Sydney, and San Francisco. 1982. xxvii + 836 pp. 16 × 23.5 cm. ISBN 0-12-181988-4. $78.00.

This volume of this continuing series provides a comprehensive reference to a variety of biochemical and biophysical methods employed in the study of visual pigments and purple membranes. The subject matter is divided into two major sections entitled "Bacteriorhodopsin" and "General Methods for Retinal Proteins". This division of the subject matter appears somewhat arbitrary, since bacteriorhodopsin and several spectroscopic techniques are discussed in both sections.

Section I is further subdivided into "Purple Membrane Preparations and Protein Structure", "Reconstituted Systems", "Molecular Structure of Purple Membranes", "Chemistry, Spectroscopy, and Photochemistry", "Specialized Physical Techniques", "Ion Transport and Physiology", "Biogenesis, Genetics, and Microorganisms", "Light-Dependent Behavioral Responses of the Intact Organism", and "Other Retinal Proteins". Section II is subdivided into "Bacteriorhodopsin and Rhodopsin Molecular Structure", "Model Chromophores", and "Physical and Chemical Methods".

This volume is a second *Methods in Enzymology* on "Visual Pigments and Purple Membranes" (Volume 81) with rather little repetition. Examination of the subject matter of the present volume indicates a wide range of techniques from genetic manipulation, to protein isolation and purification, to detailed descriptions of sophisticated spectroscopic methods. The editor has done an admirable job in bringing so many different approaches to this broad subject. Scientists with almost any interest in visual pigments or purple membrane will find useful material in this volume. In addition, many of the spectroscopic techniques have applicability to other biological systems as well. In summary, this volume will be of considerable value to protein chemists, membrane scientists, spectroscopists, biochemists, and biologists, in general, and for those who have special interests in visual pigments in particular.

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Chemical Induction of Cancer. Structural Bases and Biological Mechanisms. Volume IIIA. Aliphatic Carcinogens. By Joseph C. Arcos, Yin-Tak Woo, and Mary F. Argus with the collaboration of David Y. Lai. Academic Press, New York. 1982. xix + 780 pp. 16 × 24 cm. ISBN 0-12-059303-3. $74.50.

The coverage provided by this book, part of a series which appears at intervals, is quite thorough. Although the main body of the text seems to have been written several years ago, supplements are given for each section to furnish more current information. Discussed are direct-acting carcinogens, which includes sulfur and nitrogen mustards, haloethers, alkyl sulfates and alkanesulfonates, ethylenimines, epoxides, lactones, and sultones; *N*-nitroso compounds; hydrazo, azo, and azoxy compounds and triazenes; phosphorus-containing alkylating agents; ethionine; carbamates, thiocarbamates, and substituted ureas; miscellaneous compounds, which include aldehydes, acrylonitrile, allylisothiocyanate, peroxides, quinones, *C*-nitroso compounds, thalidomide, phthalate esters, saccharin, sulfonamides, cyclamate, and peroxisome proliferators; and some drugs (chloropromazine, oxolamine, phenobarbitol, phenytoin, pyrimethamine, methotrexate, and methapyrilene). Thus, the authors' designation of aliphatic carcinogens in the title of the book is not strictly accurate.

The discussion on each compound is quite detailed; actual data on the number of tumors induced in animals and the sizes of

experimental groups are given for most compounds. However, there is no attempt to evaluate the experiments critically or in the light of the relevance to humans. The reader must do this for himself or herself. As an example, on page 429 two investigations on malathion are reported where high dose levels were fed with negative results; sandwiched between these descriptions is one on "indirect and inconclusive evidence of possible carcinogenicity of malathion" where the pesticide was administered subsequent to a dose of 7,12-dimethylbenz[*a*]anthracene, a known potent carcinogen.

In other cases there is considerable repetition in the descriptive text; for example, the Tris incident is discussed on page 434 and again on page 442.

The value of this book comes in its inclusion of details, extensive tables on series of compounds, and in the thorough subject index, which includes all the compounds mentioned in the text. Although a critical evaluation of the animal studies is not provided, the extensive data furnished makes this a useful reference book.

[This review does not necessarily reflect the official position of the National Cancer Institute, NIH.]

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Topics in Stereochemistry. Volume 13. Edited by N. L. Allinger, E. L. Eliel, and S. H. Wilen. Wiley, New York. 1982. x + 489 pp. 16 × 23.5 cm. ISBN 0-471-05680-4. $85.00.

There are only a few good textbooks available to cover the vast area of modern stereochemistry, and by far the best one of these, "Stereochemistry of Carbon Compounds" by E. L. Eliel (McGraw Hill), is now 20 years old. One stated purpose of this series is to help individuals to update themselves without having to read the massive amount of original literature which has appeared within the last few decades. Another stated purpose of the series is to delve into some topics in greater detail than is possible in standard texts. Individual chapters, as is customary in most such series, are written by experts in the particular field and are intended to cover the subject in depth.

As is to be expected, the results of such an endeavor must, of necessity, be somewhat uneven. Presentation styles vary widely amongst different authors and there are obviously differing formats required to present widely varying subject matters. In this regard, the present volume is no exception.

The first chapter (115 pages, 138 references) "Stereoselective Aldol Condensations" (by D. A. Evans, J. V. Nelson, and T. R. Tabor), is a well-written review of a topic which Professor Evans has pioneered. This chapter appears particularly timely due to the considerable attention which has recently been devoted to natural product syntheses based upon such reactions. This chapter is considerably more than just a review, since the authors offer numerous explanations and discussions of the observed phenomena which should impart a predictive capability to a perceptive reader.

The second chapter (76 pages, 333 references), "Application of Molecular Mechanics Calculations to Organic Chemistry" (by E. Ōsawa and H. Musso), is the least helpful in the current volume. This chapter is little more than a listing of references from this field with only limited discussion, explanation, or criticism of the reported results. Even by the end of a two-page introduction the reader has already been referred to 13 references. A promising section entitled "Molecular Modeling and Drug Design", referred to in the preface by the editors, is given short thrift and is covered in just a little more than one page with eight references.

The third chapter (68 pages, 122 references), "Chiral Monolayers at the Air–Water Interface" (by M. V. Stewart and E. M. Arnett), is a good discussion of the subject, written in textbook style for the nonspecialist. Included are some detailed discussions of research results from the authors' laboratory. Of potential importance to medicinal chemists is the fact that most components of bilayer membranes are chiral, and the behavior of numerous biological compounds is exemplified throughout this chapter.

The fourth chapter (69 pages, 111 references), "NMR Chiral Solvating Agents" (by W. H. Pirkle and D. J. Hoover), is a thorough, comprehensive review of the use of such agents to dissimilarly perturb the NMR spectra of enantiomeric solutes. The coverage is that to be expected from a specialized textbook and can well serve to bring an intelligent neophyte in the subject to the current frontiers. There are numerous references to the publications from the authors' laboratory, as is appropriate since Professor Pirkle is the leading specialist in this field.

The fifth chapter (135 pages, 326 references), "Chiral Organosulfur Compounds" (by M. Mikołajczyk and J. Drabowicz), is a thorough discussion of this emerging field. Numerous organic compounds with chiral sulfur functionalities are discussed, as are the various methods which have been used to determine their absolute configuration and optical purity. The problems peculiar to the dynamic stereochemistry of sulfur compounds receive considerable attention, as does asymmetric induction in chirality transfer to other centers. This well-written chapter suffers only from a dearth of current references (there are only a handful from 1980) in this rapidly developing area, but this factor may well represent journal availability in an east-block nation.

With the exception of the last chapter, this book is surprisingly up-to-date, and most chapters include some 1981 references. This fact is a tribute to the editors in getting the material into print quickly. A minor annoyance is the use throughout of on-line references, which are easily mistaken for compound numbers. An embarrassing typographical error, in the table of contents, moves Mikołajczyk and Drabowicz from Lodz, Poland, to Urbana, IL, and does away with Pirkle and Hoover. Fortunately, this appears to be a highly visible but isolated case, and this reviewer found the book to be relatively free of such errors. In addition to a detailed table of contents, which customarily begins each chapter, there is also a subject index for this volume and a cumulative topic index for all 13 volumes published to date.

Strangely, few recent volumes in this series appear to have been reviewed in ACS journals. This volume is surprisingly price worthy in these days of rampant inflation of printed matter and is a must for any up-to-date library. This reviewer suspects that a number of investigators, in the general area of stereochemistry, may wish to procure their own copies, since the stated objectives of this volume appear to have been well met.

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Chemical and Biological Generation of Excited States. Edited by Waldemar Adam and Guiseppe Cilento. Academic Press, New York, London, Paris, San Diego, San Francisco, Sao Paulo, Sydney, Tokyo, and Toronto. 1982. xxi + 388 pp. 16 × 23.5 cm. ISBN 0-12-044080-6. $59.50.

While there are other books available specifically on chemiluminescence, bioluminescence, singlet oxygen and related species, this book attempts to present in a single volume such widely disparate and yet related processes. The initial chapter, "Photophysical Concepts in Condensed Media", presents the physiocochemical and kinetic basis involved in the generation of excited state intermediates and provides the background for the succeeding topics. The next four chapters relate to 1,2-dioxetanes, which form a major component of this book. Included are gas-phase chemiluminescence, determination of chemiexcitation yields, thermal stability, and synthesis of these cyclic peroxides. Of special interest to this reviewer was the synthetic chapter by Karl Kopecky who is the researcher responsible for the first authentic, fully characterized and isolated 1,2-dioxetane. In addition to presenting the various synthetic schemes for preparing these structures, the hazards and safety precautions in their handling are discussed. The next two chapters are related. The first involves the electro-generated chemiluminescence or electrochemiluminescence in solution-phase systems and the second relates to chemically initiated electron-exchange luminescence. This latter pathway of chemiexcitation is shown to be responsible for the generation of excited states usually from a variety of peroxides with oxidizable fluorescers.

The last four sections are related to luminescence in biological systems. The first chapter of this unit is a useful introductory one by Osamu Shimomura entitled "Mechanism of Bioluminescence". This is followed by one relating to the formation of electronically excited intermediates in dark biological sequences, a second on biochemical oxygenation reactions and chemiluminescence, and finally one on the evidence of singlet oxygen involvement in biochemical systems. It is very clear in biological processes, especially where oxygenation is involved (i.e., prostaglandin endoperoxides), that excited state intermediates are of critical importance. However, their very nature makes isolation and characterization a monumental problem.

This book provides a very useful multidisciplinary approach to the important area of excited states and their formation by chemical and biological processes. Photochemists, physical chemists, biochemists, and organic chemists with interests in transient intermediates and luminescence will find this monograph of significant importance.

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Evaluation of Analytical Methods in Biological Systems. Part A. Analysis of Biogenic Amines. Edited by Glen B. Baker and Ronald T. Coutts. Elsevier, Amsterdam and New York. 1982. xvi + 308 pp. 25 × 17 cm. ISBN 0-444-42110-6. $76.75.

Our increasing understanding of the functional neurochemistry of the brain and the mode of action of various psychotropic drugs has in the last 15–20 years become very dependent on recent advances in analytical chemistry. Virtually all of the most important methods for analyzing biogenic amines are covered in this book.

The various amines and their possible neurochemical functions are covered in chapter 1. This is followed by an interesting section on bioassay, which is, of course, less important now than in the past. Recent advances in TLC are presented in chapter 3. Fluorescence techniques which have been the mainstay of catecholamine determinations for so long are covered in the next section. Histochemical methodology, first introduced by the Swedes, is the following topic. This method of studying CNS drug action has declined in importance in recent years.

The editors themselves then provide a very useful chapter on GLC which covers detectors, columns, and derivatives, and it also has a comparative section on the advantages and disadvantages of this technique. Chapter 7 by Davis and Durden deals with the quantitative MS of biogenic amines. The basic philosophy here is that "smaller is more accurate", and the authors win the prize for having the most cumbersome abbreviation for their technique, i.e., HRTLC-HCMS-SIM!

An interesting chapter on GC–MS follows where much attention is given to practical considerations. A very popular and sensitive method of catecholamine analysis which has replaced fluorescence methodology to some extent is covered by Martin in the section on [^{3}H]methyl transfer radioenzymatic procedures. One of the most important techniques that has found increasing application in this area is that of HPLC, which is discussed in chapter 10. In addition to UV detection, the method most often used is that based on electrochemical oxidation of susceptible compounds. This is the subject of chapters 10 and 11. Radioreceptor binding assays have been very helpful in increasing our understanding of psychotropic drug action at the receptor level. In addition, they can in certain instances be used for the analysis of biogenic amines and drugs. However, their specificity is in some cases possibly questionable. The final chapter covers the radioimmunoassay (RIA) method. Like some other methods its main advantage is that of high sample throughput. A disadvantage is crossreactivity.

This is a very good book which provides up-to-date information which will be of value both to research students and other newcomers to the field, as well as to seasoned investigators.

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Advances in Experimental Medicine and Biology. Volumes 136A and 136B. Biological Reactive Intermediates-II, Chemical Mechanisms and Biological Effects. Parts A and B. Edited by R. Snyder, D. V. Parke, J. J. Kocsis, D. J. Jollow, C. G. Gibson, and C. M. Witmer. Plenum Press, New York and London. 1982. xx + 1476 pp. 17 × 25.5 cm. ISBN 0-306-40802-3. $125.00.

These volumes are the proceedings of the Second International Symposium of Biological Reactive Intermediates held at the University of Surrey, Guildford, Surrey, UK, July 14–17, 1980. The purpose of the meeting as stated by the editors was to provide a proper forum for the exchange of ideas between chemists and biologists from many fields and disciplines in order to more thoroughly understand complex toxicological and oncological events. Indeed they have recognized that toxicology, by its very nature, is a multidisciplinary science.

The papers are divided into ten titled sections each with a summary of the discussion that followed the presentation plus three sections described as "Short Communications". The titled sections are as follows: "Formation and Disposition of Biological Reactive Intermediates", "Oxygen Activation in Xenobiotic Metabolism", "Reactive Intermediates of Monocyclic Aromatic Hydrocarbons", "Reactive Intermediates of Polycyclic Aromatic Hydrocarbons", "Reactive Intermediates of Haloalkanes", "Reactive Intermediates of Haloalkenes", "Reactive Intermediates of Aflatoxins and Furans", "Reactive Intermediates of Aromatic Amides", "Reactive Intermediates of Other Nitrogenous and Sulphur Compounds", and "Reactive Intermediates and Cellular Events: Role in Human Disease". The "Short Communications" are a rather diverse collection of papers, some of which could have been incorporated into an appropriate main section. There is a list of participants and a 31-page index, which is quite adequate.

The two-book volume reports on work since the previous symposium, which took place in Finland in 1975, in the interdisciplinary fields concerned with the metabolic products of xenobiotic chemicals and their toxic and carcinogenic effects. As is generally the case with any volume that records the presentations of a symposium, the papers are of varying quality. Due to the almost 2-year delay in publication, many of the papers presented have now appeared as full publications. The only advantage for purchasing these volumes would be that of having in one place a collection of papers dealing with reactive intermediate toxicology.

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Chemistry and Pharmacology of Drugs. Volume 1. Central Analgetics. Edited by Daniel Lednicer. Wiley, New York, Chichester, Brisbane, Toronto, and Singapore. 1982. xv + 219 pp. 16 × 23.4 cm. ISBN 0-471-08314-3. $47.50.

This volume is the first of a series of monographs entitled *Chemistry and Pharmacology of Drugs*, of which Lednicer is to be the series editor. It seems fitting that for this initial volume he would be both an editor and a contributor in the form of the last chapter, "Medicinal Chemistry of Central Analgetics". There are four chapters in this book: the first is called "Pain Pathways: Potential Sites for Analgetic Action", by J. Scott Mohrland of the Upjohn Co.; the second deals with "Pharmacological Alteration of Pain: The Discovery and Evaluation of Analgetics in Animals", by Philip F. Von Voightlander, also of the Upjohn Co.; the third is entitled "The Potential of Centrally Acting Regulatory Peptides as Analgetics", by John S. Morley of Imperial Chemical Industries, Ltd.

Over the past 20 years, research in opioids received two important stimuli which reawakened interest in this field. The first was the development of agonist–antagonists as clinically useful analgesics with reduced addictive potential, and the second was the discovery of the endogenous opioid peptides in 1974. It seems that now is an appropriate time for review of the field for nonspecialists who are not able to follow the rapid developments that are taking place. In some respects, this present volume has succeeded, but in others, it is disappointing.

One of the major advances in our understanding of the properties of opioids was the introduction of the concept of multiple

opioid receptors by Martin in his seminal review which appeared in 1967. He postulated the existence of three types of receptors: μ, κ, and σ, and later Kosterlitz proposed the δ receptor on the basis of the interaction of opioids and opioid peptides in the mouse vas deferens preparation. Since that time, others have been proposed, yet very little space is devoted to a discussion of these important concepts by any of the authors. On occasion they do acknowledge these receptors, but the reader is not informed about the reasons these ideas were invoked and what properties distinguishes one opiate from another. In this connection it is unfortunate that there is no discussion of Portoghese's site-directed alkylating agents, CNA and FNA, which are key tools in characterizing opioid receptors.

Perhaps it is this reviewer's bias that inadequate attention was paid to mixed agonist–antagonists. Research in this area led to the clinical introduction of several new drug entities: pentazocine, nalbuphine, butorphanol, and buprenorphine. Von Voightlander's statement that "The pharmacological discovery of agonist–antagonists has relied on the identification of their weak analgesic activity and their ability to antagonize the effects of morphine agonists in a number of tests" is truly puzzling. The analgesic activity of pentazocine, the first of the marketed agonist–antagonists, was demonstrated first in man and not animals. By and large, these drugs are used clinically to control moderate to severe pain. The pharmacological profiles of this classs of drugs is so different from those of the morphine type that Martin was led to postulate a multiple receptor hypothesis to account for their diverse activities.

Lednicer's discussions of the biological activity emphasizes SAR studies on antinociceptive potency. If there is one lesson to be learned from studies on analgesics, it is that potency per se is of little importance in the search for an ideal analgesic. This concern for potency on the part of the author resulted in the omission of some very important uses of opioids. For example, there is no mention of the methadone maintenance program nor of the use of antagonists for preventing recidivism in postheroin addicts. The long discussion of Von Voightlander on methods for predicting abuse liability in animals would have been far more valuable if he included a discussion of how abuse liability is measured in man. His chapter would be easier to read if it followed those of Morley and Lednicer because he refers to many drugs which are unfamiliar to the reader and are discussed later. Mohrland's chapter is a minicourse in neuroanatomy and neurophysiology of pain pathways. Sometimes he forgets the audience he is addressing and lapses into the jargon of the specialist without previously defining the terms employed. Clearer diagrams would have been helpful to the casual reader.

Despite these and other shortcomings, the book does have its redeeming features. Lednicer does an excellent job of covering the chemistry of many classes of analgesics in a small space. Morley's discussion is now a bit out of date owing to some recent exciting developments but is a very helpful introduction to this field. Mohrland and Von Voightlander point out the various neurophysiological targets that can be used in new drug development programs in analgesics, and for this reason it can be recommended to the medicinal chemists who are working in the field.

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Progress in Research and Clinical Applications of Corticosteroids. Edited by Henry J. Lee and Thomas J. Fitzgerald. Heyden & Son Ltd., London. 1982. x + 302 pp. 16 × 24 cm. ISBN 0-85501-722-8. $52.95.

This book represents a collection of 18 papers presented at the Sixth Annual Clinical Symposium held in Tallahassee, FL, on February 20–22, 1981. The book includes papers on receptors (4); synthesis, metabolism, and structure–activity correlations (7); and clinical applications (7), as well as four question and answer sessions. The purpose of the symposium as stated in the preface was "to bring together many experts on corticosteroids so that the current status of theoretical and practical knowledge could be shared". Surprisingly, only one participant from a pharmaceutical company was either invited or chose to contribute to the book. As to be expected, references run through 1980. Unfortunately, the references are frequently printed without either numbers or spacing between them. In view of the scarcity of recent books on steroids, the diversity of topics covered in this book provides a useful source of information and references for each of the topics presented.

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Anthracycline Antibiotics. Edited by Hassan S. El Khadem. Academic Press, New York. 1982. xii + 285 pp. 15.5 × 23.5 cm. ISBN 0-12-238040-1. $25.00.

The clinical importance of doxorubicin as a wide-spectrum antitumor antibiotic has generated much research on the chemistry and biology of anthracycline antibiotics, in search of analogues with improved therapeutic index, wider spectrum of activity, and more favorable side-effects profiles. Written by experts from around the world, the book contains 10 chapters, each representing one of the major papers presented at the symposium on anthracyclines, sponsored by the Carbohydrate and Medicinal Chemistry Divisions of the Americal Chemical Society, that was held in New York in August, 1981.

The first chapter is, in the opinion of this reviewer, a key feature of this book. Benton Naff, Plowman, and Narayanan have undertaken the formidable task of summarizing most of the screening data on anthracyclines obtained at the National Cancer Institute over the years. They have organized the material according to structural types and within each type according to the nature of the chemical modification (i.e., side-chain modification, *N*-alkyl, *N*-acyl derivatives, etc.). For ease of comparison, they have also added to the more classical OD and T/C data an index of activity A/P (analogue to parent ratio of activity); each table is completed by a short discussion, and in the brief summary at the end of the chapter, the authors' comment on the key structure features with regard to antitumor activity. Such a formidable task has, however, some drawback: both the format chosen by authors, especially in tabulating structural information, and pagination make the chapter hard to read. Furthermore, data for any given compound are not easily retrievable, because of the lack of an index showing the content of the tables. It is, on the other hand, hard to envision a different and more effective way to present all the data reported.

The remaining nine chapters consist mainly of research data from the laboratories of the chapter's author(s), thus representing a collection of updates and indications of current and future trends from many of the leading laboratories working on the chemistry and microbiology of anthracyclines, both in academia and industry. Most contributors have placed special emphasis on structure–activity relationships, presenting and discussing in detail the biological data of the analogues reported.

The prompt publications and the commendable effort of all the contributors to include data not presented at the session and updated subjects and references make this book an excellent up-to-date review of anthracycline antibiotics.

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NATO Advanced Study Institutes Series. Series A. Life Sciences. Volume 42. Nitroimidazoles. Chemistry, Pharmacology, and Clinical Application. Edited by A. Breccia, B. Cavalleri, and G. E. Adams. Plenum Press, New York. 1982. xii + 211 pp. 17 × 25.5 cm. ISBN 0-306-40916-X. $35.00.

This volume contains 15 lectures presented at the International Conference on Nitroimidazoles: Chemistry, Pharmacology and Clinical Application held in Cesenatico, Italy, Aug, 1980. The conference was the first part of the NATO Advanced Study Institute on Radiosensitizers of Hypoxic Cells. The research on nitroheterocyclic compounds, including the nitroimidazoles, was first stimulated by the discovery of the antibacterial properties of nitrofuran. The nitroimidazole group of drugs is extensively

used for the chemotherapy of anaerobic bacterial and protozoal diseases and also for the radiosensitization of hypoxic tumors. The editors of this volume have gathered contributions from diverse fields of research on this very special drug group in order to broaden the understanding of the chemistry, pharmacology, and clinical applications of nitroimidazoles. The material presented in this volume covers areas on the pharmacology and toxicology of 5-nitroimidazoles, as well as on their synthetic methods, chemical properties, and reaction mechanisms. Also included are lectures on the use of this class of compounds as cytotoxic and antiparasitic agents, with a special focus on their applicability in cancer chemotherapy. Attention has also been paid to metabolism and pharmacokinetics. Among the most interesting compounds introduced onto the market or into clinical evaluation are the 5-nitroimidazoles dimetridazole, metronidazole, ronidazole, tinidazole, ornidazole, ipronidazole, and nimorazole, as well as the 2-nitroimidazoles benznidazole and misonidazole.

This volume is very acceptable technically with very few typographical errors. The cited references are thorough through the first half of 1980. The multidisciplinary character of this book makes it of value to researchers involved in the pharmacology, clinical pharmacology, pharmaceutics, toxicology, and the developments of drugs in the field of oncology.

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Microbial Transformations of Bioactive Compounds. Volumes I and II. Edited by John P. Rosazza. CRC Press, Boca Raton, FL. 1982. Volume I: vii + 133 pp. 18 × 26 cm. ISBN 0-8493-6065-X. $46.00. Volume II: vii + 185 pp. 18 × 26 cm. ISBN 0-8493-6066-8. $64.00.

In the preface to "Microbial Transformations of Bioactive Compounds", John P. Rosazza indicates this book in two volumes "is intended to provide a comprehensive and well-referenced look at the microbial transformation field as it exists today and to illustrate some of the current and future directions possible with it." Generally speaking, I am inclined to agree with his statement.

Volumes I and II covers a wide range of topics, with each volume organized into five chapters written by highly respected scientists with expert knowledge in special fields of microbial transformations. All of the topics are well researched and provided with current references. The authors have presented the information clearly and concisely and with illustrations and tabular summaries that are of good quality.

Volume I begins with a well-written chapter in a historical perspective of microbial transformations. Chapter 2 deals with biotransformation methods. The sections on microbiological equipment necessary for biotransformation research and microorganisms for a beginning culture collection should prove especially useful as a starting point for scientists interested in initiating a microbial transformation research program. Chapters 3–5 are comprehensively written and provide a general overview of the microbial transformation of antibiotics, prostaglandins, and aliphatic, alicyclic, and aromatic hydrocarbons.

Chapter 1 of Volume II covers the importance of microbial transformations as a useful tool in the preparation of mammalian drug metabolites. In addition, discussion of the biochemical basis for microorganisms as models for mammalian drug metabolism is provided.

Chapter 2 presents a very interesting discussion of the metabolic capability of intestinal microflora to transform xenobiotics. The pharmacological and toxicological significance of these reactions and the role of intestinal microflora in colon carcinogenesis are authoritatively written. Chapters 3–5 effectively cover the microbial transformation of alkaloids, cannabinoids, and pesticides.

The wide range of information provided should make these books a valuable adjunct to the libraries of those engaged in microbial transformation research. I recommend these books highly as an excellent resource to any scientist interested in the microbial transformation of xenobiotics.

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Derivatives of Hydrazine and Other Hydronitrogens Having N–N Bonds. By Peter A. S. Smith. The Benjamin/Cummings Publishing Co., Reading, MA. 1983. xii + 335 pp. 17 × 24 cm. ISBN 0-8053-8902-4. $49.95.

The book is the first part of a revision of the author's "The Chemistry of Open-Chain Organic Nitrogen Compounds" first published in 2 volumes in 1965–1966. Subsequent volumes to be published within 3 years will describe derivatives of ammonia and compounds having N–O bonds. The author warns that the content is not encyclopedic; some references are to early 1982, but there are probably gaping holes, and coverage of the most recent years is at best spotty. The caveat is warranted, but the omissions do not detract seriously from the value of the book.

Specific classes include (number of pages, number of references): hydrazines (42, 282); hydrazones (36, 237); hydrazides and related compounds (61, 353); diazonium and azo compounds (69, 583); aliphatic diazo compounds, azamines, and nitrile imides (50, 337); azides (38, 212); and other functions with chains of three or more nitrogen atoms (19, 112). A subject index is included.

The author claims to put emphasis on phenomenology rather than on theory, but there are good discussions of mechanism in most cases. In general, discussions are limited to the simpler compounds rather than the complex. Nomenclature, spectroscopy, photochemistry, and analytical chemistry are given more emphasis than in the earlier edition. For each class there is a good critical discussion of nomenclature, followed by class properties, reactions, preparative methods, and analytical methods.

There is little or no discussion of uses of the compounds. For example, the use of hydrazines as jet fuels is not mentioned nor is the pharmacology of compounds of interest to medicinal chemists. Olin, Inc., currently sells 21 million pounds of hydrazine each year and has available a data bank containing 20 000 references. These matters are not mentioned by the author.

From 1910 to World War II, Neil Sidgwick's "Organic Chemistry of Nitrogen" covered its subject in just 600 pages. It was the only book of its kind. Those of us who have an affection for the subject are grateful to Peter Smith for his continuing efforts to supply us with well-organized and up-to-date information. In his youth your reviewer was torn from research in diazo chemistry in much the same manner as Citizen Kane was separated from his sled *Rosebud*. He is therefore particularly grateful for Smith's chapter on aromatic diazo chemistry whose 583 references are the key to a complete up-to-date coverage of the subject.

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Contemporary Heterocyclic Chemistry. By George R. Newkome and William W. Paudler. Wiley, New York. 1982. x + 422 pp. 16.5 × 24 cm. ISBN 0471-06279-0. $39.50.

One of the most challenging tasks for authors in chemistry is to produce an understandable, well-referenced book on heterocyclic chemistry within a limited number of pages. Many people have attempted this project, but few have succeeded as well as Professors Newkome and Paudler. Using π-excessive (for example, pyrrole) and π-deficient ring systems (for example, pyridine) as their classification mechanism (which is well-defined), the authors first discuss the synthesis and reactions (electrophilic, nucleophilic, free radical, cycloaddition) of the π-excessive rings and their reduced analogues and then, similarly, present the π-deficient six-membered ring systems. Also included are discussions on mixed heteroaromatic compounds, mesoionic compounds, and three-, four-, and seven-membered and larger heterocyclic ring systems. However, it should be emphasized that the book is not just limited to cataloguing syntheses and reactions but, where necessary, appropriate elaborations are given (for example, by using a HOMO–LUMO interpretation of the regioisomeric dis-

tribution of products that results in the cycloaddition reactions to form pyrazoles from diazo compounds and alkynes).

The book is certainly as contemporary as its title states. This is evidenced by the authors inclusion of, for example, (i) metal-assisted heterocyclic syntheses that involve organometallic reagents, (ii) phosphorus, arsenic, antimony, and bismuth heterocycles, (iii) heterocyclic rings of eight and nine atoms, (iv) mesoionic compounds (which are well-defined), and (v) the ANRORC process. Two separate, well-placed chapters on naturally occurring and pharmaceutically important π-excessive and π-deficient heteroaromatic compounds contain carefully chosen, prominent examples that offer a broad spectrum of heterocyclic synthetic methods. Chapters of this type are much more meaningful, if correctly placed in the chapter sequence, than having natural product/pharmaceutical examples spread throughout the book in chapters that deal with specific ring systems. The book is further enhanced by the appendixes, which present, in tabular form, spectral (^1H, ^{13}C, and ^{15}N NMR, UV, mass) data, pK_a values, atomic electron populations, and molecular dimensions for various simple ring systems.

The book contains many accurately drawn structural formulas. This is an essential feature for a book where many readers will encounter heterocyclic molecules for the first time and must have the heteroatoms and bonds correctly placed after synthetic transformations, rearrangements, tautomerisms, etc. in order to appreciate the subject matter. The book also contains very few typographical errors.

If any flaw exists in the book, it is the brief attention devoted to nomenclature, which, more often than not, is what unnecessarily frightens many newcomers to the discipline. However, this reviewer admits this is a problem not easily overcome in a book of this size, but in future editions it is hoped that more attention can be devoted to nomenclature.

Speaking of future editions, the chemical profession would be well-served if Professors Newkome and Paudler would continue this project by presenting more of the "contemporary" developments in heterocyclic chemistry as they have done so frequently here. In the meantime, the present book is a much needed addition to the fundamental literature on heterocyclic chemistry and, considering its reasonable price, should be on the shelves of all research-oriented chemists who must deal with heterocyclic molecules.

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Books of Interest

Progress in Pesticide Biochemistry. Volume 2. Edited by D. H. Hutson and T. R. Roberts. Wiley, New York. 1982. x + 226 pp. 15.5 × 23.5 cm. ISBN 0471-10118-4. $52.00.

Behavioral Models and the Analysis of Drug Action. Proceedings of the 27th OHOLO Conference, Israel, March 28–31, 1982. Edited by Michael Y. Spiegelstein and Aharon Levy. Elsevier Scientific, Amsterdam and New York. 1982. xvii + 498 pp. 17 × 25 cm. ISBN 0-444-42125-4. $139.50.

Annual Reports in Organic Synthesis. 1981. Edited by L. G. Wade, Jr., and M. J. O'Donnell. Academic Press, New York. 1982. xiii + 498 pp. 15 × 23.5 cm. ISBN 0-12-040812-0. $26.00.