Book Reviews

ACS Symposium Series. Number 201. Calcium Regulation by Calcium Antagonists. Edited by Ralf G. Rahwan and Donald T. Witiak. American Chemical Society, Washington, DC. 1982. x + 207 pp. 15.5 × 23.5 cm. ISBN 0-8412-0744-5. $29.95 (U.S. and Canada), $35.95 (Export).

Calcium antagonist drugs are currently making a dramatic impact on cardiovascular therapeutics in the U.S. after several years of usage in Europe and elsewhere. Because of the ubiquitous regulatory role of Ca^{2+}, they are expected to be extensively utilized in the treatment of a wide range of diseases in addition to their use as research tools. This volume of the *ACS Symposium Series* is a recent addition to a number of books that review the actions of this heterogeneous group of agents. The original symposium took place in August 1981, and while the intervening 2 years have seen some advances, most notably in radioligand binding studies, each of the 11 chapters provides a reasonably current and well-documented account of the field.

Ca^{2+} antagonist drugs discussed in the 11 chapters include Ca^{2+} channel blocking agents (the major source of attention), calmodulin-specific antagonists, and the novel class of intracellular Ca^{2+} antagonists, the methylenedioxyindenes. Speculative hypotheses are also presented to include opiates and possibly antiepileptic drugs as Ca^{2+} antagonists, based on the involvement of Ca^{2+} in their modes of action. It should be pointed out that while it is of interest to note the role of Ca^{2+} in the regulation of neuronal excitability by the latter drugs, it does nomenclature a disservice to apply the term "Ca^{2+} antagonist" indiscriminately. While the majority of chapters do address themselves to "calcium antagonist" drugs, others deal more broadly with the role of calcium ions in smooth muscle contraction, platelet aggregation, and secretory events. The result is a somewhat uncomfortable mix of pharmacology, physiology, and medicinal chemistry. Readers may find that the trade-off in favor of breadth leaves this book poorly focused.

That is not to say that individual chapters are substandard. The book opens with a worthwhile effort by W. G. Nayler to subclassify Ca^{2+} channel blockers on the basis of their distinctive cardiovascular effects. This will clearly be a major thrust of future work with these compounds. Medicinal chemists will likely find greatest interest in D. J. Triggle's chapter focusing on structure–activity relationships of the dihydropyridines. W. W. Muir provides an excellent review of the influence of Ca^{2+} channel blockers on cardiovascular functions, and the editor's own chapter on the methylenedioxyindenes is also noteworthy. While other chapters do provide useful information on the topics mentioned above, they really do not sustain a focus of interest and are not well integrated with the intent of the volume as expressed by its title.

In summary, this edition of the *ACS Symposium Series* provides a collection of worthwhile papers that deal with Ca^{2+} and agents that interfere with its actions. It is recommended to those with similar interests.

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Ciba Symposium. Number 90. Receptors, Antibodies and Disease. Edited by David Evered and Julie Whelan. Pitman, London. 1982. viii + 312 pp. 15.5 × 23.5 cm. ISBN 0-272-79654-9. $35.00.

This volume consists of the papers and discussion at a symposium held in October, 1981. As the title indicates, the symposium covers a wide range of topics; consequently, I doubt that few readers will approach the book as a sum of its parts and read it cover to cover in a few sittings. The format of the book (papers plus discussion) indicates that the intention of the volume was to make the symposium accessable to those unable to attend the symposium. Because the papers are by experts in the field and are directed toward the other experts sitting around the table, the text and discussion lean toward the finer points of current thinking. For example, Rodbell's paper and the associated discussion is less instructive than his review paper in *Nature* of several years ago. The other topics discussed are the immune system and receptors for insulin, thyrotropin, acetylcholine, prolactin and β-adrenergic agonists. In each case, the reviews gave a quick overview of the approaches that are currently being used. I suspect that this book is not for every investigator's bookshelf, rather it is for the library (where it may be in heavy use for the next few years).

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Transport in Biomembranes. Edited by Renzo Antolini, Alessandra Gliozzi, and Alfredo Gorio. Raven Press, New York. 1982. xiv + 272 pp. 16.5 × 24.0 cm. ISBN 0-89004-868-1. $32.00.

This book collects the 24 papers presented at the Second Course of the School on "Fundamental Aspects of Membrane Phenomena", coordinated by the Italian Group of Membrane Science and Technology. They are grouped together under four main areas: "Membrane Model Systems", "Ionic Pores and Their Reconstitution in Planar Bilayers", "Transport Functions in Natural and Reconstituted Membranes", and "Pharmacological Application of Liposomes".

The first section includes chapters on "Kinetic Properties of Ion Carriers, Channels and Pumps" (by P. Lauger), "Polymeric Monolayers and Liposomes as Models for Biomembranes and Cells" (by K. Dorn and H. Ringsdorf), "The Liquid Crystalline Structure: An Embryo Stage Towards Biological Organization" (by Donatella Senatra), "Membrane Models of Archaebacteria" (by Alessandra Gliozzi, Ranieri Rolandi, Mario De Rosa, Agata Gambacorta, and Barbara Nicolaus), "Glycosphingolipids in Cell Surface: Modification of Lipid Bilayers Transport Properties" (by F. Gambale, M. Robello, C. Usai, and C. Marchetti), and "Photoeffects in Pigmented Bilayer Lipid Membranes (BLM and LMV)" (by H. Ti Tien).

The second section includes chapters on "Concepts and Techniques for Membrane Transport Reconstitution" (by H. Schindler), "Membrane Reconstitution Below Lipid Phase Transition Temperature" (by G. Boheim, W. Hanke, C. Methfessel, H. Eibl, U. B. Kaupp, A. Maelicke, and J. E. Schultz), "Feeling Around Inside a Channel in the Dark" (by Christopher Miller), "Hemocyanin Induced Excitability in Planar Lipid Membranes" (G. Menestrina, D. Maniacco, F. Pasquali, and R. Antolini), "Porins from Gram-Negative Bacteria in Lipid Bilayer Membranes" (by Roland Benz, Robert E. W. Hancock, and Taiji Nakae), and "Alamethicin Pore Formation in Planar Bilayers Above and Below Lipid Phase Transition Temperature" (by G. Boheim, W. Hanke, S. Uberschar, and H. Eibl).

The third section includes chapters on "Lipid–Protein Interaction: A Hydrophobic Photolabelling Study" (by Cesare Montecucco and Roberto Bisson), "The Small-Intestinal Na^+–D-Glucose Cotransporter: A Likely Model" (by G. Semenza), "Reconstitution of the Sodium–Potassium Pump (Na,K-ATPase)" (by Beatrice M. Anner), "Partial Purification and Reconstitution of the Na^+–D-Glucose Cotransport System from Renal Brush Border Membranes" (by H. Koepsell and H. Menuhr),

"Reconstitution of $\Delta\mu H^+$ Generators of the Mitochondrial Membrane" (by S. Papa, F. Guerrieri, M. Lorusso, and D. Boffoli), "Mechanism of Electron Flux and Proton Translocation in the bc_1 Complex of the Respiratory Chain" (by Giorgio Lenaz, Giovanna Parenti-Castelli, and Mauro Degli Esposti), "Reconstitution of a Light-Driven Proton Pump: ΔpH Determination in Bacteriorhodopsin/Phospholipid Vesicles" (by Rita Casadio), "Ionophore Mediated Ion Transfer in a Biological Membrane: A Study by Electrophotoluminescence" (by Daniel L. Farkas, Rafi Korenstein, and Shmuel Malkin), and "Kinetic Approach to the Transport of Branched-Chain Ketoacids Through Biomembranes" (by Katarzyna A. Nalecz and Anna B. Wojtczak).

The fourth includes chapters on "Principles of Phospholipid Pharmacology" (by A. Bruni and G. Toffano), "Liposomes Containing Doxorubicin: An Example of Drug Targeting" (by P. Rosa and F. Clementi), and "Pharmacokinetics and Pharmacodynamics of Phosphatidylserine Liposomes in Mice" (by S. Mazzari, A. Sanotti, P. Orlando, R. Raciti, and G. Toffano).

The presentations generally provide good summaries of the current state-of-the-art with literature citations through 1981. Contribution of up-to-date basic research with potential applications is an attractive feature of this volume. An added bonus is the good overview of the impressive progress the Italian membrane scientists have recently made. The book should be in the library of all chemists, physiologists, biochemists, and pharmacologists who are fascinated by the interdisciplinary opportunities biomembranes and their models offer.

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Membranes and Transport. Volumes 1 and 2. Edited by Anthony N. Martonosi. Plenum Press, New York. 1982. Volume 1: xxxiv + 688 pp. 17.5 × 26 cm. ISBN 0-306-40853-9. $75.00. Volume 2: xxxiii + 679 pp. 17.5 × 26 cm. ISBN 0-306-40854-6. $75.00.

The need for a comprehensive and critical overview of membranes has been acutely felt by scientists and their proselytes. Previous attempts have been made to produce various compilations, but none of these has been so successful as these volumes. Anthony N. Martonosi is to be congratulated for assembling 151 internationally recognized experts to produce 182 brief essays in different areas of membrane science. The coverage is extremely broad. It ranges from biophysical investigations of artificial membranes through cell recognition to transport processes in plants. Individual contributions are organized in the following chapters: I, "Molecular Architecture of Biological Membranes"; II, "Physical Properties of Biological and Artificial Membranes"; III, "Biosynthesis of Cell Membranes: Selected Membrane-Bound Metabolic Systems"; IV, "The Structure, Composition, and Biosynthesis of Membranes in Microorganisms"; V, "Bioenergetics of Electron and Proton Transport in Mitochondria"; VI, "Energy-Transducing ATPase and Electron Transport in Microorganisms"; VII, "Ion Transport Systems in Animal Cells"; VIII, "The Transport of Metabolites and Ions in Microorganisms"; IX, "Membrane-Linked Metabolite and Ion Transport Systems in Animal Cells"; X, "Channels, Pores, Intercellular Communication"; XI, "Excitable Membranes"; XII, "The Structure and Permeability of Blood Cell Membranes"; XIII, "Properties of Cell Surfaces. Recognition and Interaction of Cells"; XIV, "The Control of Cell Surfaces. Growth Regulation, Hormones, Hormone Receptors and Transformation"; XV, "Membrane-Linked Metabolic and Transport Processes in Plants".

There is a surprising uniformity of the contributions. All essays provide sufficient background. They succinctly emphasize crucial issues, bring the reader to the current frontiers, and often discuss future potentials. There is a sufficient citation of the literature, generally through 1981. Taken individually, these essays provide quick references and entries to new areas. Taken together, these volumes represent a unique and comprehensive compilation of the highly exciting and significant accomplishments of membrane science. It is strongly recommended for teachers and researchers.

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Neuroreceptors. Edited by F. Hucho. Walter de Gruyter, Berlin. 1982. xiv + 367 pp. 17.5 × 24.5 cm. ISBN 3-11-008855-X. $75.00.

The study of neurotransmission at the receptor level is a rapidly expanding body of knowledge embracing a variety of techniques and involving some of todays most talented investigators in biology and medicine. This volume is a collection of the reviews and original experimental results of primarily German workers that were presented at a meeting in Berlin during September 29–30, 1981.

Containing 28 chapters grouped into 7 sections based mainly on receptor type, heavy emphasis of the volume is placed on the nicotinic cholinergic receptor because of its relatively advanced technical level of investigation. Equally interesting and well presented is recent work on the benzodiazepine receptor, the putative THC receptor, and the photoaffinity labeling of the glycine receptor with [^{3}H]strychnine. Throughout the book, the pivotal role that radioisotopes (especially ^{3}H and ^{125}I) have played and will continue to play in neuroreceptor investigation is apparent. By and large, the chapters are technically well written and illustrated and contain sufficient references to the original literature. A useful author and subject index is included.

Having first seen this volume at a FASEB meeting last spring in New Orleans, I was very impressed with its rapid publication. However, in a quickly advancing field, such publication speed is still no assurance of producing a completely up-to-date work. For instance, the comment in Chapter 1 that "benzodiazepines do not interact with any of the already known neurotransmitters or neuromodulator receptors in the central nervous system" aside from the benzodiazepine receptor itself seems now outdated in view of the recently reported affinity that the benzodiazepine tifluadom has for the κ opiate receptor [Romer, D. *Nature (London)* **1982**, *298*, 759].

Well written and organized, this book is recommended for those involved in neuroreceptor research, especially in the cholinergic area.

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Advances in Biochemical Psychopharmacology. Volume 35. The Benzamides. Pharmacology, Neurobiology, and Clinical Aspects. Edited by M. Stanley and J. Rotrosen. Raven Press, New York. 1982. xii + 209 pp. 18.5 × 26 cm. ISBN 0-89004-639-5. $31.00.

This volume is one of the *Advances in Biochemical Psychopharmacology* series edited by E. Costa and P. Greengard. An excellent overall review of many aspects of the benzamide family of antipsychotic agents is provided in 11 chapters: (1) "The Neurobiologically Active Benzamides and Related Compounds: Some Historical Aspects", by B. M. Angrist; (2) "Behavioral Pharmacology of the Benzamides as Compared to Standard Neuroleptics", by P. Worms; (3) "The Activity of Substituted Benzamides in Biochemical Models of Dopamine Receptors", by J. W. Kebabian, K. Tsuruta, T. E. Cote, and C. W. Grewe; (4) "A Comparison of the Effect of Substituted Benzamides in Radioreceptor Binding Assays with Their Effects on Brain Dopaminergic System in vivo", by C. W. Lin and S. Wilk; (5) "Effect of Benzamide Drugs on Prolactin Secretion: Relation to the Dopamine Receptor", by H. Y. Meltzer, R. So, and V. S. Fang; (6) "The Benzamides: Evidence for Action at Dopamine Receptors—Shortcomings of Current Models", by D. E. Wazer, J. Rotrosen, and M. Stanley; (7) "Differential Antagonism of Postsynaptic (DA_1) and Presynaptic (DA_2) Peripheral Dopamine Receptors by Substituted Benzamides", by J. D. Kohli, D. Glock, and L. I. Goldberg; (8) "Specific Receptors for Substituted Benzamide Drugs in Brain", by P. Jenner, A. Theodorou, and C. D. Marsden; (9) "Pharmacokinetics and Metabolism of the Benzamides", by D. N. Bateman; (10) "Clinical Trials of Benzamides in Psychiatry", by S. D. Peselow and M. Stanley; and (11) "The Substituted Benzamides in Gastroenterology", by T. V. Nowak and K. Schulze-Delrieu. A forward and optimistic prospectus for the benzamide class of drugs is provided by S. Gershon.

This book considers the benzamides from the standpoint of selectivity as compared to classical neuroleptic agents. Differences in receptorology, biochemistry, behavioral correlates, metabolism, and clinical attributes for the important members of the series (i.e., sulpiride and metoclopramide) are discussed in-depth. Unlike the typical antipsychotics, the benzamides do not interact with dopamine-sensitive adenylate cyclase, are not significantly metabolized, have low bioavailability, and have high renal clearance; otherwise, few differences in receptor selectivity and end biological profile were detected.

The first chapter should be a delight for any medicinal chemist or pharmacologist interested in the historical aspects of drug development. It tells the story well and provides several take-home messages for the medicinal scientist.

Overall, the book is well-organized, and the chapters are authored by leading experts in the field. The text is adequately referenced. The cited references are timely and provide a valuable extension to the discusssion. The book is technically quite good with few typographical errors noted within the text; however, this reviewer believes that most medicinal chemists will be somewhat distressed by the frequent mistakes seen in chemical names and structural formulas. For example, the structures of sulpiride and sultopride found in the structure table in Chapter 3 are incorrect.

This reviewer believes that this book represents a useful guide for any medicinal scientist working specifically in the benzamide area or more generally in the dopamine antagonist–antipsychotic area. The cost of the book is reasonable in light of the wealth of information provided.

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Advances in the Biosciences. Volume 37. Advances in Dopamine Research. Edited by M. Kohsaka, T. Shohmori, Y. Tsukada, and G. N. Woodruff. Pergamon Press, Oxford. 1982. x + 428 pp. 17.5 × 25.5 cm. ISBN 0-08-0273912. $70.00.

This volume is based on the proceedings of a dopamine satellite symposium to the 8th International Congress of Pharmacology held in Okayama, Japan, July 1981. As the general title of this book indicates, the content of the 42 articles covers a wide range of dopamine research in the CNS, medicinal chemistry, neurochemistry, electrophysiology, neuroanatomy, and pharmacology related to dopamine. There are also some articles dealing with dopamine in the periphery. The book contains some reviews updating the research in various fields. Dopamine "receptology" is treated excellently by Woodruff ("Dopamine Receptors"), Langer ("Pre- and Post-synaptic DA Receptors"), Goldberg ("Peripheral DA Receptors"), and Seeman ("Multiple DA Receptors"). A review by Laduron criticizes the concept of multiple DA receptors and puts emphasis on different postsynaptic localization. Also a critical article appears about the autoreceptor hypothesis for neuronal feedback control of DA synthesis. According to Raiteri, a more likely explanation seems to be that the reuptake mechanism is involved in the feedback regulation. A neuroanatomical review on central DA pathways is presented by Lindvall and Björklund, and a new method for brain dialysis is described by Ungerstedt. Several papers are in the category of progress reports.

To the medicinal chemist, the most interesting papers are written by McDermed ("Stereochemistry of DA Agonists") and Cannon ("Indole Derived DA Agonists"). Also some articles point to design of future therapeutic agents for endocrine, vascular, ulcer, and convulsive disorders. For example, Szabo reports promising results of DA agonists for duodenal ulceration, and Neumeyer describes the anticonvulsant effect of a new aporphine alkaloid.

A few critical comments should be made. The heterogeneous material has obviously been randomly ordered, and surprisingly, an author index is totally missing. The subject index is very brief and seems to be based solely on the key words. Taken together, this doesn't make it easier for the reader. The authors' manuscripts have been reproduced directly, so the book is technically good with very few typographical errors. However, it is disappointing that it should take more than a year for the book to appear in print. The price seems to be a little high but should not prevent the DA researcher from purchasing this interesting book.

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Progress in Cholinergic Biology: Model Cholinergic Synapses. Edited by Israel Hanin and Alan M. Goldberg. Raven Press, New York. 1982. xiv + 365 pp. 16 × 24 cm. ISBN 0-89004-758-8. $69.00.

The purpose of this comprehensive collection of model cholinergic systems is to provide not only researchers in cholinergic mechanisms but also individuals in allied disciplines with concepts that might trigger new areas of research. From this viewpoint the text provides a valuable source of information that would be of value to medicinal chemists interested in entering into, continuing, or collaborating with pharmacologists in this field. The text contains a comprehensive spectrum of model cholinergic synapses. Models include invertebrate, vertebrate, isolated, and in situ preparations.

In order to illustrate the areas covered, the following list details the chapter titles (some are abbreviated) and authors: "Cholinergic Transmission: Variations on a Theme" (F.C. MacIntosh), "Aplysia Cholinergic Synapses" (R. E. McCaman and J. K. Ono), "The Torpedo Electromotor System" (R. S. Aronstam), "Heart and Parasympathetic Neuron Tissue Culture Systems" (A. Sastre and M. L. Young), "Isolated Perfused Heart and It's Parasympathetic Neuroeffector Junction" (K. Loffelholz, R. Lindmar, and W. Weide), "Reelase of Acetylcholine from the Isolated Perfused Diaphragm" (G. G. Bierkamper and A. M. Goldberg), "The Myenteric Plexus–Longitudinal Muscle Preparation" (D. A. McAfee), "The Avian Ciliary Ganglion" (G. Pilar and J. B. Tuttle), "The Vertebrate Retina in Vivo" (M. J. Neal and J. R. Cunningham) "Brain Slices" (M. H. Weiler, U. Misgeld, and D. J. Jenden), "Synaptosomes" (G. E. Gibson and J. P. Blass), and "Dynamic Properties of the Nicotinic Acetylcholine Receptor Ion Channel Complex" (C. E. Spivak and E. X. Albuquerque).

Since space precludes commentary on each chapter, I will summarize the first and last chapters, which probably would be of most interest to medicinal chemists in general.

The opening chapter by F. C. MacIntosh on cholinergic transmission is well written and also includes an account of the early work in this field. MacIntosh was a collaborator with Dale and presents the material with a sense of the historical dimension that comes only from personal contacts with the work and workers. This chapters main emphasis is on the distinctive chemical components of cholinergic synapses and their sometimes varying composition and behavior rather than the major synaptic processes, such as the synthesis, storage, release, and action of acetylcholine. The references cited are mostly recent (up to 1980) and provide a good introduction to the current literature. Some current views on the mechanisms of ACh release are briefly discussed, and it is suggested that nonquantal transmitter release observed in muscles and other tissues may be mainly an experimental artifact whose presence can compromise the interpretations of some, but not all, neurochemical experiments. Certainly, medicinal chemists wishing to answer molecular mechanistic questions will want to read this review.

The last chapter by Spivak and Albuquerque on the nicotinic ACh receptor ionic channel complex highlights the perturbations induced by drugs and selected toxins and presents a static picture of the ACh receptor with which the reader can fit subsequent data. The conformation–activity arguments for ACh based on the X-ray work of Chothia and Pauling and the nearly rigid agonist–antagonist work of Beers and Reich should give investigators with modern computer graphics systems a chance to explore in greater detail the energy and steric relationships involved in these systems. However, the authors at the end of the chapter point out something that should be appreciated by most workers seriously interested in drug design and that is that hydrophobic forces may be more important in many receptor-site mechanisms than stereochemical, ionic, or polar ones.

In general, the book appears to this reviewer to have met its goals well and I can easily recommend it for the department or school library. It, however, is probably priced too high for most readers who would like to have a personal copy. The references do not appear more recent than 1980; however, this does not detract from it, since updating of recent studies can be easily accomplished. The editors aptly point out in the preface that the information in this text will be of value not only to researchers in cholinergic mechanisms but also to individuals from a variety of disciplines interested in the concept of model systems and their application in the study of a variety of biological phenomena.

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Annual Reports in Medicinal Chemistry. Volume 17. Edited by Hans-Jurgen Hess. Academic Press, New York. 1982. xiii + 383 pp. 17 × 25 cm. ISBN 0-12-040517-2. $32.00.

This volume continues the tradition of excellence in the series, which is indispensable to anyone aspiring to keep abreast of the rapidly evolving science of medicinal chemistry. Volume 17 is organized into six sections, as has been the long-time practice, but only 10 of the 33 chapters treat the same or similar subjects as Volume 16. This very significant turnover provides each new volume with a freshness and vitality that makes the series all the more useful. In general, topic selection appears to reflect a healthy regard both for commerce and for science; drug classes such as antidepressants have been covered in each volume for a long time apparently because of continuing high levels of research activity in these fields, and this is good. Others, such as platelet activating factor and leukotriene chemistry, were evidently selected more for scientific interest. It is impossible to be sufficiently expert in all the topics covered in the volume to render informed judgment on its entire contents, but from what the reviewer can tell, all chapters are informative and authoritative.

Section I on CNS agents includes chapters continuing the coverage of antianxiety agents, analgesics, and antidepressants. There are also new chapters on serotonin receptors and on thyrotropin releasing hormone and neurotensin. Pharmacodynamic agents are covered in a section incorporating new chapters on hemorheologic agents, antianginal agents, antithrombotic agents, and agents for the treatment of peptic ulcer disease. Chapters on antihypertensive agents and antiallergy agents complete the section. Antibacterial agents, antiparasitic agents, and antineoplastic agents present new work on these previously treated topics, and the section on chemotherapeutic agents also includes new chapters on antibiotic resistance mechanisms, antifungal chemotherapy, and interferon inducers. The section on metabolic diseases incorporates further coverage on lipoxygenase, as well as new chapters on inhibitors of connective tissue degradation, leukocyte motility, and cell-mediated immunity. The topics in the biology section includes all new chapters on polyamine metabolism, disorders of bone metabolism, substance P and neurotensin, elements of recombinant DNA research, protein growth factors and, as noted, platelet activating factor. Drug metabolism continues to be covered in excellent fashion in the topics in the chemistry section, and new topics are addressed in chapters on QSAR, herbicides, nonnutritive sweeteners, strategies in natural product drugs, and leukotriene chemistry.

The authors and editors are to be congratulated for having produced yet another highly useful addition to a fine series.

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Physicochemical Principles of Pharmacy. Edited by A. T. Florence and D. Attwood. Chapman & Hall/Methuen, New York. 1982. x + 509 pp. 15.5 × 23.5 cm. ISBN 0-412-00131-4. $29.95.

This book is designed for students of pharmacy and other life sciences, providing a physicochemical background to the design and use of pharmaceutical products. The authors relate the physical chemistry of the drug or drug system to clinical usage and deal with the basic situations encountered in the progress of a drug from the dosage form to its site of action.

The contents include gases, properties of the solid state, liquids, solutions, solubility of drugs in liquids, surface chemistry, colloidal and course lyophobic dispersions, polymeric systems, principles of drug absorption and routes of administration, drug interactions and incompatibilities, and chemical stability of drugs.

Rather than being a textbook of physical chemistry for pharmacists, this is a book that bridges the gap between the basic physical chemistry taught in the first year and the more applied practice of later years.

Staff

Studies in Physical and Theoretical Chemistry. 18. Steric Effects in Biomolecules. Proceedings of the International Symposium, Eger, Hungary, October 5–8, 1981. Edited by G. Náray-Szabó. Elsevier Scientific, Amsterdam, Oxford, and New York. 1982. xiv + 417 pp. 16.5 × 25 cm. ISBN 0-444-99693-1. $107.00.

This expensive volume represents the 18th in a series generally concerned with "studies in physical and theoretical chemistry", the topics of which may or may not be related to biological systems. It is difficult for this reviewer to appreciate the high cost of this monograph, since manuscripts were not set in type and the paper is not of high quality. Nonetheless, the topics are of interest and span the areas of physical, chemical, and biological aspects of small molecules, nucleic acids, and proteins. Somewhat over half of this work is devoted to small molecules, with the remainder devoted to DNA, RNA, and proteins. Small molecules include tetracycline, enniatin and valinomycin antibiotics, dihydroergopeptines, ergolenes, neurotransmitters, ion carriers, general anesthetics, hypothalamic hormones, and peptides. Techniques include QSAR, drug–membrane interactions, photocycloadditions to nucleic acids, circular dichroism, high-field ^{1}H NMR, quantum chemical calculations, and many more. Selected topics will vary in interest depending upon the individual, but this volume has something for everyone interested in steric aspects of drugs and/or their interaction with macromolecules.

Although all chapters have something of interest to offer, none provide particular innovative insight or new approaches to the investigation of steric aspects of drugs. Common pitfalls, generally recognized, include attempts to correlate crystalline state or organic (nonphysiological) solution conformations (by NMR) with biological activity. For quantum mechanical calculations of potential energy surfaces, Richards points out that another "major complication in theoretical studies is to account for the solvent or more realistically and even more imponderably, the biological environment surrounding the molecule in its active milieu". Certain chapters on small molecules were particularly interesting to this reviewer. These involved quantum chemical calculations in the design of ion carriers and anesthetic activity and photocycloadditions to nucleic acids.

Topics relating to DNA, RNA, and proteins generally were highly theoretical and mainly of interest to individuals working in the area. Thus, considerations of aminoacylation of tRNA, accessibility vs. molecular electrostatic potential in B- and Z-DNA or tRNA, stereochemical aspects of serine and thiol proteases, NMR analysis of the active site of subtilisin and thiosubtilisin, quantum chemical calculations and the mechanism of action of serine proteases, steric substituent effects in biopolymer reactions, topics in biological catalysis, electric field of α helixes, theoretical aspects of carbonic anhydrase C-sulfonamide interactions, mechanism of enzyme action by kinetic NMR, structure–function relationship of snake neurotoxins, and protein dynamics and function were interesting to read but generally rather far removed from classical drug development. Such studies, however, likely will lay the foundation for future drug development and certainly fall within the realm of steric effects in biomolecules, a topic generally placed in perspective with other parameters throughout the book.

Although many of the topics may be found in other reviews, the authors have done a good job of discussing their specific research efforts in context with the recent literature. Selected

references are included for all chapters generally into 1981. This treatis is recommended reading for medicinal chemists.

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Pharmazeutische Chemie. Edited by E. Schröder, C. Rufer, and R. Schmiechen. Georg Thieme Verlag, Stuttgart and New York. 1982. xvii + 1138 pp. 18.5 × 24.5 cm. ISBN 3-13-6097-01. 368 DM (ca. $170.00).

Although excellent monographs on medicinal chemistry and drug research are available, they not always offer satisfactory information on chemical synthesis and/or structure and may be rather obsolete by the time they go to press. This is understandable if one considers that about 100 000 new chemical compounds are being produced annually worldwide and that only about ten of these reach the market as useful drugs.

It is commendable, therefore, that a group of chemists from Schering AG, Berlin, presents a novel text that will provide the German-speaking scientists interested in drug research with suitable information, up-to-date through 1981. This text represents Volume 4 of a series of monographs on "Arbeitstechniken der Pharmazeutischen Industrie", which is preceded by Volume 3, "Qualitätssicherung"; Volume 2, "Biopharmazie"; and Volume 1, "Pharmazeutische Technologie". Volume 4, "Pharmazeutische Chemie", is arranged into nine chapters. After an excellent introduction into the history and basic principles of drug research, the various medicinals are grouped into drugs affecting the CNS; the heart and the kidney; the muscles and tissues; hormones; drugs affecting the digestive tract; the respiratory system; chemotherapeutics; diagnostic agents; and vitamins. The carefully printed and beautifully illustrated monograph includes a considerable number of chemical structures, showing optically active representatives with their correct stereochemistry. It is apparent, however, that the Schering team focussed attention primarily on topics of interest to their company.

The chapters on THC-related compounds (marihuana), antitumor agents of the anthracycline and retinoid families, β-blockers, drugs affecting memory and learning, and specifically the chapter on vitamins, including carotenoids, are not presented in sufficient detail. Interferons and interferon inducers are discussed only casually, and recombinant DNA research and its impact on drug discovery is hardly mentioned.

Nevertheless, this monograph—1138 meticulously printed pages—introducing each topic with adequate biological and biochemical information and followed at the end by a carefully selected list of references, will provide those who can afford it with an excellent work of reference. "Pharmazeutische Chemie", though written in German, will surely find a place on the book shelves in offices and libraries of academic and industrial institutions interested in drugs and drug research.

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Pharmazeutische Wirkstoffe: Synthesen, Patente, Anwendungen. (Pharmaceutical Agents: Syntheses, Patents, Uses.) 2nd Revised and Expanded Edition. By A. Kleemann and J. Engel. Georg Thieme Verlag, Stuttgart. 1982. xxvi + 1040 pp. 17 × 24 cm. ISBN 3-13-558402-X. $110.00.

This remarkable book contains the structure, common synthetic methods, relevant patents and their priority dates, commercial uses, medicinal applications, Chemical Abstracts registry numbers, and uses of marketed and most significant pharmaceutical agents and trade names from six countries. The latter, if available, are given in the following order: Federal Republic of Germany, France, Great Britain, Italy, Japan, and USA. Knowledge of German is not necessary: the language of the book is medicinal chemistry.

A total of 1522 pharmaceutical agents are described and more than 6000 literature and patent citations are given. The authors intend to provide supplementary volumes in 3- to 4-year intervals.

The agents are arranged in the German alphabetical order using their generic names (International Nonproprietary Names, INN). Alternative generic names adopted in other countries (BAN in Great Britain, DCF in France, USAN in the U.S.A.) are given in parentheses after the title in the text. All generic names are listed alphabetically in the index of single entity agents.

The Chemical Abstracts registry numbers are given for the agents and their salts, where applicable. Medicinal applications and indications are listed for each agent. The patent citations are extensive and include priority dates. For older agents that are no longer patent protected, more modern synthetic methods found in reference books are listed.

Review articles are cited for several newer agents. Alternative industrial synthetic processes are provided for those drugs that are manufactured by more than one method.

The trade names of combination products are denoted by the abbreviation "Komb", but details of the composition are not given. Sometimes, it is noted that several combination products exist without giving the names and compositions (e.g., codein, caffein, colecalciferol, cyanocobalamin, etc.).

In addition to the alphabetically arranged index of single entity agents, five other indexes are included. One index consists of groupings of agents by chemical classes, a second by indications, a third provides an alphabetical listing of chemical intermediates used in the course of drug syntheses, a fourth lists the enzymes, microorganisms, plants, and animal organs, and the fifth index consists of an alphabetical list of the marketed preparations included in the book.

Inevitably, in a book of this magnitude (1040 pages) a number of mistakes are found. For example, the tetroxoprim–sulfadiazine combination product marketed by Roche in Germany is designated as Tibirox–Komb, and the identical product marketed by Heumann in Germany as Sterinor appears without the designation Komb (for combination product). The trade name of metoclopramide in France is Primperan not Primeran, and ampicillin in the U.S.A. under the trademark of Polycillin is marketed by Bristol Laboratories not by Squibb. Salutensin is not a single entity agent hydroflumethiazide but a combination product. These mistakes are annoying and should be eliminated in subsequent printings. Perhaps the editor should request that all companies listed review their entries.

On the other hand, the book provides an invaluable service to the medicinal chemist with a wealth of information. As opposed to narrative styles of books dealing with drug syntheses, which are of very limited value, this book is encyclopedic and provides an immediate overview of the synthetic processes and ready references.

Just as the "Merck Index", the "Index Nominum", and *Annual Reports in Medicinal Chemistry*, "Pharmaceutische Wirkstoffe" will become a standard reference on the bookshelves of medicinal chemists and is highly recommended.

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Macromolecular Chemistry. Volume 2. Specialist Periodical Reports. A. D. Jenkins and J. F. Kennedy, Senior Reporters. The Royal Society of Chemistry, London. 1982. xviii + 425 pp. 14.5 × 22.0 cm. ISBN 0-85186-866-5. $117.00 (ca. $50.00 for members).

As discussed in the introduction, the delineation of what should be included in a volume of "macromolecular chemistry" proved a prodigious task. This volume contains chapters on various types of polymerizations, on several types of natural polymers, on inorganic polymers, on techniques used to study polymers, on engineering and technology, on reactions undergone by polymers, and on reactions in macromolecular systems. There are also chapters on biomedical applications of polymers and computer applications in macromolecular science. The reporters of many of the 19 chapters make no attempt to be comprehensive or critical in their literature coverage but rather choose to review areas of widespread interest or of particular progress. Topics reviewed for the first time in this series include a brief description of the

technique or reaction. This volume is a treasure trove of information, not only because it provides current bibliographies but because many of the chapters integrate current fact with previous hypotheses. While the quality of the prose is generally very high, this reviewer found the chapters on proteins and nucleic acids particularly well-written and lucid.

In the tradition of other Specialist Periodical Reports, this work is technically well-presented. The literature reviewed is essentially that of 1979 and 1980. This reviewer suggests that, since much of this book is written in the language of the specialist, it will be of most value to those directly involved in physical and chemical studies of polymers.

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Organic Reactions. Volume 28. William G. Daubin, Editor-in-Chief. Wiley, New York. 1982. vii + 347 pp. 15.5 × 23.5 cm. ISBN 0-471-86141-3. $39.50.

The volumes of *Organic Reactions* consist of collections of chapters each devoted to a single reaction, or a definite phase of a reaction, of wide applicability. Volume 28 contains three chapters: "The Reimer–Tiemann Reaction" (H. Wynberg and E. W. Meijer); "The Friedlander Synthesis of Quinolines" (C.-C. Cheng and S.-J. Yan); and "The Directed Aldol Reaction" (T. Mukaiyama). An author index and chapter and topic index for Volumes 1–28, as well as a subject index for Volume 28, are included.

Staff

Fieser and Fieser's Reagents for Organic Synthesis. Volume 10. By Mary Fieser. Wiley, New York. 1982. 528 pp. 16 × 23.5 cm. ISBN 471-86636-9. $39.50.

This volume of reagents includes references to papers published during 1980 and the first half of 1981. This book, as in previous volumes in the series, provides references to new reagents introduced during this period, as well as recent references to reagents included in previous volumes. As in previous volumes, an index of reagents according to types, an author index, and a subject index are included.

Staff

Organic and Bio-organic Chemistry of Carbon Dioxide. Edited by S. Inoue and N. Yamazaki. Wiley, New York. 1982. xi + 280 pp. 15.5 × 23 cm. ISBN 0-470-27309-7. $49.95.

The book deals with organic and biological reactions utilizing carbon dioxide as a synthon. With a brief introduction in Chapter 1, the next three chapters (pages 5–184) are devoted to synthetic aspects of carbon dioxide ranging from the classical Kolbe–Schmitt reaction to organometallic and polymerization chemistry. Reactions of carbon dioxide on different substrates have been aptly compiled in Chapter 2 with relevant experimental details. The latter feature should prove to be of value to undergraduate and graduate students in organic chemistry. The breadth of coverage pertaining to carbon dioxide coordinated metal complexes in Chapter 3 will be welcome by the readers. The value of this chapter is enhanced by suitable use of spectroscopic data in the text. Polymerization reactions involving carbon dioxide are adequately covered in Chapter 4.

The last two chapters of the book are devoted to the biological aspects of carbon dioxide chemistry. The chapter on "Biological Carboxylations" (Chapter 5, 67 pages, 129 references) is elegantly written; the intensity of its coverage will not be found in any one modern textbook on biochemistry. The mechanistic aspects at the cellular level are succinctly presented by suitable figures, which should be appreciated by the students in the life and physical sciences. The chapter entitled "Model Reactions of Biochemical Carbon Dioxide Fixations" emphasizes the roles of carbonic anhydrase and biotin-containing enzymes.

All in all, this book provides an overview of the organic and biochemical aspects of reactions utilizing carbon dioxide as one of the synthons. Each chapter has clearly drawn chemical formulas and is well referenced. Typographical errors are few, e.g., "examplified" (page 187) and "anyhydrease" (page 253). The reviewer is intrigued with the editors' classification of carbon dioxide as an "inorganic" compound. Despite the positive aspects of this book, the $49.95 price will deter it's purchase by many interested students. Nevertheless, it should be a valuable addition to the libraries of academic institutions.

Research and Development Division **Tikam Jain**
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Sulfur in Organic and Inorganic Chemistry. Volume 4. Edited by Alexander Senning. Marcel Dekker, New York and Basel. 1982. xiv + 440 pp. 15.5 × 23.5 cm. ISBN 0-8247-1350-8. $75.00 (20% higher outside U.S.A. and Canada).

There are few areas of organic chemistry that grew as rapidly as as the chemistry of sulfur and the other chalcogens. The days are gone when Houben-Weyl's admirable volume would tell chemists all they cared to know about any class of sulfur compounds to be studied. Today sulfur chemists have available several compendia that bring knowledge about sulfur compounds up-to-date fairly frequently.

One of the most useful of these is the present series, which is thoughtfully put together, well edited, and thoroughly indexed. The present volume presents an update of the first volume that appeared 10 years ago. The various chapters cover the sulfur–silicon bond, the sulfur–nitrogen bond, the sulfur–phosphorus bond, the sulfur–fluorine bond, the sulfur–chlorine bond, the sulfur–bromine bond, and the sulfur–iodine bond. The coverage of this material is so thorough as to make this book very useful. However, it should be pointed out that the two subjects covered in volume I, likely to be of the widest interest to sulfur chemists, the sulfur–oxygen bond and the sulfur–sulfur bond, have "for reasons beyond the Editor's control" not been included in Volume 4. It is also unfortunate that, even though this book carries a 1982 publishing date, few references cited are more recent than 1978 and none more recent than 1979. Nonetheless, this volume can be recommended highly to all sulfur chemists.

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Kirk Othmer Encyclopedia of Chemical Technology. Volume 19. Third Edition. Powder Coatings to Recycling. Edited by Martin Grayson and David Eckroth. Wiley, New York. 1982. xxvi + 1010 pp. 18.5 × 26 cm. ISBN 0-471-02072-9. $165.00.

This volume includes monographs from powder coatings to recycling and contains excellent and authoritative discussion on topics of interest to medicinal chemists, such as psychopharmacological agents (Sternbach and Horst), pyrrole and pyrrole derivatives (Horst and Anderson), quinoline and isoquinoline (Holter), quinones (Finley), radioactive drugs (Green and Gruverman), radioisotopes (Martin), radiopaques (Ackerman), and radioprotective agents (Klayman and Copeland).

Staff

Clinical Biochemistry Reviews. Volume 3. Edited by D. M. Goldberg. Wiley, New York. 1982. xxvi + 477 pp. 18.5 × 26 cm. ISBN 0471-09868-X. $40.00.

This book, third in a series, represents a continuing effort by a number of the authors over 3 years. Since many of these individuals made a 3-year committment, there may be substantial changes in the series after this year. This particular edition is very similar to that of last year, except for a rather significant increase in price from $28.50 to $40.00. Slight changes in some of the topic areas are apparent in this year's volume. Topics

covered include: "Laboratory Management, Quality Assurance and Reference Values"; "Instrumentation"; "Kidney Function and Renal Disease"; "Diseases of the Gastrointestinal System"; "Selected Topics in Diabetes Mellitus"; "Biochemical Tests in Diagnosis and Monitoring of Cancer"; "Clinical Enzymology"; "Non-Polypeptide Hormones"; "Biochemistry of Pituitary Hormones"; "Biochemical Aspects of Genetic Disease"; "Toxicology and Therapeutic Drug Monitoring"; "Lipoproteins: Their Role in Enzyme Regulation"; "Hepatobiliary Disease"; and "Plasma Proteins".

Once again, the authors have exercised judgment as to which specific areas require the most coverage. For example, the enzyme chapter focuses on Prostatic Acid Phosphatase, Creatinine Kinase, and Alkaline Phosphatase.

The chapters on "Biochemical Aspects of Genetic Disease" and "Biochemical Tests in the Diagnosis and Monitoring of Cancer" are the most extensive in this volume, both offering several hundred references.

The quality of effort here is similar to that of the previous volume and again offers an interesting, although not exhaustive, overview of the literature of 1980.

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Modern Pharmacology-Toxicology. Volume 20. Endorphins: Chemistry, Physiology, Pharmacology, and Clinical Relevance. Edited by Jeffrey B. Malick and Robert M. S. Bell. Marcel Dekker, New York and Basel. 1982. xi + 296 pp. 16 × 23.5 cm. ISBN 0-8247-1687-6. $37.50.

The volume is a timely monograph on the chemistry, physiology, pharmacology, and clinical relevance of endogenous peptides with opiate-like activity. An astounding amount of literature has accumulated on these substances since the announcement in 1975 of the isolation of methionine- and leucine-enkephalin from the brain. Since then a number of other peptides of varying chain length have been reported, and the generic term "endorphin" was assigned to these compounds. Although the appellation gained considerable usage, it has not been universally accepted, and some confusion concerning the term has arisen. Many use endorphin to allude specifically to longer chain peptides related to B-endorphin, and in the light of recent knowledge, this makes good sense. It has now become increasingly clear that there are three distinct classes of peptides with varying degree of opiate-like activity with distinct biosynthetic and neuronal pathways associated, respectively, with the enkephalins, B-endorphin, and dynorphin. It may be more apropos to "opiopeptins" as the generic designation for such compounds, since these also appear to be endogenous nonpeptides that exhibit opiate-like activity.

This problem in nomenclature is addressed in the historical chapter by Simon who originally suggested the name endorphins. Since articles related to history tend to be etched in stone, I should like to call attention to some errors in the chapter and some points of issue. We were the first (1953) to attempt to use stereospecificity to differentiate stereospecificity but were unsuccessful. Loh and not Goldstein established that the purified substance responsible for stereospecific binding in the mouse brain is cerebroside sulfate. The discovery of opiate receptors greatly stimulated but did not "trigger" the search for the opiate-like factor. There were reported isolations of morphine-like substances before 1973 when stereospecific binding of opiates was conclusively established but none of the earlier studies could be corroborated.

Smyth provides some interesting insights on the biosynthesis of the opiopeptins. In prohormones containing peptide sequences with dissimilar functions, he envisages a processing mechanism for selective expression of activity that ensures only one of two bioactivities being generated at a time. Based on concepts of gene expression of molecular biology, he predicts more potent opiopeptins in the offing with varying opiate-like activity. A comprehensive but discouraging survey of the structure–activity relationship of the opiopeptins is provided by Dewey. Hundreds of pentapeptides have been synthesized with a wide range in potency, but the changes have not materially changed the specificity of action.

A handy chapter on the assay of opiopeptins is provided by Lord, Rance, and Smith. Rossier and Bloom give a good summation of the distribution of the enkephalins and the endorphins, but, regrettably, information on dynorphin has been too recent for inclusion. The chapter on "physiological function" by Cox and Baizman discusses the pharmacology of the opiopeptins; however, anatomic, metabolic, electrophysiologic, receptor, and neurotransmitter considerations have been used to extrapolate the pharmacologic effects into possible functions. The chapter is informative, comprehensive, and critical with over 500 cited references. Malick and Goldstein describe the pharmacologic profile of the opiopeptins rather superficially while alloting undue amount of pages on the modest analgetic properties of Met- and Leu-enkephalin. Terenius discusses some clinical aspects. Even though the book is already dated, it can be recommended as a useful reference and an excellent source for the literature through 1979.

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Terpenoids and Steroids. Volume 11. Specialist Periodical Reports. J. R. Hanson, Senior Reporter. The Royal Society of Chemistry, London. 1982. xi + 243 pp. 14.5 × 22.5 cm. ISBN 0-85186-346-9. $94.00.

This book continues the admirable tradition established by its predecessors. Every organic chemist and biochemist actively interested in terpenoids and steroids will want to have access to this volume and will find it and its fellow members in the series indispensable as research and reference sources. The quality of reporting continues to be outstanding; the present reviewer only regrets that in this volume, as in Volume 10, it has not been possible to include a chapter on monoterpenoids. We hope that this can be remedied in future volumes.

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Noninvasive Probes of Tissue Metabolism. Edited by Jack S. Cohen. Wiley, New York. 1982. xiv + 270 pp. 15.5 × 23.5 cm. ISBN 0-471-0889305. $49.50.

This book is a unique compendium of a variety of techniques for measuring biochemical phenomenon in intact, living systems. The contents comprise 10 chapters based principally on topics of a symposium held by the American Society of Biological Chemists.

Seven of the ten chapters are devoted to noninvasive NMR measurements. These applications are loaded with extremely interesting and, in many cases, new data on the behavior of cells and whole organ systems. One of the most scholarly chapters is that by the editor and his coauthor Lev Jacobson, which is a critical discussion on noninvasive pH measurements by NMR methods. This chapter and its related bibliography provide essential information for those who attempt to deduce hydrogen ion concentration in vivo by NMR methods (e.g., inorganic phosphorous shifts in the ^{13}P spectrum).

Noninvasive measurements of carbon-13 NMR for analyzing gluconeogenesis in hepatocytes and for discovery of the behavior of pyruvate kinase and pentose cycle activity are contained in a 38-page chapter by Sheila M. Cohen and Robert G. Shulman. This data-packed chapter is an excellent demonstration of the capability of NMR to make basic biochemical pathway and kinetic studies with a minimum perturbation of the tissues being studied.

Chapters 7–9 focus on the use of phosphorus-31 NMR for measurement of data on tissue bioenergetic state by comparison of the concentrations of creatine phosphate, adenosine triphosphate, and inorganic phosphorus and by observation of chemical shifts associated with tissue pH changes. Chapter 9 by C. D'Ambrosio, B. Chance, J. Leigh, Jr., and S. Eleff contains an excellent historical summary with examples of NMR applications to ^{31}P bioenergetics. The reader might profit by examination of

this chapter before Chapters 7 and 8. Chapter 7 by Eric Fossel and Joanne Ingwall presents the variation of creatine phosphate and ATP with cardiac cycle in the isolated, perfused rat heart. They were able to demonstrate that the concentrations of creatine phosphate and ATP change between diastole and systole and that these changes are dependent on the workload and carbon substrate availability. A remarkable finding is that the unidirectional rate constants of the creatine kinase reaction changed during the cardiac cycle as well. The companion chapter (8) by G. P. Dubé and E. A. Schwartz from Cincinnati and their collaborators, D. G. Gadian, P. M. Matthews, G. K. Radda, A. M. Seamore, and S. R. William from Oxford University, used the perfused rat heart also. They focus on the problem of the mechanism of controlled cellular respiration: cytosolic ATP–ADP ratio or phosphorylation potential. This chapter demonstrates that P-31 NMR is a useful tool for investigating these alternate mechanisms.

In addition to NMR noninvasive techniques, positron emission tomography (PET) has developed into a major investigative tool for medical science investigation of metabolism and tissue blood flow in man and animals. Chapter 10 by Michael E. Phelps is an excellent 39-page exposé of the method and details of the application of this quantitative imaging to the study of relative cerebral glucose metabolism in man.

A fifth contribution to NMR methods is the measurement of the blood composition of some NMR-sensitive elements using a vascular shunt to allow blood sampling by the NMR spectrometer. In Chapter 6 the chemical shift of 2,3-diphosphoglycerate in the blood of an animal on various concentrations of respired O_2 and CO_2 is measured. Another major example for the use of this noninvasive blood sampling technique is the measurement of the concentration of fluoroanesthetics with ^{19}F NMR.

Another chapter on the use of NMR is a detailed study of the life cycle of *A. castellanii*, a soil amoeba, with ^{13}C and ^{31}P NMR. Chapter 3 is a compendium of preliminary measurements further supporting the potentials and breadth of application of NMR to biochemical and biological studies.

Two other methods of noninvasive measurements are presented in this book. The use of fluorometry for measurement of tissue redox states and function with specific application to the corneal tissues of the rabbit is presented in Chapter 4. Noninvasive monitoring of volatile metabolites by a mass spectrometer coupled to the tissue of interest is overviewed in Chapter 2. The reader interested in the instrumentation of mass spectroscopy might not find Chapter 2 sufficiently elementary. These techniques have some unique potentials but perhaps less breadth in general applications of current interest.

In summary, this book provides the reader with a rather complete coverage of NMR in vivo spectroscopic ^{13}C and ^{31}P studies of metabolism with state-or-the-art applications and extensive literature citations. Nonmetabolic NMR proton imaging is covered in other texts. The NMR contributions are complemented by single chapters each on mass spectroscopy, fluorometry, and positron emission tomography. The book has an adequate index, and the editor has provided the reader with a consistent and convenient format for each chapter.

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The Enchanted Ring. The Untold Story of Penicillin. By John C. Sheehan. The MIT Press, Cambridge, MA. 1982. xvi + 224 pp. 13 × 20 cm. ISBN 0-262-19204-7. $15.

"A diabolical concatenation of reactive groups", a quotation of R. B. Woodward that is used by the author to underscore the problems chemists encountered as they wrestled with "The Enchanted Ring" (the β-lactam) seems an equally apt description of the personalities, institutions, and governments involved in this intriguing first-person narrative of the history of penicillin. This book provides the reader an intensely personal, well-documented account of "The Untold Story of Penicillin" and gives a rarely encountered unguarded view of events usually left for discussion among small groups of like-minded friends.

In "The Lonely Search" (Chapter 1), Professor Sheehan recounts those conditions and events that shaped his decision in 1948 to tackle a problem that was to take him 9 years to solve—the rational synthesis of penicillin. As a young chemist at Merck, for instance, he was asked to choose between two new projects, cortisone or penicillin. As we know, he chose penicillin. This decision left the cortisone project for another new young Merck chemist, Lewis Sarrett. Apparently, the fortunes of both men were influenced favorably by this single decision.

The "Early History of Penicillin" (Chapter 2) takes the reader from the initial discovery of penicillin by Fleming in 1929, through the continuing controversy over who did what first, to the Coconut Grove fire of 1942. The treatment of burn victims from this fire with penicillin placed the new wonder drug squarely in public view for the first time.

"Developing the Secret Weapon" (Chapter 3) knits together significant political, technical, and personal events from the time Roosevelt established the Office of Scientific Research and Development (OSRD) to the fall of the German black market in penicillin. Only someone as intimately familiar with the penicillin story as is the author could attempt such a detailed account of this critical period.

"The Impossible Problem" (Chapter 4) will be very enlightening to those of us grown accustomed to the current high-technology state of the art in separation and purification techniques, as well as high-resolution mass spectrometers, single-crystal X-ray spectroscopy, computer-driven data analysis, and so on. The isolation, purification, and structure elucidation of penicillin were problems faced just as these techniques were born. Professor Sheehan leads the reader through what must at the time have been frustrating events: missed sulfur, overlooked or unappreciated correct data, and strong wills locked into incorrect ideas. Throughout the book the author attempts to explain each technical point so that the nontechnical reader may understand. While the author is successful at this in most instances, this reviewer feels it is the chemist who will most intensely enjoy this chapter.

In "The Conquest of Penicillin" (Chapter 5), Sheehan achieves his goal of a rational synthesis, but he could not achieve this until he discovered a new tool for forming amide bonds. The previous failures to synthesize penicillin were inevitably due to a lack of a sufficiently gentle method to form the β-lactam at neutral pH. Sheehan's discovery that carbodiimides would serve this purpose permitted him to achieve his immediate goal and has since served many chemists wishing to form peptide or other amide bonds.

For those uninitiated to the world of patents and the all too frequent legal battles over them, "Ordinary Skill in the Art" (Chapter 6) may seem something of a sacrilege in man's holy battle against disease. But it is not that at all; it is simply what happens when something very important is invented at about the same time by different people. This chapter provides the reader a rare opportunity to vicariously experience a process few would care to experience first hand.

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The Role of Tamoxifen in Breast Cancer. Edited by Stefano Iacobelli, Marc E. Lippman, and Gioacchino Robustelli Della Cuna. Raven Press, New York. 1982. xii + 124 pp. 16 × 24 cm. ISBN 0-89004-852-5. $17.00.

This book consists of three chapters describing laboratory experiments designed to better understand the mechanism of anti-estrogen action and ten chapters exploring tamoxifen's potential as a treatment of breast-cancer patients with either early or advanced disease. Almost all the chapters in this book present recent data with brief introductory reviews of the subjects and well-chosen references to more extensive reviews. In most cases, the authors discuss their own experiments in detail. For example, Lippman and Nawata describe their previous work with anti-estrogens in the MCF-7 line, utilizing enough detail for the uninitiated reader to subsequently fully understand and appreciate their recent work with cell lines cloned from MCF-7 cells grown in and relatively resistant to tamoxifen. Other chapters describe some of the intracellular effects of tamoxifen observed in vitro as well as the effects of tamoxifen on human endocrine function. Unfortunately, these sections of the book constitute too small a proportion of the entire work.

The clinical chapters are reports of individual trials performed predominantly in Italy, in addition to one from Switzerland. Several of the trials reported are large, randomized studies of considerable importance to clinicians specializing in the treatment of breast cancer. The most notable among these is the trial by Cocconi in which patients with metastatic disease were randomized to receive either chemotherapy or combination chemotherapy plus tamoxifen as initial therapy at the time metastases were first detected; patients treated with chemotherapy only were subsequently treated with chemotherapy plus tamoxifen at the time of progression. This report includes important data both on the ability of each of these programs to induce tumor regression and the effect of each on patient survival. A similar, large trial has been performed by the Swiss group and is also described in this volume by Varini and his colleagues, but many of the other trials included represent retrospective analyses or relatively small or uncontrolled trials. These studies generally add little to our understanding of how the drug should optimally be used.

"The Role of Tamoxifen in Breast Cancer" may be of particular interest to American readers with limited knowledge of on-going European trials. However, it will not provide a comprehensive review of on-going clinical research on the use of tamoxifen. Its excellent basic research sections are quite limited, and it will have minimal value to the specialist in the area who wishes to seek out fine points.

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Marihuana: An Annotated Bibliography. Volume II. By C. W. Waller, R. S. Nair, A. F. McAllister, B. S. Urbanek, and C. E. Turner. Macmillan Publishing Co., New York. 1982. xxxv + 620 pp. 18.5 × 26 cm. ISBN 0-02-699820-3. $29.95.

This annotated bibliography on marihuana was compiled by members of The Research Institue of Pharmaceutical Sciences at the University of Mississippi and includes works published from 1975 to 1979. The previous volume covers all facets of cannabis research from 1964 to 1974. Volume II contains 2669 entries covering international scientific publications and includes structures of all different types of cannabinoids, as well as other different classes of compounds. The Addendum includes citations prior to 1975 that were omitted from Volume I. There is also a listing of patents and an expanded subject index. Although this book was designed particularly with the researcher in mind, it includes enough diversity to meet the needs of anyone with an interest in marihuana.

Staff

Methods in Enzymology. Volume 89. Carbohydrate Metabolism. Part D. Edited by Willis A. Wood. Academic Press, New York. 1982. xxx + 656 pp. 16 × 23.5 cm. ISBN 0-12-181989-2. $59.00.

This volume contains new procedures that have been published since 1974 for the enzymes involved in the conversion of monosaccharides to pyruvate or to breakdown products of pyruvate. During the 7 years since the last volumes on this subject were published, the development of new chromatographic separations utilizing affinity and hydrophobic properties of enzymes have resulted in improved procedures differing radically from those available previously. Hence, many of the enzyme purifications now involve fewer steps, are easier to carry out, and often allow separation of isozymes. As with Volumes 41 and 42, preparation of the same enzyme from a number of sources has been included. This is in recognition of the increasing spectrum of interest of investigators in, for instance, the comparison properties from a variety of sources and phylogenetic relationships.

Volume 90, soon to be published, will complete this defined region of metabolism. This volume, 89, is divided into five sections: "Analytical Methods"; "Enzyme Assay Procedures"; "Preparation of Substrates and Effectors"; "Oxidation–Reduction Enzymes"; and, "Isomerases, Epimerases, and Mutases".

Staff

ADP-Ribosylation Reactions. Biology and Medicine. Edited by Osamu Hayaishi and Kunihiro Ueda. Academic Press, New York. 1982. xxiii + 698 pp. 16.5 × 23.5 cm. ISBN 0-12-333660-0. $67.50.

This volume comprehensively treats poly- and mono(ADP-ribosyl)ation reactions. The scope of ADP-ribosylation reactions has expanded rapidly since its discovery in 1966 and now encompasses almost all types of life in a variety of biological phenomena, e.g., viral replication, bacterial intoxication, cell differentiation, and oncogenesis.

The chapters in the book are arranged in four parts. Part 1 summarizes the history and research in ADP-ribosylation reactions. Part 2 surveys NAD metabolism in eukaryotes. Parts 3 and 4 illustrate, respectively, the various aspects of poly(ADP-ribosyl)ation and mono(ADP-ribosyl)ation reactions. Throughout the book, the authors emphasize the functional role of the reactions. They present examples of such topics of current interest as activation of poly(ADP-ribose) synthesis in response to DNA damage and modulation of adenylate cyclase activity by bacterial toxin-catalyzed mono(ADP-ribosyl)ation.

The book will be of value to advanced researchers and beginners in biochemistry, molecular biology, cell biology, microbiology, endocrinology, and oncology—particularly researchers in such areas as cellular regulation, chromatin, DNA repair, carcinogenesis, and bacterial toxins.

Staff

Books of Interest

Contributions to Oncology. Volume 11. Interferon. Properties, Mode of Action, Production, Clinical Application. (Proceedings of the Third International Expert Meeting of the Deutsche Stiftung fur Krebsforschung, Bonn, Mar 13–16, 1981). Edited by K. Munk and H. Kirchner. S. Karger AG, Basal. 1982. ix + 233 pp. 15.5 × 22.5 cm. ISBN 3-8055-3482-5. $36.00 (softbound).

Preparation, Properties, and Industrial Applications of Organofluorine Compounds. Edited by R. E. Banks. Halsted Press (distributed by Wiley, New York). 1982. 352 pp. 15.5 × 23.5 cm. ISBN 0470-27526-X. $84.95.

Frontiers in Hypertension Research. Edited by John H. Laragh, Fritz, R. Buhler, and Donald W. Seldin. Springer-Verlag: New York. 1981. xxi + 628 pp. 20 × 27.5 cm. ISBN 3-540-90557-X. $39.80.

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