Book Reviews

Biotransformations. Volume 6. A survey of the transformations of drugs and chemicals in animals. Edited by D. R Hawkins. Royal Society of Chemistry, Cambridge, U.K. 1994. xxxi + 411 pp. 19 × 25 cm. ISBN 0-85186-127-X. £130.00.

This is the sixth volume in this series that surveys reported biotransformations of pharmaceuticals, agrochemicals, food additives, environmental chemicals, and industrial chemicals in vertebrates. It broadly covers the scientific literature from 1987 through 1992 with major focus on 1992. The first chapter presents an overview of novel biotransformations, mechanisms of toxicity, and notable species differences. The remainder of the book consists of referenced abstracts of reports of biotransformations of individual compounds arranged according to compound class. A cumulative index of Volumes 1–6 is included. Compounds are indexed by compound, key functional group and reaction type to facilitate access to information in the entire series.

This book will be of interest to medicinal chemists and other researchers concerned with xenobiotics and drug metabolism. Library access is recommended. The cost of the volume, a fairly large number of small errors, and timeliness are negatives.

Staff

Annual Reports in Medicinal Chemistry. Volume 29. Editor-in-Chief: James A. Bristol. Academic Press, Inc., San Diego, CA. 1994. xiv + 397 pp. 17 × 25 cm. ISBN 0-12-040529-6. $70.00 (pbk).

Volume 29 of this well-known series provides timely updates of important areas of medicinal chemistry with particular emphasis on emerging fields of research. It retains the familiar format of previous volumes. Thus, the book is divided into seven major sections, namely (I) CNS Agents, (II) Cardiovascular and Pulmonary Agents, (III) Chemotherapeutic Agents, (IV) Immunology, Endocrinology and Metabolic Diseases, (V) Topics in Biology, (VI) Topics in Drug Design and Discovery, and (VII) Trends and Perspectives. Each section is edited by an authoratative drug researcher and, with the exception of the final single-chaptered section, consists of five or six chapters by expert scientific researchers. Each chapter is 10 pages or less and is comprehensively referenced.

In Sections I–IV, some of the chapters, such as those on allergy, antiinfectives, and antivirals, present a comprehensive update the year's progress. The majority of the chapters in these Sections, however, are specifically focused and mechanistically oriented to provide the reader with the most important new results in a particular field. Included in this group of topics are some that are reviewed for the first time. These include chapters that deal with neuronal cell death, animal engineering, D_3/D_4 dopamine receptor ligands, Ras oncogene, isozyme-selective phosphodiesterase inhibitors, human leukocyte elastase inhibitors, and agents to control androgen action. Chapters reviewing subjects occasionally included in previous volumes are ones dealing with antidepressants, muscarinic agents, excitatory amino acid antagonists, endothelin antagonists, nitric oxide synthase, thrombolytics, antithrombotics, HIV protease, HIV reverse transcriptase, opportunistic infections, interleukin-1, immunosuppressants, and cell adhesion.

In Section V, topics reviewd are transcription factor NF-κB, translational control of gene expression, protein kinases and phosphatases, transgenic and gene targeting, and osteoporosis. Topics in Drug Design (Section VI) includes chapters on adenylate cyclase subtypes, antisense technology, in vitro prediction of human drug metabolism, humanized monoclonal antibodies, and ethnobotany. The final section (VII) consists of a single 24-page chapter "To Market, To Market—1993" which describes the 43 new chemical entities, including several genetically engineered molecules, introduced into the world market for the first time during 1993.

As usual, this volume has been produced in an extremely timely fashion; it is up-to-date through 1993 and contains many 1994 references. The subjects treated are of current importance to medicinal chemists and all drug reserachers. Most will find subjects of specific significance and all topics of general interest. This volume, like its predecessors, is a must for inclusion in the personal libraries of all concerned with the design, discovery, and development of new drug products.

Staff

The Year's Drug News. Therapeutic Targets. 1994 Edition. Edited by Joseph R. Prous. J. R. Prous Science Publishers, Provenza, 385–387, 08025 Barcelona, Spain. 1994. xxiv + 549 pp. 22 × 28 cm. ISBN 84-8124-041-9. $500.00.

The Year's Drug News, the first of a new annual series, has been conceived as a chronicle of the progress of worldwide pharmaceutical research during the past year. In this initial edition new drug introductions, drugs in clinical trials, new molecular entities reported for the first time, new compounds claimed in patents, and new uses, combinations, and formulations of known drugs reported from May 1993 to May 1994, as well as therapeutic targets and drug research trends described during this period, are collected, described, and referenced in a concise, clearly organized fashion. This information is quite exhaustive as it has been collected from more than 1500 journals, 80 conferences, patent literature from 10 sources, company communications, and scientific contributions. *The Year's Drug News* is organized into 17 sections and 97 chapters covering different therapeutic categories. The chapters are subdivided according to the mechanism of action of the drugs. For example, Section 1 "Analgesic and Anesthetic Drugs" consists of four chapters, namely, analgesic drugs, antimigraine drugs, anesthetic drugs, and

adjuncts to anesthesia. The chapter on analgesic drugs is subdivided according to the mechanism of action of the drugs, i.e., opioid analgesics (opioid agonists, opioid agonist–antagonists, κ-opioid agonists, δ-opioid agonists), zinc metallopeptidase inhibitors, nonsteroidal antiinflammatory drugs, PGE_2 antagonists, bradykinin antagonists, substance P antagonists, $GABA_\beta$ agonists, NMDA antagonists, and miscellaneous analgesic drugs. The final section (17) is devoted to therapeutic targets; it highlights new research efforts to discover compounds with desirable therapeutic effects. These efforts are increasingly focused on molecular targets such as receptors and enzymes. All sections are clearly presented with an introduction to the topic and a description of all new developments during the past year. Names, structural formulas, and references are clearly presented.

This book is a remarkable summary of recent research and development presented in a very timely fashion. It provides an exhaustive account of recent pharmaceutical research. All medicinal chemists, pharmacologists, and other researchers concerned with the discovery of new drugs will find this a valuable compilation that summarizes virtually all areas of drug research. Library access is recommended for all drug researchers. Unfortunately, the cost will probably prohibit inclusion in personal libraries.

Staff

Polymeric Site-Specific Pharmacotherapy. Edited by A. J. Domb. John Wiley & Sons, New York. 1994. x + 464 pp. 15.5 × 23.5 cm. ISBN 0-471-93824-6. $150.00.

A number of diseases are local in nature; that is, they do not directly affect the entire body, but rather have very local direct effects. These diseases might best be treated locally, rather than attempting to treat them by creating high circulating concentrations of the therapeutic agent to be used, and presuming that high systemic concentrations of this agent will translate to high local concentrations, as well. Unfortunately, all that these high systemic concentrations assure is high systemic concentrations, which often lead to unacceptable incidences of adverse drug reactions.

This book discusses the delivery of drugs directly to the site required, by the use of synthetic polymeric drug delivery. The chapters include an introduction to the various biodegradable polymers which are currently available, by the editor, biocompatibility and toxicity of biodegradable polymers, drug release and tissue distribution, modeling of drug delivery to the brain, polymer-conjugated drugs for cancer chemotherapy, drug delivery to the brain, polymeric delivery of neurotransmitters and neuromodulators, bone-marrow targeting, perivascular delivery systems, cardiovascular drug delivery, osteomyelitis treatment, specific delivery to the intestinal tract, systems for the eye, polymers for drug delivery to the lung, prevention of surgical adhesions, the regulation of such polymeric implants, and drug delivery to peripheral nerves.

The contributing authors are among the leaders in this newly developing field, and each writes on his special area of research interest.

Each of the 16 chapters is well-referenced, and the book contains an excellent index. It will serve as an excellent introduction to those new to the field, as well as a useful reference work for those who are attempting to treat such difficult diseases or are developing new modes of therapy.

Mark Chasin

Purdue Research Center
99-101 Sawmill River Road
Yonkers, New York 10701

Asymmetric Catalysis in Organic Synthesis. By Ryoji Noyori. John Wiley & Sons, Inc., New York. 1994. xvii + 378 pp. 16 × 24 cm. ISBN 0-471-57267-5. $54.95.

This book is an outgrowth of a series of lectures on asymmetric catalysis given by Professor Noyori in the Fall of 1990 at Cornell University. Much of the material derives from the author's own laboratory at Nagoya University, though the coverage of the topic is well-balanced by the inclusion of a great deal of work by other laboratories around the world. The author has endeavored to include most of the significant achievements up through the fall of 1992, and the result is a book packed with useful and up-to-date information on this critically important and rapidly expanding field.

The bulk of the material focuses on homogeneous organometallic chemistry. Chapters which derive largely from the author's own work include those on asymmetric hydrogenation, enantioselective olefin isomerization, and addition of organometallic reagents to olefins. A chapter on catalysis via chiral metal complexes surveys a large amount of work from other laboratories, including hydrosilylation, hydroboration, olefin epoxidation and dihydroxylation, coupling of Grignards with halides, and many others. Though necessarily not as in-depth as the other chapters, this chapter is nonetheless extensively referenced and provides an excellent beginning point for further study. Reactions in the heterogeneous phase are covered in a closing chapter.

An enormous amount of technical information is to be found here. In addition to large numbers of instructive literature references, the chapters are packed with empirical rules for predicting isomer ratios, proposed mechanistic models, kinetic data, X-ray and NMR data for chiral ligands, and a myriad of other information. Graphics are used generously and are very clear and clean throughout. The tables of reaction schemes and products alone are worth the price of the book.

With its extremely reasonable price tag, this volume probably contains more useful chemical information per dollar than any book I have seen in several years. Its purchase by chemists engaged in asymmetric synthesis, whether research scale or process, is unambiguously recommended.

Gregory S. Hamilton

Guilford Pharmaceuticals, Inc.
6611 Tributary Street
Baltimore, Maryland 21224

Advances in Experimental Medicine and Biology. Volume 340. The Design of Synthetic Inhibitors of Thrombin.. Edited by G. Claeson, M. F. Scully, V. V. Kakkar, and J. Deadman. Plenum Press, New York and London. 1993. x + 246 pp. 16.5 × 25.5 cm. ISBN 0-306-44593-X. $75.00.

This volume is based on the proceedings of the International Symposium on the Design of Synthetic Inhibitors of Thrombin held July 8–9, 1991, at the Thrombosis Research Institute in London. The book contains 23 chapters (ranging from 2 to 30 pages) which are loosely organized by analogy with the sessions of the Symposium. The first seven chapters illustrate the variety of biochemistry, physical chemistry, and computational chemistry techniques which have been utilized to determine the structure of thrombin as well as the molecular basis for its interaction with several classes of inhibitors.

The next 10 chapters exemplify how this structural data has been utilized in the design of thrombin inhibitors, with a heavy emphasis on recent work in the area of substrate related transition state analogs. In addition to discussing the structural basis for the design of their inhibitors, many of the authors in this section have taken the opportunity to thoroughly review the anticoagulant profile and *in vivo* pharmacology of representative examples from their SAR studies.

In the last section of the book, three of the four chapters discuss the biochemistry and pharmacology of recombinant hirudin and the related peptide hirulog. A summary of the phase I clinical experience with both of these agents is included. In the fourth chapter of this section, the mechanism of anticoagulation exhibited by a variety of direct thrombin inhibitors is discussed and contrasted with low molecular weight heparin, which acts by enhancing thrombin inhibition by the endogenous inhibitor, antithrombin-III.

Although a few of the tables and schemes are rather difficult to follow, most of the chapters are well-organized and clearly written. In particular, Markwardt's "Synthetic Thrombin Inhibitors as Anticoagulants: Pharmacological Aspects" is an excellent review of the field, providing an historical perspective on the development of each of the major classes of small molecule thrombin inhibitors, as well as a thorough discussion of the coagulation assays and animal models which are routinely used to study thrombin inhibitors (155 references).

The focus of this book, the biochemical and pharmacological properties of thrombin *inhibitors*, complements the previous monograph, Thrombin: Structure and Function (edited by L. Berliner, Plenum Press, New York and London; 1992), which is a more thorough treatment of the biochemistry and physiology of thrombin itself. *The Design of Synthetic Inhibitors of Thrombin* is a useful compilation of recent advances in the design of more potent and more selective thrombin inhibitors and provides an historical perspective on the development of the first clinical candidates in the field. It will serve as a useful reference for those with experience in this area as well as a nice introduction to the current state of the art for beginners.

Michael R. Wiley
Cardiovascular Research
Lilly Research Laboratories
Eli Lilly and Company
Indianapolis, Indiana 46285

Supramolecular Chemistry: An Introduction. By Fritz Vögtle. John Wiley & Sons, New York. 1993. viii + 337 pp. 15.5 × 23 cm. ISBN 0-471-92802-X. $150.00.

One thing should be noted about this volume at the outset. The author notes that the "book emerged from a series of lectures...entitled 'Modern Methods, Reactions and Structures in Organic Chemistry'." In a sense, this is both its strength and weakness. Thus there is broad coverage, but some topics that undoubtedly were fascinating to hear discussed in a lecture (*e.g.*, the mechanism of action of the weed killer paraquat) are of dubious value in the present context. A gentle view of this eccentricity is probably appropriate because there is no other single volume that attempts this broad subject. The volume of the title *Supramolecular Chemistry* by Balzani and DeCola is a proceedings volume, although Balzani and Scandola have, in *Supramolecular Photochemistry*, effectively taught a great deal of general subject matter. There is substantial overlap also with the volume by Dugas titled *Bioorganic Chemistry*; the latter being an excellent but more biological introductory volume that intersects the present one's subject matter in several places.

The present volume comprises 13 chapters. They are (1) Supramolecular, Bioorganic, and Bioinorganic Chemistry (8 pp); (2) Host-Guest Chemistry with Cations and Anions (107 pp); (3) Bioinorganic Model Compounds (6 pp); (4) Bioorganic Model Compounds (35 pp); (5) Clathrate Inclusion Compounds (24 pp); (6) Directed Crystal Formation with Tailored Additives (12 pp); (7) Photoresponsive Host-Guest Systems: Organic Switches Based on Azobenzene (24); (8) Liquid Crystals (52); (9) Surfactants, Micelles, Vesicles: Preorganization of Interface-active Compounds (8 pp); (10) Organic Semiconductors, Conductors, and Superconductors (22 pp); (11) Molecular Wires, Molecular Rectifiers, and Molecular Transistors (8 pp); (12) Light-induced Cleavage of Water (8 pp); and (13) Final Remarks (2 pp). The volume also includes author and subject indexes.

The coverage is obviously broad although the depth is varied. Indeed, the subject matter clearly reflects the particular interests of the author and his 13 "collaborators". This is neither good nor bad since not every aspect of supramolecular chemistry can be covered thoroughly in so few pages. Chapter 7 involving azobenzene may seem unreasonably long, but several principles of supramolecular chemistry are exemplified by molecules incorporating this subunit. From the medicinal chemistry standpoint, the coverage of surfactants seems meagre compared to the coverage of liquid crystals and directed crystal formation. Again, this distribution reflects the authors' expertise and interests, especially since the volume started as a lecture series rather than an attempt to prepare a textbook. The most

important critical observation is probably that the volume is built up from examples, albeit fascinating ones, rather than from principles. Thus, this monograph is more instructive than a collection of separate reviews; it is less educational than a dedicated textbook.

George W. Gokel
Department of Molecular Biology & Pharmacology
Washington University Medical School
St. Louis, Missouri 63110

Books of Interest

Membrane Protein Structure. Experimental Approaches. Edited by Stephen H. White. Oxford University Press, New York. 1994. x + 395 pp. 16 × 24 cm. ISBN 0-19-507112-3. $65.00.

Analyses of Hazardous Substances in Biological Materials. Volume 4. Edited by J. Angerer and K. H. Schaller. VCH Publishers, Weinheim, Federal Republic of Germany. 1994. xxii + 265 pp. 17 × 24 cm. ISBN 3-527-27027-2. DM 135.

Molecular Biology of Diabetes: I. Autoimmunity and Genetics; Insulin Synthesis and Secretion. Edited by Boris Draznin and Derek LeRoith. The Humana Press, Totowa, NJ. 1994. xiii + 404 pp. 16 × 23.5 cm. ISBN 0-89603-286-8. $89.50.

A Guide to the Complete Interpretation of Infrared Spectra of Organic Structures. By Noel P. G. Roeges. John Wiley & Sons, Inc., New York. 1994. x + 340 pp. 15.5 × 23.5 cm. ISBN 0-471-93998-6. $69.95.

Integrated Chemical Systems. A Chemical Approach to Nanotechnology. By Allen J. Bard, Editor-in-Chief of the *Journal of the American Chemical Society*. John Wiley & Sons, Inc., New York. 1994. xv + 324 pp. 16.5 × 24 cm. ISBN 0-471-00733-1. $49.95.

Achieving Sterility in Medical and Pharmaceutical Products. Volume 64 (Drugs and the Pharmaceutical Series). By Nigel A. Halls. Marcel Dekker, Inc., New York. 1994. v + 281 pp. 16 × 23.5 cm. ISBN 0-8247-9014-6. $110.00.

The Chemistry of Heterocyclic Compounds. Tellurium-Containing Heterocycles. Volume 53. By Michael R. Detty and (in part) Marie B. O'Regan. John Wiley & Sons, Inc., New York. 1994. ix + 511 pp. 16.5 × 24 cm. ISBN 0-471-63395-X. $125.00.