Dissociation between blood pressure and PRA has been observed by others[15] and one explanation is that a renin inhibitor must affect both circulating and tissue renin in order to elicit a blood pressure response. Thus one possibility for the low level of efficacy is that inhibitor 4 is binding to some other enzyme and is unable to reach the appropriate site of action. As seen in Table III, substitution of the thiazole for the imidazole decreased the inhibitor's specificity toward renin.[10,16]

It has been demonstrated by us[6,17] and others[18] that increasing a renin inhibitor's hydrophilicity can also lead to an improvement in efficacy. Conversely, in the present series of inhibitors, it is the more lipophilic compounds, as measured by partition coefficient and solubility (Table I), that result in superior absorption. The results reported herein clearly demonstrate that modification of the P_2 site of a molecular weight 700 peptide-based renin inhibitor can significantly improve both absorption from the gastrointestinal tract and passage through the liver into the systemic circulation. Studies currently underway are directed toward improving the efficacy of this series of renin inhibitors.

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Saul H. Rosenberg,* Hollis D. Kleinert
Herman H. Stein, Donald L. Martin, Marcia A. Chekal
Jerome Cohen, David A. Egan
Karen A. Tricarico, William R. Baker
Abbott Laboratories
Cardiovascular Research Division
Abbott Park, Illinois 60064
Received October 24, 1990

Book Reviews

Handbook of Natural Products Data. Volume 1. Diterpenoid and Steroidal Alkaloids. Edited by Atta-ur-Rahman. Elsevier, Amsterdam, 1990. vii + 962 pp. 17.5 × 24.5 cm. ISBN 0-444-88173-5. $353.75.

Prof. Atta-ur-Rahman of the H.E.J. Research Institute of Chemistry, University of Karachi, has embarked on an ambitious project involving the systematic tabulation of all known natural products, together with information on their sources, molecular formulas, melting points, and spectral characteristics. This volume represents the first installment and lists data for 971 diterpenoid and steroidal alkaloids reported until the end of 1988.

To achieve this compilation, Prof. Atta-un-Rahman has relied on more than a dozen assistants, all of whom are devoid of doctoral degrees. The relative lack of experience of the compilation team with the subject matter makes itself apparent even upon cursory inspection of this compendium. The structures are not uniformly drawn within a structural series. For example, for the steroidal alkaloids, the stereochemistry of the angular hydrogens is sometimes indicated by either thick or dotted lines, or by simply straight lines which carry no stereochemical overtones. In some other instances the angular hydrogens are just completely ignored. The five-membered ring D is sometimes drawn as a symmetrical pentagon, and at others as an asymmetrical cycle with the base either at the top or at the bottom. One can only conclude that the original literature drawings were copied by the individual members of the team without much thought toward internal uniformity or consistency.

Each alkaloid entry is duly accompanied by at least one literature reference. But it was decided to ignore accents, cedillas, and the like. The result is that Cavé becomes Cave, Döpke becomes Dopke and Şener becomes Sener. Of course, such a policy simplifies the compilers' job, but it fails to do justice to the names of the authors quoted.

Another difficulty is that the compilers have not tried to assess the literature critically and have made no attempts to correct or amend publications in the light of general knowledge or of later developments. For instance, 3-*N*-methylholarrhimine is spelled 3-*N*-methylholarrhimin simply because it appeared as such in the German literature, whereas holarrhimine is spelled correctly with an "e" at the end because it was described in English-language publications. Interestingly, the related alkaloid holarrhidine is nowhere cited.

The perfect exemplar of alkaloid compilation and tabulation to have appeared over the years has been authored by Cavé, Leboeuf, and Guinaudeau and has covered the aporphinoid alkaloids. It has appeared at intervals in the Journal of Natural Products. Any new listing of alkaloids should try to emulate this series for its consistency, accuracy, reliability, and thoroughness. The present *Handbook of Natural Products Data* unfortunately falls short of such a degree of excellence.

It should be added, however, that the project is worthwhile and deserves to be continued, provided that much greater dedication to high standards is applied. The present handbook and its future companions would then become a useful complement to the recently published Dictionary of Alkaloids by I. W. Southon and J. Buckingham, published by Chapman and Hall.

Maurice Shamma
Department of Chemistry
The Pennsylvania State University
University Park, Pennsylvania 16802

Organic Chemistry of Drug Synthesis. Vol 4. By Daniel Lednicer and Lester A. Mitscher with Gunda I. Georg. John Wiley and Sons, Inc., New York. 1990. xiii + 253 pp. 16 × 24 cm. ISBN 0-471-85548-0. $44.95.

The fourth volume of this series summarizes syntheses of drugs given a United States Adopted Name between 1983 and 1987. Arrangement of 11 chapters is by chemical class (aliphatic/alicyclic; monocyclic aromatics; polycyclic aromatics and reduced relatives; steroids; five- and six-membered heterocycles; five- and six-membered benzofused heterocycles; bicyclic fused heterocycles; β-lactam antibiotics; and twenty pages devoted to miscellaneous heterocyclic species). A bioactivity cross index, a cumulative index for volumes 1–4, references mainly in the 1980s, and comments on biological activity are provided. Many syntheses are derived from the patent literature.

These concise summaries can serve as a good starting point for chemists entering the medicinal chemical arena, but as pointed out by Alfred Burger actual syntheses by which drugs are produced are "not often divulged by the industrial chemists and engineers" (*J. Med. Chem.* 1990, *33*, 2061). Information presented could be useful as a partial source of lecture material utilized in honors courses in medicinal chemistry at the undergraduate level both in pharmacy schools and in chemistry departments. This volume is of less value to practicing synthetic chemists well-grounded in

alternative synthetic methodologies, and seasoned medicinal chemists will not derive much incite concerning concepts in drug design from this work. Emphasis is placed on relatively straightforward and successful synthetic routes to the named drugs at the expenses of a comparative analysis of alternative synthetic strategies and the use of a multitude of possible reagents.

Division of Medicinal Chemistry **Donald T. Witiak**
The Ohio State University
Columbus, Ohio 43210

Inside the Drug Industry. By Bert Spilker and Pedro Cuatrecasas. J. R. Prous, S. A., Barcelona, 1990. xvii + 109 pp. 14 × 21.5 cm. ISBN 84-86973-22-8. $15.00.

This small paperback volume identifies the world's major research based pharmaceutical firms responsible for the development and marketing of 90% of today's commercially available drugs. The well-qualified authors present an accurate and succinct description of the processes and resources required for modern drug development. They identify the enormous costs and risks involved in current drug research and development but show that drugs represent a very important but very modest fraction of total health-care costs. This volume, in fact, is an effective plea for relief from some of the major factors which make drug research so expensive and such a risky enterprise. These factors include limited patent protection, ponderous regulatory requirements, and generic competition.

This eminently readable little book should be of interest to young scientists considering a drug-research career and to those employed in the pharmaceutical industry, as well as legislators and regulatory authorities.

The volume includes a useful table of contents, indices to tables and figures, and a well-organized subject index.

15 Kinterra Road **James W. Wilson**
Wayne, Pennsylvania 19087

Comprehensive Medicinal Chemistry: The Rational Design, Mechanistic Study and Therapeutic Applications of Chemical Compounds. In six volumes. C. Hansch, P. G. Sammes, and J. B. Taylor, series editors. Pergamon Press, Elmsford, NY. 19 × 28 cm. ISBN 0-08-037059-0. $1995.00 for the set. Individual volumes not available.

The aim of the series is to present medicinal chemistry as a field in its own right. The modern role of this discipline is herein defined as the understanding of structure-activity relationships and drug design from the mechanistic viewpoint. Because of this restriction, those drugs of unknown action are not discussed. The set is organized into five volumes of text and a sixth volume which is a compendium of structures. Each volume is reviewed separately with a collective summary at the end.

Volume 1. General Principles. Volume Editor, Peter D. Kennewell. XV + 811 pp.

The first of four sections in this volume is devoted to an historical perspective of medicinal chemistry. The principal chapter among five in this section is the well-written Chronology of Drug Introductions by W. Sneader. It provides a background for this and subsequent books in the series. The other chapters are on the evolution of the pharmaceutical industry, medicinal chemistry in China, and medicine in India. Alfred Burger pleases us once more with a brief personal view of the discipline in the opening chapter.

The second section on Targets of Biologically Active Molecules is made up of six chapters. Three of these, Physiology of the Human Body, The Architecture of the Cell, and The Immune System are brief overviews. Although of value as an introduction to some readers, it is likely that a lecturer or research scientist in the field would consult texts on these subjects for a complete background. The other three chapters on Macromolecular Targets for Drug Action, Concept of Bioselectivity, and Selectivity are brief in their treatment and contain some overlap of information.

The nine chapters in the third section entitled Bioactive Materials deal mostly with methods used in developing new drugs. These include chapters on classification, lead discovery, computer-aided selection, isolation and assay, scale-up synthesis, and genetic engineering. These chapters range widely in length, five to fifty pages. There is little coherence in this section, largely isolated topics which vary in style between text and review. The three chapters on the gene are well-done.

The fourth section of this volume is entitled Socio-economic Factors of Drug Development. There are 14 chapters in this section dealing with topics such as research funding, government controls, national health care, clinical trials, marketing, surveillance, patents, information sources, and so forth. This may be useful information to some and should be accessible to those who are interested. In this series, however, it is over one-quarter of the space in this volume. It is doubtful if most medicinal chemists are going to seek out this series for these chapters.

Overall, the volume is an introduction to medicinal chemistry in a broad sense. The chapters vary widely in length, focus, and general usefulness although most are well-written. It is a good reference volume for a library.

Department of Medicinal Chemistry **Lemont B. Kier**
Virginia Commonwealth University
Richmond, Virginia 23298-0540

Volume 2. Enzymes and Other Molecular Targets. Volume Editor Peter G. Sammes. xi + 887 pp.

The first section of this volume covers "Enzymes". The topics include: Enzyme Structure, Nomenclature and Classification of Enzymes, Enzyme Catalysis, Enzyme Inhibition, and Resistance and Tolerance to Antimicrobial Drugs. The chapter Enzyme Structure may serve as an introduction for medicinal chemists not schooled in biology or biochemistry or for those who need a refresher in structural molecular biology. It is not typical of many other chapters in volume 2, in that it has more value as an introductory teaching aid than as a research review. The subtopics in this chapter are broad and sparsely covered. For example, there is one paragraph on the subtopic "protein folding" with seven references; two pages cover X-ray crystallography including diffraction theory, data collection, phase determination, and the reliability index or *R*-factor; NMR (2D) in one page, etc. The chapter on Enzyme Catalysis (fifteen pages with 48 references) is along the same lines. There is nothing on allosteric mechanisms and nothing in the subject index for volume 2 that covers allosteric properties and enzymes. Considering the recent spate of information at the molecular level on a number of important allosteric enzymes and considering the importance that allostery will play in drug interactions with allosteric proteins, it is an unfortunate omission.

The chapter on enzyme inhibition is more in-depth and less generalized, in that the subtopic categories are small enough to be specific. Also, key enzymes that have had the binding sites mapped out with the inhibitors via crystallographic studies are referenced. This chapter and the others in this section are less suited for general instruction purposes and more review oriented. The chapter on Resistance and Tolerance to Antimicrobial Drugs appears to be both descriptive and comprehensive (208 references).

The second section contains chapters on Agents Acting on Oxygenases, Electron Transport Systems and Pyridoxal Dependent Systems, Oxygenases, The Arachidonic Acid Cascade; Agents Acting on Passive Ion Transport, Agents Acting on Active Ion Transport, and Pyridoxal Dependent Systems.

The chapter on oxygenases is more oriented toward a mechanistic approach and is well-written. The description of the important oxygenase cytochrome P450 is thorough and extensive. The chapters on ion transport are descriptive but not as comprehensive. The Active Transport chapter attempts to summarize broad subtopics in a fashion similar to the Protein Structure chapter. The chapter on Pyridoxal Dependent Systems is well-written and both comprehensive and instructive.

The third section covers "Agents Acting on Metabolic Processes". The chapters include: Sulfonamides and Sulfones, Reductases, Purine and Pyrimidine Targets, and Therapeutic Consequences of the Inhibition of Sterol Metabolism. The chapter on Sulfonamides and Sulfones is brief and does not deal in depth with the diuretic aspects of sulfonamides. The reductases chapter is well-written and thorough but not descriptive with the expected

in depth crystallographic studies on binding of DHFR inhibitors mentioned in a few sentences. The remaining chapters are classic reviews with large bibliographies (305 references for Purine and Pyrimidine Targets).

The fourth section covers "Agents Acting on Hydrolases and Peptidases". The chapters include: Hydrolases, Peptidase Inhibitors, Enzyme Cascades: Purine Metabolism and Immunosuppression, Enzyme Cascades: Coagulation, Fibrinolysis and Hemostasis, Selective Inhibitors of Phosphodiesterases, Agents Acting Against Phospholipase A_2, and Protein Kinases. The chapters in this section are for the most part extensive and comprehensive. The chapter on Peptidase Inhibitors is excellent and of the character that one might like to see for the entire volume.

The fifth section covers "Agents Acting on Cell Walls". Three chapters are presented: Cell Wall Structure and Function, Beta-Lactam Antibiotics: Penicillins and Cephalosporins, and Other Beta-Lactam Antibiotics. These are the most comprehensive chapters in the volume, covering over 257 pages. This compilation of information should serve as a landmark reference reservoir for cell wall antibiotics.

The final section in volume 2 is on "Agents Acting on Nucleic Acids" and includes: DNA Intercalating Agents, DNA Binding and Nicking Agents, Agents Interfering with DNA Enzymes, Inhibitors of the Transcribing Enzymes: Rifamycins and Related Agents, and Agents That Interact with Ribosomal RNA and Interfere with its functions. There is an overall lack of nucleic acid structure presented in these chapters. Considering all of the structural work published in this area that illustrates the binding of antibiotics to DNA segments, there is little illustrative mechanistic presentation in these chapters. For the DNA Intercalating chapter, there are two references (both reviews) as sources for the crystallographic studies in this area. There is a one-half page summary of protein synthesis and no accompanying mechanisms of how antibiotics might interfere with ribosomal targets. This latter section is perhaps the weakest in the volume.

In summary, the volume will certainly be one of the first places a medicinal chemist will search for a starting reference point since the comprehensive nature of this gigantic work is unequaled in this field. However, since much of the contents of this volume are oriented toward a review format rather a basic principles format that illustrates general principles of drug action (at the molecular level if available), this reviewer believes the series could become outdated within a few years. There are some current areas of intense interest not covered (at least when the index is checked): HIV proteases, viral proteins and enzymes (especially the cold viruses), and oncogene proteins such as ras P^{21}. All of these are targets for drug invention and have the details of the atomic structures worked out.

The preface leads to an expectation of a mechanistic classification of enzyme action with numerous arrows indicating electron movement between amino acid side chain atoms and substrates or stereo pairs and colored photographs of inhibitors bound at active sites. There is little of this approach in this volume. Instead it has the tone of a more classical comprehensive topical review with one sentence or two describing the contents of a paper rather than a general more extensive treatment of several key systems which could be followed with tables and references to associated papers.

Department of Medicinal Chemistry **Donald Abraham**
Virginia Commonwealth University
Richmond, Virginia 23298-0540

Volume 3. Membranes and Receptors. Volume editor J. C. Emmett. xvii + 1280.

This volume is a very comprehensive review of topics in medicinal chemistry related to membranes and receptors. The volume is divided into six sections with 32 total chapters plus a subject index.

The first section is titled Membranes, Membrane Receptors and Second Messenger Pathways with four chapters on Structure and Function of Cell Membranes; Quantitative Analyses of Ligand-Receptor Interactions; Isolation, Purification and Molecular Biology of Cell Membrane Receptors; and Transduction Signalling, Second Messenger Analogues and Inositol Phosphates. This introductory section is an excellent review of pertinent cytology and physiology needed to fully understand the later sections and should be particularly valuable to medicinal chemists with a limited background in biology.

The second section is titled Neurotransmitter and Autocoid Receptors and has 13 chapters covering α-adrenergic, β-adrenergic, dopamine (CNS), dopamine (peripheral), histamine, acetylcholine, amino acid, benzodiazepine, serotonin, adenosine and ATP, prostanoid, platelet activating factor, and leukotriene receptors. The third section covers Peptidergic Receptors. There is a short general chapter on the design of drugs acting at peptidergic receptors followed by nine chapters concerning receptors for opioids, hypothalamic and adenohypophyseal hormones, neurohypophyseal hormones, glucagon and insulin, gastrointestinal regulatory peptide, angiotensin and bradykinin, atrial natriuretic factor, tachykinin, calcitonin, and parathyroid hormone. The next two sections each contain only a single chapter covering Drugs Acting on Ion Channels and Membranes and Lymphokines and Cytokines. The final section on Intracellular Receptors has chapters on the molecular mechanism of action of 1,25-dihydroxyvitamin D_3 and receptors for thyroid and steroid hormones.

Each chapter on a given receptor type gives extensive information on the organ sites of the receptor, the function it serves (when known), the architecture of the receptor (when known), and the SARs of agonists and antagonists. A particular strength of the reviews is the attention paid to different subtypes of receptors and the selectivity of drugs for distinguishing them. A shortcoming of many of the chapters is a lack of discussion on proposed modes of binding of the drugs covered and on the topography of the binding site (but there are some excellent exceptions). In general the chapters are well-written. There are few typographical errors, particularly for such a large volume containing so many chemical structures. This volume would be a valuable reference to any medicinal chemist, molecular pharmacologist, or student who has an interest in drugs acting at receptors. However, the unavailability of this volume separately from the entire set will probably place it beyond the reach of many who could most use it.

Department of Medicinal Chemistry **James F. Stubbins**
Virginia Commonwealth University
Richmond, Virginia 23298-0540

Volume 4. Quantitative Drug Design. Volume editor, C. A. Ramsden. xvi + 766 pp.

The volume focuses almost entirely on the use of physical properties in structure–activity analysis and drug design. The first of five sections is made up of five chapters comprising an introduction. The history by M. Tute is the best that has been written to date. He accurately describes the work of many people, going back one-half a century, who have contributed to the evolution of QSAR. The chapter on computers by the Weiningers is good, basic information of value as a text.

The second section on quantitative description of physical properties contains a mixture of subjects generally directed toward the nature and description of physical properties. A very good chapter by Loew and Burt give enough insight into quantum mechanical methods that the reader may see beyond mechanistic approaches to possibilities in pure structure–activity analyses. Regrettably just 20 pages was allotted to this important facet of drug design.

A chapter by Silipo and Vittoria on the three-dimensional structure of drugs contains the only description of topological methods in QSAR. The editors inclusion of just 10 pages on this important and emerging topic is a shortcoming in the organization of the volume. The section on biological activity and transport by Martin, Bush, Kyncl and by Dearden, respectively, are written very well in a text mode.

The section on molecular graphics is well-structured with good organization. The section on QSAR is basically a review of earlier work using partition coefficients or Free–Wilson methodology. The final section contains five chapters describing statistical

methods for drug design. These are well-done and useful as text material.

Overall, the volume presents a unidirectional focus, that of physical property-based analyses of drug action. This is the intent as stated in the preface. It is a shortcoming, however, to have omitted so much of the alternative approach to drug design, namely the purely structural descriptions of molecules, especially when the set is titled "comprehensive". These would have included quantum mechanics and graph theoretical methods. The chapters fall into three categories of design: text, review, or reference. Each has its value, depending upon what the reader seeks. Generally, the authority and quality of the chapters are high.

Department of Medicinal Chemistry **Lemont B. Kier**
Virginia Commonwealth University
Richmond, Virginia 23298-0540

Volume 5. Biopharmaceutics. Volume Editor, John B. Taylor. xvii + 756 pp.

This volume is divided into three sections: Principles of Pharmacokinetics and Metabolism, Analytical Methodology, and Chemistry and Pharmacy in Drug Development. The chapters are well-written and cover the literature primarily through 1987. On the basis of the statement in the preface, it was anticipated this important area of drug development would be covered from a "mechanistic viewpoint... integrating with its central chemistry all the necessary ancillary disciplines". This was not accomplished in this volume. All important areas of drug absorption, distribution, excretion, and metabolism (ADME) were discussed or cited; however, examples or schemes of specific regio- and stereoselective drug transformations, mechanistic pathways, or SAR studies did not reflect the scope to which the structural information in these areas have developed. The mechanistic approach to drug metabolism and toxicity was not presented in sufficient detail to provide insight into how molecular structure and physicochemical properties can affect drug biotransformations. Some of this information may have been covered in volume 2, but it was not integrated with this volume. A notable exception was the chapter on Distribution and Clearance Concepts by Gaillot, Bruno, and Montay. A more structure-oriented background in the initial chapters would have provided a better complement for the chapters on enzyme induction and inhibition, species differences, developmental drug metabolism, and pharmacogenetics. The six chapters on pharmacokinetics were well-written and informative, however, in these chapters as well as the initial chapters covering ADME, the author(s) often provided an extensive introduction to the field before covering the specific material indicated by the subject heading. It would be useful if this redundancy could be minimized by reference to the initial introductory chapters.

The section on Analytical Methodology, covering chemical methods, biological methods, and in vitro methods, was comprehensive and very well-written. It is unfortunate that the two chapters Chemical Analysis and Isolation and Identification of Metabolites overlap and could be combined into a single chapter. The remaining section on Chemistry and Pharmacy in Drug Development provides a good background in an area becoming increasingly important to the medicinal chemist. This section emphasized drug delivery and again the extensive introduction and background sections in these chapters often reviewed concepts covered in the first section.

In conclusion, the subject matter covered in this volume did not emphasize chemical structures or chemical mechanisms and did not seem to be specifically directed toward the chemist or medicinal chemist. Most of the information provided in this volume could readily be obtained in a general text on pharmacokinetics, drug metabolism, pharmacology, or pharmaceutics in more detail at a comparable or lower cost. On the basis of the cost of this series I find it difficult to recommend this text for inclusion in a small library collection.

Department of Medicinal Chemistry **William H. Soine**
Virginia Commonwealth University
Richmond, Virginia 23298-0540

Volume 6. Cumulative Subject Index and Drug Compendium. Volume Editor, C. J. Drayton. xv + 991 pp.

This volume devotes 236 pages to a cumulative subject index covering the first five volumes. Each volume has an index averaging 50 pages each, making the cumulative index somewhat unnecessary. This is particularly true since the vast majority of the entries have only a single volume cited.

The next 725 pages are devoted to a compendium of drugs and other biologically important agents. There are eight entries per page consisting of generic name, structure Chemical Abstracts registry number, molecular weight, formula, drug activity classification, company of origin, log P and pK_a data when available, pages cited in the series, and a reference to preparation and/or biological activity. The entries are alphabetical by generic name. The compilation was prepared by the use of the ChemBase program which will be available from Molecular Design Ltd.

A casual inspection of structures proves the compendium to be less than error free (for example, the structures depict the R stereoisomer of the aromatic amino acids phenylalanine, which is listed as a nutrient, tryptophan, and tyrosine, but the naturally occurring enantiomer is shown for all other amino acids). Since many of the structures included in the compendium do not appear in the preceding volumes, the compilation enhances the series. The utility of this database is limited since a search can only be made by the generic name.

Department of Medicinal Chemsitry **Richard B. Westkaemper**
Virginia Commonwealth University
Richmond, Virginia 23298-0540

Fieser and Fieser's Reagents for Organic Synthesis. Volume 15. Edited by Mary Fieser. Wiley Interscience, New York. 1990. 415 pp. 16 × 23.5 cm. ISBN 0-471-50400-9. $49.95.

The 15th volume covers the reagent literature published from mid-1988 through mid-1989. The format of this well-known series continues with its descriptions, structural formulas, and selected examples of application, providing references to new reagents as well as reagents included in previous volumes. This series remains an essential reference work for organic and medicinal chemists and should be available in all chemical libraries.

Research Biochemicals Inc. **John L. Neumeyer**
1 Strathmore Road
Natick, Massachusetts 01760

Dictionary of Drugs. Edited by J. Elks and C. R. Ganellin. Chapman and Hall Ltd., London. 1990. Vol. 1: xiii + 1303 pp. Vol. 2: vii + 755 pp. 23 × 29 cm. ISBN 0-412-27300-4. (2 volume set) $1,099.00.

The aim of this two-volume reference work is to provide the definitive source of concise, easily accessed, factual data on all of the most significant drugs currently in use or in late development worldwide. The editors have extended the term "drug" to include compounds of significant pharmacological interest which are either in the process of gaining clinical approval or which are no longer in widespread chemical use, as well as a number of biologically active compounds of plant origin which have been used in folk medicine.

The presentation of data on over 6000 drugs is uniform with the established *Dictionary of Organic Compounds*, Fifth Edition, with well-drawn structures showing stereochemistry and comprehensive bibliographies giving ready access to the important primary literature sources. Also included are therapeutic uses, tradenames, and synonyms.

Of particular value, which greatly facilitates access to the vast amount of information, are the indexes which are bound in a separate volume. Name Index includes an alphabetical listing of all names given throughout the dictionary, whether these are entry names, tradenames, synonyms, or names referring to derivatives. Molecular Formula Index includes a listing in Hill convention order of all molecular formulae and of all significant

derivatives. Chemical Abstracts Service Registry Number Index contains all CAS registry numbers in numerical order given in the dictionary. Type of Compound Index lists all drugs in the Dictionary classified according to pharmacological activity. Structure Index, contains all structural formulae (in reduced size) in entry number order.

There is no question that this latest in the series of Dictionaries will be an essential addition to any library whose clientele is involved with drugs. The data is presented in a clear and readable style and the indexes greatly facilitate the search process. As is always the case in the first edition of such a monumental task, this reviewer found some errors and some omissions. It is hoped that this dictionary will be frequently updated to reflect the rapid developments in drug research. The editors and publishers of this dictionary have a tough act to follow with the availability of the *Merck Index* now in its 11th edition which includes entries for over 10 000 drugs and biologically active compounds and contains much the same information and similar indexing as in the dictionary at a cost of $35. The price of this Dictionary will unfortunately limit its availability to libraries.

Research Biochemicals Inc. **John L. Neumeyer**
One Strathmore Road
Natick, Massachusetts 01760

Serotonin and 5-HT_2-Receptor Blockade in the Cardiovascular System. Edited by M. Gothert. Gustav Fischer, Stuttgart. 1990. 88 pp. 17 × 24 cm. ISBN 0-89573-312-4. $48.00.

This is the most recent volume of the *Progress in Pharmacology and Clinical Pharmacology* series (i.e. volume 7, number 4) and represents the results of a symposium held in Frankfurt, Germany in April 1989. The meeting and the book focus on the role of 5-HT_2 receptors in cardiovascular function and their potential clinical significance in various cardiovascular diseases.

A lead-off chapter by the volume editor very nicely (although only a brief 13 pages) reviews the current status of 5-HT receptor research, nomenclature, and second-messenger systems. In keeping with the theme of the book, emphasis is given to 5-HT_2 receptors, and, in particular, the role of 5-HT_2 receptors in the cardiovascular system. The next two chapters deal with the vascular effects of 5-HT and the effect of 5-HT_2 receptor blockade on neuronal control of circulation. The remainder of the book is divided into two sections, each consisting of three chapters. One section deals with the 5-HT_2-mediated role that 5-HT plays in the modulation/amplification of certain cardiovascular effects involving other types of receptors (e.g. in vasoconstriction and platelet aggregation). The other section details the clinical relevance of 5-HT_2 receptors in the treatment of various cardiovascular disorders.

This volume is authored by noted experts in the field; it is well-written, contains few typographical errors, and provides up-to-date information on the involvement of 5-HT receptors, particularly 5-HT_2 receptors, in various aspects of cardiovascular function. It will undoubtedly be of value to pharmacologists working in this area. Though of somewhat less value to the typical medicinal chemist, it certainly provides a concise state-of-the-art view of the field for those interested in cardiovascular and/or 5-HT medicinal chemistry.

Department of Medicinal Chemistry **Richard A. Glennon**
School of Pharmacy
Medical College of Virginia
Virginia Commonwealth University
Richmond, Virginia 23298-0581

Studies in Natural Products Chemistry. Volume 6. Stereoselective Synthesis (Part D). Edited by Atta-ur-Rahman. Elsevier, Amsterdam. 1990. x + 606 pp. 17 × 24.5 cm. ISBN 0444-88566-8. $189.75.

Professor Atta-ur-Rahman initiated this series of *Studies in Natural Products Chemistry* in 1988, and in 1990 we already have the sixth volume in hand. Clearly this represents a prodigious organizational effort. As has been the case with earlier volumes, we are presented with a "tasting menu" of reviews on many different topics. Perhaps the chief unifying criterion is that each of the themes treated is being actively pursued in at least one laboratory.

A total of thirteen chapters make up the most recent volume. J. D. Martin (Tenerife, Spain) has provided a monumental article on "Total synthesis of polycarbocyclic marine terpenoids". T. Nakano (Caracas, Venezuela) has contributed a chapter of a smaller scale, entitled "Stereoselective total syntheses of spongian-type diterpenes and scalarane-type sesterterpenes of metabolites from marine sponge organism". S. Liaaen-Jensen (Trondheim, Norway) provides an authoritative discussion of "Allenic and acetylenic carotenoids", and L. N. Mander (Canberra, Australia) has written insightfully on "Synthetic studies of gibberellins and antheridiogens". "Recent advances in the chemistry of secondary metabolites isolated from Fusarium species" are presented by M. E. Savard, R. Greenhalgh, and J. W. ApSimon (Ottawa, Canada). O. S. Chizov (Moscow, U.S.S.R.) has written a concise chapter entitlted "Amphotericin B: synthetic studies", while K. Ogura (Chiba, Japan) describes some useful methodology in "Development of dithioacetal *S*-oxides and *S,S*-dioxides as synthetic reagents".

A world famous expert on ants is reputed to have begun a lecture on the assigned subject of "the function and evolution of the gizzard in chickens" by pointing out that the really interesting thing about gizzards is that they are completely lacking in ants, and then proceeding to talk about his favorite subject for the remainder of the hour. H. Yamamoto and T. Hanaya (Okayama, Japan) explain that there are no known natural sugars containing carbon–phosphorus bonds, and then present a succinct chapter on "Sugar analogs containing carbon–phosphorus bonds". An interesting review of "Syntheses and reactions of sugar–peptide structures related to cell-wall peptidoglycan from bacteria" is provided by D. Keglevič (Zagreb, Yugoslavia), and J. C. Braekman and D. Daloze (Brussels, Belgium) have written a stimulating account of "Chemical defense in ants". "Some aspects of heterocyclic chemistry related to isoquinoline-derived alkaloids" are reviewed by J. B. Bremner (Hobart, Tasmania, Australia). The account of "Alkaloids of *Strychnos dinklagei*: structure and chemistry" by S. Michel, F. Tillequin, and M. Koch (Paris, France) includes an interesting discussion of the recently discovered iridolactams. Finally, a diversified chapter on "Chiral synthesis of natural products as semiochemicals and bioregulators" by T. Kitahara (Tokyo, Japan) proved particularly enjoyable to the reviewer.

Some of the shortcomings characteristic of earlier volumes in this series persist. There is still no author index. There is no uniformity of typeface or style for presenting structural formulas. The quality of the English remains far from even. On the other hand, the chapters are impressively up-to-date, with many recent literature references. Any organic chemist is likely to find much of the material both interesting and stimulating. The editor has once more done an excellent job of identifying and recruiting a genuinely international array of authors, all of whom have carried out their assignments admirably!

Baker Laboratory **Jerrold Meinwald**
Cornell University
Ithaca, New York 14853

ACS Symposium Series 418. Marine Toxins: Origin, Structure and Molecular Pharmacology. Edited by Sherwood Hall and Gary Strichartz. American Chemical Society, Washington, DC. 1990. xi + 377 pp. 16 × 23.5 cm. ISBN 0-8412-1733-5. $74.95.

Natural product toxins make interesting reading for people of several disciplines and this volume on marine toxins is no exception. For as anyone knows who has looked at volumes on poisonous and venomous marine animals and plants such as Halstead's *Poisonous and Venomous Marine Animals of the World* (Darwin Press, 1988), the oceans have many organisms which produce potent and at times lethal biotoxins and other pharmacologically active secondary metabolites. This volume is not comprehensive in its covering of the topic, but it does include chapters on many important toxic marine groups and certainly

those undergoing the most active research.

This book was developed from a symposium held in Woods Hole, Massachusetts under the auspices of the Commission of Food Chemistry, Applied Chemistry Division, International Union of Pure and Applied Chemistry (IUPAC) and sponsored through an interagency agreement between the U.S. Army Medical Research Institute of Infectious Diseases and the Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration. Twenty-seven chapters by 84 researchers in the field of natural product toxins are assembled in this text. The editor's stated goal is to bring together in a single volume topics of interest to the biologist, chemist, and pharmacologist/toxicologist on the most important marine toxin groups and to emphasize structure, metabolic origin, and molecular basis of toxicity. While any volume that is edited is difficult to hold to such a defined set of objectives, the contents of the various chapters do a reasonable job of adhering to these goals.

The book's 27 chapters are divided into four parts. The first part is entitled General Considerations and includes review type chapters on some of the more actively researched problems of marine toxins. These include the red tide toxins (paralytic shellfish poisons) and cyanobacteria (blue-green algae) toxins. While this later topic of cyanobacteria toxins deals mostly with freshwater cyanotoxins (in this regard one should note that the chemical structure of microcystin-LA illustrated on the jacket design is from the freshwater cyanophyte *Microcystis*), it does cover the marine cyanotoxins. This first part of the book also begins with a good review of membrane channels, particularly sodium channels, and their study by the use of selected marine biotoxins such as brevetoxin, *Anemonia* toxin, conotoxin, tetrodotoxin, and saxitoxin.

The second part covers the polyether toxins including ciguatera toxins, and brevetoxins. This section is somewhat out of date since it does not include the absolute structure of ciguatoxin which was published between the time the conference was presented and publication of this book (see: Murata et al. *J. Am. Chem. Soc.* **1989**, *111*, 8929; **1990**, *112*, 4380.). Part three of the book is entitled Palytoxin and includes six chapters dealing with all aspects of this very potent non-protein polyether toxin produced by the coelentrate genus *Palythoa*.

The final part includes selected peptide toxins of marine organisms. The eight chapters in this section focus mostly on the polypeptide toxins of sea anemone but the section also includes excellent chapters on conotoxins (sea snails), jellyfish toxins, and sea snake neurotoxins. Also included is an interesting chapter on pardaxin, a neurotoxic peptide secreted by marine flatfish which has the interesting property of being a shark repellent. Finally, in this section is a good review type chapter on marine invertebrate toxins that might have, however, been more appropriate in the first part of this book.

This volume will undoubtedly appeal to a diverse audience. It certainly held this reviewers attention and added to his understanding of marine toxins. It is unfortunate, however, that the book took over 2 years to reach publication from the time the symposium was held. In this fast-moving area of marine natural product toxins it meant that some chapters are out of date despite a certain amount of updating during the course of the publication process.

Department of Biological Sciences **Wayne W. Carmichael**
Wright State University
Dayton, Ohio 45435

Atherosclerosis Reviews. Volume 20. Biotechnology of Dyslipoproteinemias. Edited by Claude Lenfant, Alberto Albertini, Rodolfo Paoletti, and Alberico L. Catapano. Raven Press. New York. 1990. XX + 380 pp. 15 × 23.5 cm. ISBN 0-88167-616-0. $90.00.

This multiauthored book contains 37 chapters ranging in length from 6 to 14 pages. This volume presents the proceedings of the international symposium entitled "Biotechnology of Dyslipoproteinemias: Clinical Applications in Diagnosis and Control" held in Milan, Italy, May 8–10, 1989.

The book is divided into seven major areas, including: Molecular Biology of Plasma Apolipoproteins, Enzymes and Receptors Involved in Lipoprotein Metabolism, Aspects of Clinical Relevance, Techniques for Analysis of Dyslipoproteinemias, Methods for the Determination and Characterization of Plasma Apolipoproteins, Application of Molecular Biology to Medicine, and Lipid and Hemoreologic Factors of Atherosclerosis. The first two sections are highly technical, describing, for example, recent advances in the biosynthesis and processing of apolipoproteins B-100 and B-48 as well as characterizing apolipoprotein mutants and genetic defects in apoC-II deficient states. Of special interest are chapters dealing with the structure and function of acylcoA:cholesterol acyltransferase (ACAT) and receptor–ligand interactions with the low density lipoprotein receptor. These are areas that are continuing to attract attention in the research community.

The chapters dealing with aspects of clinical relevance describe clinical results with a number of lipid-regulating agents, including most of the commonly used agents. An interesting chapter describes the role of peripheral hyperinsulinemia and Na/H exchange in hypertension and atherosclerotic risk in insulin-dependent diabetic patients.

The next three topics in this volume describe techniques and methods currently used in the analysis of dyslipoproteinemias and the quantitative determination and characterization of plasma apolipoproteins. Since the technology in these areas is rapidly changing, their description are a welcome addition to this text. Specific areas discussed include new electrophoretic methods useful for the detection of apolipoprotein variants, the characterization of plasma lipid transfer proteins, application of monoclonal antibodies and synthetic peptides to apolipoprotein immunoassays, etc.

The last chapter is a potpourri of topics, including a discussion on predictive hemostatic (rheological) factors related to atherosclerotic ischemic events as well as several chapters describing the clinical efficacy of bezafibrate. The last chapter describes the initial results of an ongoing study in Brisighella, Italy, in which over 1000 residents are participating. In this study in which nutrition and education are of primary importance in reducing the risk of atherosclerosis, a 16% reduction in total plasma cholesterol was observed following the first year of the study.

This book is printed in a photo-offset style and one has to get used to reading different typefaces. Although a number of typographical errors do exist, the book is well-written considering the large number of authors. The references are up-to-date and timely. This book is of most interest to researchers active in this area and will provide an up-to-date summary of a number of interesting areas.

Wyeth-Ayerst Research **Dennis M. Ackerman**
CN 8000
Princeton, New Jersey 08543-8000

Design of Anti-AIDS Drugs. Edited by E. De Clercq. Elsevier Science Publishers B.V., The Netherlands. 1990. x + 372 pp. 17 × 24.5 cm. ISBN 0-444-88179-4. $143.50.

This is the 14th volume in a series entitled *Pharmacochemistry Library* edited by H. Timmerman. Whereas most volumes have been reports of proceedings, the present volume (edited by E. De Clercq) is an excellent up to date multiauthored review of drugs that have been or are being studied for their activity against HIV-1, the virus responsible for AIDS. Of the 13 chapters presented, Dr. E. DeClercq is author or coauthor of six, which is a reflection of the extent of his contributions in this area.

The title of the book could be misinterpreted, since it does not inform as to how to design anti-AIDS drugs, but rather what targets have been identified and hence, are available for attack, what compounds have been evaluated, and, where known, the biochemical basis for their antiviral activity.

The compounds discussed include modifications of natural nucleosides, various acyclic and carbocyclic nucleoside analogues, CD4 derivatives, polyanionic compounds, benzodiazepine derivatives, antisense oligodeoxyribonucleotides, and inhibitors of protein cleavage and glycosylation.

Various new nucleoside analogues, such as allenic 4′-hydroxy-1′.2′-butadienyl derivatives of purine and pyrimidine, oxetanocin and carbocyclic oxetanocin derivatives, carbovir (C-

D4G), 6-substituted acyclouridine derivatives (HEPT), and nucleoside analogues containing 3'-S or 3'-O atom in the sugar moiety (NGPB-21 and DD111-30A, respectively), have been described and reviewed in this book. These new nucleoside analogues were found to be active against HIV replication in vitro, some of which also inhibited the replication of retrovirus in vivo. Several new classes of compounds have been found to have potent and selective antiretrovirus activity. The syntheses and studies of these novel nucleoside analogues may lead to the discovery of a new class of anti-HIV therapeutic agents.

Compounds to date have been evaluated in cell culture systems, and the need for an appropriate animal model has been addressed by Ruprecht. A brief review of clinical studies of some of the anti-HIV-1 agents is presented by Richman.

This book will be of value to those contemplating drug development for therapy of AIDS, as well as those in the field who wish to be brought up to date in areas related to their interests.

Department of Pharmacology and Comprehensive Cancer Center
Yale University School of Medicine
New Haven, Connecticut 06510
Tai-Shun Lin

Books of Interest

Acid-Base Catalysis. Edited by K. Tanabe, H. Hattori, T. Yamaguchi, and T. Tanaka. VCH Publishers, Inc., New York. 1989. xviii + 532 pp. 18 × 25.5 cm. ISBN 0-89573-891-0. $140.00.

Immunology: Clinical, Fundamental, and Therapeutic Aspects. Edited By Bhanu P. Ram, Mary C. Harris, and Praveen Tyle. VCH Publishers, Inc., New York. 1990. x + 364 pp. 16 × 24 cm. ISBN 0-89573-763-9. $75.00.

Enzymes in Industry. Production and Applications. Edited by Wolfgang Gerhartz. VCH Publishers, Inc., New York. 1990. xvii + 321 pp. 18 × 24.5 cm. ISBN 0-89573-937-2. $85.00.

Advances in Second Messenger and Phosphoprotein Research. Volume 24. Edited by Yasutomi Nishizuka, Makoto Endo, and Chikako Tanaka. Raven Press, New York. 1990. xxxiii + 750 pp. 16.5 × 24 cm. ISBN 0-88167-670-5. $99.00.

Biosynthesis of Branched Chain Amino Acids. Edited by Z. Barak, D. M. Chipman, and J. V. Schloss. VHC Publishers, Inc., New York. 1990. xi + 530 pp. 18 × 24.5 cm. ISBN 0-89573-961-5. $120.00.

Control of Virus Diseases. Society for General Microbiology. Symposium 45. Edited by N. J. Dimmock, P. D. Griffiths, and C. R. Madeley. Cambridge University Press, New York. 1990. x + 373 pp. 16 × 23.5 cm. ISBN 0-521-38562-8. $85.00.

Protein Purification From Molecular Mechanisms to Large-Scale Processes. ACS Symposium Series 427. Edited by Michael R. Ladisch, Richard C. Willson, Chih-duen C. Painton, and Stuart E. Builder. American Chemical Society, Washington, DC. 1990. vii + 280 pp. 16 × 23.5 cm. ISBN 0-8412-1790-4. $64.95.

Chlamydial Infections. Proceedings of the Seventh International Symposium on Human Chlamydial Infections. Harrison Hot Springs, British Columbia, Canada, June 24–29, 1990. Edited by William R. Bowie, Harlan D. Caldwell, Robert P. Jones, Per-Anders Mardh, Geoff L. Ridgway, Julius Schachter, Walter E. Stamm, and Michael E. Ward. Cambridge University Press, New York. 1990. xxi + 602 pp. 19 × 25.5 cm. ISBN 0-521-39082-6. $80.00.

Nutrition and the Brain. Volume 8. Edited by Richard J. Wurtman and Judith J. Wurtman. Raven Press, Inc., New York. 1990. ix + 203 pp. 16 × 24 cm. ISBN 0-88167-628-4. $85.00.

Mutation and the Environment. Part A. Volume 340A. Basic Mechanisms. Edited by Mortimer L. Mendelsohn and Richard J. Albertini. Wiley & Sons, Inc., New York. 1990. xx + 413 pp. 16 × 23.5 cm. ISBN 0-471-56791-4. $110.00.

Mutation and the Environment. Part B. Volume 340B. Metabolism, Testing Methods, and Chromosomes. Edited by Mortimer L. Mendelsohn and Richard J. Albertini. Wiley & Sons, Inc., New York. 1990. xx + 496 pp. 16 × 23.5 cm. ISBN 0-471-56792-2. $110.00.

Mutation and the Environment. Part C. Volume 340C. Somatic and Heritable Mutation, Adduction, and Epidemiology. Edited by Mortimer L. Mendelsohn and Richard J. Albertini. Wiley & Sons, Inc., New York. 1990. xviii + 423 pp. 16 × 23.5 cm. ISBN 0-471-56794-9. $110.00.

Mutation and the Environment. Part D. Volume 340D. Carcinogenesis. Mortimer L. Mendelsohn and Richard J. Albertini. Wiley & Sons, Inc., New York. 1990. xviii + 403 pp. 16 × 23.5 cm. ISBN 0-471-56796-5. $110.00.

Mutation and the Environment. Part E. Volume 340E. Environmental Genotoxicity, Risk, and Modulation. Edited by Mortimer L. Mendelsohn and Richard J. Albertini. Wiley & Sons, Inc., New York. 1990. xviii + 385 pp. 16 × 23.5 cm. ISBN 0-471-56797-3. $110.00.

USAN and the USP Dictionary of Drug Names. 1961–1990 Cumulative List. Edited by William M. Heller and Carolyn A. Fleeger. The United States Pharmacopeial Convention, Inc., Rockville, MD. 1990. 804 pp. 23 × 28 cm. ISBN 0-913595-50-0. $85.00.

Neuromethods. 15. Neurophysiological Techniques. Applications to Neural Systems. Edited by Alan A. Boulton, Glen B. Baker, and Case H. Vanderwolf. The Humana Press, Clifton, NJ. 1990. xiii + 377 pp. 16 × 23.5 cm. ISBN 0-89603-185-3. $79.50.

Chemical Technician's Ready Reference Handbook. Third Edition. By Gershon J. Shugar and Jack T. Ballinger. McGraw-Hill Publishers, New York. 1990. xix + 889 pp. 19.5 × 24.5 cm. ISBN 0-07-057183-X.

Methods in Enzymology. Volume 187. Arachidonate Related Lipid Mediators. Edited by Robert C. Murphy and Frank A. Fitzpatrick. Academic Press, San Diego, CA. 1990. xxxviii + 683 pp. 16 × 23.5 cm. ISBN 0-12-182088-2. $85.00.

Biopharmaceutics and Clinical Pharmacokinetics. Fourth Edition. By Milo Gibaldi. Lea & Febiger, Philadelphia. 1991. x + 406 pp. 19 × 27 cm. ISBN 0-8121-1346-2. $35.00.

Spectral and Chemical Characterization of Organic Compounds. Third Edition. A Laboratory Handbook. By W. J. Criddle and G. P. Ellis. John Wiley & Sons, New York. 1990. xiii + 119 pp. ISBN 0-471-92715-5. $49.95.

Calcium and the Heart. By Glenn A. Langer. Raven Press, New York. 1990. xiv + 387 pp. 16 × 24 cm. ISBN 0-88167-617-9. $80.00.

Manual of Laboratory Immunology. Second Edition. Edited by Linda E. Miller, Harry R. Ludke, Julia E. Peacock, and Russell H. Tomar. Lea & Febiger, Philadelphia. 1991. xiv + 427 pp. 18 × 25.5 cm. ISBN 0-8121-1319-5. $39.50.

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International Reporting of Adverse Drug Reactions. Final Report of CIOMS Working Group. Edited by World Health Organization, Geneva. 1990. 66 pp. 16 × 24 cm. ISBN 92-9036-042-9. $8.00.

WHO Expert Committee on Specifications for Pharmaceutical Preparations. 31st Report. Edited by World Health Organization, Geneva 1990. 79 pp. 14 × 20 cm. ISBN 92-4-120790-6. $7.20.

Enzyme Chemistry. Impact and Applications. Second Edition. Edited by Colin J. Suckling. Chapman and Hall, New York. 1990. xii + 383 pp. 16 × 24 cm. ISBN 0-412-34970-1. $79.95.

Drug Bioscreening. Drug Evaluation Techniques in Pharmacology. By Emmanuel B. Thompson. VCH Publishers, Inc., New York. 1990. xiii + 366 pp. 16 × 18 cm. ISBN 0-89573-730-2. $35.00.

Nutrients and Cancer Prevention. Edited by Kedar N. Prasad and Frank L. Meyskens, Jr. The Humana Press, Inc., Clifton, New Jersey. 1990. xvi + 347 pp. 16 × 23 cm. ISBN 0-89603-171-3. $89.50.

Potassium Channels. Basic Function and Therapeutic Aspects. Edited by Thomas J. Colatsky. Wiley-Liss Division, New York. 1990. xiv + 348 pp. 16 × 23.5 cm. ISBN 0-471-56714-0. $79.50.

Computer Modeling of Carbohydrate Molecules. Edited by Alfred D. French and John W. Brady. American Chemical Society, Washington, DC. 1990. ix + 406 pp. 16 × 23.5 cm. ISBN 0-8412-1805-6. $84.95.