Book Reviews

A Wandering Natural Products Chemist. By Koji Nakanishi. American Chemical Society, Washington, DC. 1991. xxiii + 230 pp. 15 × 23 cm. ISBN 0-8412-1775-0. $24.95.

In 1990, the American Chemical Society, under the editorship of Jeffrey I. Seeman, initiated publication of *Profiles, Pathways, and Dreams*, a series of autobiographies of eminent chemists. The 10th volume of this 22-volume series is by Koji Nakanishi, seminal organic chemist and professor at Columbia University. Professor Nakanishi's free thinking and exuberant personality are illustrated in the style of his science and the philosophies expressed in his stories. He has contributed significantly to the development of various spectroscopic methods in organic chemistry and has been a pioneer in the elucidation of structure and mechanism in complex, unstable, and biologically active natural products. His well-known talents as a magician are also described in this fascinating book. Many photographs reflect both the professional and personal side of this highly renowned chemist.

The overall objectives of the series—to confirm the admiration of those who personally know the author and to inspire and encourage, both in science and in life, those who do not personally know him are—well met in this volume. All chemists will find this a fascinating, entertaining, and inspiring book to read.

Staff

Receptors in the Human Nervous System. Edited by F. A. O. Mendelsohn and George Paxinos. Academic Press, Inc., San Diego, CA. 1991. xiv + 258 pp. 19.5 × 23.5 cm. ISBN 0-12-490830-6. $75.00.

This compendium of nine chapters by world experts in receptor autoradiography brings together some of the latest information concerning neurotransmitter receptor localization in the human nervous system. As noted by the editors "while...there have been many reports of the distribution of receptors in the human central nervous system, there has been no integration of this information in one volume". For the systems that are addressed in "Receptors" the book achieves this goal quite admirably. I liked it, and hope the editors/authors will provide additional volumes on neurotransmitters not described in the present work.

The subject matter in "Receptors" deals with what most would refer to as the "classical neurotransmitters". Following the brief introductory remarks (Kuhar), individual chapters address the regional distribution of amino acid (GABA, glutamate, benzodiazepine; Young and Penney; chapter 2), acetylcholine, serotonin, β-adrenergic (Beigon, chapter 3; Pazos et al., chapter 4), opioid (Quirion and Pilapil, chapter 5) and angiotensin II receptors (Allen et al., chapter 6). These are followed by the S. Y. Chai et al. contribution drawing the reader's attention to the use of autoradiography to study nonreceptor systems in the brain (angiotensin-converting enzyme). Chapters 8 (Zilles) and 9 (Faull et al.) provide a cohesive ending by discussing the codistribution and localization of receptors in the brain.

The chapters are similar in format and between 20 and 30 pages in length. Each contains an introductory statement, an abbreviated methodological section, and the core material describing receptor distribution. Most end with a discussion of the data as well as brief concluding remarks on relevance or future directions. Although targeting the human nervous system, contributors made frequent comparisons to studies using nonhuman tissue, and these are useful in considering the translation of laboratory research to clinical settings. Additionally, the authors were not shy in pointing out both the power and limitations of autoradiographic methods or in attempting to link their observations to both normal and pathological chemical neurotransmission. The book contains a tremendous number of photographs and tables as well as all the essential references (current through 1990). The 14-page index is more than adequate to facilitate the quick location of topics of particular interest.

Receptors in the Human Nervous System was directed toward "researchers in the field of chemical neuroanatomy,...pharmacologists, neurophysiologists and neuroscientists". To this list I would add molecular neurobiologists, neurologists, psychiatrists, and other interested clinicians. Although somewhat pricey at $75.00, the book would also be an excellent accompaniment to medical or graduate student courses in human neuroanatomy. I most certainly recommend it be available at least in the department library.

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New Perspectives in Histamine Research. Agents and Actions Supplements. Volume 33. Edited by H. Timmerman and H. van der Goot. Birkhauser Verlag, Boston, MA. 1991. 434 pp. 17 × 24 cm. ISBN 0-8176-2507-0. $108.00.

There is nothing like a new receptor subtype to breathe new life into a biogenic amine! This was certainly true for histamine in the early 1970s, with the discovery of H_2 receptors, and their antagonists, and the same may be true for histamine H_3 receptors in the late 1980s with the discovery of highly selective ligands for this new subtype. The discovery of the H_3 receptor, which appears to control the synthesis and release of histamine in brain and some peripheral tissues, is just one realization responsible for a growing interest in the possible new biological roles for histamine throughout the body, including the brain, immulogic and neuroendocrine functions. The holding of a symposium on "New Perspectives in Histamine Research", as a satellite to the XIth International Congress of Pharmacology in the Netherlands, in 1990, was therefore timely.

The proceedings of the symposium provide an excellent record of the meeting. The editors have done a good job in compiling manuscripts from all the lectures presented

0022-2623/92/1835-4643$03.00/0

at the symposium. These include papers from the plenary lectures, on the histaminergic neuron system (Wada), neuroendocrine function (Knigge), the histamine H_3 receptor, including clinical implications of agonists (Arrang), lung receptors (Barnes), novel [^{125}I] probes (Ruat), transduction systems (Hill), astrocyte H_1 receptors (Fukai), nonsedative antihistamines (Barnett), antagonists in anesthesia (Lorenz), H_2 agonists as inotropes (Buschauer, Baumann), intracellular histamine receptors (Brandes), brain histamine metabolites (Green), and lymphocyte specific histamine derivatives (Khan). Papers based on some of the other lectures that may be of particular interest to medicinal chemists include SAR of some novel chiral H_3 agonists (Lipp), new selective H_2 agonists based on thiazolylalkylamines (Ericks), and theoretical analysis of some H_2 agonists (Haaksma).

The editors are to be commended on the prompt publication of the full symposium proceedings. However, inevitably, significant developments in histamine research have occurred subsequent to the meeting. These include the successful cloning of both H_1 and H_2 receptors. New high-affinity ligands for H_3 receptors have also been described. There are undoubtedly further exciting times ahead for histaminologists and indeed all scientists with an interest in the biogenic amine histamine.

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Progress in Basic and Clinical Pharmacology. Volume 7. β-Adrenoceptors: Molecular Biology, Biochemistry and Pharmacology. Edited by Robert R. Ruffolo, Jr. S. Karger AG, Basel. 1991. xii + 240 pp. 17 × 24 cm. ISBN 3-8055-5366-8. $196.00.

Exponential advances in our understanding of the molecular structure and function of β-adrenergic receptors have been achieved during the past few years. Three subtypes have been identified and additional ones may be anticipated. The first section of the book describes the subclassification of β-adrenoceptors. Major advances in the molecular biology of these receptors, i.e. their molecular structure and biochemical functions, are reviewed in the second section. In the third part of the book, "β-adrenoceptor signal transduction", important advances regarding the biochemical events associated with the signal-transduction processes activated via the G-protein-coupled β-adrenoceptors, and which ultimately result in the end-organ response, are explored in detail. Structure–activity relationships among agonists and antagonists of β-adrenoceptors are comprehensively reviewed in the next section. In the final two sections the functions mediated by activation of β-adrenoceptors and the therapeutic applications of agents that interact with these receptors are described.

This volume comprehensively reviews β-adrenoceptors in very broad scope ranging from the intracellular level of the nucleus, including the messenger RNA that encodes for these receptors, through the biochemical processes they activate or block through the effects mediated in intact organs and animals both in normal and disease states. This well-organized review of the most recent literature relating to β-adrenoceptors will be of interest to not only medicinal chemists but also molecular and cellular biologists, biochemists, physiologists, and pharmacologists concerned with this field of research.

Staff

Pharmacology. Second Edition. By H. P. Rang and M. M. Dale. Churchill Livingstone Inc., New York. 1991. 955 pp. 18.5 × 24.5 cm. ISBN 0-443-04110-5. $48.00.

Presented in this text is a concise overview of the principles of drug action and the properties of therapeutic agents. Emphasis is placed on fundamental biological concepts, with fully one-third of the volume devoted to basic principles of pharmacology, and a description of the anatomical, biochemical, and physiological characteristics of neurotransmitter and hormone systems. While drug action is discussed in the context of the molecular and biochemical effects of these agents, physiological responses and the interplay of organ systems are stressed. Authored by two highly respected scientists, the subject is presented in a clear and consistent manner, facilitating an understanding of the topic as a whole. Given the breadth of the field, it is not surprising that the book is uneven in its treatment of topics, reflecting the biases and strengths of the authors. Readers interested in neuropharmacology will find a wealth of information, with almost 200 pages devoted to this subject. There is less discussion of other drug classes, with cardiovascular pharmacology and chemotherapeutics covered in approximately 100 pages each.

In this second edition, new sections have been added on peptides, serotonin, amino acid neurotransmitters, cytokines, and the chemotherapy of AIDS. In their zeal to be current, the authors have included experimental agents that are undergoing, or that will soon enter, clinical trials. Risks inherent in this approach, however, are evidenced by the fact that some of these substances are no longer clinical candidates. Nonetheless, by including such agents the authors provide a sense of direction for new therapies.

In summary, *Pharmacology* is an excellent introductory text that will be of value to students and others interested in an overview of the topic from a biological perspective. This would include chemists seeking an understanding of the issues involved in the drug discovery process. Because the text emphasizes basic principles and preclinical assays as opposed to therapeutics, it will be most useful for undergraduates or in an introductory course for graduate students.

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Three-Dimensional Chemical Structure Handling. By Peter Willett. Research Studies Press Ltd., Taunton, Somerset, England. 1991. xiv + 241 pp. 15.5 × 23 cm. ISBN 0-471-93108-X. $89.95.

This book is a primer on the subject of substructure searching at the 2-D and 3-D levels. It is broken up into

0022-2623/92/1835-4644$03.00/0

discrete topics including Chemical Structure Handling Techniques, Substructure Searching in Small Molecules, Maximal Common Substructure Searching in Small Molecules, Searching in Macromolecules, and Parallel Processing Techniques.

The book provides sufficient background and detail in each chapter to enable the reader to gain a useful if not working insight into the subject. Examples are provided along with discussions of existing program packages used in this work. The conclusion chapter emphasises that the 2-D graph theoretical techniques developed 2 decades ago are now equally applicable for the representation and searching of 3-D molecules both small and large. Some challenging problems still to be solved are described. The book is a very valuable addition to the library of anymore working in information processing and database analyses.

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Protein Architecture: A Practical Approach. By Arthur M. Lesk. Oxford University Press, New York. 1991. 287 pp. ISBN 0-19-963055-0. $65.00.

This book contains six richly illustrated chapters and three appendices. The first chapter gives an introduction to molecular graphics for the uninitiated chemist, molecular biologist, or other scientist not yet using these tools in their work. It also gives an overview of X-ray crystallography and the protein data bank, including a discussion of the accuracy of the structures, all at an elementary level.

The second and third chapters contain descriptions of the geometric relationships between a molecular space to viewing space on a graphics screen. The second chapter deals with bond representations, as opposed to atom representations, giving an overview of the creation of a graphics "picture" from the atomic coordinates. The third chapter discusses the representation of atoms and contrasts the quality of the drawings produced on vector graphics devices as opposed to passive raster devices. It also describes how to represent tertiary structural interactions.

The fourth chapter, entitled Pattern and Form in Protein Structure, classifies protein structures in terms of topology and discusses how these topologies are represented on a graphics screen. There is a thorough discussion of secondary and tertiary graphics representations. Several protein topologies, protein–ligand interactions, and a DNA–protein complex are illustrated with beautiful color photographs.

Chapter five, Structure Comparison and Structural Change, promises what it delivers by discussing how to productively compare protein structures using computer graphics. Changes in structure by changes in ligation state or chain cleavage are also discussed. This chapter finishes by describing the structural relationships among related proteins. Chapter six very briefly describes the molecular graphics programs which are available for purchase. Three appendices are included which are very helpful. The first is a bibliography of protein structure determinations, corresponding to the coordinate sets deposited in the Protein Data Bank. The second appendix contains a typical table of entries from a recent Protein Data Bank newsletter, first classed by function, then classed as listed in the actual newsletter. The last appendix contains an atlas of protein folding patterns for the backbones of many proteins. The author comments that he is reminded of Goethe's remark that "architecture is frozen music" by looking at such structures, a quote that was clearly inspiration for the book's title.

This book is recommended for the beginner in molecular graphics, and for someone who desires a ready reference guide. It fills a need for basic information while keeping the reader interested with beautiful illustrations and imaginative analogies.

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Lipoxygenases and Their Products. Edited by Stanley T. Crooke and Angela Wong. Academic Press, San Diego, CA. 1991. xii + 300 pp. 15.5 × 23 cm. ISBN 0-12-197800-1. $59.00.

One has at least two expectations of a multi-authored book covering a fast-moving field of science: the contributions will be of uneven quality and the material covered will be outdated. Lipoxygenases and their products, edited by Crooke and Wong, delivers on both of these expectations. The goal of the editors in producing this book was to provide a broad review of lipoxygenases as therapeutically important targets for drug discovery, and they have enlisted a number of experts in the field to achieve this aim. A number of the contributions are of high quality, but all suffer from having apparently being written in early 1988. Thus, most of the information presented is stale and frequently irrelevant.

The book is divided into 10 chapters that cover the biology of lipoxygenase products, enzymology of lipoxygenases with a clear emphasis on 5-lipoxygenase, 5-lipoxygenase inhibitors, and leukotriene receptors and receptor antagonists. This is a fair representation of the field and if the information were current could be a valuable addition to one's library. Ford-Hutchinson's well-written chapter on development of 5-lipoxygenase inhibitors illustrates the promise and problems of this type of book; it contains an excellent review of the role of leukotrienes in disease, but contains no mention of the newer nonredox 5-LO inhibitors such as zileuton and D-2138, nor does it cover the inhibitors of 5-LO activating protein (FLAP) pioneered at his company. Similarly, the chapter by Rouzer is a competent review of the discovery of 5-LO, but contains no reference to FLAP and covers much the same ground as two other chapters.

There are a few nuggets in the book that are worth a look. DeWolf presents a lucid discussion of the enzymology of 5-LO, and Wong and Crooke's chapter on the regulation of 5-LO in cells is well-done (and does mention FLAP). It is ironic that, in a book about enzymes, one of the best sections concerns receptors. The biology of leukotriene receptors is covered in an argumentative but nevertheless worthwhile chapter by Mong, whose application of Occam's razor to the receptor field (he believes that only a single receptor exists for LTB4 and another for the peptidol-

0022-2623/92/1835-4645$03.00/0

eukotrienes) is thought provoking, but perhaps a bit premature; if anything has been learned about G-protein-coupled receptors recently it is that multiple receptor subtypes are the rule, not the exception. The only chapter with a medicinal chemistry slant is that by Lewis, Krell, and Jones covering leukotriene receptor antagonists from SKB, ICI, and Merck. The material here is somewhat fresher, as the ICI and Merck compounds remain of clinical interest. For the most part, the other contributions can be avoided, although some contain exhaustive reference lists that could be useful.

It is revealing to note what is missing from this book: discussion of FLAP and FLAP antagonists, LTB4 receptor antagonists, second- and third-generation 5-LO inhibitors, the role of leukotrienes in inflammation (!) and results of clinical trials with 5-LO inhibitors and LTD4 receptor antagonists. If this is the kind of information you desire, then look elsewhere. Is the book worth a couple of hours on an idle afternoon? Yes, but be aware that nearly 4 years have passed since most of the information presented here was published. For readers interested in a thorough review of 5-LO inhibitors, I recommend the Perspective by Musser and Kreft in this journal's July 10, 1992 issue.

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Computer Modeling of Chemical Reactions in Enzymes and Solutions. By Arieh Warshel. John Wiley & Sons, Inc. New York. 1991. xiv + 236 pp. 16.5 × 24 cm. ISBN: 0-471-S3395-5. $90.00.

The book is written as a primer for the study of enzyme mechanisms using computer analysis. The subject is developed in a systematic way beginning with the first three chapters on principles of chemical bonding, chemical reactions in gas phase, and simple solvents and chemical reactions in all-atom solvent models. This is followed by chapters on potential surfaces, modeling reactions in enzymes, general acid catalysis, different mechanistic options, and simulating metalloenzymes. A final chapter on how enzymes really work is thought provoking. The book is not a full-fledged resource book but is designed to develop the subject in a sequential manner. Illustrations references and computer programs add to the utility of the book as a text. It is recommended for scientists entering the field of enzyme studies using computer modeling.

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Progress in Medicinal Chemistry. Volume 29. Edited by G. P. Ellis and D. K. Luscombe. Elsevier Science Publishers B.V., Amsterdam. 1992. viii + 350 pp. 15.5 × 21 cm. ISBN 0-444-89472-1. $168.50.

The 29th volume of this well-known series presents eight expert reviews that focus on the relationships between chemical structure and pharmacological activity in a variety of areas of current interest in medicinal chemistry and pharmacology. Specific topics reviewed are (1) 5-lipoxygenase inhibitors and their anti-inflammatory activities, (2) an overview of class III electrophysiological agents as a new generation of antiarrythmic therapy, (3) chemical structures and biological activities of non-peptide selective κ opioid ligands, (4) pharmacologically active pyridazine derivatives, (5) centrally acting dopamine D_2 receptor agonist ligands, (6) progress in the medicinal chemistry of the herb feverfew, (7) ondansetron and related 5-HT_3 antagonists, and (8) synthetic inhibitors of bacterial and mammalian interstitial collagenases. Each chapter is followed by a compilation of references. A subject index for this volume and cumulative indexes of both subjects and authors of topics covered in volumes 1–29 are included.

As with other volumes of the *Progress in Medicinal Chemistry* series, medicinal chemists will benefit from at least institutional access to these expert reviews. Specialists involved in the areas covered in this volume may want a personal copy.

Staff

Enantiomeric Synthesis: Natural Products from Chiral Terpenes. By Tse-Lok Ho. John Wiley & Sons, Inc., New York. 1992. xii + 324 pp. 16.5 × 24 cm. ISBN 0-471-54819-7. $69.95.

This is a refreshing book. It is not still another collection of vaguely related essays by a group of authors who participated in the "*N*th International Congress of the Chemistry of Whatever", but rather a coherent, well-written, up-to-date account, by a single author, of how a very wide variety of naturally occurring compounds have been synthesized in optically active form from readily available terpene precursors. The literature coverage is excellent, with many 1990 references included.

The organizing principle of the book is simple and successful: each chapter discusses syntheses based on a single starting material or a group of closely related starting materials. In his account of each synthesis, the author provides a brief rationalization of the steps involved. Since much of the primary literature is published only in the form of brief communications, these explications will be welcomed by many readers who might otherwise have difficulty in appreciating what has actually been done. Structural formulas are given in abundance, making it relatively easy to follow each synthesis.

A good subject index allows the reader to look up any desired target compound that may be discussed. While there is no author index, the listing of all references, alphabetically by first author, at the end of the volume serves almost the same purpose.

While the title of Prof. Ho's book suggests that it is extremely specialized, this is not really the case. Each starting material has been used by the organic chemistry community in so many imaginative ways that a very useful graduate course in organic synthesis could easily be given using this book as a text, providing that the necessary background information for many of the reactions were filled in. The amount of information packed into little more than 300 pages is impressive, and the author is to be congratulated on seeking out and presenting an enormous

0022-2623/92/1835-4646$03.00/0

amount of fascinating organic chemistry in an attractive and enjoyable format!

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Prodrugs, Topical and Ocular Drug Delivery. Drugs and the Pharmaceutical Sciences, Volume 53. Edited by Kenneth B. Sloan Marcel Dekker, Inc., New York. 1992. 313 pp. ISBN 0-8247-8629-7. $99.75.

This volume in the series *Drugs and the Pharmaceutical Sciences* contains seven chapters which are rather uneven in distribution, length, and content. Six of the chapters deal with dermal–transdermal drug delivery, and only one, the last one, describes ocular drug delivery. Approximately one-half of the section of the text that discusses dermal issues has been contributed by the editor (125 pages).

The first chapter is basically a brief introduction describing the theory of percutaneous drug delivery, and some implications of the use of the prodrug approach for delivering a drug containing a carboxylic acid group. The authors conclude that the likelihood that one molecule may possess all the desired attributes for successful delivery via the prodrug approach may be small.

Chapter 2, by far the largest (100 pages), describes in detail various attempts to enhance percutaneous drug delivery using prodrugs. However, there are several basic issues that are either unresolved and/or not addressed.

Although it is recognized that in general, the assumption that increased transdermal delivery may not correlate with increased dermal delivery, the majority of the methods and approaches discussed look at transdermal delivery, even when the objective was, in fact, dermal delivery. Furthermore, while it is mentioned that chemical, as well as enzymatic, processes could activate the prodrug, it is generally accepted that enzymatic activation of the prodrug is the most desired. Accordingly, a notable omission in the entire text is the lack of discussion of the various enzymes which exist in dermal tissues. This omission is particularly important since it should form the basis for the design of any prodrug based on enzymatic activation. In addition, it should be extremely important also to address the differences that exist in the enzyme activities between various species, as well as the time dependence on enzyme activities, i.e. the differences in enzyme activity between skin that has been freshly excised and skin that has been incubated for several days.

The author provides an interesting classification of prodrugs based on the structure of the drug. Unfortunately, all of the classes described represent hydrolytically sensitive prodrugs only, while other types of enzymatic reactions which might be useful in the design of dermatological prodrugs are not mentioned at all. It is implied for drugs containing a basic amino group that no molecular modifications are necessary to improve drug delivery since they are readily absorbed. Therefore, emphasis is directed toward modification of the "acidic" NH function. For example, the dermal delivery of theophylline is thoroughly studied using several prodrug approaches, even though it is acknowledged that there is no potential use for a dermal theophylline. However, if the objective were the transdermal delivery of theophylline, then another omission in the text is apparent. All drugs considered candidates for transdermal delivery require attainment of a therapeutically effective blood level of the drug which is usually known. Moreover, the pharmacokinetic profile for the drug is also usually known as well. Accordingly, the flux through the skin required to deliver the therapeutic concentration of the drug could be estimated. Analysis of drug delivery from this perspective may be extremely important since it might suggest that delivery of the drug via the prodrug approach may not be the best choice.

Another significant omission in the text is the lack of consideration to the fate of the promoiety after it is released prior to, or after, reaching the receptor phase. Moreover, the stoichiometry of the components involved could provide important information, particularly for those prodrugs which undergo facile hydrolysis in water. For example, Mannich bases, some of which are extremely labile in water, might not survive even contact with the surface of the skin. In these instances, it is conceivable that any observed enhancement in penetration might be a direct physical enhancement as a result of perturbation of the skin by the hydrolysis products of the prodrug.

The extensive classification used in this chapter at times appears forced. There are a number of instances where the examples cited are not drugs, and other instances where whole classes are based on the results obtained using one single compound. A notable example of the latter is when the D-SH comprehensive group is for the drug 6-mercaptopurine. Discussion of the results for this drug constitutes 16 pages of the chapter.

While some of the chemistry involved in synthesizing the proposed prodrugs appears interesting, it is anticipated that many of these entities might be hydrolytically labile. The problems anticipated in the formulation of these compounds, or the stability of any dosage form are not even speculated, making an evaluation of their real potential difficult, at best.

Chapter 3 describes a mathematical model for estimating the transmembrane delivery of drugs using partition coefficient, lipid solubility, and molecular size as the most important properties of the solute. This model was investigated in the development of topical nonsteroidal antiinflammatory prodrugs. The results of these studies appear to be consistent with current knowledge, suggesting that in order to achieve maximal flux, the preparation of small molecular weight, low melting derivatives, exhibiting increased oil solubility is highly recommended.

Chapter 4 describes another model that may be useful to predict the optimization of prodrugs and analogs designed for percutaneous delivery. However, the model does not even discuss specific structural details of the prodrug. The conclusions presented are quite general in nature and tend to be consistent with the basic empirical knowledge in this field.

Chapter 5 describes an empirically based correlation between solubility parameters of the solute and solvent to correlate observed fluxes. A limited set of compounds and data, also presented in Chapter 2, are now examined for correlation between experimental data and solubility parameters calculated using group values. These calculated values, based on a summation of the group values derived from empirical results, are for some reason referred to as "theoretical solubility parameters". Considering the

0022-2623/92/1835-4647$03.00/0

simplicity of the model, and the restricted set of compounds used, the predictive value of this approach is rather dubious.

Chapter 6 is another attempt to evaluate the effect of partitioning on percutaneous transport of lipophilic drugs. The importance of enzymatic hydrolysis of the prodrug is addressed, but only the obvious is emphasized without any reference to enzyme specificity, activity, and/or distribution. It is concluded that increased enzymatic hydrolysis of the prodrug correlates with an increase in drug delivery. However, for percutaneous drug delivery only modest improvements are to be expected via the prodrug approach.

Chapter 7 is a rather comprehensive, and a very well-written chapter dealing with prodrugs and ocular drug delivery. It addresses various aspects of ocular delivery, which is a more complicated process than transdermal delivery. The variety of routes that the (pro)drug can be absorbed, the anatomy of the eye, tear flow, the enzymes present, and other issues significantly influence the transport and partitioning of drugs in the eye. The aspects described above are thoroughly addressed, and this chapter is undoubtedly the best part of this book.

In view of the many books dealing with transdermal drug delivery, and ocular drug delivery, it is difficult to see the purpose of this book. It contains the obligatory introductory material and very little specific information for the design of prodrugs useful for percutaneous absorption. The rather comprehensive and extensive classification of drug/prodrug combinations and the overly optimistic presentation might be misleading to people not familiar with this field. Although it is advertised as a text which demonstrates how to choose the best approach to design a prodrug for specific needs, after reading it, to me the approach was not immediately obvious.

On the basis of the comments above, and particularly in view of its price, I would not recommend the purchase of this book for personal libraries.

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The Alkaloids. Volume 41. Edited by Arnold Brossi and Geoffrey A. Cordell. Academic Press, San Diego, CA. 1992. ix + 252 pp. 15.5 × 23 cm. ISBN 0-471-02233-0. $85.00.

This volume contains four chapters with widely differing themes. The first, by B. Tantiswie and S. Ruchirawat, reviews alkaloids of the plants of Thailand. Most of the chapter describes isoquinoline and indole-related alkaloids, and there is a section on miscellaneous alkaloids of various structural types. The second chapter is an updated summary by J. Kobayashi and M. Ishibashi of work on marine nitrogen-containing natural products discovered since 1985. The structures of many of these compounds are fascinating and reveal in many cases novel arrays of functionality. Chapter 3, by O. Boye and A. Brossi, updates work on *Colchicum* alkaloids, and Chapter 4, by J. V. Greenhill and P. Grayshan, does the same for *Veratrum* alkaloids.

All who have used and valued this series will continue to do so; with this volume, clearly both traditional and new areas of alkaloid chemistry are visibly flourishing.

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Physiology of the Heart, Second Edition. Edited by Arnold M. Katz. Raven Press, New York. 1992. xvi + 687 pp. 16 × 24 cm. ISBN 0-88167-838-4. $55.00.

This volume contains 25 chapters ranging in length from 11 to 42 pages. Basically the book can be divided into four separate sections: basic structure, metabolism, and energetics; normal and abnormal contraction; normal and abnormal electrical behavior; and ischemic heart disease and heart failure. This volume provides an extensive update of the first edition that was published in 1977, which focused more on organ physiology and cellular biochemistry, whereas this edition incorporates topics ranging from molecular biology to clinical cardiology. The more conventional approach of using multiple authors was not utilized as the author felt this would compromise his attempt at providing a single voice to explain complex concepts. The author provides a real service to those readers interested in the history of cardiac physiology/biochemistry by including "classic" references throughout this text.

The first section of this book is similar to that seen in other textbooks on basic cardiac function. It adequately reviews cardiac structure (grossly and histologically), function, and biochemistry. The second section reviews contractile protein structure and function, excitation–contraction coupling with an excellent review of cardiac calcium channels, and the calcium pump. Although it appears to be rather basic, a chapter on receptor pharmacology was included in this section as well. The third section begins with a well-written review of the electrocardiogram and cardiac action potential. The author follows with chapters on normal cardiac conduction and several detailed chapters on the different types of arrhythmias. The last two chapters describe the ischemic heart and heart failure.

This text describes the biochemical, cellular, and, where appropriate, the molecular biology of heart disease. The clinical conditions associated with abnormal cardiac function are discussed and limited mention is made for the treatment of these disorders. The chapters are well-written, and a liberal use of appropriate current, as well as historical, references is made. A large number of diagrams are used to assist the reader in the understanding of the sometimes complex nature of cardiac function/dysfunction. Parts of this text, e.g. ion-channel structure and gene expression, are probably of greater interest to the cardiovascular researcher than the practicing cardiologist. Other parts, e.g. description of complex arrhythmias, would be of great interest to the practicing cardiologist. Thist text is well-written and should provide useful

0022-2623/92/1835-4648$03.00/0

information for both the practicing physician as well as the researcher interested in cardiac disorders.

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Serotonin Receptor Subtypes: Pharmacological Significance and Clinical Implications. By S. Z. Langer, N. Brunello, G. Racagni, and J. Mendlewicz. Karger, Basel. 1992. x + 146 pp. 17 × 24 cm. ISBN 3-8055-5550-4. $108.00.

One of the hottest topics in neurochemistry over the past few years has been the neurotransmitter serotonin. Although numerous subpopulations of serotonin receptors have been identified, and a variety of new agents have been developed, relatively little of a review nature has been published concerning the clinical significance of serotonin receptor subpopulations. The present book is the product of a workshop held in Monte Carlo (June 6–8, 1991) and sponsored by the International Academy for Biomedical and Drug Research. It is intended as the first volume of a series of Academy-sponsored workshops in the biomedical area. The book consists of 11 chapters (averaging about a dozen pages per chapter) written, for the most part, by investigators prominent in the field of serotonin. Chapter titles include (i) Molecular analysis of serotonin receptor subtypes; (ii) 5-HT1 receptor subtypes: Pharmacological heterogeneity; (iii) 5-HT2 receptors: Location, pharmacological, pathological and physiological role; (vi) Pharmacological relevance of 5-HT3 receptors; (v) 5-HT uptake mechanisms and drug development; (vi) Animal models of anxiety and aggression in the study of serotonergic agents; (vii) Electrophysiological evidence for the distinct properties of presynaptic and postsynaptic 5-HT1A receptors: Possible clinical relevance; (viii) Current concepts on the role of serotonin function in anxiety and depression; (ix) Different 5-HT receptors modulate glutamate release in cerebellum (5-HT1 and 5-HT2) and cholecystokinin release in nucleus accumbens (5-HT3): Possible relevance to cerebellar ataxias and to anxiety; (x) Serotonin and eating disorders: Pharmacological relationships; and (xi) 5-Hydroxytryptamine receptors and drug discovery.

The book is, at the same time, informative, useful, and disappointing. For someone at least moderately interested in 5-HT research, excellent state-of-the-art discussions and comprehensive reviews are provided in several appropriate areas. In contrast, many more areas could have been covered (for example, there is essentially nothing about the cardiovascular aspects of serotonergic agents), and, given the title, one might have expected more discussion of recent clinical findings. A chapter might have been devoted to some of the less popularized effects or speculative therapeutic possibilities of serotonergic agents. There is little mention of the less well investigated populations of 5-HT receptors; discussion (or speculation) regarding these populations might have served to stir up more interest on the part of medicinal chemists and pharmacologists.

The statement is made (in the general Forward) that the series is intended for, among others, medicinal chemists; however, other than for background information, there is little here to excite most medicinal chemists. For example, there is essentially no discussion of the relationship between chemical structure and either pharmacological/clinical effect or subpopulation selectivity. Furthermore, fewer than six chemical structures are presented. Even though there is a chapter on drug discovery, no clues are provided for drug design. Given the cost (or, more specifically, cost/page), this book will not be found on the desktops of most medicinal chemists; on the other hand, those working in the area would be well advised to at least browse through a library copy. Perhaps the best way to characterize the book is generally excellent, incomplete, and expensive.

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Frontiers in Molecular Toxicology. Edited by Lawrence J. Marnett. American Chemical Society, Washington, DC. 1992. ix + 294 pp. 21.5 × 28 cm. ISBN 0-8412-2428-5. $26.95.

The ACS journal *Chemical Research in Toxicology* publishes one Invited Review or Perspective in molecular toxicology in each issue. These articles from the first four volumes of the journal, grouped into four broad categories, i.e. Toxic Agents and Their Actions; Enzymes of Activation, Inactivation, and Repair; Physical Methods; and Molecular Modification, are reproduced in this book. Together these reviews and perspectives convey the opportunity and excitement that exist at the interface of chemistry and toxicology.

Many medicinal chemists will find at least selected articles in this publication of interest and useful in their research. Institutional library access is recommended.

Staff

Studies in Natural Products Chemistry. Volume 10. Stereoselective Synthesis (Part F). Edited by Atta-ur-Rahman. Elsevier, Amsterdam. 1992. xii + 718 pp. 18 × 26 cm. ISBN 0-444-89558-2. $297.25.

The tenth volume in the series *Studies in Natural Products Chemistry* edited by Atta-ur-Rahman devotes 14 chapters by authorities in their respective disciplines to the topic of stereoselective synthesis of natural products. This volume is directed at specialists in the field and is a collection of reviews on diverse topics in natural product chemistry rather than a focused presentation of selected structural types. For example, there are chapters devoted to synthesis of cembrane diterpenes (J. A. Marshall), new methods for enantioselective alkaloid synthesis (S. G. Pyne), and the synthesis of blood group oligosaccharides (A. Veyrieres). The breadth of coverage and the detail at which each topic is reviewed means that this book will not appeal to a general audience, but to specialists.

The authors of the individual chapters have adopted different strategies for their respective reviews. For

0022-2623/92/1835-4649$03.00/0

example, the chapter on the synthesis of vitamin D derivatives by Wilson and Yasmin is an excellent summary (with complete bibliography) of the synthetic results from his laboratory and the labs of many others who have made advances in this area. Kubo and Saito, on the other hand, discuss the isolation, structure determination, and biosynthesis, in addition to the synthetic investigations, concerning isoquinolinequinone antibiotics. These differences in format from chapter to chapter do not detract from the appeal of the volume.

The authors and the editor are commended because each chapter is well-written and extensively referenced (through 1990). Also an excellent index is provided. This volume, the most recent contribution to this respected series, continues to provide a breadth of valuable information for the natural product chemist and is highly recommended for those with an unlimited budget.

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Books of Interest

Methods in Enzymology. Volume 206. Cytochrome P450. Edited by Michael R. Waterman and Eric F. Johnson. Academic Press, San Diego, CA. 1991. xxxvii + 716 pp. 15.5 × 23 cm. ISBN 0-12-182107-2. $90.00.

A Specialist Periodical Report. Amino Acids and Peptides. Volume 23. A Review of the Literature Published during 1990. Senior Reporter J. H. Jones. Royal Society of Chemistry, Cambridge, U.K. 1992. xii + 328 pp. 14 × 22 cm. ISBN 0-85186-214-4. £97.50.

Recent Advances in Biotechnology. Series E: Applied Sciences. Volume 210. Edited by Fazilet Vardar-Sukan and S. Suha Sukan. Kluwer Academic Publishers Group, The Netherlands. 1992. xvii + 558 pp. 16.5 × 24 cm. ISBN 0-7923-1632-0. $178.00.

Inositol Phosphates and Calcium Signalling. Advances in Second Messenger and Phosphoprotein Research. Volume 26. Edited by James W. Putney, Jr. Raven Press, Inc., New York. 1992. xi + 404 pp. 16 × 24 cm. ISBN 0-88167-883-X. $95.00.

USAN and the USP Dictionary of Drug Names. USAN 1993. 1961–1992 Cumulative List. Edited by Carolyn A. Fleeger. The U.S. Pharmacopeial Convention, Inc., Rockville, MD. 1992. 859 pp. 21 × 27.5 cm. ISBN 0-913595-68-3. $100.00.

Biocatalysis At Extreme Temperatures. Enzyme Systems Near and Above 100 °C. ACS Symposium Series 498. Edited by Michael W. W. Adams and Robert M. Kelly. American Chemical Society, Washington, DC. 1992. viii + 215 pp. 15.5 × 23 cm. ISBN 0-8412-2458-7. $54.95.

Understanding Chemical Patents. A Guide For the Inventor. Second Edition. By John T. Maynard and Howard M. Peters. American Chemical Society, Washington, DC. 1991. xvi + 183 pp. 15 × 22.5 cm. ISBN 0-8412-1998-2. $29.95.

Organic Syntheses. Volume 70. Editor-in-Chief Albert I. Meyers. John Wiley & Sons, Inc., New York. 1992. xx + 305 pp. 15.5 × 23 cm. ISBN 0-471-57743-X. $34.95.

Advanced Organic Chemistry. Reactions, Mechanisms, and Structure. Fourth Edition. By Jerry March. John Wiley & Sons, Inc., New York. 1992. xv + 1495 pp. 16 × 24 cm. ISBN 0-471-60180-2. $54.95.

Regulation of Isopentenoid Metabolism. ACS Symposium Series 497. Edited by W. David Nes, Edward J. Parish, and James M. Trzaskos. American Chemical Society, Washington, DC. 1992. x + 270 pp. 15.5 × 23 cm. ISBN 0-8412-2457-9. $66.95.

Chemistry of Biomolecules. An Introduction. By R. J. Simmonds. Royal Society of Chemistry, Cambridge, U.K. 1992. xiv + 276 pp. 15 × 24 cm. ISBN 0-85186-883-5. £18.50.

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