

Book Reviews

Combinatorial Chemistry. Synthesis and Application. Edited by Stephen R. Wilson and Anthony W. Czarnik. John Wiley & Sons. 1997. ix + 269 pp. 16 × 24 cm. ISBN 0-471-12687-X. \$69.95.

This book is one of the first to focus, for the most part, on the emerging field of nonpeptide combinatorial chemistry. The volume is a compilation of 12 chapters written by experts in the field and covers a range of topics that will be of interest to those working in, or contemplating working in, this field.

The introductory chapter by Wilson begins with a brief history of combinatorial chemistry and a review of the literature. While it is always difficult to include the most recent references in a book, Wilson supplies a website containing combinatorial chemistry references which will give the reader the opportunity to be kept up to date in this rapidly moving field. This introductory chapter presents a nice overview of the field and the issues involved. However, I did find a few misleading statements and typographical errors in the chapter. For example, in comparing Ellman's benzodiazepine synthesis to that of the Parke-Davis group on pg 7 Wilson says "Ellman's compounds were not cleaved from the solid support". While the Parke-Davis group devised a route that allowed the final compounds to be ejected from the solid support in the final synthetic step, Ellman did, in fact, cleave his compounds in a separate step after benzodiazepine construction. The reader could be easily confused by this statement. Overall, however, the introductory chapter does a nice job of introducing the remainder of the volume.

Most of the remaining chapters are of current interest and taken together present a nice collection of techniques, approaches, and philosophies of combinatorial chemistry. For the most part, the chapters contain a significant amount of data, tables, and figures and are well written. Chapter 2, Parallel Organic Synthesis Using Parke-Davis Diversomer Technology, by DeWitt and Czarnik, is a review of the early work of the Parke-Davis group in the field of solid phase organic chemistry and concludes with some recent chemistry examples that have not been widely presented as of yet. Chapter 3, Polymer-Supported Synthesis of Organic Compounds and Libraries, by Kurth, presents the polymer-supported synthesis of 2,5-disubstituted tetrahydrofurans, introduces polymer-supported enantioselective synthesis (butyrolactones), and goes on to describe polymer-supported synthesis of small molecule libraries (β -mercapto ketones and 1,3-diols). This chapter contains plenty of detail for those readers who want to get their hands wet. Chapter 4, Macro Beads as Microreactors: New Solid-Phase Synthesis Methodology, by Rapp, describes the use of TentaGel resin for solid phase synthesis and concludes with a description of TentaGel macrobeads as polymeric microreactors. Again, this chapter contains plenty of useful data. Chapter 5, by Wintner and Rebek, Combinatorial Libraries in Solution: Polyfunctionalized Core Molecules, describes their work in preparing small molecule mixture libraries of cubanes and xanthenes in solution. This work repre-

sents a nice example of solution synthesis, screening, and deconvolution. The chapter by Sucholeiki (Chapter 6) discusses issues of concern in selecting a solid support for synthesis which should be useful for those entering the field. He then describes his work on photocleavable linkers and the use of this linker in the solid phase synthesis of biphenyl molecules through Pd-catalyzed coupling followed by cleavage. Chapter 7, Radiofrequency Encoding and Additional Techniques for the Structure Elucidation of Synthetic Combinatorial Libraries, by Xiao and Nova, discusses mass spectroscopic (both off-bead and on-bead) techniques for compound identification and deconvolution techniques (iterative and positional). The chapter then proceeds to give a very nice overview of encoding techniques that is quite up to date. This section emphasizes the radiofrequency encoding technology first introduced by Nicolaou. This is a very exciting technique which should gain rapid acceptance by practitioners of combinatorial chemistry. Chapter 8, Combinatorial Synthesis, Exploiting Multiple Component Condensations, Microchip Encoding, and Resin Capture, by Armstrong et al., compares linear vs multicomponent condensation synthesis and then nicely illustrates several of these multicomponent condensations which have been applied in library format including the use of the Passerini reaction and its application to the preparation of azinomycin analogues, the Ugi reaction, and the many useful improvements developed by these authors. The chapter concludes with a discussion of resin capture which combines the benefits of both solution and solid phase synthesis.

The remainder of the book contains a chapter by Pirrung describing indexed combinatorial libraries and their use in discovering novel enzyme inhibitors, a chapter by Taylor which introduces the field of carbohydrate libraries and some of the issues involved, a chapter by Ostresh et al. which describes split-pool technology and various deconvolution technologies and focuses for the most part on peptide libraries, and finally a chapter by Benkovic et al. which focuses on the uses of biologically generated peptide/protein libraries.

Overall, this book presents a good combination of techniques, approaches, philosophies, chemistries, and compound classes that have been explored in the field of combinatorial chemistry. Of particular interest is the volume's focus on non-peptide organic chemistry applications which will be of interest to the increasing number of researchers both entering and continuing to work in this field. The book contains good author and subject indices and each chapter contains a significant number of appropriate references. One possible concern: this volume was a long time in preparation and at least some of the chapters don't contain the most current references. This is especially an issue for a fast moving field such as combinatorial chemistry. In

conclusion, I recommend this volume to anyone working in the field.

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The Chemistry of Mind-Altering Drugs. History, Pharmacology, and Cultural Context. By Daniel M. Perrine. American Chemical Society, Washington, D.C. 1996. x + 480 pp. 17.5 × 25 cm. ISBN 0-8412-3253-9. \$39.95.

This book will provide a pleasant surprise for many readers! As the title implies, the book is not just medicinal chemistry, showing different ways to synthesize psychoactive drugs or providing a compendium of SAR details. Indeed, it is neither chemically rigorous nor encyclopedic and is easily read by the nonspecialist. It does present the essential structures and basic chemistry of the most important psychoactive drug classes, but it also provides a wealth of historical facts, cultural vignettes, and social commentaries. Beginning with a relatively well done chapter on the brain and neurotransmission that will be understandable to most chemists with little or no background in central nervous system pharmacology or physiology, the book has chapters on the opiates, depressants, stimulants, antipsychotics, antidepressants, psychedelics, dissociative agents, and cannabinoids. Anecdotes and often little-known facts are included about all these classes, ranging from their historical origins and aspects of the laws controlling their use, to the ways in which the drugs have been both used and abused. The chapters are all well documented. In fact, one *must* read the references and notes, which contain not only citations to scientific literature, but also to social, anthropological, and literary works, as well as quotations, additional commentaries by the author, and even an occasional poem! The book contains the usual number of trivial typographical slips but is remarkably free of significant errors.

The author concludes with four "appendices" that review and highlight basic organic chemistry; they will not likely be helpful to readers of *this* journal. Nevertheless, for those whose chemistry knowledge is weak or even lacking, these appendices provide a way to fill that gap, so they may more fully appreciate the book. The appendices thus extend the general educational value of this book beyond the audience of practicing medicinal chemists.

This book is particularly relevant in the 1990s because it is incumbent upon chemists, and particularly medicinal chemists, to be knowledgeable about psychoactive substances in the face of much misinformation that accompanies the current "war on drugs." The author has largely succeeded in presenting objective discussions that ought to replace what often passes for popular knowledge about these substances. While the dangers of PCP, the opiates, cocaine, and the like are not trivialized, neither are they exaggerated. This is a

book that can provide a basic understanding of what these drugs are, how they have been and are used, and how they work. The discussions of some of the social and cultural forces that shaped the patterns of use and prevailing attitudes about psychoactive drugs make the book interesting reading even for those who already have a solid knowledge of the structures and actions of these drugs. The book will be of interest to practitioners and graduate students, and could probably serve as the basis for an elective course on psychoactive drugs geared toward undergraduate or beginning chemistry or medicinal chemistry graduate students. I enthusiastically recommend it to anyone with a basic science literacy who wants a good general overview of psychoactive substances, how they were discovered, and the roles they play in medicine and in our present culture.

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Studies in Medicinal Chemistry. Volume 2. Biological Inhibitors. Edited by M. Iqbal Choudhary. Harwood Academic Publishers GmbH, Amsterdam. 1996. xiv + 378 pp. 17.5 × 25.3 cm. ISBN 3-7186-5879-8. \$150.00.

This book consists of seven reviews, five of which were written by industrial contributors who have worked in that particular drug class. The topics covered include squalene epoxidase inhibitors, dual inhibitors of 5-lipoxygenase and cyclooxygenase, cholesterol biosynthesis inhibitors, HIV proteinase inhibitors, nonpeptide antagonists at peptide receptors, conformations of thyroid hormones and analogs, and a pharmacophore for the benzodiazepine receptor. The various chapters contain numerous 1993 references and very few, if any, more recent citations. In most cases the reviews cover the field, but in a few the authors concentrated heavily on their own research. The reviews in general are not comprehensive, which is not surprising in that they average 55 pages and include numerous structures. The subject index is limited, but adequate to direct attention to appropriate sections of the reviews. There is no author index, but in this case I do not think that this is a serious omission.

The value of this type of book is that it shows the patterns of thought that can lead to the discovery of useful drugs, and the variety of structures that can have similar inhibitory activity. It also shows that although a long detailed SAR development process may lead to very potent selective agents, in some cases a different structural type may also be very useful. I think that books of this type can provide useful nondirected reading that can extend the horizons of the thinking of

medicinal chemists as well as present useful reviews of a specific area of medicinal chemistry.

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Burgers' Medicinal Chemistry and Drug Discovery. Volume 4. Edited by M. E. Wolff. John Wiley & Sons, New York. 1997. viii + 656 pp. 18.5 × 26 cm. ISBN 0-471-57559-3. \$225.00.

This volume in the series covers primarily cardiovascular drugs and chemotherapeutic agents. It is divided into four parts, beginning with radiological agents. This is a very fine chapter by Foye who has devoted a career to this research. Part 2 contains four chapters covering cardiovascular drugs. The first reviews myocardial infarction agents. This develops the pathophysiology and follows with drug treatment analyses. The next chapter on endogenous vasoactive peptides presents a good review of several neuropeptides. The illustrations are quite informative. A rich supply of references makes this chapter very useful as a resource on this topic. The chapter on hematopoietic agents is well written and informative. The coverage of investigational agents adds much to this chapter. The final chapter in part 2 is on anti-coagulants, antithrombotics, and hemostatics. This is a very good presentation of this area with useful illustrations. A large list of references enrich the value of the presentation.

Part 3 is composed of six chapters on various topics grouped as chemotherapeutic agents. The first covers synthetic antibacterial agents. This is a thorough review covering various structural types. The second

chapter reviews the β -lactam antibiotics. This is a well-written chapter with good illustrating material. Numerous references make this an excellent source of information on this topic. The chapter on anthelmintic agents covers the major infestations with good current information on effective agents. This is followed by a chapter dealing with clinical results and experience with various anthelmintic agents. Antiamebic agents are very well covered in the next chapter. A companion chapter appears next, updating the clinical results and experience of these agents. The chemotherapy of African trypanosomiasis is discussed in the following chapter. Part 3 ends with a very good chapter on antiviral agents targeting DNA. This is an excellent review of the topic with inclusion of drugs under investigation.

Part 4 on endocrine drugs contains two chapters, one on female sex hormones and the second on agents affecting the immune response. The chapter on sex hormones does a good job of reviewing the structure influence on the activity of steroids and synthetic compounds. The final chapter on the immune response agents presents a good review of the processes and agents influencing them.

The book represents an outstanding effort on the parts of the editor and the contributing authors to present well-written, authoritative information on their topics. The book is an essential addition to the library of any one conducting research, teaching, or wishing to be informed on the current status of drug treatment in a variety of categories. It is one member of a series that is truly outstanding in presenting medicinal chemistry and drug discovery to the profession.

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