Book Reviews

Crown Ether and Cryptands. Edited by George Gokel. Royal Society of Chemistry Cambridge, U.K. 1991. xiv + 190 pp. 16 × 24 cm. ISBN 0-85186-996-3. £13.50.

Crown ethers and cryptands lie at the heart of the emerging field of supramolecular chemistry, the branch of chemistry in which recognition of substrates by other entities, as opposed to the formation and manipulation of covalent bonds, represents the critical intellectual enterprise. The present volume is the third in a series of monographs in supramolecular chemistry edited by Prof. J. Fraser Stoddart of the University of Birmingham and provides an excellent introduction not only to the chemistry of crown ethers and cryptands but also into the overall field of supramolecular chemistry.

Chapter 1 is largely historical in nature and provides a detailed look at the discoveries that led to Pedersen's first synthesis of the crown ethers and to Lehn's original synthesis of the cryptands. Chapter 2 provides a more detailed discussion of synthetic methodology and gives a "behind the scenes" look at some of the factors a practitioner in the field should consider when designing a synthesis of a crown ether or cryptand. Chapter 3, which in many respects is the most pedagogically rich, gives an up-to-date overview of the methods used to assess the complexation characteristics of crown ethers and cryptands and a generalized review of the binding behavior exhibited by a large number of prototypical systems. Chapter 4, which is structural in emphasis, then serves to extend and refine this analysis of binding behavior. Here, discussion is devoted not only to the classic cation chelating capabilities of crown ethers and cryptands but also to their lesser-recognized ability to form supramolecular (i.e. noncovalently bound) complexes with neutral and anionic substrates. Chapter 5, the final scientific chapter, then provides a summary of various applications to which crown ether and cryptand compounds have been and/or are currently being applied. Many of these applications involve the ability of crown ethers and cryptands to act as solubilizing agents for cations and hence as mediators in "adjusting" normal reagent reactivity. Others, however, involve the development of sensors, carriers, and ion channels and are thus likely to be of interest to medicinal chemists. Chapter 6 is a bibliography.

This monograph is highly recommended to any chemist, medicinal or otherwise, who wants to become better informed about the exciting new area of supramolecular chemistry. It is well written in a lucid, personal, but highly informative style. This, and the fact that it is appropriately "pitched" at the senior undergraduate/beginning graduate student level, makes it a real delight to read. The only serious drawback is that literature is not directly referenced in the body of the text. As a result, the more serious reader must wade through the bibliography of Chapter 6 if he or she wants to find the relevant citation for further follow up study. This drawback, however, should not bother the vast majority of those individuals who just want a clear, easy, and informative introduction into a field that might not be their own.

Jonathan L. Sessler
Department of Chemistry and Biochemistry
University of Texas at Austin
Austin, Texas 78712

Analytical Profiles of Drug Substances. Volume 20. Edited by Klaus Florey. Academic Press, Inc., San Diego, CA. 1991. xii + 770 pp. 15 × 23 cm. ISBN 0-12-260820-8. $79.00.

Official compendia define a drug substance with regard to identity, purity, dosage, and quality. This series provides various other physical and chemical data, as well as method of synthesis, pathways of physical or biological degradation, and metabolism. In most instances complete chromatographic and spectroscopic data, with interpretations, are included. Thus, drug substances and even exipients are described in great detail.

In the present volume analytical profiles and other pertinent data are presented for amiodarone, apomorphine hydrochloride, astemizole, cefuroxime sodium, celiprolol hydrochloride, iodoxamic acid, iproniazid phosphate, anhydrous lactose, methoxamine hydrochloride, mexiletine hydrochloride, nicotinamide, norfloxacin, oxamniquine, phenolphthalein, polythiazide, terazosin, and zidovudine. In the 20-volume series, detailed descriptions are given for over 350 drug products. This information is easily accessed via the cumulative series index provided at the end of the volume.

This volume, along with entire series, offers a source of detailed information about specific compounds. Extrapolation of these data to related structures provides a vast source of information of value to medicinal chemists as well as researchers and practitioners in allied fields.

Staff

Studies in Natural Products Chemistry. Volume 9. Structure and Chemistry (Part B). Edited by Atta-ur-Rahman. Elsevier, Amsterdam, 1991. xviii + 714 pp. 17 × 24.5 cm. ISBN 0-444-89165-X. $220.50.

The relevant question to ask upon initial perusal of this book is the following: Is a book with no less than 73 contributors and a total of 24 chapters worth the effort? The answer, at least in this instance, is a definite yes.

Many of the chapters have been taken from presentations at a recent symposium on natural products held in Karachi. The book's great virtue is that it presents an excellent overview of the present state of natural products chemistry around the world. As would be expected, there are several chapters on up-to-date applications of X-ray techniques and NMR and mass spectroscopy to structure elucidation. Other topics deal with fungal metabolites, marine natural products, corticoid hormones, chalcogens, antibiotics, phenolic lipids, prostaglandins, and vitamin B_{12}.

0022-2623/92/1835-4506$03.00/0

If one were to single out for special praise one among many fine presentations, the choice of this reviewer would settle on the chapter describing three simple and inexpensive bioassays for the detection of pharmacological activity in natural products or their derivatives. The first two of these assays predict the ability to kill tumorous growths, while the third can detect herbicidal as well as plant growth stimulant activities.

Some important lessons may be drawn from the careful reading of this book, as well as from recent developments in the field. First, the isolation of taxol from the stembark of *Taxus brevifolia* by Wani, Taylor, and Wall just over 20 years ago at the Research Triangle Institute promises to be the greatest development in cancer therapy in recent decades. It, therefore, behooves the National Institutes of Health to place renewed emphasis on the isolation and screening of new natural products.

Second, since research funds are always in short supply, the added funds for the isolation of natural products will have to come from a more even distribution of resources which have hitherto been devoted to the synthesis of natural products. It is time for natural products chemistry, particularly isolation and structure elucidation, to cease being counted as a poor cousin of synthetic chemistry. In this context, the case of taxol is again relevant since the chances for the production of large amounts of this compound inexpensively through total synthesis are remote at best.

Third, the National Institutes of Health should be much more demanding in its requirements for adequate pharmacological evaluation of all isolation fractions of natural products before financial support is granted. Screening should be required even of synthetic intermediates prepared in the course of a total synthesis. Such a policy would at least partially redeem the funds expended in so many synthetic endeavors in academia where only too often a natural product may be prepared only in a few milligrams and as mostly an intellectual excercise.

Fourth, the study of natural products should be accelerated for no other reason than the ever widening destruction of our natural environment, and particularly of tropical forests.

In conclusion, so many aspects of modern natural products chemistry are so well-covered in this book that it could very well serve as a text for an advanced seminar course dealing with modern developments in the field.

Maurice Shamma

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

The Chemical Synthesis of Peptides. By John Jones. Clarendon Press, Oxford, 1991. ix + 228 pp. 16.5 × 24 cm. ISBN 0-19-855643-8. $75.00.

The synthesis of peptides from the 20 native amino acids has developed into an art that can now be performed by robotic instrumentation with a high degree of success. The peptide analogues, semipeptides, and peptidomimetics sought by the medicinal chemist, however, frequently require strategies that go far beyond the scope of "classical" peptide synthesis. Should a peptide target be selected for structure–activity studies, the medicinal chemist will be besieged on entering the literature with an aversive multitude of reagents and methods, not to mention strategies and tactics, the differences between which may border on personal preference. In the face of such confusion, it is no surprise that medicinal chemists may prefer to pursue peptidomimetics that bear little resemblance to a peptide. The discovery of novel peptides as pharmacologic leads has continued unabated since the mid 70s, however, and will continue into the foreseeable future as long as so little is known about the human genome. Thus, medicinal chemists will continue to be drawn to the field of peptide synthesis. For these practitioners a guidebook such as the current book provides a useful roadmap into the peptide-synthesis literature.

As stated by the author, "The aim of this book is to survey and exemplify the chemical methods available for synthesis of peptides and proteins of all kinds, with particular emphasis on those in actual use and the fundamental chemical principles involved." This is not the first guidebook to peptide synthesis. Miklos Bodanszky provided several books that are still eminently useful despite their age, since the main methodologies for synthesis of native peptides has varied little in the last 10 years. The present book follows the format established by Bodanszky and others in categorizing and surveying the methods of peptide synthesis. The main advantage to this book over its predecessors is an up-to-date bibliography, which alone may justify its purchase by the novice. The survey is remarkably even-handed and concise, yet entertaining, spiced with personal comments obtained from the founders of modern peptide synthesis.

The present book deals with each type of chemical transformation by first presenting the chemical principle including mechanistic considerations where important, followed by journal-style reaction schemes for specific examples. Thus, the present book might be considered a condensed, revised version of its two more lengthy predecessors: *Principles of Peptide Synthesis* by M. Bodanszky (1984, Springer-Verlag) (which surveys methods and chemical principles) and *The Practice of Peptide Synthesis* by M. Bodanszky and A. Bodanszky (1984, Springer-Verlag) (which contains specific recipes to exemplify each type of typical chemical transformation in peptide synthesis).

A novice would not be able to plan any type of peptide synthesis with this book alone. Consultation of the references is essential. The author makes no claim for exhaustive coverage and in fact boasts "ruthless selectivity...in choosing methods and examples for discussion".

For the practitioners who seek examples of semipeptide and peptidomimetic synthesis, a few examples may be found in Chapter 13, More Complex Modified Peptides. Considerations of functional group reactivities to various sets of reaction conditions and protecting group strategies for peptidomimetic synthesis, however, are not attempted, due most likely to the complex nature of the subject.

Even though peptide synthesis "is a field which labours somewhat under the weight of its literature", it is necessary to update the introductory guidebooks from time to time. Thus, for the chemist entering the field seeking an up-

0022-2623/92/1835-4507$04.00/0

to-date introductory guidebook, *The Chemical Synthesis of Peptides* may be a worthy addition to one's library.

James Samanen
Department of Peptidomimetic Research
SmithKline Beecham Pharmaceuticals
709 Swedeland Road, P.O. Box 1539
King of Prussia, PA 19406

Human Pharmacology. The Basis of Clinical Pharmacology. Edited by H. Kuemmerle, T. Shibuya, and J.-P. Tillement. Elsevier Science Publishers B. V., Amsterdam. 1991. xxii + 549 pp. 16 × 24 cm. ISBN 0-444-81448-5. $192.50.

Clearly, studying a compound's clinical pharmacology is a pivotal step in the development of a new therapeutic agent; it is at this juncture that various animal and cellular models that led to the formation of a hypothesis of the human benefits that might derive from a substance are put to the ultimate test. At this stage of examination of the pharmacological actions of a drug in humans risks taken must be limited to a minimum level. Measurements and analyses at this phase in the drug-development process must achieve maximum information with the least number and amounts of body samples. *Human Pharmacology* examines state-of-the-art techniques of analysis and measurement of drug concentration in an organism and of pharmacokinetic methods and their interpretation. The first part of the book, the analytical part, addresses the requirements for pharmacokinetics studies, drug and metabolites identification, physicochemical (e.g. fluometric, spectrometric, polarographic, electrochemical, mass spectrometric, calorimetric, etc.) methods in drug assay, and new perspectives in the assessment of drug effects. The second part of the book is devoted to various aspects of clinical pharmacokinetics, i.e. the fate of drugs in the body and different ways for obtaining, using, and interpreting the data. Recognizing the rigorously controlled conditions that must be maintained according to stringent internationally accepted criteria as data are derived, a special chapter details "good laboratory practices".

The book is intended for nonspecialists or students planning a career in pharmacology, but it is written by recognized specialists in many fields and will also interest even specialists. Medicinal chemists, as well as others involved in the development of drug products, will find the book a valuable introduction to the intricacies of clinical pharmacology.

Staff

0022-2623/92/1835-4508$03.00/0