Book Reviews

Medicinal Chemistry into the Millennium. Edited by M. M. Campbell and I. S. Blagbrough. The Royal Society of Chemistry, Cambridge, U.K. 2001. x + 398 pp. 16 × 24 cm. ISBN 0-854-04-769-7. £69.50.

According to its preface, this book represents the proceedings of sessions on new technologies in medicinal chemistry, drug metabolism and pharmacokinetics, and seven structurally distinct molecular targets presented at the International Symposium on Medicinal Chemistry held September 6−11, 1998, in Edinburgh, U.K. The targets were chosen to cover areas perceived by the pharmaceutical industry to be therapeutically important. Twenty-one chapters are written by E.U. investigators, whereas nine are from U.S. groups. In general, this well-produced book provides significant information on relevant topics. Most chapters have dozens of references; one has more than 100. However, the usefulness of these data is somewhat diminished by the age of the references—few are from 1998 or later.

It is impossible to consider all of the chapters in this volume in the limited space of this review. Inasmuch as inappropriate DMPK parameters and animal toxicity have sounded the death knell for 50% of otherwise seemingly excellent drug candidates [Kennedy, T. *Drug Discovery Today* **1997**, *2*, 436−444], I found four discussions devoted to predicting DMPK in the final portion of the book to be of special interest. Dennis Smith, in an excellent consideration of absorption and distribution, clarifies the difference between transcellular and paracellular absorption and relates these processes to C. Lipinski's "Rule of Five". Bernard Testa briefly but ably reviews the chemistry and biochemistry of toxication and detoxication, predicting drug metabolism with expert systems, prodrug design, and changes in physical properties resulting from biotransformation. Bertrand, Jackson, and Walther provide a fine overview of procedures for the rapid assessment of drug metabolism in drug discovery. A particularly intriguing paper was contributed by N. P. E. Vermeulen and colleagues who discuss modeling the active site of cytochrome P450 enzymes. In principle, this technique can give rise to models useful in computationally predicting the susceptibility of drug candidate structures to metabolic transformation. Presumably, this possibility will be enormously amplified by the recent announcement of an approach to the three-dimensional structures of biomolecules without the need for crystallization [Miao, J.; et al. *Proc. Natl. Acad. Sci. U.S.A.* **2001**, *98*, 6641−6645].

In the earlier parts of the volume, a section on new technologies comprises three chapters devoted to rational drug design. These are followed by sections on ion channels, glycine antagonists, 7TM receptors, growth factors, intracellular signaling, protease inhibition, and glycochemistry and glycobiology. Among the many informative contributions are the description of p38 MAP kinase inhibitors by Adams and colleagues and the related consideration of work on gene regulating kinases by Lewis and Manning. Here an early lead, SK&F 86002, was discovered long before the identity of the target was known. I also found a discussion of protease inhibitor design techniques by Michael Venuti and colleagues, as well as a description of cathepsin K inhibitors by Daniel Veber and associates, to be rewarding.

This book is reasonably priced and recommended to medicinal chemists, students of medicinal chemistry, and their libraries. The addition of subject and author indices would have been welcome.

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The Sigma-RBI Handbook of Receptor Classification and Signal Transduction. Fourth Edition. Edited by Keith J. Watling. Sigma-RBI, Natick, MA. 2001. viii + 231 pp. 28 × 23 cm. ISBN 0-9640548-3-3. $55.00.

This is a compilation of concise information on receptors and closely allied biological entities. A large number of authors contributed to the work, each addressing his/her expertise-specific topic. Subdivision titles of the book reflect the scope of coverage: Non-Peptide Receptors. Synthesis, Metabolism, and Transporters; Peptide Receptors and Peptide Metabolism; Ion Channels; and Intracellular Signaling Enzymes/Receptors. Each specific topic within the subdivisions is arranged on a large sideways double page and includes a narrative overview of relevant physiology/pharmacology, key references, and (for receptors) a table listing nomenclature, agonists and antagonists to the receptor, radioligand(s) of choice, and signal transduction mechanisms. For ion channels, the tables include information on conductance, activation threshold, deactivation and inactivation rates, permeation, and function, in addition to tabulation of drugs affecting the ion channel. Analogous useful information is tabulated for each of the intracellular signaling enzymes.

The narratives are well-written and authors have avoided both the extreme of excess brevity and, conversely, that of endless esoteric discussion, either of which is likely to alienate readers. The discussions are obviously aimed at a constituency of medicinal chemist readers, and the authors have hit their targets. It is gratifying to have so much useful and informative material on receptors and signal transduction concentrated in one highly readable, easily accessible source. References are current, listing many journal articles from 2000 and some from 2001. This spiral-bound handbook is a well-organized repository of a large amount of introductory information useful to medicinal chemists who are embarking upon research careers in areas involving the nervous system. Indeed, veteran medicinal chemists will likely find new information in

this book, and they will find it a useful reference for rapid recovery of specific facts.

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Advances in Chromatography. Volume 41. Edited by Phyllis R. Brown and Eli Grushka. Marcel Dekker, New York. 2001. xx + 425 pp. 15 × 23 cm. ISBN 0-8247-0509-2. $195.00.

This excellent book is a continuation of the long standing *Advances in Chromatography* series. The book is divided into 10 chapters: Fundamentals of Capillary Electrochromatography, Membrane Extraction Techniques for Sample Preparation, Design of Rapid Gradient Methods for the Analysis of Combinatorial Chemistry Libraries and the Preparation of Pure Compounds, Molecular Imprinted Extraction Materials for Highly Selective Sample Clean-Up and Analyte Enrichment, Biomembrane Chromatography Application to Purification and Biomolecule-Membrane Interactions, Transformations of Analytes for Electrochemical Detection: A Review of Chemical and Physical Approaches, High Performance Liquid Chromatography: Trace Metal Determination and Speciation, Temperature-Responsive Chromatography, Carrier Gas in Capillary Gas- Liquid Chromatography, and Catechins in Tea: Chemistry and Analysis.

The index is thorough, the chapters are well documented, and the text is supported by appropriate graphics. While all of the chapters contain information useful to the novice as well as to the experienced chromatographer, the Catechins in Tea: Chemistry and Analysis chapter provides an outstanding example of the development of an experimental method that beginners will find very instructive. The Design of Rapid Gradient Methods chapter documents the development of methods for rapid separations that workers in combinatorial chemistry and proteomics will find very useful.

This volume is an excellent review of the selected topics and it should find wide use by those involved in separation science.

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Quantitative Chromatographic Analysis. Volume 85. By Thomas Beesley, Benjamin Buglio, and P. W. Scott. Marcel Dekker, New York, 2001. xx + 378 pp. 15 × 23 cm. ISBN 0-8247-0503-3. $150.00.

The intent of this text is to provide information to the novice and to the established user of chromatographic techniques. The first chapters contain information concerning sample collection, transport, storage, and sample preparation. These chapters are well conceived, and the illustrations in the text are designed to be easily readable and are well labeled. The chapter on processing of chromatographic data is extensive, utilizing formulas and illustrations to explain processing procedures. The text does not include information concerning the impact of GMP procedures on the chromatographic process. The Gas Chromatography Applications chapter follows the chapter describing GC Apparatus for Quantitative Analysis. Although a GC/Ion Trap method is included in the Applications chapter, no mention of mass spectroscopy is found in the descriptions of detectors or in the index. This oversight is continued in the section describing Liquid Chromatographic Methods, although a line diagram of a "modem liquid chromatograph" includes a mass spectrometer. The Liquid Chromatographic Applications discussion contains a number of interesting applications, including one involving electrochemical detection of ascorbic acid, although the detector is not described in the text. The book concludes with an extensive description of Thin Layer Chromatography and Applications.

Although the text covers many topics in detail, it is unfortunate that the authors elected not to include descriptions of mass spectrometric detectors that are extensively utilized in the analysis of complex samples.

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The Handbook of Nucleoside Synthesis. By Helmut Vorbrüggen and Carmen Ruh-Pohlenz. John Wiley & Sons, New York. 2001. xii + 631 pp. 15.5 × 23 cm. ISBN 0-471-09383-1 (paper). $79.95.

The synthesis of nucleoside analogues presents considerable challenges. Control of regiospecificity and stereochemistry in the glycoside bond forming reactions commonly used to construct nucleosides is one of the more difficult synthetic transformations in common use. *The Handbook of Nucleoside Synthesis* provides an insightful and detailed analysis of the most common reactions used to prepare nucleosides, including the classical fusion and metal salt procedures as well as the Hilbert−Johnson reaction and all common variations of it. A significant amount of space is devoted to the efficient trimethylsilyl triflate procedure, which was developed by one of the authors.

The handbook presents a detailed discussion of reaction mechanisms and the effect of structure on mechanism. The outcome of Lewis acid-mediated reaction of silylated nucleobases with protected monosaccharides depends on the competition among the reactants for the Lewis acid. Details of this competition are discussed. The rationale for choosing certain combinations of reactants and Lewis acids is clarified. Regioselectivity issues, along with problems encountered with complex heterocycles, are also considered in detail.

The preparation and storage of protected sugar derivatives, the silylated bases, solvents, and Friedel–Crafts catalysts are described. This is useful information for the experimentalist. The authors devote a section to deprotection conditions and include examples that illustrate some of the difficulties that one may encounter during deprotection. Typically, methanolic ammonia is used for deacylation, but side reactions occur with pyrimidine nucleosides containing strong electron withdrawing groups attached to C5. The authors provide the reader with useful advice based on mechanistic and experimental factors. Experimental details for eight examples of nucleoside synthesis illustrating different common approaches to glycoside bond formation are included.

Although the book concentrates on glycoside bond forming reactions, a short section on conversion of ribofuranosides to 2′-deoxyribofuranosides and arabinofuranosides is included. This is useful because there are cases in which an interconversion strategy is preferable. A section on construction of nucleosides from amino sugars through de novo synthesis of heterocycles is relatively short, but it is commensurate with the level of effort in the primary literature. In addition, enzymatic glycosylation is also adequately covered.

The scope of the book is limited. The universe of nucleoside analogues contains many kinds of modifications, e.g., carbocyclic nucleosides, that are not covered in the book because they are not synthesized by conventional glycosidic bond forming reactions.

The bulk of the book is devoted to a tabulated survey of nucleoside synthesis over a 20 year period extending to 1994. This coverage is probably adequate, since most of the useful methods for nucleoside synthesis were developed during this time period. The index is only marginally useful. Relatively few terms are indexed, and there are errors. For example, the word “evolution”, which is not very important to the content of the handbook, cites page 3, although the word occurs only on page 1.

Given the importance of glycosidic bond forming reactions in modified nucleoside synthesis, particularly in the area of nucleoside analogue antivirals, the book provides a valuable resource for the practitioner and a solid foundation for those new to nucleoside synthesis.

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