Book Reviews

Second Supplements to the Second Edition of *Rodd's Chemistry of Carbon Compounds.* Volume IV: Heterocyclic Compounds. Part C: Five-Membered Heterocyclic Compounds with Two Hetero-Atoms in the Ring from Groups V and VI of the Periodic Table; Part D: Five-Membered Heterocyclic Compounds with More Than Two Hetero-Atoms in the Ring. Edited by M. Sainsbury. Elsevier, Amsterdam. 1998. xvi + 281 pp. 15.5 × 23 cm. ISBN-0-444-828702. $187.00.

As was done in the first supplement to the second edition of *Rodd's Chemistry of Carbon Compounds*, Parts C and D are combined in a single volume for the second supplement. A deficiency of this volume is the absence of an update of the chemistry of five-membered ring compounds containing two nitrogen atoms (i.e., pyrazoles, imidazoles, and their reduced and benzo derivatives) since the first supplement appeared in 1994. This deficiency is, in part, compensated for by the inclusion of a summary of reviews of the subjects that should have been covered in Chapter 16. While it is suggested that the detailed survey of the chemistry of pyrazines, indazoles, imidazoles, and benzimidazoles that appears in *Comprehensive Heterocyclic Chemistry II* (which covers the literature from 1982 to 1995) "emcompasses the period which this supplement should have dealt with", an unfortunate discontinuity of coverage nonetheless remains. Chapter 17 (by S. M. Fortt) updates the chemistry of five-membered heterocyclic compounds with two different hetero-atoms in the ring, including isoxazoles, oxazoles, thiazoles, isothiazoles, oxathioles, and selenazoles and their reduced and benzo derivatives to complete Part C.

The initial chapter of Part D (Chapter 18), covering five-membered heterocyclic compounds with three hetero-atoms in the ring, has veen divided into two subchapters in the second supplement. Chapter 18a (by S. B. Bedford) reviews the chemistry of triazoles, while Chapter 18b (by the editor, M. Sainsbury) updates oxadiazoles and thiadiazoles. Chapter 19 (by J. H. Little) reviews the chemistry of five-membered heterocyclic compounds with four hetero-atoms in the ring, including tetrazoles, oxatriazoles, thiatriazoles, oxathiadiazoles, dithiadiazoles, and phosphorus-containing heterocycles with varying numbers of nitrogen, oxygen, and sulfur atoms to complete Part D. Key literature citations and important reviews are provided throughout the narrative of each chapter to guide the reader to additional information on each topic. A comprehensive subject index for parts C and D is included as the end of the volume.

Organic and medicinal chemists interested in the properties, synthesis, and reactions of heterocyclic compounds should benefit from consulting this volume. Library access to this supplement together with the complete series of *Rodd's Chemistry of Carbon Compounds* is highly recommended.

Arnold Martin

Department of Pharmacology and Toxicology
College of Pharmacy
The University of Arizona
Tucson, Arizona 85721-0207

JM980481L

10.1021/jm980481l

A Practical Guide to Combinatorial Chemistry. Edited by A. W. Czarnik and S. H. DeWitt. American Chemical Society, Washington, D.C. 1997. xiv + 450 pp. 15.5 × 23.5 cm. ISBN 0-8412-3485. $89.95.

This 450-page text is divided into four major sections that include (1) solid-phase strategies, (2) solution-phase strategies, (3) equipment and automation, and (4) information management and biological applications. These four sections are each covered by three to four chapters.

The first section is a heavily referenced compilation of resins, linkers, cleavage conditions, etc., similar to many other recent review articles and chapters. The highlight of the section is Chapter 5 which presents a variety of analytical methods for on-bead analysis of combinatorial libraries. Several good examples are presented which illustrate the use of magic angle spinning NMR techniques and single-bead FTIR microspectroscopy for monitoring reactions and structure proof. Spectra are shown for each method, and they are explained in detail.

The title of the second section, "Solution Phase Strategies", is misleading in that no synthetic chemistry is presented. Instead, several chapters describing methods for the *analysis* of solution-phase libraries are presented. Chapter 8 is quite robust and describes a range of techniques including MS, LC−MS, and NMR.

The equipment and automation section is similar to other texts in that each manufacturer of robotics equipment is given a few pages of text and a picture. Subsequently, examples of the types of chemistry run on selected machines are presented. Not surprisingly, the syntheses of benzodiazepines and *N*-benzylglycines are included in this discussion.

As a complete work, this book is similar to others that have recently been published. However, each section is well-written and well-referenced, and they mostly contain good schemes and tables. One distinguishing feature of this book, is perhaps, its tendency to focus on the analysis of libraries, rather than the synthesis of them. Chapter 13 is a good attempt to capture issues related to data management. Those just starting to build a collection of books on combinatorial chemistry might want to consider adding this to their shelves since it does contain a lot of useful information. However, those already holding a few books on this subject might find this book to be somewhat redundant, and they

might want to consider a brief scan through its pages prior to investing another $89.95.

Donald J. Kyle

Senior Director
Computational, Combinatorial, and Medicinal Chemistry
Purdue Pharma, L. P.
99-101 Saw Mill River Road
Yonkers, New York 10701

JM980482D

10.1021/jm980482d

Analytical Chemistry. Edited by R. Kellner, J.-M. Mermet, M. Otto, and H. M. Widmer. Wiley-VCH, New York. 1998. xxv + 916 pp. 21.5 × 30 cm. ISBN 3-527-286101. $84.95.

Analytical Chemistry is designed to serve as an approved text for the FECS curriculum in analytical chemistry. As a text for a training course it includes problems, worked example problems, references, and learning objectives to guide students in their study of analytical chemistry. The excellently designed figures are well-drawn and complement the text, providing both practical and theoretical information concerning the analytical technique being discussed. The appendix includes items from statistical tables to dissociation constants arranged in a convenient and workable manner.

The well-organized chapters, which cover an extensive number of analytical techniques, are arranged so that material dealing with "The Analytical Process" and "Quality Assurance and Quality Control" precedes chapters dealing with analytical procedures. The range of topics is comprehensive, including chapters on computer interfacing of analytical instruments, LC−MS, GC−MS, and other hyphenated techniques as well as classical techniques of analytical chemistry. *Analytical Chemistry* will serve as an excellent text as well as a valued reference following completion of the student's course of study.

Jerry L. Born

College of Pharmacy
The University of New Mexico
Albuquerque, New Mexico 87131

JM9804836

10.1021/jm9804836

High-Performance Capillary Electrophoresis. Edited by Morteza G. Kahaledi. John Wiley & Sons, New York, NY. 1998. xxxii + 1047 pp. 16 × 24 cm. ISBN 0-471-148512. $150.00.

This is the most recent addition to *Chemical Analysis, a series of Monographs on Analytical Chemistry and its Applications*. This multiauthored book contains 31 chapters, organized into five sections on theory, detection systems, techniques, applications in chemical analysis, and determination of physicochemical parameters.

The first section on theory takes both beginner and expert reader through a detailed step-by-step description of capillary zone electrophoresis, micellar electrokinetic chromatography, capillary gel electrophoresis, capillary isoelectric focusing, capillary isotachophoresis, and capillary electrochromatography. Rigorous mathematical descriptions of the forces involved in separation are presented for the technically equipped reader. In addition, each chapter gives a brief, "layman's" version of the underlying separation theory for the novice.

The section on detection systems includes chapters discussing light-based detection, electrochemical detection, indirect detection, and mass spectrometric detection. The chapter on light-based methods, the most frequently used detection method in capillary electrophoresis, is particularly well-written. With this said, the other detection methods are newer, less developed, certainly difficult to review, and harder to accurately predict the future directions. The lack of more than a few commercial detectors makes this section of this book somewhat "expert"-oriented limiting its value to the beginner or the casual reader.

The techniques section includes chapters on sample introduction and stacking, coated capillaries, nonaqueous solvent systems, method validation, two-dimensional separations, and fabrication of microchips for separations. These techniques are all clearly written and should be of great interest to the expert and beginner alike.

The section on applications is excellent for those readers specifically interested in the analysis of peptides, proteins, carbohydrates, DNA, enantiomeric mixtures, inorganic ions, and pharmaceuticals. Also included are chapters covering on-line sample preconcentration, microbioanalysis and chemical analysis, and enzyme assays. The selection of these applications, while not all inclusive, clearly establishes the versatility of capillary electrophoresis.

The final section on physicochemical studies contains three short chapters on affinity capillary electrophoresis, determination of physicochemical parameters, and quantitative structure−activity relationships. These give the reader a completely different perspective in how capillary electrophoresis can be applied to obtain useful data about the physicochemical propeties of macromolecules and their interactions.

The monograph is surprisingly well-edited and reads better then most multiauthored texts. This reader found only a few errors in individual chapters. While detailed experimental procedures are not presented in each chapter, the reader is directed to carefully selected primary literature; thus, this monograph serves as a helpful guide to those new to the field. The updates presented at the conclusion of many of the chapters are somewhat disconcerting, but the listings of recent publications make this monograph very current. The figures and schemes are of high quality, and the general index is both complete and useful. This reviewer recommends this monograph for all libraries and for any

researcher currently using or seriously contemplating the use of capillary electrophoresis.

Robert J. Linhardt

Division of Medicinal and Natural Products Chemistry
College of Pharmacy and
Department of Chemical and Biochemical Engineering
University of Iowa
Iowa City, Iowa 52252

JM980484Y

10.1021/jm980484y

The Combinatorial Index. By Barry A. Bunin. Academic Press, New York, NY. 1998. xvii + 322 pp. 18 × 26 cm. ISBN 0-12-141340-3. $79.95.

Surely virtually everyone now knows that combinatorial chemistry is a rapidly growing multidisciplinary field in medicinal chemistry. The present rate of publication of research articles exceeds two papers daily, and the literature is widely scattered. Consequently it is becoming difficult for all but the most dedicated to keep abreast of current findings in an organized way. This book is a welcome aid to this process. It is an easy to use collection of reliable literature methods for all phases of medicinal chemical laboratory transformations using combinatorial techniques and places a particular emphasis on resin-based methods and the preparation of small, druglike libraries.

The book is divided into chapters describing particular laboratory transformations and procedures starting with a general background chapter and going on in turn to chapters dealing with linker technologies, specific reactions for preparing libraries, analytical methods, and solution/mixed solid-phase−solution reactions. This is followed by a series of appendixes keyed back into the preceding chapters covering a summary of functional group transformations, classification of heterocyclization reactions, unnatural biopolymers, oligosaccharides, a list of abbreviations, and then useful author and subject indexes. Each reaction covered is described in sufficient detail that a reasonably experienced chemist could perform the reaction described or use the description as the basis for developing an analogous reaction. Each reaction is also commented upon bringing out specific points of interest and ranges of utility, and each reaction or process is referenced at the point of discussion.

On the whole; this book is a very useful and practical "cook book" that many chemists will keep close at hand and refer to often. It is clearly organized and well-written and is comparatively inexpensive. Despite the magnitude of the task, it is hoped that Bunin will be able to follow through on his desire to keep the book up to date with supplements on or off the net.

All chemists who work in this key area will want to have a copy near at hand and will wear it out through constant resort. It is not, however, the sort of book that chemists will read from cover to cover. Those medicinal chemists who are not actively engaged as yet in combinatorial work will find it an excellent way to learn about it.

Lester A. Mitscher

Department of Medicinal Chemistry
Kansas University
4010 Malott Hall
Lawrence, Kansas 66045-2506

JM980487A

10.1021/jm980487a

Practical Application of Computer-Aided Drug Design. Edited by Paul S. Charifson. Marcel Dekker, Inc., New York, NY. 1997. x + 52 pp. 16 × 23.5 cm. ISBN 0-8247-9885-6. $150.00.

Practical Application of Computer-Aided Drug Design is an impressive compilation of chapters covering not only computational drug discovery techniques but also related fields in structural biology and biophysical chemistry. The authors of the various chapters have had considerable experience in their respective areas and many times provide lucid explanations of respective approaches to drug discovery. In general, the text is well-referenced and should be a valuable resource for interested researchers and students. Recent Successes and Limitations in Computer-Aided Drug Design, the topic of the first chapter; authored by Paul S. Charifson and Irwin D. Kuntz, provides a key take home message that the more "simplistic methods" have been the most successful. The fundamental concepts and techniques emphasized include molecular graphics applications, the calculation of interacting energies, molecular docking, QSAR, and pharmacophore modeling. The authors conclude that the simplistic method provides a multidisciplinary "buy-in" early in the design process and allows rapid evaluation of ideas studies permitting early incorporation of synthesis and bioavailability considerations. Clearly stated is the author's bias that structure-based approaches possess the greatest overall potential.

The second chapter on Recent Techniques and Applications in Pharmacophore Mapping by Mark G. Bures highlights in some detail recent pharmacophore mapping techniques. There are 88 references that range from very specific examples such as the work on sigma 1 pharmacophores by Richard Glennon to the more general approaches using superposition methods (DISCO) developed by Yvonne Martin and colleagues at Abbott.

The Generation and use of 3D Databases for Drug Discovery is reviewed by Renée L. DesJarlais. The chapter provides general information on the sources of 3D structures and on how to assess the quality of structure data bases as well as a review of different search methods and specific applications including pharmacophore searching (auxin transport and protein kinase C inhibitors), caveat (cyclosporine analogues and major histocompatability complex peptides), and DOCK (HIV-1 protease, thymidylate synthetase,influenza hemagglutnin, and inhibitors of parasitic proteases). The chapter, although of interest and well-presented, covers a smaller segment of the literature than the other chapters with only 20 references.

A. J. Hopfinger and John S. Tokarski summarize 3-D QSAR Analysis COMFA, Distance Geometry, and Receptor Dependent 3-D QSARS. This is an extensive, detailed, and well-reviewed contribution. Validation of 3D QSARS methods is stressed. There are 98 references. Computational Approaches to Chemical Libraries is covered by David C. Spellmeyer, Jeffrey M. Blaney, and Eric Martin. This is another well-written chapter focused on the general aspects of chemical library design. The chapter is informing without detailed specific examples (53 references). Receptor Preorganization for Activity and Its Role in Identifying Ligand-Binding Sites on Proteins (Brian K. Shoichet) briefly covers broad areas such as protein−ligand interfaces, the role of conformational change, and specificity of binding sites. Experimental and computational methods for identifying binding sites is reviewed with brief discussions on each methodology (79 references).

Manuel C. Peitsch provides a short chapter on Comparative Protein Modeling. Although protein modeling does not directly relate to computer-aided drug design, the techniques and programs discussed provide information of interest to computational chemists in an important related field (53 references). Docking Conformationally Flexible Molecules into Protein Binding Sites is covered extensively by Millard H. Lambert with a prodigious 239 references. In this chapter DOCK and distance geometry play a central role as well as Monte Carlo minimization and conformer buildup approaches. This chapter is very helpful for understanding and reviewing this important area.

Mark A. Murcko contributes an Introduction to De Novo Ligand Design. This is a very well-written and an informative addition. There are clearly described "how-to's" and an evaluation of progress in this computational field. This is another excellent contribution with 141 references. Ajay and Mark A. Murcko and Peter F. W. Stouten review Recent Advances in the Prediction of Binding Free Energy. This is a most interesting area of computational chemistry that is not often covered. The chapter is well-written, complete, and descriptive (119 references). Long Range Electrostatic Effects (Ulrich Essmann and Thomas A. Darden), 220 references, and Metals in Molecular Mechanics Force Fields and Simulations (Libero J. Bartolotti and Lee G. Pedersen), 89 references, follows. Both chapters provided needed information. It is very important to include both areas which are not often emphasized (especially long range electrostatic effects) and often needed (especially metals in force fields). The latter topic is assembled by category including most useful tables with references. The last chapter, New Vistas in Molecular Mechanics (J. Phillip Bowne and Guyan Liang), 88 references, makes this book complete.

The editor Paul S. Charifson deserves credit for putting together an outstanding review of essential topics in this field. All chapters have similar formats and make the text user-friendly. This reviewer highly recommends the text for anyone interested in computational chemistry or structure-based drug design, especially students. Unfortunately the high cost may make it primarily a library acquisition, which is a shame.

Donald J. Abraham

Institute for Structural Biology and Drug Discovery and Department of Medicinal Chemistry
School of Pharmacy
Virginia Commonwealth University
Richmond, Virginia 23219-1540

JM9804883

10.1021/jm9804883

The Laboratory Companion: A Practical Guide to Materials, Equipment, and Technique. By Gary S. Coyne. John Wiley & Sons, New York. 1997. xviii + 527 pp. 18 × 26 cm. ISBN 0-4711-8422-5. $59.95.

This book is an updated version of the previously published *The Laboratory Handbook of Materials, Equipment, and Technique* (1992). As the word "practical" in the title of the current verison implies, this book concentrates on common laboratory methods and materials used on a daily basis in most chemistry laboratories. It is this focus which sets this book apart from other general purpose laboratory manuals which might provide more complete coverage, but often in a sketchy fashion.

The author, a scientific glassblower, covers laboratory glassware in nice detail throughout the book in chapters entitled Materials in the Lab; Joints, Stopcocks and Glass Tubing; Cleaning Glassware; and The Gas-Oxygen Torch (for those who might want to perform some simple glass manipulation in the laboratory). Flexible tubing, O-rings, and other miscellaneous items (often neglected, until a problem arises) are also discussed. The unique chapter dedicated to vacuum systems is of particular note. Topics range from vacuum pumps (aspirators to diffusion pumps) and gauges to leak detection. Chapters on Measurement; Compressed Gases; and High and Low Temperature will seem familiar to practicing bench chemists. However, beginning chemists will find these chapters very informative, and experienced chemists will find them a useful resource.

Each topic is introduced from a historical perspective, followed by a brief discussion of theory. A generous, comprehensible text (accompanied by abundant illustrations and tabular data) provides comprehensive technical details, applications, and numerous handy tips. Tables containing useful data and practical comments are routinely used to summarize the sections. Safety issues are stressed throughout the book.

This book is highly recommended for those beginning their laboratory careers. More seasoned, time-impaired chemists will find this compilation of information very

helpful, and supervisors will find that a "lab copy" will pay for itself in short-order.

Thomas C. Boge
Division of Pharmaceutical Sciences
School of Pharmacy
University of Missouri—Kansas City
Kansas City, Missouri 64110

JM980489V

10.1021/jm980489v

Emerging Drugs. The Prospect for Improved Medicines. Annual Executive Briefing. Volume 3. Edited by W. C. Bowman, J. D. Fitzgerald, and J. B. Taylor. Ashley Publications Ltd., London. 1998. vi + 397 pp. 21 x 29.54 cm. ISSN 1361-9195. $690.00.

Volume 3 of this series consists of 25 well-written reviews concentrated in the cardiovascular and cancer areas but including other topics such as pain, inflammation, therapeutic vaccines, and antisense oligonucleotides. Each chapter is written by well-qualified mostly industrial investigators actively engaged in the area under discussion. Each entry is between 12 and 25 pages long and contains the following sections: summary, background, medical need, therapeutic class review, current research goals, scientific rationale, competitive environment, potential development issues, editorial analysis, and bibliography. The articles are sufficiently in depth for a pharmaceutically literate reader to get a good sense of the importance of the particular field, the rationale and current status of the approaches being followed as revealed in the literature, and some of the unique problems of developing a marketed drug in that area. The articles appear to be current with 1997 literature references. For those of us who have difficulty keeping the alphabet soup jargon straight, there is an extensive glossary. There is alsoa company index which references for each company those areas covered in this volume in which they may be active.

In summary, this volume consists of in-depth reviews of some active areas of research and development, targeting the future potential of a given hypothesis and the data describing its present status, with emphasis on compounds in the various stages of development. As indicated by the subtitle of the series, "Annual Executive Briefing", and its price, this series is not targeted specifically toward the individual laboratory investigator. As stated in the foreward to Volume One 1996, it could "provide a critical guide for those working in strategic marketing, licensing department and healthcare planning". However, it could also serve to give researchers a broad picture of a research area and provide data to suggest how their project relates. I would recommend that pharmaceutical company libraries consider acquiring this book, not only for the use of executives but also for those involved in the research and development process.

Joseph Weinstock
SmithKline Beecham Pharmaceuticals
P.O. Box 1539
King of Prussia, Pennsylvania 19406-0939

JM980502B

10.1021/jm980502b