

## Book Reviews

**Frontiers in Drug Design and Discovery. Volume 3.** Edited by Gary W. Caldwell, Atta-ur-Rahman, Mark R. Player, and M. Iqbal Choudhary. Bentham Science Publishers Ltd., Hilversum, The Netherlands. 2007. ISBN 978-90-77527-11-5. \$130.00.

This book is the third in the series. The first and second volumes were previously reviewed in this journal (Wolff, M. E. *J. Med Chem.* **2006**, *49*, 838; Salem, A. K. *J. Med Chem.* **2006**, *49*, 7555). The book comprises 22 chapters written by 74 authors from academic, governmental, and industrial laboratories in the U.S., Germany, Italy, Czech Republic, Ireland, Japan, Hungary, France, and the U.K. The book is suitable for a broader audience of industrial, academic, and governmental pharmaceutical scientists who are interested in applying structure-based design to identify potent lead drug candidates. Techniques that are covered in the book include *in silico* virtual screening, peptidomimetics, fragment-based approaches, protein crystallography, and NMR spectroscopy. Book chapters include detailed analysis of  $\alpha$  helix mimetics, HIV protease guide inhibitors, G-protein-coupled receptors, virtual docking, fragment based lead discovery, hormone receptors, peptides and quinoline/acridine based antimalarials, among others. A number of the chapters primarily focus on one drug or one disease and on the lessons to be learned from these examples. Other chapters such as the review on "Virtual Docking" or "Fragment-Based Lead Discovery by NMR" provide a general overview on their current application in drug design and discovery. In contrast to the previous volume, a strength of this book is that all of the chapters fit into the theme of applying structure-based design to identify lead drug candidates. Citations are up to date. Random spot checks on a select number of cited works in this volume revealed them to be accurate.

Overall, the book is well written with an excellent 16-page index. Similar to Volume 2, the chapters are generally well illustrated with tables to help summarize key salient points. A complete alphabetical listing of all authors listed by last name follows the last chapter. This book would be a valuable addition for libraries (industrial, governmental, and academic) and individuals who have acquired the first two volumes in this series.

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**The Synthetic Organic Chemist's Companion.** By Michael C. Pirrung. Wiley-Interscience, Hoboken, NJ. 2007. xiii + 198 pp. ISBN 9780470107072 (Paperback). \$50.00.

This book is designed to serve as a ready reference for the new or beginning synthetic chemist. Representative examples of technical discussions include searching the literature, proper methods of cutting TLC plates, removing stir bars from reactions, freeing stuck glassware joints, rescuing product lost

to a rotavap water bath, changing pump oil, NMR tube washing, and much more. In comparison with its namesake, Gordon and Ford's *The Chemist's Companion*, this book does not provide a breadth of tables and charts as one would perhaps expect, but it does include in various chapters and the appendices a number of tables and charts often affixed to the side of a fume hood, such as azeotropes, solvent signals in NMR, mixtures for cooling baths, and TLC stains. This book presents a summary of fundamental practices in synthetic organic chemistry.

The first six chapters present an introduction to the synthetic laboratory setting and tools/equipment of the trade, covering literature search tools and adapting published procedures to the benchtop, general techniques common to reactions, glassware diagrams, and step-by-step instructions for common tasks such as opening gas cylinders, reaction scale and addition of reagents, controlling temperature of reactions, and methods of drying solvents. The remaining 11 chapters focus on sequential steps from planning and carrying out a reaction to product purification, scale-up, and reaction optimization. Chapters present such primary topics as the research notebook, conducting and monitoring the reactions, transfer of material by syringe, preparing and safe handling of reagents and solvents, working up a reaction, evaporation, vacuum systems, and separation/purification of product. There are brief overviews of methods for structure elucidation for a variety of compounds, methods for removal of a variety of glassware stains, examples of writing experimental details for publication and for a laboratory notebook, and strategies for reaction scale-up and optimization. Within these 17 chapters are introduced and discussed many tips, tricks of the trade, and fundamental techniques and procedures in synthetic organic chemistry.

In general, this is an excellent book for an academic synthetic laboratory to have available as required reading for each new student (undergraduate or graduate) as they begin their training in synthetic organic chemistry. Even the intermediate or advanced synthetic chemist will pick up, or be reminded of, a tip or two. Because of the breadth of skills, equipment, instruments, and techniques employed in synthetic organic chemistry, there are topics where a book such as this can only scratch the surface of a technique or knowledge that ultimately must be mastered through experience and training (e.g., chromatographic methods, HPLC, NMR, mass spectrometry) and topics omitted (e.g., GPC, lyophilization, crystallization, and precipitation techniques) that are likely staples for synthetic organic chemists working on macromolecules, polymers, or highly water-soluble organic molecules. As indicated by the author, the book will most likely be found in the laboratory with dog-eared pages or note paper marking pages for quick reference.

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**Computational Toxicology. Risk Assessment for Pharmaceutical and Environmental Chemicals.** Edited by Sean Ekins. John Wiley & Sons, Inc., Hoboken, NJ. 2007. xxii + 814 pp. 16 × 24.5 cm. ISBN 0470049626. \$140.00.

This book is the first in the “Wiley Series on Technologies for the Pharmaceutical Industry” edited by Sean Ekins. An impressive array of scientists from academia, regulatory agencies, and industry contributed chapters.

At first sight, the book may seem lengthy and intimidating because it comprises 27 chapters, and a cover-to-cover read would be a significant endeavor. However, the chapters are organized into five major sections arranged in a logical order. Part I is entitled “Introduction to Toxicology Methods” and provides a succinct yet informative description of the discipline of toxicology and modern methods utilized to study toxicology. While this section might be viewed as merely a recapitulation of the numerous toxicology textbooks and reference books available, the material presented provides a firm foundation for the remaining four sections of this book and leads nicely into the subsequent Part II. Much appreciated in this section (as well as the others) is the layout of the material in discrete subsections, plentiful references and Web sites listed, and the numerous but appropriate tables and figures.

Part II, “Computational Methods”, comprises three chapters that succinctly describe the history and development of computational technology and the current technology (e.g., programs). Particularly interesting and helpful are the reviews of various software and methods available. Those who are not computational chemists or toxicologists will appreciate that complex concepts are often presented in clear and coherent figures.

The bulk of the book chapters is in Part III, and this section describes the application of computers to toxicological evaluation of pharmaceutical agents. Throughout this portion of the book, computational methodology used to study various targets of toxicological interest, e.g., enzymes, receptors, drug transporters, DNA (mutagenicity), is discussed in detail. Various models are presented to predict interaction of drugs/toxicants with these targets. Colorful and descriptive molecular models of drugs bound to protein are featured.

Part IV of the book consists of four chapters detailing computational methods to assess the impact of environmental chemicals on human health and ecosystems. Featured are chapters on toxicity of chemical mixtures, ecological and environmental toxicology, aquatic toxicology, and dermatotoxicology.

The last section, Part V, includes three chapters describing new and very interesting technologies for toxicology in regard to cell culture methods (e.g., cells immobilized on chips, cell-based biosensors) and the potential role of computational toxicology in human disease and therapeutics. In addition, this section features a chapter on approaches (e.g., *in silico* methods) being developed for risk assessment analysis in the regulatory field.

In summary, the book is an excellent resource on state-of-the-art and emerging computer-based technologies for the assessment of toxicity via pharmaceutical or environmental agents. As noted above, complex concepts are presented in a clear and coherent manner, often involving the use of descriptive figures. Numerous tables are provided with succinct yet adequate information that will serve as handy references (e.g., comparison of software currently available). Given the depth of each chapter in regard to background material and application of each method

discussed as well as the emphasis on both pharmaceutical and environmental chemicals, this book has the potential to appeal widely to toxicologists in a variety of locations (e.g., chemical industry, pharmaceutical industry, academia) and with differing levels of interest in computational toxicology.

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**Name Reactions for Functional Group Transformations.** Edited by Jie Jack Li. John Wiley & Sons, Hoboken, NJ. 2007. xiii + 753 pp. 19.5 × 24 cm. ISBN 0-4793-2371-1. \$130.

This is the second book in a planned series of five volumes. The editor has assembled a highly capable group of practitioners from both academia and industry to provide an up-to-date survey of prominent name reactions and reagents in organic functional group transformations. The chapters are organized into sections corresponding to the name reactions under consideration in an alphabetical order. Further, each name reaction is considered under seven subheadings as follows: (i) description, (ii) historical perspective, (iii) mechanism, (iv) variations and improvements, (v) synthetic utility, (vi) experimental, and (vii) references. Six of the seven chapters cover established name reactions used to achieve a particular synthetic outcome: (1) Asymmetric Synthesis; (2) Reduction; (3) Oxidation; (4) Olefination; (5) Amine Synthesis; and (6) Carboxylic Acid Derivatives Synthesis. The last chapter, Miscellaneous Functional Group Manipulations, consists of a selection of name reactions for achieving various transformations.

Chapter 1 surveys name reactions used in asymmetric synthesis starting with enantioselective borane reduction of ketones to chiral alcohols utilizing the Corey–Bakshi–Shibata reaction with chiral oxazaborolidine catalysts. The treatment of this reaction is quite comprehensive, covering variations and modifications that include polymer bound versions, and goes beyond their use in ketone reductions to reduction of oximes to the utility of modified variations that also act as Lewis acids in simultaneous chiral Diels–Alder addition and reductions of enones, as well as catalyst in Mukaiyama aldol reactions. The chapter is well-referenced with citations as recent as 2006. Next considered is Davis chiral oxaziridine, *trans*-2-(phenylsulfonyl)-3-phenyloxaziridine and related reagents and their use in the one-step  $\alpha$ -hydroxylation of enolates, as well as their extended use in  $\alpha$ -hydroxylation of benzyl phosphonates and oxidation of sulfides and sulfenimines. This is followed by a short section on the Midland enantioselective reduction of ketones to chiral alcohols using Alpine-Borane, its uses in chiral reductions of acyl cyanides to  $\beta$ -amino alcohols, and the reduction of  $\alpha$ -ketoesters to  $\alpha$ -hydroxy esters. The Noyori asymmetric catalytic hydroxylation is next surveyed. The utilization of rhodium(I) and ruthenium(II) catalysts with monodentate chiral ligands such as 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), modifications thereof, and new ligands to effect high-yielding homogeneous hydrogenations of ketones or alkenes to produce corresponding alcohols or alkanes with high percentage enantiomeric excess is treated in depth. An extension of the

approach to chiral reduction of imines is also touched upon. The chapter ends with the Sharpless asymmetric dihydroxylation reaction and its aminohydroxylation variant. Again, this reaction is also well illustrated with useful examples and discussions of mechanism, chemoselectivity, stereoselectivity, yield enhancements, and ease of synthesis.

Chapter 2 showcases six name reactions that are used in reductions, as follows: Eschweiler–Clark amine alkylation, applied in the reductive methylation of primary and secondary amines without quaternization; Gribble reduction of diaryl ketones or diaryl- or triarylmethanols to the methanes; Luche reduction, involving the selective reduction of  $\alpha,\beta$ -unsaturated aldehydes and ketones in a specific 1,2 manner, employing a combination of  $\text{NaBH}_4$  and cerium(III) chloride; the Meerwein–Ponndorf–Verley reduction of carbonyl compounds to alcohols; the Staudinger reaction, by which imminophosphoranes are produced from reaction of azides with tertiary phosphines; and last, the Wharton reaction for the synthesis of allylic alcohols from  $\alpha,\beta$ -epoxyketones by treatment with hydrazine. As in Chapter 1, these reactions are accorded concise and quite comprehensive treatments in which variations and improvements are highlighted quite well, and ample illustrative examples are given. The referencing is generally up to date.

Chapter 3, the longest chapter of the book, deals with many name reactions for oxidations, including many well established and useful ones such as Baeyer–Villiger oxidation, Brown hydroboration, Corey–Kim oxidation, Des–Martin oxidation, Oppenauer oxidation, Swern oxidation, and Wacker–Tsuji oxidation, among others, which are discussed extensively. Other oxidations of somewhat limited scope, such as the Woodward cis hydroxylation, are also considered. Again, accounts are comprehensive. The chapter also includes the conversion of certain silyl groups to hydroxyl with retention of configuration, using the Tamao–Kumada–Fleming oxidation, and extensive accounts on two versatile dehydrating agents, the Burgess cis-dehydrating agent *N*-(triethylammoniumsulfonyl)carbamate, which can also be used to prepare nitriles from *cis*-oximes, and Martin's sulfarane, which effects a fast elimination of secondary and tertiary alcohols to the corresponding alkenes and can be used also to catalyze amide cleavage, the synthesis of cyclic ethers and sulfilimines, and the conversion of  $\beta$ -hydroxy- $\alpha$ -amino acids to oxazolidines.

Chapter 4 is devoted to eight selected name reactions used in olefination. The Chugaev elimination reaction is considered first, and next is the Cope pyrolysis elimination reaction. The third reaction covered is the Corey–Winter olefin synthesis involving a two-step conversion of 1,2-diols to olefins via a cyclic thionocarbonate intermediate. The next subject is the Perkin reaction, which is followed by the most extensively discussed reactions in the chapter, the Perkov reaction and the Ramberg–Bäcklund reaction. The former reaction is used to generate vinyl phosphates from the reaction of alkyl phosphites with  $\alpha$ -halocarbonyl compounds, while the latter reaction involves the transformation of an  $\alpha$ -halosulfone to an olefin by reaction with a base. The last two reactions of the chapter are the Shapiro reaction and the Zaitsev elimination.

Chapter 5 is the shortest chapter, covering selected name reactions used to synthesize amines. Only three reactions are considered: the Fukuyama amine synthesis, the Gabriel synthesis, and the Leuckart–Wallach reaction. The protecting group strategy employed in the Fukuyama amine synthesis is analyzed, followed by its application to the preparation of a wide variety of secondary amines. The reaction involves the protection of a primary amine followed by alkylation with an alkyl halide or

Mitsunobu alkylation with an alcohol. Improvements and drawbacks, as well as synthetic applications, are well covered, even though the treatment is not exactly in the typical sequence of the seven organizational sections under each name reaction. An extended historical perspectives section is used to provide an analysis of efforts and limitations of various approaches to the synthesis of secondary amines, and the order of the sections on variations/improvements and synthetic utility is reversed. The references date up to 2005. The Gabriel syntheses of primary amines from alkyl halides and the Leuckart–Wallach reaction using a reductive amination strategy are next treated. References date to 2004 and 2005, respectively.

Chapter 6 is the last one focused on a specific topic, the synthesis of carboxylic acid derivatives. The following six name reactions are covered in the usual way: Fischer–Speier esterification, Mukaiyama esterification, Ritter reaction, Strecker amino acid synthesis, Yamada reaction, and Yamaguchi esterification. Fischer–Speier esterification is treated briefly with references up to 1992. Mukaiyama esterification receives a similar brief treatment but with more up to date referencing, including several from 2006. A brief treatment of the Ritter reaction for amide synthesis from reaction of alkenes with nitriles is followed by a more extended treatment of the Strecker  $\alpha$ -amino acid synthesis. The reaction is well presented with many recent references. An extensive treatment is given to the Yamada amide synthesis with a large section on synthetic utility, covering a variety of synthetic targets including bioactive natural products and synthetic agents such as anticancer agents, antibiotics, thrombolytics and antifungal agents. References date to 2004. The last reaction, Yamaguchi esterification, like the earlier esterification reactions, is also briefly discussed, and its extensive use in the synthesis of macrolides is noted. References date to 2006.

Chapter 7 contains the two longest name reaction accounts in the book. It starts with a relatively brief treatment of the Balz–Schiemann reaction for the preparation of aryl fluorides, followed by a rather extensive and insightful account of the Buchwald–Hartwig amination. A large section is devoted to the development and use of a range of ligands for this reaction that provide for the undertaking of many types of aminations. A long list of references dating to 2006 is also provided. Next are relatively short accounts of the Haloform reaction, the Hunsdiecker or Hunsdiecker–Borodin reaction, the Japp–Klingemann hydrazone synthesis by treatment with a diazonium salt (the diazo group is wrongly shown as amino group on nitrophenyldiazonium chloride reactants), the Krapcho decarboxylation reaction, the Nef reaction, and the Prins reaction. A long account of the Regitz diazo reaction then follows. The chapter ends with the Sommelet reaction.

The book is generally well-written, and most sections are succinctly presented. Unlike many previous books on name reactions, which present many reactions but treat them superficially, this book provides an excellent selection of useful name reactions, which have been given in depth, well-illustrated, instructional, and well-referenced accounts. The inclusion of a few experimental examples for each name reaction is a very good feature of the book that will appeal to graduate students and postdoctoral fellows in synthetic laboratories. A good index has been included, as well as appendices with tables of contents of the other four books in the series. This book contains a wide breadth of information and practical insights and will serve as a treasure trove of information for planning syntheses. The book will be of interest to most in the organic synthesis community and will be a good addition to chemists' shelves. The editor

and contributors have done a superb job in producing this volume. There are several typographical and structural errors that remain to be corrected.

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**Annual Review of Biochemistry. Volume 76.** Edited by Roger D. Kornberg, Christian R. H. Raetz, James E. Rothman, and Jeremy W. Thorner. Annual Reviews, Inc., Palo Alto, CA. 2007. x + 864 pp. 20 × 24 cm. ISBN 978-0-8243-0876-X. \$59.50.

This book features 33 chapters spanning a wide variety of contemporary topics in biochemistry. In addition, the volume has a cumulative index of contributing authors and chapter titles for Volumes 72–76. Each chapter contains colorful and informative figures, numerous references, pertinent definitions found in the margin and additional sections reviewing “Summary Points” or “Future Issues”.

The chapters are well-written and provide a review of numerous research areas (e.g., synapse biochemistry, structure/function of various proteins, receptors). This particular volume features a section entitled “Mitochondrial Theme”, comprising an introductory chapter (i.e., “The Magic Garden”) and five reviews on the biology and biochemistry of the mitochondria, e.g., DNA replication and protein translocation. In addition, there

are a number of reviews on recent approaches or methodology in biochemistry, such as “The Role of Mass Spectrometry in Structure Elucidation of Dynamic Protein Complexes”, “Chemical Evolution as a Tool for Molecular Discovery”, and “Studying Individual Events in Biology”. Each chapter will be of interest and utility to those working in that particular field.

While the reviews generally focus on basic biochemistry (e.g., helicases, biochemistry of methane oxidation, magnetosomes), the book will have widespread appeal to scientists in various disciplines (medicinal chemistry, pharmacology, toxicology). Numerous topics are discussed in relevance to human disease or drug design or as potential therapeutic targets. A few reviews, as examples, that fall into these categories are “Structure and Function of Toll Receptors and Their Ligands”, “Structure and Mechanism of the 6-Deoxyerythronolide B Synthase”, “Anthrax Toxin: Receptor Binding, Internalization, Pore Formation, and Translocation”, “Synapses: Sites of Cell Recognition, Adhesion, and Functional Specification”, “Lipid A Modification Systems in Gram-Negative Bacteria”, “Chemical Evolution as a Tool for Molecular Discovery”, “Modulation of the Ryanodine Receptor and Intracellular Calcium”, and “TRP Channels”.

In summary, the reviews in this book are well-written and succinct, yet they are very informative. Volume 76 is an excellent addition to the long-running series and will prove to be a superb resource for not only biochemists but also those in other biomedical fields.

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