Book Reviews

Quaternary Stereocenters: Challenges and Solutions for Organic Synthesis. Edited by Jens Christoffers and Angelika Baro. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany. 2005. xxiii + 336 pp. 17.5 × 24.5 cm. ISBN 3-527-31107-6. $170.00.

This book consists of 12 chapters contributed by experts in their fields, each chapter providing its own perspective and focus and covering a variety of synthetic approaches to the stereoselective formation of quaternary carbon atoms. The significance of quaternary stereogenic carbon, i.e., carbon bonded to four different non-hydrogen substituents, in natural products and in research efforts in the chemical and pharmaceutical industry has appropriately attracted a great deal of attention from the synthetic chemistry community. This text serves the reader with an overview of synthetic approaches and methods applied to efficient syntheses of certain natural products, pharmaceuticals, and intermediates containing at least one quaternary stereogenic carbon atom. While the individual chapters represent useful overviews of specific types of reactions (i.e., Aldol, conjugate additions, rearrangements and cycloadditions, alkylation, and radical reactions) applied to the synthesis of quaternary carbon atoms, they are not intended as a comprehensive review of the topic. Rather, most chapters provide a review of recent applications and each chapter includes references from 2004. Chapters on techniques such as phase-transfer catalysis and enzymatic processes are included. A few chapters include information on the formation of unsymmetrically trisubstituted amines or alcohols; however, these provide a valuable overview and should be included in a text such as this.

This text should be welcome by anyone involved in the practice or teaching of organic synthesis because it represents a timely overview of a significant topic. The discovery of still more efficient and robust methods to control the formation of quaternary stereogenic carbon-containing molecules is deservingly certain to remain a significant and challenging area of synthetic research and development.

Ciro J. Spagnuolo

Bristol Myers Squibb Co.
Pharmaceutical Research Institute
New Brunswick, New Jersey 08903

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Methods in Biotechnology. Natural Products Isolation, Second Edition. Edited by Satyajit D. Sarker, Zahid Latif, and Alexander I. Gray. Humana Press, Totowa, NJ. 2005. xii + 515 pp. 16 × 24 cm. ISBN 1-588-29-447-1. $135.00.

Included in this second edition of Natural Products Isolation is a comprehensive set of chapters covering everything from initial bulk extraction through scale-up isolation and follow-up or lead optimization. The book is edited nicely so that each chapter is of comparable format and style, and the editors provide an introductory chapter with an overview of natural products isolation. Included in the book are a number of more specialized chapters covering supercritical fluid extraction, crystallization, solvent extractions, planar chromatography, and low- and high-pressure techniques including both preparative and analytical scale. Also included are specialized chapters on dereplication, extraction, and purification of plant, marine, microbial, and water-soluble natural products. Also included are discussions of ion exchange, countercurrent, and hyphenated techniques. This book is very thorough and includes comprehensive references to methodologies essential for the successful isolation and characterization of natural products.

After a brief evaluation it became clear that Natural Products Isolation is extremely well suited for new graduate students involved in natural products chemistry, and I asked several students in our program to read the book and provide some written feedback regarding the usefulness of the text as required reading early in our program. Their evaluation of the book strongly supports the importance of Natural Products Isolation as an indispensable tool for new graduate students in the field and for those with an interest in a comprehensive reference to natural products purification. This book fills in important niche because historically there has not been a useful, comprehensive reference to natural products isolation techniques. I am very much looking forward to having this reference as a guide for all new students in our laboratory.

Mark T. Hamann

Department of Pharmacognosy
School of Pharmacy
University of Mississippi
University, Mississippi 38677

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Human Drug Metabolism. An Introduction. By Michael D. Coleman. John Wiley & Sons Ltd., Chichester, England. 2005. xii + 274 pp. 17 × 24.5 cm. ISBN 0-4708-6353-6 (Paperback). $50.00.

This book describes in considerable detail the three systems responsible for drug metabolism and elimination in the human body: phase I, mainly oxidative functional group changes, principally by the cytochrome P450s; phase II, conjugating enzymes that usually add large hydrophilic molecules to a drug or a phase I metabolite; and phase III, efflux pump systems that facilitate the removal of the metabolites from cells to the urine or bile. Each of these systems is discussed in turn, especially the phase I and phase II enzymes in Chapters 3−6. The Introduction in Chapter 1 discusses basic pharmacokinetic principles and the physiological role of drug-metabolizing enzymes. The threat of toxicity from drug molecules, environmental contaminants, and food toxins is presented in Chapter 2. Topics such as the induction and inhibition of the phase I enzymes are presented at some length in Chapters 4 and 5. Helpful features in the Introduction to Chapters 4 and 5 are "histories" or minicase examples of how induction and inhibition lead to adverse effects in patients. Chapter 7, "Factors Affecting Drug Metabolism", includes the influences of genetic polymorphisms plus the effects of age, diet, gender, smoking, ethanol, and disease. Chapter 8, "Role of Metabolism in Drug Toxicity", includes reversible and irreversible types of toxicity.

Overall, this is an interesting book that provides a rather comprehensive overview of drug metabolism in humans. The

author describes in the Preface that he expects that many of the readers will be studying for formal examinations, and the book may well serve as an adjunct to a textbook for students in pharmacology or another course dealing with metabolism. The author intentionally uses a minimum of chemical mechanisms and chemical structures and, as such, limits the potential use of the book as a text for an elective medicinal chemistry course on metabolism. There are a few typographical errors including "Alkyll" in the Table of Contents, but there is generally no confusion as to the intended word. The use of the drug word paracetamol instead of acetaminophen could be confusing to some readers. Citations are not used in the chapters, which is not helpful for those who would like to go directly to the literature; however, a reading list by chapter is provided after the appendices for those who are interested.

This book could be useful for many who are just beginning to learn about drug metabolism because it deals with all of the relevant aspects. It is relatively inexpensive in the paperback format, and it could thus make a good addition to many personal and school libraries.

Bruce L. Currie
Department of Pharmaceutical Sciences
School of Pharmacy
Loma Linda University
Loma Linda, California 92350

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Chemistry of Peptide Synthesis. By N. Leo Benoiton. Taylor & Francis, Boca Raton, FL. 2006. ix + 290 pp. 16 × 24.5 cm. ISBN 1574444549. $139.95.

This book provides the mechanistic basis for developing rational strategies in peptide synthesis. The first four chapters explore the fundamental reaction chemistry associated with successfully targeting these polyfunctional, chirally labile products. The fifth addresses the relative merits of solid-phase versus solution chemistries. The next two chapters bring theory to bear on the practical bench synthesis. The concluding chapter adds experiential caveats where science merges with art: fine-tuning orthogonal protecting groups, out-maneuvering stereomutations, optimizing solvent systems, selecting catalyst attributes, gauging pH dependencies, purifying products, and safe handling of reagents.

The author's unpretentious writing style belies the authoritative and sophisticated textual content. Over the course of well cross-referenced chapters, this treatise quickly transitions from offering a novice the principles of peptide science to engaging expert biochemists. The narrative flows unerringly as it guides the reader through 207 mechanism-based figures. Many such figures brilliantly superimpose the complex realities of deviant side reaction pathways onto the intended reaction course. In so doing, the study allows for the development of *predictive* skills in identifying a priori dead-end pathways.

Historical advancements in peptide chemistries read as a subtext. In this vein, the references rely significantly on older literature. A more efficient convention in tying the text to the primary literature could have saved many pages, i.e., the title-inclusive references are often repeated verbatim within the same chapter or even facing pages. The comprehensive table of contents partially offsets the sparse index. Chromatographic and spectroscopic methods for peptide separation and characterization are mentioned only in passing.

Benoiton, in the fashion of a true scholar, relishes communicating the science of peptide synthesis, a field that he has pioneered. He understands the peptide bond as only an enzyme might and, in the course of this text, has ascribed explicit personalities to amino acids, their quirks not withstanding. This extraordinary book belongs in all academic and research environments involved in peptide chemistry.

Kennerly S. Patrick
Department of Pharmaceutical Sciences
South Carolina College of Pharmacy
Medical University of South Carolina
Charleston, South Carolina 29425

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The Adrenergic Receptors in the 21st Century. Edited by Dianne M. Perez. Humana Press, Totawa, NJ. 2006. xi + 404 pp. 15.5 × 24 cm. ISBN 1-588-29-423-4. $165.00.

This book provides a focused and comprehensive update on the structure, activation, coupling, regulation, localization, and function of the nine adrenergic receptors (α_{1A}, α_{1B}, α_{1D}, α_{2A}, α_{2C}, α_{2D}, β_1, β_2, β_3). As reflected in the subtitle, a primary focus is on new techniques, such as receptor visualization, knockout and overexpression, and new methods for studying the molecular dynamics of ligand−receptor interaction and the subsequent steps. Much of this information has never been summarized in single chapters to allow easy comparison to other receptors and between adrenergic receptor subtypes. References are up to date, and a limited subject index is provided. A minor irritation is the placement of color figures at the center of the book rather than at the appropriate point in the text.

The introductory chapter on historical perspectives was a concise and very readable summary of the key discoveries made during the 100+ years that have passed since the formulation of the receptor concept at the beginning of the 20th century. Ligand binding and receptor activation are covered in detail, including an excellent review of site-directed mutagenesis studies to establish binding sites for structural elements of the catecholamine agonists, current knowledge of the molecular mechanisms involved in altering receptor conformation during activation, and a detailed presentation of classical and novel signal transduction mechanisms. While a compilation of agonists and antagonists selective for specific adrenoceptor subtypes is included, it would have been useful to have more information on these pharmacological tools, perhaps as a separate chapter, since several highly selective compounds have been recently identified. Two additional chapters on signal transduction describe regulatory proteins, homo- and heterodimerization, receptor localization, and their traffic to and from the plasma membrane. An omission is a discussion of adrenoceptor "pleiotropism", where a particular receptor sequence can have different pharmacology, depending on tissue localization. This phenomenon has led to the subsequently disproved postulation of additional adrenoceptor subtypes (e.g., α_{1L}, β_4), and it could help explain tissue selectivity not accountable to differences in receptor subtype distribution.

The physiological role of adrenoceptor subtypes and the clinical application of adrenoceptor agonists are concisely summarized, followed by a description of the exciting new techniques that allow the actual visualization of adrenoceptors using fluorescent ligands or fluorescent-labeled receptors. The

use of knockout and overexpression techniques is comprehensively reviewed. These chapters provide an excellent compilation of reported results addressing effects of knocking out one or more receptor subtypes, both under basal conditions and in models challenging various organ systems. Some of the information in the chapter on receptor overexpression duplicates that presented in the previous chapters; however, it is useful to have a tabular comparison of the effects of overexpression and knockout of a particular adrenoceptor subtype. Data from animal models are presented to show the effects of gene therapy to enhance or suppress a specific adrenoceptor, second messenger, or regulatory protein.

The final section of this book addresses adrenoceptor polymorphism and microarray analysis to identify the effect of adrenoceptor activation on gene expression. Since polymorphic loci are present in multiple adrenoceptor subtypes, the particular combination of adrenoceptor genotypes may influence susceptibility of an individual to disease and/or responsiveness to therapy. The last chapter describes the specific genes up- or down-regulated by activation of a specific α-adrenoceptor subtype, either by an exogenous agonist or by a mutation conferring constitutive activity.

This volume will be useful to anyone interested in adrenoceptor physiology/pharmacology or in the design of drugs interacting with the receptor or its signal transduction pathway.

J. Paul Hieble

Department of Pharmacology
Research & Development Division
SmithKline Beecham Pharmaceuticals
709 Swedeland Road
King of Prussia, Pennsylvania 19406

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Artificial Enzymes. Edited by Ronald Breslow. Wiley-VCH Verlag, Weinheim, Germany. 2005. xii + 181 pp. 17.5 × 25 cm. ISBN 3-527-31165-3. $99.95.

Artificial Enzymes is a selective review of efforts at the interface of synthetic organic chemistry and biocatalysis. The editor of this volume, a pioneer in the field, states in the first chapter, "I have published several reviews of our work elsewhere", and "several" turns out to be 50 reviews. Breslow has enlisted a number of experts to write chapters on various approaches to development of artificial enzymes. His introductory chapter summarizes a vast body of work on cyclodextrin-based proteases, ribonucleases, enolases, aldolases, and others.

Topics covered include pyridoxal phosphate based artificial enzymes, functionalized synthetic polymers, catalytic antibodies, and adding catalytic activity to simple binding proteins. One of the most intriguing topics is the final chapter, which describes development of artificial restriction enzymes. A typical naturally occurring restriction enzyme that recognizes a six-base sequence of DNA would cut human DNA at about 10^5 sites. To achieve complete selectivity in a genome the size of human DNA, a restriction enzyme would need to recognize a sequence of 16 or more bases. Some progress in the development of artificial restriction enzymes with this level of selectivity has been made, but much remains to be done. This is a highly promising area for further research.

As with most multiauthored volumes, there are a few pieces that do not quite fit. Chapter 1 includes eight pages of very elegant stereoselective intramolecular chemistry using cyclodextrins, but there is no turnover, so it is distinctly unenzymic. Chapter 2 also includes examples that lack turnover. Chapter 6, entitled "Hydrolytic Metalloenzymes", uses metalloenzymes as a starting point to investigate reaction mechanisms and to develop metal complexes that more nearly resemble classical chemical catalysts than enzymes; the selectivity aspect of enzymes is totally lacking. Nevertheless, this book is an excellent introduction to a key topic at the interface of organic chemistry and biocatalysis.

D. Eric Walters

Department of Biochemistry and Molecular Biology
Rosalind Franklin University of Medicine and Science
North Chicago, Illinois 60064

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Books of Interest

American Chemical Society Directory of Graduate Research. Prepared by the Committee on Professional Training. American Chemical Society, Washington, DC. 2005. xxv + 1850 + 25 Faculty Index pp. 22 × 28.5 cm. ISBN 978-08412-3975-3. $89.00. Also available online.

Phage Display in Biotechnology and Drug Discovery. Edited by Sachdev S. Sidhu. CRC/Taylor & Francis, Boca Raton, FL. 2005. xviii + 748 pp. 16 × 23 cm. ISBN 0824754662. $159.95.

The Organic Chemistry of Sugars. Edited by Daniel E. Levy and Péter Fügedi. CRC/Taylor & Francis, Boca Raton, FL. 2006. xxii + 880 pp. 18.5 × 26 cm. ISBN 0-8247-5355-0. $299.94.

Marijuana and Cannabinoid Research. Methods and Protocols. Edited by Emmanuel S. Onaivi. Humana Press, Totowa, NJ. 2005. xv + 306 pp. 16 × 23.5 cm. ISBN 1-588-29-350-5. $125.00.

Metal-Based Neurodegeneration. By Robert R. Crichton and Roberta J. Ward. Wiley, Hoboken, NJ. 2006. x + 227 pp. 17.5 × 25 cm. ISBN 0-470-02255-8. $142.50.

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