Book Reviews

New Frontiers in Asymmetric Catalysis. Edited by Koichi Mikami and Mark Lautens. John Wiley & Sons, Hoboken, NJ. 2007. xvi + 418 pp. 16 × 24 cm. ISBN 0471680265. $100.00.

Asymmetric catalysis is rapidly attracting attention because of the potential economic and environmental advantages. This book, written by international leaders in their respective fields, covers aspects of asymmetric catalysis of great interest to the synthetic chemist.

The book starts with three chapters on ligand design for catalytic asymmetric reactions. The first chapter presents successful examples of catalytic asymmetric reduction and concepts of the ligand design. The description is brought to focus on the BINAP−transition metal chemistry. The second chapter contains a discussion on ligand design for the catalytic enantioselective oxidations developed after Katsuki−Sharpless epoxidation and the Sharpless asymmetric dihydroxylation. This chapter also reviews the optical resolution during oxidation of alcohols and the catalytic enantioselective oxidative coupling of 2-naphthols developed in this new century. The third chapter deals with ligand design for C−C bond formation and focuses on the asymmetric 1,4-addition reactions under copper or rhodium catalysis and on the asymmetric cross-coupling reactions catalyzed by nickel or palladium complexes.

The fourth chapter deals with the addition of small molecules to carbon−carbon or carbon−heteroatom multiple bonds. The author prudently pays more attention to the state of the art of catalyst design rather than describing historical developments. The reactions discussed in this chapter are organized into three types of reactions: hydrometallation of olefins followed by the C−C bond formation, two C−C bond formations on a formally divalent carbon atom, and nucleophilic addition of cyanide or isocyanide anion to a carbonyl or its analogues. Asymmetric hydroformylation is finding many applications in the synthesis of natural and biologically active compounds.

Chapter 5 presents some representative results via catalytic asymmetric activation of C−H and C−C bonds in synthesis. It also summarizes representative strategies, substrates, and chiral ligands that are used in asymmetric activation of C−H and C−C bonds. A number of metathesis reactions has been possible since the discovery of Schrock and Grubbs' molybdenum and ruthenium carbene catalysts in the early 90's.

Chapter 6 presents recent progress of olefin, enyne, and alkyne metatheses. The usefulness of this type of reaction is demonstrated in the large number of applications to complex natural product syntheses. High enantioselectivities have been achieved utilizing chiral molybdenum complexes.

Chapter 7 discusses some interesting observations on the physical and chemical differences between racemic and enantiomerically pure compounds. It explains how nonlinear effects can serve to generate compounds with higher ee than the value of the chiral auxiliary or ligand. Chapter 8 discusses the development of asymmetric activation and deactivation of racemic catalysts. Addition of a chiral source to a racemic catalyst can provide high levels of enantioselctivity. Chapter 9 describes highly enantioselective asymmetric autocatalysis with amplification of chirality and asymmetric autocatalysis initiated by chiral triggers, such as circularly polarized light, chiral quartz and inorganic salts, and chiral organic crystals of achiral compounds.

Chapter 10 presents the most recent advances on desymmetrization of meso compounds, using chiral organometallic catalysts covering the literature from the past 5 years. Chapter 11 presents a history and perspective of chiral organic catalysts. We can appreciate the extraordinary growth or organocatalysis since its renaissance in the mid-1990s. Milestones in the history of enantioselective organocatalysis are illustrated. This chapter focuses on major achievements in the areas of iminium, enamine, Brönsted acid, and phase-transfer catalysis and ends with remarks on the perspective of asymmetric organocatalysts. Chapter 12 discusses recent reactions catalyzed by chiral Bronsted/Lewis acid catalysts. Lewis acids are organized by the metal. Combined acid catalysis is still in a state of infancy, and there is still much more to learn with respect to their new reactivity. The last chapter discusses chiral bifunctional acid/base catalysis.

This timely book can be used as a textbook for graduate students and as an update on the recent advances in the growing field of asymmetric catalysis. The whole synthetic community will welcome this book and appreciate the state of the art in the field.

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Chemical Biology: From Small Molecules to Systems Biology and Drug Design. Volumes 1−3. Edited by Stuart L. Schreiber, Tarun M. Kapoor, and Günther Wess. Wiley/VCH Verlag GmbH, Weinheim, Germany. 2007. lxiii + 1205 pp. 18 × 24.5 cm. ISBN 978-3-527-31150-7. $625.00.

Chemical Biology, according to the view of Editor Stuart Schreiber (*Nat. Chem. Biol*. **2005**, *1*, 64−66) seeks to identify and characterize the naturally occurring and synthetic small molecules that bind to and modulate the actions of "nature's DNA, RNA, and protein macromolecules residing within their cellular contexts". In the words of the publisher's statement on the back cover of the books, "Chemical biology has become the new buzz-word in organic chemistry and in the life sciences, describing a new era in the interplay between the two disciplines and still on the rise." Yet, as is made clear in the very first essay, chemical biology and medicinal chemistry share closely related procedures and goals, as well as an extensive network of philosophical, historical, theoretical, and experimental roots. Although it may be an overstatement to suggest, as Gough and Crews do in their discourse, that chemical biology is established on a "unique foundation", many of the contributions to this treatise, briefly considered here, are of special importance to medicinal chemists and the drug discovery community.

The three volumes comprise 39 themes edited and written by major investigators in chemical biology from 74 academic and 23 industrial institutions located in Europe (51), the U.S. (45), and Japan (1). Most articles include sections on the outlook, introduction, history and development, general considerations,

applications, future development, conclusions, and up-to-date references. An extensive index is provided in the final volume.

A number of papers are concerned with the action of naturally occurring and synthetic small-molecule "perturbogens" to produce cellular phenotypes that provide help to unravel the biochemical basis of physiological processes such as the mechanism of heat and cold sensation produced by capsaicin and menthol, respectively. Likewise, such small molecules can be used as "conditional alleles" or "inducible alleles" to "knock in" or "knock down" cell-signaling events at specific time points. A comprehensive treatment of the application of such forward chemical genetics is provided by Haggarty and Schreiber, who point out that "the logic of forward chemical genetics is a reversal of the logic of most of the current efforts in drug discovery" with a consequent "paucity of information about the phenotypic effects of large collections of small molecules". An excellent contribution by Simon and Shokat considers the effect of point mutations in controlling ligand selectivity and especially the application of such studies to the development of gatekeeper residues in the binding pocket of kinases. Through the creation of a uniquely sensitive kinase allele, it is possible to target a kinase inhibitor selectively to any one of the more than 500 kinases coded by the human genome. Claxon's outstanding discussion of chemically induced dimerization of proteins points to the creation of inducible animal models of diseases such as prostate cancer and liver disease, with obvious applications to drug development. Likewise, chemically induced dimerization of proteins has potential direct therapeutic applications.

Volume 3 comprises a group of presentations directed to specific interests of the drug discovery community. F. Douglas reviews managerial challenges encountered at Aventis in implementing chemical biology platforms. Groom and coauthors provide an extremely interesting and challenging updated categorization of the druggable genome. They determined that approximately 3500 genes encode proteins druggable via druglike small molecules, whereas only 170 are targets for approved small molecule drugs. Other papers are directed to the subjects of target families, NMR studies of kinase−ligand interactions, nuclear receptors and their interactions with ligands, GPCR targets and their interactions with ligands, protein−protein interactions, and the prediction of ADMET properties. Final discussions include the systems biology of cellular signal transduction and gene profiling by means of genome-wide expression analysis.

In general, this compendium is very well-written and produced, although some figures are too small to be useful (e.g., Figures 6.4, 6.20, 9.2-7, and 17.2-6). Figure 3.1-8, intended for color, is confusingly printed in black. This valuable and thought-provoking series is highly recommended for acquisition by individuals and libraries in the drug discovery community.

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Books of Interest

Reviews of Reactive Intermediate Chemistry. Edited by Matthew S. Platz, Robert A. Moss, and Maitland Jones, Jr. Wiley-Interscience, Hoboken, NJ. 2007. x + 472 pp. 16.5 × 24.5 cm. ISBN 0471731668. $115.00.

Enhancement in Drug Delivery. Edited by Elka Touitou and Brian W. Barry. CRC Press, Boca Raton, FL. 2006. xii + 633 pp. 18 × 26.5 cm. ISBN 0849332036. $199.95.

Fundamentals of Contemporary Mass Spectrometry. By Chhabil Dass. Wiley-Interscience, Hoboken, NJ. 2007. xx + 585 pp. 16 × 24.5 cm. ISBN 0471682292. $110.00.

Organic Chemical Drugs and Their Synonyms. Seven Volume Set. Ninth Edition. By Martin Negwer and M.-G. Scharnow. Wiley, Hoboken, NJ. 2007. xvii + 5656 pp. ISBN 978-3-527-31939-8. $2000.00

New Drug Development. Design, Methodology, and Analysis. Statistics in Practice Series. By J. Rick Turner. Wiley-Interscience, Hoboken, NJ. 2007. xxi + 270 pp. 16 × 24 cm. ISBN 047007373X. $95.00.

The GABA Receptors. Third Edition. Edited by S. J. Enna and Hanns Möhler. Humana Press, Totowa, NJ. 2007. x + 325 pp. 16 × 23 cm. ISBN 978-1-588-29-813-3. $149.00.

Bitter Nemesis. The Intimate History of Strychnine. By John Buckingham. CRC Press/Taylor and Francis Group, Boca Raton, FL. 2007. xix + 297 pp. 15 × 23.5 cm. ISBN 1420053159 (Paperback). $39.95.

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