# *Book Reviews*

**Drug Discovery Strategies and Methods**. Edited by Alexandros Makriyannis and Diane Biegel. Marcel Dekker, New York. 2004. xi + 348 pp. 16 × 23.5 cm. ISBN 0-8247-0691-9. $174.00.

This work is a further addition to the half-dozen books on drug design that have appeared in the past 4 years. In their preface, the editors state that "the topics included in this volume are not intended to be all-inclusive. Our approach has been eclectic, in an effort to bring the reader the most exciting aspects of drug discovery, along with the methods that show the most promise in enhancing the discovery process." Comprising 11 chapters, the volume has 32 industrial and academic contributors from North America, the EU, and Australia.

The opening chapter on protein crystallography for drug design includes a helpful summary of suggestions including the important advice that ligand design should be based on a liganded structure of the targeted protein. Examples of this are shown in two following chapters that consider the obtainment, analysis, and utilization of crystallographic data from signal transduction proteins and of NMR data from inhibited stromelysin and other matrix metalloproteinases. An excellent chapter by Diana and Treasurewala provides a further example of the use of X-ray crystallography and computer-assisted drug design, in this case to obtain broad spectrum antirhinovirus drugs. Appropriately, these authors go on to describe how drug development problems comprising toxicity and metabolic instability of the designed structure were successfully addressed by further chemical modification. A well organized review of linkers and resins for solid-phase synthesis presents useful information on the generation of carboxylic acids, amides, alcohols, amines, hydroxamic acids, sulfonamides, ureas, guanidines, and other functions but discusses developments only up to 1999. Two chapters coauthored by editor Makriyannis review cannabinoids and radioligands for cannabinoid receptors. An ostensibly general chapter on peptidomimetics disappointingly is limited to opioids and their antagonists. Selective discussions of allosteric modulation of GPCRs, protein misfolding, and HIV antiviral agents also appear in the volume.

This rather expensive treatise is well written and edited, attractively printed and produced by the publisher, and has a 12-page index that makes it easy to find topics of interest. Yet the editors' stated "eclectic" approach may have produced a work that is insufficiently comprehensive to justify its title. This, coupled with a paucity of recent references (fewer than 20 of its more than 800 references are later than 1999), may limit the book's suitability for acquisition by the general medicinal chemistry readership.

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**Hydrolysis in Drug and Prodrug Metabolism. Chemistry, Biochemistry, and Enzymology**. By Bernard Testa and Joachim M. Mayer. Wiley-VCH, Zürich, Switzerland. 2003. xx + 780 pp. 18 × 24.5 cm. ISBN 3-906390-25-X. $215.00

This book presents a comprehensive and well-organized look at hydrolytic reactions in the metabolism of drugs, prodrugs, and other xenobiotic molecules, with special attention to mechanistic aspects of these reactions and the enzymes that catalyze them. Moreover, the authors also clearly achieve their goal of presenting the reactions and enzymes in such a way that the reader acquires an excellent appreciation of the similarities, differences, and overall scope of hydrolytic reactions and the enzymes that catalyze them.

After an introductory chapter on general concepts of hydrolysis and hydration in metabolism and principles of prodrug design, the next 10 chapters are very logically organized into several main groups of topics. Chapters 2 and 3 provide coverage of various aspects of the enzymes responsible for hydrolysis of esters and amides. Chapters 4−6 focus on the hydrolysis of amides, lactams, and peptides. Chapters 7−9 cover the hydrolysis of esters of both organic and inorganic acids. Hydration reactions are the subject of the next two chapters, with epoxide hydrolases being covered in Chapter 10 and with Chapter 11 being devoted to various other reactions of hydration and dehydration. A final short chapter, entitled "Conclusion: The Biochemistry of Water", provides an elegant summation of the book that incorporates additional thoughts on the dual roles of water as both solvent and reagent in biological reactions, as well as the diversity of enzyme mechanisms utilized to enhance the chemical reactivity of water.

Among the many strengths of this book are its logical organization, lucid writing, and the large number of relevant examples of the concepts presented. Furthermore, there are extensive literature citations following each chapter that serve to direct the reader either to the specific original work described in the book or to more detailed monographs on a particular topic. This will be a very useful book for medicinal chemists,

enzymologists, pharmacologists, and drug metabolism scientists. While it is priced outside the range of many graduate students and postdoctoral scientists in these areas, they would likewise find it extremely useful. Medicinal chemists with interests in the design of prodrugs that are converted into their pharmacologically active metabolites through hydrolysis, hydration, or dehydration will find it exceptionally valuable. Indeed, Chapters 4, 6, 8, 9, and 11 deal extensively with various aspects of prodrugs.

In summary, this book succeeds on many levels. At once it provides a clear and well-organized introduction to hydrolysis reactions in drug metabolism and drug design, a compendium of reaction mechanisms with extensive examples, and a comprehensive and eloquent treatise on the similarities, differences, and unifying principles of these reactions in metabolism.

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