Book Reviews

Bioinformatics and Drug Discovery. Methods in Molecular Biology. Volume 316. Edited by Richard S. Larson. Humana Press, Totowa, NJ. 2005. x + 444 pp. 16 × 23 cm. ISBN 1-588-29-346-7. $125.00.

Despite its title, this book will be of great interest to chemists involved in life sciences research. The book takes bioinformatics to be all biology-related information (experimental and computational) relevant to drug discovery, and drug discovery as an interdisciplinary effort is emphasized. Indeed, the editor states in the Preface that the book is "directed to those interested in the different aspects of drug design that include academicians (biologists, chemists, and biochemists), clinicians, and scientists at pharmaceutical companies." The book succeeds admirably in illuminating the latest interdisciplinary techniques being applied to drug discovery, including target selection and validation, receptor binding site characterization and binding prediction, and use for new lead discovery. The chapters are well referenced, with many 2004 citations represented, although references for Chapter 7, Section 4 (Pharmacogenomics Standards), are unfortunately missing. Only an occasional typographical error was detected. There is a subject index but no author index.

As explained in the Preface, the first chapter describes the systematic processes of drug discovery. The next 10 chapters focus on target identification and validation, including clinical applications, and the final 4 chapters discuss protein modeling and cheminformatics, including virtual screening and in silico protein design for identification of drug candidates.

This reviewer found particularly interesting the treatment of microarray analysis in several chapters, including basic microarray techniques and applications, derivation of biological networks from microarray data, drug discovery and clinical applications of the technique, gene ontology approaches to functional genetics, construction of phylogenetic trees to track gene evolution over time or over species changes, and especially a chapter entitled "Standardization of Microarray and Pharmacogenomic Data". This last chapter, by Mayo Clinic scientists, gives an instructive summary of evolving genetic formats (from free-text to FASTA and GCG to flat-file and XML formats) and the strengths and weaknesses of each. It discusses microarray acquisition and storage formats, such as MIAME and MAGE, and emerging standards for linkage disequilibrium studies that aim to link genes to clinical disorders. It also recounts the Pharmacogenomics Knowledge Base work at pharmkgb.org and emerging HL7 clinical genomics standards that should allow comparison of results across clinical studies.

Another valuable chapter entitled "Clinical Applications of Bioinformatics, Genomics and Pharmacogenomics" by Iqbal and Fareed reviews the already extensive application of genetic data to understanding mechanism and therapy of cardiovascular diseases such as thrombophilia disorders, coronary artery disease, and others. Chapters on probing protein−protein and protein−ligand interactions by MS and by NMR are instructive, especially a chapter by Sillerud and Larson, "Nuclear Magnetic Resonance-Based Screening Methods for Drug Discovery", that admirably explains the basis of the various NMR techniques (NOE, trNOE, HSQC, TROSY, SEA-TROSY, others) and provides applications for each technique. These include determining protein structure and dynamics, protein−protein and protein−ligand structure and dynamics, and applications to screening for drug leads (HTS by NMR). Another fine chapter by Flower, entitled "Receptor-Binding Sites", reviews the nature of binding sites, experimental methods for characterizing binding sites (spectroscopic, calorimetric, sequence-based, and structure-based methods), and computational methods (with a detailed review of the many published approaches). Finally he turns his attention to virtual screening, in its many variations, for predicting receptor−ligand interaction and to molecular dynamics approaches to quantitative prediction of receptor−ligand binding. A chapter entitled "In Silico Protein Design" by Dahiyat establishes that it is now often possible to design proteins having desired structure, properties, or function by modifying available proteins or by de novo design. The chapter summarizes concepts and procedures used (including several computer programs for this purpose) and references several successful examples. A chapter by Oprea et al., "Chemical Database Preparation for Compound Acquisition or Virtual Screening", gives practical advice on creating real or virtual compound collections for screening. Since available samples are cited as surpassing 21 million (from ChemNavigator), methods for cleaning up and verifying structures, filtering for "leadlikeness", and selecting compounds for acquisition or synthesis are necessary. The final chapter describes one comprehensive "gene to lead" platform focused on development of antimicrobial agents.

Most chapters do an admirable job of explaining the basis of the subject techniques, providing general guidance in executing the methods, citing sources for materials and software as appropriate, and pointing the reader to the growing databases of genomic, proteomic, and pharmacogenomic data available for data mining and hypothesis testing. They also point out published applications of the methods appropriate for use in drug discovery or clinical therapy.

Taken as a whole, these chapters emphasize how important it is for medicinal chemists to understand how these new interdisciplinary technologies are providing important data to guide target selection/validation and new lead discovery. Armed with information supplied by these new methods, the chemistry they do is more likely to lead to successful outcomes for their projects.

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JM068001A

10.1021/jm068001a

Handbook of Reagents for Organic Synthesis. Reagents for Glycoside, Nucleotide and Peptide Synthesis. Edited by David Crich. John Wiley & Sons Ltd., Chichester, West Sussex, England. 2005. xii + 770 pp. 22 × 28.5 cm. ISBN 0-470-02304-X. $170.00.

This work is the seventh volume of the *Handbook of Reagents for Organic Synthesis* series and therefore comprises a compilation of new reagent descriptions along with relevant updates and associated entries from the original *Encyclopedia of Organic Synthesis*. In this rendition, the focus is on the various reagents

and chemical transformations used to synthesize and manipulate glycosides, nucleotides, and peptides.

The opening nine pages are a listing of appropriate and somewhat recent (1992 and later) reviews and monographs of the subject matter, namely, formation of glycoside, nucleotide, and peptide linkages. This reference information will be extremely useful to the reader who seeks to learn more of the science, including mechanistic detail and specific published works of interest, as well as the history behind the development of the chemistry and synthetic strategy employed therein. However, the vast majority of the book is dedicated to an alphabetical listing of readily available reagents that have been used to construct glycoside, nucleotide, and peptide bonds. The listing is vast and impressive. In addition to the reagents one might expect to encounter (e.g., those commonly used to make amide bonds such as HOBT + DCC), this volume also contains entries pertaining to more specialized functions (e.g., 1,1,2,2-tetramethoxycyclohexane to selectively protect 1,2-diequatorial diols in sugars). Included for each entry are molecular structure, molecular formula, chemical (CAS) registry number, and molecular weight, as well as various physiochemical data (solubility, melting point, physical state, synonyms) and sometimes reference to the synthesis and purification of the reagent itself. Within each entry, chemical schemes are clearly presented and references to primary publications are provided. At the end of the volume, a complete list of contributors is given, linking each to his/her individual entries.

As with its predecessor volumes, this handbook should prove to be a very valuable, encyclopedic addition to virtually any organic/synthetic/medicinal chemistry laboratory.

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JM068011B

10.1021/jm068011b

Frontiers in Organic Chemistry. Volume 1. Edited by Atta-ur-Rahman and Yoshihiro Hayakawa. Bentham Science Publishers, Ltd., Hilversum, The Netherlands. 2005. vi + 355 pp. 17.5 × 25 cm. ISBN 90-77527-06-0. $130.00.

Frontiers in Organic Chemistry is a series "devoted to publishing the latest and most important advances in organic chemistry". This is the first volume of the series, and it focuses on oligonucleotide chemistry. Because the volume includes only Japanese authors, it fails to achieve the stated goal of the series: to have contributions written by eminent scientists in the field. In fact, very few of the true leaders in oligonucleotide medicinal chemistry have contributed to the volume. This deficiency is exacerbated by the fact that in most of the chapters, the focus is on the research in that particular laboratory and the scope of topics covered in the book is limited. So this book is not a scholarly review and appraisal of the area so much as a collection of chapters dealing with the research interests of a number of organic chemists in Japan.

Considered in the context of chapters on topics of interest in oligonucleotide chemistry rather than a review of the area, the book does have some value. The initial chapter reviews the overall approaches to oligonucleotide chemistry. It provides useful information on advances in protection−deprotection chemistry and an update on oxidation reagents. However, such reviews have appeared before and it would have been useful to discuss advances in large-scale manufacturing of oligonucleotides in more detail.

Chapter 10 epitomizes the strengths and weakness of the book. In this chapter, the authors nicely discuss bicyclic nucleic acid modifications. However, the title of the chapter is "Sugar-Modified Nucleic Acid Analogues as Potential Materials for Genomic Technologies". Thus, the authors entirely fail to cover the topic described by the title because they ignore the vast numbers of other sugar modifications synthesized and tested. I worry that a novice reading such a chapter would leave with a distorted view of the field. Similar comments apply to virtually all the chapters. For example, in Chapter 4 the authors do a nice job of covering recent successes in 4′-thiooligonucleotides, but absent a thorough integrated review of the entire field, its value is diluted. The chapters that purport to provide such a context are simply inadequate and inadequately referenced to serve as a basis for a detailed scholarly understanding of the field. Finally, this book is specifically focused on organic chemistry. Of course, there is a place for such a contribution, but because these modifications were virtually all made with the goal of enhancing the therapeutic performance of oligonucleotides, one is left wishing for a medicinal chemistry context.

In summary, the book is a compilation of well-written chapters covering a relatively narrow portion of the field. It can be recommended for sophisticated practitioners, but it would be less useful for those seeking an introduction to the field.

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JM068005F

10.1021/jm068005f