Book Reviews

Rational Drug Design. Edited by D. G. Truhlar, W. J. Howe, A. J. Hopfinger, J. Blaney, and R. Dammkoehler. Springer-Verlag, New York. 1999. xxii + 206 pp. 16 × 24 cm. ISBN 0-387-98753-3. $69.95.

This is Volume 108 of a series of published symposia by the Institute for Mathematics and its Applications (IMA) at the University of Minnesota. The book is based on the proceedings of a workshop on "Mathematical and Computational Issues in Drug Design", a part of the 1996-1997 program on "Mathematics in High-Performance Computing". The workshop participants included researchers in computer-aided drug discovery, computational chemistry, mathematics, and computer science. The subject matter covered receptor-based binding approximations, molecular docking, and de novo design of potential therapeutic agents. Non-receptor-based applications using molecular similarity analysis, molecular dynamic simulations, and solvation between aqueous and nonpolar phases were addressed. The workshop focused on mathematical procedures and algorithms in graph theory and topology, nonlinear multidimensional optimization, and the processing and representation of information obtained from global optimization and search strategies. The oral presentations were augmented by two panel discussions.

The book opens with a summary of the two panel discussions: "Important Current Problems in Drug Design That May Be Computationally Tractable" and "New Problems That Should Be Addressed in the Next Ten Years". Considering what has happened during the past few years, it was surprising that many current and somewhat futuristic hot areas were not covered: for example, computational efforts directed toward large database management, combinatorial chemistry, high-throughput screening, and libraries designed to cover conformational space. Good suggestions were made for future inclusion of down stream development considerations to be brought into the early phases of drug discovery, as well as the need to improve methods for dealing with the physics and physical chemistry of solvation processes in general.

The chapters on molecular properties included a broad range of science from the more esoteric "Matching of Chemical and Biological Structures Using Subgraph and Maximal Common Subgraph Isomorphism Algorithms" to the more common "Molecular Similarity" and "Modeling of the Effect of Solvation on Structure, Reactivity, and Partitioning of Solutes: Utility in Drug Design". Chapters back-to-back on "Cell-Based Methods for Sampling High-Dimensional Spaces" and "A Preliminary Multiobjective Analysis of the Chemotherapeutic Benefits of Hairpin-Linked Polyamides" show the diversity of topics covered. Receptor-based modeling included three chapters: "Using Structural Information for Creative Design", "GrowMol, a de novo Computer Program and its Application to Thermolysis and Pepsin: Results of the Design and Synthesis of a Novel Inhibitor", and "Deducing the Objective Site Models by Mixed Integer Programming". These chapters reflect the heterogeneity of issues discussed with nonlinked global themes. The final four chapters are combined under the heading "Numeric Methods" ("Molecular Dynamics Information Extraction", "Ionic Charging Free Energies Using Ewald Summation", "Genetic Function Approximation: Evolutionary Construction of Novel, Interpretable, Nonlinear Models of Experimental Data", and "Applications of Distributed Computing to Conformational Searches").

In summary, the book, although outdated, contains issues of specific computational interest. The book does not live up to its title, *Rational Drug Design*, and should have a more germane title associated with the conference workshop designation "Mathematical and Computational Issues in Drug Design".

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Second Supplements to the Second Edition of *Rodd's Chemistry of Carbon Compounds*. Volume IV: Heterocyclic Compounds. Part G. Six-membered Heterocyclic Compounds with (a) a Single Nitrogen Atom in the Ring (cont'd.); Polycyclic Fused Ring Compounds, (b) an Atom of Phosphorus, Arsenic, Antimony or Bismuth. Alkaloids with a Six-Membered Heterocyclic Ring (Chapters 34−35 in this volume). Part H: Six-membered Fused-Ring Heterocyclic Compounds with a Single Atom in the Ring (cont'd.). Monocyclic Ring Compounds with Two Hetero-Atoms in the Ring from Group VIB, or One Each from Groups V and VIB. Alkaloids (cont'd.). Edited by M. Sainsbury. Elsevier, Amsterdam, 1998. xx + 650 pp. 15.5 × 23 cm. ISBN 0-444-82979-2. $402.50.

This second supplement to the second edition of *Rodd's Chemistry of Carbon Compounds* combines two chapters of *Part G*, devoted to polycyclic fused ring compounds with a six-membered ring containing a single nitrogen atom, and all of *Part H*, in one book. These topics were last reviewed as the first supplement in 1987. The chapter topics correspond to those of the first supplement. Thus, diterpenoid alkaloids (reviewed by K. J. Hale and S. Manaviazar) and steroidal alkaloids (reviewed by K. J. Hale) comprise Chapters 34 and 35, respectively, from *Part G* of the series. *Part H* begins

with alkaloids of the morphine−hasubanonine group as Chapter 36. This chapter was once again written by K. W. Bentley, who reviewed this important group of alkaloids for the first supplement. The chemistry of fused heterocyclic systems having a nitrogen atom common to two or more rings (indolizines, quinolizines, cyclazines, and certain bridged compounds) is reviewed by M. Humphries and P. Rupah. A separate chapter by I. Gasnett is devoted to recent developments in the chemistry of quinolizidine alkaloids.

The emphasis shifts from the chemistry of alkaloids for the remainder of the volume. Chapter 39 by D. T. Hurst reviews the chemistry of compounds containing two fused five- and six-membered systems, each containing a heteroatom (nitrogen, oxygen, and/or sulfur). The editor chose not to supplement Chapter 40 covering dioxanes, oxathianes, and dithianes, since information on these compounds has appeared in other volumes in the series. The volume concludes with Chapter 41, contributed by the series editor. This large chapter covers monocyclic ring compounds with one heteroatom each from groups V and VIB. It is divided into several parts as follows: (a) 1,2-oxazines, (b) 1,3-oxazines, (c) 1,4-oxazines, (d) 1,2-thiazines, (e) 1,3-thiazines, and (f) selenazines.

Each chapter is a thorough, well-written review with key literature references provided throughout the text. References to reviews that have appeared since the publication of the first supplement appear in the introductions to the chapters covering the various alkaloid topics. A comprehensive index can be found at the back of the volume. Organic and natural products chemists will find this volume particularly useful. Institutional library acquisition of this and all other volumes in the series of *Rodd's Chemistry of Carbon Compounds* is enthusiastically recommended.

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Protective Groups in Organic Synthesis. Third Edition. By Theodora W. Greene and Peter G. M. Wuts. John Wiley & Sons, New York. 1999. xxi + 779 pp. 16 × 24 cm. ISBN 0-471-16019-9. $84.95.

This third edition of a well-known book encompasses the literature in relation to the formation and cleavage of protecting groups through 1997 and is a timely update of the second edition, published in 1991. The first edition of this book had about 1500 references and described 500 protecting groups; this edition is significantly expanded and has over 5000 citations and describes 1000 protecting groups. It is divided into 10 chapters which are, as before, organized for the most part according to functional groups. Chapters 1 and 10 are devoted to the roles of protecting groups in synthesis and reactivity charts, respectively. The reactivity charts have not been changed since the first edition. Chapter 2 is on hydroxyl groups, 3 on phenols, 4 on carbonyl groups, 5 on carboxyl groups, 6 on thiols, 7 on amines, 8 on alkyne C−H (new), and 9 on the phosphate group (new).

Each chapter begins with a listing of types of protecting groups, and these are further divided into individual protecting groups. For example, Chapter 2 provides extensive coverage (228 pages) of alcohol and diol protecting groups; the first subsection includes ethers, subdivided into substituted methyl ethers, substituted ethyl esters, substituted benzyl ethers, and silyl ethers. Further subsections are esters, carbonates, and sulfonates. Thus, the exact type of protecting group is easy to locate by functional group. Alternatively, the 50-page index can be used to locate a particular moiety that has been used to protect a specific functional group, or in a general sense to find protecting group sections in the book.

Further subdivisions into individual protecting groups begin with headings for the protecting group, followed by formation, cleavage, and then a reference list. Oftentimes, specific examples are provided describing limitations or advantages of a particular method, and all is extensively referenced.

This is absolutely the most thorough, well-organized single book on protecting groups that is available. It is highly recommended for students, faculty, and industrial practitioners of organic synthesis, who will find this to be one of their most frequently used books.

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Stereoselectivity in Synthesis. By Tse-Lok Ho. John Wiley & Sons, New York. 1999. xv + 333 pp. 16 × 24.5 cm. ISBN 0471329223. $94.95.

This book provides an extensive overview of stereoinduction in organic synthesis, with approximately 800 examples reflecting primary literature through early 1997. The topic is divided into eight chapters: 1,2-Stereoinduction; 1,3-Stereoinduction; Stereoinduction at Long Distances; Group Directed Reactions and Chelation Effects; Conformational Effects; Topographical and Template Effects; Steric, Electrostatic, and Stereoelectronic Effects; and Thermodynamic Control and Kinetic Trappping. A through index allows searching by target and by selected reactions/transformations (a few major

areas such as alkylations are not indexed), but not by author. The numerous and well-chosen examples make this book attractive to any synthetic chemist and invaluable for those involved in teaching a graduate-level course in synthesis or stereochemistry. However, the weakness of the accompanying text renders the book suitable only for advanced students. Often incomplete or unclear, the written descriptions frequently detract from the graphics. Other flaws include the frequent failure to provide product ratios, the lack of emphasis on comparative stereoselection in related transformations, and the occasional lack of stereochemical descriptors in structures. Overall, *Stereoselectivity in Synthesis* is a slightly flawed answer to a pressing need.

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Topics in Stereochemistry, Volume 22. Edited by Scott E. Denmark. Wiley Interscience, New York. 1999. xii + 314 pp. 16 × 23.5 cm. ISBN 0-471-25316-2. $95.00.

This volume is a "reincarnation" of the original series launched in 1966 by E. L. Eliel and Norm Allinger and continued through 21 volumes until 1993. This volume, edited by Scott Denmark, relaunches the series, and a successful relaunch it is. The volume contains five contributions of high quality, some theoretical and some applied; a cumulative title index for the series; and a subject index.

The introductory article by Kurt Mislow, "Molecular Chirality", is a highlight of this volume. When I was asked to review this book and when I inquired about the contents, I agreed to review largely because I anticipated that the lead article might be another Mislow gem. I wasn't disappointed. In fact, I cannot do better in describing this article than to quote the editor from his preface. Prof. Denmark eloquently hit the nail on the head when he wrote: "[This chapter is] a conceptually stimulating feast...and provides an insightful analysis of molecular chirality, topological chirality, and definitions of chirality measures. Aficionados of the history of stereochemical concepts will particularly enjoy the account of how various molecular and topological models have evolved." This chapter has a discussion of molecular knots and links. I also learned that my hands would not be chiral in four-dimensional space! Such amusements are typical of a chapter in which Mislow takes some very sophisticated mathematical ideas and makes them eminently understandable to the practicing chemist. I found that the chapter effectively places the idea of chirality within the larger contexts of spacial and temporal phenomena.

The other more theoretical article closes the volume and deals with asymmetric amplification—the observation of greater enantiomeric excesses than expected in the products of a reaction. The authors, David Fenwick and Henri Kagan from the Université Paris-Sud, Orsay, have carefully developed the relevant equations and definitions and then have gone on to discuss cases of asymmetric amplification in the literature. The possible mechanisms behind this phenomenon are intriguing and clearly could be relevant to the amplification of chirality in the biological world (beyond the 1 part in 10^{17} enantiomeric excess in naturally-occurring amino acids that results from violation of parity—Mislow!).

The other articles in the volume are of a more applied nature and are also very interesting and well-written. The second article, by Donald Hilvert of the ETH in Zürich, is a thorough and lucid review of research on catalytic antibodies with an emphasis on stereoselectivity. The literature on acyl transfer, glycosyl transfer, phosphoryl transfer, additions, eliminations, substitutions, aldol reactions, and pericyclic reactions is thoroughly reviewed, and the concluding chapter on future challenges provides a useful perspective on the field.

A chapter on stereoelectronic effects on group 4 metal substituents was also intriguing. This chapter reviewed the stereoelectronic effects of Si, Ge, Sn, and Pb when these metals are at the β-, γ-, and δ-positions relative to electron-deficient sites, as well as the interaction of carbon−metal bonds with π-systems and with electron-rich orbitals at the β-position. The chapter is all about *really hyper* hyperconjugation! The last discussion is confined largely to effects on ionization potentials, but many examples from the reaction literature are present in the earlier sections.

The remaining chapter in the book, by Masakatsu Shibasaki and Hiroaki Sasai from the University of Tokyo, deals with asymmetric catalysis by chiral lanthanoid complexes. Much of the detailed discussion in this chapter is focused on "nitroaldol" (Henry) reactions, but a number of other applications are discussed as well—the asymmetric Michael reaction, the aldol reaction, and the hydrophosphonylation of aldehydes and imines. The authors not only discuss the catalytic effects but also provide structural information about the various catalysts discussed. The authors also briefly summarize earlier work on Diels−Alder reactions, Mukiyama aldol reactions, asymmetric reductions, and other reactions. One slightly annoying omission in this article was a definition of the acronym "BINOL", certainly well-known to practitioners but not obvious to a person who desires to become newly acquainted with this area. Eventually, four pages in, after the term is used repeatedly, a structure is provided.

Too often are we (or our libraries) asked to pay $200 or more for loose aggregations of virtually unedited camera-ready copy. This volume, in contrast, has been very carefully prepared. It is type-set throughout, and the figures have been drawn in the various articles with a consistent style, so that the reader does not have to compensate for variations in "benzmanship" between articles. I could find essentially no errors of chemistry, grammar, or typography. Each chapter begins with a useful outline of the chapter contents. The volume appears to be well-indexed; I was able to find entries

for all of the terms that I could devise as test cases. The editor and publisher are to be complimented for such a high standard of production.

If this volume exemplifies future releases in this series, I would expect a bright future for the "second era" of *Topics in Stereochemistry*. I enthusiastically recommend this volume to chemists interested in the topics covered as well as for those who simply want an overview of recent development in this field. The volume is dedicted to the memory of Valdimir Prelog and Derek H. R. Barton. I think their legacy has been appropriately honored.

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