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BOOK REVIEWS

**The Pyrazines: Supplement I. The Chemistry of Heterocyclic Compounds. Volume 58**. By D. J. Brown (Australian National University). Wiley-Inter--science: New York. 2002. xviii + 557 pp. $425.00. ISBN 0-471-40382-2

This book, which serves as a supplement to *The Pyrazines*, Volume 41, covers the literature between 1979 and 2000. It consists of the following eight chapters: Primary Syntheses from Aliphatic or Carbocyclic Synthons; Primary Syntheses from Other Heterocyclic Systems; Pyrazine, Alkylpyrazines, and Arylpyrazines; Halogenopyrazines; Oxypyrazines; Thiopyrazines; Nitro-, Amino-, and Related Pyrazines; and Pyrazine−Carboxylic Acids and Related Derivatives. It also contains a full appendix of all simple pyrazines reported up to 2000 (inclusive), an index to the text itself, and cross references to the original volume.

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**Advances in Chemical Physics. Volume 120. Computational Methods for Protein Folding**. Edited by Richard A. Friesner (Columbia University), I. Prigogine (University of Texas at Austin and International Solvay Institute, Université Libre De Bruxelles), and Stuart A. Rice (University of Chicago). John Wiley and Sons, Inc.: New York. 2002. xiv + 528 pp. $175.00. ISBN 0-471-20955-4.

The authors of this text thoroughly examine recent advances in computational modeling of protein folding, ranging from the simplest models to those utilizing atomic-level detail. The importance of the volume cannot be overestimated. It serves as an important reference to researchers seeking recent information on the statistical analysis of protein-folding kinetics as well as ab initio approaches to protein folding and prediction of protein binding sites and ligand binding affinities. In fact, ab initio approaches constitute a sizable portion of the book.

Volker et al. discuss the development and improvement of the potential energy function and include results showing training sets and unambiguous figures that illustrate the effects of including or excluding particular parameters. Klepeis et al. thoroughly discuss topics of generic optimization as well as approaches used to model the energies of protein interaction, protein docking, and prediction of binding affinities. The extensive description and beautifully presented algorithmic functions, tables, and figures should convince the reader of the enormous difficulty of addressing the protein-folding problem as well as the important role of ab initio approaches to resolve these quandaries.

In addition to its small size, the book is well-equipped with recent references to allow the reader to pursue any of the described topics in sufficient detail. The expansive subject index of more than 600 entries allows facile access to a particular topic of interest. The book is lacking, however, in its coverage of methods for analyzing protein sequences unveiled from the human genome project. Genetic algorithms and genetic neural network methods in the context of statistical analysis and ab initio methods are explored briefly. Membrane protein structure and function and how genomes can be mined for this type of information, two other areas of intense current interest, are not treated at all.

Nevertheless, the book does contain specific information about a wide variety of topics involving theoretical methods for studying the protein-folding problem. Each group of authors offers insightful introductions and reviews that enable the reader to understand the important questions at stake and the limitations of the tools utilized to answer the questions at hand. Equally important and interesting is the discussion of methods used to test the accuracy of predictions derived by different approaches; most of the chapters devote a lengthy section to this topic. Appropriately, the last chapter by Wallqvist et al. presents the complexities and methods to distinguish conformations of native proteins from misfolded ones using decoys. The authors conclude that the best approach to distinguish native folds from decoys involves both knowledge-based scoring potentials and the OPLS-AA molecular mechanics energy function with the surface-generalized Born solvation model.

Overall, the book fulfills its objective of presenting the complexities, advances, and various theoretical methods of approaching the protein-folding problem. This text should prove to be an excellent addition to the collection of reference texts held by scientists pursuing research in theoretical modeling of biological systems.

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**The Mechanisms of Fast Reactions in Solution**. By E. F. Caldin (University of Kent, Canterbury, U.K.). IOS Press: Amsterdam. 2001. xi +329 pp. $123.00. ISBN: 1-58603-103-1.

So many chemical transformations take place in solution that this title immediately caught my eye as a "must read." Having read the book, I can state that even beginners in the field of fast reactions will not be disappointed by this monograph; on the contrary, a great treat is in store for them as well as for more experienced researchers. The exposition is clear and up-to-date, although the author is recently deceased. Indeed, we owe much to Professor Brian Robinson who took it upon himself to produce this book after the author's death.

Chemists generally induce a reaction by mixing two solutions. In many cases, the mixing takes place on a time scale that

Unsigned book reviews are by the Book Review Editor.

exceeds the duration of the reaction under investigation. In such circumstances, we learn only that the reaction was "fast." How, then, are fast reaction rates to be measured?

Historically, the first successful attempt to measure fast reaction rates in solution was through the use of stop-flow kinetics. Here a reaction is initiated by rapidly mixing reactants by forcing solutions of them into a mixing chamber at a velocity of several meters per second. Then optical measurements (absorption or fluorescence) of the concentration versus the distance traveled by the reagent along the tube can be related to rate of reaction; this procedure can determine reaction half-lives on the order of a millisecond or less.

A conceptual breakthrough in the measurement of fast reactions was the realization that such reaction rates were measurable without the need to mix the reaction partners. One way to accomplish this is to drive the reaction mixture from equilibrium by some external perturbation, such as a mechanical or electrical disturbance, and then measure the rate at which equilibrium is restored—that is, the relaxation time. Pressure waves propagate in liquids at the speed of sound, so the use of sound waves or shock waves extends the rates of reaction to the microsecond time regime. Still faster is the use of electrical disturbances, through the use of which fast reactions can be brought to the subnanosecond regime. Finally, perturbing and probing systems using ultrafast (femtosecond) light sources allows studies on the subpicosecond time scale.

Given this context and following an exposition on diffusion-controlled reactions, this monograph provides a sequence of four chapters that introduce flash photolysis, pulse radiolysis, fluorescence quenching, and subpicosecond techniques. For me, however, the most interesting part of this book is its final two chapters on the treatment of fast electron- and proton-transfer reactions. A clear exposition is presented of what is commonly called Marcus theory, a quasithermodynamic approach that builds on transition-state theory. This theory is the closest we have come to a grand unifying theory to explain the mechanisms of fast reactions in solution.

This book is an excellent read, particularly for someone just getting started in trying to master the huge literature pertaining to fast reactions in solution.

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**Inorganic Chemistry Highlights**. Edited by Gerd Meyer, Dieter Naumann, and Lars Wesemann (University of Köln). Wiley-VCH: Weinheim. 2002. xvi + 324 pp. $75.00. ISBN 3-527-30265-4.

This volume, valuable for teachers, researchers, and advanced students, provides us with numerous brief overviews of modern/hot highlights in the field of inorganic chemistry. These span molecular, coordination, organometallic, and bioinorganic areas as well as solid-state chemistry and materials. The editors appear to have been quite successful in their endeavor.

Nineteen chapters deal with diverse and fascinating chemistry: (1) clustering in molten Zintl-phase alloys; (2) structures of and bonding in solids around the Zintl (valence compound) boundary; (3) structure predictions from first principles; (4) multivalent cation conductors in the solid state; (5) large polyoxometalate clusters; (6) olefin epoxidation with the aid of molybdenum complexes; (7) synthesis of organo-metal, organo-amide and aryoxides of the rare-earth elements; (8) structural and functional characteristics of certain phosphatase and oxidase enzymes; (9) amino-troponiminate ligands; (10) metalla-calix[4]arene-aided transformations of hydrocarbons; (11) metal carbonyl cations as superelectrophiles; (12) borylene complexes; (13) silaboranes; (14) carbaalanes; (15) reduced molecular aluminum and gallium cluster halides; (16) covalent main-group-element azides; (17) silacalix phosphinimines; (18) dinitrogen fixation; and (19) organoxenon compounds.

The chapters range between 6 and 42 pages of text, depending on the breadth of the area. Some introduce new concepts and approaches (see Chapter 3), whereas others give a thorough summary in a special field of chemistry (see Chapter 2) or feature recent developments that should be incorporated into inorganic textbooks (e.g., Chapters 13−16, 19). Many of the authors are recognized experts in their areas. Most articles are replete with references from the 1990s and from 2000 as well, although the longest and most detailed chapter on cation conductors goes back further than that. Certainly, this eclectic collection offers some attractive modern topics for everyone, although it mainly features main-group-element compounds and chemistry. The presentation is excellent, and relatively few errors were noted (a copy editor should have caught the misspellings of phosphorus, however).

This volume should have an excellent impact, particularly among those who wish to expand their breadth and understanding of modern inorganic chemistry, broadly defined. The anticipated success of this effort should also lead to a series of future volumes, but with more chapters written by a geographically broader group of authors: one-half of the contributions in this volume come from Germany, beyond which only the United Kingdom and Canada are origins of more than a single chapter. We look forward to the appearance of Volume 2, perhaps in 2004?

**John D. Corbett* and Anja-Verena Mudring,** *Iowa State University*

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**Progress in the Chemistry of Organic Natural Products. Volume 82**. Edited by W. Herz (Florida State University, Tallahassee), H. Falk (Johannes-Kepler-Universität, Linz, Austria), G. W. Kirby (University of Glasgow, Scotland), and R. E. Moore (University of Hawaii at Manoa). Biaryls in Nature: A Multi-Facetted Class of Stereochemically, Biosynthetically, and Pharmacologically Intriguing Secondary Metabolites by G. Bringmann, C. Günther, M. Ochse, O. Schupp, and S. Tasler. Springer-Verlag: Wien, New York. 2001. viii + 294 pp. $159.00. ISBN 3-211-83653-5.

"Fortschritte," as this series is commonly called, is the preeminent one on natural products chemistry and was first published in 1938. This latest volume deals entirely with biaryl natural products. Like previous volumes, the presentation is exquisite. The chemical structures, figures, schemes, and tables are of the highest quality, and the 15 color photographs of plants

are gorgeous, including periwinkle, water hyacinth, *Potentilla*, *Plumbago indica*, a liverwort, and more. There are subject, author, and reference indexes, with the latter including titles. An index to the color photographs would have been useful.

Following a 20-page Introduction, the monograph is divided into nonbridged (110 pages) and bridged (40 pages) biaryl natural products according to increasing size and structural complexity. Dr. Bringmann and his coauthors have done a masterful job of collecting, organizing, and discussing the more than 600 biaryls contained in 1360 references, including some from the year 2001. The coverage encompasses bioactivity, structure elucidation, synthesis, and biosynthesis. There is also a strong emphasis on chirality and the optical properties of these biaryl natural products, phenomena that often went unrecognized by earlier workers.

Specific examples of biaryl natural products that are covered in this monograph include simple biphenyls (aucuparin from ash trees; honokiol from magnolia), dibenzocyclooctadienes (schizandrin), diarylheptanoids (myricanone from myrtle), macrocyclic bis(benzyls) (plagiochin and the chlorine-containing bazzanins from liverworts), naphthylisoquinoline alkaloids (ancistrocladine), biflavonoids (robustaflavone), bicoumarins (orlandin from *Aspergillus niger*), perylenequinones (cercosporin from a mold), dimeric naphthalenes (gossypol from cotton seeds), dimeric carbazoles (bismurrayafolines from Indian curry leaf), dimeric indole alkaloids (cabufiline, vingramine), biaryl glycopeptides (vancomycin, eremomycin), and several more.

This monograph is an up-to-date, beautifully written survey of this relatively little-known group of natural products. I strongly recommend this book to chemistry libraries and to those natural products chemists in this field.

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**Encyclopedia of Electrochemistry. Volume 6. Semiconductor Electrodes and Photoelectrochemistry**. Edited by Stuart Licht (Israel Institute of Technology, Haifa, Israel). Series Edited by Allen J. Bard and Martin Stratmann. Wiley-VCH: Weinheim. 2002. x + 598 pp. $270.00. ISBN 3-527-30398-7.

This book is focused on the semiconductor/electrolyte interface and is the sixth volume of a planned 10-volume *Encyclopedia of Electrochemistry* (plus an index, Volume 11). It is the second monograph on this subject to become available in the last year; this follows a long drought in which no comprehensive, up-to-date book covering the area of photoelectrochemistry was published. The other monograph, *Semiconductor Electrochemistry* by Rudiger Memming (Wiley-VCH, 2001), is a more coherent work because it is written by a single author and is stronger on fundamentals; it would be more useful as a textbook or as a supplementary book to give to a new graduate student to learn the field. The present volume is more comprehensive, since it is longer, but it also contains chapters on peripheral subjects, such as inorganic fullerenes and epitaxial growth of semiconductors. The fundamentals are also covered in the first 50 pages in an easy-to-follow chapter that should give the novice the information needed to comprehend much of the following material.

This book has a much more applied flavor than Memming's, covering applications of photocatalysis and devoting full chapters to such niche subjects as optical image recording with photoelectrochemical processes and multiple band gap solar cells. Chapters concerning modification of semiconductor surfaces with molecules, dye-sensititized solar cells, and photoelectrochemical etching are particularly useful, since much of this information is consolidated for the first time in a single source.

In summary, this encyclopedia volume fits in well with the series and adequately covers much of semiconductor electrochemistry and photoelectrochemistry. It contains some valuable, up-to-date chapters on many subjects of interest to researchers using semiconductor electrodes for a variety of applications. It suffers from the usual limitations of multiple-author volumes: repetition among chapters, subjects falling between chapters, and some subjects being presented much better than others.

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**Mass Spectrometry in Drug Discovery**. Edited by David T. Rossi (Pfizer Global Research and Development) and Michael W. Sinz (Bristol-Myers Squibb, Wallingford, CT). Marcel Dekker, Inc.: New York and Basel. 2002. xi + 420 pp. $165.00. ISBN 0-8247-0607-2.

Analytical methods based on mass spectrometry are increasingly found at the epicenter of many drug discovery programs. From lead identification to pharmacokinetic profiling to quality control of bulk drug substances, mass spectrometry is often an analytical common denominator in the pharmaceutical and biotechnology sectors. However, although mass spectrometry may be a common language among many researchers in these areas, there are arguably many distinct dialects that are widely spoken in the community, the vocabulary of which often depends on the scientific background of the researchers and the specific discipline in which mass spectrometry is employed. *Mass Spectrometry in Drug Discovery* does an excellent job of bridging this "dialect gap" and gives a comprehensive view of how and why mass spectrometry is used as a quintessential tool in the drug discovery arena.

This text presents the reader with a comprehensive view of how mass spectrometry is applied in the drug discovery process from the perspective of a panel of world-class experts who actively employ mass spectrometry at major pharmaceutical companies. For the novice practitioner, this volume provides a well-written and thorough primer that educates the reader with regard to the common MS-related jargon and presents the fundamental concepts of operation of the most commonly used ionization techniques and detection platforms. This section goes well beyond providing a nuts and bolts description of the MS hardware; many commonly employed modes of operation are described in the context of biopharmaceutical applications, which serves as a nice segue to the subsequent sections describing experimental strategies and applied MS tactics.

Although the editors did a commendable job of including chapters that describe many of the mainstay applications of mass

spectrometry in a "big pharma" setting, their overall perspective was somewhat limited in this regard: of the 13 contributed chapters, only three were authored by researchers outside the "big pharma" arena. There are a number of drug discovery strategies either based on or heavily reliant upon mass spectrometry that were not discussed. Although it would be virtually impossible to describe all the novel "-omics" applications of mass spectrometry in a single volume (e.g., proteomics, functional genomics, metabalomics, pharmacogenomics, etc.), a chapter describing emerging methods would have been a welcome addition to this work. Nonetheless, this book should provide the reader with the necessary vocabulary and basic understanding of mass spectrometry to effectively assimilate recent reports of emerging MS-related techniques that were outside the intended scope of the book.

The centerpiece of the entire volume is a chapter entitled "The LC/MS Experiment," but might have been more appropriately entitled "Everything You Ever Wanted to Know about LC/MS but Were Afraid to Ask." This chapter does an outstanding job of describing and illustrating the practical aspects of LC/MS as applied to both drug discovery and general bioanalytical applications. It presents a cogent, well-organized discussion of the strategy for when LC/MS should be considered as a viable analytical technique and, perhaps more importantly, includes several industry-proven tactical approaches for actually making it work. The subsequent chapter on sample cleanup and automation nicely rounds out the section on instrumentation and experimental strategies and sets the stage for the subsequent applications section.

A few chapters are not particularly focused on MS or MS applications, but rather, play an important role in presenting concepts and analytical challenges that are at the core of the drug discovery process. These chapters may be of particular interest to the reader who has a strong background in analytical mass spectrometry or analytical methods development but would benefit from a better understanding of the bioanalytical challenges facing researchers in the drug discovery arena. For example, a chapter dealing with drug hydrophobicity and transport is presented not from the perspective of a mass spectrometrist, but rather, from the perspective of pharmaceutical researchers who use conventional chromatographic and perfusion-based techniques to characterize drug lipophilicity and transport. A few areas in which mass spectrometry might play a future role in the study of drug transport are presented in summary, but it is largely left up to the reader to put this and other non-MS discussions into the context of MS as a drug discovery tool.

The combined bibliographies of the 13 chapters contain nearly 800 references and constitute an excellent source of additional information for the interested reader. In general, the chapter bibliographies include a good mix of references to original proof-of-principle work, comprehensive review articles, and more recent publications describing optimized protocols; these are generally current up to about 2000.

In summary, *Mass Spectrometry in Drug Discovery* has something for nearly everyone working in the drug discovery sector and is an important source of information for beginning as well as seasoned practitioners of mass spectrometry; it would be an excellent addition to any university, pharmaceutical, or personal reference library. Individuals who possess a working knowledge of or expertise in analytical mass spectrometry but who have not worked in a drug discovery environment stand to gain valuable insight into a number of key roles that mass spectrometry plays in the drug discovery and development process from initial discovery to ADME (absorption, distribution, metabolism, and excretion) profiling. Moreover, this volume would make an excellent primer for managers who lack a background in analytical mass spectrometry but increasingly find themselves making decisions based on information derived from mass spectrometric analyses.

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