Book Reviews

Drugs in Inflammation; Volume 32; Agents and Actions Supplements. Edited by Michael J. Parnham, Michael A. Bray, and William B. van den Berg. Birkhäuser Verlag, Boston. 1991. 247 pp. 17 × 24 cm. ISBN 0-8176-2504-6. $79.00.

This book contains the proceedings from the first symposium on Drugs in Inflammation, of the International Association of Inflammation Societies, held on June 28 and 29, 1990, in Noordwijk, The Netherlands, as a satellite of the IXth International Congress of Pharmacology. Consistent with its association as a satellite of a major international meeting, this symposium covered four major topics in current antiinflammatory drug research. The first, Reducing the Side-Effects of Anti-inflammatory Drugs, consists of 11 papers. The lead paper, by K. Brune and W. S. Beck, reviews the aspects of nonsteroidal antiinflammatory drugs (NSAIDs) that the authors feel are responsible for their deleterious effects on gastrointestinal irritation and hepatic and renal toxicity. This is followed by a chapter by B. Goldlust and colleagues, who describe their clinical scheme to evaluate gastrointestinal toxicity. The remainder of the papers in this section deal with biological effects of several NSAIDs that are in development and includes five papers on gold complexes.

The second section is titled New Approaches to Pain Relief. It consists of six papers, one of which is a review of electrophysiological mechanisms in inflammatory pain, by H. O. Handwerker. This is followed by two additional mechanistic papers and three papers dealing with specific antiinflammatory or analgesic agents. The next section, New Treatments for Bone and Cartilage Loss in Rheumatoid Arthritis, focuses on an area of intense activity by pharmaceutical as well as academic researchers. There are 10 papers, one of which is a relatively brief, but comprehensive, review of the role of proteinases in cartilage destruction, by C. H. Evans. Several of the other papers deal with biochemical and morphological evaluation of mechanisms involved in cartilage destruction, and four deal with the effects of experimental therapies targeted to rheumatoid arthritis. The final section covers Drug Modulation of Cytokine Production. There are six papers; one, by S. Kunkel and colleagues, describes recent developments in understanding of cytokine signalling networks. The other papers describe biochemical and animal studies of inhibitors of interleukin 1 generation.

This volume was published reasonably soon after the symposium. Those who are involved in inflammation research should read it to acquaint themselves with new information in areas outside their primary interest.

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Biological Oxidation of Nitrogen in Organic Molecules (Progress in Pharmacology and Clinical Pharmacology. Volume 8, Number 3). Edited by P. Hlavica and L. A. Damani. Gustav Fischer Verlag/VCH Publishers, New York. 1991. x + 351 pp. 17 × 24 cm. ISBN 1-56081-317-2. $135.00.

This volume is comprised of 35 papers on various aspects of nitrogen xenobiochemistry, with multiple contributions being provided by certain leaders in the nitrogen-metabolism area (e.g., Ziegler and Gorrod). Although the title page suggests that this book represents the Proceedings of the 4th International Symposium on the Biological Oxidation of Nitrogen in Organic Molecules held in Munich on September 17–21, 1989, these papers were written more recently, as evidenced by the citation of 1990 literature. The volume is divided into three broad categories. The first section discusses the occurrence and analysis of N-oxidized products, describing ^{15}N NMR spectroscopic, ^{14}C radiolabeling, and TLC/HPLC chromatographic approaches to in vitro metabolic profiles and, in some cases, in vivo pharmacokinetics. The second chapter deals with the enzymology of N-oxidation and N-oxygenation, addressing aspects of mechanism, substrate specificity, isozyme multiplicity, and regulation of the flavin-containing monooxygenase and the cytochrome P-450-dependent enzyme systems. Certain phase II metabolism issues are also discussed. Papers on toxicologic aspects of N-oxidation are grouped together in the final section of the book. These include accounts on molecular mechanisms of cell toxicity exerted by several arylamines and representative nitrosamines and hydroxamic acids, as well as on the interaction of glutathione in some of these systems.

The editors' preface highlights the intention of this compilation to serve as a reference for graduates and research workers in the biochemical, biopharmaceutical, and toxicologic fields and for professionals in the drug, food, and chemical industries, in the hope of focusing attention on aspects of N-oxidation that still require more intense investigation. Undoubtedly, this volume fulfills its stated objective, and the information it contains is, for the most part, important and nonduplicative of other published material. However, as is the case in most compilations of individually authored manuscripts of this type, the coverage is somewhat spotty, and thus this volume, although valuable as a research resource, is less adequate for providing a balanced and/or unifying perspective of the field of organonitrogen metabolism.

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Principles of Nuclear Magnetic Resonance Microscopy. By Paul T. Callaghan. Oxford Science Publications, New York. 1991. xvii + 492 pp. 16.5 × 24 cm. ISBN 0-19-853944-4. $125.00.

The use of nuclear magnetic resonance microscopy, or imaging, in many areas of both the physical and biological sciences has expanded very rapidly over the past 5 or 6 years. Those of us experienced in solution-state NMR

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find the physics of NMR microscopy to be quite different from what we are familiar with. *Principles of Nuclear Magnetic Resonance Microscopy* bridges the physics gap between solution-state NMR and NMR microscopy. The text presents NMR microscopy from a mathematical point of view. The author presumes of the reader a basic knowledge of quantum mechanics and the mathematical theory of NMR. Very little general, descriptive material on NMR microscopy is included.

The text is well-written and thoroughly referenced, with 751 literature citations. It is also well-illustrated with many figures and microscopy images, including four pages of full color images. The text is divided into nine chapters. Chapter 1 presents the basic physical principles of imaging, including reciprocal space and the Fourier transformation. The second chapter presents an excellent mathematical introduction to NMR that will be very familiar to practitioners skilled in the art of solution-state NMR. Chapter 3 presents an in-depth discussion of the affects of magnetic field gradients on the observed image. The creation and application of selective pulses using field gradients is also discussed. In this chapter the concept and use of **k**-space is introduced. **k**-space which is foreign to most solution-state NMR spectroscopists, is a reciprocal space vector that may be traversed by moving either in time or in magnetic field gradient magnitude. In chapter 4 a more detailed discussion of **k**-space imaging is presented. An excellent overview of the use of **k**-space imaging in biology and material science is presented in chapter 5. This over 90-page chapter presents many interesting examples of images obtained from biological samples as well as examples from material science. I found the images of the rat brain and thorax to be particularly interesting and illustrative of the resolving power of NMR microscopy. Chapter 5 also contains an extensive biography with 256 literature references. Chapters 6 and 7 introduce the concept and use of **q**-space imaging. **q**-space is a reciprocal vector space similar to the scattering function applied to neutron scattering. Chapter 8 describes dynamic NMR microscopy, including the influence of periodic and slow motion on imaging as well as potential artifacts of dynamic NMR microscopy. The final chapter describes the instrumental requirements of the NMR microscope. Particular attention is given to the design of the magnetic field gradient coils and rf coils.

The only drawback to the text is that it is very mathematical and intended for a reader with a strong understanding of NMR and will therefore be difficult for the novice to read. The text does present a strong introduction to imaging to the scientist skilled in the art of solution- or solid-state NMR. As such, the text will help bridge the physics gap between solution-state NMR and NMR microscopy. The text would be an excellent addition to the library of any scientist interested in modern NMR experiments. The book could be used very nicely as a text book in a graduate course on NMR microscopy. As the technique of NMR microscopy becomes more common, this book will be useful to an increasing number of a wide variety of scientists.

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The Total Synthesis of Natural Products, Vol. VIII. Edited by J. ApSimon. Wiley-Interscience, New York. 1992. ix + 704 pp. 16 × 24 cm. ISBN 0-471-54507-4. $150.00.

This book comes in the worthy traditions of its predecessors in the series in being scrupulously written, with accuracy and clarity. The contrast between this multiply-authored series and some others in which the component volumes seem to have been assembled with less care and discernment is worth remarking upon at the outset.

The first chapter is a masterful summary by David Goldsmith of the current state of tri- and tetracyclic diterpenoid synthesis. Early successes in this area were followed by the discovery of much more elaborately functionalized representatives, and the synthetic approaches to them make exciting reading. N. K. Kochetkov's chapter sets the stage for the current period in polysaccharide synthesis, interest in which is driven by our understanding of the role polysaccharides play in immunochemistry. Ronald Thomson has for many years reported on the world of the natural quinones; as exciting targets proliferate and regiospecific methods are developed the focus on these compounds intensifies. His excellent chapter will be interesting to many. Spiroketal-containing natural products, sometimes containing a single carbon chain, are of great current importance: V. Vaillancourt, N. Pratt, F. Perron, and K. Albizati review synthetic methods for these, commenting first on general principles and then on particular applications.

This book will be a necessity for chemistry libraries and desirable for many individual investigators in natural products chemistry. Its contributors and editor are to be congratulated.

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The Chemistry of Sulphonic Acids, Esters and Their Derivatives. Edited by Saul Patai and Zvi Rapport. John Wiley & Sons, Ltd., Chichester, U.K. 1991. xvi + 1121 pp. 15.5 × 23.5 cm. ISBN 0-471-92201-3. $690.00.

This book is one of a series of advanced treatises *The Chemistry of Functional Groups*. It is the last volume in the subseries on sulfur-containing functional groups. Other volumes have reviewed the thiol group (1974), the chemistry of ethers, crown ethers, hydroxyl groups, and their sulfur analogues (1980), the sulfonium group (1981), sulfones and sulfoxides (1988), sulfinic acids, esters, and their derivatives (1990), and sulfenic acids and their derivatives (1990). The format of the present volume is consistent with others in the series. Thus, the initial chapter is introductory and deals with general and theoretical aspects of sulfonic acids and their derivatives. This is followed by a description of the stereochemistry, conformation, and chiroptical properties of these compounds. Subsequent chapters focus on characteristics and characterization, e.g. mass spectrometry, UV, NMR, ESR, acidity, thermochemistry, and analytical methods for sulfonic acids and their derivatives. These sections are followed by ones dealing with the preparation of sulfonic acids, esters, amides, and halides, the use of these

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compounds as synthons, their rearrangements, photochemistry, radiation chemistry, electrochemistry, and syntheses, and uses of isotopically labeled sulfonic acid derivatives and related compounds. Other chapters address directing and activating effects in reactions involving sulfonic acids and derivatives, the biological activity of sulfonic acid derivatives, sulfenes, sultones, sultams, sulfamic acids, and perfluoroalkanesulfonic acids, and polymers containing SO_3H and related groups. Each chapter is written in detail and is thoroughly referenced through 1989. In addition, the volume contains comprehensive author and subject indexes.

This volume is an outstanding source of up-to-date information and references relating to sulfonic acids and related compounds. In conjunction with other volumes of the series, it serves as a comprehensive reference source that is recommended for institutional chemistry libraries.

Staff

The Chemical Bond: Structure and Dynamics. Edited by Ahmed Zewail. Academic Press, Inc., San Diego, CA. 1992. xv + 313 pp. 15 × 23 cm. ISBN 0-12-7769620-7. $49.95.

Understanding the structure and dynamics of the chemical bond is central to all fields of molecular science. This book by some of the most influential scientists of our time—including six Nobel laureates—chronicles our emerging understanding of the chemical bond through the last 9 decades and into the future. It is an outgrowth of a symposium during Caltech's centennial year, held on the occasion of Linus Pauling's 90th birthday on February 28, 1991; it contains chapters describing the science and historical developments that have contributed to the progress achieved in the study of the structure and dynamics of the chemical bond. In the first part, "Structure", Linus Pauling, Max F. Perutz, Alexander Rich, and Francis Crick give an account of progress made in different fields with their personal historical reminiscences. In the second part, "Dynamics", Lord George Porter, John C. Polyani, Dudley R. Herschbach, Richard Bernstein, and Editor Ahmed Zewail provide overviews of the advances made in developing the molecular description of the chemical bond, in time and space, of chemical reactivity, and of the impact of recent discoveries. The interplay between theory and experiment, and bonding and dynamics, in probing the dynamics of the chemical bond is illustrated in many of the articles. The volume concludes with biographies and pictures of the all-star cast of contributors.

The Chemical Bond: Structure and Dynamics is a unique presentation describing major scientific achievements in chemistry and biology with the chemical bond playing a fundamental role. It provides lively insights on the special nature of scientific thought and discovery and will be of interest to scientists, science historians, and to all others who are scientifically inclined.

Staff

Nucleophilic Aromatic Displacement: The Influence of the Nitro Group. By Francois Terrier. VCH Publishers, Inc., New York. 1991. xi + 460 pp. 15.5 × 24 cm. ISBN 0-89573-312-9. $125.00.

Author Terrier provides an authoritative review of the importance and usefulness of the nitro group in nucleophilic aromatic substitution (S_NAr) reactions. This monograph is clearly written and comprehensive, including detailed discussions on the mechanistic aspects of the reaction and its synthetic versatility. The author discusses the reactivity of heteroaromatic systems and radical and photoinduced nucleophilic aromatic substitution reactions. The emphasis is on the nitro group as the activator of an aromatic system toward nucleophilic attack.

The book is divided into eight chapters; the first chapter provides the reader with a thorough discussion of the S_NAr reaction mechanism, separately covering the influence of the nucleophile, leaving group effects, and medium effects. Additional topics include the spectral evidence for the intermediacy of σ-complexes and base catalysis in S_NAr reactions. Chapter 2 covers the structural features of anionic σ-complexes, as well as their kinetic and thermodynamic characteristics. Chapters 3 and 4 discuss the synthetic aspects of the intermolecular substitution and intramolecular substitution (Smiles) reactions, respectively. The fifth chapter discusses hydrogen as the departing group, vicarious reactions, and the Von Richter rearrangement. Vicarious reactions are those in which the departing hydrogen of the intermediate σ-complex is promoted by the concomitant departure of part of the nucleophile addend. Chapter 6 discusses nucleophilic aromatic photosubstitutions and chapter 7 discusses the radical S_NAr reaction. Chapter 8 discusses the S_N(ANRORC) reaction. This reaction involves the nucleophilic substitution of azaaromatics, through a multistep sequence involving ring opening–ring closure (RORC) of the heterocyclic system.

References are numerous, through 1990, and are located at the end of each chapter. A multitude of useful data is arranged in the form of tables and graphs. An author index and subject index are included.

This excellent book is highly recommended to all synthetic organic chemists and should find a place in their personal libraries. The publishers should consider offering a paperback edition at a price within the reach of students.

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Advances in Drug Research. Volume 21. Edited by Bernard Testa. Academic Press Inc., San Diego, CA. 1991. xi + 299 pp. 15.5 × 23.5 cm. ISBN 0-12-013321-0. $106.00.

In his opening remarks, the editor expresses his hope that this volume will "stimulate readers by poking [the scientific fires in] their minds, disturbing settled arrangements and bringing about new combinations". Although this hope was, indeed, realized on several occasions, after reading this latest addition to the popular series, I must also express that there were other times when some of the cataloging of detail tended to smolder rather than spark.

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The first chapter, Drug Targeting Towards the Lymphatics by S. Muranishi, provides an excellent overview with enough detail to set kindling in place for both the novice and expert in drug absorption/distribution. Sparks included the potential for using the lymphatic pathway to improve the absorption of large molecules as, for example, by oral administration of peptidyl drug–cyclodextrin complexes in permeability enhancer cocktails; the potential for delivering anticancer drugs selectively to lymph nodes participating in metastases by injection of sustained release microspheres at the site of the originating tumor; and the potential to maximize immunomodulator therapy by the injection of such agents directly into the lymphatic system.

The next chapter, Recent Developments in the Field of Quinolone Antibacterial Agents by D. Chu and P. Fernandes, provides a comprehensive review of this topic since 1977, which should serve to stoke the fires for practitioners specifically interested in this field. Certainly, few investigators will challenge the authors' concluding comment that there has been a near "exhaustion of [the] potential for [producing additional] novel structures" based upon the quinolone template. Flare-ups include the design of dual-action cephalosporins which release 4-quinolone derivatives when they are inactivated by β-lactamase; and the intriguing mechanism for these agents which is thought to involve cooperative binding at sites made accessible on the DNA intermediates resulting from the action of DNA gyrase.

The final chapter, Design and Therapeutic Potential of Peptides by A. Dutta, can be initially likened to a backdraft. Its review focuses on the development of SAR data for several peptide classes and provides a rush of flames comparable to the number of papers on this topic which seem to consume entire issues within the medicinal chemistry literature these days. Included in this rush, as just one example of "disturbing settled arrangements", are considerations of potency versus selectivity during the evolutions of enkephalinase and ACE inhibitors. However, this chapter ultimately looses the force of a true backdraft in that it does not cover some very interesting newer developments associated with the field. For instance, there are essentially no discussions about developments in spectroscopy (where both X-ray and NMR have become key tools to discern the conformations and interactions of peptides/proteins), molecular modeling (where molecular dynamics simulations can now address large molecules within solvent clusters), and engineering (where, for example, epitope libraries are helping to resuscitate the role of random screening during drug discovery). Still, given the rather monumental task that this author has attempted, he should certainly be credited with having stoked the flames in this area.

In summary, I would recommend that every investigator involved with some aspect of drug discovery should have ready access to this volume, at least within a library. In this regard, the volume's subject index is reasonably complete. Scientists conducting research within one of the three fields specifically covered in the volume may want to have a personal copy as well.

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A Textbook of Drug Design and Development. Edited by Povl Krogsgaard-Larsen and Hans Bundgaard. Harwood Academic Publishers, Chur, Switzerland. 1991. x + 643 pp. 17 × 24 cm. ISBN 3-7186-5100-9. $48.00.

A distinguished group of internationally known authors has been assembled to write a textbook that covers "the separate but interconnecting areas of chemistry and biology, balancing pharmacological, biochemial, and chemical aspects". Topics in the 16 chapters range from Drug Discovery: An Overview to Structural and Physicochemical Factors in Drug Design to Bio-inorganic Chemistry to Design and Application of Prodrugs to Drug Development: From Discovery to Marketing, and there are several other more classical medicinal chemistry-based chapters. Without exception, this reviewer found the chapters to be well-written and timely. Much valuable information is to be found and many exciting ideas are presented. The topics covered in the several chapters have been well-chosen and they reflect contemporary directions and trends in medicinal chemistry.

It is this reviewer's personal prejudice that description of the volume as a *textbook* is inappropriate. Each of the 16 chapters is quite independent of the others; there is no continuity from chapter to chapter, as would be highly desirable in a textbook for students. This is a likely defect of any multiauthored book. Some of the authors have presupposed a considerable degree of familiarity of the reader with the specific chapter topic, and they immediately begin a somewhat esoteric narrative with little introductory material and definition of terms. Literature references at the end of most of the chapters are meager.

The preface statement that "all important aspects of modern drug design and development will be described and exemplified" seems overstated. No modest-sized volume can do justice to the entire field of drug design. Selected pharmacological categories in the book are generally well done, but the scope of topics covered is not comprehensive. Less than three pages is allotted to molecular modeling. The index contains no reference to atomic inversion or to hard and soft acids and bases, although a brief, unreferenced discussion of hard and soft acids and bases is found in the chapter on bioinorganic chemistry.

Despite the reservations indicated above, this reviewer highly recommends the volume as a *reference work* and a ready source of much useful contemporary information for medicinal chemistry practitioners as well as for students.

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