

Book Reviews

Medicinal Chemistry Principles and Practice. Edited by F. D. King. The Royal Society of Chemistry, Cambridge. 1994. xxiv + 314 pp. 15.5 × 23.5 cm. ISBN 0-85186-494-5. £39.50.

This book is a collation of 1-h lectures and of more extensive tutorials presented by practicing medicinal chemists from industry and academia at the 7th Royal Society of Chemistry Medicinal Chemistry School held June 28–July 3, 1993. This residential course is intended to provide an introduction to medicinal chemistry primarily for synthetic chemists who have recently joined the (pharmaceutical) industry. The chapters include An Introduction to Drug-Receptor Interactions; Signal Transduction and Second Messengers; Enzyme Inhibitors; The Biological Evaluation of New Compounds; Pharmacokinetics; Drug Metabolism; Physicochemical Properties and Drug Design; Quantitative Structure-Activity Relationships; Considerations for the Use of Computational Chemistry Techniques for Medicinal Chemists; "Patent Medicine"; Molecular Biology - A New Route to Drug Discovery; Devising a Research Strategy; Past Approaches to Discovering New Drugs as Medicines; Bioisosteres, Conformational Restriction and Pro-Drugs: Approaches to Lead Optimisation - Case History: An Example of a Conformational Restriction Approach; The Design and Synthesis of Selective Protein Kinase C Inhibitors; Discovery of 1069C - A Novel Synthetic Antitumor Agent with Low Cross-Resistance Potential; The Design And Properties of "Dipeptoid" Antagonists; Migraine Therapy - from Serotonin to Sumatriptan; and Drug Development. An appendix includes some useful tabulated information including, *inter alia*, a summary of receptor properties; a summary of ion channel properties; a table of constants useful in QSAR Analysis; and a listing and appropriate comments about common routes of administration of drugs.

Within obvious existing constraints of space and time, this "handbook" is a success. Inevitably (and appropriately), the chapters cover their topics only superficially, and some areas of medicinal chemistry are not included. However, the constituency to which the volume is addressed will find that it contains a wealth of concepts and useful information for the aspiring medicinal chemist who has no educational background in the discipline or in pharmacology. The chapters are uniformly well-written and well-organized, and for the most part, concepts, explanations, and information are presented at a level of sophistication appropriate to the readership. Graphics are extensively employed and are generally well-done and helpful. Each chapter concludes with a brief but useful bibliography to encourage further exploration of the topic(s) covered. Latter chapters in the volume are case histories of the discovery of selected new drug entities and are intended to be illustrative of the entire process of drug research. As a one-time lecturer in the Royal Society of Chemistry Residential School and as a currently active participant in similar programs in the United States, this reviewer concludes that the volume is a potentially useful adjunct

to the titanic task of converting a "pure" synthetic organic chemist into a medicinal chemist. However, the book seems to be of considerably less value as a text or as a reference for graduate students or practitioners in medicinal chemistry, pharmacology, or pharmaceuticals.

Joseph G. Cannon
College of Pharmacy
The University of Iowa
Iowa City, Iowa 52242

JM950087C

Chemistry of Nucleosides and Nucleotides. Volume 3. Edited by Leroy B. Townsend. Plenum Press, New York and London. 1994. xiii + 553 pp. 17 × 26 cm. ISBN 0-306-44474-7. \$120.00.

This book is volume 3 of a projected four-volume series dealing with the recent developments in the chemistry of nucleosides and nucleotides. These volumes are timely and very informative. As noted in the Preface, nucleosides and nucleotides (oligonucleotides included) have generated tremendous interest because of their unparalleled biological and chemotherapeutic properties. The present volume consists of five well-written chapters, written by authors who are among the leaders in the specific areas of research.

Chapter 1 (Maria Preobrazhenskaya and Ilya Korbukh; 105 pages, 317 references) presents a comprehensive review on the synthesis and reactions of the nucleosides/nucleotides of pyrrole, pyrazole, triazole, indole, indazole, and benzotriazole. Also included is a section on the conformational features of these nucleosides. The literature is covered up to 1990, and the references are located at the end of the chapter. In chapter 2 (Stanislav Chladek; 36 pages, 142 references) the synthesis, reactions, and properties of the 2'(3')-O-aminoacyl and peptidyl nucleosides, nucleotides, and oligonucleotides have been presented very effectively. This chapter provides valuable information about the mechanism of protein biosynthesis and should be of immense interest to medicinal chemists. Chapter 3 (Wolfgang Pfeleiderer; 117 pages, 233 references) deals with the syntheses and reactions of bicyclic heterocyclic nucleosides and nucleotides. The bicyclic benzo-fused ring systems included are quinoline, isoquinoline, cinoline, phthalazine, quinazoline, quinoxaline, 1,3-benzoxazine, and 1,2,3-benzotriazine. A number of bicyclic purine nucleoside analogs are discussed in which the carbohydrate moiety is linked to a six-membered pyridine/pyrimidine/pyridazine moiety. Also included are several nucleoside derivatives of nitrogen bridgehead bicyclic systems, in which the sugar is attached to the six-membered heterocyclic ring. An authoritative treatise on pteridine nucleosides and nucleotides is provided. In the fourth chapter, Gordon Shaw examines the methods of synthesis and reactions of imidazole and benzimidazole nucleosides and nucleotides. This 158-page review contains 361 references, and the literature is covered to mid-1990. This is by far the longest

chapter. The UV spectra and optical rotations of certain imidazole nucleosides and nucleotides presented in Table I and the ^1H NMR spectral data of some imidazole nucleosides (Tables II and III) are very helpful to the practicing medicinal chemist. An interesting aspect of this chapter is the discussion on the function of imidazole nucleosides/nucleotides in living systems and the involvement in the *de novo* biosynthesis of purine nucleotides. In addition, the biological properties of some imidazole nucleosides and nucleotides are briefly discussed. Recent developments in the syntheses of benzimidazole, benzotriazole, and indazole nucleosides are also summarized. In the last chapter (115 pages, 373 references), Kyoichi Watanabe has categorized the methodologies used in the synthesis of the C-linked nucleosides and discussed the chemistry of each category concisely. The synthesis of these C-nucleosides by (i) direct glycosylation of preformed aglycon, (ii) construction of the heterocyclic moiety from a C-glycosyl derivative, and (iii) interconversion of preformed C-nucleosides has been discussed very eloquently. The synthesis of C-nucleosides from non-carbohydrate material is also summarized.

The individual chapters are professionally written. Effort has been made to use illustrative figures and tables overwhelmingly and to provide extensive bibliography. A detailed subject index is also included. This reviewer found a few printing errors.

This volume, together with others in the series, presents valuable up-to-date information about nucleosides and nucleotides and should be of great interest to the basic virologists, tumor biologists, biochemical pharmacologists, and medicinal chemists.

Ganapathi R. Revankar

*Triplex Pharmaceutical Corporation
Grogans Mill Road
The Woodlands, Texas 77380*

JM950161R

Organometallics in Synthesis. A Manual. Edited by M. Schlosser. John Wiley & Sons, Inc., Chichester, U.K. 1994. ix + 603 pp. 19.5 × 25.5 cm. ISBN 0-471-93637-5. \$100.00.

This book consists of eight chapters, grouped according to metal. In all cases, the articles have been written by leading investigators in the field. Topics covered include the organic compounds of alkali metals, titanium, copper, palladium, boron, aluminum, and tin. A subject index and a formula index have been included at the end. All of the articles contain excellent introduction sections dealing with practical handling, storage, and physical properties of the title reagents, followed by clear and thorough discussions of the descriptive chemistry of the title reagents. Representative experimental procedures have been provided; however, the amount of experimental information is not consistent within the articles. For example, in the copper article, nearly every paragraph is accompanied by an experimental procedure, while the entire aluminum article contains only three experimental procedures. The experimental procedures are most convenient when titled as a representative procedure as in

most of the articles; however, in some of the articles, the procedures are unfortunately titled by the compound produced.

For the most part, the articles are well-illustrated, very clear, and extremely well-referenced; the latest references are to articles published in 1991. The first article (by M. Schlosser, 138 pages, 793 references) alone justifies the purchase of the book. This one article covers important topics such as solution and solid state structure, stabilization of carbanions, and methods for generation of organoalkali reagents. The second article (by F. Totter and P. Rittmeyer, 25 pages, 55 references) is devoted to the handling of organolithium reagents and to some extent emphasizes large-scale uses of organolithium compounds. Valuable practical information such as storage, titration, and disposal of organolithium compounds has been included in this section. The third article (by M. T. Reetz, 72 pages, 328 references) is devoted to the use of titanium compounds in organic synthesis and as a bonus includes an excellent discussion of stereoselective additions of nucleophiles to carbonyl compounds. The fourth article (by B. H. Lipshutz, 92 pages, 172 references) is devoted to organocopper chemistry. An excellent effort has been made to clarify the different types of organocopper reagents and outline the effects of additives to the system. The fifth article (by L. S. Hegedus, 69 pages, 168 references) is devoted to palladium in organic synthesis. This article begins with an excellent discussion of the advantages and disadvantages of individual sources of palladium and clarifies many confusing issues. The sixth article (by K. Smith, 41 pages, 103 references) is devoted to organoboron chemistry, the seventh article (by H. Yamamoto, 22 pages, 52 references) is devoted to organoaluminum chemistry, and the final article (by H. Nozaki, 35 pages, 183 references) covers organotin reagents.

James W. Herndon

*Department of Chemistry and Biochemistry
University of Maryland
College Park, Maryland 20742-2021*

JM950162J

The Biology of Nitric Oxide. 3. Physiological and Clinical Aspects. Edited by S. Moncada, M. Feelisch, R. Busse, and E. A. Higgs. Portland Press, London. 1994. xvii + 551 pp. 17 × 24.5 cm. ISBN 1-85578-063-1. \$212.00.

During the past several years, the importance of the L-arginine:nitric oxide pathway has become increasingly evident. Recent advances in nitric oxide research are highlighted in this volume which records proceedings from the Third International Meeting on the Biology of Nitric Oxide which was held in Cologne in October of 1993.

In the current volume are collected 3–5-page summaries of 145 meeting presentations of up-to-date physiological and clinical aspects of nitric oxide research. Topics are broadly categorized under cardiovascular effects, central and peripheral nervous system, and clinical aspects. Each report is referenced, and comprehensive author and subject indexes are included.

The *Biology of Nitric Oxide* provides timely information for researchers in the field and also provides information for clinicians and workers in other areas of research.

Staff

JM950163B

The Chemistry of Heterocyclic Compounds. Volume 52. The Pyrimidines. D. J. Brown, R. F. Evans, W. B. Cowden, and M. D. Fenn. Edited by E. C. Taylor. Wiley-Interscience, New York. 1994. xxix + 1509 pp. 16 × 24 cm. ISBN 0-471-50656-7. \$595.00.

The Pyrimidines, volume 52 of *The Chemistry of Heterocyclic Compounds*, is a unique blend of the basic concepts of traditional pyrimidine chemistry combined with some examples of new, nontraditional methodology. This treatise is not a supplement, but rather it represents a complete survey of the pyrimidine literature from start to present date. The book is broken down into 12 chapters which are followed by an extensive list of tables, the references, and a detailed subject index. The tables, which actually begin with chapter 12, contain a wealth of information on simple pyrimidines, *e.g.*, spectral and physical properties, and each entry cites the reference where this information can be found. The tables alone are worth their weight in gold.

Like its predecessors (volume 16 and supplements I and II), volume 52 examines electrophilic addition at nitrogen and carbon as well as nucleophilic addition and displacement. Chapter 1 covers these aforementioned topics as well as nomenclature. It is worth mentioning that throughout the text the use of trivial names has been minimized. Chapters 2 and 3 focus on the synthetic methods available to construct the pyrimidine ring. Chapter 3 is devoted exclusively to the *Principal Synthesis*. Chapter 4 concentrates on the preparation and reactions of alkyl- and arylpyrimidines, while chapters 5–10 cover the nitro-, halogeno-, oxo-, thio-, and aminopyrimidines and certain carboxylic acid derivatives, respectively. Synthetic approaches to these heterocycles are described, and their utility is highlighted. For example, chapter 9 which covers the aminopyrimidines explores their preparation, properties, and potential use as synthons to other bicyclic systems. Chapter 11 focuses on reduced pyrimidines, while chapter 12 covers ionization and spectral properties of pyrimidine and its simple derivatives.

The authors should be complimented on their selection of material and its presentation. This reviewer has great admiration for their ability to cover and present the highlights of all aspects of pyrimidine chemistry and to compress it into one text. Chemists interested in pyrimidine chemistry will find volume 52 indispensable.

Although the price is prohibitive for inclusion in personal collections, it should be useful to institutional libraries.

Raymond P. Panzica

Departments of Medicinal Chemistry and Chemistry
University of Rhode Island
Kingston, Rhode Island 02881

JM9501644

Hypertension. Pathophysiology, Diagnosis, and Management. Edited by John H. Laragh and Barry M. Brenner. Raven Press, New York. 1995. xiv + 3311 pp. 22.5 × 28.5 cm. ISBN 0-7817-0157-0. \$345.00 (two-volume set).

The medical community does not lack textbooks in the area of hypertension, but this encyclopedic text includes nearly every relevant topic one could imagine in the area of hypertension. This book, like its predecessor published in 1990, contains a wealth of knowledge that should be useful to any person interested in the broad area of hypertension. In providing current information in areas of active research, this book offers both the clinician and researcher a useful, detailed, easy-to-use reference book.

The text contains 189 chapters ranging in length from 6 to 41 pages. This edition is approximately 33% longer than the first edition. The all inclusive topics range from the classic description of the "Goldblatt Experiment" through the potential use of gene therapy in cardiovascular disorders. The text is divided into 10 sections: Background and Historical Aspects; Epidemiological Dimensions of Hypertension; Diet and Hypertension; Circulatory and Target Organ Pathophysiology of Hypertensive Disease; Blood Pressure Regulation in Normal and Hypertensive States; The Kidneys and the Renin-Angiotensin Aldosterone Axis: Role in Sodium-Volume Homeostasis and Arterial Tone in Pathogenesis of Hypertension; Clinical and Laboratory Evaluation of Hypertensive Disorders; Pathophysiology, Diagnosis and Treatment of Specific Forms of Hypertension; Evaluation of the Hypertensive Patient; and Treatment of the Hypertensive Patient. These sections are similar to what appeared in the first edition, although nearly each section has been dramatically increased and updated. For instance, the section in the first edition on "Future Horizons in Therapy" discussed renin inhibitors and angiotensin II antagonists as potential new therapies, whereas this edition also has chapters on endothelin antagonists and dual inhibitors of angiotensin converting enzyme and endopeptidase as well as a chapter on "Prospects for Gene Therapy in Cardiovascular Diseases".

The text is up-to-date with the most current guidelines/recommendations for treatment and references included. Tables and graphs are easy to understand and appropriately placed throughout the book. Interesting chapters such as "Low Birth Weight as a Risk Factor for Juvenile and Adult Hypertension", "Blood Viscosity as a Factor in Human Hypertension", "Hypertension, Growth Factors, and Their Relevance to Atherosclerotic Vascular Disease", and "Psychosocial Stress and Experimental Hypertension" are sprinkled throughout the

book. More standard chapters, e.g., descriptions of various classes of drugs used in the treatment of hypertension and the relationship between hypertension and various other diseases (e.g., stroke, diabetes, obesity), are included as well. The inclusion of detailed descriptions of many of the factors and mechanisms responsible for hypertension and the control of blood pressure are welcome.

This text is well written and edited. The format of the chapters is such that there is a comfortable transition from chapter to chapter although multiple expert authors have written the chapters. This text should be a standard reference for anybody who requires an all inclusive text in the area of hypertension.

Dennis M. Ackerman

*Solvay Pharmaceuticals
901 Sawyer Road
Marietta, Georgia 30062*

JM950166O

Stereochemistry of Organic Compounds. E. L. Eliel, S. H. Wilen, and L. N. Mander. John Wiley & Sons, Inc., New York. 1994. xv + 1267 pp. 18.5 × 26 cm. ISBN 0-471-01670-5. \$75.00.

This formidable 14-chapter volume might also be called "Everything you always wanted to know about stereochemistry but were afraid to ask". This long-awaited book, appearing more than 30 years after Eliel's first volume of the same title, has a little something for everyone. The authors have done a heroic job of trying to gather into one (albeit large) volume a wealth of information about "stereochemistry". Although this reviewer was a bit put off by the sheer size of the book (for which the authors apologize in the preface), it actually proved fairly easy to read and was remarkably free of typographical errors for a work of this magnitude. There are the occasional goofs, e.g., the mislabeling in Figure 11.107 and the related text of bicyclo[3.3.0]octane as bicyclo[3.3.0]nonane, and in a few places explanations or figures are wholly inadequate (e.g., the discussion of the *re* and *si* faces of the cyclobutanone in Figure 8.24).

Reading the book might also have been more enjoyable had a few humorous anecdotes or vignettes been added here and there, but the book is nevertheless well-written and easy to read; for the most part, this reader did not get bogged down. The relatively modest price for a book this size suggests that the publisher anticipates a large sales volume, which in this reviewer's opinion is a safe bet. The book has sufficient content to serve as the basis for a two-semester upper division undergraduate or graduate course in stereochemistry but at the same time will prove to be a handy reference for graduate students and academic or industrial organic chemists.

In addition to chapters on configuration, properties of stereoisomers, resolution, prostereoisomerism and prochirality, and conformation of acyclic and cyclic molecules, there is also a 155-page chapter with brief overviews of a variety of common methods for stereoselective synthesis. Although some of the chapters can stand alone, the reader should be aware that one will need to have a firm grasp of the basic definitions,

nomenclature, and symmetry operations presented in chapters 3–5. This information is used constantly throughout the later chapters of the book; it is absolutely essential to have a clear understanding of the various nomenclature terms. There is a helpful glossary at the end of the text, and the indexing appears fairly good, although some terms seem not in their most logical places (e.g., the index entry "fused rings" might be more logically searched for at "rings, fused"). There are a few terms that cannot be found. For example, "stereocenter" does not appear either in the index or in the glossary. The fact that the authors prefer "stereogenic center" does not obviate the fact that readers need to know that the two terms are taken to mean the same thing.

As another negative point, the reasoning for the order of the chapters was not completely evident. It seemed to this reviewer that the chapter on Stereochemistry of Alkenes should have been placed much earlier in the book and the chapter on Chiroptical Properties should perhaps have been placed as chapter 7, immediately following the chapter on the properties of stereoisomers, rather than as chapter 13, after stereoselective synthesis. Similarly, the last chapter, on Chirality in Molecules Devoid of Chiral Centers, might have been better placed very early in the book.

All this nit-picking aside (and after all, in a volume with this much information what reasonable person could really expect perfection?), I wholeheartedly recommend this book to all organic chemists. There is really nothing else like it—no single source with so much useful information on all facets of stereochemistry. Everyone with an interest in organic chemistry, from advanced undergraduate students on, will find helpful explanations and valuable references. The price is certainly reasonable for the size and quality of this book, and references are included up through 1993. While a future edition of this book might add additional formation, most of the material in this volume will not become dated, and it should be a handy reference source for many years to come.

David E. Nichols

*Department of Medicinal Chemistry and Pharmacognosy
School of Pharmacy and Pharmacal Sciences
Purdue University
West Lafayette, Indiana 47907*

JM950167G

Advances in Prostaglandin, Thromboxane, and Leukotriene Research Volume 23. Edited by B. Samuelsson, P. Ramwell, R. Poletti, G. Folco, E. Granström, and S. Nicosia. Raven Press, New York. 1995. xxvii + 573 pp. 16 × 24 cm. ISBN 0-7817-0238-0. \$95.00.

This volume of *Advances in Prostaglandin, Thromboxane, and Leukotriene Research* contains 116 papers presented at *The Ninth International Conference on Prostaglandins and Related Compounds* held in Florence, Italy, in June 1994. It is a timely publication appearing less than 9 months after the conference. This volume covers a variety of topics including the role of eicosanoids in the respiratory, cardiovascular, renal, and

immune systems. Other sections review advances in the study of phospholipases, cytochrome P450 and other oxygenase products, and isoprostanes. However, the main points of emphasis are the cyclooxygenase and lipoxygenase pathways of arachidonic acid metabolism, including studies on enzyme structure, mechanism, and distribution and on recent cloning and expression of leukotriene synthases and prostaglandin receptors. Fresh insights into understanding antiinflammatory drug action and side effects, based on cyclooxygenase isoforms (COX-1 and COX-2), are discussed as are prospects for developing better antiinflammatory agents with COX-2-selective inhibitors.

Several new structures, of interest to the medicinal chemist, are presented along with their pharmacological properties. These include SC-58125, a selective COX-2 inhibitor; ONO-4057 and SB-209247, LTB₄ antagonists; Latanoprost, an ocular hypotensive agent; and TTC-909 and ONO-AP-500-02, prostacyclin mimetics. There are two round table discussions. One focuses on advances in ocular prostaglandin research discussing the mechanism of prostaglandin-induced intraocular pressure reduction and some phase III clinical data with Latanoprest in patients with elevated intraocular pressure. The other focuses on the physiopathology of the erectile dysfunction and the role of PGE₁ (α -Alprostadil) in the management of male impotence. Also included in this volume are reports on PAF, on nitric oxide (NO), and on interactions between the COX and NO pathways.

This series continues to be the state-of-art reference for anyone involved in eicosanoid research. There are adequate references for most papers and the book is well-indexed by subject. I find this volume to be one of the best of the series in terms of topics covered, and I highly recommend it to anyone involved in eicosanoid research.

James F. Egler

*Central Research Division
Pfizer Inc.
Groton, Connecticut 06340*

JM950236R

Books of Interest

Ferrocenes. Edited by Antonio Togni and Tamio Hayashi. VCH, Weinheim, Federal Republic of Germany. 1995. xx + 540 pp. 18 × 24 cm. ISBN 3-527-29048-6. \$198.00.

A Practical Approach to Chiral Separations by Liquid Chromatography. Edited by G. Subramanian. VCH, Weinheim, Federal Republic of Germany. 1994. xvi + 405 pp. 17.5 × 24.5 cm. ISBN 3-527-28288-2. DM 178.00.

JM941190P