Book Reviews

Umpoled Synthons. Edited by Tapio A. Hase. Wiley, New York. 1987. xvii + 387 pp. 16 × 24 cm. IBSN 0-471-80667-6. $59.95.

The development of the umpolung concept by Seebach in accordance with Corey's "symmetrization of reactivity" had led to a concept that unifies a previously unrelated group of reaction types. *Umpoled Synthons* now presents the synthetic organic chemist with a source for the utilitarian and sometimes powerful synthetic techniques under one cover. The majority of this volume is a presentation of the important synthons of recent origin, whereas many omitted topics are conveniently referenced.

"To umpole" a synthon means to change its polarity to the opposite of its classical counterpart, usually requiring deep-seated, yet reversible, alteration at the heteroatom. This definition is elaborated upon in great detail in the introductory chapter and sets the stage for the sections that follow. The body of the book contains chapters from five contributors and is devoted to formyl anions, hydroxy carbonyl anions, heteroatom-substituted sp^3 carbanionic synthons, carbonyl α-cations, and homoenolate anion equivalents. The emphasis of these chapters is upon synthetic utility and the generality/limitations of the transformation in question, such as stereo- and/or regioselectivity. The subject matter covered in these chapters is bounded by the strict definition of umpole synthons set forward in the initial chapter, and is both comprehensive and terse in manner.

This volume would be an excellent reference source for those teaching advanced organic mechanistic and synthetic chemistry and for hard-core modern synthetic chemists. *Umpoled Synthons* is extremely terse in places, yet it is forgiving by its ready access to key references (over 2000 through 1984, some to mid-1985) provided for in the text and by reaction type in tables organized by chapter (a la Organic Reactions) in the rear of the book.

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CRC Handbook of CNS Agents and Local Anesthetics. Edited by Matthew Verderame. CRC, Boca Raton, Florida. 1986. 378 pp. 18 × 26 cm. ISBN 0-8493-3288-5. $125.00.

The 10 chapters of this volume of the CRC series in medicinal chemistry are selected to represent a systematic collection of chemical and pharmacological reference data drawn from therapeutically important drugs. However, this edition appears to confirm the saying which states that, the larger the number of contributors to a monograph, the further out-of-date its references are on the date of publication. The 19 contributors from both industry and academia seem to rely predominantly on references from the late 1970s with a cut-off at 1981. Having said this, I must also admit that in several of the chapters more frequent use of recent literature references probably would have added little of interest, e.g. those covering the local anesthetics and the barbiturates. There are, however, also creditable merits which deserve to be mentioned. The editor is to be commended for the compilation of interesting topics such as mechanism of action, structure–activity relationships, pharmacokinetics, metabolism, and toxicity of each class of agents. This information is usually not found together in an informative and easy to read fashion. Other valuable features are the IUPAC names and the physical–chemical properties of specific agents. This makes the book valuable and justifies the use of the work "Handbook" in the title.

General Anesthetics by Jacoby gives an in-depth review of the most frequently used anesthetic agents, their discovery, and physical theory of their anesthetic action. *Barbiturates* by Kotun and Alvin summarizes the pharmacological and pharmacokinetic parameters of this important class of hypnotics. *Nonbarbiturate Sedatives and Hypnotics* by Boisse and Neumeyer review the benzodiazepines with emphasis on their risk for induction of tolerance, physical dependence, and other safety aspects. *Antipsychotic Agents* by Vida and Tenthorey tries to cover the topic in 50 pages, most of these devoted to butyrophenones or phenothiazines. The contributors seem to feel uneasy about the dopamine hypothesis of schizophrenia. They have chosen no less than nine pages and four figures to illustrate various aspects of this hypothesis. A third of this material would have been sufficient. Outdated facts, such as "selective antagonists for D-1 receptors have not been found" (p 85), should have been revised. *Antianxiety Agents* by Vida and Essery gives a review divided into eight classes based upon the chemical structure of the agents. This chapter also gives a detailed presentation of the function of the benzodiazepine receptor and its interaction with the GABA receptor. *Neuromuscular Disorder Drugs* by Neumeyer and Boisse deals with antiparkinson agents and skeletal muscle relaxants. *Narcotic Analgesics and Antitussive Agents* by Eissenstat and Michne reviews the opiates and their antagonists. A valuable section on the enkephalins is included in this chapter. *Antidepressants* by Hlasta, Haubrich, and Luttinger gives an excellent compilation of both tricyclic and atypical antidepressant agents. In particular, the various metabolic fates of the tricyclics are presented in structure schemes for easy comprehension by the chemist reader. *Monoamine Oxidase Inhibitors* by Ho and Kralik is another thorough review of what was known on this topic before 1982. Structures of recently developed selective inhibitors of MAO-A and MAO-B are included, however, which makes this chapter a valuable reference. *Hallucinogens* by Nichols reviews the ergolines, the phenethylamines, the tryptamines, the phenylcyclohexylamines, and the tetrahydrocannabinols. *Local Anesthetic Agents* by Adams, Ronfield, and Takman gives an interesting section on the history of the development of these drugs as well as an in-depth account on their mechanism of action, structure–activity relationship, metabolism and pharmacokinetics, and toxicity, the common theme for all chapters. In my opinion, this volume serves well as a handbook despite the previously mentioned shortcomings.

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Laboratory Robotics. A Guide to Planning, Programming, and Applications. By W. Jeffery Hurst and James W. Mortimer. VCH, New York. 1987. xi + 129 pp. 15 × 23 cm. ISBN 0-89573-322-6. $24.95.

The authors have directed the text in this book toward anyone who is considering robotics in their laboratory. This book is not an explanation of robotics or laboratory automation, nor is it a discussion of the many different applications of laboratory robotics, but rather an introduction to the concepts, language, and reasoning behind the acquisition of a laboratory robot. Also, the authors present a few examples of how robots are currently being used in the laboratory.

In the first two chapters the authors introduce the concepts of robotics, give many examples of why an analyst should or should not consider the acquisition of a laboratory robot, and show how an automated procedure can be constructed from a manual method. The most important chapters in this book are the third and fifth. In these chapters the authors present and illustrate may examples including a valuable generalized worksheet on the justification of a laboratory robot. They also raise and answer many important questions on the expectations of a robotic system. The crucial assumption made in Chapter 3 that a robotic procedure will average about the same speed as a manual procedure could be very misleading in the true expectations of a laboratory robot. Depending on the complexity of the application, a robot might work only half as fast as a human. The fourth chapter gives

many examples of how laboratory robotics are presently being utilized throughout many industries. This chapter includes over 75 references, mostly from 1984 and 1985. The sixth chapter introduces basic aspects of general programming and a simplified explanation of the programming involved in setting up a robotic procedure. The final chapter offers some foresight into the future of laboratory robotics.

The areas of planning and applications are covered very well in this text, but the programming section is only a basic introduction to what is actually involved. Although 95% of the illustrations and examples pertain to the Zymark robotic system, this book is highly recommended to anyone who is considering purchasing any of the laboratory robots presently on the market.

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Progress in Medicinal Chemistry. Volume 23. Edited by G. P. Ellis and G. B. West. Elsevier, Amsterdam, The Netherlands. v + 281 pp. 15 × 21 cm. 0-444-80802-7. $95.00.

This is the latest in the long-established series of monographs on timely topics of interest to medicinal chemists. Included in this volume are Pharmacology and Structure–Activity Relationships of α_2-Adrenoceptor Antagonists; Radioligand–Receptor Binding in Membrane Receptor Research; Common Structural Features of Drugs, Transmitters, and Peptides in the Central Nervous System; Recent Progress in the Development of Antidepressant Drugs; Chemotherapeutic Agents for Herpesvirus Infections; and Chemical and Biological Aspects of Sparsomycin, an Antibiotic from Streptomyces.

All of the relatively short reviews are well written, and seem to be free from printing/typographical errors. Most include some literature references from 1985, but no later. The book includes an index for the volume, as well as cumulative subject and author indices for Volumes 1–23. This reviewer found the chapter on Radioligand–Receptor Binding by Marija Carman-Krzan to be an interesting and informative introduction to a topic with which many medicinal chemists are not conversant, presenting an overview of a rapidly developing research area with great relevance to medicinal chemistry and drug design. The chapter on Antidepressant Drugs by Stephen I. Ankier provides a useful "state-of-the-art" exposition of the subject, including brief descriptions of animal test methods and clinical assessment as well as discussions of recently developed drugs and experimental compounds.

As with earlier members in the series, this volume is a valuable resource for the medicinal chemist and the pharmacologist, and it is an essential acquisition for every library. However, I deplore (and cannot understand) the high cost of this slim book, and I speculate that many researchers and teachers will elect not to purchase their own copy.

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Advances in Neurology, Volume 45, Parkinson's Disease. Edited by Melvin D. Yahr and Kenneth J. Bergman. Raven, New York. 1987. xxiii + 616 pp. 18 × 26 cm. ISBN 0-88167-205-x. $98.50.

This book represents the most recent conference reviewing the advances in knowledge and new strategies directed toward gaining a better understanding of Parkinson's disease, its causes, and treatment. This is the eighth conference on this topic, the most recent one reported in this volume was held in New York City from June 9 to 12, 1985.

The 110 contributions document major clinical and research advances in the study of receptor pharmacology; the imaging of dopamine receptor sites by positron emission tomography; the introduction of novel dopamine agonists; the evaluation of sensorimotor, cognitive, and affective dysfunction in Parkinsonism; and the investigation of the causative link between the neurotoxin MPTP and Parkinsonism.

The book is organized around four major themes: epidemiological and etiological factors; biochemical and ultrastructural pathology; motor and nonmotor aspects of Parkinson's disease; and current and future approaches to therapy.

This volume presents a comprehensive picture of what is presently known and unknown about Parkinson's disease, where the potentially fruitful areas of research exist, and the practical aspects of optimally dealing with the many problems inherent in this enigmatic disease. It is in the potentially new areas of research suggested in this volume that medicinal chemists and pharmacologists will find greatest interest. The neurological community at large will find this volume a valuable stimulus to the continuing investigations of the causative factors of extrapyramidal disorders.

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Advances in Cyclic Nucleotide and Protein Phosphorylation Research. Volume 20. Edited by P. Greengard and G. A. Robinson. Raven, New York. 1986. iv + 371 pp. 15 × 23 cm. ISBN 088167-242-4. $72.00.

This volume continues the tradition of high quality which this series has established. The present volume consists of six scholarly reviews related to various aspects of cyclic nucleotide research. The contribution by Seamon and Daly on "Forskolin" as well as the chapter by Exton on "Calcium-Mobilizing Agonist Responses" are sufficiently detailed that they might exist as separate volumes. The other chapters are shorter simply because the topics under discussion have not received as much experimental investigation. All the chapters can be recommended to either the expert in the field looking for an up to the minute overview of the subject or the neophyte looking for guidance to a complex literature.

This is the kind of book that the individual investigator ought to consider owning. The depth of coverage of the topics makes the purchase of this volume appear to be a wise decision.

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Medical Style Format. An International Manual for Authors, Editors, and Publishers. By Edward J. Huth. Foreword by Stephen Lock. ISI Press. Philadelphia. 1987. xii + 355 pp. 15 × 23 cm. ISBN 0-89495-063-0. $39.95.

This comprehensive manual describes and recommends format and publication styles for journals in the medical sciences, clinical medicine, and related areas. It includes directions for spelling, capitalization, choice of type faces, symbols, abbreviations, and presentation of numerical data. Any questions anyone may have on any matters pertaining to composition, word choice, and style are answered precisely and fully in this book. An important feature is the format of references which follows essentially but not slavishly the prescriptions made by the international Committee of Medical Journal Editors embodied in the Vancouver agreement. Some journals and monographs still use the names of the authors, parenthesized with the dates, in the text and in alphabetized sequence in the references but the present manual will help to persuade them to change over to international standards, as they are followed also by *J. Med. Chem.* The stylistic recommendations for brevity, terseness, and easy understanding should be read especially by foreign authors whose native tongues lean toward verbose expressions. Punctuation, symbols and abbreviations, numbers, units of measurement and time, mathematical and statistical compilations, prose style, and a plethora of bibliographical citations and conventions fill the main body of the book. Even the treatment of translated journals is given in full.

It takes patience to read this manual and to overcome prejudices engrained in one's style since high school. However, the effort

will pay off in more uniform and readable manuscripts and more interesting presentation of one's data. The low investment in this book should be affordable by thousands of incipient and mature authors.

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Alzheimer's and Parkinson's Diseases. Strategies for Research and Development. Edited by A. Fisher, I. Hanin, and C. Lachman. Plenum, New York. 1986. xvi + 710 pp. 17 × 25 cm. ISBN 0-306-42232-8. $95.00.

This book is a standard volume of symposium proceedings. The papers were collected as a consequence of a meeting held in the first quarter of 1985. Sometime in the following year the symposium volume appears. The chapters are, for the most part, related to the stated theme of the meeting. The general headings are the following: Anatomical, Pathological and Biochemical Aspects (14 contributions); Clinical Aspects and Noninvasive Diagnostic Approaches (14 chapters); Etiological and Genetic Aspects (6 chapters); Biological Markers (10 chapters); Experimental Models (14 chapters); New Drug Development (16 chapters); and a general overview by one of the editors.

As is always the case with unedited symposium volumes, there is a wide range of quality in the chapters. Likewise, there is an overall dated quality to all the reports. In the intervening 2 years since the meeting, many of the ideas of merit have surely been published in refereed journals. These peer-evaluated reports will have greater utility to the scientific community than unedited reports in this volume. Consequently, this book is probably one better left for the library (rather than the individual) to purchase.

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Annual Review of Pharmacology and Toxicology. Volume 27. Edited by Robert George, Ronald Okun, and Arthur K. Cho. Annual Reviews Inc., Palo Alto, CA. 1987. viii + 460 pp. 16 × 23 cm. ISBN 0-8243-0427-6. $31.00.

The 27th volume in this series is composed of 20 review articles in various disciplines of pharmacology and toxicology plus another so-called "review of reviews" (by E. Leong Way). As with its predecessors, the current volume should provide at least several chapters of interest to each scientist engaged in pharmacological research and drug discovery. Almost every chapter contains an abundance of cited references, averaging 120 per review, many of which are from 1985 and 1986. In addition, the volume contains a detailed subject index as well as lists of contributing authors and chapter titles for Volumes 23–27.

Of personal interest were the review articles on platelet activating factor antagonists (by Saunders and Handley) and that on prostaglandins, leukotrienes, and platelet activating factor in shock (by Feuerstein and Hallenbeck). As a reflection of the type of material contained throughout this book, the former review contains a useful table listing references of studies performed with PAF antagonists in various animal models, and the latter review has a schematic listing of the cardiovascular effects of the leukotrienes that lead to shock. Both reviews are up-to-date accounts of their respective subject material.

Two additional chapters address interesting issues concerning adverse drug effects. The review on chemically induced immunotoxicity (by Luster, Blank, and Dean) makes it clear that the immune system is very sensitive to chemical injury. The second of these chapters (by Strom) addresses the goal of pharmacoepidemiology: the early detection of adverse drug reactions, leading to a minimization of their potential impact.

Topics in CNS pharmacology are treated in three chapters: the unit on cotransmission (by Campbell) deals with the action of two transmitters released simultaneously from a single neuron; that on drugs affecting movement disorders (by Campanella, Roy, and Barbeau) focuses primarily on Parkinson's disease; and the third (by Shiromani, Gillin, and Henriksen) discusses acetylcholine and the regulation of REM sleep.

Of particular interest to medicinal chemists is the review by Garland Marshall on computer-aided drug design. This chapter deals not only with the range of techniques available for computer modeling based upon what is known about the molecular target but also evaluates the limitations of each technique.

Rounding out this volume are chapters on inhibin (by Li and Ramasharma), carnitine (by Bahl and Bressler), purine receptors (by Williams), calcium channel ligands (by Triggle and Janis), metabolism of α- and β-adrenergic receptors (by Mahan, McKernan, and Insel), genetic analysis of hormone-sensitive adenylate cyclase (by Casperson and Bourne), and a mathematical treatment of statistical methods useful in bioassays (by Laska and Meisner).

The remaining five reviews can be classified under the toxicology heading. These chapters include health effects of exposure to polychlorinated and polybrominated biphenyls (by Kimbrough) and diesel exhaust particles (by McClellan), extracorporeal removal of drugs and poisons (by Cutler, Forland, Hammond, and Evans), safety evaluation of polymer materials (by Darby), and solvent toxicology (by Kalf, Post, and Snyder).

Missing from this issue are reviews in subject headings dealing with, for example, allergy, analgesia, inflammation, gastrointestinal pharmacology, pharmacokinetics, and renal pharmacology. However, the material covered in this 27th volume is broad-based, making it an important reference for the pharmacologist, toxicologist, and medicinal chemist alike.

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Advances in Medicinal Phytochemistry. Edited by Sir Derek Barton and W. D. Ollis. John Libbey Eurotext, London. 1986. xviii + 195 pp. 16 × 24 cm. ISBN 0-86196-092-0. $44.00.

This monograph represents the edited versions of 23 papers presented at the International Symposium on Medicinal Phytochemistry held in Marrakech, Morocco, in January 1985. The presentations run the gamut from the usual "Medicinal Plants of ..." — in this case, West Africa, Morocco, and Viet Nam— through modern methods of isolation, newer strategies in pharmacological evaluation, industrial technology, to elegant total syntheses and structural modification of analogues of the antileukemic *Catharanthus* alkaloids. Many of the papers will be seen as brief reviews of the authors' own works. Most of them offer liberal citations of recent (1980s) literature bearing on their particular fields of interest.

As disparate as the topics may seem, two themes are evident throughout which lend cogency to the argument of the natural-product medicinal chemist that there are, indeed, still-to-be-discovered compounds of potential usefulness to mankind: first, an awareness that many of the reputed medicinal properties of natural compounds or the plants containing them may be due to very subtle, indirect biodynamic activities easily overlooked in traditional pharmacological screens; second, that progress in their discovery requires a multidisciplinary approach involving, at a minimum, close collaboration between botanist, phytochemist, and pharmacologist with, as one contributor puts it (p 55), "a little luck and a lot of passion".

The book will be of interest not only to the medicinal chemist but to all scientists whose research interests involve, or relate to, the use of plant products in the pursuit of the health of mankind.

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Separation, Recovery and Purification in Biotechnology. Recent Advances and Mathematical Modeling. ACS Symposium Series 314. J. A. Asenjo and J. Hong, Eds. American Chemical Society, Washington, D.C. 1986. x + 229 pp. 15 × 22 cm. $54.95.

The ability to incorporate (and express) genes for therapeutic or other useful biologicals into bacteria, yeast, or mammalian cells

in culture is indeed a remarkable achievement. Nonetheless once expressed in the appropriate cells (itself a matter for painstaking research) purification of the desired material remains a formidable challenge. Indeed much of the cost of biologically derived materials is rooted in purification. In *Separations, Recovery and Purification in Biotechnology*, Asenjo and Hong have given us a survey of applications and approaches to product release, separation, and concentration and purification. They have been careful to focus on emerging areas, and although progress is always rapid in an expanding field, they have provided us with an adequate sampling of the state of the art. They have also presented the chapters in a well-organized fashion integrating the portions of problem solutions into a flow sheet of fermentation (growth), purification, and continuous operation. The mathematical treatments of the different methodologies should also prove useful. It is in the area of flow sheet construction and problem solving that I thought this volume might have made an important contribution. In particular to the molecular biologist suddenly discovering the need to be a protein chemist. This is particularly true since many of the concepts presented, while not new to chemical engineers, are new to many entering biotechnology. A final chapter reviewing the take-home lessons of the previous 15 chapters as a guide to the beginner would be truly appreciated. Nonetheless this review is timely and should be of interest to scientific workers in biotechnology.

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Some Modern Methods of Organic Synthesis. W. Carruthers. Cambridge University Press, Cambridge. 1986. xii + 526 pp. 15 × 23 cm. ISBN 0-521-32234-0. $99.50.

This book is the third edition of what has become one of the standard texts for students of organic chemistry. It is intended primarily for advanced undergraduate and graduate level students and aims to highlight some of the classical and contemporary organic reactions that are widely utilized in modern synthesis.

The book is divided into seven chapters: (1) Formation of carbon–carbon single bonds, (2) Formation of carbon–carbon double bonds, (3) The Diels–Alder and related reactions, (4) Reactions at unactivated C–H bonds, (5) Synthetic applications of organoboranes and organosilanes, (6) Oxidation, and (7) Reduction. Some applications of classical reactions are discussed, but the emphasis is clearly on contemporary methods. A significant number of new methods are included which have developed since the 1978 publication of the second edition. Particular attention is paid to highly stereoselective reactions such as stereoselective ketone alkylations, aldol condensations, epoxidations, and reductions and also to reactions such as the Diels–Alder in which molecular complexity is rapidly increased with high stereochemical control. More space is also devoted to the increasing use of organometallics, organoboranes, and organosilanes in synthesis.

Although a few specialized methods are omitted, and only some of the applications of particular reactions are illustrated, the reader is nevertheless presented with an excellent overview of 1985 state-of-the-art synthetic methodology. The references to the primary literature are kept to a minimum yet adequately provide starting points for additional reading in all areas. For the most part, mechanistic discussion is excluded. Particularly valuable are the discussions throughout the text which condense somewhat more complicated subjects—for example, the diastereoselectivity, enantioselectivity, and double-stereodifferentiation in the aldol condensation or the factors governing stereo- and regiocontrol in the Diels–Alder reaction—into a pleasantly readable form for the student.

Unfortunately, there are a large number of errors in the text (e.g., page number references left unfilled) and in the structures (e.g., double bonds included/excluded errroneously; products and reactants reversed). While these errors are distracting and occasionally annoying, they do not significantly decrease the value of this book.

This book was not intended to be a comprehensive reference. It is an excellent textbook, guide, and reasonably up-to-date overview of this field of organic chemistry. It should be of utility not only to the student preparing to enter the mainstream of organic synthesis but also to those scientists involved in synthesis but whose diversifications may have necessarily taken them out of the mainstream of modern synthesis.

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Cytochrome P-450. Structure, Mechanism and Biochemistry. Edited by P. R. Ortiz de Montellano. Plenum, New York. 1986. x × 556 pp. 15.5 × 23 cm. ISBN 0-306-42147-X. $69.50.

Like in all areas of life sciences, small and large alike, recent advances in the field of cytochrome P-450 reflect the rapidly accelerating change from phenomenological description to an understanding of molecular mechanisms of atomic resolution. In the case of cytochrome P-450, this ongoing change has been fuelled by the important roles this class of enzymes play in drug metabolism, the biotransformation of xenobiotics to toxic products, and in steroidogenesis and other physiological processes.

This book brings together in 13 chapters reviews on a variety of topics covering: metalloporphyrin and non-P-450 hemeprotein models of cytochrome P-450; active-site topologies of mammalain P-450 enzymes; interactions with proteins responsible for electron transfer to P-450; membrane interactions and organization of P-450; the primary and secondary structures of various P-450 enzymes; mechanistic aspects of oxygen activation and transfer; the molecular mechanisms of P-450 enzyme inhibition; the induction of hepatic P-450 isozymes; regulation, in various tissues, of the synthesis and catalytic activity of cytochromes P-450 in steroid hormone biosynthesis and vitamin D and lipid hydroxylation reactions; the role of cytochrome P-450 enzymes in sterol biosynthesis and metabolism; bacterial P-450 enzymes and the crystal structure of cytochrome $P\text{-}450_{cam}$. An appendix summarizes information regarding the multiple isozymic forms of rat hepatic cytochrome P-450 isolated by different laboratories.

No doubt due to the Editor's efforts, the book is more coherent than most multiauthor works. The excellent selection of authors (including Ortiz de Montellano himself) ensures the uniformly high quality of the various chapters. The reviews provide a selective, but sufficiently comprehensive coverage of the literature of an ever expanding field. However, with the exception of the Editor's own contributions (Chapters 7 and 8), citations seldom extend beyond 1984. The book, which stands out as a unique treatise of the subject with a "molecular focus", is highly recommended to students and professionals alike at all levels of expertise.

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