

## Book Reviews

**Practical Aspects of Modern HPLC.** Edited by Imre Molnar. Walter de Gruyter & Co., Berlin and New York. 1983. vii + 449 pp. 17 × 24.5 cm. ISBN 311-008892-4. \$77.30.

This book is a selection of the papers presented at the Symposium on "Practical Aspects of Modern High Performance Liquid Chromatography" in Berlin, Dec 7 and 8, 1981. It contains a mixture of general and specific presentations. Several of the papers deal with instrumental and column concerns, including the nature of different types of silica, special inlet ports, modern methods of detection, retention in practical HPLC, and low-volume, small-bore columns. There are also a number of general discussions covering HPLC in clinical chemistry, protein chromatography, affinity chromatography, pharmacokinetics, and fluorimetric determination of drugs in biological materials. Specific papers concern oligonucleotides, steroids, proteins, dissolution of oral contraceptives, catecholamines, (aryloxy)propanolamines, estrogen-active anabolics, and saccharides. The only work on nonbiological or nonpharmaceutical compounds is an interesting investigation of the HPLC of elemental divalent sulfur rings and nonionic sulfur compounds.

The order of the papers in the book seems rather random, though perhaps they are in the order in which they were presented at the symposium. In more than a few instances, the reader encounters awkward or ungrammatical English, which often obscures the author's point. The book does not appear to have been edited by anyone fluent in the language in which it is written. It might, however, be a worthwhile investment for those researchers heavily involved in the application of HPLC to problems in medicinal, biological, or clinical chemistry. Extensive bibliographies in several of the general discussions, as well as a convenient and well-constructed index and list of chromatograms, enhance the usefulness of the work.

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**Biological Magnetic Resonance. Volume 4.** Edited by Lawrence J. Berliner and Jacques Reuben. Plenum Press, New York and London. 1982. xx + 340 pp. 16 × 23.5 cm. ISBN 0-306-40968-2. \$42.50.

This volume consists of four chapters on the applications of ESR (electron spin resonance) to problems in medicine, Cd-113 NMR studies, principles and applications to biological systems of the photochemically induced dynamic nuclear polarization technique, and applications of ring-current calculations in structural studies of biological macromolecules.

Chapter 1, entitled "Spin Labeling in Diseases", discusses membrane structure and function, the spin-labeling technique, applications of spin labeling in neurological disorders, neoplasia, sickle cell anemia and other diseases, the future of spin-labeling in the study of disease, and recent developments in spin labeling.

Chapter 2, entitled "Principles and Applications of <sup>113</sup>Cd NMR to Biological Systems", begins with the basic principles in the acquisition and interpretation of <sup>113</sup>Cd NMR data in a variety of biological problems. The remainder of the chapter is a review of <sup>113</sup>Cd NMR studies of biological systems over the past 5 years. <sup>113</sup>Cd NMR studies of alkaline phosphatase, <sup>113</sup>Cd NMR studies of metallothionein, and other <sup>113</sup>Cd NMR applications are discussed.

"Photo-CINDP Studies of Proteins" is the title of Chapter 3, which covers the application of CINDP to biochemical problems, in particular, the efforts to obtain structural information on biological macromolecules and on their interactions with ligands. One section describes the laser photo-CINDP experiment, another

the basic CINDP effects of amino acids. The results of investigations of a number of specific proteins, such as bovine pancreatic trypsin inhibitor (BPTI), ribonuclease, lysozyme, α-lactalbumin, colipase, phospholipase A<sub>2</sub>, and others, are presented.

The final chapter, which is the largest, Chapter 4, entitled "Application of Ring Current Calculations to the Proton NMR of Proteins and Transfer RNA", is a review chapter that examines the role of ring-current concepts as a link between spectroscopy and structure of the aromatic ring in the macromolecule and as a key for appreciation of the significant biological properties of macromolecules from <sup>1</sup>H NMR studies. Details are given to the reader for applying ring-current concepts, for performing calculations, and for guidance in interpretation of ring-current effects. Specific sections describe ring-current theories, protein crystallography and protein structures, ring calculations and computer programs, shift calculations in protein NMR, applications of ring-current calculations to proteins, proteins with known crystal structures, proteins and peptides without crystal structures, and ring current calculations and transfer RNA.

There is an appendix consisting of three parts: (1) "Johnson-Bovey Program for Ring Current Tables"; (2) "Subroutines for putting H Atoms onto X-ray Coordinates"; (3) "Random Coil Chemical Shifts". All chapters are extensively referenced, with most literature citations being recent. Numerous diagrams and tables are used throughout the text.

This text should be of great interest and value to the chemist, biochemist, or biologist working in the field of biological magnetic resonance.

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**Topics in Antibiotic Chemistry. Volume 6.** Edited by P. G. Sammes. Halsted Press (Distributed by Wiley), New York. 1982. 345 pp. 16 × 24 cm. \$74.95.

Volume 6 in the series, "Topics in Antibiotic Chemistry", is a continuation in this series with three chapters as follows: Part A (97 pages), "Modern Synthetic Antifungal Agents" (by George J. Ellames); Part B (122 pages), "The Biochemistry of Nucleoside Antibiotics" (by J. Goodchild); and Part C (104 pages), "The Chemistry of Nucleoside Antibiotics" (by J. G. Buchanan and R. H. Wightman).

Part A, after a brief introduction to fungal diseases, proceeds into a limited discussion on the known non-imidazole-based antifungals (the polyene macrolides, flucytosine and griseofulvin) and the imidazole-based drugs (clotrimazole, miconazole, and econazole), leaving much of the detailed material referenced to more specialized reviews on the subject. The chapter begins to come to life on its own, however, with a discussion on eight newer drug candidates in a section "Future Imidazole Based Antifungal Agents". References are cited through 1980 in discussions on the chemistry and biological activity, along with some information related to clinical and preclinical evaluation of these compounds. A large section is devoted to "Synthetic Approaches to Novel Antifungal Agents". Clearly, to the new researcher in this field, this section will prove most useful, since the synthetic routes to a variety of the newer imidazole-type antifungals are outlined, together with data on biological activities of the synthetic congeners. The chapter is concluded with two sections on laboratory testing and the mode of action of antifungals. Combined, the sections in this chapter provide what seems to be adequate coverage of the field through ca. 1980.

Part B assumes a limited knowledge of the field and begins with a brief introduction on the structure and nomenclature of nucleosides, followed by a more detailed account of nucleoside biochemistry (including functions, biosynthesis, antibiotic mechanisms, resistance mechanisms, and transport). A section

on "Enzymes of Nucleotide Metabolism" covers all of the more important enzymes acting upon nucleosides, as well as inhibitors and nucleosides resistant to these enzymes. For the medicinal chemist, the final section on "Analogues of the Common Nucleosides", which provides a wealth of information on modified nucleosides, their biological activities, and mode of action, will perhaps be the most used portion of the chapter. References, though abundant, are not exhaustive, yet the chapter does provide an accurate, readable account of the area into at least a part of the 1981 literature.

Part C delves into the chemistry of the naturally occurring nucleoside antibiotics. Detailed discussions, with processes illustrated with schemes for the more complex syntheses, provide a good account of the synthetic work in this area up through most of 1981. Critical analyses of the processes to a given nucleoside have been made, and, generally, the most efficient, up-to-date processes are presented. Although synthetic chemistry is emphasized, the authors provide some coverage on the more important aspects of biosynthesis and isolation techniques, which are valuable adjuncts to synthesis. All in all, the syntheses of some 45-50 nucleosides, including a few important C-nucleosides, are discussed. References total 384.

It is noteworthy that approximately two-thirds of this book is devoted to a discussion of nucleosides. No attempt is made to cover all nucleosides, the emphasis being restricted to known nucleoside antibiotics. As such, the two chapters when taken together comprise a rather comprehensive treatment of the subject, much as is done in Suhadolnik's two volumes, "Nucleoside Antibiotics" (1970) and "Nucleosides as Biological Probes" (1979). While considerable overlap exists between Part B and Suhadolnik's treatment, the chemistry is given more in-depth treatment in Part C of this volume.

All in all, Volume 6 of "Topics" is a good piece of work, well written with few noticeable errors. The book can be recommended for all medicinal-chemical libraries, but, unfortunately, the price is out of reach for most personal collections.

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**Metal Ions in Biological Systems. Volume 15. Zinc and Its Role in Biology and Nutrition.** Edited by Helmut Sigel. Marcel Dekker, New York and Basel. 1983. xxii + 493 pp. 15.5 × 23.5 cm. ISBN 0-8247-1750-3. \$75.00.

About 160 zinc metalloenzymes have been identified, and they are involved in every aspect of metabolism, including the replication and translation of genetic material. A volume devoted to the biological roles of this important metal ion is therefore of much current value. The present development of knowledge concerning structure and function of zinc in metalloenzymes has awaited the application of X-ray crystallographic techniques to these enzymes; much of the findings reported here is therefore of recent determination.

Since the observation of Keilin and Mann that carbonic anhydrase contains zinc, this metal ion has been found in enzymes in all of the six classes recognized. Its functions cover the range of catalytic, structural, regulatory, and noncatalytic (or unknown) activities. Determination of the active sites of zinc enzymes and the coordination spheres of the zinc ion have been determined for several of the more researched enzymes; on many of the lesser known enzymes, information regarding structure and function is not yet available; a number of zinc-containing proteins are also known for which enzymatic properties have not been discovered. Nutritional aspects of zinc and clinical manifestations of zinc deficiency states are also undergoing current development.

The individual chapters are well presented and reflect a remarkable uniformity of style. The introductory chapter on the categories of zinc metalloenzymes is most useful to medicinal chemists or biochemists in describing the structure and function of the zinc ion. Other chapters include a discussion of models for zinc binding sites in enzymes, and the role of metal substitution in providing information on active sites. The role of zinc in DNA and RNA polymerases and in snake toxins is discussed, and spectroscopic properties of metallothionein introduce the role of

metal-thiolate clusters. Subjects of more health interest include the interaction of zinc with erythrocytes, zinc absorption and excretion in relation to nutrition, and nutritional influence of zinc on the activity of enzymes and hormones. The final chapter is concerned with the zinc deficiency syndrome during parenteral nutrition in humans.

There is both an author and subject index, which cover 55 pages. Previous standards of printing and depiction of structures have been maintained and are quite good. This volume should be of particular interest to medicinal chemists and biochemists, as well as to clinicians, clinical pharmacists, and nutritionists, and may be said to have been "long awaited". The editor and authors are to be commended for particularly well-presented treatments.

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**Advances in Pharmacology and Chemotherapy. Volume 19.** Edited by S. Garattini, F. Hawking, A. Goldin, and I. J. Kopin. Academic Press, New York. 1982. x + 294 pp. ISBN 0-12-032919-0. \$38.00.

This neat and compact volume, just as the preceding ones of this series that have appeared annually, contains several independent review articles on various topics in the general area of chemotherapy. At least three of the seven chapters in the present volume are of primary interest to the medicinal chemists, while the remainder provide relevant information of more biological or medical nature.

The first article, on "Chloroethylnitrosourea Cancer Chemotherapeutic Agents", by R. J. Weinkamp and H.-S. Lin, reviews the present state of information concerning the various physical, chemical, and pharmacokinetic properties (lipophilicity, alkylating and carbamoylating activities, chemical and metabolic transformations), as well as the cytotoxicities and *in vivo* antitumor activities of various (chloroethyl)nitrosoureas. An apparent lack of consistent correlation between the physicochemical properties and biological effects is noted in this series. The authors conclude that "the rather unpredictable influence of structure on activity is apparently due to specific interactions that influence the biodistribution and chemical activation of these agents". A. Mantovani, under the title "Interaction of Cancer Chemotherapeutic Agents with Mononuclear Phagocytes", reviews the effects of several representative antitumor drugs on the activation and functions of the mononuclear phagocyte system, which is believed to have an important role in contributing to the efficacy of antitumor chemotherapy. The effects of these drugs are not always suppressive; they can be heterogeneous and relatively selective toward different functions of cells of the monocyte-macrophage lineage and on the lymphokines (MIF) involved in their regulation. A better understanding of these effects is still needed for effective chemoimmunotherapy design. A review by H. Van den Bosche, F. Rochette, and C. Horig, on "Mebendazole and Related Anthelmintics" contains an extensive coverage of available data concerning the pharmacokinetics and toxicology of eight benzimidazole carbamate anthelmintics, their effects against a variety of worm infections in various domestic and wild animals, and their use in the treatment of various nematode and cestode infections in human medicine. This is followed by an article on the "Chemotherapy of Human Intestinal Helminthiasis, with Particular Reference to Community Treatment", by D. Sturchler, which reviews some of the biological and medical aspects of this group of diseases.

A perfect example of the medicinal chemistry approach is presented under the title "Development of Radiosensitizers: A Medicinal Chemistry Perspective" by V. L. Narayanan and W. W. Lee. Based on a wealth of relevant information obtained, in part, from a systematic study of "electron-affinic" radiosensitizers currently conducted under two NCI research contracts, these authors present a very interesting analysis of the effects of judiciously selected structural variations on the physicochemical properties and radiosensitizing activities of several types of nitroaromatic (including nitroheterocyclic) compounds, particularly nitroimidazole derivatives. It is noted that even in this relatively narrowly defined structural group, where the radiosensitizing

activity (at least in vitro) usually parallels the electron affinity (or redox potential), the latter may not be the only determining factor; other mechanisms (alkylation, thiol addition) were also invoked in several cases to explain "anomalous" results. This review provides much valuable insight into the structural and mechanistic aspects of "hypoxic" radiosensitizers; it will greatly aid in the design of new agents aiming to optimize the results within the theoretical limits of the electron-affinic approach. Other mechanisms and approaches for selective radiosensitization of tumors are clearly possible and will be explored, hopefully, in a similarly systematic manner in the future.

"The Effects on Antineoplastic Therapy on Growth and Development in Children" by U. Bode and A. Oliff, is, of course, of primary interest to the clinical oncologists. The last article in the volume, on the "Biological Properties of ICRF-159 and Related Bis(dioxopiperazine) Compounds", by E. H. Herman, D. T. Witiak, K. Hellmann, and V. S. Waravdekar, deals with the chemistry, structure-activity relationships, biological characteristics, and the pharmacological and clinical evaluation of this unique class of anticancer agents having "antimetastatic" and "angiometamorphic" (ability to normalize the tumor neovascularity) effects. From the point of view of the medicinal chemists, the section dealing with the stereoselectivity of the antimetastatic activity is of particular interest. On the whole, this volume appears to be well worth its list price and is recommended as reading and reference for those interested in the above topics.

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**Pharmacological and Chemical Synonyms. 7th Edition.**  
Edited by E. E. J. Marler. Elsevier, New York. 1983. 514 pp.  
17.5 × 24.5 cm. ISBN 0-444-90227-9. \$76.50.

This alphabetical compilation of names used for drugs, pes-

ticides, and other substances of pharmacological or biochemical interest has now reached its seventh edition. This comprehensive international dictionary has been brought up to date since the sixth edition (published in 1978) and features extensive cross-indexing. Consistent chemical nomenclature is used: systematic, unambiguous, fully numbered names are given in most instances. Alternative chemical names are included for some more complex compounds, which could be systematically named in a number of ways.

"Marler's PCS" will find an important place in all libraries involved with drugs and other substances of biological interest.

Staff

#### Books of Interest

**Heparin—New Biochemical and Medical Aspects.** Edited by Irene Witt. Walter de Gruyter & Co., Berlin. 1983. 17.5 × 24.5 cm. xv + 372 pp. ISBN 3-11-008637-9. \$70.50.

**Methods in Enzymology. Volume 92. Immunochemical Techniques. Part E. Monoclonal Antibodies and General Immunoassay Methods.** Edited by John J. Langone and Helen Van Vunakis. Academic Press, New York. 1983. 16 × 23.5 cm. ISBN 0-12-181992-2. \$65.00.

**Kirk-Othmer Encyclopedia of Chemical Technology. 3rd Edition Volume 22. Sulfonation and Sulfation to Thorium and Thorium Compounds.** Wiley, New York. 1983. xxvi + 10002 pp. 19 × 26 cm. ISBN 0471-0205-3. \$180.00.