

71507-20-5; **2d**, 71507-12-5; **2e**, 38539-99-0; **3a**, 60413-79-8; **3b**, 13648-01-6; **3c**, 72166-52-0; **3d**, 71507-21-6; **3e**, 71507-13-6; **4a**, 20051-76-7; **4b**, 13647-38-6; **4c**, 71507-82-9; **4d**, 71507-78-3; **4e**, 71507-14-7; **5a**, 89999-20-2; **5b**, 13647-39-7; **5c**, 71507-83-0; **5d**,

71507-79-4; **5e**, 71507-15-8; **6**, 4248-66-2; **7**, 13074-00-5; **8**, 17597-25-0; **9**, 89999-17-7; **10**, 13648-06-1; **11**, 60413-80-1; **12**, 89999-18-8; **14**, 89999-19-9; progesterone, 57-83-0; corticosterone, 50-22-6; cortisol, 50-23-7.

Book Reviews

Chemical Information. By Yechezkel Wolman. Wiley, New York. 1983. xiv + 199 pp. 15.5 × 23.5 cm. ISBN 0-471-10319-5. \$24.95.

The book bears the subtitle "A Practical Guide to Utilization" and was developed for a formal course in chemical literature at the Institute of Chemistry, Hebrew University of Jerusalem. It is printed in reduced typescript (with a sprinkling of typos) that does not allow use of bold face or italics. In an effort to crowd as much as possible into the text pages, lists of books, periodicals, and other types of literature are given in paragraph form rather than in tables. The book includes an index, a glossary of acronyms, and an appendix of 12 recent developments that are keyed to specific pages of the text.

The 14 chapters bear conventional headings, but they are not accurate descriptions of the chapter contents. Who would expect to find long discussions of "Bielstein", "Gmelin", and the "CA Subject Index" in a chapter on "Obtaining Numerical Data", especially when Beilstein was used as an alternative data source when a melting point couldn't be found in "Heilbron's Dictionary" or the "CRC Handbook"? There is a 4-page discussion on obtaining translations buried in a chapter on "The Library". The description of Landolt-Bornstein is found in a subsection dealing with crystallographic data. Phase diagram data sources are discussed under "Solubility Data". In an effort to avoid undue repetition, the author makes extensive use of a cross-reference system involving elaborately numbered paragraphs.

The unusual organization of the material is probably an expression of the author's lecture technique and also the result of his use of several specific search examples. The latter usually involve locating specific data, but there is one detailed description of a subject search (for Moebius dromaticity). The chapter on "How to Conduct a Literature Search" consists of just a 2-page exposition of 13 suggestions, the last of which is "know when to stop".

Among the deficiencies that must be a consequence of the book's brevity are inadequate coverage of the literature of chemical engineering, government publications, statistical data, chemical marketing, and biomedical properties. On the other hand, there are unusually complete discussions of current awareness techniques, spectral data, kinetics, the major treatises, and of Chemical Abstracts and its various indexes. The description of online searching is brief, but many references to extended discussions are given.

The literature of occupational hygiene, safety, toxicity, environmental impact, etc., is covered, but the author recommends that the ordinary chemist should not include safety literature in updating his reading program. He should rely on secondary sources even though they may be less or even more reliable than the original. There are so many such secondary sources today that one wonders where chemists can be found to prepare them. (Perhaps they use unemployed lawyers as authors.)

Dr. Wolman recommends that chemists today should devote 5-10 h per week in a personal current awareness program, supplemented by \$500-1000 per year for computer service. An effective personal filing system should be developed. The use of a personal minicomputer is suggested to replace wives, now that the ladies no longer stay home to maintain the files.

The ACS Committee on Professional Training has recently completed a revision of the 1977 guidelines that emphasizes increased attention to information retrieval and states that students need formal instruction in this area. The book under review, along

with 10 similar ones published during the past 10 years and with the help of commercially available tapes that teach the use of "Beilstein", "Gmelin", etc., collectively provide all that is needed for sound instruction in the use of the literature of chemistry. None of these texts addresses the critically important question of data quality; perhaps that can be learned only by bitter experience!

Amherst, Massachusetts

Edward R. Atkinson

The Benzodiazepines: From Molecular Biology to Clinical Practice. Edited by Ermineo Costa. Raven Press, New York. 1983. xiv + 432 pp. 16 × 24 cm. ISBN 089004-885-1. \$39.50.

In the period since the benzodiazepines were introduced into clinical practice over 20 years ago their popularity has increased until they have now become one of the most commonly prescribed classes of drugs in the world. The sheer volume of their usage combined with occasional reports of withdrawal symptoms or adverse reactions have, however, been reason for concern both by drug regulatory agencies and by the general public. This important topic of possible overuse or abuse of the benzodiazepines was a subject for thoughtful discussion by several authors in this compilation of papers presented at a World Congress of Biological Psychiatry symposium held in Stockholm in July 1981. It was further considered in a round table discussion by leading investigators from around the world and chaired by Dr. Leo Hollister.

Other clinical papers in this volume deal with the possible use of benzodiazepines for treating a variety of centrally mediated disorders, including schizophrenia, endogenous depression, and epileptic syndromes, in addition to their use for treating insomnia and anxiety. Their intravenous use in anesthesiology was also discussed. The safety of the benzodiazepines was considered from several points of view, including their interaction with other substances, particularly alcohol or other depressants, their metabolism, pharmacokinetics and use in patients with impaired liver or kidney function, their use in elderly patients, and their effect on performance, especially when used chronically for treating anxiety or insomnia.

As important as these topics are, especially for the practicing physician, in my opinion they are overshadowed by the remarkable strides that have been made on elucidating the mechanism by which the benzodiazepines interact with the central nervous system. These discoveries will undoubtedly have a tremendous impact on our understanding of central nervous system function and may lead to new approaches for therapeutic intervention in a variety of diseases. The "benzodiazepine receptor" is now considered to be an integral part of a GABA-receptor complex which also includes a GABA recognition site, a regulator protein (GABA modulin), and a chloride channel. It is believed that the "benzodiazepine receptor" is the recognition site for a co-transmitter that appears to decrease the action of GABA on the receptor. Interaction of the anxiolytic benzodiazepines with this recognition site increases the B_{max} for GABA binding and, thus, increases GABAergic transmission. It is possible that the insight gained through these investigations of the GABA receptor may be applicable to other transmitter systems. If so, it suggests that it might be possible to find useful chemical modulators for other transmitters or perhaps different, more selective modulators for the GABA system. This volume includes excellent discussions of the mechanism of benzodiazepine action, including discussions

of GABA transmission, the GABA receptor, the "benzodiazepine receptor" and its *in vitro* use for ligand binding studies, and a short chapter on the relatively new benzodiazepine antagonists.

Although this book contains a wealth of useful information about the pharmacology, mechanism of action, toxicology, and clinical use of the benzodiazepines, it does not live up to the evaluation given in its preface. It is *not* a "comprehensive report of the state-of-the-art in this field". Of the 25 chapters, 6 were written by members of the Hoffmann-La Roche staff. No other pharmaceutical company is represented. A great body of research and several important therapeutic advances in this field have thus been virtually ignored. Because of this bias it would appear that the symposium may have been organized and sponsored by Hoffman-La Roche. If so, this should have been clearly noted in the preface of this volume, to alert the reader to the possible slant of the publication.

This volume includes a brief subject index but no author index.

The Upjohn Company
Kalamazoo, Michigan

Jackson B. Hester

The Alkaloids. Volume 21. Edited by Arnold Brossi. Academic Press, New York. 1983. xix + 368 pp. 16 × 23 cm. ISBN 0-12-4659 721-3. \$49.50.

This volume breaks new ground for the series by including reviews on nitrogen-containing substances derived from mammals, amphibians, fish, and microorganisms, as well as from plants. The restriction of the term alkaloid to bases of plant origin is wholly artificial, and the inclusion of materials from other sources in this book is justified by the complexity and interest of the chemistry described and by the medicinal importance of some of the compounds either as medicinal agents or as tools for studying physiological processes.

Two chapters, on simple isoquinoline alkaloids and quinazolinocarboline alkaloids, are updating reviews of areas covered in earlier volumes, and the first of these includes a valuable summary of the scope and limitations of and recent improvements in general methods of synthesis of isoquinolines.

A complementary chapter on simple isoquinolines and β -carbolines that are essential participants in or consequences of biochemical processes in mammals makes equally interesting reading.

An excellent chapter on four groups of antibiotics obtained from actinomycetes and sponges and all derived from isoquinoline-quinones gives full details of the activity and mode of action of the compounds, as well as the determination of their structures and methods of total synthesis. One compound, camptothecin, which shows antitumor, antiviral, plant-growth regulating, and insect sterilant properties, is the subject of another chapter covering the whole of the chemistry and 18 syntheses of camptothecin or its close analogues, and another chapter deals only with acronycine, unique among acridone alkaloids in showing very encouraging antitumor activity.

The longest chapter deals mainly with the chemistry, stereochemistry, and syntheses of a variety of neurotoxins isolated from amphibia but includes a section on the topology of receptors and mechanisms of ion transport that could provoke new lines of thought in this area of medicinal chemistry.

Literature surveys for all of the chapters are extensive, terminating in 1982, and the standard of production of the volume is excellent. In the preface, the series editor indicates that the broadening of the scope of the work begun with this volume will continue in future issues, and that is welcome news.

K. W. Bentley

Advances in Biochemical Psychopharmacology. Volume 37. CNS Receptors—From Molecular Pharmacology to Behavior. Edited by Paul Mandel and Francis V. DeFeudis. Raven Press, New York. 1983. xxii + 506 pp. 16 × 24 cm. ISBN 0-890040827-4. \$48.00.

The exponential expansion of studies on CNS receptors during the past decade has received impetus from new radioligand-binding techniques, in addition to improvements in other tech-

nologies, such as electrophysiology, autoradiography, and photoaffinity labeling. Despite these very significant advances, a direct relationship between ligand-receptor interactions and the mechanisms underlying the elicitation of a pharmacological response is lacking in most instances. Eventually it appears that isolation and characterization of receptors, reconstitution in a manner emulating the natural environment, and careful examination of the mode of interaction with agonists and antagonists will be required before receptor-related events can be understood with clarity. It is with this recognition that the present volume in this series, which records the proceedings of an international symposium held in the Couvent Ste-Odile, France, September 1-3, 1982, addresses studies directed toward the biochemical and physiological levels in an attempt to better understand physiological mechanisms and certain behaviors in terms of CNS function.

The book is divided into eight parts, namely, "Receptors for Inhibitory Amino Acids", "Receptors for Excitatory Amino Acids", "Benzodiazepine Receptors", "Dopamine Receptors", "Cholinergic Receptors", "Serotonin Receptors", "Adrenoceptors", and "Other Receptors and New Techniques". The list of contributors is very impressive, consisting of experts in each of the topics being addressed. Each of the eight general receptor classes is discussed in the form of a brief presentation of specialized studies that in most instances includes a significant amount of new research. In general, this enables the reader to gain some background information relative to the specific receptors and, in addition, to learn of new findings and methodologies that have advanced our understanding of drug-receptor interactions.

The book is published from "camera-ready" copies that result in a lack of typographical uniformity but expedite the publication process to enable more timely presentation. Despite this, it is now more than a year since most of the articles were prepared. Thus, as a consequence of the rapid advances in the area of drug receptor research, some of the presentations, for example, in the area of dopamine receptors, are already becoming dated.

The articles are uniformly well written; they are remarkably free from errors, contain many recent references, and are published on high-quality paper. An adequate subject, but no author, index is included. The overall impression of this reviewer is that this compilation of symposium presentations, as is so frequently the case, includes a great deal of new and relevant information without a clearly instructive orienting review format. As a result, continuity between the subject matter of the individual articles is lacking. Thus, the book, as perhaps is appropriate for a series such as this, is of a journal nature and will be a useful addition to appropriate scientific libraries, but will be of value as a desk copy to only extremely specialized CNS and receptor scientists.

Research and Development Division
Smith Kline & French Laboratories
Philadelphia, Pennsylvania 19101

Carl Kaiser

Anticancer Drug Development. Proceedings of the 1st International Symposium on Management and Realization of Anticancer Drug Development. Granada, Spain, March 25-26, 1982. Edited by P. Hilgard and K. Hellmann. J. R. Prous, Barcelona, Spain. 1983. xi + 223 pp. 15.5 × 22.5 cm. ISBN 84-499-6141-6. \$50.00.

Anticancer drugs include a broad spectrum of chemical structures that lack specificity in inhibiting cell proliferation. This nonspecificity is responsible for the dose-limiting toxic effects on normal dividing tissues. The majority of the drugs available today have been identified by means of an antitumor screening program. The early introduction of new antineoplastic drugs with demonstrated efficacy in the screens into phase I clinical trials has been a concern of oncologists and the regulatory agencies. The progression to clinical trials involves preclinical animal toxicology and often pharmacology. Phase I trials of anticancer drugs, unlike others, in humans are primarily concerned with elucidating toxicities and the establishment of the maximum tolerated safe dose. Phase II clinical trials today are generally concerned with the evaluation of efficacy in specific malignancies. An overview

of current approaches, strategies, and the problems in each of these areas of anticancer drug development are presented in this volume, based upon lectures presented at the symposium that was held at Barcelona, Spain, in March, 1982.

The book consists of 24 chapters written by a total of 49 authors. Five of the symposium papers are concerned with the selection of agents based upon antitumor activity screening. An assessment of the ability of various mouse tumor models to predict the efficacy of clinically effective drugs demonstrated that most of the established drugs exhibit a broad spectrum of activity. The new screening panel of tumor models in mice employed at the National Cancer Institute is described. Of interest are the new screening methods presently under evaluation. The chapter on the human tumor clonogenic assay describes a recently developed method employing human tumor fresh biopsy samples which is designed to predict whether a given agent would be effective in the treatment of that tumor. The clonogenic assay is of considerable current interest and is presently under evaluation by the National Cancer Institute to determine whether it will prove useful for the identification of new effective anticancer drugs. The use of autochthonous (carcinogen or radiation) induced tumors as a new model for the screening of new agents is the subject of another chapter. One chapter is devoted to the preclinical evaluation of anticancer drug toxicity and very briefly describes the results of a study conducted by European Organization for Research on the Treatment of Cancer (EORTC) Screening and Pharmacology Group. These presentations served as the basis for the discussions of the current criteria employed for bringing a drug into clinical trial.

The majority of the chapters are concerned with the design and analysis of clinical trials. The chapter devoted to the problems associated with the clinical evaluation of anticancer drugs in the U.S. currently and strategies for the design of effective clinical trials is especially valuable. Other chapters concerned with the work of the Early Clinical Trials Group of the EORTC and the approaches to the clinical development of anticancer drugs in Switzerland, the countries of mutual economic assistance (Hungary, Czechoslovakia, and the GDR), and the Netherlands will be of particular interest to oncologists in the U.S. These chapters provide a summary of recent phase I and II trials with selected investigational drugs and afford considerable insight into the current status of clinical anticancer drug development in Europe. The efficacy of combination chemotherapy in the treatment of many malignant tumors is well established. The importance of drug scheduling is addressed in a chapter on the therapeutic use of the combination of methotrexate and 5-fluorouracil. Clinical pharmacologists will find repeated reference to the importance of both preclinical and clinical pharmacology to clinical anticancer drug trials; however, except for a very brief chapter on the relevance of pharmacokinetics to these trials, little information regarding these studies has been presented. In addition, there is a chapter documenting the need for improved methods of postmarketing surveillance of anticancer drugs.

Researchers concerned with bringing to clinical trials will find an excellent review of the current regulatory requirements of the U.S. Food and Drug Administration of investigational new drug applications for antineoplastic agents. There is also a particularly lucid account of the processes employed for reconciling the regulatory requirements for drug development within the European Economic Community.

In the preface, it is noted that the book is directed to persons interested in anticancer drug development at the scientific, administrative, or regulatory level. The presented material represents a concise review of the topics, most often including the viewpoints of the reviewers and, as is typical of a symposium proceedings, the quality is variable. The volume conveys the intrinsic difficulties in the development of these drugs, and its value stems from the critical examinations of the problems by many of the authors. Except for two incorrect chemical structures, the chapters appear to be well edited. Unfortunately, a subject index is lacking. The book can be recommended to medicinal chemists seeking an overview of the problems associated with the development of anticancer drugs, since the development of these agents differs markedly from that of other drugs. Researchers in cancer chemotherapy will have a particular interest in current approaches to the clinical development of anticancer drugs in

Europe.

College of Pharmacy
The Ohio State University
Columbus, Ohio 43210

Louis Malspeis

Peptide and Protein Reviews. Volume 1. Edited by M. T. W. Hearn. Marcel Dekker, New York. 1983. v + 256 pp. 16 × 23.5 cm. ISBN 0-8247-7053-6. \$35.00.

In the preface of the first volume of "Peptide and Protein Reviews", the editor states that the major purpose of this new series is to bridge the information gap existing between peptide/protein chemists and biomedical researchers working in areas such as endocrinology, immunology, etc. This concept of demonstrating the role and potential of peptide/protein chemistry in interdisciplinary biomedical research is certainly useful and particularly attractive because currently existing series of volumes in the peptide and protein field are primarily technique oriented. The stated goal of the editor has been nicely achieved in chapters 2 to 6 of this first volume, which describe the application of both classical and more novel techniques and concepts of protein/peptide chemistry to a number of important problems in structural biology.

These review articles are preceded by a chapter on methodology by A. S. Bhowm and J. C. Bennett, which provides a clear and concise update on recent advances in peptide/protein sequencing techniques. Included in this chapter are a critical appraisal of sequencers currently available on the market and various suggestions for modifications of these instruments. The many practical hints given by the authors (optimization of coupling, sample extraction, etc.) will be particularly appreciated by the reader who has relatively little experience in protein sequencing. In chapter 2, R. F. Colman expertly reviews the characterization of both TPN- and DPN-specific isocitrate dehydrogenases. The studies discussed in this article involved mainly more classical techniques of enzymology and protein chemistry, and the results obtained to date permitted the formulation of a hypothetical molecular mechanism of isocitrate decarboxylation in the case of the TPN-specific enzyme. The functional, structural, and conformational homology of cytochromes *c* and ribonucleases from various sources is examined in chapter 3 (Y. B. Myer) based on information from X-ray crystallography and CD and NMR spectroscopy. The author reaches the interesting conclusion that the conformational state of the ligand-enzyme complex but not of the free enzyme has to be homologous in order to obtain functional homology. In chapter 4, R. Anholt, M. Montal, and J. Lindstrom report on the impressive progress that has recently been made with regard to the incorporation of acetylcholine receptors into model membranes. Novel techniques permitting the reconstitution of acetylcholine receptors both in lipid vesicles and in lipid bilayers are described in some detail. Clearly, these new techniques have now been developed to a stage where unambiguous conclusions regarding the functioning of acetylcholine receptors in the natural membrane environment can be drawn from such studies. In the longest chapter of the book, the neurophysin-oxytocin/vasopressin system is comprehensively reviewed and clearly presented by I. M. Chaiken, D. M. Abercrombie, T. Kanmera, and R. P. Sequeira. The review covers biosynthesis, sequence determinations, and studies on the conformational/aggregational behavior of neurophysins and on molecular details of the neurophysin-oxytocin/vasopressin interaction. The occurrence, function, and biological significance of the neurophysins and the neurohypophysial hormones are discussed somewhat less extensively. This chapter demonstrates very nicely how the use of the large spectrum of methods available to date, ranging from sophisticated physicochemical techniques and novel biochemical approaches to recombinant DNA experiments, has led to a detailed structural understanding of an important peptide-protein complex. In the last chapter, M. J. S. DeWolf, A. R. Lagrou, H. J. J. Hilderson, G. A. F. VanDessel, and W. S. H. Dierick discuss the role of enzymes, cell membranes, and subcellular components in the normal and in the pathological thyroid gland. The authors present a reasonably clear summary of the biochemical mechanisms regulating the function of the thyroid gland, but there is little emphasis on methodology.

The type of review presented in this volume is of great interest to biomedical researchers who would like to assess the potential of modern techniques of peptide and protein chemistry with regard to their own research problems. Because of its high didactic value, this volume is also very well suited for use in undergraduate and graduate courses. On the other hand, the researcher who is already an expert with a restricted interest in one or the other of the fields covered in this book may be less inclined to buy it because of the diverse nature of the topics.

The volume is, in general, well written and relatively error free. It would have been somewhat more convenient for the reader if a summary of the subtitles had been listed at the beginning of each chapter. All chapters contain a list of both up-to-date and pertinent older references, but a general subject and author index is not provided at the end of the book. However, because of the mainly didactic nature of the reviews such indexes are not really necessary.

In conclusion, Volume 1 of "Peptide and Protein Reviews" fulfills the principal goals set by the editor and it can be expected that future volumes of this well-conceived series will continue to illustrate the important role of peptide and protein chemistry in biomedical research.

Laboratory of Chemical Biology and Peptide Research
Clinical Research Institute of Montreal
Montreal, Quebec H2W 1R7, Canada

Peter W. Schiller

Peptide and Protein Reviews. Volume 2. Edited by M. T. W. Hearn. Marcel Dekker, New York. 1984. vii + 296 pp. 16 × 23.5 cm. ISBN 0-8247-7135-4. \$52.50.

In the second volume of "Peptide and Protein Reviews", both the general concept stated in the preface of volume 1 and the original form of presentation of the book are retained.

In Chapter 1, H. Ponstingl, M. Little, and E. Krauhs present an authoritatively written and well-coordinated review on tubulin. Structural aspects, including amino acid sequences, posttranslational modifications, and the assembly of tubulin into microtubules, are described in detail. Genes, biosynthesis, and evolutionary aspects of tubulin, as well as its interactions with various drugs, are also covered. A useful, up-to-date, and fairly comprehensive review on neurotensin was compiled by S. A. St-Pierre, R. K  rouac, R. Quirion, F. B. Jolicoeur, and F. Rioux (Chapter 2). Tissue distributions of the 13-peptide are reviewed, and its various central and peripheral effects are expertly described. However, it is obvious that as in the case of many other neuropeptides, a well-defined role of neurotensin as a neurotransmitter or neuromodulator remains to be established. The biological activities of nearly 80 neurotensin analogues in central and peripheral assays are conveniently tabulated in the final section of the chapter. Structure-activity studies seem to have been limited to mostly classical amino acid substitutions and so far have resulted in a few analogues with slightly enhanced potency or with weak antagonist properties. A clear and concise description of the events involved in the termination of polypeptide biosynthesis is presented by W. P. Tate in chapter 3. While progress has recently been made in elucidating molecular details of some of the steps leading to the release of the completed peptide chain from the ribosomal complex, other steps are still poorly understood. The author proposes an interesting scheme for polypeptide chain termination which most certainly will be useful as a working hypothesis for the design of further experiments. The final chapter provides an excellent report on parathyroid hormone (PTH) research by M. Rosenblatt, who has been a pioneer in this area for many years. Biosynthesis, precursor processing, secretion of PTH and its various mechanisms of action, and structure-activity studies are authoritatively and elegantly reviewed. Among recent achievements, the two most important ones are the synthesis of a peptide segment corresponding to the precursor-specific region of PreProPTH and the development of a PTH-(1-34) analogue with antagonist properties *in vivo*. The experimental approach taken by the author and his colleagues undoubtedly represents one of the most convincing demonstrations so far of the great potential of innovative peptide fragment and analogue synthesis

in the elucidation of the molecular endocrinology of peptide and protein hormones.

Laboratory of Chemical Biology and Peptide Research
Clinical Institute of Montreal
Montreal, Quebec H2W 1R7,
Canada

Peter W. Schiller

Organic Reactions. Volume 30. Edited by William G. Dauben. Wiley, New York. 1984. ix + 579 pp. 16 × 23.5 cm. ISBN 047-89013-8. \$54.50.

Volume 30 of this classic series contains two chapters, each devoted to a single reaction. The first chapter, "Phytocyclization of Stilbenes and Related Molecules" (F. B. Mallory and C. W. Mallory), consists of 456 pages and 708 references. The second chapter, "Olefin Synthesis by Deoxygenation of Vicinal Diols" (E. Block), consists of 110 pages and 189 references. An author index and a chapter and topic index for Volumes 1-30 are also included, as is a subject index for Volume 30.

Staff

Compendium of Organic Synthetic Methods. Volume 5. By Leroy G. Wade, Jr. Wiley, New York. 1984. xvi + 552 pp. 16 × 23.5 cm. ISBN 0471-86728-4. \$37.50.

By their compilation of volumes 1 and 2 of this compendium, Ian and Shuyen Harrison filled one of the great needs of the synthetic community: a method for rapidly retrieving needed information from the literature by reaction type rather than by the author's name or publication date. Volume 5 of this series presents the functional group transformations and difunctional compound preparations of 1980-1982. This volume closely follows the classification schemes of the first four volumes. The experienced user will require no additional instructions on the use of this volume. It remains an invaluable tool for synthetic organic chemists.

Staff

Review of Organic Functional Groups. By Thomas L. Lemke. Lea & Febiger, Philadelphia. 1983. x + 131 pp. 15 × 23.5 cm. ISBN 0-8121-0905-8. \$10.50.

Most teachers of undergraduate medicinal chemistry in Schools of Pharmacy encounter entering students who have taken fundamental undergraduate organic chemistry courses at various junior colleges and/or 4-year colleges, and, thus, the backgrounds of the students vary widely. Consequently, either special introductory medicinal chemistry courses reviewing concepts of organic chemistry particularly relevant to the biological system are established or significant portions of the basic medicinal chemistry courses are devoted to the review of these concepts. This book is designed to provide entering pharmacy students with the proper background for formal medicinal chemistry courses by reviewing the chemistry of functional groups commonly encountered in bioactive substances. The 16 chapters are entitled (1) "Water Solubility and Chemical Bonding", (2) "Alkanes", (3) "Alkenes", (4) "Aromatic Hydrocarbons", (5) "Halogenated Hydrocarbons", (6) "Alcohols", (7) "Phenols", (8) "Ethers", (9) "Aldehydes and Ketones", (10) "Amines", (11) "Carboxylic Acids", (12) "Functional Derivatives of Carboxylic Acids", (13) "Sulfonic Acids and Sulfonamides", (14) "Thio Ethers and the Nitro Group", (15) "Heterocycles", and (16) "Predicting Water Solubility". A very useful appendix reviewing the concepts of acidity and basicity is also included. Each chapter is organized by reviewing common and IUPAC nomenclature, physical properties related to water and lipid solubility, chemical properties related to the stability of the functional group under environmental conditions which might affect the storage of a drug, and metabolic properties of each functional group. Most chapters contain review questions at their conclusion.

The concise manner in which the material is presented should serve to hold the attention of the reader. Minor deficiencies

include the lack of sufficient examples of nomenclature within each functional group and a relatively weak chapter on chemical bonding. Additionally, the endeavor would have been enhanced by the inclusion of a greater number of review questions (only 35 review questions are presented in the 16 chapters) and by an introduction to drug nomenclature. The paperback format permits a modest price, bringing it within reach of all students. Because of the need for such an effort, this book is recommended as a supplemental resource to the standard medicinal chemistry texts and should prove to be a valuable tool in the teaching of medicinal chemistry at the undergraduate level.

School of Pharmacy
University of Mississippi
University, Mississippi 38677

Ronald F. Borne

Organic Functional Group Preparations. Volume 2. By Stanley R. Sandler and Wolf Karo. Academic Press, New York. 1983. xiii + 492 pp. 16 × 23.5 cm. ISBN 0-12-618552-2. \$75.00.

This is volume 12/II of *Organic Chemistry, a Series of Monographs*, and constitutes volume II of "Organic Functional Group Preparations". This work describes the preparation of some 17 functional groups, including allenes, ortho esters, sulfites, enamines, ynamines, ureas, pseudoureas, semicarbazides, carbodiimides, *N*-carbamates (urethanes), *O*-carbamates, imines, azides, azo compounds, azoxy compounds, and *C*-nitroso and *N*-nitroso compounds. Special and important features of this work are that the preparation of a given functional group is described from a variety of starting materials and by a variety of different preparative methods. For example, the chapter on imines describes the syntheses of these important intermediates from condensation of amines with carbonyl compounds, condensation reactions involving nitriles (preparation of ketimines), and the reaction of imine or imine derivatives with other reagents. In addition, the preparation of imines via oxidation or reduction reactions is also presented, albeit the yields are not always practical in the preparative sense. In the chapter on imines, the preparation of ethylenimines (aziridines) is also presented. A number of less versatile, but none the less important, methods are listed at the end of each chapter under miscellaneous methods. The other 16 chapters in the book also follow this same useful format.

The strength of this work, in this reviewer's opinion, is the experimental procedures, which have been clearly written into the work and in most cases, as the authors point out, have been checked in their own laboratories. The criteria for the choice of procedures were as follows: (1) the laboratory operations should be safe and free from the danger of explosion, (2) the procedures should afford the highest yield possible of compounds of reliable structure, (3) the procedures should be relatively uncomplicated, and (4) the procedures should be generally useful for a wide range of organic structures. Certainly for the most part these criteria have been fully met. Moreover, the tables of various transformations that have been carried out are presented in most cases with yields and with references. These clearly indicate the versatility of the preparation of the given functional group under discussion.

This reviewer's major criticism is that the volume (copyright 1971) does not contain any references dated after 1970, and therefore modern methods for synthesis of these organic functional groups have doubtless had to be omitted. It is unfortunate that it has taken so long for the book to be published. Consequently, it is felt this book can now be considered a classical approach to these transformations and is better suited for advanced undergraduate students, graduate students, and research workers in organic or medicinal chemistry who want to know exactly "how" to carry out the synthesis of one of the 17 functional groups. Because the latest reference was reported in 1970, this book cannot be considered an exhaustive treatise on the preparation of the functional groups so described; nonetheless, it is a valuable reference source for organic and medicinal chemists who are actually "doing" chemistry.

Department of Chemistry
University of Wisconsin
Milwaukee, Wisconsin 53201

James M. Cook

Presynaptic Receptors. Edited by J. deBelleruche. Ellis Horwood Ltd., Chichester. 1982. 223 pp. 16 × 23.5 cm. \$69.95.

During the past 10 years, the study of neurotransmitter receptors has moved ahead at a rapid pace. One area of special interest is the topic of presynaptic receptors, those neurochemical recognition sites that modulate neurotransmitter release either through positive or negative feedback mechanisms and are also thought to mediate the interaction of different receptor types. Although the literature concerning these receptors is increasing in the form of original and review articles, little is still known about the details of how such presynaptic receptors exert their control. This volume is based on contributions from leading European researchers at a Neurochemical Group Meeting of the Biochemical Society about presynaptic receptors.

Containing 12 chapters, this book is divided into four main sections concerning autoreceptors for catecholamines, presynaptic muscarinic receptors, transmitter interactions, and, finally, electrophysiological studies. For the most part, each chapter is technically well written, and all of them are well referenced. It is inevitable that in such a fast moving field, specialized texts like this soon become somewhat dated. For instance, may chapters posed unanswered questions about presynaptic receptors. It is very likely that the tools to answer such questions will quickly be identified, and the answers themselves will soon be forthcoming. By and large though, the book provides a superb basis for familiarity with a field of burgeoning interest and promising therapeutic potential. Stressed throughout the book is the key role that radiolabeled (especially ³H and ¹²⁵I) receptor ligands play in elucidating the location and function of presynaptic receptors. Such a role will no doubt expand in this area of increasing importance.

Authoritative and well written, this book is recommended for a varied readership of research workers in the area, as well as students desiring an introduction to the subject of presynaptic receptors.

New England Nuclear,
a DuPont Company

Crist N. Filer

Chronicles of Drug Discovery. Volume 2. Edited by Jasjit S. Bindra and Daniel Lednicer. Wiley, New York. 1983. IX + 272 pp. 16 × 23.5 cm. ISBN 0471-89135-5. \$44.95.

This second volume of descriptions of the processes leading to new drugs, written by those responsible, is an excellent addition to the first volume (reviewed in *J. Med. Chem.* 1983, 26, 117). Chapters listed by authors (drug) are as follows: M. A. Ondetti, D. W. Cushman, and B. Rubin ("captopril"); P. A. J. Janssen and J. P. Tollenaere ("Pimozide"); M. Gorman, R. R. Chauvette, and S. Kukulja ("Cefaclor"); J. W. McFarland ("Pyrantel, Morantel and Oxantel"); B. Ekström and B. Sjöberg ("Bacampicillin"); W. O. Gotfredsen ("Pivampicillin"); F. J. Lund ("Pivmecillinam"); F. Arcamone ("Doxorubicin"); J. A. Montgomery ("The Nitrosoureas"); H. Kawaguchi and T. Naito ("Amikacin"), and K. H. Büchel and M. Plempel ("The Azole Story"). The last includes such antimycotic imidazoles as clotrimazole. The rationale and history of the work leading to each active compound or series of compounds are given, and those arrived at from random screening leads or incorrect working hypotheses are acknowledged, as well as those resulting from very elegant reasoning, and some in between. The mix is an honest report of the real world, to which younger scientists and students might be exposed with advantage. Apart from the use of "biproduct analog inhibitor" (p 10) for "inhibitor analogous to both products", which is clumsier but would avoid coining a homonym of "byproduct", both the writing and the material are excellent. The seemingly obligatory errors noticed are few: the structure 8 on page 173 is not daunomycin, as stated on pages 174 and 175, but its *N*-trifluoroacetyl derivative, and the sentence (p 175) on the conversion of 9 to 10a or 10b does make sense if a comma is inserted after "daunomycinone" on l. 17. Another comma after "10b" in the same sentence would convert it to proper English. The volume is well-produced with clear chemical structures and pertinent tables. Perhaps the cost of excellence accounts for the one negative feature, a decrease of 4% in the number of pages and an increase

of 38% in the price over Volume 1.

This book is recommended for those interested in the process of drug discovery and any who would like a group of pleasant and fascinating scientific "reads". Future volumes are promised on an irregular basis.

Organic Chemistry Department
The Burroughs Wellcome Co.

M. Harfenist

Pharmacology of Histamine Receptors. Edited by C. R. Ganellin and M. E. Parsons. Wright, Bristol. 1982. xvii + 521 pp. 24 × 16 cm. ISBN 0-7236-0589-0. \$69.50.

Histamine, first isolated at about 1910, is a normal constituent of most tissues and blood of animals, including those of man. It is stored mostly in mast cells in tissues and in basophils in blood. Its vascular effects, coupled with its local storage and synthesis, make it a likely candidate for local control of tissue homeostasis, yet little is known about the chemical nature of histamine receptors or their precise locations. Affinity labeling and binding studies using radioactive antagonists have produced much progress, and hypothetical histamine receptors are now being drawn and analyzed. It is the right time, therefore, to read, understand, and inwardly digest a book written on this topic, linking together the chemical and biological components.

This book is exciting and a great stimulus not only to those experimentalists who work in the field of histamine but also to those clinicians interested in the biological effects of histamine released within the body. It is edited by two prominent scientists from the industrial world (working mostly to obtain safer and more selective antagonists) and written by experts from the U.K., U.S.A., and France. Its 11 chapters cover the main areas of chemistry, pharmacology, and pathophysiology of histamine where developments have occurred during the past 10 years. After the early studies with conventional antihistamines (which are now known as histamine H₁ receptor antagonists) in the treatment of allergies resulting from histamine release, the discovery of other selective agonists and antagonists showed the world that a second type of pharmacological histamine receptor might exist (now known as the histamine H₂ receptor). The presence of at least two types of receptor led to clinical applications, particularly in the treatment of peptic ulcers. Cimetidine, an H₂-receptor antagonist, was first marketed in the U.K. in 1976 and has since been introduced in over 100 countries. Like histamine, it is an imidazole derivative with a structurally specific side chain that differs from the naturally occurring amine in being longer and not basic. Nevertheless, lots of other H₂-receptor antagonists, such as ranitidine, possess a structure resembling histamine in the side chain yet are not imidazoles.

The opening chapter in the book guides us through the development of the classification of histamine receptors and is followed by a first-class description of the chemical properties of the amine in relation to tissue components on which it can bind and, therefore, produce its effects. The size of the chapter (nearly 100 pages) illustrates the depth and detail of the approach, ending with the suggesting that the H₂-receptor antagonists act at a highly polar site on the cell membrane surface where the dominant interactions are hydrogen bonding. Chapters on gastric secretion, the heart and blood vessels, the lung, the alimentary and genitourinary tracts, and the brain follow, as well as certain biochemical approaches to the problem of histamine receptors. Each is described fully enough to satisfy most histaminologists. Finally, advances in the pathophysiology and immunology of histamine are adequately dealt with, emphasis being laid on the potential therapeutic uses of H₁ and H₂ antihistamines. All in all, the book is stimulating to read and gives the impression that even greater advances in the field of histamine receptors and histamine antagonists will soon develop in the next decade.

I can thoroughly recommend this book, since it is good value for the price. Published on good paper, it is well presented. I very much liked the arrangement of having references at the end of each chapter given in full (that is, each contains the full title and first and last page numbers). The index is well-arranged and most valuable. However, it would have been a help to the reader if the contents of each chapter were not only collected at the start of each chapter but the page numbers given as well.

I found very few errors in the text, and these were all minor. Examples are on page 120 (where the first column of Table 3.5 is labeled Cell (pg/cell) when it should be simply Cell), pages 121 and 377 (where it is not compared to but *with*), and page 312 (where believes is incorrectly spelt in line 26 and *by* is omitted in line 28). Furthermore, I am not in favor of figures and tables being set out in two directions, sometimes next to each other but on opposite pages. Examples of this are on pages 62 and 63, 70 and 71, and 80 and 81, where one illustration is set in the text and the other is at right angles to this.

Department of Paramedical Sciences
North East London Polytechnic
London, E15 4LZ, England

G. B. West

Advances in Neurology. Volume 37. Experimental Therapeutics of Movement Disorders. Edited by Stanley Fahn, Donald B. Calne, and Ira Shoulson. Raven Press, New York. 1983. xx + 319 pp. 16 × 24 cm. ISBN 0-89004-695-6. \$45.

Parkinsonism is one neurological disease whose pathological basis is clearly delineated—there is a loss of dopaminergic neurons in the *substantia nigra*. Rational therapies are based on giving L-Dopa to increase the amount of dopamine in the basal ganglia or treatment with dopamine agonists, such as bromocriptine. Unfortunately, the beneficial effects of such treatments are not always clear cut, consistent, or permanent, and there are considerable side effects. The aim of this volume is to present some of the newer approaches that are being tested in attempts to improve the treatment of Parkinsonism and other movement disorders. The latter include dystonias, tremors, and tardive dyskinesia.

The various chapters are written by clinicians for clinicians. Individual reports tend to be sketchy, and the documentation often consists of a few tables describing the percentage improvement in a small group of patients, together with a listing of side effects. Statistical evaluations tend to be rudimentary or entirely lacking. In general, very few of the newer therapies seem to provide a real advance over present treatments.

Direct reports from the clinical investigators who are actually carrying out such studies can provide a useful overview of new treatments for practicing neurologists. For the reader whose main interest is neuroscience research, it would be preferable to have a critical review by one author who could also cover basic studies of the neurochemical mechanisms that supply the rationale for clinical trials. This book is useful for clinicians to leaf through. It is not likely to be of lasting interest to them or anyone else.

Department of Biochemistry and
Pharmacology
Tufts University School of Medicine
Boston, Massachusetts 02111

Louis Shuster

A Guide to the Chemical Basis of Drug Design. By Alfred Burger. Wiley, New York. 1983. x + 300 pp. 17 × 24 cm. ISBN 0471-86828-0. \$45.00.

"In this book I have no intention of reviewing the whole field of medicinal chemistry". So says Professor Burger in the introduction, but this is probably the broadest and most sweeping view of this bewildering field that has ever been written, in only 300 small pages. This task is so awesome that very few practitioners of the field would have tried it, and it stands to reason that only Alfred Burger could succeed at it. In order to ascertain that the job was done properly, he tried it in three different ways: first, from a historical point of view (Chapter 1: "History of Medicinal Chemistry"); second, from a modern perspective (Chapter 2: "Recent Research"); and, finally, at close range (Chapter 3: "Selected Examples of Drug Design"). There is obviously a fourth way, but that book has already been published, it is the three-volume "Burger's Medicinal Chemistry", edited by M. E. Wolff and written by 82 experts. Has Professor Burger been successful at this herculean task? I think he has. I, personally, liked Chapters 1 and 2, more than Chapter 3, and I am sure that many specialists might find fault with some of the statements in their "own" specific fields, but they will surely gain from the broader

view they will obtain on the other fields. This book does not provide a set of specific "recipes" to guide the process of drug discovery because nobody could. Drug discovery or drug design is a multifactorial process that is easily exemplified but difficult to explain and interpret, except a posteriori, and those interpretations are always to be taken with "a grain of salt". This guide teaches by exemplification, and the readers should decide whether the interpretation can be extended to their own particular problem. With the help of 1500 references, it should be relatively easy to reach deeper into any specific area. For most of us who have practiced the chemistry of drug design without having been specifically trained in medicinal chemistry, Professor Burger's book will be profitable reading.

The Squibb Institute for Medical Research Miguel A. Ondetti
Princeton, New Jersey 08540

Decision Making in Drug Research. Edited by Franz Gross. Raven Press, New York. 1983. xii + 244 pp. 16 × 24 cm. ISBN 0-89004-4. \$34.00.

The years between the end of the Second World War and the early 1960's saw the introduction of an unparalleled number of new effective drugs into clinical practice. The mainstays of drug therapy for numerous diseases were, in fact, first marketed in that period. One need mention in that connection only the thiazides, the H₁ antihistamines, and the corticosteroids. Though its origins date back further, this decade of success formed the mold for the research-based pharmaceutical companies. What is often overlooked, however, is that the great preponderance of the drugs developed in this so-called Golden Era were, in fact, products of serendipitous discovery. There is also a tendency to measure the health of the industry by the number of new chemical entities marketed. The enormous numerical success of that era was due in no small part to the fact that each drug in a new class was quickly followed by a large number of almost identical me-too competitors: chlorothiazide, for example, spawned at least half a dozen very closely related marketed analogues. The situation today is radically different; for a variety of reasons, market introductions dropped off sharply, starting in the mid 1960's. Though this decrease in new drugs is popularly ascribed to regulatory interference, the increasing difficulty of therapeutic targets probably plays an at least equally important role. There is in this reviewer's mind no denying that many of the new entities introduced in the post drug lag period are as fully as important as the drugs that first saw the light of day in the Golden Era. It must, however, be admitted that the process of drug development has become more expensive, more protracted, and far more difficult. The consequent smaller rate of new drug introductions has led to many studies, such as Wardells, conferences and general soul searching.

"Decision Making in Drug Research" represents the proceedings of a conference addressed in a very general way to the problems facing current industrial pharmaceutical research. The undertone to the meeting is put most plainly by one of the participants (G. Bartholini): "progress in terms of original compounds has been far below par in the last decade". In an interesting sidelight, this reviewer was unable to find anywhere in the volume details as to where or when the conference was held or as to its backing, beyond thanks to the Smith Kline Foundation for its hospitality and for finding such a marvelous spot on the Italian coast. The 25 participants represented both industry and academia, with the former predominating. Though affiliations are given, the lack of functional identification makes it somewhat difficult to set some of the comments in perspective. (From personal knowledge, it is imputed that the 17 companies were represented at levels ranging from chief executive officer to department manager.)

The book is divided into eight sections representing the corresponding conference topics: "Objectives for Research and Development in Drug Industry", "Criteria for Selecting Areas for Drug Research", "Criteria for Setting Priorities for Projects", "External Factors Influencing Decision Making", "Organization of Industrial Drug Research", "Decision Steps Within a Research Project", and "Cost of Research and Management Problems in Drug Research". Each of these topics is addressed by anywhere

from two to eight participants. This wide-ranging conference consisted of some 25 individual presentations, punctuated by 16 discussions periods (published in transcript); since this seems to have been crammed into a 2-day period, the presentations are of necessity on the brief side. The book, as a conference proceedings, reflects this lack of depth. On the positive side, it must be admitted that the book clearly identifies all the problems inherent in current industrial pharmaceutical research, ranging from the proper research funding levels through recruiting and maintaining a productive research staff.

The several presentations that address the role of the medicinal chemist in modern pharmaceutical research will be a particular interest to readers of this Journal. The traditional part played in drug discovery by chemists as the fount of all innovation is being increasingly challenged. It is felt by some that the day is at hand where the body of knowledge relating to molecular pharmacology is sufficient to be able to design new drugs on those principles; proponents of that view are increasingly tending to the point of view that the day of the imaginative insightful chemist is drawing, or should have drawn, to a close. Those chapters (particularly Bartholini's) and the ensuing discussions make for lively reading.

In sum, this conference proceedings addresses a very important topic in uneven, somewhat cursory fashion. Those picking up this book hoping to come up with answers on decision making in drug research will come away disappointed. On the other hand, the book will offer reassurance that others are asking the same questions. There is a sufficient sprinkling of examples as to how various research organizations are trying to cope with common problems to make a perusal of the book an interesting exercise.

Pharmaceutical Sciences Daniel Lednicer
Adria Laboratories Inc.
Columbus, Ohio 43216

Advances in Heterocyclic Chemistry. Volume 33. Edited by A. R. Katritzky. Academic Press, New York. 1983. ix + 336 pp. ISBN 0-12-020633-1. \$65.00.

Of the five chapters in this volume, three are updates of subjects previously dealt with in this series. The first chapter, "The Photochemistry of Oxygen- and Sulfur-Containing Heterocycles", is a continuation by S. T. Reid of his earlier review in Volume 11 (1970) and is a companion piece to his article on the photochemistry of nitrogen-containing heterocycles in Volume 30 (1982). Only the most blasé photochemist will fail to be impressed by the array of transformations which would be incredibly difficult to affect by classical synthetic techniques. The chapter makes for particularly fascinating reading.

"Reactivity of Naphthyridines toward Nitrogen Nucleophiles" (by H. C. van der Plas, M. Woźniak, and H. J. W. van den Haak) is authored by researchers whose contributions dominate the field. They describe the replacement of halo by amino groups on nitrogen heterocycles as taking place by the following types of substitution: "ipso" (leaving and incoming groups at same location), "cine" (leaving and incoming groups removed by one carbon atom), and "tele" (leaving and incoming groups are separated by two or more carbon atoms).

The related "Recent Developments in Naphthyridine Chemistry" (by W. W. Paudler and R. M. Sheets) is an update of Paudler and Kress's review in Volume 11 (1970). The authors state that an "explosion" of papers on naphthyridines has taken place since the appearance of the latter review and that contention is borne out by the marked increase in the rate of publication on this subject. The ¹³C NMR spectra of the six types of naphthyridines are given in a table in which data missing from the literature was provided by the authors. A small section is devoted to medicinal applications of naphthyridines.

"Pseudoazulenes" (by H.-J. Timpe and A. V. El'tsov) describes compounds in which a CH=CH bond of either or both of the two rings of the azulene ring system is replaced by a heteroatom (O, S, Se, or NR) while maintaining the aromaticity of the system. The authors have cataloged 39 different heterocyclic systems that fit this definition of pseudoazulenes. They admit that with such an abundance of structural types it is difficult to generalize about their synthesis, although they have identified threads of similarity

that run through them. Once prepared, we learn that the pseudoazulenes tend to be unstable to air, light, acid, and base. Hence, the main interest in them seems to lie in the physicochemical comparisons with azulenes.

"The Chemistry of Pyrido[1,2-*a*]pyrimidines" (by I. Hermezc and Z. Mészáros) had been reviewed previously in 1957 and contained 43 references. This review, which covers the literature until late 1981, contains 492 references. Interestingly, names given in the cited references, if they are Hungarian, i.e., Hermezc and Mészáros' nationality, are carefully given all appropriate diacritical marks, whereas Yugoslav names, which have as great a need for these marks, are deprived almost totally of theirs. Is there a message here? This chapter, like all the others, is a very lucid and informative account of the subject matter. Volume 33 continues in the high standard of this excellent series.

*Division of Experimental
Therapeutics*

Daniel L. Klayman

*Walter Reed Army Institute of
Research
Washington, DC 20307*

Chemistry and Biology of Pteridines. Pteridines and Folic Acid Derivatives. Edited by John A. Blair. Walter de Gruyter, New York. 1983. xxxiv + 1070 pp. 17.5 × 24.5 cm. ISBN 3-11-008560-7. \$128.00.

This book records the proceedings of the Seventh International Symposium on Pteridines and Folic Acid Derivatives held in St. Andrews, Scotland, from September 21–24, 1982, at which 274 participants from 24 countries were present. As with the previous symposia, a wide range of topics was presented. This symposium had much larger coverage of tetrahydropterin chemistry and biochemistry than previously, reflecting the present considerable upsurge of interest. It was also apparent that there is a great increase in the sophistication of studies in the areas represented at the symposium, a trend to be greatly welcomed.

In organizing the symposium and, thus, the general structure of this book, leading scientists were invited to give keynote lectures summarizing recent developments in their field of expertise which will be of value to those readers who wish to inform themselves of developments outside their own special interests. The many contributions from other authors describe the most recent developments in research in the chemistry and biochemistry of pteridines. This volume provides a detailed survey of the present state of this fascinating and important field of chemistry and biology.

Brief reports of the discussions and papers presented at each session and an author and subject index have been included.

Staff

Drug Fate and Metabolism. Volume 4. Methods and Techniques. Edited by Edward R. Garrett and Jean L. Hirtz. Marcel Dekker, New York. 1983. xiv + 485 pp. ISBN 0-8247-1849-6. \$75.00.

Methodology is of critical importance when investigating the fate of drugs in man or animals. This volume is the fourth in a series covering this topic and continues the theme of methodological critiques. The books comprising the series appear at irregular intervals, and the contents of each is in no way uniform. This applies to the present volume, which deals with pharmacokinetics, parameters affecting drug analysis, isotope derivitization analysis, electron-capture GLC, animal species, and the use of quantitative EEG measurements in bioavailability studies.

One of the editors, Dr. Garrett, in conjunction with Dr. Balant have contributed a massive 150-page chapter that deals competently with the use of computers in pharmacokinetic studies. This occupies one-third of the whole volume, but one inevitably feels that by the time such a chapter is read, techniques in this area will have advanced beyond what was written some time previously.

A small chapter by Dr. Valentine was the highlight of the book for me. The author undertook a detailed discussion of all those preanalytical factors that can affect subsequent drug analysis; all those factors that seldom rate high enough to receive space

in publications. I learned much from Dr. Valentine's contribution; its content is an example to us all.

The following chapters on isotope derivitization and electron-capture GLC were complete but left me feeling that if I could possibly avoid the complexity of analysis required for such analysis then I would use other approaches. For isotope derivitization, analysis of 40–50 samples per week is claimed; for a busy analytical laboratory this would seem less than adequate. Dr. Hucker returned to the theme of which species to use in drug metabolism studies when the object is to determine what occurs in man. Inevitably, the final conclusion is that only man mimics man and that other species are different. However, there is much useful comparison across species in the chapter, particularly when it is desired to study a specific metabolic route. Lastly, Drs. Itil and Krynicki deal with how to use quantitative EEG analysis to determine bioavailability of centrally active drugs. They conclude that this is almost as easy as plasma measurements but with the distinct advantage of being noninvasive and relating to effect rather than just to peripheral drug levels. Certainly, such techniques will become more widely used in the future.

Overall, there are a number of interesting contributions; however, the topics are too widespread for individuals to purchase a volume of this kind. Finally, one is left wondering when some of the chapters contained in the volume were written. The bibliography only extends to the 1980's in a few places; the majority of references are to work carried out in the later 1970's. This gives the impression that the book has been in preparation for some considerable time.

*Department of Neurology
Institute of Psychiatry
De Crespigny Park
London SE5 8AF, England*

Peter Jenner

New Approaches to the Design of Antineoplastic Agents.

Edited by Thomas J. Bardos and Thomas I. Kalman. Elsevier Biomedical, New York. 1982. vii + 337 pp. ISBN 0-444-00724-5. \$68.00.

This book is a compilation of papers presented at the 22nd Annual Medicinal Chemistry Symposium held in May, 1981, and sponsored by the Department of Medicinal Chemistry, State University of New York at Buffalo. The organizers intended the symposium to provide an overview of progress in the design of drugs for treatment of cancer and to encourage, both in formal presentations and informal discussions, the articulation of novel approaches to drug design. I consider that the organizers' objectives were attained and that the book is a useful resource not only for scientists actively involved in anticancer drug development but also to those interested in a clear and reasonably concise exposition of biochemical and pharmacological rationales for anticancer drug design. The editors selected an excellent group of investigators to review past accomplishments and to provide guidelines for future work. An attractive feature of the book is the inclusion of detailed discussions, some quite lively, of individual papers, as well as general panel discussions on agents altering the DNA template and enzyme inhibitors and their role in combination chemotherapy. These discussions often presented insights that enhanced the value of the preceding paper(s).

D. W. Henry's chapter on "Receptor Based Drug Design" provides a good introduction to the volume and properly distinguishes between design of molecules that bind to isolated receptors and design of useful drugs. N. R. Bachur's concise chapter on "Biochemical Activation of DNA Complexing Agents" provoked an excellent discussion. Bachur paid particular attention to the role of free radical species in determining cytotoxicity produced by anthracyclines and related compounds. A. C. Sartorelli's article on "Design of Hypoxic Cell Selective Chemotherapeutic Agents" delineates the physical and biochemical bases for approaches to treatment of poorly vascularized tumors with low growth fractions. In this chapter, as well as in the previous chapter, material covered in the discussion suggested that the published summary does not include material presented orally. J. W. Lowry's contribution on "Synthesis and Properties of New Antileukemic 2-Haloethylnitrosoureas" provides a detailed description of an investigative area that is of considerable current

interest. A chapter by K. W. Kohn and L. C. Erickson on "Mechanistic Bases for the Development of New Nitrosoureas" nicely complements Lown's contribution. This well-organized chapter gives due attention to capacity for repair of damaged DNA as a determinant of cellular response to drugs that induce such damage. "Model Parameters of DNA Reactive Agents" are discussed by H. S. Schwartz and P. M. Kanter; this chapter summarizes work by these authors on the interaction of drugs with DNA polymerase-monopolymer template systems and on production of structural damage to DNA.

The second section of the book starts with an article by R. E. Parks, Jr., T. M. Savarese, and S.-H. Chu on "Analogues of 5'-Methylthioadenosine as Potential Chemotherapeutic Agents". This is a well-crafted chapter that provides useful information about a relatively new target for antimetabolite development. F. M. Sirotnak contributed a chapter on "Rationales for Improved Antifolate Therapy of Cancer at the Level of Membrane Transport". This chapter describes evidence for subtle structural determinants of folate analogue membrane transport in neoplastic and normal tissue and implications for design of new agents. An especially useful section of this chapter deals with the contribution of enhanced lipid solubility to the antitumor activity of "nonclassical" antifolates.

J. A. Montgomery's presentation on "The Role of Congener Synthesis in Cancer Chemotherapy" summarizes advances in several areas of anticancer drug design with some emphasis on studies of analogues of established antimetabolites. This chapter provides a succinct description of goals and approaches to the attainment of those goals, in programs of congener synthesis. R. L. Kisliuk contributed a paper on "Homofolates and Other 2-Amino-4-Oxy Antifolates" that provides an interesting review of the biochemistry and pharmacology of folate homologues but does not specify targets for future synthetic efforts. A brief discussion of related folate antagonists including "dideaza" analogues (quinazolines) is included.

R. C. Jackson's paper on "Uridylate Trapping in Experimental Chemotherapy" describes approaches to management of hepatomas that are derived from biochemical studies of galactosamine-induced hepatotoxicity. These approaches involve combinations of galactosamine with several drugs that perturb pyrimidine metabolism (e.g., arabinosylcytosine, 3-deazauridine, etc.).

H. L. Elford and his colleagues discussed "New Cancer Chemotherapeutic Agents that Inhibit Ribonucleotide Reductase". Their paper stresses studies with poly(hydroxy) and poly(amino)benzene derivatives; the studies are presented in a well-organized manner, and the paper describes several compounds that are of interest not only as biochemical tools but also as potential components of combination chemotherapy regimens.

The third and final section of the book is organized under the heading "Diverse Mechanisms and New Approaches". R. K. Boutwell's short chapter on "Inhibition of Chemical Carcinogens" describes a strategy based on inhibition of steps in the process of tumor promotion. Information presented in this chapter is intended to help establish a rational basis for cancer prevention.

A chapter on "Control of Cancer Cell Proliferation by Biological Agents and their Analogs" by A. Bloch addresses the potential role of such approaches as the use of biological response modifiers in improvement of cancer treatment. Bloch briefly discusses induction of differentiation by biopolymers, conventional cancer chemotherapeutic agents, retinoids, and prostaglandins.

Y.-C. Cheng and D. Derse consider "Approaches and Limitations in the Development of Selective Antiherpes Virus Agents"; the inclusion of this contribution in the symposium presumably is due to the association of viruses with some malignant disease.

"Specificity in the Cytotoxicity of Showdomycin: Inherent and Derived" is discussed by M. Rabinovitz and Y. Uehara. Rabinovitz and Uehara point out the importance of competitive relationships for drug transport as possible determinants of selective drug damage.

T. J. Bardos and Y.-K. Ho provide an "Update on Antitemplates" that summarizes their studies of analogues of the templates for nucleic acid polymers with emphasis on studies of polynucleotides containing mercaptopurimidine units.

The latest references in the book are for the year 1981, and this is a disadvantage. On balance, I consider this a valuable book because it presents an organized body of information that will

provide medicinal chemists, pharmacologists, and others involved in anticancer drug design with new perspectives and insights on drug action that can catalyze the development of new drugs and drug combinations for treatment of cancer.

Vermont Regional Cancer Center John J. McCormack
Department of Pharmacology
University of Vermont
Burlington, Vermont 05405

Advances in Chromatography. Volume 23. Edited by J. C. Giddings, E. Grushka, J. Cazes, and P. R. Brown. Marcel Dekker, New York. 1984. xvi + 249 pp. 16 × 23.5 cm. ISBN 0-8247-7075-7. \$49.75.

Volume 23 is the latest addition to the long-standing and highly respected previous volumes in the series *Advances in Chromatography*, perhaps one of the more respected collections of review papers dealing with various areas of gas, thin-layer, and, more importantly, high-performance liquid chromatography. Indeed, more than half of these particular reviews in Volume 23 deal with aspects of HPLC, although GC is also represented. As in the past, each of the authors of these reviews is usually a recognized expert in his particular area, and thus each writes with a degree of authenticity, expertise, and sophistication expected from *Advances in Chromatography*. The Editors have once again done their jobs admirably, not only in carefully choosing just who will contribute here, but also in the final chapters/reviews published. Clearly, for anyone who has closely followed previous volumes in this series, this is yet another welcome addition to your library, despite the ever increasing price for recent volumes. The *Advances* are not published by photocopy methods, they do not use camera-ready copy, and thus the quality here is quite good, perhaps justifying the current price. The publication details are excellent: high-quality artwork, high-quality paper and print, excellent detail to proofreading, and lack of minor flaws, all of which further improve the readability and acceptability of the final product.

Volume 23 contains but six individual chapters, which comes to a bit less, on the average, than 40 pages per chapter. In all cases, lists of references are extensive and up-to-date, and the reviews are not only thorough and concise but also critical and evaluatory of future trends, directions, and possibilities. The first chapter deals with laser spectroscopic methods for detection in liquid chromatography (HPLC) and is written by E. S. Yeung, who has already published and presented widely in this field. He first describes the ideal LC detector and properties of lasers and then discusses individual laser-based LC detectors, such as RI, UV-Vis, FL, light scattering, optical rotation, photoionization, and, finally, photoconductivity. Everything one wanted to know in the area of laser-based detectors for HPLC is described and discussed here, even to the point of areas of possible future development and application not yet described.

Henderson and O'Connor next discuss low-temperature HPLC for the separation of thermally labile species. This chapter emphasizes the theory of temperature effects in HPLC, instrumentation and methods available for low-temperature HPLC, and finally, of course, individual literature applications in this field. These authors have also presented and published widely in this very area, and thus they too are able to present the topic with a high degree of expertise, experience, sophistication, and finesse. Chapter 3 involves a discussion of the use of HPLC for the kinetic analysis of enzymatic reactions and is written by D. L. Sloan. In essence, this chapter is devoted to newer HPLC-based techniques for following enzymatic reactions, using HPLC assays for starting materials, intermediates, and/or final enzymatic reaction products. For anyone intending to study such reactions, this particular chapter is surely an excellent introduction and synopsis of the entire area of HPLC applications for enzyme-based/initiated reactions.

Farooqui and Horrocks have contributed Chapter 4, which deals with a particular type of Sepharose-based affinity chromatography that utilizes heparin as the bound moiety responsible for the final separations. Some discussion is provided of the basic heparin-protein interactions, as well as methods for the attachment of heparin to various solid supports, such as Sepharose. The use of the final heparin-Sepharose affinity support for purification

of enzymes is then discussed, along with other possible uses for this type of affinity chromatography. Finally, the authors end this chapter with a discussion of the various advantages and disadvantages of heparin–Sepharose chromatographic methods.

Hu has reviewed the somewhat newer area of chromatopyrography, which is really an off-shoot of pyrolysis–GC, but now developing a method that permits the determination of the chemical characteristics of a compounded polymeric material. This is achieved in two or three separate steps: first by describing the specific formulation by the analysis of volatile components with conventional GC operating temperatures, second by using pyrolysis–GC to define the polymeric structure, and third by using inorganic analysis for determination of any residual, nonvolatile, and perhaps inorganic matter left after the first two steps in the overall method. Chromatopyrography is mainly a combination of a chromatogram and a pyrogram. Its main use is clearly for polymeric analysis and characterization, much as pyrolysis–GC has been used in the past, but now refining that approach to provide greater reproducibility and valid information.

The final chapter in this volume of *Advances in Chromatography* deals with the area of inverse gas chromatography and is written by S. G. Gilbert of Rutgers University. This is apparently an area of gas chromatography that emphasizes what happens to the stationary phase in GC, rather than the analytes, during a typical GC separation process. These studies are considered “inverse” in that the area of investigation is the nonvolatile, stationary phase. Although there are valid reasons for better understanding what occurs to the stationary phase during gas chromatography, since this could eventually lead to significant improvements in final separations, the vast majority of the analytical chemists and perhaps even chromatographers are perhaps less interested in this area than in the final separations and separation processes. This reviewer found this particular chapter a bit less interesting and relevant to current research interests than the other chapters in this volume. However, inverse gas chromatography has been of major use in polymer characterization, now using gas phase probe molecules to determine solute–solvent interactions where the polymer serves as the stationary phase or solvent.

In summary, this latest volume of *Advances in Chromatography* would appear to have something for everyone interested in the separation sciences, with extensive up-to-date references and bibliographies for each chapter. For the experts in HPLC, three or four of these chapters should be of direct interest; for those interested in bioanalysis, two or three chapters are important; and for those interested in GC or polymer analysis, at least two such chapters are relevant, if not vital. This is a collection of reviews in chromatography that should find widespread acceptance by the analytical community and which keeps very much alive this continuing series of *Advances*.

Northeastern University
Boston, Massachusetts 02115

Ira S. Krull

Myocardial Infarction and Cardiac Death. Edited by Erwin Margulies. Academic Press, New York. 1983. XIV + 220 pp. 16 × 23.5 cm. ISBN 0-12-471350-5. \$32.50.

Erwin Margulies conceived the scope and contents of this monograph and engaged the authors to write the chapters. Before the volume was completed, however, Dr. Margulies was killed in an automobile accident. Thus, his friend and colleague George de Stevens completed the task of editing and preparing this volume and has dedicated it to the memory of Dr. Margulies. Dr. de Stevens is editor-in-chief of this series of *Medicinal Chemistry Monographs*, of which this is Volume 18.

In seven chapters, 12 authors have described various aspects of myocardial infarction ranging from coronary microcirculation and basic mechanisms to the design and execution of clinical trials. With the focus of attention in recent years on experimental and clinical research into the causes and consequences of infarction, this has become a large and rapidly changing field. Only a few selected topics can be covered in a monograph such as this one. Nevertheless, the authors without exception have done a creditable job of describing state-of-the-art knowledge, each in his own field of expertise, and this volume provides an excellent review of

experimental and clinical results. The book has a thorough and useful index. Methods and findings are well documented, and the references are pertinent and up to date. The bibliographies do have one troublesome drawback, in that the format used in this volume does not permit inclusion of the titles of references cited.

In the initial chapter of the book, Mary Wilderman describes the structure, function, and pathophysiology of the coronary microvasculature. This chapter is very nicely illustrated.

Drs. Gerald Kelliher, Robert Dix, and Betsy Soifer discuss animal studies in an extensive second chapter. The authors describe contemporary methods and models, as well as review the subjects of experimental ventricular arrhythmia and myocardial infarct production. This chapter has a comprehensive reference list with 202 entries.

In the third chapter, William Frishman and Edmund Sonnenblick review the pharmacology of β -blockers, lipid-lowering agents, and antithrombotic drugs and their role in the prevention of myocardial infarction and sudden death.

Reflecting Dr. Margulies' preferences, the most thoroughly treated subjects in this text are the role of platelets in coronary disease and the pharmacology and therapeutic use of antiplatelet agents. One section of the chapter by Drs. Frishman and Sonnenblick, as well as the entire fourth chapter by Marian Packham and J. Fraser Mustard (416 references), deals with these subjects. The key role of platelets in the development and progression of atherosclerotic heart disease and thromboembolic myocardial infarction are presented in a separate chapter by Sean Moore.

In the remaining chapters of this monograph, Sidney Goldstein reviews the clinical pathogenesis of infarction and sudden death, while Michael Gent and Joel Singer provide a thorough discussion of the design, execution, and interpretation of clinical trials in cardiac mortality.

CV Preclinical Research Department Jeffrey E. Byrne
Bristol-Myers Pharmaceutical Research
Evansville, Indiana 47721

Pharmacology of Alcohol. By Dora B. Goldstein. Oxford University Press, New York and Oxford. 1983. xii + 179 pp. 16 × 24 cm. \$24.95.

In the Preface, the author, who has devoted nearly a lifetime to the study of addictive drugs, including alcohol, and who received the Research Society for Alcoholism's award for research excellence in 1981, offers two basic tenets that are stressed in this book, viz., alcohol requires high tissue concentrations to exert any pharmacological activity, and the consequence of such concentrations (a) causes deleterious effects on biological membranes and (b) overtaxes the liver, which must metabolize it.

The first chapter discusses the basic principles of ethanol absorption, distribution, and elimination and introduces the enzymes responsible for ethanol metabolism. These principles are further expanded on in a later chapter on the effect of ethanol on biological membranes, the work for which she is noted. That ethanol fits the classical Meyer–Overton relationship between lipid solubility and pharmacological activity is clearly illustrated, and the hypothesis is presented that expressions of intoxication, tolerance, and physical dependence (to ethanol) may be explained by membrane effects alone.

Although Goldstein herself does not consider acetaldehyde—the first metabolic product of ethanol oxidation—of major consequence in alcoholism, she nevertheless discusses the role of acetaldehyde in the sympathomimetic effects of ethanol ingestion and on biogenic amine metabolism and the formation of tetrahydroisoquinolines (TIQs), the latter a subject of initially intense, then waning, but again revitalized interest. The relationship of inadequate acetaldehyde clearance to the genetics of alcohol deterrence in humans and in rodent species is covered in some detail, as this has great bearing on voluntary alcohol intake.

The biochemical and pathological effects of alcohol on the liver are treated only briefly; understandably, more attention is paid to tolerance, physical dependence, and effects on neurotransmitter systems, as these are subjects of her specialty. Goldstein writes in a clear but simple style, which makes for pleasant reading. Many basic principles of pharmacology applicable to ethanol, as

well as to other drugs, are presented in this book, but the material covered is not sufficiently detailed to serve as a textbook for a graduate course on the pharmacology of ethanol. Rather, as the author points out, this is an introductory text to serve as a foundation upon which the specialized information can be systematically added. This book, therefore, serves an important base for all graduate students in pharmacology and medicinal chemistry, and is also recommended for any scientist with even peripheral interest in alcoholism.

VA Medical Center
Minneapolis, Minnesota 55417

Herbert T. Nagasawa

Neurobiology of The Trace Elements. Trace Element Neurobiology and Deficiency. Volume 1. Neuro Toxicology and Neuropharmacology. Volume 2. Edited by Ivor E. Deosti and Richard M. Smith. Humana Press, Clifton, NJ. 1983. Vol 1: 374 pp. Vol. 2: 320 pp.

These two volumes deal with the role of metals in biological systems, focusing special attention on the nervous system. They aim to provide a perspective of the rather broad and diverse roles of these metals for the general medical and scientific audience. The first volume examines the participation of a number of elements (Cu, I, Zn, Se, Co, and Fe) on the normal development and function of the nervous system and the pathological effects of their deficiencies. The second volume deals with the importance of Pb, Cd, Mn, Hg, Al, and Li to the fields of toxicology and/or pharmacology. The emphasis of both volumes is on the mammalian nervous system, with special attention to that of humans. The bases for the production of these two volumes at this time are defined by the editors and the introductory remarks of Sir Mac Farland Burnett. They call attention to the dramatic expansion that has taken place in the understanding of the biochemistry, anatomy, physiology, and pathology of the nervous system. Concurrently, they point to the fact that metallobiochemistry also has become established as a well-defined field of its own. Furthermore, the impact of metals on nearly all aspects of cellular function and the diverse but profound effects of both their excess and deficiency now have been delineated. The latter has led to the conclusion that the developing nervous system of the fetus is one of the most predominant target tissues affected by many of these metals. As a consequence, there has been a resurgence of interest in, as well as a need to present the known information on, these metals as they relate to these issues.

Overall, this has been accomplished partly by these two volumes. Each chapter is accompanied by an extensive list of references. However, in Volume I the treatment accorded to each metal is variable; there is no consistent division of the component parts in terms of, for example, anatomy, biochemistry, and pathology. Most chapters review the known information but some do not provide an integration of that information or define clearly the areas that require future experimental examination. The latter would have helped to fulfill the editorial promise to create the "new" discipline of "trace element neurobiology".

There are a number of valuable aspects to this volume, however, which merit mention. In the chapters on copper, for example, there are compiled the relative amounts of this metal present in different parts of the nervous system. This provides a concise, valuable source for the interested clinician and researcher. The reviews on the effects of copper deficiency, particularly the biochemical consequences, are good, although description of the clinical aspects of genetic diseases associated with the deficiency are very sparse.

There is included a section on iodine deficiency that is well written and substantiated, particularly the discussion of the clinical presentations. The syndrome resulting from iodine and thyroid hormone deficiencies are clearly differentiated and will be of interest to the general reader.

The bulk of the volume deals with zinc and its involvement in the development and function of normal tissues. There are three separate chapters dealing with the role of this metal in biochemistry, cell division, and teratology, as well as analytical information on its presence in different segments of the brain, particularly the hippocampus. In general, the first section dealing with the biochemical and teratological effects of zinc and its

deficiency are very phenomenological. Unfortunately, most of the known information on the biochemistry of zinc has dealt with tissues other than the nervous system, but better use of that information could have been made. Similarly, better advantage could have been taken of histological and microscopic techniques to define the pathological consequences of zinc deficiency on the brain.

The chapters on the effects of zinc and iron on behavior are intriguing, since they suggest a potential role for these metals. However, the information presented is insufficient to make any conclusions at this time.

The chapters on selenium and cobalt are well written. In particular, the one on cobalt is the most complete of the text. In large measure, this is probably the result of the fact that so much more is known about cobalamin deficiency. The chapter is well organized, the presentation is systematic, and the illustrations are clear and defined.

The second volume is generally well written and presents physiological and clinical information needed for the understanding of the toxicology of each of the metals discussed. There are included brief discussions of the chemical basis for the effects of the elements, particularly with lead, though not as extensively as found in more specialized texts.

The initial chapter discusses the effects of lead and mercury on behavior, dealing with the approaches used to measure toxicity in both animals and humans. It is a good survey of the available literature. The section on cadmium, its physical chemical properties, sources of pollution, metabolism, and toxicology, as well as its teratogenic effects on the central nervous system, are concise and informative. Similarly, several chapters dealing with lead, mercury, manganese, and aluminum survey critical aspects of their absorption, tissue distribution, and functional consequences. A final chapter on lithium provides the single instance of an element that is presently used as a pharmacological agent in the treatment of a psychiatric disease.

In summary, the two volumes provide needed perspective on the importance of metals to the function and pathology of the nervous system.

Center for Biochemical and Biophysical Sciences and Medicine
and the Department of Medicine
Brigham and Women's Hospital
Harvard Medical School
Boston, Massachusetts 02115

Kenneth H. Falchuk

Chemistry and Biochemistry of Amino Acids, Peptides and Proteins. Volume 7. Edited by Boris Weinstein. Marcel Dekker, New York and Basel. 1983. 408 pp. 23.5 × 16 cm. ISBN 0-8247-7027-7 \$69.75.

The explosive growth in the literature of peptide and protein chemistry prompted several major efforts toward comprehensive reviews. Yet in some special areas that are outside of the mainstream of research, the investigators' need for information often remained unfulfilled. Therefore, the endeavor initiated by the late Boris Weinstein to summarize the advance in such highly specialized fields deserves praise and recognition. The six previous volumes of this series are still valuable sources of information, and the seventh volume is no less important in this respect. The dedicated editorial work of Boris Weinstein was interrupted by illness and his untimely death, and the editing of Volume 7 was finished with the help of Drs. Orton and Pickart. It is as excellent as the first six volumes.

The first chapter, by R. K. Olsen, is a detailed account of recent research on quinoxaline antibiotics. Isolation, structure determination, biological activities, and aspects of conformation are treated with much thought for organization. The review is concluded with biosynthesis of quinoxaline depsipeptides and with their synthesis in the laboratory and extends to the properties of synthetic triostins as well.

The next chapter, by R. Rocchi and V. Giormani, reports research results in the complex area of glycoproteins. This comprehensive review is both concise and clear. After a discussion of the nature of the carbohydrate-protein linkage, an account of the methodology leading to synthetic O- and N-glycosides follows.

The synthesis of pseudoglycoproteins is also included. To cover the extensive literature, 275 references are listed.

The chemistry and biochemistry of open-chain imino acids is the subject of Chapter 3, by J. Tempé. This is a unique area made more accessible by the thorough review of 274 publications.

The intriguing group of ionophores, of which valinomycin is the best known member, is the subject of Chapter 4, entitled "Ion-transporting Peptides". The authors, R. W. Roeske and S. J. Kennedy, wrote an excellent summary of recent developments. In addition to small cyclic ionophores, such as valinomycins, enniatins, and beauvericin, new developments in the chemistry of channel-forming peptides, like alamethicin, and the open-chain gramicidins are covered as well.

The concluding chapter, by A. F. Spatola, is very timely. Numerous attempts toward long-acting or inhibitory analogues of biologically active peptides are based on modifications of the peptide backbone. The author skillfully organized the extensive material according to the chemistry in the modifications. Changes at the amide nitrogen, the α -carbon, or the amide carbonyl are discussed in separate sections, as are modifications of the entire amide bond or extensions of the backbone, e.g., by the incorporation of β -amino acids. The chapter is concluded with the biochemical properties of the backbone-modified peptides, e.g., their resistance to proteolytic enzymes.

Handling of the rich and complex material in the volume is facilitated by the Author Index and the Subject Index.

Department of Chemistry
Case Western Reserve University
Cleveland, Ohio 44106

Miklos Bodanszky

Brain Peptides. Edited by Dorothy T. Krieger, Michael J. Brownstein, and Joseph B. Martin. Wiley-Interscience, New York. 1983. xi + 1032 pp. 17 × 24 cm. ISBN 0-471-09433-1. \$97.50.

"Brain Peptides" is a timely sourcebook for current neuroscience or neuroendocrinological research. It is a scholarly effort by the editors, medical neuroscientists with proven leadership in the development of the neuropeptide field. There is a clear organization such that the reader can find an isolated topic easily. There are 39 chapters written by investigators noted in the field discussed. The material is divided into four parts, with the initial sections treating broader aspects of neuropeptide biology and function and the later sections presenting more specific aspects of known peptides. I think Parts 2 and 4 could have been given better titles. Not all the processes discussed in Part 2 are homeostatic systems, and naming Part 4 "Specific Peptides" implies specificity of pharmacological and physiological actions, as well as the intended meaning, i.e., particular peptides.

The first chapter begins with a thorough and interesting description of the structure and evolution of peptide hormone genes, such as those of the pituitary hormones and insulin family, as well as of somatostatin and calcitonin. The treatment would have been complete if the structures of the preproenkephalin and preprodynorphin genes were included and their similarity to the POMC gene was discussed. The ensuing chapters deal with the cell biology and enzymology of neuropeptide biosynthesis and degradation. The chapter by Peng Loh and Hal Gainer is one of the fairest treatments of the research on pathways of biosynthesis that have been written. However, the nomenclature of the enzymes involved in these processes needs to be simplified. The

rest of Part 1 describes the cell biology and neurophysiology of neuropeptides in nonmammalian organisms such as molluscs, crustaceans, and insects, where the systems are better defined.

The next part contains chapters on the role of peptides in the functioning and homeostasis of systems of the organism, such as feeding behavior, thermoregulation, and nociception, etc. The chapter on "Memory, Learning and Adaptive Behaviors" by George Koob and Floyd Bloom is good. These chapters are worthwhile for chemists or neuroscientists specializing in one neuropeptide. The third part of the book describes methodologies used commonly in neuroscience. "Competitive Binding Assays" is a chapter that specifically deals with radioimmunoassay techniques and not receptor binding. This is another equivocal title. Some of the techniques described in Miklos Palkovits' chapter on neuroanatomy, the Jans' chapter on neurophysiology, and Kwen-Jen Chang's and Pedro Cuatrecasas' chapter on molecular pharmacology of receptors are part of the exciting advances being made today.

The last part is comprised of chapters describing the localization, identification, regulation, and function of neuropeptides known in the CNS. Almost all of the chapters cover the particular field well. The earlier known peptides, such as neurotensin, substance P, TRH, and somatostatin, are described in substantive chapters. Some neuropeptide hormones have a more limited distribution and role in the CNS. This perspective is clarified in the chapters on oxytocin and vasopressin by Earl Zimmerman and on the pituitary hormones by Anthony Liotta and Dorothy Krieger. On the whole, the fourth part of the book is probably the most useful as a collection of research reviews on the individual peptides.

"Brain Peptides" covers the neurobiology of peptides in the CNS. As we know, for some neuropeptides many analogues have been made, and extensive structure-activity studies are ongoing. These aspects of interest to medicinal chemists are excluded from the scope of this book.

Experimental Therapeutics Branch
NINCDS, NIH
Bethesda, Maryland 20205

Martha Knight

Mucopolysaccharides—Glycosaminoglycans—of Body Fluids in Health and Disease. Edited by Rajendra Varma and Ranbir S. Varma. Walter de Gruyter & Co., New York. 1983. xv + 647 pp. 17.5 × 24.5 cm. ISBN 3-11-008471-6. \$132.60.

This monograph provides a reference source for an up-to-date, comprehensive integration of literature on virtually all the biological fluids for diagnosis, prognosis, and treatment of the pathology of the connective tissue. This book will help the experts in broadening their knowledge and equally help a new investigator with the needed information.

Staff

Books of Interest

Enzyme Technology. Preparation, Purification, Stabilization, Immobilization, Recent Advances. Biotechnology Review No. 2. Chemical Technology Review No. 222. Edited by S. Torrey. Noyes Data Corp., Park Ridge, NJ. 1983. xi + 308 pp. 16.5 × 24 cm. ISBN 0-8155-0956-1. \$42.00.