nature of the copper enhancement of INH action, it is not due to a conformational change induced in INH upon formation of the Cu(II) complex.

Acknowledgment. Support was from National Institutes of Health grants CA 15879 and NS 09839 and from the Medical Research Council of Canada. We thank L. H. Jensen for suggesting the problem and for use of his diffractometer.

Supplementary Material Available: A listing of observed and calculated structure factors (2 pages). Ordering information in given on any current masthead page.

Book Reviews

Progress in Pharmacology. Volume 3. Number 1. Structure–Activity Relationships in Clonidine-Like Imidazolidines and Related Compounds. By P. B. M. W. M. Timmermans, W. Hoefke, H. Stahle, and P. A. van Zwieten. Gustav Fisher Verlag, Stuttgart and New York. 1980. vi + 104 pp. 17 × 24 cm. $42.50.

The monograph "Structure–Activity Relationships in Clonidine-Like Imidazolidines and Related Compounds" is a logical continuation of the first book on this subject published by Van Zwieten in 1975. This new book, Volume 3, is considerably enlarged over the previous contribution, mainly due to the results taken form the Ph.D. thesis of Timmermans and those of other experts such as Hoefke, Stähle, and Van Zwieten. This volume is organized into six parts: a brief introduction and five major sections which are concerned with the chemical (Chapter 2) and physical (Chapter 3) properties of clonidine-like derivatives, SAR (Chapter 4), followed by a comparison between various pharmacological actions (Chapter 5), and finally by QSAR (Chapter 6) using the Hansch method. This volume contains 62 figures and 39 tables with numerous pharmacological and chemical data (e.g., pD_2, ED_{50}, α_1 and α_2 actions, log P, pK_a, etc.).

The over 200 literature references given in alphabetical order and followed by a subject index are also useful. Unfortunately, the references go only up to 1978 with the exception of a few author's references which are from 1979. It is regrettable that the paragraph devoted to the site of action of clonidine is omitted. Also, it has been recently shown that in the nucleus reticularis lateralis, clonidine inhibited excitatory neurons. The authors, on the contrary, state that the hypotensive action of clonidine is accounted for by an "increased activity of hypothetical inhibitory neurones" (pp 2, 1, 35). With regard to the paragraph devoted to the nature of α-adrenoceptor (p 85), I hope that the reader will understand that the work of Timmermans et al. in 1977 confirmed previous results from several researchers. Nevertheless, this volume can be considered essential for anyone working or undertaking research in adrenergic drugs. Researchers not directly involved in that field might find it interesting because this monograph gathers contributions from physical and medicinal chemists, biochemists, and pharmacologists. The price of $42.50 for this volume containing 104 pages might be discouraging.

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Specific GABA Receptor Agonists and Uptake Inhibitors: Design, Development and Structure–Activity Studies. By Povl Krogsgaard-Larsen. Login Brothers, Chicago. 1980. 198 pp. 15.5 × 22 cm. $12.50.

Professor Krogsgaard-Larsen is a major contributor to the medicinal chemistry of γ-aminobutyric acid (GABA), an inhibitory neurotransmitter. This monograph presents a clearly written account of his research in the period 1972–1979 which has resulted in the discovery of many selective GABA agonists and GABA uptake inhibitors and has advanced our knowledge of the structure–activity relationships of these agents. Many of the compounds reported are widely used by biologists to study GABA function, including the interaction of GABA with other neurotransmitters and with benzodiazepines. The GABA agonist, 4,5,6,7-tetrahydro[5,4-*c*]pyridin-3-ol (THIP), synthesized during the course of this research, is a potent analgesic now undergoing clinical trials. The monograph, Professor Krogsgaard-Larsen's thesis for the Doctor of Pharmacy from the Royal Danish School of Pharmacy, is recommended to workers in the field as offering a perspective not available in previous publications and to students of medicinal chemistry as an account of excellent and successful research in the emerging field of amino acid neurotransmitters. Its utility is hampered somewhat by the lack of an index, but the table of contents is quite detailed.

Chapter I, "Introduction", briefly reviews the evidence that GABA is an inhibitory neurotransmitter. Since decreased GABA function is implicated in the pathogenesis of certain diseases (Chapter II, "GABA Dysfunctions and Neurological and Psychiatric Disorders"), Chapter III, "Pharmacological Interventions in the GABA System", reviews the potential for increasing GABA neurotransmission with inhibitors of GABA metabolism, inhibitors of GABA uptake, and GABA agonists. Chapter IV, "Biochemical and Pharmacological Evaluation of Gabaergic Compounds", describes the methods used to assess GABAergic activity and selectivity. Chapter V, "Specific GABA Receptor Agonists: Design and Development", and Chapter VI, "Specific Inhibitors of GABA Uptake: Design and Development", present the rationale for selecting muscimol as the starting point for the research and detail the structural changes, results, and hypotheses that led to the discovery of the title compounds. Chapter VII, "Neuropharmacology of GABA Receptor Agonists", and Chapter VIII, "Neuropharmacology of GABA Uptake Inhibitors", review the metabolism, distribution, potential prodrugs, and selected pharmacology of the title compounds. Chapter IX, "Syntheses of Heterocyclic GABA Analogues", outlines the synthesis of compounds discussed in preceding chapters. Chapter X is a "Summary in Danish".

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Chemotherapy of Cancer. Second Edition. By Stephen K. Carter, Marie T. Bakowski, and Kurt Hellmann. Wiley, New York. 1981. 379 pp. 13.5 × 21 cm. $18.50.

The revised edition of *Chemotherapy of Cancer* appears 4 years after the first edition and reflects the considerable changes that have taken place in clinical cancer chemotherapy. This book has a strong clinical orientation and is notable for its lack of chemical structures. As with the first edition, the authors have divided the book into four sections, each containing two to four clearly written and compact chapters. The emphasis on conciseness, however, leads to an inability to discuss some topics in detail; for example, the mechanism of drug action, pharmacokinetics, and drug metabolism are poorly developed themes. Nevertheless, the unusually straightforward and uncomplicated style makes this book ideally suited for medical and graduate students, postdoctoral fellows, residents, and researchers and clinicians who have recently become involved in cancer research or therapy.

The introductory section presents the general stratagies and concepts of cancer chemotherapy and the current steps involved in clinical testing of new antineoplastic agents. Although less than

5% of the text is allocated to basic concepts of cancer chemotherapy, the authors outline the major points in a lucid fashion. The discussion of clinical trial is extensive and is a valuable chapter in the book.

The second section deals with individual anticancer drugs. After a brief discussion on the elements of drug development, routes of drug administration, determination of optimum drug dosage, and mechanisms of antitumor activity, the authors list specific information concerning the pharmacology and toxicology of the 50 most commonly used antineoplastic agents in the U.S. Drugs are classified loosely according to their mechanism of action.

The third section of the book contains a detailed description of the chemotherapeutic approaches for various advanced adult solid tumors, pediatrics solid tumors, and hematologic malignancies. Representing more than half the book, this section is an orderly, well-referenced and concise review of the current therapeutic stratagies in cancer medicine. Each chapter has been extensively modified to afford a major improvement over the previous edition. One relatively minor flaw, however, is the omission of an introduction to this section, which results in an unnecessary disruption in the flow of the text.

The final section outlines a variety of new analogues and therapeutic approaches which are currently being investigated in both the clinic and the laboratory. Drugs such as mAMSA, PALA, anthracyclines analogues, vindesine, prednimustine, DON, and methyl-GBG are mentioned, in addition to the exciting work in the areas of in vitro tumor sensitivity assays, toxicity amelioration, bone marrow transplantations, radiation sensitizers, and biologic response modifiers.

Although this elementary book is directed primarily toward those involved in the clinical practice of treating cancer, scientists interested in drug development may find it exceedingly useful. The book clearly outlines the disease states for which new therapies are required and the limitations of our current approaches. The appealing format and a very good index make locating information both easy and enjoyable.

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Chemical Analysis: A Series of Monographs on Analytical Chemistry and Its Applications. Volume 59. Affinity Chromatography: Bioselective Adsorption on Inert Matrices. By William Scouten. Wiley, New York. xiii + 348 pp. 15 × 23 cm. $42.50.

This book marks only the second effort of this collection in the area of biochemical techniques. It is, as the author states, an introductory guide to the field of affinity chromatography and is designed as a primer for the novice and a possible textbook for an advanced undergraduate or graduate course in protein biochemistry. Viewed from this perspective, I believe the book easily accomplishes these modest, yet not readily achievable, objectives.

The chapters follow a normal, logical development that is fairly standard for reviews on affinity chromatography, starting with a description of chromatography support matrices, spacer arms, and coupling procedures, and continuing with chapters on theory, the use of general affinity ligands, bioselective elution, and several chapters on special techniques. Of particular interest are the very thorough chapters on nucleic acid affinity chromatography and hydrophobic chromatography. There is also a very fine chapter on the chemistry of affinity chromatography, with good descriptions of synthetic procedures. Indeed, this is the book's main strong point, with most chapters containing adequate experimental details to enable its use as a source book for affinity chromatography. A good selection of key references, many from 1978 and some as recent as 1979 and 1980, enables the reader to carry out a more extensive literature search if required.

The book does lack an adequate discussion of adsorption chromatography in general and does not include a section on ligand quantitation, two somewhat bothersome oversights. There are also a large number of typos, unexpected for this kind of book, which occasionally lead to ambiguous statements and might make the researcher hesitant to follow a synthetic procedure without double checking. However, these are relatively small complaints for a work which, overall, has much merit.

In a field in which there have been a number of reviews and books, Professor Souten has given us a fine, basic text at a competitive, though not inexpensive, price. The book's style is very readable and the experimental procedures are clearly presented. The medical researcher, the biochemist, and the student will find this to be a valuable addition to their library if they do not already possess a recent overview in this rapidly expanding field.

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Nucleic Acids and Proteins. Edited by Shen Zhao-wen. Science Press, Beijing, China (Distributed by Van Nostrand-Reinhold, New York). 1980. xiv + 662 pp. 16 × 24 cm. $42.00.

This book records the proceedings of a symposium on nucleic acids and proteins organized jointly by the Chinese Academy of Sciences of the Peoples Republic of China and the Max Planck Gesellschaft of the Federal Republic of Germany and held in Shanghai in October of 1979. It consists of 90 communications, including reviews on ribosome structure (H. Wittmann), insulin structure (Z. You-shang), and molecular mechanisms of virus maturation (E. Kellenberger), research papers on the chemical synthesis of ribonuclease A (H. Yajima and N. Fujii), drug resistance conferred by plasmids (H. Meng-min et al.), the cloning of bacteriophage DNA fragments (C. Yan et al.), enkephalin involvement in acupuncture analgesia (Z. Kang et al.), nitrogenase cofactors (Nitrogen Fixation Study Group, Jilin University), sleep peptide synthesis and action (J. Ai-xue et al.), and many, many more. It is heartening to read these papers and note the vigorous, up-to-date interest in biochemistry and molecular biology in the Peoples Republic of China. The world scientific community will surely benefit from continued international cooperation so well exemplified in this book.

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Topics in Antibiotic Chemistry. Volume 5. Edited by P. G. Sammes. Ellis Horwood Limited, Chichester (Distributed by Wiley, New York). 1980. 312 pp. 15.5 × 24 cm. $87.50.

Volume 5 of this important series contains four different parts, each of which is concerned with one particular aspect of antibiotic chemistry and biochemistry. Part A, written by J. M. Ghuysen of the University of Liege, is titled "Antibiotics and Peptidoglycan Metabolism". This part is complex and difficult reading for one not familiar with the area, but it is well worth the effort. It begins with a detailed description of the composition and assembly of bacterial cell walls and then discusses the biosynthesis of peptidoglycans. The specific steps in biosynthesis that are inhibited by various kinds of antibiotics, such as D-cycloserine, tunicamycin, bacitracin, and vancomycin, are carefully noted. Thus, one can form a clear picture of the overall process. Following this discussion, the structure–activity relationships among β-lactam antibiotics are given with particular attention to conformational analysis of their side chains. Part A is completed by thorough descriptions of the enzymes of the peptidoglycan cross-linking system, the mechanistic properties of β-lactamase and DD-carboxypeptidase/transpeptidase enzymes, and the properties of enzyme active centers. The discussion of processes occurring at the active center of the serine DD-carboxypeptidases/transpeptidases is especially thoughtful. Overall, the presentation of ideas and experimental results on the β-lactam antibiotics is most valuable. It complements nicely the material on the chemistry and antimicrobial activity of new synthetic β-lactams that was the topic of Volume 4 in this series.

Part B, written by D. H. Williams, V. Rajanada, M. P. Williamson, and G. Bojesen of Cambridge University, is devoted to the vancomycin and ristocetin group of antibiotics. This group also includes actinoidin, avoparcin, and A35512B. The ristomycins have been shown to be identical with the ristocetins. Compounds in the vancomycin family consist of a polypeptide aglycon to which a carbohydrate moiety is attached. Their antibacterial activity

is based on the formation of 1:1 complexes with UDP-acetylmuramylpeptide precursors that have a D-Ala-D-Ala residue at the carboxyl terminus. The authors present a very precise and lucid picture of the structure of this type of complex through their use of the results available from UV difference spectra, proton NMR spectra with emphasis on the nuclear Overhauser effect, X-ray crystallography, and model-building studies. They also describe the discovery, isolation, and structure elucidation of members of the vancomycin–ristocetin group.

The properties and action of kirromycin (mocimycin) and related antibiotics, such as aurodox, efrotomycin, heneicomycin, kirrothricin, and azdimycin, are the subjects of Part C. A timely review on this new family of antibiotics has been written by A. Parmeggiani and G. Sander of the Ecole Polytechnique, Palaiseau Cedex. Kirromycin and its analogues inhibit bacterial protein synthesis by a unique and specific effect on elongation factor (EF) Tu. This factor is a monomeric protein that increases the rate and specificity of positioning aa-tRNA on the ribosomal acceptor site A. It does this through a process that begins with the formation of a ternary complex with GTP and aa-tRNA, followed by hydrolysis of the γ-phosphate of GTP, release of the EF-Tu–GDP complex from the ribosome, and interaction of the α-amino group of aa-tRNA with the peptidyl transfer center on the ribosome. The authors review a number of experiments to support their conclusion that kirromycin binds to EF-Tu in a 1:1 complex that can further add GTP and aa-tRNA; however, because of the presence of kirromycin, GTP hydrolysis is inhibited and aa-tRNA is not placed on the peptidyl transfer center. Also described in Part C are the isolation and properties of the antibiotics, their antibacterial activities, and the development of resistance by bacterial mutation.

Part D, a review of the actinomycins, is written by A. B. Mauger of the Research Foundation of the Washington (DC) Hospital Center. A number of reviews on the actinomycins have appeared in recent years, and there is some question as to whether this one really was needed. However, it is an excellent review which can be recommended highly on its own merits. It is concerned with the broad picture of actinomycins, including such topics as production and nomenclature, separation and characterization, structure determination, chemical reactions, synthesis, biosynthesis, mechanism of action, structural conformation, preparation of analogues, and structure–activity relationships. The discussion of conformational analysis is a particularly valuable feature of this review.

The variety of topics contained in this volume makes it difficult to target a selected group of readers who might have a compelling interest in it. Possibly those people involved with β-lactams would find it especially valuable. And the limited number of people working with compounds of the vancomycin, kirromycin, and actinomycins will find their particular reviews essential. Beyond these special interests, the volume, as well as the entire series, can be recommended for libraries. This particular volume should have a broad appeal to chemists, biochemists, molecular biologists, and microbiologists. The high price probably will discourage the reader with a general interest in antibiotics from purchasing a personal copy.

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Recent Advances in the Chemistry of β-Lactam Antibiotics. Special Publication. Number 38. Edited by G. I. Gregory. The Royal Society of Chemistry, Burlington House, London. 1981. ix + 378 pp. 15 × 21 cm. £16.00.

This softback volume contains 30 chapters stemming from the papers presented at the Second International Symposium on β-Lactam Chemistry which was held in Cambridge, England, in June of 1980. The first symposium had taken place in 1976 and also resulted in a book. The β-lactam antibiotic field has undergone a remarkable revitalization in recent years spurred by their continued economic/medical success and by the discovery of novel ring structures and relatively efficient new methods for partial and total synthesis. A comprehensive, though brief, review at this time is welcome. The chapters in this book are brief synopses of recent advances on a wide range of topics and, although there is the anticipated variation in interest and quality, the overall level is quite good. The individual chapters are photo-offset from the authors' manuscripts, and the quality of the printing and binding is excellent. An enormous amount of technical information is presented in brief and very readable fashion, and medicinal chemists who do not normally follow this field will find that the book provides easy access to novel chemical reactions and interesting elements of drug design. Chapter 1, by R. Bucort of Roussel, provides a clear and concise account of the methods of preparation of clinically important cephalosporins and the prospects for economical partial and total synthesis. Chapter 2, by B. Wetzel et al. of Boehringer-Ingleheim, discusses interesting QSAR studies directed toward improvements in pyrimidinylureido ampicillin/amoxycillin types. The cefuroxime/cefotaxime groups are represented by chapters by W. Duerckheimer et al. of Hoechst and G. G. Weingarten et al. of Glaxo. The bioisosteres are described in a collection of chapters by M. Narisada et al. of Shionogi (1-oxacephems), A. K. Bose et al. of Stephens Institute (1-dethia-2-thiocephams), M. Hashimoto et al. of Fujisawa (3-azacephalosporins), M. J. Pearson et al. of Beecham (1-azacephems), and J. Marchand-Brynaert et al. of Louvain University (2-oxopenicillins). Much effort and novel chemistry has resulted, in many cases, in reasonably efficient entries into new ring systems sometimes possessing substantial biological activity worthy of further exploration. Narisada, in a particularly interesting contribution, points out that optimization requires a careful consideration of the interplay of functional groups and that knowledge gained in one ring system will not automatically apply in another. Biosynthetic studies are described by E. P. Abraham et al. of Oxford (a well-written account of exciting work on cell-free studies with cephalosporins), B. W. Bycroft et al. of Nottingham (on penicillins), and S. W. Elson of Beecham (with a fascinating account of the complex clavulanic acid story). Clavulanic acid chemistry is recounted by C. E. Newall of Glaxo, B. C. Ross of Hoechst, and P. H. Bentley et al. of Beecham. Newall's chapter on conversion of clavulanic acid into new structural types was particularly well-written. Recent olivanic acid chemistry was clearly described in chapters by D. F. Corbett et al. and by R. Southgate et al. of Beecham. The thienamycin field was surveyed by B. G. Christiansen et al. of Merck and S. Oida of Sankyo. H. R. Pfaendler of the Woodward Institute described, in an interesting chapter, the geneology of the penems, and additional chapters on this general topic were presented by J. Gostelli et al. of the Woodward Institute, S. Betty et al. of Glaxo, and P. Ward et al. also of Glaxo. Much of this work involves chemical hybridization. Mode of action studies were contributed by J. M. Ghuysen et al. of Liege (mapping the active site of penicillin-sensitive cell-wall transpeptidases), H. Vanderhaeghe et al. of Leuven, by G. W. Ross et al. of Glaxo (SAR of penetration, β-lactamase resistance and affinity to penicillin-binding proteins), and by M. I. Page et al. of Huddersfield Polytech (on the mechanisms of several important reactions of β-lactam antibiotics). The chapters of Ghuysen, Ross, and Page were particularly thought provoking. Finally, chapters by P. G. Sammes et al. of Oxford and Leeds and by J. E. G. Kemp of Pfizer on the 6-β-bromo- and 6-β-iodopenicillanic acids as β-lactamase inhibitors round out the collection.

In sum, this book is economical, well-produced, timely, full of references, and has interesting insights into an important medicinal chemical area; therefore, it should be bought by all libraries and by most medicinal chemists.

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Nucleic Acids Symposium Series. Number 7. Nucleic Acid Synthesis: Applications to Molecular Biology and Genetic Engineering. Edited by Hubert Köster. Information Retrieval Ltd., London. 1980. 396 pp. 16 × 23 cm. $40.00.

This volume consists of 32 reports presented at the International Symposium on Chemical Synthesis of Nucleic Acids held in Egestorf, GFR, in the spring of 1980. It is written in the

tradition of the *Nucleic Acids Research, Special Publication* series which, starting with the previous volume 6, was renamed the *Nucleic Acid Symposium Series*.

The material is loosely grouped into two sections. The first covers synthetic methologies and the second deals mainly with applications of synthetic oligonucleotide fragments, often with the assistance of recombinant DNA technology, to specific problems of molecular biology. The volume is presented as containing "details of the latest methods in oligonucleotide synthesis from practically all the leading laboratories in the world". This claim is to a large extent correct. There is an abundance of international participation which comprises a valuable feature. For example, important and elegant work done in the USSR, primarily at the Shemyakin Institute in Moscow, could be of interest to many American scientists who may not be familiar with it, since pertinent papers were published only in the Russian literature. However, a word of caution is warranted. This is not a "how to" book for the uninitiated; a point we will come to again later.

The introduction defines concisely the scope of the oligonucleotide synthesis and includes a brief but up-to-date list of references and reviews. It is followed by a fascinating account of the pioneering work currently being carried out in that field. Almost all important aspects of oligonucleotide synthesis are represented, including both the di- and triester variations, the $2' \rightarrow 5'$ link formation, the preparation of viral "cap" structures, the use of T4 RNA ligase, and the phosphite triester method. The growing interest in synthetic methodologies employing solid supports is evidenced by the fact that they are the subject of six reports. A variety of solid supports are described. These include HPLC grade silica gel, cellulose, polyacrylmorpholide, polydimethylacrylamide, polystyrene, and polyvinylpyridine or polyacrylonitrile grafted with Teflon. The comparative advantages of such materials are not clear from the presentations, and the assessment of their usefulness must be left to the experimenter. It is conceivable that in practice the selection will be ultimately dictated by the availability of commercial systems. In this context, the lack of a discussion on the adaptation of the phosphite triester method to solid-phase synthesis, developed by Ogilvie's group at McGill University, for both ribo- and 2'-deoxyribooligonucleotides represents an important omission.

The degree of experimental detail given in the reports varies. It is perhaps unavoidable that in such a volume emphasis will be given primarily to a discussion of strategies and methods rather than procedures, which is not objectionable in principle. Reference to the literature where experimental methods and the characterization of important intermediates are described should be adequate. It is troublesome, however, when, as, for example, in the synthesis of mRNA "cap" structures, most of the original papers have appeared in condensed form in rapid-publication journals such as *Tetrahedron Letters*, *Chemistry Letters*, etc. Attempts to even duplicate such work would be a tedious experience. On balance, the volume is a virtual gold mine. There are nuggets of information scattered throughout the volume regarding blocking reagents, deblocking methods, condensing agents, chromatographic separations, etc. The reader who is patient enough to examine its contents carefully and systematically will be richly rewarded.

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Safe Handling of Chemical Carcinogens, Mutagens, Teratogens, and Highly Toxic Substances. Volumes 1 and 2. Edited by Douglas B. Walters. Ann Arbor Science Publishers, Ann Arbor, MI. 1980. Vol. 1: xiv + 381 pp. Vol. 2: xiv + 277 pp. 16 × 24 cm. $33.95/volume.

The handling of chemicals associated with potential human health hazards is a complex and controversial problem. Various government agencies and private organizations are becoming increasingly concerned with the use of known and potential highly toxic substances. Policies relating to the handling of chemical carcinogens, mutagens, and teratogens require an interaction of the chemist with toxicologists, industrial hygienists, safety and health personnel, and engineering professionals. Most of the material in these two volumes was derived from the 1979 American Chemical Society/Chemical Society of Japan Chemical Congress symposium program, "Safe Handling of Chemical Carcinogens, Mutagens, and Teratogens—The Chemist's Viewpoint". Realistically, effective control of these toxicants requires separate procedures, depending on whether the operation is in an industrial, academic, or research setting. The emphasis of these books is on control and use of hazardous agents in a research organization, although with modification the approaches suggested could be adapted for industrial or academic laboratories. The books have their origin in the hazardous chemical agent use protocol concept developed at the National Institute of Environmental Health Sciences. Walters details the protocol system, appropriately designed laboratory and disposal facilities, and informational and personnel requirements necessary for establishing and maintaining health and safety regulations which are effective but also flexible enough to accommodate various research programs and anticipated future needs.

The two volumes are each divided into three major sections. The first section concerns appropriate laboratory design, handling and management procedures, and packaging and transportation of hazardous compounds. The emphasis of this section is on the use of the principles of containment and engineering controls for workers, laboratories, and environmental protection. An overview of several representative facilities and programs is presented. The next section deals with methods for monitoring the chemicals in the laboratory and outside environment, as well as in personnel. The format for interaction of the research staff with medical and safety personnel is presented in discussions about medical surveillance programs. The third section deals with information and classification systems for chemicals. The chapters in this unit present organizational grouping procedures for categorizing chemicals by functionality, reaction, and structure.

Beginning in the second volume, the fourth section leads from chemical classification to the use of structure–activity for toxicity prediction. Although currently of limited specific potential, structure–activity predictions help indicate properties, mechanisms of interaction, hazards, and handling requirements which can be planned for in advance. Physiochemical properties are determinants of chemical reactivity and stability which are important factors in containing and disposing of chemicals. Spill control, degradation, detoxification, and deactivation are covered in the following section. The last section discusses disposal methods for hazardous chemicals and emphasizes incineration methods. The need for appropriate monitoring of incinerator stack effluents for detection of hazardous chemicals from a specific analysis viewpoint rather than general emission criteria is also covered. These books offer a useful and up-to-date compendium for chemical safety procedures and will be a valuable reference for chemists involved with health and safety issues in the laboratory.

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Advances in Enzymology. Volume 51. Edited by Alton Meister. Wiley, New York. 1980. v + 317 pp. 16 × 24 cm. $29.50.

This volume of *Advances in Enzymology* contains several chapters which might be of particular interest to medicinal chemists. One article by L. F. Thompson and J. E. Seegmiller deals with adenosine deaminase deficiency and severe combined immunodeficiency disease (SCID). The authors review the clinical manifestations of adenosine deaminase deficiency, as well as the evidence for a biochemical relationship between this enzyme deficiency and a defect in the immune system. Therapeutic approaches to treat SCID are reviewed. In addition, the authors describe the use of adenosine deaminase inhibitors as immunosuppressive agents and in combination chemotherapy. Other types of immunodeficiency syndromes associated with deficiences of enzymes in the purine salvage pathway, including T-cell immunodeficiency and B-cell dysfunction, are reviewed.

Another article of potential interest to medicinal chemists deals with the enzymology of 2,3-diphosphoglycerate (2,3-DPG). The importance of 2,3-DPG in red blood cell physiology, in general, and oxygen affinity for hemoglobin, in particular, makes this chapter very interesting. This article by Z. B. Rose is primarily devoted to the enzymology of phosphoglycerate mutase, which catalyzes the interconversion of glycerate 3-phosphate and glycerate 2-phosphate, and diphosphoglycerate synthase, which catalyzes the formation of 2,3-DPG from glycerate 1,3-diphosphate. Another chapter written by R. C. Bray deals with the reactions and the structure of molybdenum centers in enzymes. This chapter is of particular interest because of the molybdenum centers present in nitrogenase and nitrate reductase, enzymes of obvious environmental interest because of their involvement in the nitrogen cycle. The other topics covered in this volume include cryoenzymology in aqueous media, written by P. Douzou, and the utilization of binding energy in coupled vectorial processes, written by W. P. Jencks.

Some of the topics reviewed in this volume are of substantial current interest, making the volume worth the rather modest price tag. The editor, Alton Meister, is to be congratulated for continuing to maintain a high level of quality in the articles which appear in this series.

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Advances in Enzymology. Volume 52. Edited by Alton Meister. Wiley, New York. 1981. 408 pp. 16 × 24 cm. $32.50.

Volume 52 of *Advances in Enzymology* contains several very interesting articles, including one by A. L. Fink and G. A. Petsko on X-ray crystallographic cryoenzymology. This technique has the potential to define in more detail the structure of each intermediate and transition state in an enzyme-catalyzed process. This article describes the use of subzero temperatures and fluid cryosolvents to stabilize normally transient intermediates in the crystalline state so that their atomic structures may be determined by X-ray diffraction methods. Such molecular information would be extremely valuable to medicinal chemists in their efforts to design mechanism-based and transition-state inhibitors of enzymatic reactions. X-ray cryoenzymology appears to supplement conventional crystallography, adding the important capability of detailed mechanistic studies, including "time-lapse" pictures of an enzyme in action at atomic detail.

Another article in this volume deals with the interactions of dinitrogenase and dinitrogenase reductase. The complex of these two proteins is referred to as nitrogenase, which is the system capable of fixing N_2, that is, reducing N_2 to $2NH_3$. The article reviews the information which is available concerning the mechanism of association of dinitrogenase and dinitrogenase reductase to form the nitrogenase complex, as well as the kinetic data available on the catalytic capability of the complex. This is an extremely interesting system from a biochemical standpoint but equally interesting and important from both environmental and economical viewpoints.

In another chapter in this volume a review is provided of glycosyltransferases and their use in assessing oligosaccharide structure and structure–function relationships. This article provides a survey of the various glycosyltransferases and describes their actions in oligosaccharide biosyntheses and their use in structure–function analysis of oligosaccharides. The final chapter in this volume deals with the role of futile cycles in the regulation of carbohydrate metabolism in liver. This chapter surveys the current state of knowledge about the three cycles occurring in the glycolytic/gluconeogetic pathway. For each cycle the author describes the relevant regulatory properties of the enzymes involved and the role of the cycle in the regulation of glucose metabolism.

The articles in this volume are well-written, comprehensive, and timely, making it a worthwhile addition to one's library.

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Protective Groups in Organic Synthesis. By Theodora W. Greene. Wiley, New York. 1981. xiii + 349 pp. 17 × 24 cm. $37.50.

This much needed book on protective groups by Theodora Greene includes up-to-date procedures for protecting functional groups such as hydroxyl, amino, carboxyl, carbonyl, and sulfhydryl. The stated aim of this book is to provide concise yet complete information on the most useful of these groups, including the best methods of formation and cleavage, as well as an indication of the scope and limitations of each group, with references through 1979. The author has surely met her objectives in this handy volume. The advantage of this book over others published on this subject is not only the timeliness of the references and methods but also the incorporation of reactivity charts which give an overview of the best procedures and stability of the reaction products. This book will find a place on the shelf of any modern synthetic organic chemist.

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Aliphatic and Related Natural Products Chemistry. Volume 2. Specialist Periodical Reports. By F. D. Gunstone, Senior Reporter. Royal Society of Chemistry, Burlington House, London. 1981. xiii + 265 pp. 15 × 22.5 cm. $104.00.

This second volume in the new series follows the format and the content of its predecessor, covering the literature of 1978–1979, with the exception of the chapter on "Marine Aliphatic Natural Products", which was omitted by reason of "unforseen difficulties".

These books are written by specialists for specialists who, under normal circumstances, may be expected to be au courant with the literature of their respective fields anyway. Unfortunately, the individual medicinal chemist and his institutional library for whom these and the related series serve as valuable references may find the rapidly escalating cost of these pocket-sized volumes a deterrent to the use they deserve.

Staff

Annual Review of Pharmacology and Toxicology. Volume 21. Edited by R. George, R. Okun, and A. K. Cho. Annual Reviews Inc., Palo Alto, California. 1981. ix + 670 pp. $20.00.

No annual compilation can reasonably cover all of pharmacology and toxicology. I look to Annual Reviews for a sampling of topics and areas that are currently generating research interest and excitement. The present volume fulfills these expectations. I have arbitrarily divided the topics covered here into six main areas.

(1) *Neurotransmitters and Their Regulation.* The study of excitatory amino acids has reached the point of using specific antagonists such as D-α-aminoadipate, uptake blockers such as *threo*-3-hydroxyaspartate, binding assays, selective lesions, and measurements of neuronal conductance.

The discussion of hypothalamic releasing factors, pituitary peptide hormones, and their regulation by classical neurotransmitters suggests that progress in this field is being hindered by the lack of methods for measuring directly the release of hypothalamic hormones.

The area of presynaptic receptors is covered broadly, with emphasis on defining a logical foundation for assessing such receptors. The involvement of both pre- and postsynaptic receptors in adaptation to centrally acting drugs receives detailed consideration in a separate chapter.

The discussion on the mechanism of action of barbiturates highlights the emerging role of GABA and also describes other changes relating to the development of tolerance and physical dependence.

The neurotransmitter that receives the most attention in the review on the pharmacology of migraine is serotonin. Studies in this field have revealed a therapeutic activity of propranolol that is unrelated to the blockade of β-receptors.

The chapter that deals with the possible role of neurohormones

and peptides in the pharmacology of memory is a progress report on a shadowy area that still has many more vague hypotheses than solid benchmarks.

(2) *Pharmacogenetics.* This field is represented by two chapters. One is devoted largely to genetics of the adenylate cyclase system in cultured mouse lymphoma cells that are killed when cAMP accumulates. The other deals with the genetics of the induction of cytochrome P_{450} activities in mice, with emphasis on the Ah receptor and multiple forms of cytochrome P_{450}.

(3) *Immunopharmacology.* A review of the integration of chemotherapy with immunology in the treatment of childhood acute lymphocytic leukemia stresses the need for information about the effects of chemotherapeutic agents on B and T cells. The chapter on the pharmacological control of immediate hypersensitivity discusses the use of agents that raise cAMP levels to inhibit antigen-stimulated, IgE-mediated histamine secretion.

(4) *Environmental Toxicology.* A discussion of factors that promote the development of respiratory cancer covers the role of cocarcinogens and particulates, as well as nutrition and infections. The review on neurotoxicity after organophosphorus esters presents a detailed summary relating chemical structures to toxicity and advances the hypothesis that the target consists of axonal rather than neuronal proteins.

(5) *Advances in Physiology.* Under this heading I would classify topics that do not deal with drugs or poisons directly, but are of great interest to pharmacologists. These include a discussion of prostaglandins and related compounds and a chapter on the actions of nerve growth factor and anti-NGF antibodies.

(6) *New Approaches and Methodologies.* The effect of structural changes in diuretics related to ethacrynic acid is discussed in relation to protein binding, tubular secretion, biotransformation, and ototoxicity. The SAR approach has still not reached the point of permitting valid predictions or an understanding of the exact role of different chemical groups. The same problem arises in the chapter on SAR and drug disposition. There is a useful tabulation of equations correlating physicochemical properties with permeability, diffusion, protein binding, metabolism, and excretion. Do these correlations simply describe colligative properties or do they explain what is happening?

A descriptive chapter in stereology contains many equations but few answers. It emphasizes the correlation between calculated and observed changes in enzyme activities and the structure of endoplasmic reticulum after treatment with phenobarbital. At the moment, this approach does not seem to promise fundamental new insights.

The chapter on radioimmunoassay contains many practical pointers and an illuminating discussion of the advantages and disadvantages of using monoclonal antibodies.

The availability of a bewildering variety of in vitro and in vivo assays has prompted a timely presentation of the use of the decision point approach in the testing of compounds for carcinogenicity. The recommended progression is from tests for mutagenicity and transformation to in vivo tests for the initiation or promotion of tumors. What is still lacking is a description of how this approach works in practice.

A related chapter on screening for teratogens suggests that cultures of dispersed cells of *Hydra attenuata* might provide a useful regenerating, developing test system. Again there is no indication of whether this system is actually useful.

There are the usual accessory chapters. K. K. Chen discusses his training in China and the U.S. and the discovery of ephedrine. A novel feature this year is a review of eight new drugs or delivery systems, based on data obtained from the Food and Drug Administration. The descriptions are brief, there are no references, and no attempt is made to evaluate the animal and human studies which form the basis for claims of efficacy. I do not feel that this material, useful and interesting though it is, belongs in Annual Reviews.

The concluding review of Reviews continues to reflect the erudition and special interests of E. Leong Way and includes a perceptive evaluation of the new edition of Goodman and Gilman's "Pharmacological Basis of Therapeutics".

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Books of Interest

Encyclopedia of Chemical Technology. Third Edition. Volume 13. By Kirk-Othmer. Wiley, New York. 1981. xxvi + 993 pp. 19 × 26 cm. $145.00.

Encyclopedia of Chemical Technology. Third Edition. Volume 14. By Kirk-Othmer. Wiley, New York. 1981. xxvi + 981 pp. 19 × 26 cm. $145.00.

American Drug Index. By Norman F. Billups. J. B. Lippincott, Philadelphia. 1981. ix + 732 pp. 15 × 21 cm. $21.00.

The Condensed Chemical Dictionary. Tenth Edition. By Gessner G. Hawley. Van Nostrand Reinhold, New York. 1981. xi + 1135 pp. 17 × 24 cm. $42.50.

Parkinson's Disease. Current Progress, Problems and Management. By U. K. Rinne, M. Klingler and G. Stamm. Elsevier/North-Holland, New York. 1981. xviii + 401 pp. 16 × 23 cm. $65.00.

New Frontiers in Psychotropic Drug Research. By Stuart Fielding and Richard C. Efflanf. Futura Publishing Co., Mount Kisco, NY. 1979. xviii + 262 pp. 16 × 23.5 cm. $28.50.

Basics of Electroorganic Synthesis. By Demetrios K. Kyriacou. Wiley, New York. 1981. xiii + 153 pp. 15.5 × 23.5 cm. $27.50.

Atherosclerosis Reviews. Prostaglandins and Cardiovascular Disease. Volume 8. By Ruth Johnson Hegyeli. Raven Press, New York. 1981. xiii + 203 pp. 16.5 × 24 cm. $25.00.

Coordination Compounds of Porphyrins and Phthalocyanines. By B. D. Berezin. Wiley, New York. 1981. xiii + 286 pp. 16 × 23.5 cm. $53.95.