Conclusion

The above results clearly show that replacement of the ribofuranose oxygen of all three adenosine residues of 2-5A core 5′-monophosphate results in a major reduction in ability to interact with the 2-5A-dependent endonuclease from a variety of sources. The decreased binding activity may be related to a loss of interaction of one or more of the ribofuranose oxygens with some site on thee endonuclease. Certainly the methylene group would introduce considerable hydrophobicity into a previously hydrophilic site. Alternatively, the conversion of oxygen to methylene may bring about a conformational change in the 2-5A molecule, and this could be detrimental to optimal binding interactions. In this regard, both UV and CD spectra suggested that the aristeromycin analogue **14** possesses less base stacking than the parent p5′A2′p5′A2′p5′A.

Acknowledgment. We are grateful to Dr. M. Nishikawa (Takeda Chemical Industries) for a supply of aristeromycin, to Professor H. Hirai, Y. Gotob, and M. T. Kawamura for their assistance in determining 400-MHz NMR spectra, and to Dr. S. Higuchi for his help in measuring CD spectra.

Book Reviews

The Alkaloids. Volume 22. Chemistry and Pharmacology. Edited by Arnold Brossi. Academic Press, Orlando, FL. 1983. xviii + 342 pp. 16 × 23.5 cm. ISBN 0-12-469522-1. $50.00.

This well-established series of volumes on the most beautiful of all natural products, the alkaloids, continues to go from strength to strength. Since the publication of Volume 1, edited by R. H. F. Manske and H. L. Holmes, in 1950, the series has been devoted to a series of reviews on the different classes of alkaloids which are again reviewed when sufficient new data has been accumulated. Volume 21 saw a change in editor and in Volume 22 we see also a marked change in two of the five chapters presented. One chapter is devoted to one of the sophisticated physical techniques which has been used for the determination of novel structures of alkaloids and one concentrates on a specific chemical method which has proved valuable in alkaloid synthesis. Further reviews of this type are promised for future volumes, and hence it is of interest at this early stage to note the scope and contribution of these new departures.

The chapter on "Elucidation of Structural Formula, Configuration and Conformation of Alkaloids by X-Ray Diffraction" briefly outlines the experimental procedure, interpretation of data, and evaluation of the results. Applications to the problems of establishing structure, configuration, and conformation are described and then a series of examples are given. Among the examples used are a series of alkaloids from neotropical poison frogs, morphine agonists and antagonists, and some bisindole and bisditerpene alkaloids. The chapter illustrates quite clearly the dramatic effect which X-ray diffraction techniques have had on natural product chemistry by examples in the alkaloid field.

"Application of Enamide Cyclizations in Alkaloid Synthesis" is the title of the second departure from traditional "Manske and Holmes" chapters. This versatile synthetic method is discussed in detail, and the two techniques of photocyclization and thermalcyclization are described. Applications of the method to the synthesis of numerous alkaloids are given and include the Amaryllidaceae alkaloids, benzophenanthridines, protoberberines, yohimbines, and ergot alkaloids.

For those who may think that all is not well with the world, I should add that tradition has not been thrown completely out of the window and that their chapters on "golden oldies" such as the "Ipecac Alkaloids" and the imidazole alkaloids of the pilocarpine-type are still there. Both these areas continues to be the subject of considerable research and are of interest to medicinal chemists because of the range of pharmacological properties shown by these compounds.

The remaining chapter reviews in some detail the putrescine, spermidine, spermine, and related polyamine alkaloids. Such alkaloids occur as mixtures and are very difficult to separate and even when separated the results obtained from spectral or chemical analyses are equivocal. This timely review is a valuable contribution to our understanding of these alkaloids.

What of the change of approach? I welcome the new emphasis and the two new chapters bring the promise of further interesting reviews on the physical and chemical techniques which are so important in alkaloid chemistry.

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Allenes in Organic Synthesis. By Herbert E. Schuster and Gary M. Cappola. Wiley-Interscience, New York. 1984. xvi + 358 pp. 17 × 24 cm. ISBN 0-471-87284-9. $47.50.

The purpose of the book, as stated by the authors in the preface, "is to describe the synthesis of a variety of functionalized allenes and their application to the preparation of a variety of interesting chemical intermediates and natural products", a coverage that is not adequately indicated by the title of the book. Overall, the authors have done an excellent job in accomplishing the stated purpose of the book.

Chapter 1, "Allenes: An Introduction", is a very short chapter (seven pages) that includes very brief sections on ^{1}H and ^{13}C chemical shifts and optical properties and chirality.

Chapter 2, "Alkyl, Aryl and Cyclic Allenes", describes the many methods of syntheses of these classes of substituted allenes.

Chapter 3, "Additions to Allene Hydrocarbons", describes reduction (hydrogenation) and electrophilic, nucleophilic, and miscellaneous additions. Interestingly, free-radical additions are not discussed. Cycloaddition and dipolar cycloaddition reactions are covered later in a separate chapter. Most of the references cited in this chapter are rather old (only a few being post-1980) and have been reviewed previously. The inclusion of this material, however, does provide for a complete and comprehensive review of the synthesis of substituted allenes.

Chapters 4–8 cover the syntheses and reactions of various types of substituted allenes: "Allenes Containing Unsaturated Substituents", Chapter 4; "Hydroxy and Oxo-Substituted Allenes", Chapter 5; "Allenic Acids and Their Derivatives", Chapter 6; "Hetero-Substituted Allenes", Chapter 7, including alkoxy- and acetoxy-substituted allenes, sulfur-substituted allenes having sulfur in various oxidation states, and nitrogen-, phosphorus-, silicon- and boron-containing functions; "Haloallenes", Chapter 8. The syntheses of many natural products containing these functions, or in which these functionalized allenes were used as synthetic intermediates, are described.

Chapter 9 is devoted to a discussion of cycloaddition reactions of substituted allenes, including allene–allene dimerizations, allene–ketene and allene–olefin cycloadditions, and allene–enone photochemical cycloadditions. The chapter concludes with a discussion of the synthesis of heterocyclic systems via dipolar cycloaddition reactions. These areas are the subject of active research today, and some of the statements appearing in this chapter are not correct in terms of results published in late 1983 and 1984. For example, in the section on allene–olefin cycloaddition reactions it is stated that "the stereochemistry about the alkene is retained in the cycloaddition". This is not universally

true, some cycloadditions occurring with complete loss of stereochemistry.

The final chapter entitled "Miscellaneous Reactions of Allenes" is very short (12 pages) and consists of two sections: one on organometallic allenes (lithium, silver, and titanium only) and the second on oxy, thio, and amino Claisen rearrangements. The authors admit these reactions "do not belong to any of the previous chapters" and that "only those reactions of practical synthetic value are discussed here". In fact, lithioallenyl compounds and oxygen-, sulfur-, and nitrogen-containing allenes had been discussed earlier, and these few reactions could well have been described in those chapters.

Overall, the book is well written. The discussions of the chemical reactions are very adequately illustrated by chemical equations. There are very few typographical errors, and the structures are clearly and carefully drawn. Literature references are given, appearing at the end of each chapter. The references cover up until late 1982, material from one 1983 reference appearing in an Addenda in Chapter 7. The index (14 pages) appears to be quite adequate. It is a book well worth having for anyone interested in allene chemistry or synthesis.

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Logical and Combinatorial Algorithms for Drug Design. V. E. Golender and A. B. Rozenblit. Research Studies Press, Letchworth, England (distributed by Wiley). 1984. xiii + 289 pp. 15.5 × 23.5 cm. ISBN 0471-90266-7. $63.95.

This book provides detailed descriptions of the authors' methods of computer-assisted design of biologically active molecules. Logical analysis of structure–activity data reveals substructural features associated with a particular biological property. Combinatorial methods permit similarity and dissimilarity analysis of graph (connections between atoms) and matrix (distances between atoms) descriptions of structure. Since all but two of the citations to their own work are to works written in Russian, much of the discussion will be new to English-speaking readers.

The first chapter is an excellent literature review of available methodologies for computer-assisted molecular design. It plus the excellent bibliography alone might justify the book's inclusion in the libraries of institutions that employ or train medicinal chemists. The subsequent three chapters discuss in turn (1) computer languages for structure description oriented to selection of biologically important features, (2) principles of selection of features important to biological activity, and (3) algorithms for the manipulation of computer-coded chemical structures. The final three chapters discuss the author's implementation of these principles: (1) the STRAC software for QSAR or other analysis of user-input data; (2) the ORACLE system that inspects a data base to find molecular fragments predictive of membership in an activity class; (3) the TOPOLOG system for the prediction of biological activity by analysis of either topological (connections of atoms) or topographic (distance between atoms) matrices.

The book is aimed at users and designers of computer-aided drug design methods and specialists in related areas of structure information handling or design of synthetic pathways. Because much of the discussion relies on symbolic logic, matrix manipulation, and graph theory, most American medicinal chemists will find this book very difficult. However, the rest of the target audience may discover some fresh insights from this book.

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Reductions in Organic Chemistry. By Milos Hudlicky. Ellis Horwood Ltd., New York. 1984. xvi + 309 pp. 16 × 23.5 cm. ISBN 0-470-20018-9. $45.00

Surveyed and analyzed in numerous articles and monographs, the topic of reductions in organic chemistry might at first seem too overdone to merit further discussion. However, most of the literature on the subject considers particular techniques such as catalytic hydrogenation or deals with specialized reagents. In contrast to such tightly focused discussion, this book addresses all types of reductions in the context of a wide assortment of organic compounds. A product of the authors lengthy familiarity with the area, the book critically reviews the reduction of organic functional groups, employing the literature up to 1982, and recommends those methods noted for consistently high yields. Special emphasis too is placed on chemo- and regioselective reductions. Representative of this concern is the discussion of the selective reduction of polynitro aromatics on page 74 and cyclic anhydrides on page 147. Practicing organic chemists will undoubtedly find this perspective the book's most valuable feature.

Containing over 300 pages, the arrangement of this volume was well thought out. It begins with a historical yet practical coverage of the several reduction categories including catalytic hydrogenation, hydride reduction, electroreduction, and reductions with metals and non-metals. The greater part of the book next highlights the methods of choice to accomplish the high-yield specific reduction of functional group families. The order of functional class review is reminiscent of the Beilstein arrangement. Correlation tables follow and afford a rapid summary of reduction technique options for various functionalities and are conveniently cross-referenced with the preceding text. Following these tables, 50 detailed experimental procedures, including yields, illustrate specific reduction examples. The volume concludes with over 1000 original literature references and a useful author and subject index.

Technically, the book is well assembled. I noticed only one typographical error; namely, the correct year for ref 1 on page 219 is 1874 not 1974. Timely and authoritative, this book should well serve the varied needs of synthetic organic chemists in both the chemical industry and academia.

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Drug Dynamics for Analytical, Clinical, and Biological Chemists. By B. J. Gudzinowicz, B. T. Younkin, Jr., and M. J. Gudzinowicz. Marcel Dekker, New York. 1984. vii + 176 pp. 16 × 23.5 cm. $39.75.

Numerous technicians and analysts working in analytical chemistry, biochemistry, clinical chemistry, and toxicology laboratories in industry, academic settings, and hospitals contribute to drug investigations through analyses of drugs and metabolites in biological fluids. Yet, many of the same personnel may have little understanding of the disposition and actions of drugs in man and other mammals. Gudzinowicz, Younkin, Jr., and Gudzinowicz have addressed this concern through the preparation of a brief volume that is proposed as a "basic primer" on drug dynamics. The authors also suggest that their work may be useful to laymen.

The book is composed of five major sections: 1, "Drug Administration: Routes of Entry"; 2, "Principles Governing Drug Absorption and Distribution"; 3, "Major Pathways of and Factors Influencing Biotransformation of Drugs"; 4, "Elimination or Excretion of Drugs"; 5, "Mechanisms of Drug Action". These sections are composed of elements of biopharmaceutics, pharmacokinetics, biochemical pharmacology, drug metabolism, and medicinal chemistry. In general, the topics and coverage are right for baccalaureate-level chemists and biologists. The treatment of the material, however, is often confusing or unclear.

Beside errors in terminology (e.g., the use of "parenteral" to describe percutaneous and intravaginal administration of drugs [page 3]) and confusing discussions (e.g., description of the disintegration rate of a solid drug instead of disintegration and dissolution of dosage forms [page 6] and inadequate distinction between enantiomers and diastereomers [page 113]), the book contains several diagrams and figures (e.g., pages 33, 34, 42, and 52) that are unclear or in error. For example, the structures in Figure 9 seem to depict the oxidation of 2-methyldecalin to a rearranged and ionized primary alcohol that is subsequently converted to a decalin with a "CH_2O^{2-} Glucuronide" moiety! It is difficult to understand how such errors survived a peer review process. Unfortunately, the types of errors described can be the source of much confusion for the novice, thereby making it difficult

to recommend the book for its stated purposes.

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Essentials of Pharmacology. Third Edition. Edited by J. A. Bevan and J. H. Thompson. J. B. Lippincott Co., Philadelphia. 1984. xxiii + 916 pp. 19 × 26 cm. ISBN 0-06-140462-4. $35.00.

This, the third edition of an enjoyable, intermediate textbook in pharmacology, has been enlarged and improved over the previous edition published in 1976. Nine new chapters have been added to this edition, including often overlooked, but necessary, chapters in "Principles of Drug-Receptor Interactions and Pharmacokinetics". The book includes 83 diverse chapters, organized into three sections: "General Pharmacology and Pharmacologic Principles", "Systemic Pharmacology" (i.e., the primary section found in most pharmacology texts), and "Special Topics".

A particular strength of the book is its diversity. It devotes over 100 pages to the consideration of general principles, which are esential in the proper understanding of the basis of pharmacology, particularly for pharmacy and nursing students, but which is given scant attention in most texts intended for undergraduates. It also includes unusual information such as chapters on "Information Sources", "Parenteral Nutrition", and "Therapeutic Agents Available in Europe" and is also scattered with historical vignettes. The preface to the first edition states that the text is intended for medical and dental students who have completed their preclinical courses and reflected the almost "outline" approach of the earlier editions. The present edition is much more detailed, and most chapters follow a general pattern of mechanism of drug action, effects, therapeutic uses, and tables of comparative information among different agents. The chapters also include representative exam questions. This edition, therefore, is probably better suited to a preclinical course, particularly one where there is no need for a ponderous "reference" text.

As is the case with most multiauthored texts, there is some lack of uniformity among the different chapters, some of which contain extensive comparative information, while others do not. There is little structure–activity information that would appeal to a medicinal chemist, but this is, arguably, not the function of a pharmacology text. It would, however, be quite appropriate for those medicinal chemists who want to acquire a good, rapid familiarization with general pharmacology. In summary, this is an informative, reasonably easy to read, but not overwhelming, textbook of pharmacology.

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Novel Approaches to Cancer Chemotherapy. Edited by Prasad S. Sunkara. Academic Press, New York. 1984. xiv + 388 pp. 16 × 23.5 cm. ISBN 0-12-676980-x. $65.00.

The focus of this book is new and emerging theories in tumor biology and approaches to cancer therapy based on these theories. This work, which is the latest in the distinguished *Cell Biology* series, consists of 11 chapters, each of which describes a difference between cancer and normal cells and presents an approach to cancer treatment that is based upon each difference. Chapters one, two, six, and seven focus on the manipulation of the host's immune system as an approach to cancer treatment. In particular, interferons as potential anticancer agents and adjuncts for use with traditional therapies, monoclonal antibodies in diagnosis and treatment of cancer, lymphokines as activators of macrophages, and the natural tetrapeptide tuftsin as an immunomodulator are presented and evaluated. Chapter three includes a review of the biochemistry of polyamines and their role in growth and development. The medicinal chemist will especially appreciate the inclusion in this chapter of a table of inhibitors of polyamine biosynthesis and the discussion of (difluoromethyl)ornithine, a mechanism-based inhibitor of ornithine decarboxylase and polyamine biosynthesis. Chapter four connects the arachidonic acid cascade to cancer and emphasizes the role of prostacyclin in tumor cell metastasis. Chapter five is a critical survey of the current status of liposomes as vehicles for delivering drugs to cancer cells. Included here are preparative methods and properties of liposomes. Chapters eight and nine describe the physiologic role of steroid 5α-reductase in prostate cancer and of aromatase in breast cancer and the therapeutic potential of mechanism-based irreversible inhibitors of these enzymes. Chapter ten is a provocative discussion of the cancer cell membrane as a target for selective drug therapy. Here, the biochemistry of 2-deoxy-2-aminoglucose is reviewed, and the selective cytotoxicity of this reagent is described. Chapter eleven explores the basis for cancer therapies directed toward disruption of ion flux in tumor cells.

Each chapter is interestingly presented and extensively outlined for easy readability. Many useful tables are included, and most chapters have a summary. This work is well referenced and contains some 1984 references. An eight and one-half page index is included.

Novel Approaches to Cancer Chemotherapy provides a refreshing vista of the area of cancer treatment and should prove a valuable source of ideas and information for established investigators and for those contemplating entering the field of cancer research.

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Highlights in Receptor Chemistry. 2nd Camerino Symposium on Recent Advances in Receptor Chemistry, Camerino, Italy, 1983. Edited by C. Melchiorre and M. Gionella. Elsevier Science Publishers, Amsterdam and New York. 1984. viii + 305 pp. ISBN 0-444-80569-9. $65.00.

This volume is a collection of manuscripts contributed by the participants of the 2nd Camerino Symposium on Recent Advances in Receptor Chemistry held in Camerino, Italy, Sept 5–8, 1983.

Receptor research today constitutes a wide area, with exponentially growing interest from a variety of different disciplines, including chemistry, biochemistry, pharmacology, biophysics, and physiology. The multidisciplinary approach is certainly contributing to a better understanding of receptor structure and function. This symposium was designed to provide a favorable forum for the meeting of chemists and biologists working in the receptor field by emphasizing both the chemical and pharmacological aspects of receptor research. This volume includes the plenary lectures of a distinguished group of scientists working in the most promising areas in the field such as receptor theory, acetylcholine, dopamine, histamine, amino acid, α- and β-adrenergic, and opiate receptors. Also discussed are the coupling of receptors to adenylcyclase, biochemical aspects of ion channels, quantitative structure–activity relationships, and computational procedures for rationalizing drug–receptor interactions. An author and subject index is also provided. This book will be of particular interest to pharmacologists, biochemists, molecular biologists, and medicinal chemists wishing to bring themselves up to date in the rapidly expanding field of receptor chemistry.

Staff

Books of Interest

Annual Drug Data Report. Volume VI–1984. Edited by J. R. Prous et al. J. R. Prous, Barcelona, Spain. 1984. x + 485 pp. 18 × 24.5 cm. ISBN 0-379-412-1. $200.00.