Book Reviews

Taxane Anticancer Agents: Basic Science and Current Status. Edited by Gunda I. Georg, Thomas T. Chen, Iwao Ojima, and Dolatrai M. Vyas. ACS Symposium Series 583. American Chemical Society, Washington, D.C. 1995. xiii + 353 pp. 15.5 × 23.5 cm. ISBN 0-8412-3073-0. $99.95.

Although taxanes were discovered in the early 1960s, it took 20 years for the scientific community to appreciate the enormous potential of these compounds as cancer chemotherapeutic agents. There has been a virtual explosion of interdisciplinary activity in this area over the last decade, encompassing chemistry, biology, pharmacology, and medicine. This excellent compilation of past and present efforts in taxane research by Georg, Chen, Ojima, and Vyas, all pioneers in taxane research in their respective fields, is therefore very timely. Analysis of the diverse frontiers of research in the chemistry and biology of taxol makes this book, which is based on three symposia held by the Chemical Health and Safety, Medicinal, and Organic Divisions of the American Chemical Society, respectively, a useful tool for taxane researchers in all fields.

Commencing with a summary of the different frontiers of taxane research and a sketch of possible future work by M. Suffness, a personal account on the isolation of taxol by Wall, results of clinical trials, environmental issues, biosynthetic work, and the search for taxol-producing microorganisms follow. Metabolism, formulations and problems thereof, prodrugs, and photoaffinity studies form the major part of the rest of the book, which encompasses the structure−activity relationship (SAR) studies undertaken by various groups. The final section is comprised of the total syntheses of taxol by Holton and Nicolaou together with accounts by Paquette and Wender on their synthetic approaches.

While the biology and pharmacology of taxane research have adequate treatment, the emphasis on SAR studies probably reflects a bias of the editors, a majority of which are involved in this area. Holton's and Nicolaou's accounts reiterate their seminal papers on the first total syntheses of taxol. The Paquette and Wender accounts offer more detailed and subjective analyses.

Much of what is said in the introduction to each of the chapters is repetitive. Perhaps the editors felt this approach would be useful for readers who would restrict themselves to individual chapters. Nonetheless, the book is timely and recommended for both taxane and non-taxane researchers.

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An Introduction to Medicinal Chemistry. By Graham L. Patrick. Oxford University Press, New York. 1995. xiv + 336 pp. 19.5 × 25 cm. ISBN 0-19-855872-4. $59.00.

The author's preface states that this book was written for undergraduates who have a basic grounding in chemistry, but no previous knowledge of biology, and who are contemplating a career in the pharmaceutical industry. The first chapter addresses the role of the medicinal chemist in drug discovery, and the next several chapters present introductory level discussions of protein structure, enzyme chemistry, receptor site theory and drug−receptor interactions, nucleic acids, drug development, pharmacodynamics, and quantitative structure−activity relationships (QSAR). Each of the next three chapters is devoted to a single pharmacologic category (*e.g.*, antibacterial agents, the peripheral cholinergic nervous system, and opium analgesics), illustrating the application of the fundamental chemical and biological concepts presented in the first portion of the book to the understanding of drug design and of drug actions and effects.

Creation of an introductory medicinal chemistry textbook for undergraduate chemistry students is a laudable endeavor, and the author has presented the subject material in a readable style at an appropriate level of chemical and biological sophistication. He has largely succeeded in demonstrating that medicinal chemistry is (and must be) an amalgamation of organic, physical, and biochemistry with biology. He has not attempted to cover all categories of therapeutic agents, but he wisely elected to demonstrate the application of chemical and biological principles to three widely different therapeutic categories of drugs. The book reaches a crescendo in its final chapter which recounts the still fascinating saga of the discovery of cimetidine.

Chemical structures are well and carefully reproduced, and there are many well-drawn diagrams and drawings which elucidate and complement the chemical and biological concepts discussed in the narrative.

However, there are aspects of the book which this reviewer found less appealing. Some material presented as factual is not correct; some explanations or discussions are incomplete, vague, and/or subject to misinterpretation. Typical examples include the following: (p 12) "Anesthetics work by interacting with the lipids of cell membranes..."; (p 49) definition of the term *receptor* mentions only protein molecule components of cell membranes and leaves the reader to infer that this is the only location and chemical type of receptors; (p 122) aspirin is described as a prodrug to salicylic acid, and no reference is made to aspirin's direct effect on the arachidonic acid cascade; (p 123) the description of pargyline (consistently misspelled in the narrative) as a prodrug for propiolaldehyde represents at best an obscure property of the drug. The prodrug discussion ignores perhaps the most frequent application of the strategy: alteration of solubility/partitioning characteristics for enhanced absorption or transport.

The statement (p 123) that "a bioisostere is a chemical group which can replace another chemical group without affecting biological activity" is inadequate and misleading. The cryptic comment (p 224) that hyoscine "has been used as a truth drug" may titilate the reader, but it seems inappropriate to the discussion of which it is a part. The contention (p 244) that there are no metabolic pathways in mammals which can convert a phosphorus−sulfur double bond to a phosphorus−oxygen double bond is incorrect, and the ensuing rationalization of species differential toxicity of the insecticide *parathion* is thereby compromised.

The book ends with a compilation of 12 references for "further reading". Some of these date from the late 1970s and early 1980s, and some of these and others are not what this reviewer would have recommended for expansion of an undergraduate student's general knowledge of medicinal chemistry. It is disappointing that the author did not list specific supplemental readings at the end of each chapter. It would have been helpful to this reviewer had he documented some of the controversial/questionable statements in the book.

The first chapter of the volume contains a series of large and largely pointless cartoon drawings; p 85 consists of a full-page cartoon drawing. This excessively cute material seems, to this reviewer, completely out of place for a text intended for university-level science students.

The book is bound in what appears to be an insubstantial paper binding, which is not likely to withstand the frequent openings and closings to which undergraduate textbooks are subjected.

This book did not attain the putative admirable goals of the author; it was a disappointment, and it cannot be highly recommended.

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Fluorine-containing Amino Acids. Synthesis and Properties. Edited by V. P. Kukhar' and V. A. Soloshonok. John Wiley & Sons, Inc., New York. 1995. x + 411 pp. 15.5 × 23.5 cm. ISBN 0-471-95203-6. $140.00.

This volume is a complete and thorough treatment of the chemical aspects of fluorinated amino acids. Reference is made to biological studies, but this is not the overall emphasis. Six chapters out of 11 are concerned with synthetic methods and the remainder with purification and biology. There is not much overlap among the chapters, and the diverse chemical approaches, i.e., homogeneous catalysis, enzymatic methods, etc., are clearly delineated. There are two chapters on chromatography and resolution of chiral amino acids. A comprehensive table in the chapter by V. Tolman, which lists all of the classically synthesized fluorinated amino acid analogues as well as yields and number of steps required, should be especially helpful in designing new synthetic routes and target compounds.

Three chapters (those by J. T. Welch et al., H. L. Sham, and K. L. Kirk) provide much detail on biological applications of fluorinated amino acids, such as renin inhibition. Undoubtedly this field is expanding and will require periodical updating. There are many examples of the magic of substitution of hydrogen with fluorine, e.g., completely changing the receptor selectivity of a biologically active ligand or transforming an agonist into an antagonist. Also the use of fluorine in protease inhibition is featured. This is an approach that may find yet great application in research on HIV-related enzymes and other enzymes. There is no separate chapter on use of ^{18}F in PET scanning, although references to imaging are scattered throughout the book. Thus, this volume will be a very valuable reference for medicinal chemists, fluorine chemists, and also pharmacologists desiring up-to-date reviews.

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The Biology of Nitric Oxide. Part 5. Edited by S. Moncada, J. Stamler, S. Gross, and E. A. Higgs. Portland Press Ltd., London. 1996. xxx + 353 pp. 21 × 29 cm. ISBN 1-85578-102-6. $160.00.

This is the sixth book relating to the biology of nitric oxide that has been published by Portland Press since 1992. This, along with the approximately 60 oral communications and 400 posters presented at the Fourth International Meeting on the Biology of Nitric Oxide that was held at Amelia Island, FL, in September 1995, proceedings of which are contained in the present volume, attests to the intense current research and interest in this subject. *Part 5* provides a timely update on nitric oxide biology research as it presents communications and abstracts from over 1350 specialists on a variety of areas, ranging from the role played by nitric oxide in cancer and tissue rejection to methods for detecting and measuring it in biological systems. The 335 1-page papers included in this volume are subdivided into those from oral and poster communications and according to subject, i.e., biochemistry, molecular biology, immunology, chemistry, pharmacology, physiology, therapy, and "hot topics". Comprehensive author and subject indexes facilitate information retrieval. As a result of the direct reproduction used in assembling the reports, there is a lack of uniformity; however, the overall print quality is remarkably good.

As with any proceedings report containing such a large number of varied topics, this book will likely be of most value as a retrieval source of information. Its timeliness, excellent indexing, and overall quality enhance its value for this purpose.

Staff

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Chemometric Methods in Molecular Design. Edited by Han van de Waterbeemd. VCH, Weinheim. 1995. xix + 359 pp. 17.5 × 24.5 cm. ISBN 3-527-30044-9. DM 188.00.

This book is volume 2 in the new series *Methods and Principles in Medicinal Chemistry*, edited by R. Mannhold, P. Krogsgaard-Larsen, and H. Timmerman. In covering a wide variety of chemometric methods in molecular design, it represents an excellent companion to Hugo Kubinyi's fine volume on Hansch analysis, and related approaches, which opened the series.

The brief introduction by the editor introduces the concept of chemometrics as applied to the design of new molecules and divides the large variety of methods into convenient categories. The chapter includes two useful tables filled with general and specialized software packages for carrying out statistical analysis.

The remainder of the book is divided into four sections dealing with Molecular Concepts, Experimental Design, Multivariate Data Analysis (by far the largest portion of the book), and Statistical Validation. The section on Molecular Concepts contains two chapters reviewing molecular and atomic descriptors. The next section begins with a chapter reviewing Experimental Design followed by three chapters entitled (1) Applications of Statistical Experimental Design and PLS Modeling in QSAR, (2) Total Response Surface Optimization, and (3) Disjoint Principle Properties of Organic Substituents. The emphasis of the book is methods of Multivariate Data Analysis of Chemical and Biological Data, which includes chapters on (1) Principal Component and Factor Analysis, (2) Graphical Analysis an Aid in Medicinal Chemistry, (3) SIMCA Pattern Recognition and Classification, (4) PLS for Multivariate Linear Modeling, (5) Spectral Mapping of Drug Test Specificities, (6) Display of Multivariate Data using Non-linear Mapping, (7) The Use of Cononical Correlation Analysis, (8) Discriminant Analysis for Activity Prediction, and (9) Cluster Significance Analysis. The book ends with a very important section on Statistical Validation which includes a chapter on Validation tools and a chapter on Choosing the Proper Statistical Method.

Most of the chapters begin with a discussion of the statistical model which can get unavoidably dry but provides the theoretical background necessary to appreciate the methods applicability. It is the wealth of applications provided which makes this volume particularly valuable for the medicinal chemist as well as the modeler. The book is well written and includes many up-to-date references. The figures and tables are well chosen to help the reader follow the discussion, and the index is well organized. I recommend this volume as an excellent one-stop practical reference to medicinal chemists who want to understand and/or apply the latest statistical methods to their project.

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