Book Reviews

5-Hydroxytryptamine-3 Receptor Antagonists. Edited by F. D. King, B. J. Jones, and G. J. Sanger. CRC Press, Boca Raton, FL. 1994. 363 pp. 16 × 24 cm. ISBN 0-8493-5463-3. $169.95.

The first sentence of the Introduction aptly presents the book's contents: "This book describes a fascinating episode in the history of drug discovery in which academic research led ultimately to the development of selective 5-HT3 receptor antagonists, a class of drugs initially of uncertain therapeutic value." Serotonin (5-HT) is one of the neurotransmitters that dominated research during the 1980s. One particular population of 5-HT receptors, namely 5-HT3 receptors, has received considerable attention both in academia and the pharmaceutical industry and has led to the identification of several novel therapeutically useful agents. This book focuses on the discovery, medicinal chemistry, and pharmacology of 5-HT3 antagonists.

The book gets off to a rough beginning. The Introduction contains numerous errors including spelling errors, reference to literature citations that do not appear in the list of references, and incorrect literature citations. However, once beyond the Introduction, one encounters smoother sailing. The book consists of 13 chapters. The first chapter is an excellent and comprehensive presentation of the current state of knowledge regarding the structure–activity relationships of 5-HT3 antagonists. The second chapter is a review and critique of various molecular modeling studies conducted with 5-HT3 antagonists. Chapters 3–6 deal with the basic pharmacology of 5-HT3 receptors (e.g., molecular characterization, receptor localization, electrophysiology, assay techniques for evaluating 5-HT3 antagonists), and the remaining seven chapters individually describe the role(s) or potential role(s) of 5-HT3 receptors/ligands in anxiety, schizophrenia, cognitive disorders, drug abuse, nociception, emesis, and gastrointestinal function.

The book must have long been in the making because encounters with references more recent than 1991 are few and far between. The authors of one chapter note that their literature survey was completed in 1991. Authors of two other chapters thoughtfully included Addenda to some 1992 and 1993 literature. Nevertheless, as a whole, the book is not as up to date as possible, considering that it bears a 1994 publication date. And, although true to its title (and, therefore, beyond fault), the book might have contained at least one chapter on 5-HT3 agonists. Various 5-HT3 agonists are mentioned throughout the book, and a brief discussion of these (albeit few) agents would have been helpful. In toto, however, this book is excellent; it will certainly make for interesting reading for those in the neurosciences, and is a "must" for those working in the 5-HT area or in one of the therapeutic areas in which 5-HT3 receptors may be involved. Medicinal chemists should particularly enjoy the first two chapters.

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Nucleosides and Nucleotides as Antitumor and Antiviral Agents. Edited by Chung K. Chu and David C. Baker. Plenum Press, New York. 1993. X + 336 pp. 17 × 25 cm. ISBN 0-306-44520-4. $85.00.

This book is dedicated to the memory of Professor Tohru Ueda, and most of the 17 chapters represent contributed papers given at a Memorial Symposium held in San Francisco, CA, on April 7, 1991. The subject matter covers a wide range of topics which should be of interest to all in the nucleoside/nucleotide field. Chapter 1 by A. Matsuda and co-workers concentrates on *ara*-C derivatives: derivatives which are resistant to cytidine deaminase, are potential substrates for 5′-kinases, and have a reactive chemical functionality at C2′ designed to be activated *in vivo*. Their synthesis and possible mechanisms of action as antitumor agents are discussed. Chapter 2 by H. Tanaka *et al.* provides a concise review on the regioselective lithiation of uracil-type acyclo- and ribonucleosides to provide either C5 or C6 substituted pyrimidine derivatives, analogues which are not easily obtained by conventional chemical methods. A portion of this chapter is devoted to the design, synthesis, and biological properties of HEPT and its derivatives. Chapter 3 by K. W. Pankiewicz and K. A. Watanabe focuses on past and present problems encountered in preparing fluorosugar nucleosides. A variety of improved direct methods of fluorination are discussed. Conformational factors of the sugar moiety are also examined and their effect on product formation is considered. In the next chapter, J. Zemlicka deals with the synthesis and antiretroviral activity of certain *N*-allenol derivatives of nucleic acid components. The challenging synthetic strategies developed in his laboratory and in those of others are reviewed. The mechanism of antiretroviral action of selected analogues is also a topic of discussion.

Chapter 5 by E. J. Prisbe *et al.* examines the synthesis and structure–activity-relationships (SARs) of certain 4′-substituted-3′-functionalized-2′-deoxy-β-*D*-*erythro*-nucleosides (mostly pyrimidines) and discusses their HIV-1 inhibition. The chapter that follows by M. J. Robins and co-workers considers 5′-α-halo thioethers, sulfoxides, and sulfones of adenosine (and several of uridine) as potential inhibitors of *S*-adenosyl-L-homocysteine hydrolase

(AdoHcy hydrolase). A detailed discussion on the synthetic methodology leading to these nucleosides and the pitfalls encountered along the way is followed by a short section on their activity and possible mode of inhibiting AdoHcy hydrolase. Chapter 7 by V. Nair concentrates on a series of novel, regioisomeric pyrimidine and purine dideoxynucleosides, nucleosides in which the heterocyclic aglycon resides on C2′ of the dideoxy sugar moiety rather than C1′. Synthetic strategies leading to the preparation of key, isodideoxynucleosides possessing the *S,S*-chirality are discussed in depth. The next chapter by S. W. Schneller *et al.* dovetails into Nair's chapter in that it begins with the synthesis of isodideoxy-7-deazapurine nucleosides having the *R,R*-configuration. Schneller then focuses on the synthesis of carbocyclic 7-deazaoxetancin G followed by approaches to cyclopentyl derivatives of 7-deaza-G. Chapter 9 by E. Abushanab highlights the use of D-isoascorbic and L-ascorbic acid to provide chirons for a host of biological molecules. Their application in the preparation of a variety of 1′,2′-*seco*-nucleosides/tides, and their respective phosphonates is provided. Abushanab also demonstrates how molecules like (+)-EHNA and certain suitably protected 2′-deoxypentofuranosides can be conveniently prepared from these chirons and how the latter 2′-deoxy sugars can be used in a stereospecific synthesis of β-D-2′-deoxynucleosides.

Chapter 10 by T.-S. Lin and M.-C. Liu examines, in detail, the SARs of 3′-azido, 3′-amino, and certain 2′,3′-unsaturated and dideoxypyrimidine and pyrimidine-type nucleosides with several retroviral cell lines. Another part of this chapter is devoted to the preparation of nitrosourea and phosphamide-type nucleosides and their potential role in cancer treatment. The next chapter by M. Nasr and S. R. Turk provides a detailed review of 2′,3′-dideoxy and 2′,3′-didehydro-2′,3′-dideoxypyrimidine (U, C, and T) nucleoside SARs which are compiled from an extensive computerized database. This analysis aims at the future design of new nucleoside entities for HIV treatment. Tables 1–4 allow the reader to have a quick, overall view on how structural changes, whether large or small, affect activity in various *in vitro* cell lines. Chapter 12 by J. W. Beach and co-workers is split into two parts. The first part examines a very timely issue: that of stereochemical control in the preparation of deoxynucleosides. They cover the influence of solvent, catalyst, and bulky groups on the α/β ratio of nucleoside formation. The second part is centered on the chemical preparation of heteronucleosides: a new class of nucleoside analogues having either a dioxolane or oxathiolane ring for the sugar component. The following chapter by H. Machida and S. Sakata focuses on the synthetic and antiherpetic aspects of 5-substituted arabinofuranosyluracil nucleosides and compliments the earlier chapters by Matsuda, Tanaka, and Lin. Throughout the chapter the authors point out how changes in the sugar moiety, from a 2′-deoxy to an arabinosyl, affect antiviral activity and metabolism of these nucleosides. The next two chapters by V. E. Marquez and co-workers and P. Van Roey and C. K. Chu examine the solution and solid-state conformations of dideoxynucleosides and how these physical parameters relate to activity. Both chapters compliment each other, are well-written, and are worth a careful reading. Marquez *et al.* show how solution conformational changes on the dideoxysugar moiety caused by fluorine-induced rigidity (*gauche* interactions) affect their nucleotide anabolism and thus their biological profile. The chapter which follows by Van Roey and Chu centers on selected X-ray crystallographic data of four classes of dideoxynucleosides. Again, their detailed analysis of these crystal structures is aimed at how they influence substrate specificity for kinases and thus why or why not they possess HIV activity. The last two chapters by J.-L. Imbach and co-workers and Y. S. Sanghvi and P. D. Cook cover modified oligoribonucleotides (ONs) as potential chemotherapeutic agents. Imbach *et al.* focus on synthesis, stability, and HIV activity of certain α-ONs prepared in their laboratory whereas Sanghvi and Cook discuss the very interesting aspect of synthetic backbone modifications of ONs. Their synthetic approach to these modified ONs is discussed in a concise, straightforward manner. They point out how chirality, solubility, and availability will determine the future role of ONs in drug therapy.

In conclusion, this book is well worth its price and not too expensive for inclusion in personal collections. The information presented is up to date and well-referenced. This reviewer gives it a "thumbs up". This text along with the three recent L. B. Townsend volumes (Plenum Press) are valuable resources for those academicians and industrial chemists involved in all aspects of nucleic acid chemistry.

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Chemistry and Biology of Pteridines and Folates. Edited by June E. Ayling, M. Gopal Nair, and Charles M. Baugh. Plenum Press, New York. 1993. xxiv + 825 pp. 17 × 25.5 cm. ISBN 0-306-44581-6. $159.50.

This book contains over 160 short papers covering presentations made at the 10th International Symposium on the Chemistry and Biology of Pteridines and Folates held in March 1993. It also includes full papers presented as plenary lectures by E. C. Taylor and W. Pfleiderer, the former describing his elegant work on the design and synthesis of inhibitors of folate-dependent enzymes. The book summarizes the current state of the art of this most important class of biologically significant compounds. This symposium, like its predecessors, brought together leading members of the international community engaged in all facets of pteridine research. Thus the topics covered included pteridine synthesis, physical and analytical chemistry, biosynthesis, molecular biology, medicinal chemistry, enzymology, pharmacology, and clinical medicine. Some of the major areas covered include tetrahydrobiopterin, the urothione family of molybdopterin cofactors, and the folates. The folates play a key role in one-carbon metabolism and cancer, the biopterins are involved in hydroxylations and nitric oxide biosynthesis, while the urothiones are molybdenum cofactors for sulfite oxidase, xanthine dehydrogenase, and aldehyde oxidase which are required for normal human development.

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This book is essential reading for all those interested in any of the facets of pteridine research. It is detailed enough to bring those not fortunate enough to have attended the symposium a good sense of the current status of the field and to act as a source of inspiration for future research directions. Regretfully, the high cost of this book, which is justified by its size and quality, will discourage individual purchasers, but it should find a place in biochemical and pharmaceutical research libraries.

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Books of Interest

Neural Networks for Chemists. An Introduction. By Jure Zupan and Johann Gasteiger. VCH Publishers. Weinheim, Federal Republic of Germany. 1993. xix + 305 pp. 19.5 × 26 cm. ISBN 3-527-28603-9. DM 68.00.

Tietz Textbook of Clinical Chemistry. Second Edition. By Carl A. Burtis and Edward R. Ashwood. W. B. Saunders, Philadelphia, PA. 1994. 2368 pp. ISBN 0-7216-4472-4. $125.00.

ACE Inhibitors: Central Actions. By John M. Starr and Lawrence J. Whalley. Raven Press, New York. 1993. xii + 254 pp. 15.5 × 23.5 cm. ISBN 0-7817-0072-8. $75.00.

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