# Book Reviews

**Studies in Natural Products Chemistry, Vol. 11, Stereoselective Synthesis (Part G).** Edited by Atta-ur-Rahman. Elsevier, Amsterdam. 1992. xiv + 502 pp. 17 × 24 cm. ISBN 0-444-89744-5. $250.00.

It has now reached the stage where to keep up with recent developments in synthetic organic chemistry it is almost a requirement to consult the series of books entitled *Studies in Natural Products Chemistry*, edited by Atta-ur-Rahman. The latest addition to this collection is Volume 11 which consists of 11 chapters written by synthetic chemists from Japan, the U.S.A., Canada, and Italy.

The first chapter, by L. A. Paquette, is a lucid, thorough, and exciting presentation of contemporary efforts at the construction of the pharmacologically very important taxanes. This is followed by other excellent discussions on synthetic approaches to the quassinoids (T. Murae and M. Sasaki), biomimetic syntheses of aromatics via polyketides (M. Yamaguchi), conformational control in macrolide synthesis (N. Nakajima and O. Yonemitsu), stereochemistry of natural products biosynthesis (K. A. Reynolds and H. G. Floss), chiral approaches to the indolizidines (C. Kibayashi), synthesis of Aristotelia alkaloids (H.-J. Borschberg), synthesis of mevinolin and compactin (D. L. J. Clive, K. S. K. Murthy, A. G. H. Wee, P. S. Prasad, G. V. J. da Silva, M. Majewsi, and P. C. Anderson), synthesis of vitamin D (Y. Tachibana and M. Tsuji), the use of $\alpha$-halo boronic esters in synthesis (D. S. Matteson), and finally higher carbon sugar synthesis (G. Casiraghi and G. Rassu).

This book is recommended to the devotees of synthetic natural products chemistry trying to keep up with some of the latest advances in the field.

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**The Design of Drugs to Macromolecular Targets.** Edited by C. R. Beddell. John Wiley and Sons, Chichester, U.K. 1992. xiv + 287 pp. 15 × 23 cm. ISBN 0-471-92080-0. $145.00.

The Burroughs Wellcome UK researchers, many of whom are authors in this book, including the editor, were among the first to design, synthesize, and test drugs using macromolecular targets. Therefore, it was not surprising that many of their chapters were written with a historical perspective. Surprisingly and disappointedly, Peter Goodford, who directed and championed this novel effort, did not contribute a chapter or write the **Introduction** which contained general and philosophical statements about each topic without revealing content. The material in the book is not rigorous concerning quantitative approaches to understanding molecular interactions, molecular mechanics, or crystallography; but, is more pictorially and concept oriented, making many of the chapters easy to read. This approach may be due to the fact that many of the authors chosen are not developing specific molecular tailoring technology but scientists that have worked at the interface between medicinal chemistry, crystallography, and computational chemistry-molecular modeling.

The first chapter by Garland Marshall on **"The Role of Macromolecules in Drug Action"** is an excellent and up to date review. The chapter begins with small molecules as receptors and then proceeds to discuss nucleic acids and enzymes as drug receptors. Finally, membrane, membrane proteins, and viral receptors are covered. Another small section on transport and metabolism is included. I found this chapter to be very useful for learning, teaching, and research purposes. Marshall gives good advice as well in recommending that the paper by Marmorstein and Sigler on the structure–activity relationships of tryptophan analogs be required reading for all medicinal chemists (from their work on the crystal study of a DNA–repressor complex). By its comprehensive nature, this chapter touches upon a number of subjects treated more in depth by other authors (hemoglobin, DNA, etc.).

The **"Ligand Fitting Methodology"** chapter by Alwyn S. Gilbert and John N. Champness contains a discussion of molecular interactions, molecular mechanics and dynamics, visualization methods, and four protein examples (ACE-Renin, hemoglobin, dihydrofolate reductase, and hemagglutinin). Much of the work presented is from the Wellcome UK group efforts, and information provided on the treatment of the molecular interactions, molecular mechanics, and molecular dynamics is not detailed but qualitative in nature.

The third chapter, **"Compounds Designed to Bind to Haemoglobin"** by Ray Wootton, is an extensive treatment of molecules that bind to hemoglobin. The highlight of the chapter is the design, testing, and binding site determination of the antisickling agent BW12C. BW12C is generally regarded as the first molecule to be designed **de novo** from the three-dimensional structure of the protein that has reached clinical trials.

Unfortunately, there are a number of errors or misstatements in the chapter: for example, on p 66, BZF analogs were not diluted as suggested and are active in whole blood; suggested reasons for the increased activity of the urea and carboxyamido BZF analogs from the crystal structures *is* quoted in the referenced paper on p 66, but was ignored for some reason on p 65, where the statement is made that increased potency was not apparent from crystal structures; on p 67, the negative suggestions on the use of dithionite in binding assays for deoxy Hb is not correct (the binding of dithionite in high salt crystals of Hb has been reported); comments on the same page concerning the Scatchard plots of hemoglobin ligands are not appropriate since the assays were run at very high hemoglobin concentrations and analyzed with Klotz's concerns considered; and no reference given on p 75 to show that ethacrynic acid analogs increase red cell rigidity.

Overall, the chapter is a Wellcome history and view of hemoglobin–ligand research detailing their pioneering work.

**"Drug Interactions with Target Enzymes of Known**

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**Structure"** by Barbara Roth and David K. Stammers reviews the literature on three enzymes that represent therapeutic targets: dihydrofolate reductase (DHFR), carbonic anhydrase, and D-Ala-D-Ala-peptidase. The majority of the chapter (23 pages) focuses on DHFR where the greatest amount of information has been published. The five pages on carbonic anhydrase follow that literature through 1988. The statement that "the number of known proteins of established structure which represent a target of action for drugs on the world market can easily be counted on one hand" is certainly no longer the case. Missing are HIV enzymes, especially the protease, renin, and a number of cancer-related protein and DNA macromolecular targets.

**"Multiple Modes of Binding of Thyroid Hormones and Other Iodothyronines to Human Plasma Transthyretin"** (P. de la Paz, J. M. Burridge, S. J. Oatley and C. C. F. Blake) is extensive (54 pages in length), well-illustrated, and interesting; however, all of the references are for work published through 1983 or before, except for two in 1984, two in 1986, and one in 1987.

**"Computer Modeling of Drug–DNA Intercalative Interactions"** by Steve Neidle nicely covers this area (references through 1991) starting with DNA structures followed by methodologies for Drug–DNA modeling and then to specific examples. The chapter would be a good starting point for those interested in this area of research.

**"Crystallographic Investigations of Glycolytic Enzymes from *TRYPANOSOMA brucei*: Potential Starting Points for the Design of New Sleeping Sickness Drugs"** (W. G. J. Hol and R. K. Wierenga) treats one disease state from a to z, starting with a description of the disease, followed by the biochemistry of trypanosomes, rational drug design, crystallography-based structure–function, and modeling. This is a well-written chapter summarizing work in this laboratory through mid-1990. The all-inclusive approach presented (see p 213, figure 7.1) can be used as a model for rational drug design.

The final chapter, **"Drug Discovery and Invention: Some Approaches Compared"** (A. S. Gilbert and R. M. Hyde), illustrates how the process of modeling ligands to (3-D) macromolecules can be enhanced by combination with or consideration of QSAR principles. This is a brief but necessary discussion on the need to integrate other factors, such as hydrophobicity and QSAR into 3-D drug design.

Editor Chris Beddell, in his preface, indicates that "the primary aim of the book is to indicate the current state of expertise and the ways in which this expertise might develop in the immediate future for molecular tailoring to be as successful as possible." This is a high standard for any book on the subject. Considering that a number of chapters are outdated, and chapters covering some of the modern expertise being used for molecular tailoring are missing, such as multidimensional NMR, I believe that the material presented will still be useful to individuals interested in understanding the concepts behind this field of drug design and how they developed. From this point of view, the book is extremely user friendly for the bench chemist, graduate student, or those interested in the history of development of modern drug design based on macromolecular targets. The high cost may preclude its use in academic course work or for personal home copies.

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**Radiopharmaceuticals. Chemistry and Pharmacology.** Edited by Adrian D. Nunn. Marcel Dekker, Inc., New York. 1992. x + 435 pp. 15.5 × 23 cm. ISBN 0-8247-8624-6. $165.00.

The area of radiopharmaceuticals has been the focus of numerous monographs, reviews, and international meetings for a number of years. Since nuclear medicine can be divided into two disciplines with complementary imaging technology, the purpose of this particular book is to provide a timely comparison of both positron emission tomography (PET) and single photon emission tomography (SPECT). It is not intended to exhaustively relate the synthesis and use of every radioactive substance employed for these methods, but to offer some philosophical and practical direction as to which technique is most advantageous under a given set of circumstances. Twelve distinguished authors from both the pharmaceutical industry as well as academia contributed to the book. It is divided into three sections: Perfusion, Receptor Binders, and Excretion, within each section individual chapters deal with such subjects as single photon radiopharmaceuticals for imaging myocardial perfusion (chapter 3), the influence of structure modification on the metabolic transformation of radiolabeled estrogen derivatives (chapter 9), and renal radiopharmaceuticals (chapter 10). Indexed at the end of the volume, the book also collectively contains over 1000 valuable references to the original literature. This text admirably succeeds in its purpose of updating current investigators in a rapidly advancing area along with those who are unfamiliar with it. It should therefore be useful and appreciated not only by radiopharmaceutical, organic, and medicinal chemists but also physicians and regulatory workers.

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