Total Synthesis of Natural Products: The 'Chiron' Approach. (Organic Chemistry Series, Vol. 3). By STEPHEN HANESSIAN. Pergamon Press, Inc. Maxwell House, Fairview Park, Elmsford, NY 10523. 1983. 291 pp. 15 × 23 cm. Price: $20.00.

The present generation of organic chemists considers no total synthesis of a natural product to be truly satisfactory unless it also yields an optically pure product. One of the ways of achieving this objective is to begin the synthesis with a substrate drawn from the chiral pool so bountifully provided by nature: amino and hydroxy acids, terpenes, and carbohydrates, many of which are readily available and relatively cheap. In this book, Professor Hanessian, one of the leading practitioners of the art of using carbohydrates as precursors in asymmetric total synthesis, presents both a personal approach to this field and a thorough review, with much informative commentary, of successful syntheses employing carbohydrates as starting materials.

Part 1 of the book describes those features of compounds from the chiral pool—variety in carbon framework, sense of chirality, number of asymmetric centers, functional group sequences—that make them versatile springboards from which to launch asymmetric syntheses. All important, of course, is the designer's perception of the structural and stereochemical relationships between these "chiral templates" and the target structure. Parts 2 and 3 of the book, entitled "Design" and "Discovery" respectively, present guidelines on how to establish the appropriate "visual dialogue" (a functional, if not particularly felicitous, phrase). The central feature of the approach is the identification and selection of "chirons"—suitably functionalized, defunctionalized, or otherwise modified versions of the chiral templates which, after activation, may be assembled to give the target product.

The rest of the book, and by far the largest part, is devoted to "Execution," a detailed discussion of selected carbohydrate-based asymmetric syntheses. These syntheses fall into three main groups: those in which the targets contain reasonably obvious carbohydrate-type symmetry; those in which such symmetry is partially hidden; and those in which only the most hardened fans of the approach would have looked for a carbohydrate precursor in the first place. Each section is further subdivided into chapters according to the types of molecules being synthesized. The relatively straightforward chiral targets (acyclic compounds, tetrahydrofurans, tetrahydropyrans and the like) predominate the earlier chapters and more complex products (*i.e.* prostaglandins, heterocyclic antibiotics, macrolides, and ansa compounds) dominate the later sections. In almost all cases, the syntheses chosen for illustration are of compounds with substantial pharmaceutical significance. The book ends with a brief discussion of a possible role for computers in the visual recognition of chiral templates within target structures.

Not the least virtue of this book is the abundance of flow-sheets (more than 150) for the syntheses discussed. In most cases, the flow sheets show both a retrosynthetic analysis from target via chiron to chiral template, as well as the forward steps, with reagents, of the completed synthesis. It appears that every reference of importance in the field has been included, and the index is reasonably comprehensive. There appear to be very few errors. Those whose chief fascination is the art and philosophy of organic synthesis will certainly read this book with avidity, even if they remain unconvinced that carbohydrates necessarily provide the ideal solution to the problem of introducing asymmetry into a synthetic scheme.

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Molecular Aspects of Anti-Cancer Drug Action. (Topics in Molecular and Structural Biology. 3). Edited by STEPHEN NEIDLE and MICHAEL J. WARING. Verlag Chemie International Inc., 303 N.W. 12th Ave., Deerfield Beach, FL 33441. 1983. 404 pp. 16 × 24 cm. Price: $97.50.

This book, the third in a series on *Topics in Molecular and Structural Biology*, contains eleven chapters dealing largely with Drug-DNA interactions of a number of cancer chemotherapeutic agents currently of high interest. Literature is covered through 1981 with the occasional appearance of a few later citations. Based on a random survey, the book is remarkably free from typographical errors. The text is printed in small (but clear) type. In most cases chemical structures, figures, and tables are easily read; however, in some cases the codes to structural formulae were difficult to read. The selection of topics includes: acridines, three chapters on topics related to anthracycline drugs, quinoxaline antibiotics, bleomycin, platinum compounds, alkylating agents, and methotrexate and analogues. In addition, there are reviews of the chemical and biological damage by certain antitumor drugs.

The chapter on acridines by Denny, Boyuley, Cain, and Waring is an excellent review of the enormous work of the group that was headed by the late Bruce Cain. It culminates in amsacrine and describes the studies (largely by Polish workers) on nitracrine—an active but toxic 1-nitro-acridine derivative—and of the bifunctional acridines. The interactions of daunomycin and adriamycin with nucleic acids is covered in a brief but useful chapter by Neidle and Sanderson; however, this subject has been covered in greater detail in earlier reviews. J. R. Brown presents a timely chapter with much new material on synthetic anthracycline drugs that will be of particular interest to medicinal chemists seeking a rational basis for the synthesis of new agents in this class.

Bifunctional intercalation is again reviewed by Waring and Fox in a chapter dealing with quinoxaline antibiotics. Although this group has not attained clinical significance, the techniques discussed in the study of molecular interactions may be of general use. Another review by Roberts and Pera dealing with the action of platinum antitumor drugs is presented in an authoritative manner. Lown briefly surveys the chemistry of DNA damage by a large number of antitumor agents. This chapter should be of particular value to medicinal chemists.

Molecular Aspects of Anti-Cancer Drug Action will be useful to medicinal chemists seeking rational approaches to the synthesis of antitumor agents. Unfortunately, the high cost of this volume ($97.50) may restrict purchases to technical libraries.

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A Guide to the Chemical Basis of Drug Design. By ALFRED BURGER. John Wiley & Sons, Inc., One Wiley Drive, Somerset, NJ 08873. 1983. 300 pp. 16.5 × 23.5 cm. Price: $45.00.

The contributions of Professor Alfred Burger to the discipline of medicinal chemistry, particularly the literature of medicinal chemistry, have long been noted and acknowledged. His current effort attempts to recount those experiences of the medicinal chemist which, in cooperation with biologists and pharmacologists, have resulted in the chemical design of therapeutically useful drug substances. It is the broad scope of this endeavor which accounts for both the success and failure of this latest effort. The success of this overview of drug design resides mainly in those areas in which Professor Burger provides personal insight. This guide, afterall, recounts many ideas and examples which "are results of a lifetime in medicinal chemistry." After a brief introduction in which he traces his early interest in the chemistry of medicinally useful agents, and thus traces the development of medicinal chemistry, the book discusses drug design from three distinct, but oftentimes redundant, viewpoints. Chapter 1 begins as a fascinating discussion of the history of medicinal chemistry but develops into a chapter which lacks direction and depth. Chapter 2 presents areas of research interest with particular emphasis on antihypertensive agents, anti-inflammatory agents, antiviral and antitumor agents, antihistaminics, analgetics and antihyperglycemic agents. It is in this chapter that general aspects of drug design, molecular modifications and quantitative structure-activity relationships are presented. The discussion in each of these areas represents a general overview of the subject and precludes any discussion in depth. For example, in the discussion of recent research in the area of antihypertensive agents the role of presynaptic α_2-adrenoceptors in the action of newer agents such as clonidine is neglected. On the other hand, the discussion of the development of analgetic research is particularly interesting. Chapter 3 is intended as a discussion of selected examples of drug design. Many aspects of drug design of analgetic, anti-inflammatory, anticholinergics and antihistaminic agents discussed in Chapter 2 are repeated in the early part

of this chapter. The bulk of the chapter is devoted to a discussion of the development and design of chemotherapeutic agents. Again, the major drawback to this chapter, for the most part, is a lack of in-depth discussion of many key areas as exemplified by the brief discussion of antitumor agents.

To offset the problems associated with attempts to cover these broad areas in 300 pages, Professor Burger has extensively documented this coverage by citing 1512 references. Most of these are up to 1980, but several key post-1980 references are included. Unfortunately, several errors appear. For example, isoproterenol is described as the *N*-isopropyl homologue of epinephrine possessing "maximal α-adrenergic properties" (p. 20). Several structures are incorrectly drawn and other seemingly minor, but important, errors occur. For example, chlorisondamine is described as a drug lacking quaternary ammonium groups when, in fact, the opposite is true (p. 33).

Overall, while this project may have been somewhat too ambitious, it does represent another important contribution to the literature of medicinal chemistry by Professor Burger. The book should be of particular interest as background preparation for the organic chemist preparing for a research career in medicinal chemistry.

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NOTICES

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