may limit the circulation of this text to library collections and faculty offices.

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Monosaccharide Sugars. By Zoltán Györgydeák and István F. Pelyvás. Academic Press, San Diego, CA. 1998. xviii-508 pp. 15.5 × 23.5 cm. ISBN 0-12-550360-1. $89.95.

This book is a compendium of the literature on methods for C−C bond formation, degradation, and epimerization of monosaccharides. It contains approximately 1700 references and is divided into three parts. The first and largest part, 370 pages, describes the ascending synthesis of monosaccharides by long-known methods, such as the formose or cyanohydrin reactions, as well as more recent methodologies using nitroalkanes, malonesters, phosphoranes, and organometallics. The second part, 95 pages, covers the degradation of monosaccharides and related acids to smaller chiral synthons. The final part, 20 pages, deals with sugar epimerization.

Each chapter is illustrated by relevant examples taken from fields as diverse as *C*-saccharide, antibiotic, nucleoside, and isotopically labeled saccharide synthesis. Despite these useful examples, little or no mechanistic information is given on the reactions presented. Collections of known sugar derivatives are summarized in many tables, and the influence of experimental conditions on the reaction products is briefly discussed. Suitable experimental protocols are given for each type of transformation. While this is helpful, particularly for older chemistry published in difficult to obtain or foreign language journals, it is likely that most chemists would want to return to the original literature before attempting a synthesis.

Although the authors use systematic carbohydrate nomenclature, recently established by IUPAC, it would have been helpful for the authors to have included a primer on carbohydrate nomenclature for the nonexpert. There is no author or compound index, limiting the value of the compendium as a fast reference. The subject index is very simple and generally useful to find syntheses of a given type of sugar or examples of particular reactions. While some references are quite old (1860s), more recent, important references (1995−1997) are discussed in a brief addendum.

The utility of this book is as a general overview and compendium, comparing useful strategies for synthesis of higher-carbon sugars and related chiral synthons from simple carbohydrate derivatives. This book has little value for the carbohydrate chemist, focused primarily on oligosaccharide targets of biological and pharmaceutical importance, as constituent monosaccharides must be designed and protected with a specific target in mind. This book is somewhat more useful for the medicinal and synthetic chemists wishing to investigate the use of monosaccharides as chiral building blocks to prepare more complex targets.

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Reviews in Computational Chemistry, Volume 11. Edited by Kenney B. Lipkowitz and Donald B. Boyd. Wiley-VCH, Inc., New York, NY. 1997. xxiv + 431 pp. 16 x 24 cm. ISBN 0-471-19248-1. $120.00.

The book is number 11 in the series started in the mid-1980s to cover recent advances in the burgeoning field of computational chemistry. In the decade since the first Gordon Conference on computational chemistry, we have witnessed amazing advances in the field. It is fair to say that computational chemistry as an element of the discovery process for new materials and drugs has become mainstream. With some refinements, and more powerful machines and algorithms, we use essentially the same force fields as a decade ago and the same fundamental theory in ab initio calculations. The bigger strides in recent years are in the application of computational methods and the linkage of thermodynamic theory to quantities like receptor structure, ligand structure, and molecular electronic properties.

The preface of the book starts with a philosophical note by explaining that the theme of the volume is "computer aided ligand design" and "modeling of biomolecules". It is further explained that "ligand design", not "drug design", is the proper nuance for what is being described, because the design of a drug encompasses a large number of downstream scientific analyses and disciplines beyond the strictly computational. The editors assert: "One of the best ways for the computational chemist to influence the drug discovery process is to supply essential information and good ideas, which, when implemented help drive a pharmaceutical project toward a successful conclusion." Thus the thrust of the book is how to optimize the role of computational chemistry in drug discovery.

Briefly, Chapters 1 and 2 discuss the multitude of new methods which have been developed for de novo design of ligands. Chapters 3 and 4 survey and discuss current advances in 3-D QSAR methods. In Chapter 5, the emphasis is on using computational methods to calculate partition coefficients, which are important in classical drug design work. Chapter 6 details recent work in the treatment of counterions in the modeling and simulation of DNA structures. Finally, the volume is concluded with an appendix entitled "Compendium of Software and Internet Tools for Computational Chemistry."

The book appropriately begins with two complementary chapters on de novo design of ligands. The first chapter provides a general introduction. The author systematically reviews and explains each of six major classes of methods: fragment location, site point con-

nection, fragment connection, sequential buildup, whole molecule, and random connection. To set the stage, he presents factors to consider, when evaluating the methods: How is the target represented? How are hits scored? Is the method systematic or random? Can the method make anything? Is the method an idea generator or a ligand generator? Is the receptor or ligand flexible? Two practical tradeoffs are articulated—hesitancy on the part of the synthetic department to embark on a complex synthesis because the molecule was suggested by a relatively unknown computer method and the scarcity of published examples of the success of these methods due to industrial proprietary concerns. Following a comprehensive discussion, the chapter concludes with recommended issues to be addressed in fugure research: speed, scoring functions, synthetic accessibility, novelty, filters, and testing strategies.

In the complementary Chapter 2, several specific de novo design methods are compared and contrasted in the context of the steps that occur in their application. This is viewed as an iterative process which includes constraint definition, structure generation, structure scoring, analyzing and prioritizing generated structures, verification of selected structures, and synthesis and testing of preferred designs. As an example, the structure generation section of the chapter discusses atom and fragment library approaches, building strategies, and handling molecule and receptor flexibility. Woven into this discussion are the programs LUDI, HOOK, PRO_LIGAND, SPROUT, GROW, and MCSS. The other sections take a similar approach, which solidifies the readers' understanding of the subject through this comparative overview. The chapter concludes with literature citations to published design examples which are complementary to the target or similar to other known ligands and a review of several validated examples.

Chapters 3 and 4 discuss various aspects of 3-D QSAR methods. As most medicinal chemists are familiar, the fundamental hypothesis of QSAR is that macroscopic properties (e.g., bioactivity) are related to molecular structure. Systematic variations in structure should have concomitant effects in observed activity, which can be used interpretively or predictively.

These chapters begin with a short discussion of the basic notions of classic QSAR. Following this basic foundation, the discussion enters the realm of 3-D QSAR. In the 3-D practice, one is trying to take explicit account of the influence and location of various substituents in the molecular architecture. A good QSAR model has the qualities of robustness, predictive power, explanatory power, relevance, simplicity, and uniqueness. Current methods are compared and contrasted with regard to their treatment of a number of variables which enter into the analysis, such as representation of the molecules and calculation of interaction energies.

The authors have generalized the underlying assumptions of 3-D QSAR: (1) it is the modeled compound that is responsible for the observed effect; (2) the modeled geometry is the bioactive conformation; (3) only a single conformation is considered in the binding and effect; (4) the binding site is the same for all compounds; (5) the target property is mainly explained by enthalpic processes; (6) entropic terms are the same for all compounds; (7) the system is at equilibrium, and kinetic effects are not considered; (8) solvent and diffusion are not included.

Lipophilicity, as quantified in the octanol−water partition coefficient, is the most well-known correlate of bioactivity in classical QSAR. Chapter 5 considers computational approaches. In the past, it has been considered as a primarily experimental technique. The large volume of literature following Hansch attests to its robustness and applicability in studies of bioactivity, toxicity, and other relevant drug properties. This is somewhat hampered by the need to synthesize an unknown compound in order to measure its experimental lipophilicity, so that some relevant bioactivity can be predicted. The result of this prediction might lead to the paradoxical conclusion that the compound is not, in fact, worth synthesizing. In the era of combinatorial libraries of many thousands of compounds and virtual libraries in the millions, clearly an expedient means of computing log *P* is important. Methods are reviewed and discussed, which range from fragment-additive methods through theoretical methods to direct simulation methods and techniques which also include the contributions of multiple conformers.

In the case of DNA, which is the subject of Chapter 6, the negatively charged phosphate groups in the backbone are neutralized by first- and second-row alkali metal cations. These and the swarm of water molecules are collectively called the "ion atmosphere" of the DNA strand. This is one of the most complex problems in an atomic-level simulation. Getting it right is critical to understanding and interpreting the thermodynamics of these systems reliably and correctly. This assumes even more vital importance as the structures and interactions of transcription factors, DNA-binding molecules and enzymes, and DNA itself are considered as therapeutic targets for current drug research.

The discussion in the chapter focuses on underlying physical theory, simulation methodology, ion and water placement, and simulation protocols. There is extensive coverage of the treatment of nonbonded interactions, including shifting functions, cutoffs, and constraints. Validation is one of the most important aspects of an effective simulation method. An acceptable model will account for all important observables, including experimentally determined structures, thermodynamics, and H-bonding patterns. These are treated in the context of numerous examples from recent research activities.

The excellent appendix on software and the internet is one of the most exciting additions to this volume. One hardly has to mention why this is important—the internet connects 16 million plus computers and "tens of millions of users". Connectivity is the sine-qua-non for modern computational chemists—to stay in touch, to obtain software, and to access a virtual library of information in the field.

In this part of the book, Don Boyd has provided useful tables listing URLs of search engines, web sites of general interest to computational chemists, web sites of organizations of interest to computational chemists, web sites for software and of software vendors, web sites of publishers and journals, web sites of computer manufacturers, and e-mail addresses of relevant bulletin boards.

The current volume of the series continues the excellent tradition of its predecessors, by offering the reader comprehensive and current information on several subjects of importance to specialists in computational chemistry as well as their medicinal chemistry colleagues. Each of the six chapters and the appendix are written by well-known leaders in their respective fields who provide fascinating demonstrations of their extensive expertise. The breadth of computational topics covered makes the volume important to those wishing to gain insight outside of their core area of expertise.

The table of contents is surprising in its high level of detail. This is particularly helpful, since it reads more like an outline of the chapters. The volume provides comprehensive indices: an index of authors cited, an excellent subject index, and a list of contributors and their affiliations. There is also a complete listing of the contents and authorship of the previous 10 volumes in the series.

The book is a high-quality production, all around. It is recommended for individuals, researchers, and institutional libraries.

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From Chemical Topology to Three Dimensional Geometry. Edited by Alexandru T. Balaban. Plenum Press, New York, NY. 1997. xviii + 420 pp. 16 × 23 cm. ISBN 0-30645462. $125.00.

Graph theory, a branch of mathematics, was discovered in the 19th century; present day chemists probably are familiar with graph theory and chemical topology as representations of chemical molecules as lines and points or as a connectivity matrix. There is a burgeoning literature in this field, particularly as it relates to QSAR.

The 10 chapters of this book by Balaban and 16 coauthors span the spectrum from organic to biological to inorganic molecules and size ranging from small alkanes to Fullerenes and transmembrane proteins. With the exception of the QSAR and protein chapters, the emphasis is on research and theory.

QSAR based on graph-theoretical descriptors reflects computational efficiency. Instead of high-level quantum mechanical calculations, algebraic indices derived from connection tables of molecular graphs may be computed and correlated to biological activity of compounds. However, one commonly encountered objection is the seeming "2-dimensional" nature of graph theory descriptors. Chapters 1−3 discuss approaches to making the indices reflect the "3-D" nature of real molecules, including 3-dimensional geometry, conformations, and chirality. In the first chapter, molecular similarity attributes are ranked in order of importance for biological activity, including *disposition* of electrical charges, of polar groups, of H-bond donors and acceptors, and of lipophilic and hydrophilic regions. *Disposition is* a 3-dimensional concept.

Chapter 4 treats one of the most important problems of medicinal chemistry: the extraction of a QSAR equation from biological data. The equation can be used predictively to evaluate the therapeutic potential and toxicity of new molecules, prior to synthesis. The effective use of topological descriptors takes on an added urgency in light of the mainstream importance of combinatorial chemistry. Virtual libraries of millions of molecules can be computationally screened with an efficient predictive equation, based on quickly computed descriptors. Real examples of these QSAR equations are given in physical properties, lipophilicity, chromatographic retention time, analgesic potency, and enzyme inhibition.

In the present age of bioinformatics, the relationship between gene sequence and the primary structure of its expressed protein product is understood. However, the problem of protein folding to the tertiary structure is largely unsolved. As Chapter 5 points out, the 3-D structure of a protein is a necessary prerequisite to rational design of small molecule ligands. The sequences of over 30 000 proteins are known, but only 3000 experimental structures are known. Chapter 5 adds to the armamentarium of protein prediction with-theory and practical examples. The treatment of transmembrane proteins, of which the neurotransmitter receptors are the most important, provides a valuable insight into these molecules.

Chapter 6 concentrates on the representation and characterization of molecules, rather than similarity or structure−property relationships. The characterization discussion focuses on defining structural invariants which are mathematical properties of a structure. These are unique for a given structure, but they do not allow reconstruction of the structure. In this chapter the authors proceed from the fundamentals of graph theory through methods which characterize the 3-D nature of real molecules and finally to a consideration of chirality.

Chapters 7−9 deal with Fullerenes, which are of interest because of their unique position in molecular orbital theory. A fundamental category of chemical structures is the one where the members are composed of a single element, carbon being the most notable. Chapter 7 deals with Fullerenes in the context of the connection between geometry and electronic structure. Methods of chemical topology are applied to define a Fullerene, the number possible for a given carbon number, and their structures and properties. In Chapter 8, the possibility of toroidal Fullerenes is introduced. They are predicted to be stable, and at least by analogy, they are not less likely than the hollow spheres which are now known. The central importance of carbon and the large number of conjugated species are treated in the broad context in Chapter 9. Structural enumeration, electronic stability, and properties are interrelated with topology.

The formation of a mathematical graph by the vertices and edges of polyhedra leads to a connection to coordination chemistry and crystal packing. With a reasonable level of mathematical formality in symmetry operations and graph theory, Chapter 10 establishes the