Book Reviews

Structure and Reactivity. Edited by Joel F. Liebman and Arthur Greenberg. VCH Publishers, Inc., New York. 1988. xiii + 385 pp. 16 × 24 cm. ISBN 0-89573-712-4. $84.00.

This volume contains eight chapters dealing with various aspects of, and approaches to predict, chemical reactivity. The first chapter by Politzer and Murray discusses their bond deviation index and relates it to molecular strain and to electrostatic potential. The second chapter, by Klein and Stevens, presents electron density distribution and electrostatic potential from an experimentalist's point of view. This is a particularly instructive chapter for theorists who usually have a limited understanding as to how such properties are measured. Cremer and Kraka develop the concept of molecular strain within the framework of modern quantum chemistry in the third chapter. The next two chapters are more specialized in content, one dealing with the possible implications of twisted bridgehead bicyclic lactams on their reactive properties, and the other chapter focusing on planar effects on the lability of carbon-carbon bonds. Chapter 6 by Krygowski examines crystal structures of molecules and describes them in terms of contributions of canoni reference structures. Iyer and Slagg discuss the structural features common to molecules of explosives and other high energy compounds in Chapter 7. The final chapter by Schulz and Schweig discusses the merits of combining ultraviolet photoelectron spectroscopy and matrix isolation to study reactive species.

This book should be useful to computational chemists working in molecular design. A variety of molecular properties related to chemical reactivity are defined and discussed. Some of these properties may be helpful in designing molecules. The discussions of molecular strain are particularly well done, and suggest roles this property might play in bioactive compounds. The topics covered in this volume are extensive and diverse. It might have been better to select more closely related subjects so as to present a common theme to the reader.

Department of Medicinal Chemistry and Pharmacognosy
University of Illinois at Chicago
Chicago, Illinois 60680
A. J. Hopfinger

Computer-Assisted Modeling of Receptor–Ligand Interactions. Theoretical Aspects and Applications to Drug Design. Edited by Robert Rein and Amram Golombek. Alan R. Liss, Inc., New York. 1989. ix + 512 pp. 16 × 24 cm. ISBN 0-8451-5139-8. $96.00.

This is Volume 289 of *Progress in Clincial and Biological Research* and contains the contents of most of the invited talks and a few selected papers from the 1988 OHOLO conference held at the King Solomon Hotel in Eilat, Israel, on April 24–28. The central objective of the conference was to strengthen the dialogue between theoretical and experimental scientists in the receptor and drug design fields. The book provides a broad overview of protein modeling and analyses of protein–ligand interactions especially as they relate to processing transmembrane signals. The book is organized into the five sections that were covered at the conference: (I) Computational Methods in Protein Modeling and Analysis of Protein–Ligand Recognition, (II) Physical Methods in Drug Design, (III) Receptors and Transmembrane Signaling, (IV) Receptor-Directed Drug Design, and (V) Round-Table Discussion.

As would be expected for a book that summarizes the proceedings of a meeting, there is little relation between one paper and the next (except in Section III), and a large range of variance exists in the effective treatment given to each topic. A number of the papers have reference lists that stop several years before the meeting date, while others contain several 1988 references. Some papers provide titles in references and others do not. The variance in papers even extends to the type of print and paper (photo duplication with some articles printed on glossy paper). The editors did an excellent job in getting the material to press in a reasonable time frame from the date of the meeting.

The following list of authors and paper titles are presented to illustrate the extensive topics and areas covered in the book:

Section I contains 11 contributions which include papers by Harold A. Scheraga, Some Computational Problems in the Conformational Analysis of Polypeptides and Proteins; Cyrus Levinthal, Modelling the Structure of Highly Constrained Proteins; Mitiko Go and Michiko Nosaka, Assorted Modules in Protein Architecture; Masayuki Shibata and Robert Rein, A Computer Modeling Study of Acetylcholine Receptor–Ligand Interactions; O. Tapia and J. Åqvist, Molecular Dynamics as a Tool for Structural and Functional Predictions: The Retinol Binding Protein and Chloroplast C-Terminal Fragment of the L12 Ribosomal Protein Cases; Barry Honig, Kim Sharp, and Michael Gilson, Electrostatic Interactions in Proteins; Fred E. Cohen, Lydia Gregoret, Scott R. Presnell, and I. D. Kuntz, Protein Structure Predictions: New Theoretical Approaches; Peter S. Stern, Normal-Mode Dynamics as a Tool for Predicting Antigenic Sites on Proteins; Morris Krauss and Walter J. Stevens, A Theoretical Model of Metal Binding Sites in Proteins; Yechiel Becker, Computer Modeling of Membrane-Anchored Cellular and Viral Proteins: Organization and Function; and Rick L. Ornstein, C–H···X Hydrogen-Bonded Pseudo-Watson–Crick Base Pairing with 7-Deazanebularin and Canonical Bases in DNA and RNA.

Section II has 6 papers: Oleg Jardetzky, Oliver Lichtarge, James Brinkley, and Marcela Madrid, The Structure of Proteins and Their Binding Sites: NMR and Artificial Intelligence; Elisha Haas, Folding and Dynamics of Globular Proteins Studies by Time Resolved Fluorescence Spectroscopy; J. L. Sussman, M. Shoham, and H. Harel, Protein Adaptation to Extreme Salinity: The Crystal Structure of 2Fe–2S Ferredoxin from *Halobacterium marismortui*; Sasson Cohen, Zipora, Brif, Frank Haberman, and Zivi Liron, Partial Molal Volume and Pharmacodynamic Activity; Joel Bernstein, Polymorphism in Drug Design and Delivery; and Elisha Berman and Michal Kam, The Solution Conformation of the Antibiotic Anticancer Chromomycin A_3 by Two-Dimensional NMR Spectroscopy.

Section III contains 11 contributions: H. Robert Guy and G. Raghunathan, Structural Models of α-Helical Membrane Peptides and the GABA Receptor Channel; Jon Lindstrom, Paul Whiting, Ralf Schoepfer, Michael Luther, and Manoj Das, Structure of Nicotinic Acetylcholine Receptors from Muscle and Neurons; Laurent Boulu and G. M. Crippen, Voronoi Receptor Site Models; Edward M. Kosower, A Structural and Dynamic Model for the Nicotinic Acetylcholine Receptor; N. Steinberg, J. Grunwald, E. Roth, R. August, E. Haas, Y. Ashani, and I. Silman, Conformational Differences Between Aged and Non-Aged Organophosphoryl Conjugates of Chymotrypsin; B. P. Doctor, K. K. Smyth, M. K. Gentry, Y. Ashani, C. E. Christner, D. M. De La Hoz, R. A. Ogert, and S. W. Smith, Structural and Immunochemical Properties of Fetal Bovine Serum Acetylcholinesterase; Enrique Ortega, R. Schweitzer-Stenner, and Israel Pecht, Receptor–Effector Coupling Processes Probed by Monoclonal Antibodies; J. Ramachandran, E. G. Peralta, A. Ashkenazi, J. W. Winslow, D. H. Smith, and D. J. Capon, Structural and Functional Diversity of Muscarinic Acetylcholine Receptor Subtypes; Jonathan M. Gershoni, Modelling the Cholinergic Binding Site: Considerations; Hermona Soreq and Catherine A. Prody, Sequence Similarities between Human Acetylcholinesterase and Related Proteins: Putative Implications for Therapy of Anticholinesterase Intoxication; E. E. J. Haaksma, G. M. Donné-Op den Kelder, H. Timmerman, P. Vernooijs, and W. Ravenek, Comparison of the Interaction of the Histamine H_2-Antagonists Histamine and Dimaprit.

Section IV contains 8 papers: James D. Petke, Gerald M. Maggiora, and Ralph E. Christoffersen, Quantum Mechanical

SCF/CI Studies as Probes of Macromolecular Structure: Methodological Aspects of Spectral Comparisons; Jonathan Greer, Karl W. Mollison, George W. Carter, and Erik R. P. Zuiderweg, Comparative Modeling of Proteins in the Complement Pathway; Gustavo A. Mercier, Roman Osman, and Harel Weinstein, A Molecular Theoretical Model of Recognition and Activation at a 5-HT Receptor; Gilda Loew, Lawrence Toll, John Lawson, Gernot Frenking, and Wilma Polgar, Opiate Receptor Heterogeneity: Relative Ligand Affinities and Molecular Determinants of High Affinity Binding at Different Opiate Receptors; Rebecca C. Wade and Peter J. Goodford, The Role of Hydrogen-Bonds in Drug Binding; Amiram Goldblum, Hydrogen Bonding in Protein Ligand Interactions: A Theoretical Dimension of Aspartic Proteinase Crystallography; Sid Topiol and Michael Sabio, Computational Studies of Ligand/Receptor Interactions; Richard K. Gordon, Ruthann M. Smejkal, Eli Breuer, and Peter K. Chiang, Design and Synthesis of Antimuscarinics Based on Physical and Mechanical Attributes.

Section V summarizes the round-table discussion. The panel members were Drs. Harold A. Scheraga, Jonathan Greer, Barry Honig, Edward K. Kosower, Michael Levitt, Jon Lindstrom, Garland Marshall, and Israel Silman.

In summary the book provides a good starting point for scientists interested in learning about or initiating research in the receptor and transmembrane signaling field. From this standpoint sections III and IV make a valuable contribution. Section I lacks depth with a number of prominent groups in that area missing and would require a symposium of its own to adequately cover the topic. Section II, Physical Methods of Drug Design, does not contain many papers related to drug design, as such, and the section title would have been better if the words Drug Design were left out. The round-table discussion makes for interesting reading. The comments by the panel members about the value of integrating modeling with experimental data are sobering as well as the comment by Michael Levitt that "often just picking up plastic models and playing with them is as useful as using giant computers". Garland Marshall notes that "A model...evolves with time...it is part of an intellectual process, it is not a distinct thing, just a tool that goes with experimental science". Even if future modeling studies produce nothing close to the elegant and fundamental ideas that produced the models of the α-helix and DNA, the method has been vindicated as a worthy intellectual process.

Department of Medicinal Chemistry **Donald J. Abraham**
School of Pharmacy
Medical College of Virginia
Virginia Commonwealth University
Richmond, Virginia 23298

Fluorine-Containing Molecules—Structure, Reactivity, Synthesis, and Applications. Edited by J. F. Liebman, A. Greenberg, and William R. Dolbier, Jr. VCH Publishers, Inc., New York. 1988. xvii + 346 pp. 16 × 24 cm. ISBN 0-89573-705-1. $84.00.

This book, published as a member of the series *Molecular Structure and Energetics*, consists of 12 autonomous reviews of research areas relating to fluorine-containing molecules. In Chapter 1, Rahman et al. discuss reactions of atomic carbon with perfluorocarbons to form such reactive intermediates as CF, CF_2, CF_3, and CF_2O_2. Chapters 2–6 concern the effects of fluorine substitution on energetics, structure, and reactivity of organic molecules. Filler reviews inter- and intramolecular arene–polyfluoroarene interactions, and relates energetics of these interactions to chemical reactivity. Chapter 3, by Skancke, consists of a mainly theoretical treatment of the effects of fluorine substitution on several properties of charged and neutral aromatic systems. Dolbier and Koroniak review the remarkable effects of fluorine on the stereochemistry of the electrocyclic ring opening of cyclobutenes, and discuss mechanistic interpretations of these effects. In Chapter 5, Bumgardner and Whangbo discuss the influence of secondary orbital interactions on behavior of fluorinated organic compounds. Koch and Koch follow this with a chapter describing the effects of fluorine on the partitioning of carbanion intermediates in alcoholic media. Chapters 7 and 8 relate more directly to organic synthesis. Welch and Eswarakrishnan review the effects of fluorination on enolates and enolate equivalents. In Chapter 8, Burton discusses the preparation, stabilities, and reactivities of a series of perfluoroalkenyl organometallics, including vinyl cadmium, vinyl zinc, and vinyl copper reagents. In chapter 9, Jache provides a comprehensive review of the inorganic chemistry of hydrogen fluoride. In Chapter 10, Peters and Allen discuss structure and bonding in compounds containing only N, O, and F. Chapter 11, by Bergstrom and Swartling, provides a review of fluorine-containing nucleic acid components, including analogues containing fluorine on the carbohydrate, phosphate, and heterocyclic ring. Syntheses and structural effects are emphasized, and a summary of biological data is provided. In Chapter 12, Liebman discusses mimicry rules by which the behavior of nonfluorinated molecules may by used to predict the behavior of fluorinated compounds.

As can be seen, a broad range of topics is covered, and this breadth represents both a strength and weakness of this volume. The individual chapters are well-written and well-referenced, and the authors are authorities in their fields. The range of topics covered makes it probable that most readers will find material of value in this book. On the other hand, it is less likely that many will find the entire book pertinent to their work. Nonetheless, the underlying theme of the series, molecular structure and energetics, is well-served by this volume. Indeed, the chapters dealing with the effects of fluorine on structure and reactivity and on intramolecular and intermolecular interactions, as well as the theoretical discussions provided in other chapters, should be particularly valuable to both organic and medicinal chemists interested in fluorinated molecules.

Laboratory of Chemistry **Kenneth L. Kirk**
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland 20892

Strategies and Tactics in Organic Synthesis. Volume 2. Edited by Thomas Lindberg. Academic Press, Inc., San Diego. 1989. xv + 469 pp. 16 × 23.5 cm. ISBN 0-12-450281-4. $75.00.

In the second volume of this series on multistep organic synthesis the editor, Dr. Thomas Lindberg, continues the theme of "behind-the-scenes looks at organic synthesis from the perspective of outstanding organic chemists," so successfully established in 1984 with Volume 1. The contributors Dale Boger, Steven Burke, Bruce Dorsey, Thomas Engler, Burt Fraser-Reid, Michael Greco, Paul Helquist, Peter Jacobi, Michael Jung, Alan Kozikowski, Stephen Martin, William Roush, Amos Smith, Daniel Sternbach, Ray Tsang, and David Williams describe their efforts to develop efficient synthetic routes to structurally complex natural products with established or potential biological activity. Most of the chapters start with a brief history of the target compounds detailing highlights of structure elucidation and biological activity, then proceed to a retrosynthetic analysis before describing the actual evolution of the syntheses themselves. On the whole, the authors present candid accounts of their work, including naive assumptions and serendipitous discoveries en route to the final solution of the synthetic problem. In this regard they admirably achieve the stated purpose of the volume. The narratives are generously endowed with schemes, figures, tables, equations, and interspersed structural formulas strategically placed to aid the reader. Furthermore, the accounts are well-documented with literature citations. Thus, the work could serve as a valuable source book of synthesis methodology. Unfortunately, the index is a sparse 3 pages and includes only 165 terms, mainly reagents, reaction types, and compound names.

Considering the number of authors and the diversity of subjects, the work is remarkably unified. The ChemDraw quality structural formulas and type-set text contribute to its uniformity and make the book a pleasure to read. Each of the accounts offers interesting chemistry and several are so well written I felt compelled to finish them without interruption. The only down side of this well-recommended volume is the high price, which will likely limit its accessibility to graduate students and postdoctorals.

Department of Chemistry **James A. Marshall**
University of South Carolina
Columbia, South Carolina 29208

Cocaine, Marijuana, Designer Drugs: Chemistry, Pharmacology and Behavior. Edited by Kinfe K. Redda, Charles A. Walker and Gene Barnett. CRC Press, Boca Raton, FL. 1989. 238 pp. 18.5 × 25 cm. ISBN 0-8493-6853-7. $115.00.

This publication resulted from a symposium held at the Florida Agricultural and Mechanical University in Tallahassee, FL, during March 1986. It brought together health professionals, social workers, and scientists focusing primarily on the subject of cocaine and marijuana. After the symposium, the editors expanded the scope of the discussion to include relevant and timely topics such as designer drugs and uses, misuses, and abuses of anabolic steroids by athletes.

The term "drug abuse" is a timely and important issue that the editors set out to address from various points of view—sociological, psychological, medical, legal, and moral. This book attempts to do all things for all people, but unfortunately is too broad in scope and lacks sufficient depth in either the chemistry, pharmacology, or behavioral sciences of abused drugs to be of great interest to individuals working in this area.

The book is organized into 17 chapters written by 26 contributors and contains a subject index. Most references are pre-1986, and few of the authors have attempted to update their literature citations. The excessive cost for the 238 pages will further limit interest in this book.

Section of Medicinal Chemistry **John L. Neumeyer**
Northeastern University
Boston, Massachusetts 02150

Protecting Scientific Ideas & Inventions. By Ramon D. Foltz and Thomas A. Penn. CRC Press, Boca Raton, FL. 1988. vii + 249 pp. 21.5 × 28 cm. ISBN 0-944606-03-2. $49.95 (paperback).

This book has been written by R. D. Foltz, a corporate patent lawyer, and Thomas A. Penn, an R&D manager. In it they have translated the laws, concepts, and legal procedures into the language of a layman. They have utilized unique diagrams and examples to simplify complex concepts, to draw conclusions and provide guidance, to create worksheets and checklists to make it easy to keep records and to give legal experts the information they need, and to minimize the costs of getting a patent. This guide is presented in a form that enables ready referral and even includes samples of registration forms and easily copied, ready-to-use, legal letters and contracts. The book is so detailed and practical that it even provides a map to and of The Public Search Facilities of the U.S. Patent & Trademark Office Complex in Crystal City.

This book is clearly a very valuable compilation that guides one through the patent process in a practical, yet comprehensive fashion. It will be of value to all interested in protecting scientific ideas and inventions, but most especially to those relatively inexperienced in the patent process. The only minor criticism is the lack of a subject index.

Staff

Allosteric Modulators of Amino Acid Receptors: Therapeutic Implications. Fidia Research Foundation Symposium Series Volume 1. Edited by E. A. Barnard and E. Costa. Raven, New York. 1988. xviii + 404 pp. 16 × 24 cm. ISBN 0-88167-432-6. $79.00.

Divided into three sections on $GABA_A$, $GABA_B$, and excitatory amino acid (EAA) receptors, the present volume contains 25 chapters on the molecular pharmacology, biochemistry, and electrophysiology of receptor function and is the result of a meeting held in London in November 1987. With the exception of a chapter on the neuroprotective effects of MK 801 by the Merck Neuroscience Group, the therapeutic implications of allosteric modulation mentioned in the title receive minimal consideration and the title is thus misleading.

The chapters on receptor structure and electrophysiology are of a uniformly excellent quality and special mention should be made of the chapter on $GABA_B$ transduction mechanisms by Wojcik et al. While nearly half of this volume concerns EAA receptors, given the intense activity in the area of excitatory amino acid research, much of the information in this section is unfortunately dated and has appeared elsewhere.

Seven of the chapters in this volume (approximately 25%) are from the Fidia-Georgetown Neuroscience Group and provide an opportunity to become acquainted with the research focus at this institute. Some may, however take exception to the glutamate receptor nomenclature in use in Southwest Washington and to Costa's thought-provoking statements on the iatrogenic effects of isosteric antagonists versus allosteric modulators. The latter idea, developed in the first chapter of this volume, reflects an increasing interest in indirectly acting ligands as "side effect free" therapeutic agents although the complexity of ligand interactions with the benzodiazepine and NMDA–receptor complexes tends to defy rationalization in terms of drug specificity. Some literature substantiation of the statement (page 5) that "in nature, signal transduction at transmitter receptors is never regulated by resorting to isosteric inhibition: allosteric modulation prevails" would have been welcome. As to "never", I am sure the chorus of *H.M.S. Pinafore* would have some relevant comments on such blanket negatives especially in light of how little we know regarding drug actions and mechanisms at the transductional level. As a monograph, this volume is uniformly well produced but is one to be consulted in the library rather than purchased for one's own collection.

Pharmaceutical Products Division **Michael Williams**
Abbott Laboratories
Abbott Park, Illinois 60064

Synthetic Peptides: Approaches to Biological Problems. Edited by James P. Tam and Emil Thomas Kaiser. Alan R. Liss, Inc., New York. 1989. xxi + 344 pp. 16 × 23.5 cm. ISBN 0-8451-2685-7. $72.00.

It has become evident in recent years that peptides, proteins, and their analogues and mimics are the drugs of the future as well as essential reagents and tools for the examination and understanding of many biological processes. From this perspective, this book can provide important information on emerging ideas and methods that are being used in the design, synthesis, and evaluation of peptides in the context of their biological applications and uses. This volume includes 25 articles from a UCLA Colloquium of the same name as the book title, which was held at Park City, UT, January 31–February 4, 1988. The meeting was held concurrently with the UCLA Symposium on Technological Advances in Vaccine Development. Perhaps for the latter reason, the emphasis of the book is on peptides and their potential uses and applications in the area of immunology, with 15 of the 25 chapters primarily devoted to this subject, with contribution in the Sections on Methods and Applications (6 articles), Synthetic Peptide Based Vaccines (5 articles), and Determinations of Antigenic Domains (4 articles). Other topics covered are Prediction of Peptide and Protein Structures (4 articles), Bioactive Conformations of Peptide Hormones (2 articles), and Peptide Hormones and Growth Factors (4 articles).

The usefulness of conference proceedings books such as this monograph to other investigators depends on three critical issues: (1) the quality of the chapters in the book; (2) the time that elapses between the conference and its publication; and (3) the efforts made by the publisher to bring the book to the attention of interested readers. The latter area often is the most neglected but crucial component, and it is hoped that publishers will put more effort into this important issue.

On the second issue the publishers of this volume have done quite well, with a publications date of approximately 1 year after the conference was held. This is excellent, especially in view of the tragic and untimely death of Professor Kaiser. Professor Tam is to be congratulated for pushing forward to ensure a reasonably rapid publication of the book. The book has been printed by direct reproduction from original manuscripts, and the editors have done a good job of maintaining a consistent format. Furthermore a useful subject index is provided.

On the whole, the quality of the papers in the book is high. As previously mentioned, the emphasis in the book is on the application of peptides to problems in immunology. Most important areas are covered, including novel methods of investigating peptide–antigen interactions (e.g., Geysen et al., Smith, and Tam), and design of specific vaccines (e.g., Brown, Kumar et al., etc.).

The coverage of the other areas of current interest in synthetic peptide design is more limited. In the Peptide Hormones and Growth Factor areas, 30 or more peptides are under active investigation at this time, so that any effort to cover all of the topics would be difficult. In addition, numerous neuropeptides also are under active investigation. Similarly numerous efforts are in progress to determine the "bioactive conformations" for a variety of peptide hormones and neurotransmitters. Nonetheless, a number of very useful insights into current approaches to peptide design and synthesis are provided in the chapters found in this book. The four papers on prediction of peptide and protein structure are particularly well written and provide good discussions that will be useful to everyone, from the new initiate to the most seasoned practitioner.

In summary, this is a useful new book in an area which is currently under rapid development into many new areas with important medical applications. Timely updates and insights into several specific areas of current peptide research makes the book a useful and necessary addition to any library, and important reading for the novice and long-time participant in this important area.

Department of Chemistry **Victor J. Hruby**
University of Arizona
Tucson, Arizona 85721

The Alkaloids. Volume 34. Edited by Arnold Brossi. Academic Press, New York. 1988. ix + 410 pp. 15.5 × 23.5 cm. ISBN 0-12-469534-5. $89.00.

This book continues the fine tradition of its predecessors in the series by highlighting advances in selected areas of alkaloid chemistry and presenting well-written, contemporary reviews by recognized experts. The first chapter, by T. Hino and M. Nakagawa, reviews the cyclic tautomers of tryptamines and tryptophans. Here we encounter first the rich chemistry of the simple pyrroloindoles, followed by oligomeric derivatives and the structurally more elaborate fungal toxins such as the sporidesmins. R. Mechoulam then reviews the alkaloid chemistry of *Cannabis sativa*, beginning with nineteenth century investigations of hashish contaminated with tobacco and continuing with a discussion of the spermidine alkaloids which have been identified as genuine constituents of this plant. T. Amiya and H. Bando present a review of developments in the *Aconitum* alkaloids, emphasizing synthetic progress. Synthesis is also a feature of the chapter by M. Onda and H. Takahashi on the protopine alkaloids, but studies of the conformations of these 10-membered aminoketones in solution and the solid state are also interesting. G. Massiot and C. Delaude present a thorough review of the state of knowledge of African *Strychnos* species, incorporating enthnobotany, structure elucidation, biosynthetic pathways, synthesis, and pharmacology. Finally R. Verpoorte reviews advances in the *Cinchona* alkaloids, with an emphasis on recent synthetic and spectroscopic results. Altogether this is an excellent volume which will be of interest to many scientists.

Northeastern University **Philip W. Le Quesne**
Boston, Massachusetts 02115