Book Reviews

Biomedical Frontiers of Fluorine Chemistry. Edited by Iwao Ojima, James R. McCarthy, and John T. Welch. ACS Symposium Series No. 639. 1996. xi + 356 pp. 15.5 × 23.5 cm. ISBN 0-8412-3442-6. $99.95.

The book resulted from three ACS symposia held in 1995 dealing with Fluorine in Drug Design, Medicinal Chemistry, and in Biological Chemistry. Two of the symposia were sponsored by the Divisions of Medicinal Chemistry and Fluorine Chemistry at 210th ACS National Meeting in Chicago. The third was an ACS-sponsored symposium at the 4th International Chemical Congress of Pacific Basin in conjunction with the Chemistry Society of Japan and the Canadian Chemical Society. Many of the 94 authors were invited speakers at the symposia.

The individual 23 chapters are short and are entitled (1) Recent Advances in the Biomedicinal Chemistry of Fluorine-Containing Compounds; (2) Practical Synthesis of Enantiopure Fluoroamino Acids of Biological Interest by Asymmetric Aldol Reactions; (3) Synthesis and Incorporation of α-Trifluoromethyl-Substituted Amino Acids into Peptides; (4) Trifluoromethylated Amino Alcohols: New Synthetic Approaches and Medicinal Targets; (5) Asymmetric Synthesis of Functionalized Fluorinated Cyclopropanes and Its Application to Fluoromethano Amino Acids; (6) Synthesis and Properties of Novel Fluoroprostacyclins: Potent and Stable Prostacyclin Agonists; (7) Preparation of Fluorinated Amino Acids with Tyrosine Phenol Lyase: Effects of Fluorination on Reaction Kinetics and Mechanism of Tyrosine Phenol Lyase and Tyrosine Protein Kinase Csk; (8) Efficient Synthetic Routes to Chiral 6-Deoxy-6,6,6-trifluorosugars via Intramolecular 1,2-*O*,*O*-Silyl Migration; (9) Fluoroamino Acid Containing Analogues of Folic Acid and Methotrexate; (10) Fluoro-olefin Iosteres as Peptidomimetics; (11) Molecular Design of Fluorine-Containing Peptide Mimetics; (12) Mechanistic Studies of the Prenyl Transfer Reaction with Fluorinated Substrate Analogs; (13) Elucidation of the Mechanism of Inhibition of Human Immunodeficiency Virus 1 Protease by Difluorostatones; (14) Fluorine-Containing Peptidomimetics as Inhibitors of Aspartyl Proteases; (15) Inhibition of Ornithine Aminotransferase: A New Target for Therapeutic Intervention; (16) Fluorinated Vitamin D_3 Analog with *In Vivo* Anticancer Activity; (17) Syntheses, Biological Activity, and Conformational Analysis of Fluorine-Containing Taxoids; (18) Design of a Fluoro-olefin Cytidine Nucleoside as a Bioprecursor of a Mechanism-Based Inhibitor of Ribonucleotide Reductase; (19) Synthesis and Biological Activity of 2-,2′-Difluorodeoxycytidine (Gemcitabine); (20) Fluorinated Sugars as Probes of Glycosidase Mechanisms; (21) ^{19}F-Labeled Amino Acids as Structural and Dynamic Probes in Membrane-Associated Proteins; (22) Fluorinated Amino Acids in Nerve Systems; and (23) ^{18}F-Labeled Tracers for Positron Emission Tomography Studies in the Neurosciences.

Chapter 1 gave reasons why substitution with fluorine is desirable. It also gave many examples of enzyme inhibition, increase in compound stabilities, and use in mechanistic probes achieved by incorporating F in various molecules. Fluorine has been used to replace H whereas CF and CF_2 have been used to replace oxygen. Many of the resulting compounds are on the market or are at various stages of clinical trials as anticancer, antiviral, antibacterial, antimaterial, antifungal, CNS agents, and hypolipidemic and antidiabetic drugs. Many other applications in medicine and as components of liposomal membranes and vesicles were given. Haven made a strong case for incorporation of F into various biomolecules; the next seven chapters focused on how to achieve such incorporation synthetically. The other chapters were grouped into various sections such as enzyme inhibitors, fluorosugars and nucleosides, and fluorine-containing biomolecules as probes for biochemical problems. This is a good reference book dealing with why, how, and some results of incorporating fluorine into various biological molecules. It is straight to the point and contains references up till 1995. It is an excellent text for both novice and expert in this field. It is highly recommended for individual and library acquisition.

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Genetic Algorithms in Molecular Modeling. Edited by J. Devillers. Academic Press, London. 1996. x + 327 pp. 15.5 × 23.5 cm. ISBN 0-12-213810-4. $55.00.

This is a book exploring the nature of genetic algorithms and their applications to QSAR and drug design. In 12 contributed chapters, several workers in this new field have written of their research and the nature of this new paradigm. The editor, J. Devillers, begins with an explanation and an overview of this Darwinian-based optimization method, exploiting a large listing of software and numerous references. The second chapter by Luke gives an extensive overview of the many genetic methods. Leardi follows with a chapter on feature selection using genetic algorithms. Two QSAR examples illustrated the use and power of this approach. In the fourth chapter Rogers expands on the issues that arise in applications. The lack-of-fit score is discussed, and three evolutionary modeling techniques are compared.

The fifth chapter covers genetic partial least squares in QSAR. These two methods of problem solving are combined and applied to previously studied QSAR data. Chapter six discusses applications of genetic algorithms to QSAR problems and to guiding molecular diversity experiments. Chapter seven is an extensive review of the author's work on the prediction of progesterone receptor binding affinity among a large set of steroids. This is a thorough review of the steps involved in

utilizing this method. The next chapter describes a procedure for construction of atomic-level receptor site models in the absence of a receptor crystal structure. Applications are extended to molecular recognition and chemical structure handling in the next chapter. Chapter ten describes genetic selection of aromatic substituents for designing test series. Neural networks and genetic algorithms are integrated into property prediction and structure construction from properties. The final chapter uses neural nets and a genetic algorithm to design biodegradable molecules.

The book is an essential part of a library of the medicinal chemist and drug design specialist who aspires to be at all creative in the new millennium. Computer-assisted design and in silico experiments are the ingredients of a productive approach to new drugs and, with the help of books like this, become more prominent in graduate curricula.

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Biological NMR Spectroscopy. Edited by John L. Markley and Stanley J. Opella. Oxford University Press, New York, 1997. x + 360 pp. 16 × 24 cm. ISBN 0-19-509468-9. $65.00.

This excellent text is the result of a Symposium on Biological NMR held at Stanford University in March of 1994 to honor the 65th birthday of one of the great pioneers in the area, Professor Oleg Jardetzky. The Epilogue of Professor Jardetzky's chapter highlighting the history of the application of NMR techniques to biological problems is in itself noteworthy. In his epilogue he discusses the importance to daydream and to be an explorer of science, and not to be just an exploiter of existing knowledge. Professor Jardetzky leaves us with these words, "A society that increasingly thinks only in terms of directing and channeling craftsmanship in the pursuit of clearly visible goals is cutting itself off from the source of all innovation." His thought-provoking epilogue should be required reading for all scientists, particularly those who sit on grant review panels.

The text is divided into four sections containing 23 chapters dealing with all areas of NMR related to the investigation of biological problems. The first section discusses the history of biological NMR spectroscopy. These four chapters provide an insight into the major challenges which have been overcome in the past 30−40 years. For the graduate student and recent Ph.D. who are accustom to and familiar with the application of modern NMR techniques for the determination of protein structure, these chapters provide an insight into the process of the development of these techniques. This historical perspective provides a valuable insight into the creativity, as well as the hard work, which went into the development of these powerful techniques. The second section, which is divided into 13 chapters, is devoted to a discussion of the application of NMR to protein structural studies. The application of both solution and solid state NMR methods to determine protein structure, protein folding, protein specificity, ligand receptor binding, and enzyme action are discussed in a clear and concise manner. The third section contains three chapters devoted to the study of nucleic acids. Topics discussed include determination of the structure of ribosomal RNA, characterization of DNA, and determination of conformational transitions. The fourth and final section presents a discussion of *in vivo* spectroscopy. These three chapters discuss the application of MRI methods to the study of the brain, and cancer cell metabolism.

This text should be required reading for all scientists interested in, or involved with, the application of NMR to biological problems. The text provides not only a clear overview of the state of the art in the field but also, in my opinion, an equally important overview of the history of the field.

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Encyclopedia of Cancer. Volumes 1−3. Edited by Joseph R. Bertino. Academic Press, Inc., San Diego, CA. 1997. xxxviii + 2134 pp. 22.5 × 28.5 cm. ISBN 0-12-093-230-X. $475.00 (3 volume set).

The *Encyclopedia of Cancer* is an ambitious three-volume compendium containing 163 articles on various topics relating to the disease of cancer, including its molecular and genetic processes, its epidemiology, its prevention, and its treatment. As defined in the glossary of this encyclopedia, cancer is "a multistep genetic disease resulting from specific alterations in the function of one or more genes, disrupting the control of cellular growth and differentiation, with the outcome of uncontrolled cellular proliferation and transformation to a neoplastic state." This description provides sufficient detail of the underlying complexities which make this disease a worthy subject for an encyclopedic collection of knowledge.

The encyclopedia is thoughtfully organized and presented, and includes at the very beginning a brief, helpful Guide to Using the Encyclopedia. All articles are arranged alphabetically by title. Each volume contains two complete Table of Contents for the entire encyclopedia. One Table of Contents lists articles as they are arranged in the encyclopedia, alphabetically by title. A second, more useful Table of Contents lists articles alphabetically by subject area. Fourteen specific subjects are presented in this second Table of Contents: Antisense, Ribozymes; Biological Treatment; Biology of Cancer; Chemical Carcinogenesis; Chemoprevention; Chemotherapy; Drug Resistance; Epidemiology/Tumor Genetics; Gene Therapy; Invasion and Spread of Cancer; Oncogenes; Radiation Therapy; Tumor Suppressor Genes; and Viral Carcinogenesis.

A uniform format for each article includes a brief outline of the general content, a short glossary of key

terms, an introductory paragraph that defines the discussed topic and summarizes the article's contents, cross references to other topics in the encyclopedia, and a brief bibliography of key review articles and research papers. A subject index containing more than 10 000 entries is located at the end of Volume 3 and offers the most convenient way to access a specific subject. In addition, Volume 3 contains a complete glossary of key terms just preceding the subject index. Clearly, significant effort has gone into organizing the material in ways that will not only enable readers to quickly locate information on a specific topic but will also encourage them to browse and read other articles of interest throughout the encyclopedia.

Basic scientific research is continually revising and expanding our understanding of cancer, and an encyclopedia devoted to this disease must cover a wide range of fundamental topics (e.g. cell cycle control and differentiation, carcinogenesis, chemotherapy, drug resistance), as well as timely topics (e.g. gene therapy, chemoprevention). In this respect, the editor has succeeded admirably in assembling, in encyclopedic form, a comprehensive, well-chosen collection of topics, contributed by a group of highly regarded scientists. This encyclopedia should be of interest to a wide range of scientists, biologists and chemists alike. Medicinal chemists will find throughout the encyclopedia many valuable summaries of highly relevant subjects that relate to the biology and treatment of cancer. Students in various disciplines of life sciences will also find the encyclopedia useful because they can easily access authoritative articles on a wide range of topics related to cancer. The reasonable cost of this three-volume set should make it a feasible acquisition for departmental libraries.

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Molecular Modeling: Principles and Applications. By Andrew Leach. Longman, Edinburgh. 1996. xvi + 595 pp. ISBN 0-582-23933-8. $35.00.

The book is a text covering the elements of the broad field called molecular modeling. It begins with a chapter on the useful concepts including potential energy surfaces, molecular graphics, coordinate systems, and associated mathematics. The second chapter is a review of quantum mechanical models. This is concise and well-written. This is followed by a chapter on empirical force fields in molecular mechanical applications. This is a wide-ranging review of the various terms in molecular mechanics calculations. Chapter four explores energy minimization as it relates to exploration of energy surfaces. It is well illustrated and clearly written. The next chapter describes computer simulation methods including molecular dynamics and Monte Carlo methods. Examples of simple thermodynamic properties that can be calculated are listed and described. The following two chapters are devoted to detailed descriptions of molecular dynamics and Monte Carlo methods. This set of chapters is quite useful in presenting these dynamic simulation methods with good illustrations punctuating both chapters.

Chapter eight presents the subject of exploration of conformational space. Several methods are described, and it is a very good discussion of these subjects. Chapter nine addresses three challenges in molecular modeling, free energies, solvation, and simulation of reactions. Again the illustrations enhance this presentation. The final chapter reviews the use of molecular modeling to discover and design new molecules.

This book is an excellent piece of work that should be a part of the library of every graduate student in medicinal chemistry. This should be the new essence of medicinal chemistry graduate education supplanting the classical emphasis on synthesis.

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Neural Networks in QSAR and Drug Design. Edited by J. Devillers. Academic Press, London. 1996. x + 284 pp. 15.5 × 23.5 cm. ISBN 0-12-213815-5. $65.00.

This book is a collection of articles exploring the subject of neural networks as data processing tools in compound design. It assumes some prior orientation to the subject as it moves quickly into the back propagation algorithm in the first chapter, written by the book editor, J. Devillers. This is a thorough overview with illustrations, comparisons, and software sources. The next four chapters illustrate the applicability of neural networks in log *P* estimations, organic chemical biodegradation, odor relationships, and odor threshold modeling. These chapters reveal the potential for neural nets to organize information into useful patterns leading to predictive models. Copious references accompany each of these four chapters, providing the reader with a rich source of information for deeper involvement in this paradigm. The editor has brought in several authors for these chapters who have contributed significantly to neural net technology. All are well written. Chapter 6 explores the pattern recognition capability of the adaptive resonance theory of Grossberg. These classifiers are shown to be of significance in computer-aided molecular design.

Chapter 7 shows the value of neural nets in multivariate data display. Chapter 8 is a QSAR study of nicotinic agonists using neural nets. The last three chapters describe applications to the evaluation of molecular surface properties, nonlinear neural mapping, and fuzzy clustering to classify protein classes. All very well presented by authorities in these areas. This book, and others in these emerging areas of modeling, stand as signposts to the new approaches to molecular design. The medicinal chemist who aspires to professional success in the new millennium must have a rich back-

ground in these areas. It is no longer just sufficient to synthesize and test; experiments are played out in silico with prediction, classification, and visualization being the necessary tools of medicinal chemistry. This book is in this new mainstream.

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The Ionotropic Glutamate Receptors. Edited by Daniel T. Monaghan and Robert J. Wenthold. Humana Press, Totowa, NJ. 1997. x + 378 pp. 16 × 23.5 cm. ISBN 0-89603-4756-9. $135.00.

This book is the 13th entry into the "Receptor" series edited by David Bylund and others. As with earlier books in this lineage, *Ionotropic* attempts to provide an up to date and reasonably thorough "overview of (the) most recent wave of information (and a) fresh understanding of glutamate receptor properties at the molecular level." As noted by the editors, (they) "face(d) the challenge of covering a rapidly growing and changing field that is perhaps already too broad for complete coverage in a single volume." The reviewer tends to agree. That being said, within the practical limitations of a book, *Ionotropic* offers a reasonable coverage of the biochemical, physiological, and pharmacological properties of recombinant ionotropic glutamate receptors and attempts to compare these to the properties of native glutamate receptors expressed in the central nervous system.

Ionotropic contains 14 chapters that are broadly divided into four main topic areas. The first chapter, an historical review of the area by David Lodge, is thoroughly delightful reading which should be requisite material for graduate students entering the area. Chapters 2−6 focus on molecular properties of glutamate receptor subunits with the last two of these detailing receptor modulation by phosphorylation. Chapters 7−9 present a description of the anatomical localization of specific glutamate receptor subunits as determined by *in situ* hybridization and immunohistochemistry. The last five chapters describe the pharmacological and physiological properties of NMDA and non-NMDA receptors. Notably, there is an emphasis to present molecular cloning data in such a way as to help explain the vast earlier (precloning) literature on glutamate receptors.

By the way of specifics, the 14 chapters are authored by 27 contributors, each of whom is easily recognized as a leading expert in the area. Nine chapters (Lodge, Hollmann, Sommer, Soderling, Watanabe, Petralia, Huettner, Verdoorn, and Morrisett) have only one author. Chapters range from 10 to 40 pages. Each contribution is thoroughly referenced, although most citations are pre-1996, suggesting either little of relevance occurred that year or that the chapters were written about a year ago. References are provided in full format, facilitating further searching of the subject area. The five and a quarter page index is somewhat limited for a book of this size.

Overall, *Ionotropic* achieves its principal aims of presenting an overview of this rapidly growing area of research. While the information contained within is already somewhat dated, the book would be useful to students entering the area, or more senior researchers desiring a quick introduction to ionotropic excitatory amino acid neurotransmission. With a price tag of $135.00, *Ionotropic* is most suitable for the department or institutional library.

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