Book Reviews

PCR. A Practical Approach. Edited by M. J. McPherson, P. Quirke, and G. R. Taylor. The Practical Approach Series. Series Editors: D. Rickwood and B. D. Hames. IRL Press at Oxford University Press: Oxford, New York, and Tokyo. 1991. xxii + 252 pp. $55.00. ISBN 0-19-963226-X.

Polymerase chain reaction (PCR) is unquestionably a powerful technique in molecular biology. This most recent in the series of Practical Approach books provides wide ranging uses of the PCR technique. The PCR concept, that of rapid amplification of specific DNA sequences using appropriate primers and a thermostable DNA polymerase is adequately explained in Chapter 1. Most of the remaining chapters are concerned with a multitude of applications for the technique. These 12 chapters all rely upon the basic PCR amplification concept in order to generate ample quantities of the desired nucleic acid fragment for sequencing or further testing. Since each application relies upon the same general amplification concept, one might think that the various chapters are somewhat redundant, but one does not obtain this impression. Since amplification of minute quantities of DNA is described using sources such as blood and archival materials, some of the valuable information in each chapter is that related to the procedures employed to extract and prepare the DNA samples prior to actual PCR amplification.

A number of chapters describe the use of PCR in some basic applications such as genetic diagnosis (Chapter 2), the analysis of genomic sequence variations (Chapter 4), the detection of deletions and point mutations (Chapter 5), the generation of cDNA libraries (Chapter 10), and its general application to gene cloning and manipulation (Chapter 12). Additionally, there are descriptions of some variations in the basic PCR concept such as "inverse" PCR (Chapter 9), which employs a circularized restriction fragment. The inverse PCR approach can be used when sequence information is available in only one region. The text and the procedures in these chapters and throughout the book are clearly written and often aided by the use of graphics and photographs of key elements.

In some respects, one of the most important chapters for scientists who wish to begin using PCR procedures is Chapter 14, authored by Eckert and Kunkel. These authors describe the fidelity of a number of DNA polymerases used in PCR applications. Tables of error rates for a series of conditions involving variations in the pH or concentrations of Mg^{+2} and dNTPs are prominently displayed throughout the chapter. This will be a critical chapter to consult in order to estimate the fidelity of the amplified materials. The fidelity of the synthesized sequences is, in my opinion, an important enough aspect of PCR technology that it should have appeared in a more prominent position in the book (Chapter 2?). But this is a minor quibble with what is otherwise an excellent presentation and organization of procedural materials related to PCR.

As a final comment, this reviewer would like to note positively the hard cover and ring binding used in this publication. The former should provide many years of service to the owner, while the ring binding permits the book to lie open on a bench or desk for easy "no hands" consultation.

Larry W. McLaughlin, *Boston College*

Statistical Thermodynamics for Chemists and Biochemists. By Arieh Ben-Naim (The Hebrew University, Jerusalem). Plenum Press: New York and London. 1992. $85.00. ISBN 0-306-43848-8.

Given the plethora of statistical thermodynamics textbooks available, the question inevitably arises: Why write another? The answer is that statistical thermodynamics is a subject of such wide applicability that one needs books written particularly for each subspeciality. *Statistical Thermodynamics for Chemists and Biochemists* written by Professor Ben-Naim covers, among other topics, three that lie somewhere at the interface between chemistry, structural biology, and biophysics, namely binding, macromolecular conformation ("structure"), and solvation effects. The book thus fills a useful niche in the field of statistical thermodynamics. The book should appeal to chemists who study complex systems and physically inclined biochemists, although the latter will find the book's formal level of presentation, by the author's own admission, difficult. Of particular value is the thorough treatment of the thermodynamics of binding, including simple binding, interacting sites, cooperativity, allostery, and models for enzyme regulation. Some useful analogies between adsorption and fluid state theory applied in one or two dimensions are also developed. There is also a good treatment of helix-coil transitions. A good portion of the book is devoted to water and aqueous solvation, in which the author is one of the leading authorities.

The presentation is at a formal level and is aimed for research scientists, although it's also appropriate for graduate students with thermodynamic and some statistical mechanics background. The references are up to date but often refer to other books. Consequently the chemists would perhaps wish for more references to recent research articles in liquid state theory, water simulations, etc. Biochemists might find the sections dealing with protein binding and folding somewhat abstract and wish that the author had "put some numbers in" to illustrate how large this or that effect is in real proteins. For example the section on oxygen binding to hemoglobin is a case where there are many reliable binding and equilibrium constant measurements that could be used to illustrate the use of the author's equations. Overall, however, *Statistical Thermodynamics of Chemists and Biochemists* is a valuable addition to the researcher's bookshelf.

Kim Sharp, *University of Pennsylvania*

Comprehensive Chemical Kinetics. Volume 33. Catastrophe Theory. By A. Okniński (Warsaw University of Technology). Translated from Polish by A. Przyjazny. Elsevier: Amsterdam and New York. Polish Scientific Publishers: Warsaw. 1992. xvi + 285 pp. $159.00. ISBN 0-44498742-8.

Catastrophes have been of considerable interest to a growing band of chemists, physicists, biologists, and chemical engineers over the last 20 years under the rubric of oscillating chemical reactions and/or chemical instabilities. This work has become a subject of some importance, not only because of the interesting chemistry involved but also because of its implications for the many other areas in which similar nonlinear dynamic laws occur. However, the mathematical bases of nonlinear behavior usually are not covered in standard undergraduate or graduate programs in chemistry. Chemists who work in this area must dig it out for themselves, and many of the standard mathematics/physics texts available are a bit too abstract for the usual physical chemist or even chemical physicist. This book connects the abstract and the practical by taking the reader through a geometrical discussion of various types of catastrophes possible and their relationship to bifurcation theory, *i.e.*, the standard mathematical machinery used in this area, to application of these concepts to a number of physical, biological, and chemical examples. The strength of the book is that it is not full of abstract mathematics. It is instead full of examples that show the mechanics of deriving insights concerning the behavior of the various models treated. It is accessible to a person with the mathematical skills of a good physical chemistry graduate student, and it is a good beginning place to learn the rudiments of the trade. The treatment is classical in that it gives the basics but does not discuss the current state of the art, although there are some recent references. Unfortunately, no exercises are provided, numerical methods are not covered, and differential-difference equations and iterative mappings are not discussed. It also is unfortunate that, even considering its price, the book clearly was not edited by a native English speaker; the language use if often awkward, and there are a number of obvious typos.

Richard J. Field, *University of Montana*

Chemistry and Biology of N-Nitroso Compounds. By William Lijinsky (Frederick Cancer Research Facility). Cambridge University Press: Cambridge and New York. 1992. xvi + 464 pp. $175.00. ISBN 0-521-34629-0.

Chemistry and Biology of N-Nitroso Compounds is the latest addition to the series Cambridge Monographs on Cancer Research, which describes carcinogenesis by a variety of different chemical types. This particular volume covers the N-nitroso compounds, which are important because they are the most versatile chemical carcinogens known, serving as models for almost every kind of human cancer. Since humans are exposed to some N-nitroso compounds in significant quantities, they are believed to be involved in causing certain types of cancer. The author, William Lijinsky, is an internationally recognized authority on N-nitroso compounds who has contributed immensely to our knowledge of their biological properties, particularly mutagenicity and carcinogenicity. The book is logically divided into chapters on the occurrence of N-nitroso compounds, their chemical properties, and their metabolism and cellular interactions, followed by chapters on their toxicity, mutagenicity, and carcinogenicity. The latter three chapters comprise about half of the book.

The greatest strength of this book is the compilation of biological data on N-nitroso compounds—toxicity, mutagenicity, and carcinogenicity. Dr. Lijinsky draws mostly on his own data in compiling these properties. This is reasonable because most of the relevant assays were carried out

under standardized conditions, allowing ready comparison of structure–activity relationships, which are extremely interesting. Dr. Lijinsky is careful to recognize the contribution of other groups who have evaluated the carcinogenicity of N-nitroso compounds and quotes the appropriate reviews of work in other laboratories, the results of which for the most part agree with his own. This book will therefore be very useful as a source of information on the toxicity, mutagenicity, and carcinogenicity of N-nitroso compounds.

Dr. Lijinsky also presents a realistic discussion of the potential involvement of N-nitroso compounds in human cancer. This is placed nicely within a historical context by the author, whose career spans the entire period of intense interest in N-nitroso compounds, which began in 1956 when Magee and Barnes demonstrated the hepatocarcinogenicity of *N*-nitrosodimethylamine in rats. Initially, these compounds were seen mainly as models for inducing tumors in laboratory animals, but subsequent work as described by Dr. Lijinsky has shown that they are probable causative agents for some human cancers.

Despite these strengths, there are aspects of this book which are annoying. Most of the references to work other than that carried out by the author or his colleagues are rather outdated, with less than 5% later than 1987. This in itself would perhaps not be so detrimental if it did not have such a negative influence on the text. As an example, the discussion of the role of cytochrome P450 enzymes in the metabolism of *N*-nitrosamines is hopelessly outdated, without even a single mention of cytochrome P450 2E1, which has been known for some time to be a high-affinity enzyme involved in the metabolism of *N*-nitrosodimethylamine. Another example is Dr. Lijinsky's discussions of cyclic nitrosamine–DNA adducts, in which he fails to cite several key papers, some of which are not even recent. These lapses are surprising and detract from the scholarly qualities of the book.

Dr. Lijinsky uses both literature data and his own studies in support of his general thesis that the formation of specific DNA adducts is not sufficient to explain structure–activity relationships in nitrosamine carcinogenesis. Most scientists involved in chemical carcinogenesis would probably agree that DNA adducts are necessary but not sufficient for induction of cancer by N-nitroso compounds. However, this important topic is not treated in an objective manner. The many other factors known to contribute to the carcinogenic process such as repair and persistence of DNA adducts as well as effects on cell replication are not thoroughly discussed. Instead, Dr. Lijinsky appears to be determined to prove that DNA adducts are unimportant in carcinogenesis by N-nitroso compounds and fails to present a balanced picture.

In summary, I would recommend this book as a reference work for those interested in the fascinating structure–activity relationships among the N-nitroso carcinogens, as well as the historical aspects of the field, but not as a source for an objective discussion of the literature concerning their mechanisms of carcinogenesis.

Stephen S. Hecht, *American Health Foundation*

Cyclic Organonitrogen Stereodynamics. Edited by Joseph B. Lambert (Northwestern University) and Yoshito Takeuchi (University of Tokyo). VCH Publishers: New York, Weinheim, and Cambridge. 1992. x + 293 pp. $125.00. ISBN 0-89573-773-6.

An introductory chapter by Professor Lambert outlines the two dynamic processes of primary interest in organonitrogen compounds: rotation about single or partial double bonds and inversion about nitrogen. Serious study of these has been possible only with the availability of modern research tools, and a third of the book is devoted to these methods: NMR (22 pp, Y. Takeuchi), rotational and vibrational spectroscopy (31 pp, P. Groner and J. R. Durig), and theoretical studies (41 pp, R. D. Bach and M. Raban).

The remaining chapters divide nitrogen heterocycles into four groups: strained rings (54 pp, W. B. Jennings and D. R. Boyd) five-membered rings (9 pp, F. G. Riddell), six-membered rings (84 pp, J.-J. Delpuech), and azabicyclic systems (35 pp, T. A. Crabb). Barriers to nitrogen inversion are the sole question in strained rings, and Chapter 5 provides a large and useful tabulation of inversion barriers for three- and four-membered rings. The heart of this volume is the long and unusually well-written analysis of conformational dynamics in piperidines in Chapter 7, including chair–chair interconversion, nitrogen inversion, pH effects, and the anomeric effect.

This volume (a second will follow on acyclic nitrogen compounds) is a valuable summary of a field which has developed over several decades. About a quarter of the references are to publications of the last ten years. A majority of the examples in the chapter on spectroscopic methods are acyclic molecules, and there is an unfortunate use of the double-headed resonance arrow to represent equilibria, but otherwise very few errors were noted. Sufficient mathematical detail is given, particularly in the chapters on NMR and piperidines, for a graduate student to comprehend the calculation of rate constants and equilibria from the analytical methods used. This slim volume will provide a very useful source of data about conformational equilibria and rates in nitrogen heterocycles, as well as an understanding of the methods which can be applied to these challenging molecules in which the nitrogen inversion process is superimposed on more common conformational changes.

Richard K. Hill, *University of Georgia*

The Organic Chemistry of Drug Design and Drug Action. By Richard B. Silverman (Northwestern University). Academic Press, Inc.: San Diego, CA. 1992. xiv + 422 pp. $55.00. ISBN 0-12-643730-0.

This book is a tour de force in the title area. The author approaches the broad, interdisciplinary subject of medicinal chemistry from a fundamental perspective, with a felicitous integration of organic chemistry, biochemistry, enzymology, molecular biology, and pharmacology. At every turn, organic chemical principles, concepts, and reactions are plied as tools to dissect, develop, and understand the diverse subfields presented. The book has breadth but is not intended to be comprehensive in its treatment. It is organized into the following chapters: Introduction (Medicinal Chemistry Folklore, Discovery of New Drugs), Drug Discovery, Design and Development, Receptors, Enzymes (Catalytic Receptors), Enzyme Inhibition and Inactivation, DNA, Drug Metabolism, and Prodrugs and Drug Delivery Systems.

The organization of this book is excellent, and the writing style is crisp and captivating. The author has a special sense for communicating sufficient key points in each area without getting bogged down with details. Because the author must effectively instruct on such varied material, comprehensiveness would only destroy the seamless exposition and the flow. In consideration of this chosen approach, the author not only cites many supportive references from the original literature but also furnishes general references on specific topics for further in-depth reading.

In the late 1970s, the book *Essentials of Medicinal Chemistry* (A. Korolkovas and J. H. Burckhalter, John Wiley & Sons, 1976) was instrumental to the entry of many chemists into this area. That book touched on many basics and was an excellent introductory, background source at the time. Although some good comprehensive and more recent texts are available (such as *Comprehensive Medicinal Chemistry* or the classic *Burger's Medicinal Chemistry*), an adequate, up-to-date book for introducing scientists to the field is lacking. The Silverman book nicely satisfies this need.

Moreover, as rational drug design is becoming the essence of medicinal chemistry in the 1990s, it is significant that this book adopts a novel format that focuses on the rational chemical underpinnings to both drug discovery and drug development. It seeks to illuminate the workings of drugs at the molecular level. Thus, this book contrasts with the traditional presentation which is organized around various classes of drugs.

This book would be appropriate for advanced undergraduate students and graduate students and would probably be well suited as a text for course applications, especially at the graduate level. It is strongly recommended to scientists who are seeking an efficient introduction to medicinal chemistry, background in a specific drug principle or category, or a dose of inspiration.

Bruce E. Maryanoff, *R. W. Johnson Pharmaceutical Research Institute*