Book Reviews

NMR Spectroscopy, Second Edition. Basic Principles, Concepts and Applications in Chemistry. Edited by Harald Gunther (University of Siegen). John Wiley & Sons, New York, NY. 1995. xx + 581 pp. 15 × 22.5 cm. ISBN 0-471-95201-X. $39.95.

The text is a clearly written nonmathematical description of NMR spectroscopy that is appropriate for graduate and advanced undergraduate biochemistry, organic, and medicinal chemistry students. The text is also appropriate for those senior scientists, who have been away from NMR for a few years, to use to update themselves on topics such as two-dimensional and gradient-enhanced experiments.

The first six chapters provide an introduction into the basic theory of NMR spectroscopy. In addition, an excellent discussion of the structural features that control the observed values of chemical shift and coupling constants are presented. Once the reader understands the influence of electron density, ring current, and other factors on the observed chemical shift and coupling constant data, he is introduced to the analysis of high-resolution NMR spectra. Using chemical shift and coupling constant data, the reader learns to predict molecular structure. Chapter 6 presents an excellent discussion of the effect of molecular symmetry and chirality on proton spectra, which will be of particular interest to organic chemists. The first six chapters are an excellent reinforcement and expansion of the material, related to NMR, normally presented in an undergraduate organic course.

Chapter 7 introduces the basic theory of Fourier transform NMR spectroscopy. In this chapter, a limited number of vector diagrams are used to describe the effect of rf pulses on the equilibrium magnetization vector **M**. Two-dimensional NMR is discussed in Chapter 8 using vector diagrams and example spectra. The 2D *J*-resolved and COSY experiments are discussed in detail. The product operator formalism is also discussed is sufficient detail for a student to calculate the effect of a simple pulse sequence on the equilibrium magnetization. However, a more detail study of the product operator formalism is required to apply it to the analysis of complex pulse sequences. In this chapter, short introductory discussions of gradient-enhanced and three-dimensional experiments are also presented. The discussion of three-dimensional NMR should be expanded in my opinion to increase its usefulness.

The influence of dynamic effects on NMR spectra is presented in Chapter 9. The topics of kinetics, inversion of configuration, internal rotations, as well as dynamic process in organometallic compounds are discussed. A very good discussion of the effect of temperature on these processes is presented.

Chapter 10 is a collection of short discussions of specific NMR experiments such as rotating frame (ROESY and TOCSY) and solid state experiments. These topics are presented in sufficient detail for the reader to develop a basic understanding of the experiments. Chapter 11 is devoted solely to carbon-13 NMR. Chapter 12 is a collection of 14 appendices, covering such topics as ring current effects, the Bloch equations, and the Hamiltonian operator.

In summary, the text is a very good first book for the study of NMR spectroscopy. It provides the necessary basis of knowledge to build on with further study.

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Modern Countercurrent Chromatography. Edited by Walter D. Conway (State University of New York at Buffalo) and Richard J. Petroski (U.S. Department of Agriculture). American Chemical Society, Washington, DC, 1995. x + 238 pp. 15 × 22.5 cm. ISBN 0-8412-3167-2. $69.95.

This volume of 17 chapters written by different authors is based on a symposium which took place at the 1993 American Chemical Society National Meeting in Chicago. It provides a useful complement of information to the two main textbooks on the newer techniques of countercurrent chromatography (CCC): *Countercurrent Chromatography—Theory and Practice* by N. B. Mandava and Y. Ito and *Countercurrent Chromatography—Apparatus, Theory and Applications* by W. D. Conway.

The first chapter of the book is a brief summary of the apparatus, theory, and advantages of CCC. The remainder is divided into three parts, starting with some theoretical studies, then describing certain applications, and finishing with a very large section on pH-zone-refining CCC. This latter technique, which has only recently been introduced, allows increased sample size (by at least 10-fold, compared to conventional CCC) for ionizable solutes, without increasing the dimensions of the apparatus.

In the theoretical part, Chapter 2 emphasizes the importance of phase density difference for stationary phase retention, while Chapter 3 investigates the efficiency of CCC separations. Chapter 4 is a rather specialized discussion on the different parameters associated with the cross-axis coil planet centrifuge, and Chapter 5 describes some work on the optimization of conditions for a Sanki centrifugal partition chromatograph.

The section on applications contains a relatively small selection of short articles, the subject matter of which ranges from the separation of plant constituents to the purification of synthetic peptides and the isolation of lipoprotein fractions from human serum. There is also a chapter on the optimization of solvent systems by the use of TLC and distribution of the sample between the two phases of the solvent system in question. This is an aspect which is essential for obtaining good separa-

tions. Chapter 12 discusses the interfacing of CCC instruments with a mass spectrometer. This detection method eliminates problems involving base-line noise and weak chromophores. Applications with peptides and erythromycins are presented, using an analytical CCC instrument, a moving belt interface, and FAB ionization. The section is rounded off in Chapter 13 with a description of the measurement of partition coefficients.

The rest of the book is comprised of an introduction to pH-zone-refining CCC. There is a good description of this technique, which resembles displacement chromatography and is suitable for ionizable compounds. Few applications have been published up to the present time, but gram quantities can be separated in a matter of hours. A model for predicting and optimizing separations is presented in Chapter 15, and applications are described with reference to the dye tetrachlorofluorescein in Chapters 16 and 17. The important contribution of Y. Ito to the development of zone-refining CCC is underlined by the fact that he is coauthor of all four chapters.

On the whole, this is a well-written and well-presented book. There are one or two minor anomalies (such as the shading of bars in figure 4, p 25), and some parts will probably only be appreciated by the really experienced users of CCC. However, Conway and Petroski have produced a volume which will be of value to anyone currently involved in CCC liquid−liquid separation techniques and especially to researchers who wish to find out more about the pH-zone-refining method.

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Anthracycline Antibiotics. New Analogues, Methods of Delivery and Mechanisms of Action. Edited by Waldemar Priebe (M. D. Anderson Cancer Center, The University of Texas). American Chemical Society, Washington, DC. 1995. xi + 332 pp. 15 × 22.5. $99.95. ISBN 0-8412-3040-4.

As the editor states in the preface, doxorubicin is a *front line chemotherapeutic agent in the treatment of numerous cancers*. But the clinically used anthracycline antibiotics have certain limitations: they are toxic and have a narrow spectrum, and tumors which are initially sensitive often develop resistance. Discovery scientists still use the validated approach of trying to perfect the imperfect and to understand the almost impossibly complicated; the anthracyclines are ideal target drugs. This book is an excellent and comprehensive selection of various chemical and biological approaches to solving these problems and was created from talks given at an American Chemical Society symposium.

The collection begins with a discussion on unresolved SAR issues, and results using the National Cancer Institute's 60 human tumor cell line panel are presented which highlight more than one mechanism of action for anthracyclines. There is a large section on synthetic approaches, including the preparation of non-cross-resistant anthracyclines and the synthesis of analogues of anthracyclines and glycosylated products with fluorine on the A or D ring and the side chain, and in a related report, the preparation of daunorubicin and doxorubicin analogues with the fluorine at position 2 of the sugar is discussed. There is a thorough account of experiments addressing the chemistry of oxomorpholinyl radicals and anthracycline redox chemistry. 3′-Morpholino derivatives are further discussed by Suarato *et al*. who also address the effects of this substitution on multiple drug-resistant tumor cells. The synthesis of linked anthracyclines is discussed with comments on chemistry and biological activity.

The mechanism of action of anthracyclines is presented in a number of articles: experiments addressing the recognition of DNA by daunorubicin and the specific binding of the two molecules are discussed in a chapter by Chiares, and this is further explored by Wang *et al*. who present a wealth of complex molecular detail. The significance of DNA toposiomerases and the effect of anthracyclines on these enzymes is discussed by Pommier, again with an excellent bibliography, and this is followed by a chapter on antihelicase activity. The next two articles address the importance of the cell membrane in the action of anthracycline, and these are followed by a discussion on the protein in resistant cells which transports these drugs. The cardiotoxic effects are covered in the two penultimate chapters and include data from experiments using an EDTA analog, as well as a much wider review of the field. The final chapter covers the use of drug carriers to help overcome the toxic effects and to improve the therapeutic index.

Clearly, drug discovery and development is not simple. Most of the talks included in this book were authored by academic scientists, and it would be interesting to know the amount of collaboration between the groups with innovative chemistry and novel analogues and those with innovative and different bioassays. By using as many pharmacological and chemical combinations as possible, perhaps some of the problems associated with this group of compounds can be resolved even more efficiently. This is possibly recognized by some of the authors; *e.g.*, Guidi *et al*. state that "published data are not adequate for the comparative evaluation of potential anti tumor efficacy of different compounds."

This collection should be of interest to those involved in drug discovery and development, especially workers in anticancer research. Academic groups, particularly medicinal chemistry and natural products scientists and their students, would predictably find this collection very interesting and of great utility. $100 per copy seems a reasonable price.

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Theoretical & Physical Principles of Organic Reactivity. Edited by Addy Pross (Ben-Gurion University of the Negev). John Wiley & Sons, New York, NY. 1995. xv + 294 pp. 15.5 × 23 cm. ISBN 0-471-55599-1. $59.95.

In a sense, this book is as much philosophical as it is scientific in its approach to organic reactivity. The book is unique in that it presents organic reactivity from an entirely different perspective via the use of valence bond theory and electronic configurations, i.e., the valence bond configuration-mixing model or so-called curve-crossing model. According to this approach, a reaction coordinate diagram is constructed on the basis of an avoided crossing of the reactant (Ψ_R) and product (Ψ_P) configuration curves. Conversion from Ψ_R to Ψ_P can occur via either a single electron shift or a spin shift. Although this approach may at first seem "alien" to many readers (and certainly this review does not do the theory justice), the important point is that these concepts are developed extremely well in the text. Moreover, these concepts are nicely illustrated using common organic reactions such as S_N2, S_N1, and radical, pericyclic, and numerous other organic transformations.

The first section of the book (Chapters 1−4) deals with theoretical principles. Chapter 1 is mostly philosophical, and it provides a brief overview and comparison of MO theory and the valence bond approach. The second chapter provides an introduction to MO theory, dealing with topics such as the LCAO approach, variation principle, Hückel theory, etc. The third chapter delves into qualitative valence bond theory, introducing valence-bond configuration mixing diagrams and the principles (rules) for constructing them. Chapter 4 details the actual construction of free energy diagrams.

Classical physical organic principles are covered in the second major section of the book (Chapters 5−8). Chapter 5 provides a brief introduction to topics such as chemical kinetics, reaction mechanisms, the Hammond Postulate, the Bell−Evans−Polanyi principle, 3-D potential energy diagrams, Marcus theory, and the reactivity−selectivity principle. These different approaches are nicely compared and interrelated. Chapter 6 deals with linear free energy relationships (e.g., the Hammett and Bronsted equations). Ionization potential, electron affinity, redox potentials, charge transfer complexes, etc. are introduced and discussed in Chapter 7. (This order of presentation was somewhat curious in that IP and EA were used in earlier chapters of the book dealing with valence bond theory, MO theory, etc.) Solvent effects on reactivity are discussed in Chapter 8. Overall, this section provides a good overview and would be especially interesting and informative to an individual who has had some experience with these topics. However, because of its brevity, it is unlikely that this section would be adequate for a "first-time" exposure to fundamental physical organic chemistry.

The final section of the book (Chapters 9 and 10) applies the concepts developed in earlier sections to specific processes such as nucleophilic substitution, electrophilic aromatic substitution, radical reactions, and pericyclic reactions in the context of the curve-crossing model.

The advantage of the valence bond approach (vs. MO theory) is that it is qualitative. The mathematical basis of the theory is de-emphasized, and the author makes the point that different valence bond configurations can be thought of in terms of resonance structures. In addition to providing a satisfying (and alternative) rationalization to common organic reactions, this approach to reactivity also provides a unifying basis for understanding seemingly disparate processes (e.g., the relationship between polar and single electron transfer processes). According to the preface, the book is intended as a text "for advanced undergraduate and graduate students as well as researchers in organic chemistry." While the book is excellent reading (and would likely be appreciated by advanced undergraduates and graduate students), by itself, the book would not suffice as an introductory physical organic text. The sections dealing with MO theory, kinetics, thermodynamics, linear free energy relationships, etc. are simply not comprehensive or detailed enough to provide an adequate introduction to classical physical organic chemistry. In addition, there are no problems in the book which would reinforce these concepts for a beginning student. Consequently, as a textbook it would best be used in the context of supplemental reading for an introductory physical organic chemistry course or perhaps as a text for a special topics course. For the more advanced reader with an interest in organic reactivity, I would highly recommend this book because of its unique perspective.

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