

Additions and Corrections

Analysis of the Structure and Stability of a Backbone-Modified Oligonucleotide: Implications for Avoiding Product Inhibition in Catalytic Template-Directed Synthesis [*J. Am. Chem. Soc.* **1998**, *120*, 3019–3031]. PEIZHI LUO, JOHN C. LEITZEL, ZHENG-YUN J. ZHAN, AND DAVID G. LYNN*

Page 3022: Figure 2 and the legend were incorrect as published. The correct Figure 2 and its legend are shown below. The data were fit as described in the text.

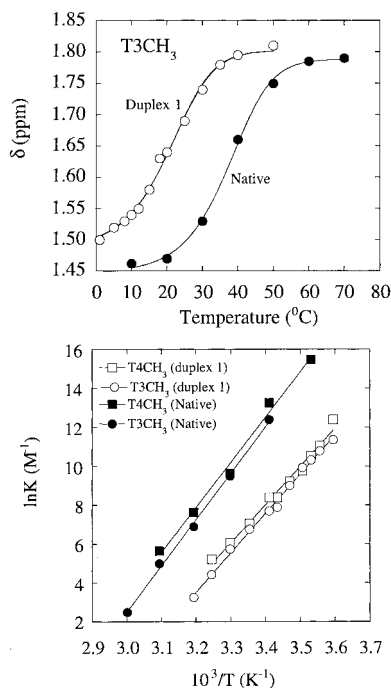


Figure 2. (a, top). The chemical shift change of the T3 methyl groups in the native (●) and the modified duplex 1 (○) as a function of temperature. The curves through data points are fit to eq 5 using a nonlinear least-squares method. Two lines through each melting profile were fit with floating or fixed base line parameters in δ_s and δ_d . The difference in T_m between native and modified duplex 1 is ca. 17 $^{\circ}\text{C}$ in 2 mM solutions in D_2O , 100 mM NaCl, 10 mM NaH_2PO_2 , 2 mM NaN_3 , pH6 buffer. (b, bottom). The van't Hoff plots of the thermal unfolding profiles for the native (solid symbols) and modified duplex 1 (open symbols). Note that van't Hoff plots of T3CH₃ and T4CH₃ from the same duplex are very similar. Therefore, the thermodynamic parameters derived from these two probes of each duplex are in good agreement (see Table 1).

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Book Reviews

Reductions by the Alumino- and Borohydrides in Organic Synthesis. Second Edition. By Jacqueline Seyden-Penne. Wiley-VCH: New York, Chichester, Weinheim, Singapore, and Toronto. 1997. xiv + 224 pp. \$74.95. ISBN 0-471-19036-5.

The present monograph, which encompasses the reduction of organic compounds by a gamut of simple and complex boron and aluminum hydrides, is the second edition of an authoritative treatment first published in English in 1991. Its stated purpose is to offer guidance to the chemist seeking to apply such reagents for selective reductions

in organic synthesis. The author has sought to accomplish this goal by emphasizing the following aspects: (1) the locoselectivity of the reductant (which locus or functional group out of several is preferentially attacked); (2) the degree or stage of reduction to which a functional group is reduced; (3) the regio- and stereoselectivity of such reductions; and (4) the strategies of asymmetric reduction. It is stressed that "all these hydrides are easy to use, and the book is organized so that the reader can match the appropriate reagent to a given transformation".

What follows in this organization is first a chapter which describes

the properties and reducing characteristics of 21 metal hydrides in a summary fashion, as well as giving a listing of 10 metal hydride-transition metal salt combinations often used as reducing agents. Then in the succeeding four chapters the reductions of individual functional groups, presented in 20 principal categories, are exemplified through equations of successful applications of these metal hydride reductants. Copious literature references (~1000), some extending into 1996, guide the interested reader to the original experimental procedures. In the discussion accompanying these numerous examples the various kinds and degrees of selective reduction observed are treated largely on an ad hoc basis. Only for the stereoselective reduction of aldehydes and ketones is a more general mechanistic analysis considered, wherein a comparison of the relative merits of the Felkin-Ank and the Houk models is made. Finally, about 10 pages of synoptic tables are included, which summarize by general formula the various ways a given reduced functionality, such as an alcohol, for example, can be derived by metal hydride reduction from a diverse array of starting materials. A brief but useful index of reductants and reducible substrates completes this treatment.

In compiling this summary of a huge amount of experimental information, the author has greatly alleviated the organic chemist's task of identifying the most appropriate metal hydride and the most promising experimental conditions to achieve a particular reduction in synthesis. Although the author is to be congratulated for this achievement, such a treatment has serious limitations and liabilities that both curtail its usefulness and conceal the experimental hazards posed by these metal hydrides. In describing the characteristics of these hydrides in Chapter 1, the author occasionally mentions the moisture sensitivity of the hydride (as with LAH, Red-H, or AlH_3), but nowhere is mentioned the necessity of working with the most reactive hydrides under nitrogen or argon. In the page devoted to DIBALH, neither its explosive reaction with water nor its pyrophoric reaction in air is even alluded to. The mandatory techniques for manipulating, analyzing, or ultimately hydrolyzing such hydrides are not explicitly referenced. This lack of information is accompanied by the proclamation that "these hydrides are easy to use".

The second unsatisfying aspect of this monograph is the wholly empirical recitation of many experimental observations: the factual outcome of which products are generated under what experimental conditions. Any mechanistic considerations of the primary chemical process underlying all these reductions, namely, hydrometalation, are totally lacking, despite the abundant mechanistic evidence that has been published over the last 25 years on the interaction of boron, aluminum, and transition metal hydrides with unsaturated organic substrates, and critically reviewed in the 1982 and 1995 editions of *Comprehensive Organometallic Chemistry* and the 1991 edition of *Comprehensive Organic Synthesis*. Any active practitioner of modern organic synthesis, with whom this reviewer is acquainted, would not choose a particular reagent for a critical chemical transformation without making a searching analysis of the known mechanistic features of the reaction. Since the days of R. B. Woodward the skillful applications of reaction mechanistic insights have proved to be the key to achieving masterly stereoselective total syntheses of formidable complexity.

Because of these two failings, this reviewer could recommend this monograph only to chemists seeking ready-made procedures to meet their needs for individual reductions that they might be satisfied with achieving empirically and who do not wish to deal with mechanistic principles in order to maximize the reduction's selectivity. But such chemists who are not completely familiar with the physical and chemical properties of these hazardous hydrides surely deserve explicit warning concerning the toxic, pyrophoric, and explosively hydrolyzable hazards of these reagents that the author is recommending for various uses in organic synthesis. Any such warning being lacking in this printing, this reviewer urges the author and the publisher to prepare an addendum page bearing appropriate precautions concerning the hazards attendant upon manipulating such reagents and giving literature references to

proper techniques. They should then take steps to provide every copy of this monograph, purchased or not, with such a caveat.

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Purinergic Approaches in Experimental Therapeutics. Edited by Kenneth A. Jacobson (National Institute of Diabetes) and Michael F. Jarvis (Abbott Laboratories). Wiley/VCH: New York. 1997. xiv + 581 pp. \$89.95. ISBN 0-471-114071-6.

This book tackles the difficult task of bringing together under a single cover the present and future potential for purine-based drugs in the treatment of a broad range of human diseases. This is no mean feat. The research literature on the role of extracellular purines has expanded almost exponentially over the last few years, and there are now few mammalian tissues that are unaffected by either adenosine or ATP. Most of this literature has focused on dissecting the diverse physiological roles of purines, identifying receptors and their tissue distribution, and defining the pharmacological status of a host of purinergic receptor agonists and antagonists. Clearly the time has come for an integrated text that focuses attention on the vast clinical potential for purine-based drugs that specifically target either purinergic receptors or metabolic pathways. The editors of this text, K. A. Jacobson and M. F. Jarvis have been in the forefront of this field for many years and have assembled 53 contributors representing some of the top laboratories in the world. The book contains 28 chapters and is neatly organized into four parts. Part I, Historical Perspective (M. Williams and G. Burnstock), highlights the central theme of the book. It also provides one of the best and, with over 160 references, complete overviews of the purine field that I have seen in recent years. Part II, Molecular Pharmacology, includes three chapters that review the current status of adenosine and P2-purinergic receptors and their signal transduction pathways (G. Stiles, T. Filtz et al., J. Linden). A separate chapter (J. D. Geiger et al.) summarizes the current basic research in adenosine transport and metabolism and at the same time presents possible strategies for regulating tissue levels of adenosine to therapeutic levels. Part III, Medicinal Chemistry, includes a chapter summarizing the comprehensive structure-function approach that has been used in the design of purinoceptor agonists and antagonists (K. Jacobson and A. M. van Rhee) as well as inhibitors and modulators of adenosine metabolism (A. IJzerman and N. van der Wenden). What I especially liked in these two chapters and in the book in general is the attention given to the figures illustrating the important chemical structures. The last and largest section of the book, Part IV, Therapeutic Implications, comprises nearly two-thirds of the book and addresses the central theme of the book. These chapters discuss the possible therapeutic targeting of purinergic receptors in cardioprotection and cardiovascular functions (G.-S. Liu et al., C. Kennedy et al., L. Belardinelli et al., P. Leff et al.), in pulmonary (J. Fedan), renal (E. Jackson), and gastrointestinal (F. Christofi and M. Cook) functions, in diabetes (M.-M. Loubatières-Mariani et al.), and in inflammation (B. Cronstein, S. Rosengren and G. Firestein, M. A. Jacobson and T. Bai). Purine nucleosides (adenosine) and nucleotides (ATP) are now firmly established in the research literature as neurotransmitters and neuromodulators, and not surprisingly, several chapters are devoted to the nervous system. More recently, purines have been implicated in pain transmission, and the possibility that purine-based drugs may represent a new generation of analgesics and anesthetics is an exciting development that is reviewed in several chapters (A. Fukunaga, J. Sawynok). Additional sections with extensive and recent literature focus on purines in neurodegeneration and development (M. Abbraccio, S. Rivkees), epilepsy (L. Knutsen), and ischemia (T. Dunwiddie and B. Fredholm, D. von Lubitz). Adenosine also affects behavior and psychomotor activity (M. Jarvis) and is involved in sleep disorders (D. Carley and M. Radulovacki). The anticancer activity of ATP has been recognized for some time, and ATP is currently under clinical trials for the treatment of advanced stage lung cancer (E. Rapaport).

This book primarily targets researchers in all areas of basic and clinical research on purines and is an essential addition to their collection. For the uninitiated with only a passing interest in the field,

it is challenging but rewarding reading. Nevertheless, this text should also find a broad audience among those in other areas of pharmacology who are looking for a highly readable up-to-date review of the field. I would also recommend it to the medicinal chemist who might find the diverse medical relevance of purines an irresistible challenge. It is a text that is long overdue. At a hefty 581 pages of fairly small print, *Purineric Approaches in Experimental Therapeutics* is solidly packed with information and is a steal at any price.

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Handbook of Instrumental Techniques for Analytical Chemistry. Edited by Frank A. Settle. Prentice Hall: Upper Saddle River. 1997. xxi + 995 pp. ISBN 0-13-177338-0.

The book entitled *Handbook of Instrumental Techniques for Analytical Chemistry* has for a general goal to provide scientists and engineers from many disciplines with an easily understood reference to current established techniques of chemical analysis. Substantial efforts have been invested to standardize the presentation of each technique and to provide simple concepts of what the techniques can yield in terms of analytical results, general boundaries of applicability, information as to instrument manufacturers, instrument pricing, and relevant literature references that can provide further details to the reader.

The book is structured in eight sections, each dealing with a particular topic, that seek to provide a general overview of current techniques involved in modern chemical analysis. Sections deal with (i) sample preparation, (ii) separation methods, (iii) qualitative optical spectroscopy, (iv) quantitative optical spectroscopy, (v) mass spectrometry, (vi) electroanalytical techniques of analysis, (vii) microscopic and surface analysis methods, and (viii) polymer analysis. Within each section and each technique, a standardized format has been used in order to facilitate understanding of the basic principles of the method, the instrumentation required, the analytical information it can provide, its fields of applications, manufacturers of the instruments, and pertinent references on the techniques themselves.

In a way, the objectives of the book have been achieved in the sense that it provides an inventory of current analytical techniques that can be used to solve analytical problems in many areas. Furthermore, adequate information is provided in terms of what the techniques can generally offer and where instruments or accessories can be purchased. The information and technical content have been kept to a low level that can be easily understood by almost anybody with some scientific background. Thus, the book provides general analytical information that is easily accessible.

The strengths of the book also reveal its weaknesses. Although there is a need for this type of a handbook, the simplicity of understanding that has been emphasized can also represent a deficiency. Throughout the book, the information that is presented can be deceptive. The chapters presented are, on average, so general that it becomes difficult to get the useful information that may be required and that one would expect to be able to find in a handbook. The book is closer to a "repertoire" of analytical techniques than it is to a handbook in which specific details are usually found. In many chapters, the information on the techniques themselves is so minimal that the reader is referred to textbooks or articles in the literature. Some of the chapters provide information at a reasonable level. Thus, the value of the handbook is essentially lost because the reader has to consult other sources on simple matters which takes time. Basic information as to the principles underlying the techniques, the instrumentation, analytical parameters, and conditions of use are described so vaguely that the resulting effect is to provide information that is commonly known to most scientists and the few additional details that may be helpful are absent.

The desire to cover a wide range of topics in such a short fashion, which has governed the authors, eventually defeats the purpose of the book and reduces its value to the chemical community. There are many instances where oversimplification leads to a void of useful information. Either there is a lack in basic principles or in instrumentation or other elements that would be useful to the reader to order to rapidly obtain the information that is required to solve the problem at hand. References in a handbook should be given to provide detailed information, but it is essential that enough information be provided in

order for the reader to access sufficient primary information on the subject. It is the role of a handbook to condense information for easy and rapid access.

In summary, this book has achieved its goal to provide a repertoire of analytical techniques that can be used to solve analytical problems. However, in trying to oversimplify the technical aspects, it has sacrificed the useful information that one usually seeks in a handbook that is supposed to condense the essential information, not eliminate it or give reference to it elsewhere. Most people involved in chemical analysis from any standpoint usually possess the information given in this book and seek more details that will enable them to profit from a reference work. The book is short on that score because it does not provide sufficient information to really be helpful as a handbook. It appears more as an introduction to a handbook than a handbook itself as we traditionally know them and use them. It is a real challenge to cover many complex topics in such a short number of pages, but it is also important by reducing the information not to omit things that are essential to the usefulness of the work. The simplified and qualitative nature of the book, which is its strength for nonchemists, appears to be a strong weakness when it is considered as a handbook or a reference book for analytical chemistry. Nevertheless, it is an excellent "repertoire" of analytical techniques for people that are very remote from the field.

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Nuclear Magnetic Resonance Spectroscopy in Environmental Chemistry. Edited by Mark A. Nanny (University of Oklahoma), Roger A. Minear (University of Illinois at Urbana-Champaign), and Jerry A. Leenheer (U.S. Geological Survey). Oxford University Press: New York. 1997. viii + 326 pp. \$65.00. ISBN 0-19-509751-3.

Advances in NMR instrumentation, e.g., the introduction of stronger magnets, the development of new pulse techniques, and the building of better probes, have increased the range of applications and accessible nuclei available for study by high-field NMR. The text *NMR Spectroscopy in Environmental Chemistry* assesses the impact of the aforementioned developments on studies involving the transport and fate of chemicals in the environment. Three major application areas, demonstrating the diversity and breadth of environmental research problems that NMR spectroscopy can address, are highlighted in the text. These areas are (1) the chemical and physical interaction of contaminants with complex environmental matrixes, (2) the chemistry of important environmental species in solution, colloidal, and condensed phases, and (3) the characterization of natural organic matter.

The book is divided into three sections. The first section entitled Contaminant Interactions examines the noncovalent interactions of organic pollutants with humic and fulvic materials. These interactions are very important because they increase the apparent solubility of hydrophobic chemicals in soil and sediment pore water. Using standard NMR techniques, information about these interactions can be obtained for heterogeneous and complex environmental systems. For example, Bortiajtnski (Chapter 2) studied these interactions by measuring the changes in T_1 of the ^{13}C nucleus as phenol interacted with soluble humic material. Anderson (Chapter 3) took advantage of changes in chemical shifts and line widths to study the interaction of pesticides with soluble humic acids. Herbert and Bertsch (Chapter 4) used ^{19}F NMR to examine the interaction of nonionic solutes with surfactants and humic acids and compared these results with those from a solvent polarity study to obtain an indication of the association. The NMR sorption studies described in the text required the labeling of the sorbate molecule with NMR sensitive nuclei at or near the chemically active site.

The second section of the text entitled Solution and Condensed Phase Characterization presents studies that examine the chemistry of environmentally important species in solution, colloidal media, and condensed phases. The focus of this section is the chemistry and speciation of Al in the environment. The incentive to study Al can be attributed to concerns raised about the effects of dissolved aluminum on the health of plants, animals, and man. Using ^{27}Al NMR, Vivit (Chapter 8) and Thomas (Chapter 9) examined aluminum chemistry in dilute aqueous solution. Laboriau (Chapter 10) describes an NMR-

based approach to understand the interaction of aluminum ions with smectite clay. The studies described by Vivit, Thomas, and Laboriau have only recently become possible because of the introduction of probes fabricated with aluminum-free material, which reduces baseline roll due to acoustic ringing.

The third section of the text is entitled Nutrient and Natural Organic Matter (NOM) Cycling in the Environment. It focuses on research exploring phosphorus and nitrogen cycling in the environment, using either solid-state or solution NMR to investigate the structure of NOM under nondegradative conditions. Most of the NOM studies reported in this text utilized ^{31}P or ^{15}N NMR, as organic oxygen or sulfur is not amenable to either solution or solid-state NMR. The studies on NOM research presented in this section include P in organic wastes and fertilizers, the chemical characterization of nitrogen in plant composts and humic materials, and ^{13}C CP/MAS NMR studies of organic carbon in aquatic sediments and soil with low carbon content.

Each section of the text contains an overview chapter, which provides the reader with the necessary background to understand how NMR has advanced research in a particular area. The overview chapters promote continuity, which is often a problem with multi-authored texts. The final chapter of this book summarizes a panel discussion held at the end of the symposium NMR Spectroscopy in Environmental Science and Technology that was presented at the National ACS Meeting in Denver, Colorado, in 1993. Evidently, the symposium and panel discussion played a pivotal role in the development of this text. My overall opinion of the text is favorable. The references in the text are current and complete. The scientific level of the text is high. Clearly, this book will be a useful reference for chemists who require a basic knowledge of NMR for environmental systems or environmental engineers who seek to incorporate NMR techniques into their research.

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X-Ray Charge Densities and Chemical Bonding. IUCr Texts on Crystallography 4. By Philip Coppens (State University of New York at Buffalo). Oxford University Press: New York. 1997. xiii + 358 p. \$85.00. ISBN 0-19-509823-4.

This book has been eagerly awaited by those active in the field specified in the title. The author is well-known for his seminal contributions to the subject as well as his clear, lucid, and pedagogical lectures and writings. This book fulfills that expectation. But it is not just a monograph for those in the field. I would recommend it as a textbook for a graduate level course as well as supplemental reading for an undergraduate course in crystallography. Some exercises are included as well as a large number of references. Importantly it can be used for self-study by nonspecialists, e.g., a chemist who wants to be able to use the concepts and results from electron density studies in their own work.

But what is meant by X-ray charge densities? One is aware that in crystallographic structure determinations the scattered data are fit in a least-squares sense to a superposition of spherical atomic form factors situated at the atomic centers. The residuals are the remaining electron density as well as the errors. As quoted in the preface, the late Fred Hirshfeld said, "An accurate set of nuclear coordinates and a detailed map of the electron density can be obtained, by X-ray diffraction, only jointly and simultaneously, never separately or independently."

The book contains 12 chapters in a logical order from the fundamentals to applications to specific types of systems in the final three chapters, i.e., transition metal compounds, extended solids, and molecular crystals. The first chapter goes into the theory of scattering of X-rays and neutrons. The second chapter discusses the important topic of the effect of thermal vibrations on the intensities of the diffracted beams including anharmonic effects. In the third chapter the relationship between the chemical bonding and the scattering formalism is presented. The breakdown noted above in the independent-

atom model for the electron density (i.e., superposition of spherical atoms) is explored, and the improved scattering models needed are given. Included are multipolar methods and the κ refinements.

In chapters four and five least-squares and Fourier methods are given as well as the recent technique of maximum entropy enhancement. However, little mention is made of the latest developments in density matrix refinements. The next three chapters contain methods for spatial partitioning and topological analysis of the charge density as well as the electrostatic moments and electrostatic potential. In Chapter 9 the role of the charge density in the cohesive energy of crystals is examined.

The author has been very careful in the presentation of the material. For example, he cautions the reader in presenting the Gram-Charlier expansion that the Hermite polynomials employed are not those familiar from the quantum mechanical treatment of the harmonic oscillator. The latter involve the n th-order derivative of $\exp(-x^2)$; the former, used mostly in statistics, involve the n th-order derivative of $\exp(-1/2x^2)$ and are sometimes given the symbol $He_n(x)$ to avoid confusion with the latter, denoted by $H_n(x)$.

Many concepts from quantum chemistry including density functional theory are introduced and used in the book. However, I would suggest that in the next edition an appendix be added in which some of the language and methods of modern computational chemistry are mentioned. This would include basis set nomenclature and quality descriptors. Another useful appendix would provide information about the needed computer programs and their sources.

As expected there are some typographical errors which do not detract from one's progress through the book. Gremlins have left their tracks in eq 1.50 and Figures 11.10, L.1, and L.2. The caption of Figure 1.7 is confusing because this figure is a plot of f' vs f'' . One thing that I like to check is how a book treats a fundamental theorem in Hartree-Fock theory. In one line on p 186, it is called Koopman's theorem; two lines later it is correctly named Koopmans' theorem.

This book is a worthy member of the series of books sponsored by the International Union of Crystallography (IUCr). It opens up this area to a wider audience. Not only is it valuable to the specialist as a reference but it can help refresh one's mind on the technical aspects of the subject.

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Progress in the Chemistry of Organic Natural Products, #71. Edited by W. Herz (Florida State University), G. W. Kirby (University of Glasgow), R. E. Moore (University of Hawaii), W. Steglich (Universität München), and Ch. Tamm (Universität Basel). Springer: Wein, Germany. 1997. \$219.00. ix + 358 pp. ISBN 3-211-82850-8.

This is the current volume of a long-standing series on the chemistry of organic natural products. This volume masterfully maintains the tradition of the series by presenting its subject matter in a clear, organized, thorough, and visually appealing style. There are three chapters of varying lengths on insect neuropeptides by G. Gäde, sesquiterpenes from *Thapsia* species by S. B. Christensen, A. Andersen, and U. W. Smitt, and pregnane glycosides by D. Deepak, S. Srivastav, and A. Khare. Each review is thorough, accurate, and carefully referenced, covering isolation, structure elucidation, and biological activity. References are current through 1995, and there are detailed subject and author indices. This book will be an essential addition to the bookshelves of all chemical libraries, and will be an invaluable reference source for workers interested in natural products chemistry.

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