Book Reviews

Chemometric Methods in Molecular Design. Methods and Principles in Medicinal Chemistry, Volume 2. Edited by Han van de Waterbend (Hoffman-LaRoche Ltd., Basil, Switzerland). VCH: New York. 1995. xix + 359 pp. $110. ISBN 3-527-30044-9.

This volume is divided into four major sections: molecular concepts, experimental design, multivariate data analysis, and validation. There are two papers in the section on molecular concepts which deal with molecular descriptors. A relatively complete discussion of traditional two-dimensional (2D) descriptors and graph-based descriptors is given. Kier includes an overview of the development and application of atomic field indices. The only mention of three dimensional (3D) descriptors is molecular volumes and surface areas by Jurs and colleagues.

There are four papers in the section on experimental design. Three of the papers have sections on design strategies which, in composite, are quite insightful and useful. The paper by van de Waterbend and colleagues mentions how principles of experimental design might be applied in the generation of molecular diversity and in combinatorial chemistry.

The larger part of this volume focuses upon multivariate data analysis of chemical and biological data. There are nine papers in this section of the volume. At first thought one might wonder how much new and novel information might be given in this seemingly well-discussed topic area. Yet, a major strength of this volume is in both the quantity and quality of new ideas presented in the various papers. DeVillers and Chessel, for example, discuss the graphical representations of data analysis in terms of aiding the dissemination of information in medicinal chemistry. Lewi describes how spectral mapping analysis is particularly well-suited to extract information on drug action specificity. Ford and Salt also approach the problem of analyzing multiple biological responses from each of a set of compounds in terms of generating structure−activity models. They suggest the use of canonical correlation analysis and nicely define and apply this formalism.

Validation of QSAR results is the final section in this volume. While there are only two papers, both with Wold as a coauthor, on this timely topic, several useful validation procedures, strategies, and ideas are given. The Four Tools for Model Validation are particularly instructive and useful.

This volume should be very useful to researchers in chemometrics, molecular design, and molecular diversity. I am not sure that newcomers to any of the fields mentioned above will find this volume straightforward and intuitive. The papers are oriented more toward the experienced practitioner. 3D-QSAR does not receive too much attention in this volume although many of the techniques, approaches, strategies, and concepts given can be readily tailored to 3D-QSAR applications. Overall, this volume is composed of well-written, informative, and state-of-the-field papers, and it will be a valuable resource wherever chemometrics impacts a problem in chemical research.

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JA9551998

Organomagnesium Methods in Organic Synthesis. By Basil J. Wakefield (University of Salford, U.K.). Academic Press: London. 1995. xvi + 249 pp. $50.00. ISBN 0-12-730945-4.

This book, like others in the *Best Synthetic Methods* series, is a compact and practical summary and guide to the application of an area of organic chemistry to the craft of organic synthesis. Since the field of organomagnesium chemistry is relatively mature, the emphasis is not on introducing or promoting the use of newer chemistry but on updating, summarizing, and making accessible the older.

The book begins with a very brief introduction (Chapter 1), discussion of a number of general considerations (Chapter 2), and survey of methods for preparation of organomagnesium compounds (Chapter 3). The bulk of the book consists of 13 subsequent chapters, each devoted to the reactions with various functional groups or the formation of particular carbon−heteroatom bonds. Each chapter includes discussions and illustrations of the reactions and their variants, referenced tables of examples, and experimental procedures for representative preparations. References are plentiful and many are quite recent. Generally, the discussion is informed and critical. The relative effectiveness of magnesium and lithium reagents is frequently compared. Mechanistic explanations are minimal; the emphasis is strongly on the practical application. As such, the book should prove a valuable resource to the chemist considering the appropriateness of an organomagnesium reaction in a synthetic application or wanting models or helpful tips for the laboratory.

Although the author has been quite successful in achieving his stated goals, this reviewer did note a number of details which might have made the book more useful or convenient. Some examples and procedures appear to be relatively exotic or atypical, without appropriate caveats, and so may be poor models. The tabulated examples are drawn mostly from *Organic Syntheses* rather from the primary research literature. More mechanistic commentary could provide useful guidance for synthesis; a particular instance is in substitution reactions at carbon, in which halides or other leaving groups are displaced. Answers to some unanswered questions (if they do indeed exist) would be helpful: What is the stoichiometry necessary in forming R_2Mg compounds by precipitation with dioxane? In routine Grignard reactions, should the Grignard reagent be separated before use from excess magnesium (or should an excess be used)? Why use ammonium chloride; or what other work-up alternatives exist? Commercial sources of Grignard reagents are given, but it might also be helpful to include sources of magnesium apart from the usual "for Grignard reagents" grade. Distillation from lithium aluminum hydride is listed as a technique for drying THF, but without warning of the potential dangers from decomposition of the hydride. A minor annoyance appears in the reference lists; previously cited references appear as, for example, "see section 2.1, Ref [6]", although this infrequently saves a line of text. Finally, there are a number of typographical errors, the older-style lower case "liter" abbreviation is used, and in at least one location, there is confusion in the meaning of the "M" symbol for concentration or molar scale.

In summary, despite minor shortcomings, this is a useful book, which responds to a real need. In these days of proliferating literature, the student or practicing chemist who has access to this and similar references will have the edge.

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JA955313M