Organic Process Research & Development **2003**, *7*, 609−612

Book Reviews *

On-line LC NMR and Related Techniques. Edited by Klaus Albert. John Wiley & Sons: New York. 2002. 290 pp. £70.00/EUR115.50/$105. ISBN 0-471-49649-9.

This book offers a comprehensive review of the theory behind LC−NMR and related techniques, and describes practical applications of these techniques. Each chapter has been compiled by experts in the different fields, with 18 authors contributing. The book is well referenced, with literature coverage to 2001, and thus provides up-to-date information on the theory and practical applications of LC−MR.

The book is divided into eight chapters, with the first two chapters dealing with the theory and practical use of LC−NMR. In chapter one, Klaus Albert, the editor, provides substantial detail concerning theoretical and experimental aspects. This encompasses design of continuous-flow NMR probes and other practical considerations, which include a discussion of the advantages and disadvantages associated with solvent signal suppression. Chapter two deals with automation of LC−NMR. The practical use of LC−NMR and LC−NMR/MS is discussed as is the different working modes, for example, on-flow, direct stop-flow, and loop storage/loop transfer and measurement procedures.

The next four chapters cover various applications of LC−NMR ranging from biomedical and pharmaceutical applications to drug metabolism studies, natural product analysis, and even environmental analysis. Throughout the applications chapters, practical advice is given and detailed graphical illustrations are provided, of both experimental setups, including typical chromatograms and NMR spectra. The book is primarily aimed at providing a detailed review of successful applications of LC−NMR to date, whilst simultaneously pointing out current shortcomings of this technique and highlighting areas where further developments are required.

The book generally fails to describe any application of these techniques to areas of direct relevance to the industrial chemist. From an industrial chemist's point of view, chapter three on biomedical applications is of particular interest, where reference is made to applications of LC−NMR in combinatorial chemistry, analysis of chemical impurities, and trapping of reaction intermediates. Although these examples are in the context of biomedical applications, one can easily see the relevance of LC−NMR in the area of organic process research and development, in particular as an analytical tool during optimization studies. One feels that the book could have had a much bigger impact, if it had also highlighted other potential application areas and identified potential shortcomings of these techniques in such areas.

The application of LC−NMR to discovery research is exciting, and chapter five discusses the current scope of this technique's application in the area of natural product analysis, including analysis of functional foods and biological tissues. Although there is still some limitation in this area, it is clear from recent applications that in years to come these techniques will have a major impact in this field. In particular, in bioactivity guided, high-throughput screening approaches, LC−NMR could have a major impact.

Chapter 7 deals with related techniques, and the final chapter provides a glimpse of what future developments could be expected in this field. From these two chapters it is clear that this is a rapidly growing area. As the editor points out, the recording of continuous flow ^{13}C NMR spectra will constitute the next major breakthrough, and two approaches, currently under development, are described. The other important growth area described in the last chapter focuses on development of different techniques for parallel NMR data acquisition.

The book is well produced, with few errors and omissions. It provides a concise guide to the current state of LC−NMR and related techniques with a comprehensive review of all practical applications in this field. It is a useful book, in particular to anybody who isconsidering investing in the acquisition of such equipment or who is looking for enhanced performance of existing equipment. It is also important reading material to the industrial chemist as innovative developments and applications of LC−NMR could potentially contribute to the acceleration of process development and optimization activities.

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OP020084R

10.1021/op020084r

Encyclopaedia of Pharmaceutical Technology, 2nd edition. Edited by J. Swarbrick and J. C. Boylan. 2002, Marcel Dekker: New York. 2002. 3 Volumes. 3032 + 64 pp. ISBN 0-8247-2822-X (Vol. 1), 0-8247-2823-8 (Vol. 2), 0-8247-2824-6 (Vol. 3), 0-8247-2825-4 (Prepack), 0-8247-2825-4 (Online).

Encyclopaedias are always valuable as a first port of call when researching a new area. Thus, for the chemist/chemical engineer Kirk Othmer and Ullmann provide valuable insight into selected topics, with a strong industrial bias. *Encyclopaedia of Pharmaceutical Technology* provides the same service for the pharmaceutical industry, and the previous edition was well-received. The first edition's first volume was published in 1988, and the last, volume 20, in 2000,

*Unsigned book reviews are by the Editor.

10.1021/op020084r CCC: $25.00 © 2003 American Chemical Society
Published on Web 03/14/2003

the whole work encompassing 9000 pages. The second edition, at 3000 pages, is much more condensed and focuses on a list of topics relevant to the discovery, development, regulation, manufacture, and commercialisation of drugs and dosage forms. The second edition has tried to match the breadth of coverage of the previous edition, but with a consistent format and style, difficult for a multi-author work. Over 300 chapter-authors have been used.

A chapter in an encyclopaedia should give a comprehensive, but short, review of the topic, with a good list of references to key works so that the reader can explore further if he/she wishes to have more in-depth knowledge. Most of the chapters do this very well. For example, chapters of interest to process chemists in Volume 1 include Calorimetry in Pharmaceutical R & D, Chiroptical Analytical Methods, Chromatographic Methods of Analysis, Contract Manufacturing, Crystallisation, Design of Drugs, and Drying and Dryers.

As one would expect, the authors concentrate more on dosage forms rather than on the bulk-active (e.g., in Drying and Dryers), but nevertheless, these are useful chapters for the process chemist. Each chapter is approximately 10−20 pages long with 5−80 references at the end. References tend to be to U.S. books and literature—for example, the chapter on Drying and Dryers does not mention the key book by van't Land on this topic.

Chapters in volume 2 which may be of interest include Equipment Cleaning, Evaporation and Evaporators, Excipients (four chapters), European Agency for the Evaluation of Medicines (EMEA), Filters and Filtration, FDA, Freeze-Drying, Good Manufacturing Practices − An Overview, Harmonisation of Pharmacopeial Standards, Hydrolysis of Drugs, Optimisation Methods, Particle Size Characterisation, and Patents (both international and U.S.A. perspectives). The latter chapter has useful discussion on process patents and is an excellent example of how to summarise an extremely complex subject in only 12 pages. In contrast the six-page chapter on Generic Drugs and Generic Equivalency barely covers the surface, and in common with many other chapters, takes a U.S. view rather than examining the international scene.

Volume 3 includes sections on Pharmacopeial Standards (European, Japanese, and U.S.A.), Polymorphism-Pharmaceutical Aspects, Process Chemistry in the Pharmaceutical Industry, Scale Up and Post approval Changes, Spectroscopic Methods of Analysis (six chapters), Thermal Analysis of Drugs and Drug Products, and X-ray Powder Diffractometry.

The chapter on Polymorphism is by Harry Brittain, author of many books on the subject, and is an excellent summary and is well referenced. It has a number of typos, however, and, in a list of solvents, quotes the boiling point of NMP as 80°!

The chapter on Process Chemistry in the Pharmaceutical Industry is a great disappointment—what an opportunity lost! A stimulating chapter on this subject would have emphasised to other disciplines the importance and value of process chemistry. However, the 14 pages are virtually a quick summary of one author's book of the same name. Of the 23 refs five are to chapters from this book. No mention is made of Lee and Robinson's book, Anderson's excellent and more recent monograph on Process Development, or even our journal, *Organic Process Research & Development* (OPRD). The authors briefly discuss biotransformations, polymorphism, and automation, all of which have had recent special issues in this journal, without any reference to OPRD. If the authors had read these special issues, their chapter would have been more up to date. The chapter also fails to direct the reader to the important reviews of process R & D published elsewhere. On the subject of enzyme catalysis, the key works of Patel, Faber, Roberts, etc. are not referenced. Although the work of Pisano at Harvard Business School is referred to, his important book, *The Development Factory*, is not referenced. Overall, this chapter fails to impart the importance of process chemistry in the pharmaceutical industry and the way it interfaces with other disciplines.

With a compendium of such size, one would expect some variability in quality, and the above criticism should not deter readers and potential purchasers. Overall, the quality of the individual chapters is good, and the value of the encyclopaedia is in its tremendous breadth, so that it can be a first port of call—along with the first edition—when needing knowledge of some new aspect of pharmaceutical technology.

The encyclopaedia, which has an excellent 64-page index, is highly recommended and should be in the library of any company or institution involved in pharmaceuticals.

OP0340356

10.1021/op0340356

Developing an Industrial Chemical Process: An Integral Approach. By J. Mizrahi. CRC Press: Boca Raton, FL. 2002. 229 pp. $140 (Paperback). ISBN 0-8493-1360-0.

The first implementation of a novel industrial chemical process brings many problems, which are discussed in this book, which begins with the "whys" and "wheres" and then looks at the organisation, activities, design, construction, and start up. Almost from the language of these statements, one can gather that this is a book for engineers involved in bulk-chemicals manufacture using dedicated plants operating continuous processes, rather than multipurpose batch processing. The book claims to be the first professional reference to examine the actual process development practices of industrial companies, research organisations, and universities. The author, however, does not reference any of the excellent books written on process development by chemists and engineers in the last 10 years (Anderson, Lee and Robinson, Gadamasetti, Repic, Doraiswamy) not even a book by his fellow countryman, Agam.

Nevertheless, this is a very readable account which focuses much more on the management of process development. Chapter headings include "Why a new industrial chemical process could be needed", "Starting the development of a new process", "Essential resources needed...", "Process

definition and feasibility tests", and "Economic analysis...". However the emphasis is firmly on engineering and not on chemistry.

A major weakness is in the discussion of process safety, where hazard and operability studies are not mentioned. In fact, the subject of safety is only allocated half a page. It deserves a whole chapter—it should be a vital part of management culture in the modern chemical industry.

Case studies discussed include processes to recover salts from the Dead Sea, production of pure phosphoric acid, citric acid by fermentation, and solvent extraction. The author demonstrates his practical knowledge with delightful statements such as, "One of the main enemies of industrial solvent extraction is the *crud*, consisting of fine solid precipitates, which accumulates at the interface between the two liquid phases and may prevent their separations and cause emulsions." He then goes on to discuss remedial methods.

At the end of each chapter, the author has a useful section, usually less than a page long, entitled "Worth another thought". All through the book the author is concerned about patents, patentability, and know-how and how it can be used to advantage.

In summary, the author has produced a very readable summary of the steps required to manage and implement a process on plant. It is a little old-fashioned, in that safety and environmental issues, such an essential part of modern process development, are not given enough space. However, it is recommended particularly for managers involved in process R & D, where lessons from the bulk chemical industry may be usefully adapted to fine chemicals and pharmaceuticals.

OP034039A

10.1021/op034039a

Chemometrics: Data Analysis for the Laboratory and Chemical Plant. By Richard G. Brereton. John Wiley & Sons: Chichester. 2003. 489 pp. Paperback. £39.95/EUR 66.00. ISBN 0-471-48978-6.

Much of chemical research, development, and processing is now dominated by instrumental techniques—such as FT-NMR, FT-IR, diode-array HPLC, HPLC−MS, etc.—which produce thousands of data points to describe each sample. The task of chemometrics is to mine this extensive data for the few nuggets of genuinely useful information. Ordinarily, the necessary routines are built into the instruments themselves, and the chemists need only interpret the final output—e.g. the NMR spectrum rather than the Free Induction Decay. This book is intended for those wishing to look behind the scenes at the mathematical manipulations involved.

The main topics are Experimental Design, Signal Processing, Pattern Recognition, and Calibration. The chapters on Signal Processing deal with the interpretation of chromatograms and spectra. They cover the theory of peakshapes, baseline correction, smoothing functions, time series analysis, and Fourier transforms. Pattern recognition is one of the most useful applications of chemometrics, for example, in recognising the nature of a compound through its spectral properties, or assigning the origin of a sample on the basis of its chromatogram. The methods discussed here include principal components analysis, cluster analysis, discriminant analysis, and SIMCA. Various approaches are described for calibration—particularly in relating sample compositions to spectral properties. These include multiple linear regression, principal components regression, and partial least-squares regression. Experimental Design is probably the topic most relevant to organic chemistry R&D. The chapter gives a concise account of the most commonly used designs: factorial and fractional factorial designs, Plackett−Burman and Taguchi designs, central composite designs, simplex centroid and simplex mixture designs. There is also a discussion of the simplex optimization technique.

In each case the discussion is built around the manipulation of a few example data sets, with step-by-step instructions and graphical illustrations. Each chapter ends with a collection of problems, usefully set out in a stepwise manner with hints on what do to at each stage. Although no answers are given in the book, these can be obtained freely from an associated website. The book is only really worthwhile if the reader is prepared to follow these detailed mathematics, and it would help to come to it with a basic grounding in linear algebra (matrix manipulation). The calculations themselves are easily performed with the aid of a spreadsheet program; the appendix provides a thorough account of how to use the Excel and Matlab packages for these purposes. Purchasers of the book can also download a number of macros which simplify the routine tasks.

A slight irritation for the reader arises from poor editing, with many obvious grammatical and syntax errors left uncorrected. Otherwise, this gives a useful introductory overview of a wide range of chemometric techniques.

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OP030005R

10.1021/op030005r

The Organic Chemistry of Enzyme-Catalysed Reactions. By Richard E. Silverman. Academic Press: London. 2002. 717 pp. £59.95. ISBN 0-126-43731-9.

This volume is a revised version of the 2000 edition, but has changed little. It has the same number of pages as the 2000 edition, and the references do not seem to have been updated. The only changes appear to be correction of typos.

The earlier edition was highly recommended to organic chemists in industry. The author was trained as an organic chemist and moved into enzymology later. This means that he understands the way in which organic chemists think. The chapters are arranged in terms of functional group chemistry rather than enzyme classifications. Thus, there are chapters on isomerisation, eliminations aldol, Claisen, formylation,

rearrangements carboxylation, decarboxylation as well as oxidation and reduction and hydrolysis.

The book is ideal for any organic chemist who knows little about enzyme reactions but wishes to know more and is a good reference text. As mentioned earlier, the references have not been updated so that the literature coverage is to 1999. No doubt future editions—and I am sure there will be future editions—will have a full update of the text and literature. Highly recommended and reasonably priced!

OP0340513

10.1021/op0340513

Solvent-Free Organic Synthesis. By K. Tanaka. Wiley−VCH: Weinheim. 2003. 433 pp. £80. ISBN 3-527-30612-9.

This book is a real disappointment and a lost opportunity to discuss the merits and disadvantages of solvent-free organic synthesis. There is no discussion of issues in the volume; instead, 537 examples from the literature are compiled under 14 different chapters. For each example, a reaction scheme and experimental procedure are given together with a reference. However, the experimental information is not always sufficient to carry out the reaction, and one would need to go back to the original reference to find out the exact conditions (stoichiometry, weights, etc.). There is no commentary on each reaction. Such a volume should have discussed issues such as energy saving, prevention of solvent waste, hazards (particularly of scale-up), and toxicity issues.

Of course, when the reactions are described as solvent free, this does not include the work-up, which invariably includes solvent extraction or crystallisation. The author should discuss this issue in depth, but there is no comment on any of these controversial topics.

In conclusion, this volume cannot be recommended. This contrasts with the excellent related volumes from Wiley−VCH on Ionic Liquids and Supercritical Fluids which have appeared in the past few years.

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