*Book Reviews**

Computational Organic Chemistry. By Steven M. Bachrach. Wiley-Interscience: New York. 2007. 528 pp. $120. ISBN -13: 9780471713425.

The increasing desire to rationalise reaction pathways and understand the principles behind certain classes of transformations has no doubt motivated the urge to compile the seven chapters of this book. The author, Professor Steven Bachrach at Trinity University, Texas, has focused on a topical approach, paying attention to certain transformations (such as Pericyclic Reactions) that have classically been ideal substrates for computational chemistry. The increasing importance of modelling the reaction conditions for a synthetic transformation has also been acknowledged in this book in the form of a chapter on Solution-Phase Organic Chemistry. Of note, a very interesting and informative component is the inclusion of a series of interviews with various prominent Professors, including Professor K. N. Houk, Professor P. von R. Schleyer, Professor W. T. Borden, Professor H. Schaefer, Professor C. J. Cramer, and Professor D. Singleton, relating their various career choices, insightful parcours, and current opinions on the topic.

Chapter 1 provides an extensive summary of Quantum Mechanics approaches, starting from the Hartree−Fock method, and subsequently introducing electron−electron interactions with post Hartree−Fock strategies (Perturbation Theory, Coupled-Cluster Theory, Multiconfiguration SCF and Composite Energy methods).

Chapter 2 introduces the relevant Fundamentals of Organic Chemistry through a number of case studies on bond energies, acidity, ring strain energy and aromaticity.

Chapter 3 is devoted to pericyclic reactions. Classically, Diels−Alder, Cope and Bergman cyclisations are included, along with more unusual ones in the "Pseudopericyclic Reactions" and "Torquoselectivity" subsections.

Chapter 4 emphasises species that bear one or more unpaired electrons, such as radicals, diradicals and carbenes. Various cases are introduced, notably methylene, phenylnitrene, phenyl carbene, tetramethyleneethane and benzynes. The reactivity of radicals is exemplified in a series of internal additions to alkenes and cascade processes.

Chapter 5 covers the reactivity of anions, starting with the S_N2 reaction in the gas phase, and also investigates the solvent effects. Interestingly, this chapter introduces one of the major grails for an organic chemist: asymmetric control. The first example is the control of asymmetry during the addition to a pro-chiral carbonyl compound. The second example is the asymmetric organocatalytic aldol reaction, with instances of amine- and proline-catalysed reactions, a discussion about the analogous Mannich reaction and the use of water as a solvent.

Chapter 6 follows up on the previous chapter, by focusing on the notion of solvation. It illustrates the various approaches with three examples, an aqueous Diels−Alder reaction, the solvation of glucose and the structure of nucleic acid base pairs in solution.

Chapter 7 considers the dynamic nature of an organic reaction by introducing the intrinsic reaction coordinate and the minimum energy paths. Several examples of nonstatistical dynamics are presented, where the dilemma between concerted and diradical mechanism is mentioned.

In summary, the book provides an excellent and authoritative panorama of the various approaches to modelling important organic intermediates and their reactivities. Although the book could be out of reach for pure organic chemists because of the intensive technical jargon used, it does provide examples of very detailed mechanistic considerations. The spirit of this book is very much in line with the school of thought of a pragmatic approach to molecular modelling pioneered by Houk, and for that reason, may attract organic and physical chemists alike.

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Asymmetric Organic Synthesis with Enzymes. Edited by V. Gotor, I. Alfonso, and E. García-Urdiales. Wiley-VCH: Weinheim. 2008. 325 + xiv pp. £122. ISBN 978-3-527-31825-4.

In the last 10 years there have been some excellent books on the subject of biocatalytic processes. This one is clearly aimed at organic chemists. The editors have assembled some well-known names (Reetz, Bäckvall, Turner, Nakamura, Mihovilovic, Fessner, etc.) to write chapters on their specialised subjects, and of course, the editors themselves have contributed chapters. It all works well, with some excellent reviews, although most have few references after 2006.

The opening chapter on Medium Engineering discusses interesting solvent effects on enzymatic processes and is an important (and probably unique) review on this topic. This is of real interest to industrial process chemists wanting to tweak reactions, fine-tuning them for increased yield, enantiomeric excess, or throughput.

Manfred Reetz then discusses Directed Evolution in an organic chemist-friendly way with lots of examples of interest to industrial scientists. This is followed by a chapter on the

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"Search for New Enzymes" (J.-L. Reymond and W. Streit). Subsequent chapters focus on synthetic chemistry including Dynamic Kinetic Resolutions (B. Martin-Matute and J. E. Bäckvall), Deracemisation and Enantioconvergent Processes (N. J. Turner), and Transesterification and Hydrolysis of Carboxylic Acid Derivatives, Alcohols and Epoxides (R. Chênevert, P. Morin, and N. Pelchat).

The editor then chips in with an interesting short chapter on Aminolysis and Ammonolysis of Carboxylic Acid Derivatives, in which the formation of amide bonds as well as their hydrolysis is discussed. Given the difficulty of forming amide bonds selectively using chemical reagents, organic chemists will appreciate this introduction to an enzymatic approach.

The Japanese authors, K. Nakamura and T. Matsuda, discuss Enzymatic Reduction Methods, focussing almost entirely on carbonyl reductions, not C=C bond reduction. This chapter has much more detailed case studies which will be of interest to industrial readers, since it discusses how to modify biocatalysts, change reaction conditions, and prevent inhibition to produce an efficient process.

A timely review of Bioxidations in Chiral Synthesis (M. D. Mihovilovic and D. A. Bianchi) covers regioselectivity as well as enantioselectivity, deracemisations, and kinetic resolution including oxygenation of nonactivated carbon centres (usually hydroxylations), epoxidation, Baeyer−Villager oxidation, and dihydroxylation of aromatics.

The final chapter on Aldolases (W.-D. Fessner) is a comprehensive review illustrating that carbon−carbon bond-forming reactions can be carried out diastereoselectively and enantioselectively using enzymes, and there are now important industrial applications.

Overall, there are some excellent and very readable reviews in this compilation. The book is an ideal work for organic chemists interested in enzymes. Admittedly many of the authors have written reviews on similar topics in journals and elsewhere, but it is good to have them updated and all together in one bound volume on one's book shelf. The editors are to be congratulated on producing a fine volume.

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Theilheimer's Synthetic Methods of Organic Chemistry, Vol. 72. Edited by G. Tozer-Hotchkiss. Karger: Basel, Switzerland. 2008. 456 + xxiv pp. Euro 564.50. ISBN 978-3-8055-8928-4.

It is over 40 years ago when I was recommended to look at Theilheimer by the late Professor Sir Derek Barton, who was a great fan of the series. I remain a great fan of the series, too. For those organic chemists who have not used Theilheimer, I recommend you get hold of a copy soon. It is the best summary of the previous year's synthetic methods you will find, in a form that is easy to locate what you want. This is because the system of indexing that Theilheimer uses is based on disconnections and key bond-forming reactions. Once you get used to the system, it is very easy to use.

The current volume, which covers the literature of 2007 (although the reviews section lists some 2008 references), maintains the high standards of previous volumes. As always, it has an extensive subject index which makes it easy to locate, say, a named reaction or any reaction not easy to classify by bond formation.

Outstanding!

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The Management of Chemical Process Development in the Pharmaceutical Industry. By Derek Walker. John Wiley and Sons, Inc.: New York. 2008. 387 pp. £52.95. ISBN 978-0-470-17156-1.

In my opinion, this book is a very personal account of the management of Process Research & Development; it is based very much on the experiences the author gained across several decades and organisations, but all appear to have been large pharma. In the Introduction the author states the book is "about the management of the people, organisation and main disciplines which have to be integrated to create and develop a chemical process to meet all needs". Excited by this prospect, I set about reading the book with enthusiasm to discover how the author's experiences of several decades, spread through several companies and departments, might assist those within management structures of chemical and pharmaceutical companies.

Chapter 2 presents a personalised view of the key attributes required for management of chemical process development by giving examples of key people the author has worked with, either as colleague, subordinate or supervisor. It made interesting reading, and I am sure everyone will recognise a number of the attributes in the people they have encountered in their career tracks. I question whether its position should take such prominence in the book and whether it perhaps could have been better placed as an acknowledgment.

In later chapters each gives a nice overview of subject matter such as process safety, the environment, regulatory affairs and patents, but as I progressed I was left with the impression that it is more like a set of memoirs. As I reflected on the stated content of the book in the Introduction, I became increasingly disappointed as the book fell short of my expectations. In the final chapter, the author presents some personal views on the impact of bureaucracy and development strategies in the pharmaceutical industry, making a number of provocative statements and inviting readers to challenge the comments. This I did and disagreed with many of them which is, again, a personal opinion.

As for the more practical aspects of presentation in the book, the equipment diagrams were small but clear; however, I found that the reaction schemes were difficult to read because of the small size and the use of roman numerals.

For me, the title does not reflect the content, which seems to fall between a management and technical text, though not

fulfilling the needs of either. The title led me to expect to glean insights into the management structures used in various companies and to see the types of strategies used to manage both people and systems to best effect. Instead, I read what for me was a very personal account of one man's experiences and views, which on several occasions clashed somewhat with my own.

Overall, this is not a text I can suggest for the academic or industrial workplace library; rather, it is something individuals might want to read to examine their perspectives on the world of chemical development.

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Process Chemistry in the Pharmaceutical Industry, Vol. 2. Edited by Kumar Gadamasetti and Tamim Braish. CRC Press: Boca Raton, FL. 2008. 494 pp. $249.95. ISBN 0-8493-9051-6.

The first volume in this series, edited by Kumar Gadamasetti on his own, was an interesting mixture of case studies with one or two extra chapters on specific areas of technology, such as phase transfer catalysis. This second volume, with Tamim Braish as coeditor, has expanded this idea, and alongside some excellent case studies are chapters on topics such as Designing Robust Crystallisation Processes for Active Pharmaceuticals, PAT and the Use of *in situ* Monitoring Techniques, and Trends in Outsourcing, and Sourcing Pharmaceutical Products in China and India which add to the content which is spread over 29 chapters.

There are also chapters on synthetic methodology such as Chiral Amine Synthesis, Unnatural Amino Acids, Organic Reactions in Water, Oxetan-3-one: Chemistry and Synthesis, and Microwave Technology in Process Optimisation. The case studies are uniformly good and also varied in the types of compounds discussed. Some case studies, for example, describe the chemical development of the commercial route to marketed compounds such as sildenafil and varenicline; other case studies describe in some detail the various synthetic route options examined and the optimisation of specific routes necessary to produce material during the development programme and the challenges associated with this. Other compounds described did not make it to market but still provide some interesting chemistry and scale up problems. In addition there are chapters on the PEGylation of biological macromolecules and Process Development Considerations for Therapeutic Monoclonal Antibodies in Mammalian Cell Culture.

This is an excellent book, but if I had to find a fault I would suggest that some of the technology chapters are not strictly "Process Chemistry in the Pharmaceutical Industry" although they are undoubtedly of interest to process chemists in the pharmaceutical industry and in other related industries, too. Overall this book is definitely recommended, and the editors are to be congratulated on a job well done.

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High-Throughput Analysis in the Pharmaceutical Industry. Edited by Perry G. Wang. CRC Press: Oxford, U. K. 2008. 432 pp. £84. ISBN 978-1-420-05953-3.

Whilst most of the chapters in this industry-oriented book will be of little interest to organic process chemists and engineers (though analytical chemists will enjoy reading about how to improve their productivity in the laboratory), there is one chapter which is a gem. Entitled "High-Throughput Analysis in Support of Process Chemistry and Formulation R&D in the Pharmaceutical Industry" and written by Zhong Li of Merck U.S.A., it is a first-rate review of the latest developments and looks to the future. It should be required reading for all organic process and process analytical chemists.

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Process Systems Engineering: Volumes 3 and 4: Supply Chain Optimization - parts I and II. Edited by Efstratios Pistikopoulos, Michael Georgiadis, Vivek Dua, and Lazaros Papageorgiou. Wiley-VCH; New York. 2007. Part I: 348 + xix pp; Part II: 349 + xix pp. £105. ISBNs: 978-3-527-31693-9, 978-3-527-31906-0.

I was hoping by reading these two multiauthor volumes to gain some insight into the subject of supply chain management as it relates to the chemical/pharmaceutical industry. However, as I perhaps should have realised (these books are volumes 3 and 4 in a series on process engineering), the books have little relevance to fine chemicals and none to pharmaceuticals. An extensive chapter on "Short-Term Scheduling of Batch and Continuous Processes" offered promise of more of the information I was looking for, but it turned out, as much in the two volumes does, to be focused on modelling, and even the three examples are more related to bulk chemical processes. Similarly, a chapter on "Chemical Supply Chain Redesign" was again focussed on bulk chemicals in dedicated plants.

Overall, these volumes are not likely to be of interest to *Org. Process Res. Dev.* readers.

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Pharmaceutical Pre-Approval Inspections: A Guide to Regulatory Success (Drugs and the Pharmaceutical Sciences, Vol. 181, 2nd ed.). Edited by Martin D. Hynes, III. Informa Healthcare: New York. 2008. 278 pp. $229.95, £115.00 (Hardcover). ISBN 978-0-8493-9184-2.

Preapproval inspections (PAIs) of pharmaceutical premises have been a feature of the regulatory landscape in the United States since the late 1980s. The FDA's PAI programme arose partly as a reaction to the "generic drug scandal", which made them reluctant to continue taking data submitted in companies' drug applications entirely on trust. Thus, the PAI has a different focus from a routine GMP inspection, its main purpose being to review the adequacy and accuracy of information provided in the regulatory submission—although manufacturing standards would be evaluated as well. In the intervening decades, significant changes have occurred in the FDA's approach. Their "Quality Systems Approach" was introduced in 2002, followed shortly by a new risk-based strategy to prioritise inspections—rather than attempt to inspect all applications. A dedicated Pharmaceutical Inspectorate was inaugurated in 2003. Also, the advent of electronic submissions (eCTD format) has been a boon to field inspectors, who are now able to review much more of the relevant documentation in advance of their inspection, rather than waiting for hard copies to be provided on site.

The overall goal of this present book is "to help the reader prepare for an FDA pre-approval inspection so that (it) will produce a rapid regulatory approval [...] and not become an impediment". In this it is only partially successful. It consists of a series of essays by experts from pharmaceutical companies (Eli Lilly, Wyeth) and several regulatory consultancies, and few of them are really to the point. Only three out of the twelve chapters contain significant information about inspections as such. The introductory chapter details "The Evolution of the FDA: Pre-New Drug Application Approval Inspections". This is followed by an account of "FDA's Risk-Based Approach to Inspections". A later chapter deals with "The Systems-Based Pre-Approval Inspection". Together these provide a good overview of the agency's current expectations. However, the only practical advice to companies for dealing with inspections comes in a three-page section of the chapter on "cGMP Risk Assessment and Management Strategy".

Other chapters deal with Pharmaceutical Product Development, Training Requirements, Concepts in Quality by Design, Equipment Cleaning, Stability Studies, Computer Systems Validation, and The Quality Assessment Program. While these usefully contribute to an understanding of regulatory issues in pharmaceutical development, they only tangentially address the advertised subject of the book. I found the final chapter "All Dressed Up but No Approval to Go: The Consequence of Failing an FDA Pre-Approval Inspection" particularly disappointing, since it fails to provide any detailed examples.

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