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Book Reviews *

Polymeric Materials in Organic Synthesis and Catalysis. Edited by Michael R. Buchmeiser. Wiley Interscience: Weinheim. 2003. xxxiii + 559 pp. 159 Euro/235 SFR. ISBN 3-527-30630-7.

The attractive features of polymer-supported (PS) reactions, be they reactions using PS substrates, PS reagents, PS catalysts, or PS scavengers, have been very well documented in recent years. Major advantages of using such reactants include the simplified product isolation procedures, the possibility of automating these procedures, and the possibilities of high throughput and combinatorial chemistry.

The study of PS reactions is by no means new. They began to be studied seriously in the 1940s and early 1950s following the introduction of various commercial ion-exchange resins. Typical studies then involved using resin beads bearing sulfonic acid groups as catalysts for esterifications, ester hydrolyses, acetalizations, and acetal hydrolyses. Ion-exchange resins were also used to remove acids or bases from reaction products. Often in such cases the use of the PS species was not even mentioned in the paper title or abstract. Today these would be regarded as applications of PS catalysts or PS scavengers.

The study of PS reactions received an enormous boost in 1963 when Merrified and also Letsinger reported the first examples of "solid phase" peptide synthesis. Letsinger also reported the first studies of "solid phase" oligonucleotide synthesis, the forerunner of the technique used extensively today in connection with genetic engineering.

In the early 1970s several research groups sought to extend Merrifield's and Letsinger's ideas to organic chemistry in general, and many examples of reactions using PS substrates, PS reagents, PS catalysts, or PS scavengers were reported. By 1980 over a thousand relevant references were to be found in the primary literature. Several books and entire international conferences were devoted to the subject. A wide variety of supports was investigated. The importance of the correct choice of reaction solvent, the ideas of site isolation and microenvironmental effects were identified, studied, and substantially understood. The pros and cons of using PS substrates, PS reagents, and PS catalysts were clearly recognized, and it was obvious that, in general, reactions using PS substrates were the least attractive of these three types because every reaction needed to proceed in close to 100% yield. Thus, for every reaction the conditions needed to be very carefully tuned: a labor-intensive and time-consuming task. It was recognized that a much better way forward was to use PS reagents and, preferably, PS catalysts.

Interest in the field of PS organic chemistry slowly waned, basically because it consisted of excellent techniques in search of applications, until the ideas of combinatorial chemistry were introduced in the late 1980s by Furka, by Lam, and by Houghten. Surprisingly, in view of the previous experiences, reactions using PS substrates were now the reactions studied most extensively. "Linkers" became very important. The technique was belatedly christened "solid phase synthesis". Eventually after 10 years or so it is again recognized that, for many purposes, reactions using PS reagents or PS catalysts plus, if necessary, PS scavengers are the often the best way forward. This approach has now been christened "solution phase synthesis".

Over the years numerous books on PS organic synthesis have been published. The stage has now been reached, however, where the subject is too large for comprehensive coverage in just one book. The present book covers various aspects of recent research on PS reactants. It is entitled *Polymeric Materials in Organic Synthesis and Catalysis*. The word "materials" in the title may be a bit misleading since it is used as a collective noun for the various types of reactive solid supports and not in the more common sense of chemically inert solid polymers for use in physical applications.

The book consists of 559 pages divided into 13 chapters, plus a subject index. Each chapter is prepared by one or more authors active in the relevant field. There are chapters describing recent research on solution-phase synthesis (by Ley et al.), solid-phase synthesis (by Gil et al.), synthesis using soluble polymers (by Janda et al.), and methods for monitoring reactions on polymers (by Yan). Because coverage is not comprehensive and focuses on more recent work, many of the earlier references to work in these fields are absent, and some of the important earlier work on, for example, site−site interactions, is only briefly covered. Solid-phase peptide synthesis and oligonucleotide synthesis are not specifically covered.

Of particular interest are the chapters describing the many recent developments in polymer supports (Sherrington et al.), PS catalysts of various types (Kirschning et al.), the applications of olefin metathesis in the context of PS reactions (Buchmeiser et al. and Hoveyda et al.), and biocatalyzed reactions on polymer supports (Reents et al.). The latter chapter covers some aspects of PS oligosaccharide synthesis.

Other chapters discuss some of the approaches to carrying out PS reactions where the supports are not only serving as handles to facilitate separations, i.e., where some organization of the reactive species on the support has the potential to bring further novel aspects to the reactions. Thus, there is chapter on dendritic polymers as supports (Haag and Roller), one on functional systems assembled on surfaces (Jordan) including, for example, self-assembled monolayers and polymer brushes, and on micellar catalysis (Nuyken et al.). These present interesting and novel systems, but they are either of low capacity, are difficult to prepare, are fragile,

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and/or not easily recovered. Thus, they throw light on the complexities and potential of supported systems, but they can only be expected at this stage to have limited commercial applications.

Finally there is a chapter on the use of membranes (by Keurentjes) to achieve reactions, separations, or both at the same time. This will undoubtedly be a growth area in the future, especially with the recent developments in membrane technology.

In summary this is an excellent and stimulating book that describes recent work on many parts of the subject and which reviews many developing areas. It is a reference book to update established researchers and a very good starting point for researchers new to the field. To the reviewer it is gratifying to see the gap between polymer chemistry and organic chemistry gradually narrowing as the years go by. Nature makes great use of both macromolecules and small molecules *working together* to provide the "machine of life", with the macromolecules often providing data storage, recognition, catalysis, and structural materials whilst the small molecules ferry between them to achieve the required chemical conversions. Future researchers in the field of PS reactions definitely need both the skills of the organic chemist and the polymer chemist to maximize progress.

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Chemical Micro Process Engineering: Fundamentals, Modelling and Reactions, 10th ed. by V. Hessel, S. Hardt, and H. Löwe. Kluwer Academic Publishers: Dordrecht. 2003. Wiley-VCH: Weinheim. 2004. xxxviii + 674 pp. £135. ISBN 3-527-30741-9.

The appearance of this work, along with its companion volume *Chemical Micro Process Engineering: Processing, Applications and Plants* by the same authors is timely. It is four years since the excellent *Microreactors* appeared, and the technology has moved on tremendously with over 1500 publications in the past few years. Unfortunately, many of these publications are in conference proceedings, rather than in full peer-reviewed journals, and often lack the experimental detail necessary to critically appraise the results. Also many of the publications are from companies and organisations making and possibly selling microreactors, where there can be a tendency to overstate the importance of microreactors with respect to conventional technology.

The authors therefore faced a difficult task but have decided on excellent formulae for overcoming these challenges. The word "benchmark" appears on countless occasions, and when the literature is referenced, the reader is shown how many references are to peer-reviewed journals and how many to conference proceedings. Of course, the authors, all from the Institut für Microtechnik Mainz GmbH, are probably the leaders in their field; therefore, many references are to their own work. Dr. Hessel is an organic chemist so that several sections of the volume are devoted to detailed organic reactions carried out in microreactors.

There are only five long chapters, but each chapter is broken down into sections, subsections, and even further subdivided—the contents pages which list these subdivisions take 23 pages!

Chapter 1, A Multi-faceted, Hierarchic Analysis of Chemical Micro Process Technology (124 pages with 342 references), outlines the key aspects of the technology including design, principles and concepts (e.g. process intensification, green chemistry), microreactor consortia, impact on chemical engineering, mixing, heat transfer, fouling, industrial process development, impact on process results (conversion, selectivity, yield, optical purity, etc.), as well as impact on society and ecology. The latter section includes a subsection on "The Micro Reactor Echo in Trade Press and Journal Cover Stories"). which lists examples. but seven pages of examples is surely too much for a technical readership. This chapter is a useful overview of the subject and includes forward-looking observations, discussing problems to be solved before microreactors become widespread in chemical manufacturing.

When references are listed, the title of the publication is given in addition to the authors and the journal. This helps the reader to decide whether this reference is relevant and warrants further investigation.

Chapter 2 (132 pages), on Modelling and Simulation of Micro Reactors, discusses flow phenomena, CFD, flow distribution, heat transfer, mass transfer and mixing, and chemical kinetics. Chapter 3 covers gas-phase reactions (124 pages), chapter 4 reviews liquid and liquid/liquid-phase reactions (198 pages), and chapter 5 (80 pages) describes recent advances in gas/liquid reactions, with emphasis on direct fluorination processes. Direct fluorination is not possible in conventional technology since the radicals generated and the high heat evolution cause numerous byproducts. With microreactor technology, both problems can be controlled.

Chapter 4 will be the one of most interest to organic process chemists. It describes the various types of reactor used—36 are detailed including electrochemical and photochemical microreactors. Each type of chemical reaction is covered (and the scope is the whole of organic synthesis) by breaking down the "process" into the following;

- drivers for performing the reaction in microreactors
- beneficial microreactor properties for the reaction
- the reaction itself investigated in the microreactor
- experimental protocols
- typical results

I found this approach comprehensive but rather cumbersome and not so easy to read. There are excellent sections on Suzuki and Sonagashira couplings, but the tendency is to use homogeneous catalysis, rather than the often cheaper heterogeneous, presumably for fouling reasons.

The chapter focuses on the actual reactions, whereas the workup and product isolation, when the process has departed

the microreactor, is rarely mentioned. If microreactor technology is to be integrated into pilot scale and production of fine chemicals by multistep processes, then this is an issue which ought to have more discussion. Is the workup/product isolation to be carried out continuous or batchwise? For crystallisation, the most common mode of purification, continuous crystallisation, takes longer to develop than batch, but the integration of batch unit operations into a continuous process is not ideal from a scheduling viewpoint.

In conclusion, this is an excellent, comprehensive summary of the state-of-the-art in microreactors and should be read by all process chemists and engineers interested in the field. The book is reasonably well produced, although I found some incorrect formulae, some mistakes (reduction instead of oxidation), and more than the usual number of typos. The high price may deter all but the most ardent devotees of this fascinating subject. However, every industrial library involved in process R&D and chemical manufacture should purchase a copy.

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The Chemistry of Process Development in Fine Chemical & Pharmaceutical Industry. By C. Someswara Rao. Asian Books Private Limited: New Delhi. 2004. 1277 pp. ISBN 81-86299-50-5.

This is a remarkable book. Apart from one short chapter of 43 pages, the rest of the book (over 1200 pages) has been written by a single author. I do not know how long it took him, but it is an act of great determination and dedication. The key word in the title is chemistry; this is an organic chemistry book and the focus is on organic chemistry from an industrial, process R&D and manufacturing viewpoint. This is reflected in the chapter titles.

The book begins with an overview of the nature of process development and then surveys some organic reactions in detail (Grignard, Wittig, ozonolysis, Mitsunobu, etc.) from the viewpoint of the process chemist, with particular emphasis on scaleability. This is followed by a 70 page chapter on Chiral Technology.

Subsequent chapters include "Strategies for the simplification of Organic Reactions and Processes" (121 pages); Reagent Modification and Rate and Order of Addition of Reagents; Additives for Reagents − Fine Tuning of Organic Reactions; (100pp) Choosing a Reagent; (166pp) Byproducts from Side Reactions; Solvents and Solvent Effects; Phase Transfer Catalysis; Work-Up, Purity and Purification (96pp); and Safety Assessment of Chemical Process Technology. The latter chapter is written by Dr. Khan of the Indian Institute of Technology.

There is a wealth of information here; it is a phenomenal literature survey, with many examples taken from Organic Process Research and Development. The list of references at the end takes 200 pages! The literature coverage is comprehensive and is to 2003.

The chapter on "Choosing a Reagent" is particularly useful; the author discusses the choice of reagent based on safety/toxicity, efficacy, and workup convenience. For example there are sections on avoiding pyridine, safe reagents for chloromethylation, alternatives to dimethylsulphate, avoiding Bu_3SnH, and substitutes for DCC.

In the chapter on "Strategies for Simplification of Organic Reactions and Processes", the author covers in situ generation of reagents and substrates (e.g., chlorine and bromine), telescoping, and consecutive l-pot reactions and multicomponent reactions. The whole book is full of useful tips for the practising organic chemist, and the comprehensive lists of examples and tables provide something for everyone. It is rather like an encyclopaedia of organic reactions from a process viewpoint.

Throughout the book, the author discusses chemistry and processes from a green chemistry viewpoint. It is clear from the text that Dr. Rao has extensive experience in process development and manufacture and that he has concern for environmental issues, as well as safety and economics.

The book, however, has some significant weaknesses. It is not easy to find your way around, since the extensive tables, which can be a few pages long, interrupt the text and the publisher has not distinguished (e.g., by use of different typeface or use of bold lettering) between tables (which have lots of structures in) and schemes/figures. The index (only 15 pages) is poor, so that it is difficult to find what you are looking for. Given that there is so much useful information in the book, this is particularly disappointing. I found it hard to locate particular topics which I wanted to re-examine after reading the book cover-to-cover.

Despite these criticisms, all organic chemists in process R&D will wish to have access to this comprehensive text. Since the book is well used, it is a pity that the binding is poor; already my copy is starting to disintegrate after a few weeks.

In conclusion, all industrial libraries should have a copy of this remarkable book. Chemists in universities, particularly students about to take up a job in process R&D, would also learn a lot from perusing this "encyclopaedia".

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