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Book Reviews

Handbook of Functionalized Organometallics: Applications in Synthesis (Volumes 1 and 2). Edited by P. Knochel. Wiley-VCH: Weinheim. 2005. £175. 652 + xix + 17 (index) pp. ISBN 3-527-31131-9.

The editor, Paul Knochel, has brought together an excellent group of reviewers to produce an outstandingly useful pair of volumes. He begins with a short introduction, and this is followed by chapters covering the various metals (lithium, boron, magnesium, silicon, tin, and zinc in volume 1; copper, nickel, manganese, zirconium, and titanium in volume 2). In addition, volume 2 contains chapters on electrophilic multi-hapto-organometallics in organic synthesis, metal carbenes for organic synthesis, and organodimetallics for organic synthesis.

The emphasis is on polyfunctional compounds, and this will appeal to the process chemist looking to find ways to synthesise complex molecules. Perhaps the most useful chapter for process chemists will be the one on magnesium organometallics. The authors begin by discussing the various ways of preparing Grignard reagents, with lots of practical hints and the advantages and disadvantages of each method. Since one of the chapter authors is the editor, we would expect that his recent work on exchange reactions is given prominence, and the safety advantages of using ^{i}PrMgBr for some substrates rather than direct magnesiation in large-scale processes is emphasised with an example from Merck Process R&D.

The review emphasises that Grignard reagents containing a wide range of functional groups (e.g., NO_2, CN, CO_2R) can be prepared by the exchange method at low temperature that could not have been made using magnesium metal directly, and this is further elaborated in the following pages where a wide range of reactions are discussed in detail. Most of these are, of course, carbon−carbon bond-forming processes. Examples, in general, in this chapter are kept to simple aromatic and heterocycles with multifunctionality rather than complex natural products, and this again should appeal to the process chemist.

The other chapters are usually organised in a similar way, and process chemists will find something of interest in most of the chapters. I particularly liked the chapters on organozincs, organocopper, and organomanganese reagents.

The weakest chapter was on organonickel chemistry, where the excellent format of previous chapters was not followed. There was no section on preparation methods, with the chapter launching into homocoupling reactions on the first page. I found this chapter to be a catalogue of reactions with little attempt to aid in understanding the reactivity and mechanistic details of the processes. Nevertheless, skipping through the reaction schemes will give every chemist lots of synthetic ideas, and the chapter is well referenced.

In general, references are up to 2004 with an occasional 2005 reference, and the chapters have few typos—most of the ones I detected were surprisingly in the bold subtitles. One typo which was amusing was the awarding of the Nobel "Price" to Grignard—I did not realise you had to pay for these!

If I have one criticism, it is that the work could have included a conclusion which focused on synthetic transformations and compared and contrasted the advantages and disadvantages of each metal for each transformation. Or this could have been briefly discussed in a longer introduction. The excellent index helps the reader to carry out this task for himself to some extent.

In conclusion, this pair of volumes should be in every medicinal and process chemist's library. The main problem will be: will it still be on the library shelf since it is likely to be so heavily used. Best to buy your own copy!

Wiley-VCH now have an excellent series of books on organometallic chemistry with recent titles on "Modern Organonickel Chemistry", "Ruthenium in Organic Synthesis", "Metal-Catalysed Cross-Coupling Reactions", "Titanium and Zirconium in Organic Synthesis" and "Transition Metals for Organic Synthesis". Knochel's book on Functionalised Organometallics maintains the very high standard of this series.

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Cyclic Separating Reactors. By Takashi Aida and Peter L. Silveston. Blackwell Publishing: Ames, IA, Oxford. 2005. 386 pp. $239.99. ISBN 1-4051-3156-X (hardback), ISBN 978-14051-3156-8.

This book is mainly a bibliographical review of the state of the art regarding the cyclic separating reactors. After a brief introductory section that defines the scope of the book as well as provides useful definitions the authors separate the subject in two main parts; Part II of the book is focusing on chromatographic reactors, while Part III provides information on pressure and temperature swing reactors. The fourth part of the book provides methodology to select and develop a continuous reaction process. In the final part the authors are providing their point of view regarding the future development of the technology.

The two main sections, Parts II and III of this book, provide an extensive review of the literature with references from the 1960s up to 2003. Part II is dedicated to chromatographic reactors making the distinction between the counter current moving bed and the simulated moving bed. This section is organized logically and provides important information regarding the process and its variations. However,

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the process descriptions are a bit confusing. The authors are reporting a large amount of results and examples from the bibliography, and the resulting discussions are brief and somewhat incomplete for a reader with no previous knowledge of the process discussed.

Part III which discusses the swing reactors is organized also logically and makes the distinction between pressure and temperature swing operations. Again the authors are providing a large amount of information in terms of mode of operation and modeling. But the resulting discussions are also brief and assume that the reader has already a more than basic knowledge of the technique.

Parts IV and V of the book could have been more developed since they talk about selecting the type of reactor depending on the application, how to design it, and how the technology should evolve in the next few years.

This book provides a good bibliography review of the cyclic reactors, a rapidly developing technique. It is recommended to engineers and researchers that are already working in this field or wish to learn more about these processes. However, further information needs to be sought from the rich bibliographic source provided to get a more complete understanding of the process.

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Industrialization of Drug Discovery. Edited by Jeffrey S. Handen. Taylor & Francis/CRC Press: Boca Raton, FL. 2005. 305 pp. $139.95. ISBN 0-8247-2391-0.

Glancing at the title, I was expecting a manual detailing high throughput screening cascades and automation equipment. I was most pleasantly surprised to read an engaging, though-provoking, and up-to-date overview of modern elements of the drug discovery process. The book, which does not necessarily require a scientific background, is a must for managers who wish to clearly understand the issues pertinent to the drug discovery process with a view to formulating informed strategic decisions. With 10 chapters contributed by no less than 18 authors ranging from large pharma, biotech, consulting firms as well as academia, it covers a comprehensive breadth of subjects whilst remaining digestible. The "must-know" and classic examples are placed in context and explained. The collection of wisdom in the decision-making chapters is astonishing.

As aptly stated in the first chapter, effective integration of a sound set of strategies (rather than a single strategy) should increase the size of the needle and decrease the size of the haystack. The book aims to equip the reader to do just that. If you have never heard of the Taguschi and Poke Yoke Approaches or cannot see what lessons pharma can learn from Henry Ford, then chapter 3 is enlightening. Although chapters 4 and 5 on compound management and HTS are not comprehensive enough to enable the reader to design an automation facility, it nevertheless provides a good overview of compound storage, plate duplication, and screening cascades to name but a few. The authors use facts, figures, costs, and statistics to attack anti-intellectual clichés about HTS. Chapter 6 is probably among the most "science based" chapters and explains what ADMET is, what assays are available, and it gives a valued judgment on their uses and limitations. The challenge of "making knowledge work productive" is candidly addressed in chapter 7 which is outstanding in clarity and in the wisdom of the advice provided on knowledge management. Chapter 8 is effectively a management training course for informed decision making and makes excellent reading. Chapter 9 convinces the reader that a productive and mutually beneficial collaboration should be based on suitable partner selection as well as the application of emotional intelligence.

The book is excellent at putting "measurables" on such a broad topic as drug discovery and should make informative reading for medicinal chemists as well as pharmacologists. Its insightful content is particularly pertinent to managers and consultancy partners involved in this field.

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Catalyst Separation, Recovery and Recycling: Chemistry and Process Design. Edited by D. Cole-Hamilton and R. Tooze. Springer: Dordrect. 2006. 250 pp. £96. ISBN 1-4020-4086-5.

This excellent volume is number 30 in the series "Catalysis by Metal Complexes" published by Springer over the last 30 years. It continues the high standard, set by previous volumes, and the strong industrial focus.

The short opening chapter by the editors on "Homogeneous Catalysis − Advantages and Problems" summarises what the book is about, namely that homogeneous catalysis has a number of disadvantages which means that the large number of reactions discovered have not been applied in industry. Catalyst stability and catalyst recovery and recycling are the key issues discussed in the book.

Chapter 2 summarises clearly the classical separation technologies for homogeneous catalysts from an industrial perspective and uses as the main example hydroformylation of olefins. This example is used by all chapter authors and provides an excellent unification of the whole book. In this chapter the references are mostly from the patent literature, and the author (David Bryant) has used his own inside knowledge from his days at Union Carbide to interpret what really is used in industry.

There follows chapters on "Supported Catalysis" which covers the immobilisation of tailor-made homogeneous catalysts; "Separation by Size-Exclusion Filtration", which discusses membrane reactors; "Biphasic Systems" which

covers water−organic processes particularly those operated at Celanese. The work in this chapter has been covered at greater length in monographs such as *Aqueous-Phase Organometallic Synthesis* (Wiley-VCH, 2nd ed., 2003) and *Aqueous Organometallic Catalysis* (Kluwer: Dordrecht, 2001).

An excellent chapter on "Fluorous Phase Catalysis" ends with a discussion on process synthesis of 1-octene by hydroformylation. This chapter contains a projected costing for manufacture of 100,000 t/a by a continuous process and makes assumptions regarding cost of fluorous phase and recovery of rhodium catalyst. The following chapter on "Ionic Liquids" is also well described from an industrial viewpoint and has a similar projection for butanol production using ionic liquids on 100,000 tonne scale. At a solvent cost of 15 Euros/kg, the process could be economic but depends initially on rhodium recoveries. "Supercritical Fluids" with emphasis on carbon dioxide are covered in the next chapter, and again, an economic evaluation and the potential for scale-up and manufacture are discussed using the hydroformylation of 1-octene to 1-nonanal as an example.

The final chapter, again written by the editors, discusses "Areas for Further Research" and has a section for each of the previous chapter headings. The conclusion is that none of the alternative strategies discussed in the book has reached the point where it can be commercialised for rhodium-catalysed hydroformylation of long-chain alkenes, and there are few commercial applications in lower-volume products.

Inevitably, the focus in the book has been on the bulk chemical industry. Perhaps one chapter could have been devoted to the use of new technologies in the fine chemicals/pharmaceutical areas, using batch and semibatch processes, where the cost constraints may not be so tight.

Overall, the editors have done an excellent job on unifying a multi-author work and have emphasised how important it is for academic research to be aware of the industrial applications, and for industry to be aware of what new academic research can bring to industrial process R&D and manufacture. Highly recommended.

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Thin-Layer Chromatography: A Modern Practical Approach. By Peter E. Wall. Royal Society of Chemistry: Cambridge. 2005. x + 184 pp. £69.95. ISBN: 0-85404-535-x.

Thin-Layer Chromatography (TLC) is still one of the most inexpensive ways to analyse for impurities and to follow reactions qualitatively and quantitatively. Although HPLC remains the favourite technique of the modern organic chemist, TLC is a useful and lower cost alternative, which can be fast and accurate. It has one major advantage over HPLC; everything is visible, if the correct visualisation technique is used, and non-UV absorbing compounds can be seen. Younger chemists brought up on HPLC would do well to investigate TLC as an option, particularly when working in manufacturing, where TLC can be of benefit.

The appearance of this latest book on the subject is therefore most welcome. The title is the 11th in the RSC Chromatography Monographs series, previous volumes of which have been well received. The author of the latest volume begins with an introduction and then devotes more than 50 pages to sorbents and TLC layers and follows this with shorter sections on sample pretreatment and sample application. The main chapter on development techniques (47 pages) is thorough, but I would have liked more examples which have helped me in solvent selection. Chapters on Detection and Visualisation; Quantification and Video Imaging; and TLC Coupling Techniques complete the monograph.

Overall this is a very readable account of how to begin to use TLC from first principles and with lots of very practical advice. What it lacks are detailed case studies of where TLC has been used and how problems of difficult resolutions have been solved, except when looking at complex natural product mixtures. The short sections on HPTLC and quantification show how the technique can be used for accurate analysis and can be coupled to other techniques in a similar way to HPLC.

Overall this book can be recommended to industrial chemists wishing to refine their TLC expertise, and it will help them to understand how to achieve better separations.

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Hydrolases in Organic Synthesis, 2nd Edition. By U. T. Bornscheuer and R. J. Kazlauskas. Wiley-VCH: Weinheim, 2006. xii + 355 pp. £100. ISBN 3-527-31029-0.

The previous edition of this volume was well received when it appeared in 1999. The authors have updated the text but have focused on new areas, new insights, and new frontiers rather than adding a comprehensive set of additional data. The extra 20 pages compared to the first edition include new chapters on protein sources, optimisation of biocatalyst performance for organic synthesis, and catalytic promiscuity, and the sections on dynamic kinetic resolution, immobilisation, and directed evolution have been considerably expanded. These enhance the work considerably. So for those who have not previously purchased the first edition, this is an excellent buy.

If you already have the 1999 volume in your library, I am not sure whether the new edition is sufficiently different to justify the expense. One of the things I liked about the first edition was the comprehensive nature of the table and figures, where substrates, yield, and ee in the transformation and a reference were given. This was most useful. Unfortunately, the authors have decided that most of these figures should *not* be updated, and therefore large sections are identical to the first edition. This seems to be a lost opportunity to replace some older examples with references from the literature 2000−2005.

The reference list at the end covers over 90 pages, partly because the full title of each reference is given, a most useful

attribute for the reader. Less than 20% of the references, however, are new, even though there has been tremendous activity in the field in the past 6−7 years.

The subject matter is discussed from the viewpoint of the organic chemist, and the chapters are arranged by functional group transformations rather than by enzyme type. This makes for an easy-to-read text, nicely separated by schemes and figures, all beautifully produced.

In conclusion, this second edition should be in every library interested in organic synthesis. If your library already owns the 1st edition, it may be more difficult to persuade the librarian, if such a person still exists, to "fork out" for a slightly expanded version of the first edition.

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