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Book Reviews *

Regulatory Chemicals Handbook. Jennifer M. Spero; Bella Devito; Louis Theodore. Marcel Dekker: New York, Basel. 2000. 1036 pp. $195.00. ISBN: 0-8247-0390-1.

The *Regulatory Chemicals Handbook* provides a compendium of information on about 600 chemical substances controlled by three pieces of U.S. legislation: hazardous air pollutants (HAPs) as defined by the Clean Air Act; priority water pollutants (PWPs) as defined by the Clean Water Act; and OSHA chemicals, as defined by the Occupational Safety and Health Act. The book treats these as three separate lists, each organised alphabetically. There is, naturally, some duplication, although not as much as might be thought. For example, anthracene and other fused aromatic hydrocarbons are listed as PWPs, but surprisingly, they do not feature in the OSHA list.

The information provided depends to some extent on which list the substance appears in. For all listed substances there are details of: CAS registry number, U.S. Department of Transport identification number, synonyms, physical properties such as melting and boiling points, density and vapour pressure, solubilities, and chemical properties such as sensitivity to heat, moisture, strong acids or bases, oxidants, etc. Details of biological properties and bioaccumulation are provided for the 126 PWPs only. No molecular structures are given—only molecular formulae and MWs.

For the majority of entries, a great deal of useful handling information is provided, for example on toxicity, acute and chronic health risks and symptoms, explosion and fire concerns, recommendations for storage, exposure, personal protection, spill clean up, fire-fighting, first aid, and disposal. There are also details of the regulatory status of the substances and of the regulations applying to them. One curious feature is that animal toxicity data (e.g., rat LD_{50}) is provided not under "toxicity" but rather under "general comments".

As a work of reference, this will be most immediately useful to chemists and managers in the U.S.A. who need to organise their work to comply with the respective legislation. More generally, it can be a source of valuable data for incorporation into in-house Material Safety Data Sheets. For most substances handled, the chemist will have to seek this information elsewhere, but this book will at least provide corroboration and perhaps additional data for the substances it does cover.

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Polymer Modification: Principles, Techniques, and Applications. Edited by J. J. Meister. Marcel Dekker: New York. 2000. 914 pp. Price $235. ISBN 0-8247-0078-3.

This edited text has been produced by 14 contributors including the editor. It appears to have been prepared "camera-ready" since there is considerable variety in the font, font size, structure packages, and so forth used throughout. The relatively poor production quality overall detracts from the content.

The strength of the book is its overall subject matter "polymer modification" coupled with the reasonably comprehensive coverage of key polymeric materials, both natural and synthetic. Although it is possible to find information in the literature on polymer modification, to find it concentrated in one text is rare.

The editor in his preface indicates that the book was designed as both an advanced text for a course (chemistry? polymer chemistry?) in polymer modification, and a reference work for professionals in polymer science and engineering. Perhaps this dual objective has led to the book's falling between two stools! There is an odd mixture of information dealing on one hand with simple ideas in polymer chemistry, to on the other hand, for example, very detailed ^{13}C NMR assignments of model compounds relevant to phenol−formaldehyde. Since it is in part an instructional text, each chapter ends with a list of questions, answers to which are presented in Appendix I. Appendix II continues the instructional element with 68 pages constituting a primer on polymer structure, molecular weight, polymer types, polymerisation methods, solvents and solution properties, and glass transition temperature. It is difficult to see why Appendix II has been included in a book on "polymer modification" and why some basics of polymer science were included and yet others not. Surely directing readers unfamiliar with basic polymer science to an existing introductory text would have been more sensible and saved 68 pages!

The "polymer modification" chapters deal with cellulose, lignin, starch, other natural gums, polyethylene, polystyrene, PVC, Nylon, epoxy resins, phenol−formaldehyde, and oddly, polymer liquid crystals. The term modification is taken very loosely and covers anything from specific chemical derivatisation to plasticization. Very disappointingly, many of the chapters are rather retrospective with few references after ~1990. In some cases this simply reflects a mature area and there can be no objections to this, but in others this is simply not so, and there is a feeling that the author has not bothered to research contemporary work, or is oblivious to it.

Had I seen this title in a book list dated 2000, with my own interest in a particular aspect of "polymer modification", I would have been keen to acquire it. Having now had the privilege to examine the content more fully, without resort to my own budgets, I realise that the text holds little value

*Unsigned book reviews are by the Editor.

for me personally. However, for those new to the area, and particularly for those who might want background information on a fairly broad range of macromolecules, the book is a reasonable starting point.

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OP0001133

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Designing and Operating Safe Chemical Reaction Processes. Health & Safety Executive (UK). HSE Books: Sudbury, UK. 2000. 78 pp. £12.50. ISBN 0-7176-1051-9.

The latest guidance from HSE is aimed at small to medium-sized manufacturing companies using batch and semi-batch processes to produce intermediates, fine and speciality chemicals, pharmaceuticals, dyestuffs, polymers, resins, etc. The approach is essentially regulatory and is aimed at management, particularly those responsible for the development, design, and operation of chemical plants and processes. It explains how to prevent and control the risk of exothermic runaway reactions, with sections on chemical process hazards, hazard assessment, selecting and specifying a basis of safety, and finally, management of chemical processes (process instructions, management of change, training, maintenance, audits, emergency procedures).

This is a useful booklet with excellent up-to-date references. Readers will need to use the reference books since the book provides guidance but not enough technical information to decide how to follow the guidance. There is also a useful glossary, though again some terms are rather inadequately defined (e.g., accelerating rate calorimeter (ARC): a type of adiabatic calorimeter). There is no index, and the glossary does not refer to the page where the term is used, and thus it cannot suffice as an index.

Essentially this is a volume which will enable British companies to comply with the law. It will be useful to chemists and engineers in other countries, but it has, of course, been aimed at the U.K.

I would have liked to see more chemical examples in the text. It is clear the volume has been written by chemical engineers and aimed at chemical engineers. Some examples of inherently safer synthetic routes to complex molecules should have been included (e.g., new routes avoiding hazardous reagents, not just simple reagent substitutions in an existing route). In the section on "predicting reactivity and stability" it is suggested that nitrogen-containing compounds (e.g., amides, imides, nitrides, azides, etc.) may be energetic or hazardous. I think the amides referred to are sodamide and simpler inorganic compounds and not organic amides such as NMP or DMF which are commonly used as solvents. In the same section, oxygenated compounds of halogen are listed without specific reference to perchlorates, and peroxides are specifically included without mentioning other peroxo compounds such as hydroperoxides, peracids and esters, etc.

In the section on interpreting screening data it suggests that for small companies testing houses and consultancies could be used but fails to provide an appendix of suitable companies, which would have been useful.

Whilst the differences between laboratory- and plant scale are mentioned, the largest scale ups are often from lab to pilot plant, when multipurpose plant is often used. Guidance on this scale is distinctly lacking. What the chemist or engineer needs to do at each scale of operation would have been useful, and although it is recognised that this will vary from case to case, some real examples would have helped with interpretation.

Runaway reactions have often occurred when something abnormal in the process occurs (delay in processing owing to equipment breakdown, different quality of raw material or solvent but still within the specification, often caused by a change in supplies, etc.)

This aspect is not really addressed, that is, that testing the normal process may give a basis of safety, but this may not be valid without a great deal of process R&D and additional safety studies. With the current trend of "speed to market", the detailed process studies may not be carried out before the first scale ups are operated.

Two concepts used in pharmaceutical bulk active manufacture, GMP and process validation, have, in my view, helped to produce safer processes by minimising the chances of process operator error and by having a better understanding of the **critical process** parameters which affect rates of reaction and by-product formation. These concepts not only help companies to produce products to tight specifications but also put better control on processes—this has to be good for safety.

Despite these comments, this slim, low-priced volume should be read by all process R&D managers, chemical engineers, and safety professionals. Ideally they should have their own copy.

OP000102+

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Pharmaceutical Fine Chemicals - Global Perspectives. R. Bryant. Informa Publishing: London. 2000. 129 pp. $790. ISBN 1-86067-4755.

This is a Chemical Industry report concerned with market intelligence—hence the high price. The author defines pharmaceutical fine chemicals (PFCs) as covering:

- raw materials and intermediates
- finished bulk drugs (including generics)
- custom synthesis
- toll manufacture

The total sales per annum are estimated at 60 billion U.S. dollars. He analyses the different customers and the chemical producers in depth, defining the different sectors and their individual requirements. The analysis is presented with strong opinions, a lot of insight, and occasionally with humour, making it a fascinating report to read.

The main chapters include the demand for PFCs, supply of PFCs, business aspects, customers for PFCs, companies

involved in producing PFCs, technology, current state of the industry, and outlook.

The analysis is truly global, covering in detail the rise of India and China as sources of PFCs, as well as U.S.A. and Europe. The report is filled with tables of data relating to company sales and market value and has some useful information on who owns whom, although current frenetic merger and acquisition activity has already made the information a little out of date. The report is quite critical of some recent mergers and acquisitions, stating that "the individual parts do not always act in concert. Central decision-making can be slow, and it has been the case that poor performing operations have not been dealt with sufficiently quickly".

Some useful data on global manufacturing capacity of key raw materials, intermediates, and building blocks as well as bulk actives is tabulated—this is information that is not easily found or estimated.

The report emphasises that companies supplying intermediates and final products to the pharmaceutical industry may rely heavily on a highly qualified workforce of process chemists and it is this group's ability to meet short deadlines and produce high quality processes and products which is critical for success. New technologies in themselves do not win business, without the backup of good chemists. The author here clearly betrays his background as a process chemist in industry. Readers of OPR&D will, no doubt, wholeheartedly agree with him!

In summary, the report will be of value to those working in the chemical and pharmaceutical industries, particularly in business development, outsourcing, and contract manufacture and marketing.

OP000125O

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Catalysis of Organic Reactions. Edited by Michael E. Ford. Marcel Dekker: New York. 2000. 672 pp. $195. ISBN 0-8247-0486-x.

Catalysis of Organic Reactions continues the series of the same name, which comprise the contributed papers from the conference organised by the Organic Reactions Catalysis Society. The proceedings contain 58 chapters, which originated at the 18th Conference held in Charleston, South Carolina, in May, 2000. The editor and publishers have, therefore, done an excellent job of getting the proceedings in print so quickly. The contents are a mixture of industrial and academic case studies on homogeneous and heterogeneous catalysis, with the latter predominating.

Chapters which are of interest to process chemists include the following:

- A new type of heterogeneous nickel−aluminium catalyst which is active in reductions but is easier to filter and reuse. The preparation is much less exothermic than usual Raney nickel catalysts, and foaming is less. Scale up is relatively easy.
- Selectivity between batch slurry and continuous fixed-bed hydrogenation, including full cost analysis—a case study from Dixie Chemical
- Safety and economic considerations in the design of an industrial hydrogenation facility—a case study from Searle/Monsanto
- The safe handling of activated nickel catalysts—a case study from Hoffman-La Roche and Degussa Huels
- Production of aromatics catalysed by commercial sulphated Zirconia solid acids
- Vapour-phase synthesis of indole and its derivatives
- Carbons as catalysts (for ester hydrolysis)
- LiOH-modified sponge catalysts for control of primary amine selectivity in the nitrile hydrogenation
- Catalytic hydrogenation of benzonitrile over Raney nickel—influence of reaction parameters on rates and selectivities
- Reaction pathways in the catalytic reductive *N*-methylation of polyamines
- Reductive alkylation of 2-methylglutaro-nitrile with Pd catalysts
- The synthesis of amines by catalytic hydrogenation of nitro compounds
- Novel preparation of 5-α-dihydroethisterone from androst-4-ene-3,17-dione
- Selective epoxidation of allylic alcohols with amino-modified titania−silica aerogels
- Heterogeneously catalysed conversion of substituted methyl aromatics to aromatic aldehydes and nitriles
- The Heck reaction as a clean alternative to Friedel−Crafts chemistry
- Chiral modifiers for supported metals
- Anchored homogeneous catalysts

The proceedings are required reading for all process chemists and engineers interested in catalysis, particularly heterogeneous catalysis. The emphasis of the volume is practicality and industrial application.

Highly recommended!

OP000130S

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Biopharmaceutical Process Validation. Edited by Gail Sofer and Dane W. Zabriskie. Marcel-Dekker: New York. 2000. 382 pp. $150.00. ISBN: 0-8247-0249-2.

This is the 25th volume in the Biotechnology and Bioprocessing series of monographs. Its publication is timely when one considers the progress being made towards the commercial introduction of increasing numbers of biopharmaceutical products and the challenges which face the emerging companies in the biotechnology sector.

Advances in the characterisation of biopharmaceuticals have led to a greater understanding of the critical parameters which control their production and quality. Changes in the regulatory environment for biological products, particularly in the United States, have also postponed the point at which the manufacturing process and the site of commercial manufacture must be fixed. These two factors have combined to create an opportunity to develop more economic, efficient, and reproducible manufacturing processes along the lines

with which those involved with NCE development and manufacture will already be familiar. This opportunity also comes with a "price" of an increased requirement to carry out formal equipment and process validation, although, as one of the contributors to the book points out, such validation is rewarded by improved process performance with fewer failures, etc.

The book is a collection of contributions from a large number of specialists, mainly based in the United States where the industry is more established. It is organised in a logical manner with a few introductory chapters being followed by detailed works on each stage of the biopharmaceutical manufacturing process in the sequence in which they occur in practice. Extended references and data sources are provided at the end of each chapter. These make the book suitable as a general introduction to those new to the subject as well as a more detailed treatise for those seeking more specific information. The early chapters are especially useful in allaying the fears of many who might regard the whole issue of validation as a black art! An organised approach is promoted along with careful preparation and a good technical understanding of the critical process parameters. This theme extends into the more detailed chapters and contributes to a very readable volume.

One criticism concerns the lack of reference to the issue of process validation at contract manufacturing facilities. The contributors to this volume are primarily based in companies which have their own manufacturing facilities and hence have more direct control over activities in these areas. For emerging biotechnology companies such facilities might not be available, and manufacture of early clinical trials supplies is contracted out. However, it is at this stage that much of the process development and preliminary validation has to be carried out. The strategy of the company might assume that full-scale manufacture will be the responsibility of some future partner, but the partner might not arrive in time to take on the full scope of process development and validation. The challenge of carrying this out in the interim by a third party is not to be underestimated and would have been worthy of a reference.

This is a minor criticism, and the book is to be recommended to all who are actively involved in this subject and also to those who wish to gain more insight into an area of increasing importance in the pharmaceutical industry.

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Perspectives in Organopalladium Chemistry for the XXI Century. Edited by J. Tsuji. Elsevier: New York. 322 pp. $147.00. ISBN 0-444-50197-5.

Palladium is undoubtedly the most important transition metal used for organic synthesis. It catalyses a broad range of very useful transformations, and indeed most complex syntheses usually employ a palladium-mediated step en route to the target.

This book, edited by one of the fathers of modern organopalladium chemistry, brings together 21 leading authorities to describe their contributions to the field. Each chapter describes the author's own work and usually describes the mechanisms, scope and limitations, and which catalysts/cocatalysts are required, together with a brief explanation for their choice. This latter aspect is especially useful as it allows the reader to extrapolate to new situations. Many of the authors focused on their own work which I found frustrating although this is what the editor asked them to do. For example, the chapter by Helmchen on asymmetric allylic substitution does not include the excellent ligands developed by Trost for cyclic substrates. In contrast, the chapter by Buchwald on amination of aryl halides and sulfonates does include Hartwig's contributions, but there is a significant bias towards the authors own ligands.

Although most of the leading authors are presented (e.g., Herrmann, Grigg, Negishi, Helmchen, Suzuki, Buchwald), a number are absent (e.g., Trost, Bachvall, Tsuji). As such, there is no discussion of Pd(II)-catalysed additions of nucleophiles to alkenes or dienes, which seemed like an important omission. Carbonylation in relation to organic synthesis is also absent although its application in polymerisation is covered.

These criticisms notwithstanding, I found the chapters highly informative with important subtle pieces of information concerning catalysts and cocatalysts. These subtleties arise from the myriad of possible mechanistic pathways through which palladium may catalyse even a single transformation (there is an excellent chapter on mechanism by Amatore). However, armed with such information one may go some way in transforming a failed palladium-mediated process into a successful one. This book should therefore be in every library although it is rather expensive for individual collections.

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