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Book Reviews *

Pharmaceutical Substances 2.4 . By Axel Kleeman, Juergen Engel, Bernhard Kutscher, and Dietmar Reichert. Thieme: New York, Stuttgart. 2006. Online Product Available by Annual Subscription at www.thieme-chemistry.com. Price on Application

Pharmaceutical Substances is an online compendium of some 2400 of the most significant pharmaceutical compounds of industrial interest.

For each drug the following information can be accessed:

(i) chemical structure

(ii) synthetic route (graphical representation)

(iii) intermediates

(iv) nomenclature (INN standard, trivial names, synonyms)

(v) CAS registry numbers (including intermediates)

(vi) ATC codes

(vii) medical applications/therapeutic category

(viii) toxicological data

(ix) patent information (number, origin, holder, and application date)

(x) commercial information (e.g., formulations)

(xi) bibliographic information (including CASSI codes)

The database is searchable by structure and substructure (including reaction searching), which will be of particular use to those designing synthetic routes to active pharmaceutical ingredients, intermediates, and related compounds. The system supports ChemDraw and ISISDraw and has a built-in JAVA applet so that researchers can use whichever is their preferred structure drawing tool.

The database is updated reasonably regularly (at least once per year), which ensures that newly approved substances are included. The bibliographic information provided is good, although the criteria for inclusion or exclusion of information are not apparent. There are certainly missing pieces of information. For example, the entry for amlodipine fails to include the published patents describing the most effective and direct method for resolving the enantiomers. The references would certainly be much more useful (and more searchable) if the titles of the papers and patents were included.

Text searching is weak and has not been improved, despite the recommendations of this reviewer 2 years ago (P. L. Spargo, *Org. Process Res. Dev.* **2004**, *8(*6*)*, 1084).

The following examples illustrate the textual search limitations.

(i) A search for "polymorph" yielded only two hits, while "polymorphic" yielded four (different) hits and "polymorphism" two (different again!) hits. A search for "crystal form" gave three hits and "crystal modifications" another three (different) hits.

(ii) Searches for "pde5" and "PDE5" gave no hits, but "PDE 5" gave four hits (including sildenafil and vardenafil, but not tadalafil, although the latter is present in the database). "PDE V" gave two hits (not including sildenafil or vardenafil). A complementary search for "phosphodiesterase" gave five hits (tadalafil plus four others, but neither sildenafil nor vardenafil!).

(iii) Amazingly, a search for "statin" gave only one hit (atorvastatin) although the other statins are, of course, present in the database!

(iv) Textual inconsistencies meant that to find all mesylate salts one would have to search for "mesilate" as well as "mesylate". (A substructure search using the mesylate counterion was a more fruitful, if cumbersome, approach to this search.)

Overall, this is a useful compendium for those working in the pharmaceutical and allied industries. The structure and substructure searching capability is very good, and the database is particularly useful when directly searching for a known drug, as opposed to classes of drugs. However, the textual searching is weak, and the data within is not comprehensive.

Pricing depends on the number of potential users in an institution. The price for a 1 year subscription for up to 20 users in 2007 is 4,330 Euro. At that price, more comprehensive information might be expected, and the text searching and indexing function should be better. Until such improvements are made, the full potential of this otherwise admirable online resource cannot be realised.

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Thiophenes. By Salo Gronowitz and Anna-Britta Hörnfeldt. Elsevier: Oxford, 2004. xxii + 964 pp. $323.00. ISBN 0-1230-3953-3

This text is one of the *Best Synthetic Methods* (BSM) series, a well-known and much-admired collection of review articles focused on modern synthetic methodology. As the title suggests, the subject matter contained in this addition to the BSM family spans pretty much all of the wide range of chemistry associated with this class of heterocycles, so one would expect the text to be lengthy, and it is (reaching nearly 1000 pages). The content is divided systematically into 15 separate chapters, with 6 of these giving a thorough and meticulous description of the preparative methods most often used to prepare thiophenes functionalized with Groups

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I−III and V−VII appendages; additionally, there is a more detailed focus upon thiophenes bearing carbon substituents, such that the remaining 5 chapters describe the preparation of thiophenes bearing the whole gamut of sp3-, sp2-, and sp-hybridized carbon moieties. The text concludes with a lengthy chapter devoted to the preparations of oligothienyls, a very justifiable inclusion, given the great applied and academic significance of these hetarenes during the recent past.

This book is a tour-de-force, representing a superb review of this subclass of heteroaromatic chemistry, and it will likely become a *vade mecum* for practitioners of this particular organic art. The organization of the manuscript makes the (occasionally dense) subject matter very amenable to the curious amateur and consummate professional alike, and the critical description of the methodology described is both insightful and informative. The detail provided is considerable, and although the visual presentation is occasionally a little "old school" (especially in the diagrams), the exhaustive coverage of pertinent experimental data more than compensates for any perceived deficiencies in the format. There are a few minor typographical errors and some linguistic compromises, but these slight peccadillos do not detract from the power and appeal of this mighty tome. Recommended unhesitatingly.

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Synthesis of Acetylenes, Allenes and Cumulenes: Methods and Techniques, 1st ed. by Lambert Brandsma. Elsevier Academic Press: Boston, Amsterdam. 2004. xxxii + 469 pp. $249. ISBN 0-1212-5751-7.

Lambert Brandsma has produced several laboratory manuals over the years, and this volume combines and updates some of them. The organisation of the chapters will be familiar to those who have used those earlier works. Unfortunately, there is too much similarity to those previous books when what is really needed is a thorough overhaul and updating. Take chapter one on Procedures and Equipment, for instance. While it contains some handy hints, and some useful diagrams of experimental set ups, it is oddly dismissive of that staple of the lab, the magnetic stirrer. Curious to note, too, is that the rotary evaporator and TLC earn no mention. Chapter two, on the other hand, covers the Preparation, Purification and Storage of Some Solvents and Reagents. This is all useful information.

Subsequent chapters cover different classes of reactions, from the familiar to the obscure. Chapter three concerns the Generation of Metalated Acetylenes, Allenes and Cumulenes. Synthesis of some acetylenes from 1,2-dibromides by elimination is also included, as are some allene−alkyne isomerisations. The isomerisation of alkynes from internal to terminal is also in this chapter, although oddly the reference given is not to the (more convenient) *Organic Syntheses* procedure. There is a wealth of detailed information in this chapter, and numerous helpful tables.

Chapter four covers alkylation reactions, including epoxides. There is rather too much emphasis on liquid ammonia for my taste, although some THF and DMSO procedures are scattered around. Chapter five, Reactions and Aldehydes and Ketones, and Chapter six, Carboxylation, Acylation and Related Reactions follow. Both chapters have a good range of useful examples. Chapter Seven, Silylation, Stannylation and Phosphorylation starts with how to make TMS acetylene—very helpful for chemists with limited means. Most of the chapter involves using Me_3SiCl, but there are sufficient tin and phosphorus reactions. The use of heteroatoms continues in Chapter 8, Sulfenylation and Related Reactions. The chapter is rather longer than the subject deserves. Halogenation is covered in Chapter 9.

Chapter 10 discusses Elimination. Some of the coverage here impinges on chapter 3. All the main methods are represented, and the molecules range from the everyday to the exotic. Chapter 11 is devoted to allenes and their formation from dihalocyclopropanes—the Skatterbøl reaction.

Chapter 12 moves into transformations, with a wide range of substitution and alkylation reactions. A curious omission here is the formation of optically active allenes from propargyl derivatives using conjugate hydride addition. Chapter 13 focuses on the copper (I)-catalysed Mannich chemistry of acetylenes. This is where one might expect to find the Searles−Crabbe reaction—probably the best, most general method for making terminal allenes. Professor Brandsma comes very close to this reaction (he would have it if he tried $R = i$-Pr in expt 13.2.2!) but shies away at the last moment. I find this an even stranger omission than rotavaps in chapter 1.

Chapters 14, 15, and 16 show Brandsma at his most modern, covering coupling reactions: Chadiot−Chodkiewitz, Glaser and Sonogashira. The last of these is thoroughly covered, with numerous examples.

Chapter 17 covers base-catalysed isomerisation of acetylenes. Chapter 18 covers sigmatropic rearrangements, including the very handy formation of allenic sulfoxides from propargyl alcohols, but not their further transformations.

Chapters 19 and 20 cover a whole range of miscellaneous reactions, largely functional group transformations. A large section here is devoted to S_N' displacements of propargylic substrates.

The book concludes with useful tables of data. These are quite comprehensive but show their age as much of the ^1H NMR data lists CCl_4 as solvent. IR data—highly characteristic with these classes of compounds—is absent. Appendices B and C function as the index. The book, as in previous books by the author, lacks a proper index.

It is easy to be disappointed with this book. You will find no discussion of the place of these functional groups in synthesis, no "big picture". It is not really a book about cumulenes. Acetylenes take centre stage, and allenes have a secondary role with some of their important reactions being

ignored. I could not find the excellent Searles−Crabbe reaction anywhere! The definition of cumulenes is rather odd: a few 1,2,3-trienes are in, but heterocumulenes are out. The standard of citing of the literature is patchy with a unhealthy over-citing of the author's own work. Many of the procedures strike this reviewer as old-fashioned. Many ways to follow reactions which have been standard and every-day for so long such as TLC and gas chromatography are ignored. Many of the procedures have a "sameness". There is little variation in technique thoughout the book—for example, alkylations are more often than not in liquid ammonia, Sonogashira couplings are in excess amine.

Nevertheless, if the prospective purchaser is able to overlook these shortcomings, the book can be a good buy. If what you want is detailed, even meticulous, experimental procedures to make and use acetylenes, then you should look no further. The procedures described cover a wide range of compounds, even if the range is not as wide as the title might imply. The procedures are clearly and thoroughly written; obviously, these have been done and refined in the author's laboratory and not extracted from the literature. On the other hand, if you want an up-to-the-minute book, putting acetylenes and cumulenes into their current context, you will be disappointed.

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Biocatalysis in the Pharmaceutical and Biotechnology Industries. Edited by Ramesh N. Patel. CRC Press: Boca Raton, FL; London. 2007. 893 pp. $169.95, £99. ISBN-10 0-8493-3732-1.

This mammoth multi-author volume contains 34 chapters on all aspects of biocatalysis, with subjects such as Nitrilases and Nitrile Hydratases, Biocatalytic Deracemisation, Flavin-Containing Oxidative Biocatalysts, Industrial Processes using Lyases, Enzymatic Synthesis of Modified Nucleosides, etc. In fact, the volume covers all the major areas one would wish to see in such a tome and contains some excellent reviews of individual topics. So why am I dissatisfied with certain aspects?

First, there is no introduction to the work and no final summing up or conclusions. This would have been an ideal opportunity to summarise the state of play in industrial biotransformations and to look forward to the future, possibly highlighting where the gaps in the biocatalytic armoury are lacking, As a result, although the individual chapters are fine, there is a lack of an overall picture.

Second, there is some overlap between chapters. While this can be acceptable if the authors have coordinated their chapters well, in this case the chapter headings indicate that the overall scheme of the book has not been properly thought out, for example, three different chapters on the synthesis of chiral intermediates and two on the synthesis of optically active amines.

Third, for a book title which has the word "industries" in it, I would have expected the majority of chapter authors to have been based in industry; yet only 17 out of the 78 authors listed are from pharmaceutical or biotechnology companies. As a result, the emphasis is not as industrial as one would expect from the title. However, the academic authors have given insight into the potential uses in industry which is valuable, given the time it takes for academic inventions to become used in industrial processes.

Nevertheless, despite these overall criticisms, I enjoyed the individual chapters, and each author has made an attempt to give an idea of the future perspectives in his area. The chapters are extremely well referenced, and the titles of the references, which help the reader to determine whether the references are worth following up, are given in some, but not all chapters. Most chapters include references up to 2004, so already the chapters are a little dated. This is, of course, not the fault of the author but of the publisher, who has taken so long to convert the manuscripts to the finished product. A comprehensive 44-page index assists the reader in locating individual topics, although the chapter headings will usually have indicated where to find the desired information.

There is no doubt that this work should be in the libraries of all who have interests in biocatalysis, whether in academia or in industry, and this volume complements the previous work by the same author, which was published in 2000. Although there have been many books on biocatalysis and biotransformations in the past few years, this work does not duplicate any of the previous works and provides relatively up-to-date data on a very wide range of topics in a highly readable format. Recommended, with the limitations expressed earlier.

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