Organic Process Research & Development

BOOK REVIEW

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# Book Review of Pharmaceutical Process Chemistry for Synthesis, Rethinking the Routes to Scale-Up

**Pharmaceutical Process Chemistry for Synthesis, Rethinking the Routes to Scale-Up**. By Peter J. Harrington. John Wiley & Sons: Hoboken, NJ. 2011. 369 pp. Price £83.50/€100.20/$125.00. ISBN 978-0-470-57755-4.

This book contains 9 chapters and covers the process chemistry used to make 8 of the top 10 selling drugs in the world in 2007−8. The list includes Actos (pioglitazone hydrochloride), Lexapro (escitalopram oxalate), Effexor (veblaxafine hydrochloride), Seroquel (quetiapine hemifumarate), Singulair (montelukast sodium), Prevacid (lansoprazole), Advair Diskus (salmeterol xinafoate), and Lipitor (atorvastatin calcium). The author (formerly with Roche) has only included drugs where he had no previous detailed knowledge of the process chemistry and so deliberately omitted any Roche compounds.

For each target the author selected typically 3−4 building blocks as the basis for a thorough literature and patent search. Each chapter begins with a short overview of current and past marketplace information for the target, followed by a detailed discussion of the process chemistry described in the literature. This is not an easy book to read as there is so much detail included. In many cases it seems as if one is reading a series of experimental procedures. For example there are 15 paragraphs describing slightly different variations on the pivalic acid catalysed Paal−Knorr pyrrole synthesis to make the same pyrrole intermediate en route to Lipitor, when the information could probably have been better presented as a table.

The book is aimed at a wide audience including synthetic chemists interested in making these top selling drugs, process chemists looking for methods proven on scale up, discovery chemists seeking to understand the strategies used by generic companies to develop noninfringing processes, and also for use as a possible core information source for a one semester course on process chemistry in universities. As almost every conceivable way of making each target is described, this book could be invaluable for chemists in generic pharmaceutical companies except that they have probably acquired all this information already as most of these products are either off patent already or are due to go off patent over the next 5 years. The other audiences will find the necessary information in this book but will have to sort the wheat from the chaff to find it. I only found one omission−the simulated moving bed chromatographic separation to generate the chiral centre in escitalopram which is used in production.

The book is at its best when the author gives his own views on particular aspects of the chemistry described, and at the end of each chapter there is a section on what the author considers to be the "best process available today". The author does occasionally display the typical pharmaceutical process chemist's prejudice against certain reactions and reagents. Oxidation reactions for example are described as either using toxic reagents and/or are volume inefficient. Similarly diazotisation reactions are described as being difficult to scale up even though they are the backbone of the dyestuffs industry, but these are relatively minor quibbles.

The author is to be applauded for the amount of work he has clearly put in to preparing this book, but in my view a better book would have resulted if he had included more of himself and less literature detail. There are some really useful nuggets of information and comments and suggestions in the book; it is just that there is so much detail to wade through to find them. Overall the book is recommended, but with some reservations.

**Will Watson**
Scientific Update

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