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Walter Cabri and Romano Di Fabio, **From Bench to Market: The Evolution of Chemical Synthesis**

Oxford: Oxford University Press, 2000. 266 pages hardback and paperback. Hardback £60.00 Paperback £19.99
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Reviewed by D. M. Andrews, Stevenage, England

It is perhaps very appropriate that a book devoted to the optimisation of process research and development chemistry (PR&DC) should emanate from Italy – not only one of Europe's prime locations for pharmaceutical R&D, but also one of the most important European locations for bulk generic manufacturers.

The aim of this book is neatly set out in the first chapter at overview level – it aims to illustrate how the creativity and skills of PR&D chemists can determine the most efficient strategies for the bulk synthesis of drug material in an increasingly competitive marketplace. The book describes how modern bulk synthesis needs to take account of such diverse factors as the patents in effect on pre-existing processes; regulatory requirements and procedures; laboratory-to-pilot plant scale-up problems; environmental concerns; cost of intermediates; and competition between companies.

The authors have been personally involved in several of the processes described and in all cases it is clear that they are able to draw extensively upon experience gained with some of the pre-eminent PR&DC groups, both in Italy and internationally.

The main body of the book is devoted to nine case histories – descriptions of industrial syntheses of molecules spanning five of the main therapeutic areas. The examples have been carefully chosen to carefully illustrate the impact of stereoselective methodology and enzymatic and organometallic catalysis on modern industrial synthesis. Nearly all of the examples are marketed proprietary products which are now (or soon to be) subject to generic competition and thus also illustrate the impact of competitor activity. The only exception is the case history for sanfetrinem, which has not yet been marketed by its originator. Furthermore, its inclusion fails to add any significant concepts not already covered in the other four chapters covering anti-infectives. This is a minor criticism however – in all cases the authors present a very comprehensive and detailed account of the chemical challenges.

For each case history the format is the same: a description of the pharmacology and mode of action of the compound concerned follow a general introduction. This is then followed by a retrosynthetic analysis at a strategic level before an exhaustive description of the different chemical routes and processes detailed in the literature. The entries for nabumetone and acyclovir are typical in that each describes 13–15 distinct synthetic approaches – this in spite of the fact that both are relatively simple molecules. Herein lies one of the main strengths of the book – an extraordinary range of chemistry is covered in great depth, including information about yield, purity and solvents used, as well as isolation methods. The strengths and weaknesses of each route are considered in isolation, as well as their patent status (novelty *vs.* freedom-to-use *vs.* infringement of prior art). Each chapter ends with a summing up of all the pertinent factors and an analysis of the factors that lead the authors to conclude which is the most effective route.

The final chapter looks to the future and describes the ways in which pharmaceutical companies are searching for a new paradigm in discovery research to allow them to maintain their current rates of growth and secure future optimised financial returns within the fairly static G7 market. The book ends on a positive note: "This pressing need to create more powerful tools for synthesis promises a bright future for skilled organic chemists working in the pharmaceutical industry."

The book itself is well laid out with a very helpful table of contents. By contrast, the index is rather too brief to be of very great utility and could be significantly

enhanced in any future editions. The presentation of the references (which are collected together at the end of each chapter) will present no problem to experienced industrial chemists. This group is familiar with the need to distinguish abandoned patents from those that are continuations-in-part and from divisionals of US patents. Academic readers may find fault with this format on two counts: they may not find it easy to follow and they may not have easy access to many of the sources quoted. Given that in several cases the coverage is rather selective, a more pragmatic arrangement might be to adopt an even more abbreviated format – presentation of just enough summarised material to allow the interested reader to generate more extensive in-house patent searches.

Who should buy this book? The first and concluding chapters of this book provide a perfect overview to the context and future perspective of modern PR&DC. These chapters will be of general interest to members of any of the scientific disciplines who are active within the field of pharmaceutical research, since all of the principles and challenges of launching drugs into today's markets are described in non-specialist terms.

I found this book to be a thoroughly enjoyable read and it should appeal to all practising synthetic, organic and medicinal chemists. Indeed, the natural audience of this book is likely to be rooted firmly within the chemistry community – it should prove to be inspirational reading for PhD and BSc chemists alike, especially those who are seeking careers within any aspect of pharmaceutical chemistry. To paraphrase the preface: The challenge the industrial chemist faces stimulates rather than hampers our creativity – our ability to behave like craftsmen in working with atoms and molecules.

Dr David M Andrews is currently Head of the Department of Medicinal Chemistry at GlaxoSmithKline Research & Development, Stevenage, where he is engaged in research into new antiviral therapies. He has been involved in various medicinal chemistry research programmes at GSK over the past 11 years.