Organic Process Research & Development

BOOK REVIEW

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The Art of Process Chemistry

The Art of Process Chemistry. Edited by Nobuyoshi Yasuda. Wiley VCH: Weinheim, 2010, 298 + xv pages, £100, ISBN 978-3-527-32470-5

In the preface, the editor explains why he has chosen the word "Art" in the title and how it can apply to organic synthesis, especially when creativity is involved. I think it is justified in relationship to the topic covered in this book—process chemistry—which requires great ingenuity and flair.

This beautifully produced book comprises nine chapters—all case studies—from 10 process chemists all working at Merck in the United States. Each case study is of a different drug substance or group of related substances and discusses the medicinal chemistry route, and new routes, with optimisation and development of each stage in the synthesis. While some of the case studies have been published or presented at conferences, the value of this compilation is that the choice of route and how it was developed is discussed in detail, along with mechanistic understanding where necessary. However, it is often this understanding which leads the scientist to further improvements and to control (e.g., of stereochemistry).

The book will be of great value to students looking to move into a career in process research; the enthusiasm and commitment of the authors comes over in the text, and the attention to detail and emphasis on mechanistic evaluation is a lesson to all.

Those in academia will find much material that can be used in teaching.

Process researchers will also find hidden in the text some key practical tips on synthesis, as well as product extraction and isolations.

The case studies include compounds of which only a few kilograms have been made (and maybe are still under development) as well as those made on many tonnes scale, and which are already on the market (Efavirenz, finasteride, raltegravir, etc.). A minor criticism of the approach is that scale up is rarely discussed, and the problems we all have on scale up are only occasionally mentioned. Thus, a typical quotation after detailed synthetic and mechanistic work has been carried out is "The first-generation process was rapidly and successfully scaled up to provide multi-tonne quantities of bulk drug to adequately supply needs through phase III drug filing and launch".

The implication from statements such as this is that there were few problems and that this was straightforward. I doubt it! Only occasionally are hints given about issues such as crystallisation problems, hazards, etc. Even though one synthesis uses a large excess of alkylating agent in the last step, the question of genotoxic impurities is not mentioned.

So, in conclusion, this is an outstanding book which discusses the art of process research and developing process understanding. Issues usually encountered on scale up to pilot plant and beyond are less adequately covered here, but are likely to be covered in a new edition of Anderson, due out shortly.

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Editor

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