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*Book Reviews**

The Claisen Rearrangement: Methods and Applications. Edited by Martin Hiersemann and Udo Nubbemeyer. Wiley-VCH Verlag GmbH and Co. KGaA: Weinheim. 591 pp. £155. ISBN 978-3-527-30825-5.

This book comprises 11 chapters devoted to the Claisen rearrangement and its variants.

The Preface remarks on the fact that Claisen published the rearrangement in 1912 with the all-carbon variant published some 38 years later by Cope, so it is perhaps curious that the Claisen rearrangement should also be known as the 3-oxa-Cope reaction. More significantly, the editors comment that, when carrying out key word literature searches for hetero-Claisen reactions, one should be mindful that terms such as 3-aza-Cope and 3-thia-Cope need also to be used to avoid missing substantial portions of the literature. A useful word of warning for those wanting to pursue the literature further for any of the reaction categories

The book introduces the topic of the Claisen rearrangement by discussing the biotransformation using the enzyme chorismate mutase which catalyses a Claisen reaction of chorismic acid. This is a key branch point intermediate in the biosynthesis of aromatic amino acids in microorganisms and plants. The chapter provides an interesting insight both into the Claisen rearrangement and more specifically into this biosynthetic pathway. The chapters that follow are then dedicated to the many variants of the rearrangement, and all are well presented with many examples and brief discussion of the pertinent points, then closing, for the most part, with examples of applications in synthesis. Since I have had only cursory contact with the Claisen rearrangement over the past 25 years, it was refreshing to read some details of the mechanism as well as learn more about the tactics used to control the transition state in order to gain a high degree of control over the stereochemical outcome in the products. On this subject, I found chapter 2 particularly interesting in which metal-catalysed reactions were discussed along with the impact different metals can have on influencing chair vs boat transition states and hence the product stereochemistry. The chapter discussing the Ireland−Claisen rearrangement was also especially interesting to me, providing good background information to the control of enolate geometry and clearly underlining the importance of this in the overall outcome.

Since first being introduced to the Claisen rearrangement as a chemistry undergraduate I have always been both intrigued by and interested in rearrangement chemistry, and this interest encouraged me to pick this book up in the first place. The final chapter deals with the mechanistic aspects of the aliphatic Claisen rearrangement. The author of the chapter has provided a chronological review of the literature, so that the reader gets a sense as to how the understanding has developed since the early views of Hurd and Pollack in 1938. The progression through the literature shows how the mechanism unfolded using key reports concerning substituent effects and the transfer of stereochemistry. The chapter concludes that "the mechanism for the aliphatic Claisen rearrangement in the absence of strong acid proceeds through an early transition state, which is characterised by a concerted but asynchronous bond-breaking and bond-making process. However, the extent of bond-breaking and bond-making is highly dependent on substituents and solvents, as is the geometry and energy of the transition state." Thus, it is gratifying to read that my undergraduate lecture of some 25 years ago remains broadly valid in this rapidly changing world of science and technology!

Overall, this is a useful text for the academic library with some interest for the industrialist. It is notable that there did not appear to be any examples of synthetic use from large-scale industry application, which may at least in part be a result of the fact that, where isomeric products are possible, the rearrangements are rarely stereospecific, and although high selectivity is possible, the challenges of removing even small percentages of an isomeric side product may be too great at industrial scale. Nevertheless, the rearrangement reaction remains a very powerful tool for carbon−carbon bond formation, especially quarternary carbon centres, and should not be overlooked by industrial chemists when evaluating synthetic routes to a target, whether in Discovery or Development laboratories.

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Pharmaceutical Manufacturing Handbook. Edited by Shayne Cox Gad. Wiley-Interscience. 2008. 1370 + xiii pp £103. ISBN 978-0-470-25958-0.

Whilst this compendium is mostly related to secondary manufacturing, there are some chapters which are of interest to readers of *Organic Process Research & Development* (OPRD). The editor has done an excellent job of recruiting more than 60 experts in the various fields to cover issues related to the seven themes of Manufacturing Specialties, Aseptic Processing, Facility, Normal Dosage Forms, New Dosage Forms, Tablet Production and Role of Nanotechnology. The longest section, over 500 pages, is on new

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dosage forms and methods of drug delivery, and the next is tablet production, about 240 pages. There are 34 chapters in the 7 sections.

Chemists and chemical engineers working in API production will be interested in the chapter on From Pilot Plant to Manufacturing: Effect of Scale Up on Operation of Jacketed Reactors by B. Wayne Bequette, but the 20 pages is mostly devoted to heat transfer issues. Readers are referred to the excellent paper by Ed Paul in *Chem. Eng. Sci.* **1988**, *43*, 1773−1782 for mixing and mass transfer issues rather than the excellent and more up-to-date book on mixing by the same author.

OPRD readers will also enjoy the chapters on Pharmaceutical Preformulation: Physicochemical Properties of Excipients and Powders and Tablet Characterization and Role of Preformulation in Development of Solid Dosage Forms. These chapters, with some duplication between the two, discuss issues such as physical/bulk characteristics of solids for example crystallinity and polymorphism, hydrates, amorphates (briefly), particle characteristics, flow and compressibility, as well as salt selection and solubility characteristics. In this section neither the excellent book *Pharmaceutical Salts* by Stahl and Wermuth nor the thought-provoking work by Bernstein are referred to, and there are a number of typographical errors in other references. An excellent chapter on Effects of Grinding in Pharmaceutical Tablet Production is also well worth reading, although the effect of grinding on crystal form is not discussed in detail.

Other chapters which may interest OPRD readers include Radiopharmaceutical Manufacturing; Sterile Product Manufacturing; Clean Facility Design, Construction and Maintenance Issues; Solid Dosage Forms; Liquid Dosage Forms; Controlled-Release Dosage Forms, Tablet and Production Systems and Biotechnology-Derived Drug Product Development. A four-page index, inadequate for a volume of over 1000 pages, is provided.

In summary, this is a useful overview of pharmaceutical, particularly secondary, manufacturing with many chapters being relatively up-to-date, (i.e., to 2006), covering issues such as QbD and the current regulatory climate. The compendium can be recommended for library (if yours still exists!) purchase.

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