

Crystallization of Organic Compounds

Crystallization of Organic Compounds. By Hsien-Hsin Tung, Edward L. Paul, Michael Midler, and James A. McCauley. Wiley: New York, 2009; 289 + x pages, £66.95, ISBN 978-0-471-45780-9

For chemists and engineers working in process research and development, or even in production, this is the best book on crystallisation. For those in other disciplines or in academia, wishing to get a perspective on industrial problems in crystallisation, polymorphism, salt formation, etc. and how to solve them, this would also be a valuable book.

The authors all previously worked at Merck (U.S.A.) on crystallisation-related issues and are all now retired; they must be sorely missed. One hopes that their decades of experience have been passed on to others at Merck. This book will additionally help to spread the knowledge outside Merck.

The content is backed up by 30 case studies which exemplify the discussions in many chapters. These case studies describe real examples of what can go wrong in development and production, and how the problem was solved. Some of these case studies have previously been presented at conferences on process R&D, scale up, or chemical engineering, or have been published in a wide range of journals. So it is good to have them described in detail in this format, where more discussion and critical analysis can be allowed.

Chapters which process chemists and engineers will find particularly useful are the four that describe the different methods of crystallisation, namely cooling, evaporative, anti-solvent, and reactive. The special features needed to control and optimise each type of crystallisation with respect to impurity control, particle size distribution, crystal habit, or polymorph/solvate are clearly elucidated and exemplified in each chapter.

Nevertheless, the early chapters covering fundamentals are also treated from a practical perspective and are well worth exploring. Of particular importance is the chapter on mixing and crystallisation (one of the authors—E.L.P.—has also written books on Mixing) which discusses the effect of mixing on nucleation and crystal growth as well as on scale up of industrial processes. Both batch and continuous operations are included in many chapters, perhaps a surprise for many readers since the authors are all from the pharma industry where few continuous processes have been developed. These authors were clearly ahead of their time.

One minor criticism: when a particular drug is mentioned—particularly with respect to polymorphism—it would have been useful to have the chemical structure drawn out; this would also help to make the molecular views (e.g., Figures 3-23 and 3-24) more understandable, particularly in terms of hydrogen bonding. Where structures are provided in the book, they are often poorly drawn with incorrect bond angles.

On the back of the book the authors indicate that they had two goals:

- (1) Build a deeper understanding of the fundamental properties of crystallisation as well as the impact of those properties on crystallisation process development.
- (2) Improve readers' problem-solving abilities by using actual industrial examples with real process constraints.

I think they have achieved both of these goals admirably and in a very readable and enjoyable format.

No lab, office, or library should be without a copy!

Trevor Laird
Editor

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