

MS34 Crystallization Techniques and chemical reactions driven by solid state interactions

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Chaperone Compounds for Co-Crystallization of Small Molecules

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Abstract

Modern instrumentation and processing techniques enable high-quality 3D structure analysis – including absolute structure determination – often in less than an hour, i.e. faster and more comprehensively than many spectroscopic methods can achieve. However, many small or highly flexible organic molecules remain intractable to current crystallization methods, including the crystal-sponge method[1]. A new chaperone-aided crystallization method[2] based on tetraaryladamantanes (Figure1) has delivered high quality co-crystals in a fair number of cases, allowing for the structure determination of analytes, including their stereochemistry. The adamantine chaperone approach works well for analytes that are liquid at room temperature and adds an important tool to the toolbox for both synthetic organic chemists and crystallographers, facilitating the investigation of small molecules, such as new natural products, synthetic intermediates, pharmaceutically active ingredients, or fragrances.

The chaperone-aided crystallization method is easy to apply and crystals suitable for the determination of absolute configuration are typically obtained within minutes or hours. With modern X-ray instrumentation the method can provide very fast access to the full 3D structure of an important class of organic analytes.

Salient features include:

- Structures in hours or days rather than weeks
- Small quantities of analyte required
- No solvent screening required

Four chaperone compounds are being made available, helping to obtain suitable crystals with ordered analyte in the unit cell, allowing for determination of relative or absolute configuration.

We will discuss the method and demonstrate rapid crystal growth for examples, such as the two enantiomers of limonene.

References

- [1] Inokuma, Y.; Yoshioka, S.; Ariyoshi, J.; Arai, T.; Hitora, Y.; Takada, K.; Matsunaga, S.; Rissanen, K.; Fujita, M. *Nature* **2013**, 495, 461–466.
- [2] Krupp, F.; Frey, W.; Richert, C. *Angew. Chem. Int. Ed.* **2020**, 59, 15875–15879.

Fig1: Chaperones based on tetraaryladamantanes

