MS28 Navigating crystal forms in molecular and pharmaceutical materials

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The mystery of a co-crystal disappearing polymorph – case solved with quantum crystallography methods

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Abstract

In the last decade, with the variety of possible applications of multicomponent materials, polymorphism in co-crystals has become more common or maybe more investigated by the scientific community. [1]

On the one hand, obtaining different forms of a co-crystal can lead to new materials with significantly different physical properties. However, in many cases, control over the obtained crystal phases containing more than one building block can be more challenging than in single-component materials. Performed experiments can lead to the concomitant polymorphs being difficult to separate and to so-called disappearing crystal phases.

Here we present the case of three polymorphs of urea barbituric acid co-crystals, which were obtained for the first time in 2008 by one of us [2]. Two phases were centrosymmetric ($P2_1/c$ and P-1), whereas the third was polar, crystallizing in the Cc space group. After the form $P2_1/c$ was obtained the Cc polymorph was not reproduced using the same or modified experimental conditions, neither in our home lab, nor by other researchers [3]. Therefore, it was considered to be one of the cases of metastable, disappearing polymorphs.

Using modern quantum crystallography tools, we understood the process of the polar co-crystal formation. Electron density studies combined with calculations of interaction energies gave us an idea for an advanced cocrystallization experiment used to reproduce the missing co-crystal form. Not only were we successful, but we also established ideal conditions for obtaining the remaining two polymorphic modifications [4,5]. This work gives a foundation for using quantum crystallography to study concomitant polymorphism phenomena in multicomponent materials.

References

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Figure 1