Poster

Experimental electron density distribution in cocrystals of theophylline and pyromellitic acid.

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Co-crystals, systems of two or more neutral compounds crystallizing in one structure (with all the due reservations – excluding solvates, hydrates etc, cf. quite a vivid discussion some time ago), are recently subject of quite intensive studies due to their expected properties, for instance solubility of pharmaceutically important compounds. Due to the very nature of these crystals the number of high-resolution structures of cocrystals is quite small (e.g. [1 - 3]).

For some time, we have been studying the cocrystals of alkaloids with pyromellitic (1,2,4,5-benzenetetracarboxylic) acid (PMLA). In the course of these studies a series of well-diffracting samples of cocrystals of theophylline (TPH) were obtained, including two polymorphic forms of 2:1 TPH – PMLA, hydrate TPH-PMLA-H_2O (1:1:2) and methanol solvate TPH-PMLA-MeOH (2:1:1). High resolution data of good quality were collected and the analysis of experimental electron density was performed with Hansen-Coppens multipolar model [4]. The examples of the obtained static deformation maps are presented in Fig. 1.

Additionally, we were able to determine the experimental conditions allowing to obtain certain polymorphic form, for different crystallization methods: form the solution, by grinding and using microwaves.

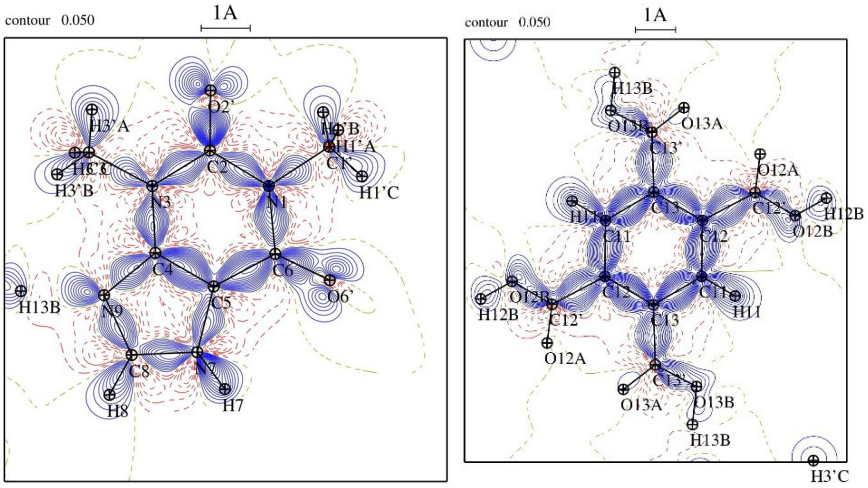

Figure 1. Static deformation maps for the polymorph II of TPH – PMLA: theophylline (left), and acid (right)

The results allow for comparison of the intermolecular interaction in polymorphic forms as well as in solvates of appropriate cocrystals. Also, the estimation of the charge transfer between the coformers could be done, electrostatic potential and topology of the electron density distribution are analyzed in detail.

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