Crystal Engineering through Solvent Mediated Control of Molecular Conformation: The Case of 5-Hydroxynicotinic Acid

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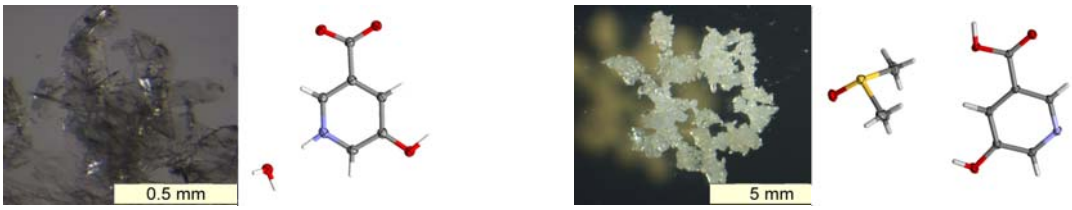
The importance of molecular conformation for polymorphism and its consequent repercussions in terms of tight control over the industrial production crystalline organic materials with highly reproducible physicochemical properties has long been recognized. Efforts to understand how a crystallization solvent can direct the formation of a polymorph containing a specific molecular conformation are, however, relatively scarce. Nicotinic acid (NA) and its hydroxyl derivatives (2-, 4-, 5-, and 6-hydroxynicotinic acids) are very good models for such studies. Indeed, regardless of the solvent, NA always crystallizes as a single polymorph with the molecule in the same neutral conformation. In contrast, the hydroxyl derivatives are prone to polymorphism and solvate formation and, depending on the crystallization conditions, the molecules in the crystal lattice can exhibit hydroxyl, oxo, or zwitterionic conformations [1].

Here we describe study of 5-hydroxynicotinic acid (5HNA) showing that by judicious selection of the solvent it is possible to obtain 1:1 solvates, where solvation memory is not completely lost and the tautomer preferred in solution persists in the crystalline state: zwitterionic in 5HNA·H_2O and neutral in 5HNA·DMSO. Nevertheless, upon thermal desolvation the obtained materials evolve to the same unsolvated form where the molecule is in a zwitterionic conformation. The structures of 5HNA·H_2O and 5HNA·DMSO obtained from single crystal-ray diffraction are discussed and compared with that of 5HNA solved from powder data. The energetics of the dehydration/desolvation prcess was also fully characterized by thermogravimetry (TG), differential scanning calorimetry (DSC) and Calvet microcalorimetry.



(a) (b)

Fig. 1. Crystals and molecular conformations of the 5-hydroxynicotinic acid hydrate (a) and DMSO solvate (b).

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