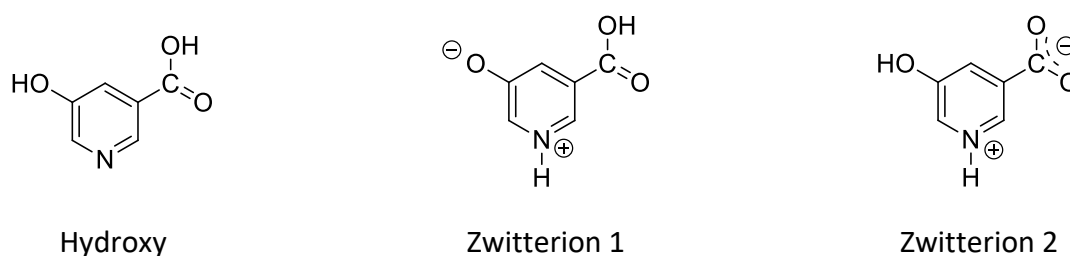


## Solvent Mediated Control of 5-Hydroxynicotinic Acid Molecular Conformation in the Crystalline State

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Crystallization from solution is the most widely used method to obtain and purify compounds. Nevertheless, despite being used by man for millennia, there is still little understanding on how molecules associate in solution to form crystalline materials. A particular unexplored aspect within this scope is how tautomeric equilibria in solution can influence the crystallization of molecules in a particular conformation. The hydroxyl derivatives of nicotinic acid (which have biological importance and ample applications, including the manufacture of pharmaceuticals, herbicides and insecticides), are very convenient models for these studies, since they exhibit competing tautomeric forms.<sup>1</sup>

In this work the crystallization of 5-hydroxynicotinic acid (5HNA; Figure 1) from a protic (water) and an aprotic (DMSO) solvent, was used as a model to investigate possible relationships between the dominant molecular conformation in solution and in the corresponding crystallized material. Single crystal X-ray diffraction analysis showed that crystallization of 5HNA from water and DMSO led to a hydrate and a solvate, respectively, of 1:1 stoichiometry. Furthermore, the conformation adopted by the molecule in the hydrate is zwitterionic (Zwitterion 2 in Figure 1) and in the DMSO solvate is hydroxylic (Hydroxy in Figure 1) which, according to NMR evidence, correspond to the predominant tautomers found in the corresponding mother solutions. This work, therefore, suggests that the formation of hydrates and solvates, where the memory of solution is not completely lost, may provide a mean to control the molecular conformation in crystalline materials.



**Figure 1.** Tautomeric forms of 5-hydroxynicotinic acid.

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