Poster Prize Competition | Are you eligible? | NO

The role of proton transfer in multicomponent crystals of pyridine derivatives with carboxylic acids

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The estimation of the extent of proton transfer between proton donor/electron acceptors and proton acceptor/electron donor moieties, both in intra- and inter-molecular cases, can be considered an emerging approach in crystal engineering, aimed at predicting the strength and the nature of hydrogen bonding interactions.[1] This is particular important in the field of pharmaceutical cocrystals, due to the presence of aromatic base (e.g. pyridine) and/or carboxylic acid functionalities in many compounds of pharmaceutical relevance[2,3]. In general terms, shared proton between unprotonated pyridine and carboxylic group leads to neutral co-crystal formation, while completely transferred proton, associated with the formation of charge-assisted H bonds between carboxylate anion and pyridinium cation, leads to a molecular salt [4,5]. To predict whether multicomponent systems in solution would co-crystallize as molecular salts or neutral co-crystals, the evaluation of ΔpKa = pKa(protonated base) - pKa(acid) could be of help: according to the so-called "rule of three", a salt is expected if the ΔpK_a ($pK_{a-(base)} - pK_{a(acid)}$) is greater than 2 or 3 units, while the formation of a cocrystals is observed if the ΔpK_a is smaller than 0 [1,6].

The present case study deals with the formation of molecular salts/ co-crysta containing pyridoxine, the alcohol derivative of pyridine, well known as vitamin B6, that widely used both in therapy and food supplementation, and aromatic acids or other coforme from the FDA-GRAS (Generally Accepted as Safe for Food Additives by the Food &Dr Administration) list [2,3].

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