Oral presentation

Modification of intermolecular interactions by inducing proton transfer in multicomponent crystal based on malonic acid and 4,4′-bipyridine

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The nature of interactions between entities can be an indicator of different types of multicomponent crystals. In cocrystal the hydrogen bonds most commonly govern aggregation, while in salts Coulomb interactions between ions are the most significant. When the crystal is built of Brønsted-Lowry acid-base pairs the ΔpKa rule can be used to predict which one will be formed. According to the original version of this empirical rule the formation of a salt is expected when ΔpK_a ($\Delta pK_a = pK_a$ [protonated base] − pK_a [acid]) is higher than 2 or 3 [1]. For low values of $\Delta pK_{a,}$ formation of cocrystals will be preferential. More precise categorization was proposed based on the analysis of almost 6500 structures of ionized and non-ionized acid–base pairs [2] deposited in the Cambridge Structural Database [3], and recently, it has been shown that values of the boundaries strongly depend on the crystal packing and molecular structure [4].

The H-bonds in cocrystals direct molecular aggregation in a manner that transfer of a proton between entities involved in hydrogen bond is structurally possible if appropriate stimulus is applied, enabling formation of a salt. One of such stimuli is high pressure. It is known to strongly affect solid matter leading to a wide range of transformations, including proton-transfer reactions [5].

In this study, a model cocrystal (BIPYMA) based on 4,4′-bipyridine (BIPY) and malonic acid (MA) was investigated under pressure using X-ray diffraction and Raman spectroscopy techniques, supported by DFT calculations, in order to induce and confirm cocrystal-to-salt transformation [6]. The reaction was structurally possible as molecular aggregation is controlled by O-H···N hydrogen bonds binding BIPY and MA molecules alternately into chains. When BIPYMA cocrystal was compressed up to ca. 3.3 GPa intricate modifications to its protonation states were revealed (Fig. 1), showing pressure-controlled switching between hydrogen and ionic bonds These results were then confronted with existing studies on proton transfer in multicomponent crystals to correlate the ΔpK_a with the pressure required to induce proton-transfer reaction to add additional dimension to the $\Delta p\,K_a$ rule by extend its applicability to variable pressure conditions.

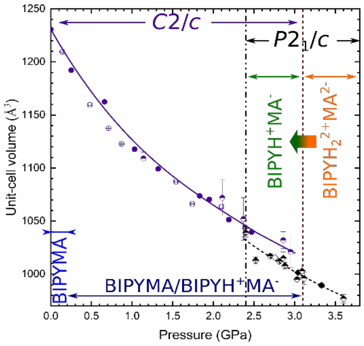

Figure 1. Pressure dependence of unit-cell volume with the stability regions for BIPYMA in different protonation states, and pressure ranges in which specific crystal symmetry is observed, marked with arrows.

[1] Stahl, P. H. & Wermuth, C. G. (2002). *Handbook of Pharmaceutical Salts: Properties, Selection and Use.* Weinheim: VHCA: Wiley-VCH.

[2] Cruz-Cabeza, A. J. (2012). *CrystEngComm*, **14**, 6362.

[3] Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.*, **B72**, 171.

[4] Cruz-Cabeza, A. J., Lusi, M., Wheatcroft, H. P. & Bond, A. D. (2022). *Faraday Discuss.,* **235**, 446.

[5] Boldyreva, E. V. (2014) *Z. Kristallogr,* **229**, 236.

[6] Patyk-Kaźmierczak, E., Izquierdo-Ruiz, F., Lobato, A., Kaźmierczak, M., Moszczyńska, I., Olejniczak, A. & Recio, J. M. (2004) *IUCrJ,* **11**, 168.

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