

Synthesis and Energetics of Maleic acid-Glycine and Fumaric acid-Glycine Binary Crystals

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Multicomponent crystals have attracted considerable interest in recent years as a means to tune the properties of crystalline products without changing the molecule of interest.¹ Two prevalent types of multicomponent crystals are binary salts and binary co-crystals, which differ by the fact that two counterions or two neutral molecules are present in the crystal lattice, respectively. This strategy has been particularly useful, for example, to improve the solubility of active pharmaceutical ingredients (APIs) or food additives.

Different preparation methods can lead to different products, even if starting materials from identical batches are used. The assessment of the stability of a specific binary co-crystal or salt relative to its precursors, therefore, becomes of considerable importance.

A recent theoretical work predicted that the formation of co-crystals from their precursors is generally enthalpy driven.¹ This is not, however, a necessary condition, as shown by the recent report of an entropically stabilized cocrystal.²

Another relevant issue is that for neutral precursors with ionizable protons the preference for salt or cocrystal formation depends on the tendency for proton transfer between the potential donor and acceptor counterparts.

This preference was analyzed in this work for two systems: maleic acid-glycine (MA-Gly) and fumaric acid-glycine (FA-Gly). It was found that a MA-Gly salt and a FA-Gly cocrystal were always obtained regardless of the preparation method used: crystallization from solution or mechanochemistry. The differences in crystal structure between the obtained materials were evaluated based on single crystal X-ray diffraction data. Finally, the relative stability of MA-Gly and FA-Gly relative to their precursors was assessed in terms of lattice energy, based on calorimetric measurements.

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References

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