

Structural characterization and mechanism for crystal desolvation induced by polymer-assisted grinding

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Many compounds take up solvent molecules into their structures during synthesis or storage, often resulting in new crystal structures with different physicochemical properties. The opposite process, desolvation, is important for preparing industrial products such as the processing of food and pharmaceuticals, organic synthesis, and activation of porous compounds. Heating is generally the primary lever for desolvation, but other methods include pressure control and mechanical stresses. In this study, we demonstrate the possibility to achieve tunable desolvation using polymer assisted grinding.

The crystalline sesquisolvate of theophylline (THP) and 2-pyrrolidone (PYR) (2:3 THP:PYR) [1] was ground with a wide variety of different polymers. Interestingly, this process leads to varying degrees of PYR desolvation. Both the type and amount of polymer were found to affect the amount of PYR removed, leading to three different cases: 1. no significant solvent removal, 2. partial removal to varying extents, or 3. step-wise removal, with the ability to return the crystalline monosolvate (1:2 THP:PYR) and pure crystalline THP. To better understand the mechanisms involved, representative polymer-sesquisolvate systems were characterized by x-ray diffraction, pair distribution function (PDF) analysis [2], and Raman spectroscopy to elucidate the nature of structural and chemical changes in different components. Differential PDF analysis showed changes in the local structural ordering, which correlated with the strength of desolvation response and morphology of the polymer backbone. This was complimented by simulations to estimate the relative reaction energies for the different solvation processes. Altogether, the results indicate that the behavior is driven by a balance between the energy penalty needed to desolvate theophylline and the energy released upon solvation of the polymer.

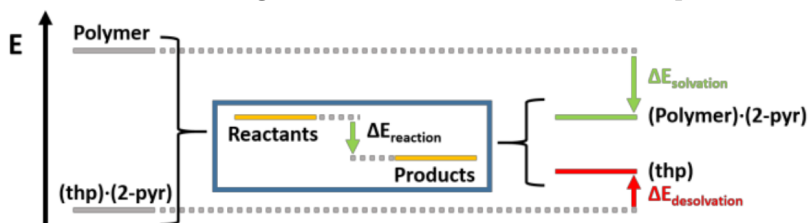


Fig. 1 Energy balance for the desolvation process.

- [1] D. Hasa, M. Pastore, M. Arhangelskis, B. Gabriele, A. J. Cruz-Cabeza, G. S. Rauber, A. D. Bond, W. Jones. On the kinetics of solvate formation through mechanochemistry. *CrystEngComm*, 2019, 21, 2097-2104.
[2] M. W. Terban, S. J. L. Billinge. Structural analysis of molecular materials using the pair distribution function. *Chem. Rev.* 2021, DOI:10.1021/acs.chemrev.1c00237