

MS28-2-6 Stability of Co-crystals - a Density Functional Theory study
#MS28-2-6

R. Fox ¹, J. Klug ¹, D. Thompson ², A. Kellett ¹, A. Reilly ¹

¹Dublin City University - Dublin (Ireland), ²Dublin City University - Limerick (Ireland)

Abstract

Co-crystals are crystals of more than one molecule held together through dispersion interactions such as Hydrogen bonding, dipole-dipole interactions, and Van der Waals interactions. Co-crystals have also been more stable than their single-crystal counterparts, as indicated by their higher lattice enthalpy.^[1] In literature, hydrogen bonding has been the main focus to account for the stability of co-crystals.^[2] However, other dispersion interactions like Van der Waals could be necessary for stabilising co-crystals.

Various Density functional theory (DFT) methods have been used to calculate the lattice enthalpy of experimentally made thermodynamically stable co-crystals. These methods include Tkatchenko and Scheffler (TS) and Many-Bodied dispersion (MBD) dispersion corrections. This co-crystal set includes simpler molecules, 4,4'-bipyridine and oxalic acid, and more complex active pharmaceutical ingredients, aspirin and paracetamol; these are all experimentally made structures. Previous work has shown that most co-crystals are thermodynamically stable, so calculations are expected to have a negative enthalpy.^[1]

Using the DFT method, simple systems of oxalic acid and 4,4'-bipyridine were calculated to be more stable than their single-component counterparts, with the calculations predicting negative lattice enthalpies. Whereas with more complex systems of aspirin and paracetamol, the DFT methods predict that some of the co-crystals are less stable than their single-component counterparts, with some co-crystals producing positive lattice enthalpies.

The prediction might not predict might not accurately calculate the lattice energy of the complex systems by the DFT methods. However, the geometry optimisation does not consider that kinetic effects might play a role in the stability of these co-crystals.

References

- 1 C. R. Taylor and G. M. Day, Evaluating the Energetic Driving Force for Cocrystal Formation, *Cryst. Growth Des.*, , DOI:10.1021/acs.cgd.7b01375.
- 2 A. V. Yadav, A. S. Shete, A. P. Dabke, P. V. Kulkarni and S. S. Sakhare, Co-crystals: A novel approach to modify physicochemical properties of active pharmaceutical ingredients, *Indian J. Pharm. Sci.*, 2009, 71, 359–370.