EXPLORING POLYMORPHISM OF MOLECULAR MATERIALS USING HIGH PRESSURE - OPENING UP NEW DIMENSIONS IN POLYMORPH SCREENING

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The importance of polymorphism in crystallisation processes is widely recognised and is the subject of intense academic and industrial interest. Although the use of high pressure has been shown by physicists and geoscientists to be a powerful method for accessing new polymorphs of metals, alloys, ceramics, and minerals, there have been relatively few studies on the effects of high pressure on intermolecular interactions in simple molecular compounds. Recent work at Edinburgh has shown that direct compression of either single crystals or powders, and crystal growth from the melt are two methods that can be used to prepare new polymorphs of simple organic compounds. These new forms have been structurally characterised by X-ray and neutron diffraction. For more complex materials, such as pharmaceuticals, pigments, or explosives, we have developed methods for *in situ* growth of single crystals *from solution* at pressures in the range 0.5-20 kbar. This has allowed a much wider range of compounds to be studied, including pharmaceuticals, and has also enabled us to prepare new solvates. Using diamond-anvil cells, spectroscopic and structural characterisation of these materials can be performed *in situ*.

Since pressure influences intermolecular interactions so strongly and is so effective in changing the relative thermodynamic stabilities of crystalline forms, its use adds another valuable dimension to polymorph/solvate screening. This presentation will therefore demonstrate how pressure can be used to prepare polymorphs and solvates of a selection of typical pharmaceutical substrates, and how these may be characterised *in situ* using spectroscopic and diffraction techniques (both powder and single-crystal). The presentation will also describe how "bulk" quantities of metastable polymorphs/solvates can be recovered to ambient pressure for subsequent use in seeding experiments under ambient conditions.

References

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[2] Fabbiani, F.P.A., Allan, D.R., Parsons, S., Pulham, C.R., *CrystEngComm.*, (2005), **7**, 179.