Probing Polymorphism with High Pressure

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In recent years, work at Edinburgh has shown that pressureinduced crystallisation of simple organic compounds from the pure liquid results in the generation of new polymorphs [1]. Attempts to induce polymorphism in more complex, higher melting compounds (such as pharmaceuticals) have been much less successful. This is because thermal decomposition usually occurs long before the pressure-elevated melting temperature is reached.

We have instead developed a technique for growing single crystals from solution at high pressure that removes excessively high temperatures and provides an opportunity to study high-pressure crystallisation from different solvent systems [2]. We report how the power of this technique, in combination with ambient-pressure conventional polymorph screening processes, is not only successful in identifying known polymorphs of organic molecules, but also completely new polymorphs, and solvates, as illustrated by the nootropic drug piracetam, for which new polymorphs and hydrates were prepared and characterised at pressures below 1.0 GPa [3].

We believe that this methodology has the potential to make a significant impact for the discovery of new polymorphs and solvates.

[1] Allan D.R., Clark S.J., Ibberson R.M., Parsons S., Pulham C.R, Sawyer L., *Chem. Commun.*, 1999, 751. [2] Fabbiani F.P.A., Allan D.R., Dawson A., David W.I. F., McGregor P.A., Oswald I.D.H., Parsons S., Pulham C.R., *Chem. Commun.*, 2003, 3004. [3] Fabbiani F.P.A., Allan D.R., Parsons S., Pulham C.R., *CrystEngComm., in press.*

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