MS32-P3 A thermal gradient approach towards polymorph selection in thin films

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Polymorphism can be defined as the intrinsic ability of a solid material to exist in two or more crystal forms which may differ in the molecular conformation and/or crystal packing. The phenomenon is generally understood in terms of nucleation, i.e. once a nucleus of a given phase has appeared, growth continue in the same phase without any subsequent phase transition. Polymorphism is central to crystal science and is of great importance for industrial sectors like pharmaceuticals, fertilizers, explosives, pigments, and organic electronics because it has a dramatic influence on properties of materials. Although an extensive body of research is available in this topic, some elements key to the understanding of polymorphism is still missing. To this extent we sought to understand the role of heat flux in polymorphic control and phase transitions with a model system, acetaminophen. This is experimentally facilitated by a temperature gradient heating stage which essentially consists of two independent heating elements separated by a distance of 2.5 mm. One of the heating elements is set at a temperature, above the melting temperature (hot side) while the other at a temperature below the crystallization temperature (cold side) of acetaminophen. Structural evolution is then followed as thin films of acetaminophen are translated from the hot zone to the cold zone. Thin films are ideal model systems, because of the absence of convection, heat transport occurs only by diffusion. In this presentation, we report on the crystallization of polymorphs of acetaminophen as a function of thermal gradient parameters (magnitude of the gradient, sample velocity) in a thin film geometry. The thin film samples were displaced at a given rate ($1 \leq v \leq 75$ μm/s) to control direction and the rate of crystal growth. This allowed us to decouple nucleation and growth. A detailed structural analysis combining polarized optical microscopy (POM) and X-ray diffraction (out-of-plane, in-plane) has been carried out to characterize different crystalline forms produced by the thermal gradient technique.

Keywords: Polymorphism, Thermal Gradient, Thin film, X-ray Diffraction

MS32-P4 Re-investigating the structures of *trans*-$[Cu(NO_3)_2(en)_2]$ and *trans*-$[Cu(NO_3)_2(pn)_2]$; Tales of twinning and a reversible phase change leading to a new polymorph.

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The structure of *trans*-bis(1,2-diaminoethane) -dinitrato-copper(II), $[Cu(NO_3)_2(en)_2]$, has been reported twice previously,[1] including once as a private deposition to the CSD. On both occasions the data were collected at room temperature with a 4-circle serial diffractometer and the *R* factors at *ca*. 4% suggest there is little more to understand. Our recent re-determinations at low temperature on a CCD area detector system reveal both merohedrally twinned and non-twinned diffraction patterns from a single batch of crystals. We will describe the handling of the twinning and hence a halving of the *R* factor.

The structure of *trans*-bis(1,2-diaminopropane) -dinitrato-copper(II), $[Cu(NO_3)_2(pn)_2]$, has also been reported twice previously.[2,3] As above, both determinations were at room temperature on serial diffractometers. The first determination did not include H atoms and had an *R* factor of 12.2%. The second however, did include H atoms and refined to $R1 = 3.3\%$. A close inspection of the published ORTEP plot however, with hindsight, now provides clues to our new findings. A reduction in temperature leads to a loss of molecular symmetry and, primarily, a significant movement of both the nitrate ligands (Fig. 1). On re-warming the crystal, the original structure is obtained, albeit with a little de-lamination of the crystal. We will describe our experiments and the structural changes observed.

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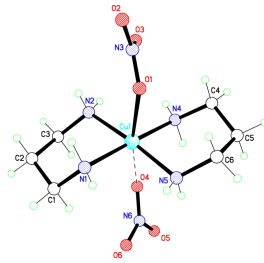

Figure 1. New unsymmetrical polymorph of $[Cu(NO_3)_2(pn)_2]$ at 160K.

Keywords: Polymorph, twinning, coordination complex.

MS32-P5 Cocrystal Systems of Cyanopyridines and Carboxylic acids

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In the recent past, multicomponent crystals like cocrystals, salts and solvates became more and more interesting due to their upcoming applications in pharmaceutical use and materials science.[1] The understanding of the formation of those compounds is an essential part of crystal engineering to achieve more knowledge about multicomponent crystal aggregation and subsequently to use this information to tune chemical and physical properties of active pharmaceutical ingredients (API) like solubility, bioavailability, melting point and stability.[2, 3]

In some cases it can be preferable to synthesize a cocrystalline compound instead of a salt, for example based on the poor predictability of salt structures in respect of their chemical and stoichiometric composition.[4] To select suitable compounds for targeted cocrystal growth, the pK_a-rule is a helpful tool. The ΔpK_a of a two component system (defined as $\Delta pK_a = pK_{a[base]} - pK_{a[acid]}$) can give reliable information concerning cocrystal or salt formation.[5-8]

In order to study the applicability of this method, selected compounds were chosen for a cocrystal screening. Different cyanopyridines, acting as bases with relatively low pK_a-Values were intended to be formed into cocrystals via solution crystallization with selected carboxylic acids as cocrystal-former.

In our studies, the pK_a-rule turned out to be a very accurate instrument for specific cocrystal approach. Depending on this rule we were able to design various cocrystals consisting of pyridine derivatives and carboxylic acids.

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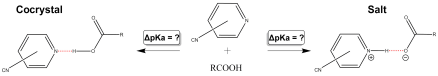

Figure 1.