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.

[1] D. Yan, A. Delori, G. O. Lloyd, T. Friščić, G. M. Day, W. Jones, J. Lu, M. Wei, D. G. Evans, X. Duan, *Angew. Chem.Int. Ed.*, **2011**, 50, 12483.

[2] P. Vishweshwar, *J. A. McMahon*, J. A. Bis, M. J. Zaworotko *J. Pharm. Sci.*, **2006**, 95, 499.

[3] N. Qiao, M. Li, W. Schlindwein, N. Malek, A. Davies, G. Trappitt, *Int. J. Pharm.*, **2011**, 419, 1.

[4] C.B. Aakeröy, M.E. Fasulo, J. Desper, Mol. Pharm., **2007**, 4, 317.

[5] D.A. Haynes, W. Jones, W.D.S. Motherwell, *CrystEngComm* **2006**, 8, 830.

[6] M. J. A. Bowker, P.H. Stahl, C.G.Wermuth, *Handbook of Pharmaceutical Salts*, **2002**, VHCA, Wiley-VCH: New York.

[7] R. Bhogala, S. Basavoju , A. Nangia, *CrystEngComm*, **2005**, **7**, 551.

[8] K. Molčanov, B. Kojić-Prodić, *CrystEngComm* **2010**, 12, 925.

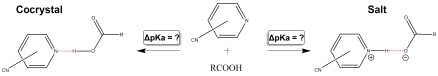

Figure 1.

Keywords: Cocrystal, Polymorphism, Intermolecular potentials, Hydrogen bonds, Carboxylic Acid, Cyanopyridine

MS32-P6 Dehydration of paroxetine hydrochloride forms I and II

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Paroxetine hydrochloride has two hydrate forms: a stoichiometric hemihydrate (form I) and a non-stoichiometric hydrate (form II). Both forms can be dehydrated to give two distinct anhydrous forms, which are isostructural with their respective parent hydrates.[1,2]

The water content and unit cell volume of form II change rapidly, continuously and without any noticeable hysteresis in response to changes in relative humidity at 30°C. Form I, on the other hand, shows a clear first order phase transition on heating, producing the pure dehydrated form after *ca.* 1 h at 100°C. Dehydrated form I converts back to hemihydrate form I at room temperature at relative humidities as low as 1%.

The dehydration process was monitored in-situ using synchrotron powder diffraction experiments. There was no evidence of any intermediate phase and the data allowed structure determination of form I dehydrate. It was revealed that both form I and its dehydrate are isostructural with the corresponding paroxetine hydrobromide forms.[3]

Comparison of the structures gives an explanation of the different stabilities and transformation kinetics observed. Form II contains solvent pockets separated by easy-to-open gates, and consequently it behaves as a channel hydrate. Molecular dynamics simulations show the mechanism of opening the gates, which are formed by hydrophobic rings with only weak intermolecular interactions between them. In form I, however, water molecules are separated from each other by strongly hydrogen-bonded chloride ions, so their removal is much more difficult. The dehydrates show poor hydrogen bond coordination,[4] which explains their low stability and easy conversion back to the isostructural hydrate form.

1. M. F. Pina, J. F. Pinto, J. J. Sousa, L. Fábián, M. Zhao, D. Q. M. Craig, *Mol. Pharmaceutics* 2012, **9**, 3515.

2. M. F. Pina, M. Zhao, J. F. Pinto, J. J. Sousa, C. S. Frampton, V. Diaz, O. Suleiman, L. Fábián, D. Q. M. Craig, *Cryst. Growth Des.* 2014, **14**, 3774.

3. P. S. Carvalho Jr., C. C. de Melo, A. P. Ayala, C. C. P. da Silva, J. Ellena, *Cryst. Growth Des.* 2016, **16**, 1543.

4. P. T. A. Galek, J. A. Chisholm, E. Pidcock, P. A. Wood, *Acta Cryst.* 2014, **B70**, 91.

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