Characterisation of the Metastable Form in Coffein Samples

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Caffeine is well known to exist in two polymorphic forms.[1-4] Several studies deal with the transformation behavior of the metastable form (mod. I or a-form) to the enatiotropically related stable form (mod. II or ß-form) including processing related conditions[5-7], but the fact that it is almost impossible to purchase or produce caffeine samples that contain only the thermodynamically stable form (II) is almost consistently ignored. The polymorphism of caffeine is in many respects a special case which is the consequence of its molecular features. The intermolecular interaction forces are generally weak and the planar molecules form stacked arrangements in the crystal structure. A recent structure determination of anhydrous caffeine from powder data[8] confirms the presence of orientational disorder and the structure of the high temperature form (mod. I) has never been solved because it is highly disordered. The purpose of this study was to gain insight into the order-disorder phenomena of this compound and to determine the ratio of the two polymorphic forms in caffeine samples, which were crystallized in different ways.

Caffeine was crystallized from various solvents in several ways and samples of mod. I were annealed at different temperatures below the transition point (140°C) in order to and obtain the thermodynamically stable state. The ratio of mod. I and the state of disorder was estimated by analyzing the transition endotherm (enthalpy, temperature, peak splitting) using DSC and to display the structural differences, XRPD and FT-Raman spectroscopy were applied.

The amount of stable mod. II in samples crystallized from solvents ranges from 14 to 92 % whereas this fraction is generally lower in samples obtained by evaporation of the solvent. We could not see a clear dependence on the solvent properties, except that nitromethane favors the crystallization of stable form with a low degree of disorder. Additionally, we found a new crystal form of caffeine (acetic acid solvate). Solvent mediated transformation leads to almost pure mod. II whereas annealing of mod. I between 90 and 120°C gives samples with splitted transition endotherms but high transition enthalpies. Available samples of mod. I, which were produced at different temperatures and stored for 8 years under controlled moisture conditions showed that moisture accelerates the transformation rate to mod. II but the samples still consist of 20 to 70% of mod. I. However, the results clearly show that all conventional production ways of “anhydrous caffeine” (crystallization from solvents, via the hydrate) results in a mixture of polymorps, respectively in some degree of disorder and that extra effort is required in order to obtain highly “physical pure” anhydrous caffeine.

References

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