

Selective Polymorph Transformation of Anthranilic Acid via Solvent-drop Grinding

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Each crystal packing arrangement of a particular chemical compound will possess a unique set of physicochemical properties such as dissolution rate, melting point and hygroscopicity. The discovery, selection and preparation of such polymorphs pertain to a variety of disciplines including pharmaceuticals, dyes and pigments. Because polymorph selection enables physical property optimization, novel methods of generating different crystal forms garner interest from both a scientific and an intellectual property perspective.

In general, polymorphs are often obtained by evaporating or cooling a saturated solution of the target compound, sublimation, crystallization from melt as well as solid-state grinding. Recently it was shown that solid state grinding in the presence of several drops from a pipette of a particular solvent increased the kinetics of cocrystallization and directed a solid state cocrystallization product to a specific polymorph [1-2]. Given these results, we chose to determine whether this 'solvent-drop grinding' method may offer improvement or selectivity in the crystallization of polymorphs of *single*-component systems, thereby offering much wider applicability [3].

Anthranilic acid that exhibits a trimorphic nature (structures of form I, II and III have been well determined) is a pharmaceutically interesting compound. We herein report specific polymorphic transformation of anthranilic acid via solid-state grinding. In particular, form I can transform to form II and III by solid-state dry grinding and solvent-drop grinding with heptane, respectively. Form II can transform to III by solvent-drop grinding with chloroform. In addition, form III can transform to form I and II in the solid state by grinding in the presence of water and heptane, respectively.

[1] Trask A.V., Shan N., Motherwell W.D.S., Jones W., Feng S., Tan R.B.H., Carpenter K.J., *Chemm. Commun.*, 2005, *in press*. [2] Trask A.V., Motherwell W.D.S., Jones W., *Chemm. Commun.*, 2004, 890. [3] Shan N., Toda F., Jones W., *Chemm. Commun.*, 2002, 2372.

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