Poster Presentation

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Hydrogen bonding structure and polymorphism in agrochemicals

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Polymorphism of crystals, crystal habit and crystal growth are important factors that must be controlled for any commercial crystallization process. Pharmaceuticals and agrochemicals are two of the most industrially-important, active-molecule systems for which the physical properties are strongly correlated to their crystal structure. While pharmaceuticals have attracted more academic interest to date, the market for agrochemicals is also very considerable, amounting to $15 bn annually. Given the potential significant toxicity of some agrochemicals, the ability to control physical properties such as solubility and dissolution rates, which depend on the crystal structure of the agrochemical itself, represents a way of optimizing the ratio between the amount of product used and its efficiency, improving its function and reducing its environmental impact. Hydrogen bonds play a crucial role in the spatial arrangement of the active molecules and the crystallization process. However, high accuracy and precision of the hydrogen atom positions can only be achieved through single crystal neutron diffraction (SND). SND experiments have been performed on three herbicides - isoproturon (IPU), pendimethalin (PDM), and diflufenican (DFF) - and the fungicide cyprodinil (CYP) [1][2]. All four structure refinements show a ten-time improvement in precision in the hydrogen atom positions compared to SXD with accurately determined nuclear positions. For cyprodinil, which crystallises as two polymorphs, A and B, differences in the hydrogen bonding network have been determined. Form A is governed by single, linear hydrogen bonds between two molecules, while the B form is characterized by the presence of dimers linked through pairs of hydrogen bonds, leading to a stable 8-membered ring. These differences in structure are reflected in the physical properties of the two polymorphs such as melting point and the observed slow inter-conversion that takes place during storage.

[1] *European Patent EP 0655441 A1, 1995,* ***[2]*** *Syngenta Limited, WO 2010/038008, 2010*

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