„A COMPUTER SIMULATION BASED SCREENING METHOD FOR CRYSTALLIZATION PROCESSES“

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Crystallization of organic solids from solution is often a difficult task because phase transitions, formation of solvates or complexation could occur. Therefore it is important to find out the solvent properties which have a positive influence on the crystallization of the desired polymorphic form. It is very material and time consuming to obtain values of solvent properties by experimental methods. In the Fraunhofer ICT we developed a data base which includes a collection of solvents and their properties calculated by computer simulations. We used a SGI Octane workstation using program Cerius 4.2 (Accelrys) for determining solvent properties like dipole moment, molecular surface and electrostatic potential by using Force Field (cff 91_950_1.01) [1] and semiempirical methods (WinMopac) [2].

We developed a screening plan for crystallization with 32 solvents, representing twelve different functional groups and the four influence factors: dipole moment, electrostatic potential, molvolumina and solubility. It`s known that the electrostatic potential of a molecular surface is related to solvent properties like the H-bond donating parameter α and the H-bond acceptor parameter β [3]. It seems therefore necessary to include the electrostatic potential as an important influence factor. Each solvent stands for a combination of different solvent property values. In our crystallization device Quest from Argonaut we recrystallized the nitramine ε-CL-20, a metastable polymorphic form, at ambient temperature. The recrystallized samples were analyzed by x-ray diffraction (XRD), REM and DSC to characterize polymorphic forms, donor-acceptor complexes and morphology of the crystals.

We found high correlations between polymorphic phases and the solvent properties dipole moment and the electrostatic potential. Furthermore we understand the solution mechanism and could explain solvent effects like complexation or formation of pseudopolymorphs. In a following modelling step we obtained quantitative solvent property values and could predict the most suitable solvent for crystallization process of ε-CL-20.

Literature

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