„Monte-Carlo Simulation as a Promising Tool for Polymorph Screening“

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Introduction:

The searching for suitable solvents for crystallization processes with experimental trial and error methods is often a time and material consuming task. The situation is getting further complicated if polymorphism or incompatibilities between solute and solvent occur. Therefore, a systematic crystallization screening requires detailed information about the molecular structure and the interaction between a given solute and the solvents.

Experimental and Results:

HNIW, an energetic nitramine with four stable phases at RT and p(atm), was recrystallized in different solvents and the samples were analyzed by X-ray diffraction. Simultaneously, solvent parameters and solute-solvent interaction energies were determined with the semiempirical Computer Simulation program WinMOPAC (Fujitsu) and the Force-Field based Monte Carlo program „Blends“ from Accelrys. By correlation of simulated with experimental data, we obtained solvent requirements for the crystallization of the desired polymorph, ε-HNIW.

ε-HNIW is only soluble in dipolar aprotic solvents. Solvents with a dipole moment of $\mu > 2{,}6$ D or a low ionization potential with $I_{Ion} < 10{,}47$ eV induce phase transitions or complexation with HNIW. The Coulomb interaction energies E_{Coul} between solute and solvent, calculated by the Monte Carlo method, is the most important influence factor. HNIW is only soluble in solvents, in which $|E_{Coul}|$ is higher than 0,5 kcal/mol. But to crystallize the ε-HNIW phase in high yields $|E_{Coul}|$ must be lower than 2,6 kcal/mol, otherwise phase transitions occur.

Conclusion:

The simulation of solvent parameters and solvent-solute interactions by Monte Carlo methods are promising tools to understand solvent induced polymorphic phase transistions and to predict suitable solvents for crystallization processes.