4bk Monte Carlo Simulations to Study Polymorphism and Relative Polymorph Stability in Solids

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Several different Monte Carlo simulation techniques are employed to determine relative stability of different polymorphs of organic solids modeled using the Transferable Potentials for Phase Equilibria (TraPPE) force field. Solid-slab Gibbs ensemble Monte Carlo (GEMC) methodology is applied to calculate the vapor pressures of several different polymorphs of n-propylbenzene. The differences in obtained vapor pressures allow a ranking based upon the relative stability of the polymorphs. Another technique of relevance for the pharmaceutical industry calculates the solubilities of different polymorphs in, primarily, aqueous solvents. The difference in solubilities gives an estimate of the relative stabilities. In accordance, solubilities of different polymorphs of phenol are studied in water and water/ethanol mixtures using expanded ensemble Monte Carlo simulations. The results obtained agree with the vapor pressures of the phenol polymorphs obtained using solid-slab GEMC simulations. An additional method of direct evaluation of the free energy difference between two different polymorphs using lattice switch Monte Carlo method is also explored.