Extending the SAFT-Gamma Mie Approach to Model Benzoic Acid, Diphenylamine, and Mefenamic Acid: Solubility Prediction and Experimental Measurement

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The prediction of the thermodynamic properties, and in particular of the solid-liquid solubility, of active pharmaceutical ingredients (APIs) is a significant challenge of interest in pharmaceutical applications and solvent selection processes. Here, we extend the table of group-group interactions of the SAFT-gamma Mie group-contribution equation of state to model the phase behavior and solubility of mefenamic acid, a nonsteroidal anti-inflammatory drug, in a range of solvents. In addition to mefenamic acid, we also consider its molecular synthons: benzoic acid and diphenylamine. New experimental solubility data are presented for the three molecules in a range of solvents, and three new SAFT-gamma Mie groups are defined (aCCOOH, aCNHaC and CH3CO) and characterized, together with their unlike interactions with solvent groups. Literature data of vapor pressure, single-phase density, saturation density, vaporization enthalpy, bubble temperature, dew temperature, and bubble pressure are used to characterize the new group-group interactions. Solubility data are used to characterize the new group-group interactions only if there are no other experimental data available. The transferability and predictive accuracy of the new models are assessed by comparison of the theoretical predictions with the experimental solubility data. Our comparison includes alcohols, ketones and esters as families of solvents and included mixed-solvent solubility predictions.