



Solubility predictions of acetanilide derivatives in water: Combining thermochemistry and thermodynamic modeling



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ABSTRACT

Knowledge about solubility in water is required for crystallization processes, for the development of structure–property relationships, for the establishment of solubility scales, assessing environmental contamination, and for validating thermodynamic models. Approaches are desired that allow predicting solubility without the use of any experimental solubility data. Most methods that have been proposed to predict aqueous solubility of organic compounds face low prediction reliability and the lack of model interpretability. This work proposes the use of a thermodynamic approach for the prediction of solubility of acetanilide and its derivatives in water. This approach requires fusion enthalpy and fusion temperature as well as the activity coefficient of the respective acetanilide derivative. The latter was obtained by the equation of state PC-SAFT, which uses thermochemistry data as input for model parametrization. The thermochemical data on acetanilide and its derivatives (vapor and sublimation pressures, sublimation and fusion enthalpies) were collected from the literature and evaluated for internal consistency. In order to validate the final solubility prediction model, aqueous solubility of acetanilide and 17 derivatives were predicted and compared to experimental solubility data from literature at 298.15 K as well as to an ideal solubility model, which assumes ideal mixture behavior. The results showed that mixtures of acetanilides + water are highly non-ideal, and the average deviations between solubility data and ideal solubility model could be reduced by two orders of magnitude by using PC-SAFT for the solubility predictions. More promising, PC-SAFT was found to allow predicting the temperature dependence of the aqueous solubility accurately, while ideal solubility model failed to quantitatively describe temperature-dependent solubility.

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1. Introduction

Knowledge about solubility is required for the design and optimization of crystallization processes, for the development of structure–property relationships [1,2], for the establishment of solubility scales [3,4], for waste-water treatment [5], and for validating thermodynamic models [6–10] and solubility estimation

procedures [11] in which intermolecular interactions are crucial. Aqueous solubility is further used as characteristic scale in diverse classification systems. Classification systems, solubility scales or structure–property relationships are increasingly used in the early stages of research or process design in order to evaluate the economic benefit of processes under investigation. The reason behind that is the fact that measuring solubility is usually time-consuming and often requires a high amount of substance, thus being also cost-intensive. Thus, a method for predicting the aqueous solubility of organic compounds is most desirable in academia and research areas in chemical engineering, biotechnology, pharmaceutical and cosmetic science. This is especially important for compounds with very poor aqueous solubility as in these cases experimental solubility values might be highly uncertain.

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