Melting Properties of Amino Acids as an Access to the Solubility Modeling

New values for melting properties allows consistently modeling of solubility in water

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Knowledge about the melting properties of biomolecules is extremely important for process design, as such data influence the solubility behavior in solvents, and such data are required for solubility modeling. However, melting properties for amino acids were not accessible before this work because the amino acids decompose upon slow heating. By means of 'fast scanning calorimetry', a method that applies very high heating rates, the melting properties of 20 proteinogenic amino acids were measured in this work. The new data were further used as an input data for thermodynamic modeling, which is used to predict amino-acid solubilities in water. This is the maximum equilibrium amount of amino acid in the liquid phase at defined temperature and pressure. The model prediction results were in very good agreement to the experimental solubility data. The successful modeling results were accompanied by new experimental solubility data, pH measurements of the liquid phase, and X-ray diffraction of the solid phase, which are important data to validate the model predictions.

The separation and purification of amino acids is usually realized through crystallization, for which the knowledge of solubility is essential. Due to cost-intensive and time-consuming determination of experimental solubility, the solubility modeling based on physical data such as melting properties is highly desired.

Modeling solubility requires a solid-liquid equilibrium between the amino acid in the saturated phase and in the solid phase. In this work, the temperature dependency of the melting enthalpy was taken into account by considering the difference in the heat capacities of the solid and liquid state Δc_{p0i}^{SL}. Assuming a pure compound in solid state the solubility x_i^L can be calculated with Eq. (1) with the assumption of a linear temperature dependency of Δc_{p0i}^{SL} in Eq. (2)

$$\ln\left(x_i^L \cdot \gamma_i^L\right) = \frac{\Delta h_{0i}^{SL}}{R \cdot T_{0i}^{SL}}\left(1 - \frac{T_{0i}^{SL}}{T}\right) - \frac{1}{R \cdot T}\int_{T_{0i}^{SL}}^{T} \Delta c_{p0i}^{SL}(T)\,dT + \frac{1}{R}\int_{T_{0i}^{SL}}^{T} \frac{\Delta c_{p0i}^{SL}(T)}{T}\,dT \quad (1)$$

$$\Delta c_{p0i}^{SL}(T) = \left(a_{c_{p0i}^L} - a_{c_{p0i}^S}\right) \cdot T + \left(b_{c_{p0i}^L} - b_{c_{p0i}^S}\right) \quad (2)$$

with γ_i^L as the activity coefficient of component *i*, *R* the universal gas constant, Δh_{0i}^{SL} the melting enthalpy, and T_{0i}^{SL} the melting temperature. The function $\Delta c_{p0i}^{SL}(T)$ was described by the parameters $a_{c_{p0i}^L}$, $a_{c_{p0i}^S}$, $b_{c_{p0i}^L}$, and $b_{c_{p0i}^S}$.

Access to γ_i^L was provided by PC-SAFT. All pure-component parameters were taken from the literature. Figure 1(a) shows that the solubility of glycine, L-alanine, L-valine and L-leucine can be modeled with high accuracy in a broad temperature range. It can be seen that the amino acid with highest melting temperature does not necessarily has the lowest solubility.

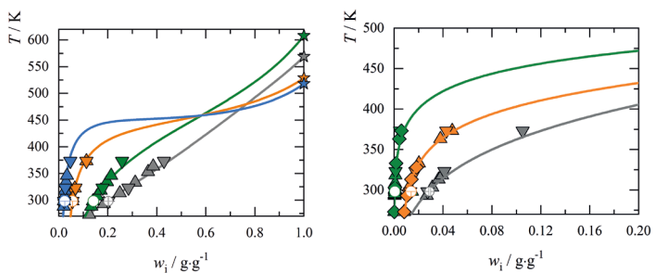

Figure 1: Temperature-dependent solubility of amino acids in water at p = 1 atm in weight fraction at pH = pI. Triangles represent literature data sets; empty circles represent the solubility measurements from this work; lines represent PC-SAFT modeling; stars represents the melting temperatures measured with the FSC. **LEFT:** Amino acids with non-polar substituents: glycine (grey), L-alanine (green), L-valine (orange), L-leucine (blue). **RIGHT:** Amino acids with aromatic substituents: L phenyl alanine (grey) L-tyrosine (green), L-tryptophan (orange).

Figure 1(b) shows that PC-SAFT allowed modeling also for very low-soluble amino acids (Phe, Tyr and Trp). The values for $\Delta c_{p0i}^{SL}(T)$ considerably contributed to the success of the modeling results. The influence of the activity coefficients is also pronounced on the result of Eq. (1), they were found to vary between three orders of magnitude for the conditions under study. Moreover, X-ray diffraction detected crystal changes in solubility experiments for several amino acids, which excluded application of Eq. (1).

To conclude, the melting properties of 20 proteinogenic amino acids determined by means of FSC were used to model solubility successfully. The modeling results and the data were in good agreement in a broad temperature range. The synergy between new FSC data, pH and X-ray diffraction measurements and PC SAFT allowed an accurate and reliable solubility modeling. This opens the door for the future for modeling solubility of any biomolecules that decompose before melting upon slow heating.

Publications:
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