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ARTICLE *in* INDUSTRIAL & ENGINEERING CHEMISTRY RESEARCH · MAY 2009

Impact Factor: 2.59 · DOI: 10.1021/ie801567w

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Thermodynamic Modeling of Several Aqueous Alkanol Solutions Containing Amino Acids with the Perturbed-Chain Statistical Associated Fluid Theory Equation of State

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The perturbed-chain statistical associated fluid theory EoS was applied to model the solubilities of glycine, DL-alanine, L-serine, L-threonine, and L-isoleucine in pure water, pure alcohols (ethanol, 1-propanol, and 2-propanol) and in mixed solvent systems. Three pure component nonassociating parameters for the amino acids were fitted to the densities, activity and osmotic coefficients, vapor pressures, and water activity of their aqueous solutions. The solubilities of amino acids in pure and mixed solvent systems were calculated on the basis of the phase equilibrium conditions for a pure solid and a fluid phase. The hypothetical melting properties of each amino acid were fitted, to accurately correlate the solubilities in pure water. Only one temperature independent binary parameter is required for each amino acid/solvent pair. The model can accurately describe the solubility of the amino acids in water, but the correlation for the solubility in pure alcohols was not so satisfactory. The solubility in mixed solvents (ternary systems) was predicted on the basis of the modeling of the solubility in pure solvents, without any additional fitting of the parameters, and the results achieved were reasonable. Fitting the binary parameter for the pair amino acid/alcohol not to the solubility in pure alcohol, but to the solubility in the mixed solvent system, the description of the solubility in the mixed solvent systems was clearly improved and the results were in fair agreement with the experimental data for all mixture compositions. The results showed a global root-mean-square deviation in mole fraction of 0.0032 for correlation and 0.0070 for prediction.

1. Introduction

The biological and industrial importance of amino acids is well-known as well as the knowledge of their physical and chemical properties. Although some studies have been published concerning the measurement and thermodynamic modeling of aqueous solutions of amino acids with alcohols, a great lack of information, on solubility data, still remains in terms of studied systems and/or condition (e.g., temperature range). In an attempt to overcome the drawbacks found in the representation of phase equilibria and achieve an acceptable quantitative performance for industrial applications, thermodynamic models, namely g^E models or equations of state for the correlation and prediction of the thermodynamic properties have been applied. An overview was given recently[1−3] and it is possible to observe that despite the relative success obtained with the foregoing models, they exhibit limitations and for some of the fitted parameters there is no physical meaning. The work development in this field is still a growing challenge. The results produced using the g^E models are quite acceptable; however, the equations of state become a very attractive alternative. Since experimental data are often scarce, from a practical and critical point of view, an equation of state is more robust for predictions beyond the region where model parameters were estimated.[4,5]

The application of an EoS in the representation of amino acid solubilities in mixed solvents is almost unknown. To the best of our knowledge Fuchs et al.[3] were the only pioneers in this subject, calculating the solubility of amino acids (DL-methionine, glycine, and DL-alanine) in water and alcohols (from methanol through 2-propanol) using the perturbed-chain statistical associated fluid theory (PC-SAFT) equation of state. Pure-component parameters of amino acids were fitted to vapor pressures and to densities of their aqueous solutions. One constant (temperature-independent) binary parameter k_{ij} for each solute/solvent system was introduced to correlate the solubility data of the amino acids in pure solvents. On the basis of those binary systems, the solubility in water at different pH values, as well as in water−alcohol mixtures, was predicted without the addition or refitting of model parameters, and the results showed a fair agreement.

The main goal of this work is to extend their findings for other amino acids in mixed aqueous alkanol solutions (L-serine, L-isoleucine, and L-threonine) and to describe with accuracy other thermodynamic properties such as water activity and osmotic and activity coefficients. Inversely to Fuchs et al.,[3] amino acids are here considered as nonassociating molecules allowing the reduction of the number of parameters to be estimated. The solubilities in mixed solvent systems were predicted using the pure component and binary parameters without fitting any additional parameters and the results were reasonable. Fitting the binary parameter for the pair amino acid/alcohol to the solubility in the mixed solvent system instead, the description of the solubility in the ternary systems was

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10.1021/ie801567w CCC: $40.75
Published on Web 04/23/2009

clearly improved. The results show a global root-mean-square deviation (rmsd) in mole fraction of 0.0070 and 0.0032 for prediction and correlation, respectively.

The glycine and DL-alanine PC-SAFT parameters were refitted and relevant comparisons with the results achieved by Fuchs et al.[3] are presented. For densities and solubility in pure water there are very minor differences between the two correlations. All other thermodynamic properties are reproduced with a much better agreement using the approach proposed here.

2. Theory

On the basis of the phase equilibrium conditions for a pure solid and a fluid phase, an equation of state can be used to calculate the fugacity of the solute ($\hat{f}_s$). If the fluid phase is liquid the equilibrium is given by the following equation:

$$f_s^{liq}(T,P)\,\gamma_s^{L}(T,P,n)\,x_s^{L} = \hat{f}_s = f_s^{solid}(T,P) \tag{1}$$

where x_s^L represents the mole fraction of the solute in the liquid phase, γ_s^L is the symmetric activity coefficient of solute in the liquid phase, and f_s^{liq} and f_s^{solid} are the reference state fugacities of the solute in the liquid and solid phases, at system pressure and temperature, respectively. The relation between the reference state fugacities can be calculated according to

$$\ln\frac{f_s^{liq}(T,P)}{f_s^{solid}(T,P)} = \frac{\Delta H_o}{RT_o}\left(\frac{T_o}{T}-1\right) - \frac{\Delta C_p}{R}\left(\frac{T_o}{T}-1\right) + \frac{\Delta C_p}{R}\ln\frac{T_o}{T} \tag{2}$$

where ΔH_o and ΔC_p correspond to the change in enthalpy and heat capacity upon melting, respectively, and T_o is the melting temperature of the pure solute.[6] The symmetric rational activity coefficient (γ_s^L) is defined as

$$\gamma_s^{L} = \frac{\hat{\varphi}_s(T,P,n)}{\varphi_s(T,P)} \tag{3}$$

where $\hat{\varphi}_s(T,P,n)$ and $\varphi_s(T,P)$ are the fugacity coefficients of solute s in the mixture and as a pure component, respectively.

Therefore, the solubility of a substance at atmospheric pressure can be given by the following equation:

$$x_s^{L} = \frac{1}{\gamma_s^{L}}\exp\left[-\frac{\Delta H_o}{RT_o}\left(\frac{T_o}{T}-1\right) + \frac{\Delta C_p}{R}\left(\frac{T_o}{T}-1\right) - \frac{\Delta C_p}{R}\ln\frac{T_o}{T}\right] \tag{4}$$

The fugacity coefficients are here calculated using PC-SAFT EoS. The model development was derived in detail by Gross and Sadowski.[4,7] Molecules are assumed to be chains of freely joined spherical segments and the residual Helmholtz energy (A^{res}) of the systems is considered to be the sum of different contributions:

$$A^{res} = A^{hc} + A^{disp} + A^{assoc} \tag{5}$$

where A^{hc} accounts for the repulsion, A^{disp}, accounts for attractions, and A^{assoc} denotes the contribution of the association interactions.[7] The PC-SAFT EoS requires three pure-component parameters; the segment number, m; the segment diameter, σ; and the dispersion energy, ε/k for nonassociating molecules, and two additional pure-component parameters; the association energy, $\varepsilon^{A_iB_i}$; and the association volume, $\kappa^{A_iB_i}$ for associating molecules.

In the reference and dispersion terms, the conventional Berthelot−Lorentz combining rules for the binary mixture properties are applied and the correction of the dispersion-energy parameter for the mixture is given by the introduction of one constant temperature independent binary parameter (k_{ij}):

$$\sigma_{ij} = \frac{1}{2}(\sigma_i + \sigma_j) \tag{6}$$

$$\varepsilon_{ij} = (1 - k_{ij})\sqrt{\varepsilon_i\varepsilon_j} \tag{7}$$

The strength of cross-associating interactions between two associating substances is described by applying simple mixing and combining rules.[8] Those rules are applied without any adjustable correction parameter and are written as

$$\varepsilon^{A_iB_j} = \frac{1}{2}(\varepsilon^{A_iB_i} + \varepsilon^{A_jB_j}) \tag{8}$$

$$\kappa^{A_iB_j} = \sqrt{\kappa^{A_iB_i}\kappa^{A_jB_j}}\left[\frac{\sqrt{\sigma_{ii}\sigma_{jj}}}{1/2(\sigma_{ii}+\sigma_{jj})}\right]^3 \tag{9}$$

Table 1. Experimental Data Used to Estimate the Pure Amino Acid PC-SAFT Parameters

amino acid	density	vapor pressure	water activity	activity coefficient	osmotic coefficient	total
			Glycine			
NDP[a]	149	14	183	151	−	497
temp range (K)	278−318	298	298	298		
data source	9−14	15	12, 16−20	16, 18−20[b]		
			DL-Alanine			
NDP	162	13	99	−	67	341
temp range (K)	278−318	298	298		298	
data source	9−12, 14, 21	15	12, 17, 19, 20, 22		19, 20, 22	
			L-Serine			
NDP	78	13	46	−	9	146
temp range (K)	278−328	298	298		298	
data source	14, 23	15	15, 17, 24		24	
			L-Threonine			
NDP	60		24	−	24	108
temp range (K)	288−328	NA[c]	298		298	
data source	23, 25, 26		27		27	
			L-Isoleucine			
NDP	106					106
temp range (K)	278 − 328	NA	NA	NA	NA	
data source	9, 28					

[a] Number of data points. [b] Calculated. [c] NA = not available.

3. Results and Discussion

3.1. Estimation of PC-SAFT Parameters. In this work, amino acids were treated as nonassociating molecules and, since amino acids exist only as solids under normal conditions, the three pure-component parameters required were fitted to all binary aqueous mixture data compiled in our database (Table 1). A larger database was used here, when compared to the work by Fuchs et al.[3] Even if in both works the same two kinds of independent experimental data were used, density and vapor−liquid equilibrium, consistent and widely applied information on osmotic coefficients, fundamental for a reliable description of water/amino acid binary systems, was also included.

To characterize the association of water, a two association site model (2B model) was considered. Although a four-site model would reflect best the physics of water molecules, a two-site approach yields better agreement between model and reality.[4] Besides that, using only two association sites, instead of four, decreases the computational time. The water pure component PC-SAFT parameters used were taken from Fuchs et al.[3] A temperature dependent segment diameter was intro-

Table 2. Pure Component PC-SAFT Parameters for Amino Acids

	segment number		segment diameter		energy parameter			
amino acid	m	SD	σ	SD	ε/k	SD	$d_{crystal}$	d_{calcd}
glycine	5.0503	2.4×10^{-2}	2.27	7.8×10^{-3}	204.81	1.0	1.607[29]	1.413 (1.623)[3]
DL-alanine	4.3623	6.9×10^{-3}	2.65	5.2×10^{-3}	226.02	1.5×10^{-1}	1.424[29,30]	1.418 (1.504)[3]
L-serine	5.2266	3.3×10^{-3}	2.48	4.1×10^{-3}	167.54	2.1×10^{-1}	NA[a]	1.537
L-threonine	5.3468	4.7×10^{-3}	2.66	1.2×10^{-3}	218.91	7.3×10^{-2}	NA	1.559
L-isoleucine	3.0000	---	3.62	6.6×10^{-3}	257.26	3.2	1.2[31]	1.199

[a] NA = not available.

Table 3. Binary PC-SAFT Parameters of Amino Acid/Solvent Systems

	k_{ij}						
	water	ethanol		1-propanol		2-propanol	
glycine	−0.10	0.22	0.15[a]	0.21	0.12[a]	0.24	0.14[a]
DL-alanine	−0.10	0.18	0.12[a]	0.17	0.11[a]	0.16	0.13[a]
L-serine	−0.12	0.35	0.23[a]	0.38	0.21[a]	0.40	0.20[a]
L-threonine	−0.10	0.18	0.12[a]	0.20	0.11[a]	0.22	0.12[a]
L-isoleucine	−0.03	0.31	0.26[a]	0.31	0.22[a]	0.38	0.25[a]

[a] k_{ij} adjusted to the mixed solvent systems.

duced by the authors to improve the description of the water densities at low temperatures.

For fitting the pure component PC-SAFT parameters for each amino acid, the objective function (FOBJ) chosen was the minimization of the sum of squared relative deviation:

$$\text{FOBJ} = \sum_k \left[\frac{Q_k^{\text{calcd}} - Q_k^{\text{expt}}}{Q_k^{\text{expt}}} \right]^2 \tag{10}$$

where Q means thermodynamic property for each experimental data point k. The superscripts "expt" and "calcd" mean experimental and calculated quantities, respectively.

Generally, all the thermodynamic properties of the aqueous solutions with amino acids are reproduced by the PC-SAFT EoS with very good agreement; maximum ARD of 0.10% for density data, and 0.47% for vapor−liquid equilibrium data. It is worthwhile to mention that the literature survey shows a considerable lack of information for some amino acids: for L-isoleucine, only densities in aqueous solutions were found.

The estimated parameters for the amino acids and the respective standard deviation (SD) are given in Table 2. To have a good description of all thermodynamic properties, a binary interaction parameter (k_{ij}) for each amino acid/water pair was introduced. These are listed in Table 3. The estimation of k_{ij} followed an iterative procedure, first k_{ij} was fixed and the three pure component PC-SAFT parameters estimated, then the k_{ij} was changed, and the parameters refitted. To follow a reliable procedure and to obtain reasonable sets of parameters the calculated density for the pure amino acid in a hypothetical liquid state should be of the same order of magnitude of the crystal density. The calculated densities (d_{calcd}) from this work and from Fuchs et al.[3] as well as the density of the pure crystal ($d_{crystal}$), at 298.15 K, are also given in Table 2. The calculated densities in this work are lower than the density of the pure crystal, specially for glycine. For L-isoleucine, since the number of experimental data is very limited, the SD of the parameters was very high, so the segment number was fixed and only the segment diameter and energy parameters estimated.

3.2. Solubility in Pure Solvents and the Estimation of Hypothetical Melting Properties. Since most amino acids decompose before melting, the lack of data on melting properties is natural. Therefore, to apply eq 4, melting properties were treated as adjustable parameters, as hypothetical properties with no physical meaning, and were fitted to the experimental solubility data of the amino acid in water at different temperatures. Figures 1 and 2 show the correlated solubility curves of the amino acids in water, where x_s^L is the amino acid mole fraction. The symbols represent experimental data and the curves were calculated with PC-SAFT EoS. The solubility of the 5 amino acid in pure water can be described with a very good accuracy. For L-serine, the experimental data presents some scattering, especially at higher temperatures, and for this reason the ARD observed in Table 4 is much higher than the one obtained for the other amino acids. In that table the estimated hypothetical properties are also shown.

By reducing the number of adjustable parameters, and since there was no difference in the ARD values, the influence of the

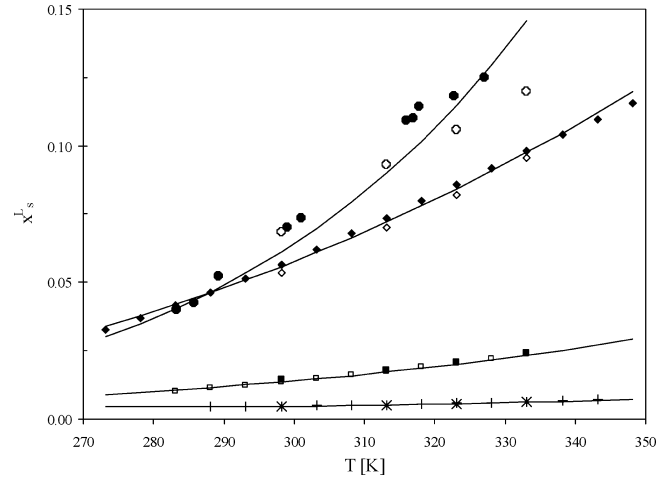

Figure 1. Solubility of the amino acids in water at different temperatures. Glycine: (♦) Dalton and Schmidt,[21] (◊) Ferreira et al.[1] L-Serine: (○) Ferreira et al.,[2] (●) Luk and Rousseau.[35] L-Threonine: (■) Ferreira et al.,[2] (□) Profir and Matsuoka.[36] L-Isoleucine: (×) Ferreira et al.,[2] (+) Zumstein and Rousseau.[31]

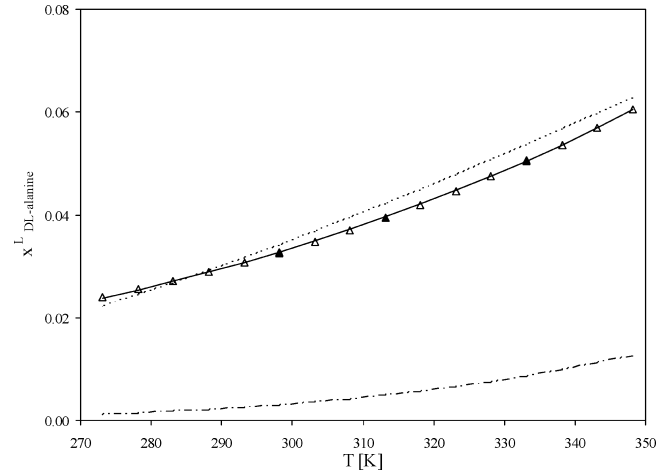

Figure 2. Solubility of DL-alanine in water at different temperatures. Data from Ferreira et al.[1] (▲) and Dalton and Schmidt[21] (Δ). PC-SAFT:[3] (- –) $k_{ij} = 0.0$, (- - -) $k_{ij} = -0.0598$. PC-SAFT, (—) $k_{ij} = -0.10$ (this work).

Table 4. Hypothetical Melting Properties for Amino Acids

	enthalpy of melting ΔH_o (kJ mol^{-1})		melting temperature T_o (K)		heat capacity ΔC_p (kJ mol^{-1} K^{-1})			
amino acid		SD		SD		SD	solubility data source	ARD[a] (%)
glycine	21.97	1.8×10^{-1}	489.78	2.4		ignored	1, 21	1.68
DL-alanine	15.98	3.2×10^{-2}	581.72	1.0		ignored	1, 21, 32	0.33
L-serine	24.54	9.8×10^{-1}	375.28	3.7		ignored	2, 33−35	8.19
L-threonine	17.72	1.6×10^{-1}	637.12	5.8		ignored	2, 36	1.45
L-isoleucine	11.27	8.9×10^{-1}	621.28	3.7×10^{1}	0.073	6.1×10^{-3}	2, 31	1.08

[a] ARD = 100/NDP $\sum_{k=1}^{NDP} |(x_{aa,k}^{calcd} - x_{aa,k}^{expt})/x_{aa,k}^{expt}|$.

change in heat capacity could be ignored, except for L-isoleucine, where an estimation was mandatory to obtain the desired accuracy. The objective function for fitting the hypothetical melting properties was the same as described before (eq 10) where Q corresponds to the solubilities of the amino acid in water (x_s^L).

To model the solubility of amino acids in pure alcohols, the methodology applied by Fuchs et al.[3] was followed. To characterize the association of the alcohols, two association sites were assigned (2B model). The pure PC-SAFT parameters for the alcohols as well as the binary k_{ij} parameter for water and alcohol were taken from Fuchs et al.,[3] while the amino acid parameters are the ones summarized in Table 2. For each binary amino acid/alcohol system a binary parameter k_{ij} was introduced to correlate the solubility data. These parameters are also given in Table 3. Since the solubility temperature dependence of glycine, DL-alanine, L-serine, and L-threonine was not correctly described; the binary parameters (amino acid-alcohols) were fitted to the solubility data at 298.15 K only. Only for L-isoleucine, the correlation results for the solubilities in pure alcohols are satisfactory.

3.3. Modeling Amino Acid Solubilities in Mixed Solvents. The solubility of the amino acids in different water−alcohol mixtures was predicted using only information from the binary systems estimated so far. The temperature dependency was in good agreement with experimental data. However, it was observed that the predicted solubilities, for all ternary systems, are always below the experimental data. Accepting a worse amino acid solubility description in pure alcohols, the binary amino acid/alcohol parameter was, after, treated as an adjustable parameter not to the solubility in pure alcohol but to the solubility in the mixed solvent system. The new binary amino acid/alcohol parameters are summarized in Table 3.

Figures 3 and 4 show the predicted and correlated solubilities of L-threonine and L-isoleucine in different aqueous alcohol mixtures. In these figures the ratio of alcohol (2) and water (1) in the equilibrium solutions is given by x_2/x_1. Since the solubility in pure alcohol is very small, the amino acid solubility axis was extended for better reading. The results for the correlation are in better agreement with the experimental data while the predicted solubilities are always underestimated. Particularly, like shown in Figure 3, the correlation results for the L-threonine solubility at medium solvent ratios of ethanol are now in very good agreement with literature data. However, the amino acid solubilities in pure alcohol became poorly correlated, which is more evident observing Figure 4. For L-isoleucine solubility in water/1-propanol mixed solvent it is possible to observe (Figure 4) the difficulties to obtain an agreement of the same quality as the previous case. Nevertheless, the improvement from prediction to correlation is even more evident. Additionally, the solubility of the L-isoleucine in alcohol−water mixtures shows a particular behavior especially for the system with 1-propanol at 333.15 K. Observing Figure 4, at this temperature, the solubility expressed in mole fraction is higher than the solubility

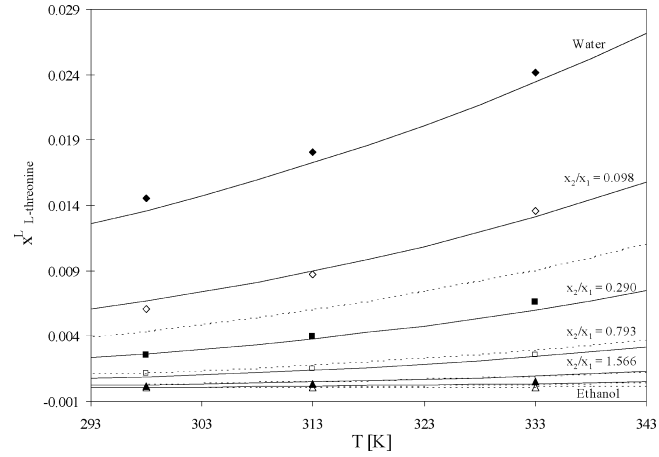

Figure 3. Solubility of L-threonine in different water (1)−ethanol (2) mixtures. Experimental data from Ferreira et al.:[2] (♦) water, (◇) x_2/x_1 = 0.098, (■) x_2/x_1 = 0.290, (□) x_2/x_1 = 0.793, (▲) x_2/x_1 = 1.566, (Δ) ethanol, (---) PC-SAFT prediction, (—) PC-SAFT correlation.

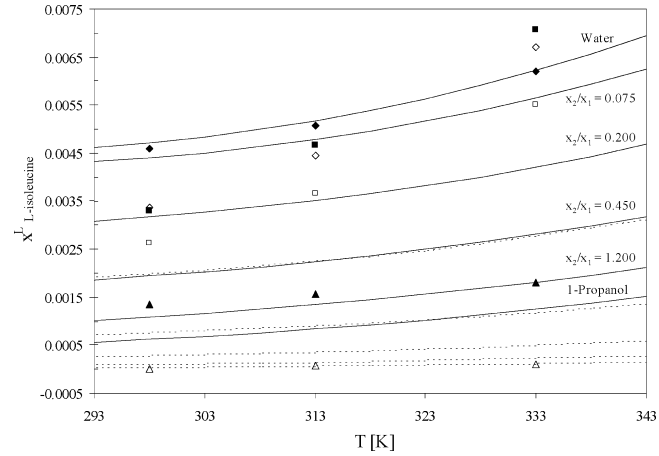

Figure 4. Solubility of L-isoleucine in different water (1)−1-propanol (2) mixtures. Experimental data from Ferreira et al.:[2] (♦) water, (◇) x_2/x_1 = 0.075, (■) x_2/x_1 = 0.200, (□) x_2/x_1 = 0.450, (▲) x_2/x_1 = 1.200, (Δ) 1-propanol, (---) PC-SAFT prediction, (—) PC-SAFT correlation.

in pure water, but PC-SAFT EoS cannot describe this behavior. The PC-SAFT EoS correlations were only in agreement with experimental data for higher alcohol ratios. The same was observed for the solubility of L-isoleucine with the other alcohol systems studied, larger deviations were obtained for the medium and low solvent ratios.

The rmsd values in mole fraction for the prediction and correlation in each system and the number of data points (n) are given in Table 5. Naturally, the rmsd's found for the correlation are much lower than for the prediction, especially for mixed solvent systems containing DL-alanine, glycine, or L-threonine.

In a new attempt to improve the results, with special attention to the systems with L-isoleucine, association was also considered

Table 5. rmsd Values for Each Alcohol System with the Different Amino Acids

		ethanol		1-propanol		2-propanol	
glycine	this work	0.0019[a]	($n = 24$)	0.0013[a]	($n = 6$)	0.0018[a]	($n = 6$)
		0.0071		0.0063		0.0078	
	Fuchs et al.[3]	0.0023		0.0022		0.0027	
DL-alanine	this work	0.0009[a]	($n = 18$)	0.0013[a]	($n = 18$)	0.0013[a]	($n = 18$)
		0.0043		0.0060		0.0035	
	Fuchs et al.[3]	0.0029		0.0024		0.0044	
L-serine	this work	0.0082[a]	($n = 18$)	0.0030[a]	($n = 11$)	0.0077[a]	($n = 15$)
		0.0159		0.0033		0.0154	
L-threonine	this work	0.0004[a]	($n = 18$)	0.0007[a]	($n = 18$)	0.0006[a]	($n = 18$)
		0.0018		0.0035		0.0029	
L-isoleucine	this work	0.0007[a]	($n = 18$)	0.0012[a]	($n = 18$)	0.0010[a]	($n = 18$)
		0.0013		0.0026		0.0023	

[a] Correlation.

for the amino acids. Two different types of association sites (of equal strength), each of them having two sites were assumed to characterize the association of amino acids.[3] The five pure PC-SAFT parameters required for an associating molecule, the binary amino acid/solvent parameters and the hypothetical melting properties were estimated. The experimental data used in the correlation was the same used before (Tables 1 and 4), and the order of magnitude of the standard deviation of the parameters was, as expected, very high. Similar results to the ones presented before, with no association, were obtained for the binary systems, but there was no improvement for the prediction or correlation of the ternary systems. Thus, the introduction of the association was left out of consideration.

3.4. Comparing Results: This Work and Fuchs et al.[3] The results obtained in this work and the ones achieved by Fuchs et al.[3] for glycine and DL-alanine are now compared and discussed. To characterize the association of amino acids, Fuchs et al.[3] considered two different types of association sites, each of them having two sites and both types were assumed to be of equal strength. As mentioned before, only vapor−liquid equilibrium data and densities of aqueous solutions were used by Fuchs et al.[3] to determine the amino acid parameters and when the solubility of the amino acid in pure solvents was considered, one constant (temperature independent) binary parameter k_{ij} for each binary solute/solvent system was introduced to correlate the solubility data quantitatively. Figure 2 demonstrates that with a $k_{ij} = 0.0$ the solubility of DL-alanine in pure water is poorly correlated and the introduction of a k_{ij} was necessary to have a good agreement with the solubility data.

Using the PC-SAFT parameters estimated by Fuchs et al.[3] it is possible to conclude that the k_{ij} parameter introduced to correlate the solubility data quantitatively has a very minor effect on the calculated densities, but a pronounced effect on the calculated vapor pressures, osmotic coefficients, and water activities as shown in Figure 5 for the osmotic coefficients of the system water/DL-alanine at 298.15 K. To quantitatively represent solubility data, Fuchs et al.[3] estimated a k_{ij} ($k_{ij} = -0.0598$), which overestimates considerably the values for the osmotic coefficients. Using a $k_{ij} = 0.0$ those authors achieved results comparable to ours. In fact, in the work by Fuchs et al.[3] it is not possible to represent simultaneously solubility and other thermodynamic properties of aqueous amino acids solutions.

In both works, the melting properties were treated as adjustable parameters but with one difference. In this work they were estimated without any restraint while Fuchs et al.[3] used a group-contribution method to have a reasonable range for the hypothetical enthalpy of melting and let the hypothetical temperature of melting to be freely estimated. The values obtained in both works for those properties are very similar for

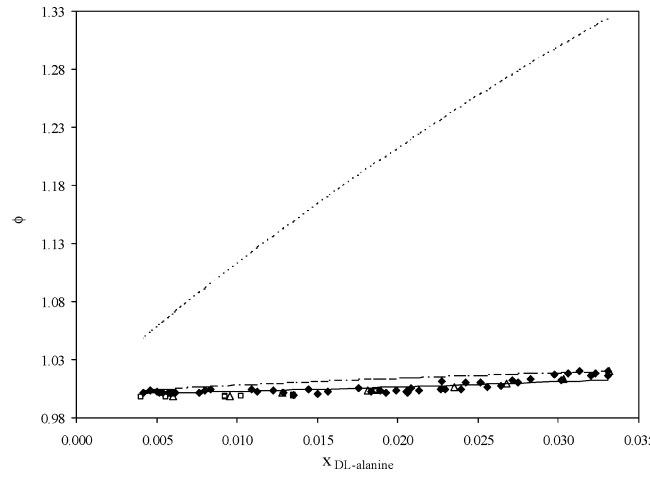

Figure 5. Osmotic coefficients in aqueous of DL-alanine solutions at 298.15 K. Data from Romero and González[19] (□), Smith and Smith[20] (♦), and Robinson[22] (Δ). PC-SAFT:[3] (- −) $k_{ij} = 0.0$, (---) $k_{ij} = -0.0598$. PC-SAFT, (—) $k_{ij} = -0.10$ (this work).

the glycine but not for the DL-alanine. Regarding the melting temperature, an experimental interval for glycine was found in the literature, between 508.35 and 510.15 K.[37] Comparing the experimental value to the ones given in Table 4 and by Fuchs et al.,[3] the deviations found are 4 and 11%, respectively. While the temperature of melting for glycine presents a reasonable value, the value estimated by Fuchs et al.[3] for DL-alanine is very high (963.22 K), almost reaching the temperature of melting of ionic compounds. The melting properties found in this work are more satisfactory and, as shown in Figure 2, the correlated solubility data in pure water is better.

In regard to the modeling of amino acids solubilities in pure alcohol, none of the works are successful. Figures 6 and 7 show the predicted solubilites of glycine and DL-alanine, in various water−alcohol mixtures, given by Fuchs et al.,[3] which are compared with the results found in this work using the binary parameters amino acid/alcohol adjusted to the mixed solvents systems. Figure 6 demonstrates that the divergences at medium solvent ratios of ethanol for glycine solubility were improved.

As displayed in Figure 7, the modeling of the solubility of DL-alanine in aqueous 2-propanol systems shows a much better agreement with experimental data, and similar results were observed for the other systems with ethanol and 1-propanol. Nevertheless, in this work, at high solvent ratios, and pure alcohols the results present larger deviations, for both amino acids. The rmsd's (Table 5) found using Fuchs et al.[3] parameters show better predictions than the ones obtained in this work; however, none of the predictions present the high accuracy given

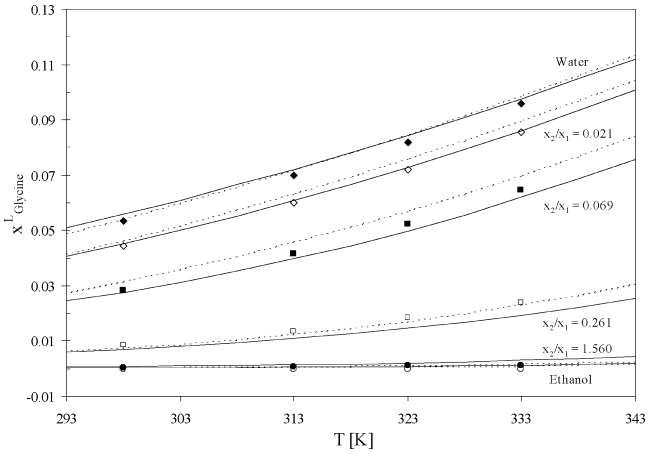

Figure 6. Solubility of glycine in different water (1)−ethanol (2) mixtures. Experimental data from Ferreira et al.[1] and Orella and Kirwan.[38] (♦) water, (◇) $x_2/x_1 = 0.021$, (■) $x_2/x_1 = 0.069$, (□) $x_2/x_1 = 0.261$, (●) $x_2/x_1 = 1.560$, (○) ethanol, (---) PC-SAFT prediction,[3] (—) PC-SAFT correlation (this work).

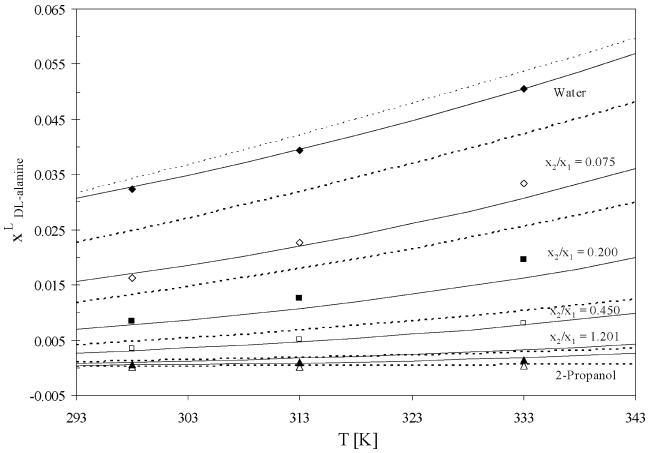

Figure 7. Solubility of DL-alanine in different water (1)−2-propanol (2) mixtures. Experimental data from Ferreira et al.[1] (♦) Water, (◇) $x_2/x_1 = 0.075$, (■) $x_2/x_1 = 0.200$, (□) $x_2/x_1 = 0.450$, (▲) $x_2/x_1 = 1.201$, (Δ) 2-propanol, (---) PC-SAFT prediction,[3] (—) PC-SAFT correlation (this work).

by the correlations developed in this work adjusting only one k_{ij} for each amino acid/alcohol pair.

4. Conclusions

The recently developed thermodynamic equation of state, the perturbed-chain SAFT model[4,7] was applied to model the solubilities of glycine, DL-alanine, L-serine, L-threonine, and L-isoleucine in pure water, pure alcohols (ethanol, 1-propanol, and 2-propanol) and in mixed solvent systems. The amino acids were treated as nonassociating molecules and the pure component parameters were estimated by fitting simultaneously the densities, activity and osmotic coefficients, vapor pressures, and water activity of their aqueous solutions. One binary solute/solvent parameter was necessary for each system to correct the dispersive interactions. Good correlation results were obtained.

The hypothetical melting properties were treated as adjustable parameters and were estimated fitting the solubility curve in water. Even though the model was able to accurately correlate the solubility of the amino acids in water, the correlation results for the solubility in pure alcohols were not so satisfactory.

The solubility in mixed solvent systems was predicted using the pure component and binary parameters without fitting any additional parameters. With the exception of the L-isoleucine systems, the predictions were reasonable. Fitting the binary parameter for the pair amino acid/alcohol to the solubility in the mixed solvent system instead, the description of the solubility in the mixed solvent systems was clearly improved.

In Fuchs at al.[3] study the amino acids were considered as associating substances and the five pure-component PC-SAFT parameters were fitted using only experimental densities and vapor pressures. The binary parameter amino acid/water used by Fuchs et al.[3] has a very minor effect on the correlation of the densities but a pronounced effect on the correlated vapor pressures, activity coefficients, and water activities. To represent accurately the solubility of amino acids, the k_{ij} values estimated by Fuchs et al.[3] introduced some inconsistencies and large deviations to the experimental values measured for those last properties.

The glycine and DL-alanine PC-SAFT parameters were refitted, and the comparison with the results given by Fuchs et al.[3] was presented. For densities and solubility in pure water there are very minor differences between the two correlations, while the other thermodynamic properties are reproduced with a much better agreement and consistency using the parameters proposed here.

In this work considering the amino acids as nonassociating molecules the number of estimated parameters was reduced. The model performance, regarding the modeling of amino acid solubilities in pure water and in solvent mixtures, was kept, and very good improvements were observed specially for the description of the osmotic and unsymmetric molal amino acid activity coefficients. Attempts to introduce association parameters did not improve the correlations.

The correlation and prediction results obtained for the description of aqueous alkanol solutions containing amino acids showed satisfactory results with global rmsd values in mole fraction of 0.0032 and 0.0070, respectively.

Acknowledgment

The authors acknowledge the financial support from the national research project FCT/POCTI/EQU/40179/2001 and by LSRE financing by FEDER/POCI/2010. L. A. Ferreira acknowledges her Ph.D. scholarship (SFRH/BD/17897/2004) from Fundação para a Ciência e a Tecnologia (Lisboa, Portugal).

Nomenclature

List of Symbols

A = Helmholtz free energy
C_p = heat capacity (J.mol^{-1}.K^{-1})
d = density (g.cm^{-3})
$\hat{f}$ = fugacity
g = Gibbs energy
H = enthalpy (J.mol^{-1})
k = binary interaction parameter
m = segment number
n = mole number, number of data points
P = pressure (Pa)
R = ideal gas constant (J.mol^{-1}.K^{-1})
T = absolute temperature (K)
x = mole fraction

Greek Letters

γ = molal activity coefficient
Δ = property difference
ε/k = energy parameter, dispersion
ε = association volume

κ = association energy parameter
σ = segment diameter
φ = fugacity coefficient
Subscripts
1 = water
2 = alcohol
calcd = calculated
crystal = crystal
i,*j* = any species
k = experimental data point
s = solute
o = pure substance, melting property
Superscripts
A, *B* = association sites
assoc = association
calcd = calculated by the model
disp = dispersion
E = excess property
expt = experimental
hc = hard chain
L, liq = liquid phase
res = residual
solid = solid phase
* = unsymmetric
Abbreviations
ARD = average relative deviation
EoS = Equation of State
FOBJ = objective function
Q = thermodynamic property
NA = no data available
NDP = number of data points
PC-SAFT = perturbed-chain SAFT
rmsd = root mean square deviation
SAFT = statistical associating fluid theory
SD = standard deviation

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Received for review October 17, 2008
Revised manuscript received March 20, 2009
Accepted April 3, 2009

IE801567W