Enthalpies of Dilution of L-Alanine in Dimethylsulfoxide + Water and Dimethylformamide + Water Mixtures at 298.15 K

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The dilution enthalpies of L-alanine in dimethylsulfoxide (DMSO) + water and dimethylformamide (DMF) + water mixtures at 298.15 K have been determined, respectively, using an isothermal titration calorimeter. On the basis of the McMillan−Mayer theory, the homochiral enthalpic interaction coefficients h_{XX} of L-alanine in both of the mixtures of various mass fractions ($w_2 = 0$ to 0.3) have been calculated. It was found that h_{XX} is positive at lower DMSO or DMF concentrations, but it becomes less positive and even negative with the increasing concentration of DMSO or DMF. The results were interpreted from the point of view of solute−solute interactions mediated by these two aprotic cosolvents.

Introduction

As the fundamental building blocks of native protein, L-α-amino acids have drawn a lot of attention. Great interests have been focused on the thermodynamic properties of amino acids in pure water, aqueous solutions of electrolyte or nonelectrolyte, as well as some organic solvents. From the thermodynamic data, such as dilution enthalpies, dissolution enthalpies, and viscometric and volumetric properties, useful information can be obtained about the weak, noncovalent interactions, which govern the native structure of proteins, between the amino acid residues and between these residues and the aqueous environment.[1] A great deal of research papers on the thermodynamic properties of aqueous solutions of amino acids have been reported in the past several decades. These include amino acids in pure water,[2,3] in aqueous solutions containing cosolutes or cosolvents such as urea,[4,5] alcohol,[6] saccharine,[7–10] aliphatic amides,[11,12] electrolytes,[13–16] and so on. Most of these studies were performed by flow or batch microcalorimetry which characterizes a time-consuming process and demands a large sample amount. In this paper, dilution enthalpies have been determined following a titration microcalorimetric method proposed by Fini and Castagnolo.[17] The main advantage of this method is that it consumes smaller quantities of reagents and samples and therefore is suitable for substances available only in a small amount. The thermal effects determined by this method can still be analyzed according to the commonly used thermodynamic approach developed by McMillan and Mayer.[18]

Both dimethylsulfoxide (DMSO) and *N*,*N*-dimethylformamide (DMF) are widely used as highly polar aprotic solvents with large dipole moments and high dielectric constants. They can mix with water over the whole mole fraction range. Proteins are completely unfolded at higher mole fractions of DMSO ($x > 0.75$) and in pure DMSO, while at lower mole fractions, DMSO has a nearly undetectable effect upon the secondary structure of protein.[19] DMF, with a large dipole moment ($\mu = 3.8$D) and a high dielectric constant ($\varepsilon = 37.7$ at 298.15 K),[20] often serves as a model compound for the study of small peptides and is of particular interest in view of the lack of hydrogen bonding in its pure state and of the structure alteration ability to its aqueous mixture.[21] Both DMSO and DMF are also widely used in molecular biology, polymer science, and the pharmaceutical industry.

As a continuous investigation on enthalpic pairwise interactions of α-amino acids in aqueous solutions containing other interesting compounds,[22–25] the dilution enthalpies of L-alanine in DMSO + water and DMF + water mixtures at 298.15 K have been determined, respectively, using an isothermal titration microcalorimeter, and the effects of these two highly polar aprotic cosolvents on homochiral enthalpic interaction coefficients were discussed. The main differences between this work and our previous work are:

(1) Most of the previous works were performed by flow or batch microcalorimetry, while this work was performed by the ITC (isothermal titration calorimeter) technique which is timesaving and requires less sample.

(2) Compared with the previous works which aimed to explore the enthalpic interactions between solute and solvent, this work focused on the enthalpic interactions between the same two solvated solute molecules and the influence of solvent alteration over a wider composition range. The mixed solvent is considered to be a changing environment factor which has a great effect on solute−solute interaction.

Experimental Section

Glycine, L-alanine, and L-serine are products from Sigma and used as received. DMSO and DMF (AR grade) were twice distilled under reduced pressure over molecular sieves (0.4 nm), finally collected at 314.15 K, and then dried by molecular sieves for 24 h before use. The two mixed solvents (DMSO + water and DMF + water) were prepared by weight using an electronic balance with a precision of 0.1 mg, and with a range of cosolvent mass fraction $w_2 = 0\sim0.3$. All amino acid solutions were prepared by weight using an electronic balance with a precision of 0.01 mg. The Milli-Q water (Millipore Elix5/Milli-Q Academic system) was used in all the preparations.

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Table 1. Experimental Dilution Enthalpies of Glycine, L-Alanine, and L-Serine in Pure Water at 298.15 K[a]

N	$\frac{m_{N-1}}{\mathrm{mol\cdot kg^{-1}}}$	$\frac{m_N}{\mathrm{mol\cdot kg^{-1}}}$	$\frac{\Delta H(m_{N-1}\rightarrow m_N)}{\mathrm{J\cdot mol^{-1}}}$	$\frac{m_{N-1}}{\mathrm{mol\cdot kg^{-1}}}$	$\frac{m_N}{\mathrm{mol\cdot kg^{-1}}}$	$\frac{\Delta H(m_{N-1}\rightarrow m_N)}{\mathrm{J\cdot mol^{-1}}}$
		L-alanine			L-serine	
2	0	0.00617	−200.85 (0.50)	0	0.00411	391.3 (0.54)
3	0.00617	0.01229	−197.53 (4.11)	0.00411	0.00819	384.8 (0.23)
4	0.01229	0.01837	−194.66 (−0.05)	0.00819	0.01225	379.5 (0.24)
5	0.01837	0.02441	−192.15 (−0.05)	0.01225	0.01627	372.1 (−0.32)
6	0.02441	0.03041	−189.38 (−0.16)	0.01627	0.02027	367.2 (−0.22)
7	0.03041	0.03636	−187.86 (0.37)	0.02027	0.02424	360.8 (−0.52)
8	0.03636	0.04227	−184.30 (−0.16)	0.02424	0.02818	356.0 (−0.39)
9	0.04227	0.04814	−181.82 (−0.16)	0.02818	0.03209	351.5 (−0.17)
10	0.04814	0.05397	−178.60 (−0.55)	0.03209	0.03598	346.0 (−0.23)
11	0.05397	0.05975	−176.54 (−0.28)	0.03598	0.03983	341.1 (−0.12)
12	0.05975	0.06549	−173.65 (−0.46)	0.03983	0.04366	336.1 (0.00)
13	0.06549	0.07119	−171.53 (−0.29)	0.04366	0.04746	330.6 (−0.06)
14	0.07119	0.07685	−169.40(0.00)	0.04746	0.05123	326.8 (0.40)
15	0.07685	0.08246	−167.60(0.41)	0.05123	0.05497	321.3 (0.34)
16	0.08246	0.08803	−165.73(0.79)	0.05497	0.05867	315.3 (0.13)
		glycine				
7	0.01704	0.02041	341.9 (−0.75)			
8	0.02041	0.02377	341.4 (−0.12)			
9	0.02377	0.02712	341.0 (0.59)			
10	0.02712	0.03046	337.1 (0.24)			
11	0.03046	0.03379	334.9 (0.42)			
12	0.03379	0.03710	331.1 (0.09)			
13	0.03710	0.04040	328.9 (0.27)			
14	0.04040	0.04369	324.7 (−0.18)			
15	0.04369	0.04697	322.3 (−0.06)			
16	0.04697	0.05023	318.6 (−0.38)			
17	0.05023	0.05349	317.1 (0.03)			
18	0.05349	0.05673	314.0 (−0.09)			
19	0.05673	0.05996	311.0 (−0.16)			
20	0.05996	0.06318	309.4 (0.19)			

[a] The values in parentheses are the evaluated uncertainties: $100[\Delta H_{XX}(\mathrm{exptl}) - \Delta H_{XX}(\mathrm{calcd})/\Delta H_{XX}(\mathrm{exptl})]$; all $\Delta H_{XX}(\mathrm{calcd})$ are calculated from eq 17 (see Supporting Information).

The dilution enthalpies were determined by an isothermal titration calorimeter (VP-ITC, MicroCal) at 298.15 K. The accuracy of the apparatus and method was testified by dilution experiments of glycine, L-alanine, and L-serine in water at 298.15 K. All the solutions were degassed thoroughly before use. The sample cell was loaded initially with solvent, and the 250 μL syringe was filled with amino acid solutions. A titration run consisted of consecutive injections of 10 μL (or 15 μL) volume and 20 s duration each, with an interval of 4 min between them. The heat effect $\Delta H(m_{N-1},m_N)$ per injection was determined by automatic peak integration of thermal power vs time curve. The thermal effects relating to the friction from each injection were considered to be negligible in all experiments.[17]

Theoretical Basis

According to Fini and Castagnolo,[17] the value of dilution enthalpy per injection in ITC can be expressed as

$$\Delta H(m_{N-1} \rightarrow m_N) = \Delta H(m_{N-1}, m_N)/n_p \tag{1}$$

where N indicates the number of injections and n_p is the moles of solute in each injection volume (V_{inj}), which can be calculated as follows

$$n_p = V_{inj}\rho_{sol}m_0 \tag{2}$$

In which ρ_{sol} and m_0 are the density and the concentration of the solution in the syringe, respectively. m_0 is defined as moles of solute in 1 g of solution. Since the solutions used were at lower concentrations, the densities of them were assumed to be that of pure water.

The thermodynamic formula commonly used to deal with the excess enthalpy of a binary solution containing solute X and solvent Y (Y = pure water or aqueous mixed solvent) can be expressed as follows

$$H^E(m_X) = h_{XX}m_X + h_{XXX}m_X^2 + \cdots \tag{3}$$

in which h_{XX}, h_{XXX}, etc. are known as pairwise, triplet, and higher-order enthalpic interaction coefficients, respectively. To evaluate these coefficients, the dilution enthalpies of a binary solution (X + Y) are needed. The method of measuring dilution enthalpy by ITC was described in ref 17 (see also Supporting Information).

Results and Discussion

To check the accuracy of the apparatus and method, dilution experiments of glycine, L-alanine, and L-serine in pure water at 298.15 K were done first. The determined enthalpies of dilution, ΔH, are presented in Table 1, and the calculated enthalpic interaction coefficients together with the corresponding literature values are given in Table 2. As an example, the typical titration curve of L-serine in water at 298.15 K can be seen in Figure 1, and the experimental values of $\Delta H(m_{N-1}\rightarrow m_N)$ of L-serine in water plotted as a function of the injection number N are given in Figure 2.

For the three amino acids in water, the calculated values of h_{XX} differ slightly from those reported by Palecz.[26] It is reasonable for this difference since his calorimetric method used is different from ours. However, the higher-order coefficient, h_{XXX}, differs to a larger degree with the literature data. Since it is very difficult to elucidate the complicated interaction contributions to h_{XXX}, great attention has been commonly paid to h_{XX}.

Table 2. Enthalpic Interaction Coefficients of Glycine, L-Alanine, and L-Serine in Pure Water at 298.15 K[a]

enthalpic coefficients	this work	ref 26	R^2	SD	σ
		glycine			
h_{XX}/J·kg·mol^{-2}	−401	−424	0.9895	0.09	−5.74
h_{XXX}/J·kg^2·mol^{-3}	39	60			
		L-alanine			
h_{XX}/J·kg·mol^{-2}	205	206	0.9963	0.04	−0.49
h_{XXX}/J·kg^2·mol^{-3}	24	−5			
		L-serine			
h_{XX}/J·kg·mol^{-2}	−645	−709	0.9976	0.07	−9.9
h_{XXX}/J·kg^2·mol^{-3}	−28	120			

[a] Notes: R^2 is the square of the correlation coefficient, and SD is the standard deviation of regression. σ: (the relative deviation) = $100[h_{XX}(\text{exptl}) - h_{XX}(\text{ref})]/h_{XX}(\text{exptl})$.

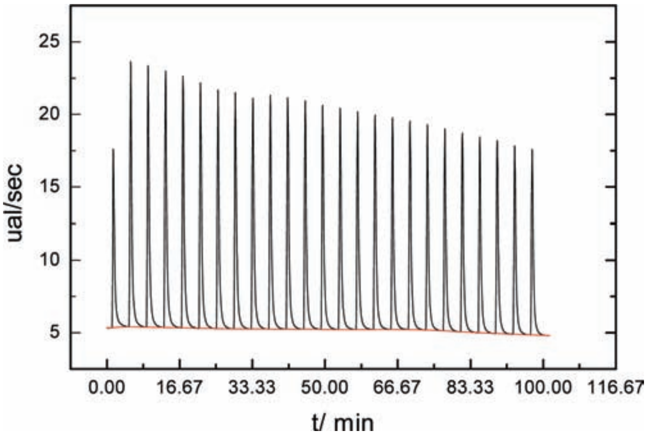


Figure 1. Typical titration curve of L-serine in water at 298.15 K.

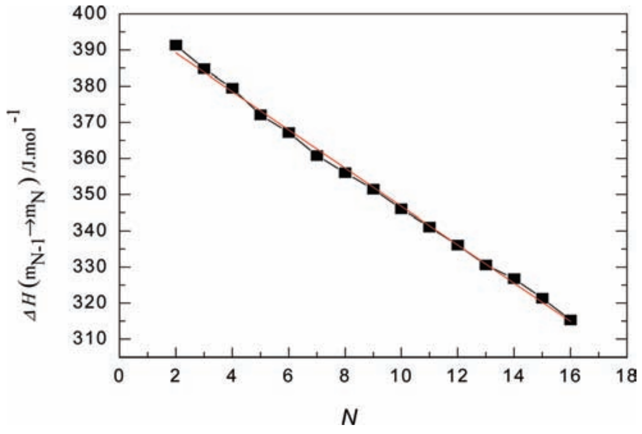
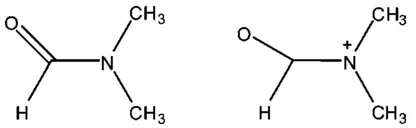


Figure 2. Experimental values of $\Delta H(m_{N-1} \rightarrow m_N)$ of L-serine in water as a function of injection number N at 298.15 K ($R^2 = 0.9976$, SD = 0.07).

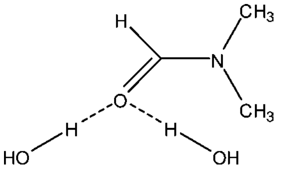
The experimental values of $\Delta H(m_{N-1} \rightarrow m_N)$ as a function of N from the dilution experiments of L-alanine in aqueous DMF or DMSO solutions of different mass fractions (w_2) are listed in Table 3. The values of h_{XX} were calculated from the slopes of linear regression of the experimental data based on eq 17 (see Supporting Information), all with the squares of correlation coefficients $R^2 > 0.95$. The trends of h_{XX} with the mass fraction of DMF or DMSO in the aqueous mixed solvents are illustrated in Figure 3, and the corresponding values are reported in Table 4. From Figure 3, it can be observed that h_{XX} of L-alanine in aqueous DMF or DMSO solutions has an interesting bidirectional effect. At lower DMF or DMSO concentrations, it is positive. As the increasing concentration of DMF or DMSO, it becomes less positive and even negative. A similar result has been reported by Liu[27] for the system of L-alanine in aqueous ethylene glycol solutions and for N-methyl-L-alanine and N-acetyl-L-alanine in DMF by Somsen.[28,29] All imply that energetically favorable interactions take place between the DMF molecule and the side chain of alanine.

One of the main factors affecting the direction of h_{XX} can be ascribed to the structure alteration of the mixed solvents since the enthalpic interaction coefficient reflects the solvent-mediated interactions among solvated solute molecules. Any changes in the structure of the solvent can lead to corresponding energetic effect which reflects directly in h_{XX}.

On one hand, the addition of DMF to water diminishes the dielectric constant and results in strengthened electrostatic interaction arising from the formation of hydrogen bonds between DMF and water molecules. Hydrogen bonds between water and the carbonyl oxygen of the DMF molecule which has a strong electron pair donating ability are stronger than those between water molecules, and this effect is strengthened by the nitrogen atom due to the resonance structure of DMF. According to Chu[30] et al., DMF has the following resonance structure



Hence, in aqueous solutions, DMF molecules are bound by two water molecules with its amide oxygen in the first resonance structure, while the nitrogen atom can not take part in the formation of hydrogen bonds for its free electron being protected by two methyl groups. The structure can be illustrated as follows



As these electrostatic interactions occur, the structure of water molecules is broken. When the solvated DMF molecules interact with the charged zwitterion heads of amino acids, there is a relaxation of solvent molecules to the bulky solvent that results in a negative contribution to the value of h_{XX}. This tendency becomes even more obvious as the concentrations of DMF in mixtures increase since DMF molecules are considered to be structure-breakers toward water[12] and enable peptide to adopt "folded" conformations that exist in the interior of the globular protein.

On the other hand, both the hydrophobic−hydrophobic interactions between nonpolar methyls of two L-alanine molecules and the hydrophobic−hydrophilic interactions of the methyl of L-alanine with the polar −CO− in DMF predominate over all the interactions in the studied system and result in positive contribution to h_{XX}. The overall sign and magnitude of h_{XX} would be a result of the competitive balance of all interaction factors mentioned above. The possible interactions between L-alanine and DMF can be stated as follows:

(a) Hydrophobic−hydrophobic interaction between CH_3− of L-alanine and CH_3− of DMF, which has a positive contribution to h_{XX}.

(b) Hydrophobic−hydrophilic interaction between CH_3− of L-alanine and the polar −CO− in DMF, which has a positive contribution to h_{XX} as well.

Table 3. Experimental Dilution Enthalpies of L-Alanine in DMF + Water and DMSO + Water Mixtures, Respectively, at 298.15 K

N	m_{N-1} / mol·kg^{-1}	m_N / mol·kg^{-1}	$\Delta H(m_{N-1}\rightarrow m_N)$ / J·mol^{-1}	m_{N-1} / mol·kg^{-1}	m_N / mol·kg^{-1}	$\Delta H(m_{N-1}\rightarrow m_N)$ / J·mol^{-1}
			L-alanine in DMSO + water			
		$w_2 = 0.0548$			$w_2 = 0.1090$	
2	0	0.00616	−168.56 (−0.96)	0	0.00412	−84.71 (−0.01)
3	0.00616	0.01228	−164.89 (−0.04)	0.00412	0.00820	−83.96 (0.39)
4	0.01228	0.01836	−162.84 (−0.10)	0.00820	0.01226	−82.62 (0.10)
5	0.01836	0.02440	−160.81 (−0.16)	0.01226	0.01629	−81.84 (0.48)
6	0.02440	0.03039	−158.19 (0.14)	0.01629	0.02029	−80.21 (−0.19)
7	0.03039	0.03634	−155.94 (0.22)	0.02029	0.02427	−79.43 0.20)
8	0.03634	0.04225	−153.95 (0.12)	0.02427	0.02821	−77.67 (−0.65)
9	0.04225	0.04811	−151.46 (0.36)	0.02821	0.03213	−77.36 (0.35)
10	0.04811	0.05394	−149.34 (0.35)	0.03213	0.03602	−75.82 (−0.24)
11	0.05394	0.05972	−147.00 (0.50)	0.03602	0.03988	−74.44 (0.63)
12	0.05972	0.06545	−145.08 (0.36)	0.03988	0.04371	−73.92 (0.14)
13	0.06545	0.07115	−142.87 (0.42)	0.04371	0.04751	−72.49 (−0.33)
14	0.07115	0.07680	−141.07 (0.18)	0.04751	0.05129	−71.35 (−0.40)
15	0.07680	0.08241	−138.79 (0.29)	0.05129	0.05504	−70.43 (−0.17)
16	0.08241	0.08798	−136.88 (0.13)	0.05504	0.05875	−69.43 (−0.04)
17	0.08798	0.09351	−135.67 (−0.55)	0.05875	0.06244	−68.54 (0.23)
18	0.09351	0.09899	−132.93 (−0.11)	0.06244	0.06611	−67.29 (0.00)
19	0.09899	0.10440	−131.11 (−0.34)	0.06611	0.06974	−66.48 (0.42)
20	0.10440	0.10980	−129.54 (−0.79)	0.06974	0.07334	−65.41 (0.46)
		$w_2 = 0.1627$			$w_2 = 0.2159$	
2	0	0.00411	−31.79 (−1.91)	0	0.00411	−31.87 (−4.38)
3	0.00411	0.00819	−31.72 (−0.44)	0.00411	0.00820	−32.98 (0.40)
4	0.00819	0.01224	−30.25 (−3.39)	0.00820	0.01225	−32.23 (−0.40)
5	0.01224	0.01627	−31.04 (−0.88)	0.01225	0.01628	−32.08 (0.63)
6	0.01627	0.02026	−30.44 (0.73)	0.01628	0.02027	−31.99 (−0.03)
7	0.02026	0.02423	−29.83 (0.51)	0.02027	0.02424	−31.47 (−1.81)
8	0.02423	0.02817	−29.45 (1.13)	0.02424	0.02819	−30.81 (−1.25)
9	0.02817	0.03208	−29.33 (2.62)	0.02819	0.03210	−30.11 (0.57)
10	0.03208	0.03596	−28.75 (2.53)	0.03210	0.03598	−29.36 (−0.47)
11	0.03596	0.03981	−28.00 (1.86)	0.03598	0.03984	−29.13 (0.55)
12	0.03981	0.04364	−27.17 (0.85)	0.03984	0.04367	−28.62 (0.46)
13	0.04364	0.04744	−26.47 (0.27)	0.04367	0.04747	−28.15 (0.50)
14	0.04744	0.05120	−25.68 (−0.66)	0.04747	0.05124	−27.17 (−1.27)
15	0.05120	0.05494	−25.14 (−0.63)	0.05124	0.05498	−27.18 (0.52)
16	0.05494	0.05866	−24.46 (−1.21)	0.05498	0.05870	−26.75 (0.75)
17	0.05866	0.06234	−24.04 (−0.70)	0.05870	0.06238	−25.63 (−1.69)
18	0.06234	0.06600	−23.35 (−1.31)	0.06238	0.06604	−25.57 (−7.82)
19	0.06600	0.06962	−22.94 (−0.78)	0.06604	0.06967	−25.00 (−0.40)
20	0.06962	0.07322	−22.50 (−0.31)	0.06967	0.07327	−24.33 (−1.10)
		$w_2 = 0.2685$			$w_2 = 0.3207$	
2	0	0.00819	72.21 (1.25)	0	0.00482	68.37 (0.18)
3	0.00819	0.01626	69.86 (0.17)	0.00482	0.00957	66.91 (0.28)
4	0.01626	0.02422	67.83 (0.48)	0.00957	0.01426	65.45 (0.43)
5	0.02422	0.03206	66.26 (−0.48)	0.01426	0.01888	63.70 (0.06)
6	0.03206	0.03979	64.44 (−0.86)	0.01888	0.02344	62.07 (−0.08)
7	0.03979	0.04741	63.31 (−0.17)	0.02344	0.02792	60.34 (−0.41)
8	0.04741	0.05492	61.71 (−0.19)	0.02792	0.03234	58.55 (−0.86)
9	0.05492	0.06231	60.14 (−0.19)	0.03234	0.03670	57.23 (−0.50)
10	0.06231	0.06959	58.76 (0.15)	0.03670	0.04098	55.89 (−0.18)
11	0.06959	0.07675	57.28 (0.33)	0.04098	0.04520	54.44 (−0.04)
12	0.07675	0.08381	55.05 (0.83)	0.04520	0.04935	52.72 (−0.38)
13	0.08381	0.09074	54.67 (1.37)	>0.04935	0.05344	52.16 (1.50)
			L-alanine in DMF + water			
		$w_2 = 0.0473$			$w_2 = 0.0949$	
2	0	0.00411	−92.83 (1.74)	0	0.00411	−34.20 (1.56)
3	0.00411	0.00819	−89.85 (−0.23)	0.00411	0.00819	−33.27 (−0.66)
4	0.00819	0.01224	−88.62 (−0.29)	0.00819	0.01224	−33.00 (−0.30)
5	0.01224	0.01626	−87.30 (−0.47)	0.01224	0.01627	−32.98 (0.79)
6	0.01626	0.02025	−85.99 (−0.62)	0.01627	0.02027	−32.23 (−0.34)
7	0.02025	0.02422	−84.88 (−0.56)	0.02027	0.02423	−31.62 (−1.03)
8	0.02422	0.02815	−83.85 (−0.39)	0.02423	0.02817	−31.57 (0.00)
9	0.02815	0.03206	−82.78 (−0.27)	0.02817	0.03208	−31.21 (0.10)
10	0.03206	0.03594	−82.05 (0.27)	0.03208	0.03597	−30.82 (0.06)
11	0.03594	0.03979	−80.65 (0.00)	0.03597	0.03982	−30.60 (0.59)
12	0.03979	0.04362	−79.42 (−0.06)	0.03982	0.04365	−29.98 (−0.17)
13	0.04362	0.04741	−78.01 (−0.37)	0.04365	0.04744	−29.46 (−0.64)
14	0.04741	0.05118	−77.19 (0.09)	0.04744	0.05121	−29.31 (0.14)
15	0.05118	0.05492	−76.33 ((0.50)	0.05121	0.05495	−29.02 (0.48)

Table 3. Continued

N	$\frac{m_{N-1}}{\text{mol}\cdot\text{kg}^{-1}}$	$\frac{m_N}{\text{mol}\cdot\text{kg}^{-1}}$	$\frac{\Delta H(m_{N-1}\rightarrow m_N)}{\text{J}\cdot\text{mol}^{-1}}$	$\frac{m_{N-1}}{\text{mol}\cdot\text{kg}^{-1}}$	$\frac{m_N}{\text{mol}\cdot\text{kg}^{-1}}$	$\frac{\Delta H(m_{N-1}\rightarrow m_N)}{\text{J}\cdot\text{mol}^{-1}}$
		$w_2 = 0.1428$			$w_2 = 0.1909$	
2	0	0.00411	−39.42 (−2.45)	0	0.00343	36.85 (2.85)
3	0.00411	0.00819	−39.38 (−1.45)	0.00343	0.00683	34.80 (−1.39)
4	0.00819	0.01224	−39.74 (0.58)	0.00683	0.01021	35.19 (1.27)
5	0.01224	0.01626	−39.25 (0.49)	0.01021	0.01356	34.12 (−0.26)
6	0.01626	0.02025	−39.35 (−1.92)	0.01356	0.01689	33.28 (−1.16)
7	0.02025	0.02422	−38.87 (1.86)	0.01689	0.02020	32.64 (−1.48)
8	0.02422	0.02816	−38.07 (0.95)	0.02020	0.02348	32.19 (−1.23)
9	0.02816	0.03207	−37.52 (0.70)	0.02348	0.02674	32.27 (0.66)
10	0.03207	0.03595	−37.18 (1.01)	0.02674	0.02998	31.14 (−0.89)
11	0.03595	0.03980	−36.16 (−0.55)	0.02988	0.03319	30.75 (−0.74)
12	0.03980	0.04362	−35.40 (−1.42)	0.03319	0.03638	30.30 (−0.46)
13	0.04362	0.04742	−35.27 (−0.54)	0.03638	0.03955	29.92 (0.07)
14	0.04742	0.05119	−34.94 (−0.20)	0.03955	0.04269	29.87 (1.74)
15	0.05119	0.05493	−34.25 (−0.90)	0.04269	0.04581	29.16 (1.18)
		$w_2 = 0.2394$			$w_2 = 0.2881$	
2	0	0.00410	50.86 (0.36)	0	0.00308	147.76 (1.42)
3	0.00410	0.00816	49.63 (1.35)	0.00308	0.00612	143.84 (1.01)
4	0.00816	0.01217	48.13 (−0.27)	0.00612	0.00914	139.35 (0.17)
5	0.01217	0.01614	46.95 (−1.28)	0.00914	0.01212	135.98 (0.12)
6	0.01614	0.02007	46.21 (−1.37)	0.01212	0.01507	131.84 (−0.53)
7	0.02007	0.02396	45.74 (−0.87)	0.01507	0.01799	127.62 (−1.26)
8	0.02396	0.02780	44.90 (−1.17)	0.01799	0.02088	125.51 (−0.36)
9	0.02780	0.03160	44.20 (−1.18)	0.02088	0.02373	121.71 (−0.78)
10	0.03160	0.03536	43.85 (−0.39)	0.02373	0.02655	117.14 (−1.88)
11	0.03536	0.03908	43.44 (0.30)	0.02655	0.02934	114.39 (−1.46)
12	0.03908	0.04275	42.49 (−0.28)	0.02934	0.03210	111.98 (−0.73)
13	0.04275	0.04638	42.14 (0.57)	0.03210	0.03483	108.72 (−0.72)
14	0.04638	0.04997	41.75 (1.36)	0.03483	0.03752	107.95 (1.63)
15	0.04997	0.05352	40.89 (0.99)	0.03752	0.04019	106.56 (3.53)

(c) Hydrogen bonds between the carbonyl oxygen of DMF and water that lead to the structure of water molecules being broken as well as partial dehydration of the hydration shell of L-alanine zwitterions, both of which have negative contributions to h_{XX}.

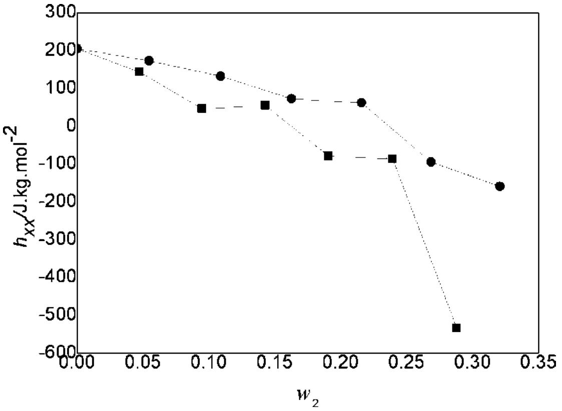


Figure 3. Homochiral enthalpic pairwise interaction coefficient h_{XX} of L-alanine in two aqueous mixed solvents as a function of mass fraction w_2 at 298.15 K (●, DMSO; ■, DMF).

Table 4. Enthalpic Interaction Coefficients h_{XX} of L-Alanine in DMF + Water and DMSO + Water Mixtures, Respectively, at 298.15 K[a]

DMF + water		DMSO + water	
w_2	h_{XX}/J·kg·mol^{-2}	w_2	h_{XX}/J·kg·mol^{-2}
0	205.00 (±1.00)	0	205.00 (± 1.00)
0.0473	143.20 (± 0.11)	0.0548	173.22 (± 0.14)
0.0949	46.70 (± 0.25)	0.1090	132.13 (± 10.72)
0.1428	54.76 (± 1.48)	0.1627	72.63 (± 0.51)
0.1909	−78.63 (± 0.34)	0.2159	62.30 (± 0.16)
0.2394	−86.21 (± 0.05)	0.2685	−94.56 (± 0.04)
0.2881	−533.94 (±0.01)	0.3207	−159.03 (± 0.01)

[a] Note: the values in parentheses are the evaluated errors.

Therefore, it can be concluded that at lower DMF concentrations interactions (a) and (b) predominate the sign and magnitude of h_{XX}, with the increasing concentration of DMF, and interaction (c) plays a more important role.

From Figure 3, it can be seen that the tendency of h_{XX} for L-alanine in aqueous DMSO solutions is almost similar to that in aqueous DMF solutions. This is because there are two methyl groups in the DMSO molecule, and they are the same in molecular structure. It is reasonable to refer that the methyl moieties play a pivotal role during the dilution process. According to van der Vegt and van Gunsteren,[31] the methyl moieties in DMSO can bind to the hydrophobic solute, and the binding process occurring at the expense of entropy is driven by a favorable solute−solvent energy and causes "salting-in" of the hydrophobic solute.

Salting-in of solutes is driven by preferential binding of the cosolvent to the solute, whereas salting-out is driven by a preferential exclusion of the cosolvent from the solute surface.[31] During the dilution process, the cosolvent molecules go through reorganization, after which a correct size cavity used to accommodate the solute molecules comes into being.

Therefore, at low DMSO concentrations, DMSO salts out L-alanine as the result of a favorable solute−solvent entropy change. This salting-out process is caused by strong cosolvent−water interactions that impede the opening of the cavities to the solute and then causes the nonpolar solute to be more preferentially hydrated, with a positive contribution to h_{XX}. Preferential binding of the L-alanine to DMSO that is driven by a strongly favorable change of the solute−solvent energy with increasing DMSO content occurs, with a negative contribution to h_{XX}.

Supporting Information Available:

Detailed information of the theoretical basis about the method of measuring dilution enthalpy by ITC (isothermal titration calorimeter). This material is available free of charge via the Internet at http://pubs.acs.org.

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