

ENTHALPIES OF SOLUTION AND DILUTION OF SOME *L*- α -AMINO ACIDS IN WATER AT 298.15 K

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Abstract

The enthalpies of solution and dilution of glycine, *L*- α -alanine, *L*-valine, *L*- α -leucine, *L*- α -serine and *L*- α -threonine in water were measured at 298.15 K. The results were applied to calculate the enthalpic coefficients of homogeneous interactions between zwitterions of *L*- α -amino acids in aqueous solutions.

Keywords: aqueous solutions of *L*- α -amino acids, enthalpies of solution and dilution

Introduction

Amino acids and their derivatives incorporate some of the structural features present in globular proteins. They are useful as models of specific aspects of the more complex proteins in aqueous solution. Studies on the thermodynamic interactions between amino acids molecules in aqueous solution can promote an understanding of the conformational stability and unfolding behaviour of globular proteins in aqueous solution.

The present work reports the results of calorimetric measurements of the dissolution and dilution enthalpies of *L*- α -amino acids in water. The results obtained are discussed from the point of view of homogeneous molecular interactions, on the basis of the McMillan-Mayer model [1], as modified by Franks [2] and Desnoyers [3]. It is well known that the McMillan-Mayer enthalpic interaction coefficients can be considered a measure of intermolecular interactions in aqueous solution.

Experimental

Glycine (G) (99.5% from Merck), alanine (A), valine (V), leucine (L), serine (S) and threonine (T) (all 99% from Merck) were crystallized from a water-methanol mixture and dried under reduced pressure at 323 K. The water used in the experiments was deionized and distilled twice.

The enthalpies of solution were determined with a calorimeter of the isoperibol type [4, 5]. The temperature sensitivity was about $4 \cdot 10^{-5}$ K, and the temperature stability of the thermostat was better than 10^{-3} K. The standard enthalpies of solution ΔH_s° of these amino acids were calculated as the mean of the results of 10 to 12 independent measurements carried out in the molality range from 0.001 to 0.02 mol kg⁻¹ water.

Calorimetric measurements of the enthalpies of dilution were carried out with a Setaram MS-80D isothermal calorimeter at 298.15 K. Both the ampoules used for measurement of the enthalpies of solution and the calorimeter measuring cells were weighed by means of a Sartorius RC 210D balance.

Results and discussion

The enthalpies of solution of the *L*- α -amino acids in water in the amino acid concentration range 0.001–0.02 mol kg⁻¹ water were measured at 298.15 K. On the basis of the dissolution enthalpy values, the standard solution enthalpies of the amino acids in water were calculated. The data are listed in Table 1 (the numbers of measurements are given in parentheses) together with the corresponding standard enthalpies of solution reported in the literature. The calculated values are seen to be in good agreement with the literature data. Only the results obtained by Abu-Hamdlyyah and Shehabuddin [6] on threonine are appreciably lower than those obtained in this study.

Table 1 Standard enthalpies of solution ΔH_s° of *L*- α -amino acids in water at 298.15 K

<i>L</i> - α -amino acid	$\Delta H_s^\circ/\text{kJ mol}^{-1}$ (this work)	$\Delta H_s^\circ/\text{kJ mol}^{-1}$ (Ref.)
Glycine	14.20 \pm 0.06 (15) [17]	14.08 [6], 14.13 [8], 14.18 [9]
Alanine	7.67 \pm 0.05 (12)	7.54 [6], 7.36 [10]
Valine	3.12 \pm 0.07 (10)	3.10 [9]
Leucine	3.41 \pm 0.07 (10)	3.46 [6], 3.46 [8]
Serine	11.49 \pm 0.06 (12)	
Threonine	10.33 \pm 0.06 (10)	9.78 [6]

The enthalpies of dilution of the aqueous *L*- α -amino acid solutions were measured in water, using a Setaram MS-80D isothermal calorimeter and an isoperibol calorimeter [4, 5]. The initial molalities (m_i) of the *L*- α -amino acids were calculated so as to arrive at a final molality (m_f) of from 0.001 to 0.02 mol kg⁻¹ water (which corresponded to the range of concentrations used to determine the standard enthalpies of solution). The results of the calorimetric measurements of the dilution enthalpies ΔH_{dil} are presented in Table 2. The resultant enthalpies of dilution were used to find homogeneous enthalpic pair interaction coefficients

h_{xx} in water, according to the modified McMillan-Mayer model [1, 3]. The experimental values of the enthalpies of dilution ΔH_{dil} were described by the second-degree polynomial [3, 11]

$$\Delta H_{dil} = h_{xx}(m_f - m_i) + h_{xxx}(m_f^2 - m_i^2) + \dots$$

where h_{xx} and h_{xxx} are the homogeneous enthalpic pair and triplet interaction coefficients of the amino acids in water (Table 3). The enthalpic pair interaction coefficients h_{xx} constitute the sum of the energy effects of the interactions between the hydrated molecules in water, including a direct interaction between two zwitterions ($-\text{CHCOO}^-\text{NH}_3^+$) of the investigated amino acid in an exothermic process, and a partial dehydration of the hydration shells of the amino acid molecule, polar portions interacting with each other in an endothermic process.

Table 2 Enthalpies of dilution ΔH_{dil} of aqueous amino acid solutions at 298.15 K

m_i^j	m_f^j	ΔH_{dil}^j	m_i^j	m_f^j	ΔH_{dil}^j
mol kg ⁻¹		J mol ⁻¹	mol kg ⁻¹		J mol ⁻¹
Glycine					
0.3648	0.0154	141.2	0.9296	0.0185	331.6
0.5248	0.0175	196.8	1.4231	0.0241	474.3
0.5248	0.0198	198.5	1.7170	0.0178	533.5
0.6101	0.0199	230.2	1.9421	0.0183	592.5
0.6101	0.0226	223.8	2.1014	0.0192	610.1
0.8105	0.0253	296.0	2.4846	0.0267	683.3
<i>L</i> - α -Alanine					
0.4851	0.0152	-94.9	0.8852	0.0728	-165.7
0.4851	0.0354	-92.6	0.9852	0.1178	-173.5
0.5981	0.0295	-114.3	1.2532	0.1008	-235.1
0.5981	0.0379	-116.5	1.2532	0.1201	-223.2
0.7231	0.0384	-139.7	1.6292	0.1249	-303.9
0.8852	0.0445	-167.3	1.6282	0.1853	-281.6
<i>L</i> - α -Valine					
0.1018	0.0098	-79.8	0.2852	0.0175	-230.8
0.1508	0.0102	-122.2	0.3015	0.0182	-242.3
0.1854	0.0135	-148.4	0.3416	0.0198	-276.1
0.2232	0.0169	-179.1	0.3962	0.0253	-318.2
0.2501	0.0202	-197.8	0.4241	0.0265	-342.0

Table 2 Continued

$m_i/$	$m_f/$	$\Delta H_{dil}/$	$m_i/$	$m_f/$	$\Delta H_{dil}/$
mol kg ⁻¹		J mol ⁻¹	mol kg ⁻¹		J mol ⁻¹
<i>L</i> - α -Leucine					
0.0551	0.0099	-55.9	0.1285	0.0125	-142.7
0.0793	0.0102	-86.9	0.1505	0.0155	-167.1
0.0843	0.0101	-89.7	0.1531	0.0192	-161.8
0.1005	0.0119	-109.4	0.1608	0.0202	-172.7
0.1152	0.0153	-121.8	0.1608	0.0168	-177.1
<i>L</i> - α -Serine					
0.3543	0.0185	222.6	0.9245	0.0253	532.3
0.4951	0.0182	310.9	1.2521	0.0199	693.7
0.4951	0.0199	305.1	1.6307	0.0155	825.4
0.7025	0.0204	424.9	1.9852	0.0232	926.1
0.7025	0.0242	416.5	2.0081	0.0195	916.7
0.8605	0.0281	510.8	2.3616	0.0220	987.3
<i>L</i> - α -Threonine					
0.2305	0.0124	19.4	0.4538	0.0242	32.1
0.2305	0.0225	18.0	0.5002	0.0275	35.2
0.3242	0.0154	26.6	0.5882	0.0175	41.9
0.3242	0.0194	25.2	0.5882	0.0274	39.5
0.3781	0.0210	29.5	0.6176	0.0454	40.2
0.4538	0.0148	35.0	0.6176	0.0348	41.3

For amino acids with alkyl groups, this process is superimposed by an additional effect of hydrophobic hydration, causing reinforcement of the hydrogen-bonds between the water molecules surrounding these alkyl groups [12, 13]. Investigations of the structure of water in solutions of various amino acids by Bango *et al.* [14] and Hechte *et al.* [15] indicated that the water–water hydrogen-bonds in the water zones surrounding the alkyl groups of the amino acids are stronger than those in bulk water, and that the size of the water clathrate around the hydrophobic side-chain increases with increasing alkyl group size. In consequence of the co-operation of the hydrogen-bonds, this effect is transferred on to the hydration layer of the zwitterion, which reinforces the interaction between the water molecules and the amino acid polar portion. This makes direct interaction between two amino acid zwitterions difficult, since the removal of water

molecules from the hydration shells of interacting molecules requires a higher energy supply. Consequently, the effect of partial dehydration of the reinforced hydration layers of the zwitterion becomes more endothermic.

The enthalpic triplet interaction coefficients h_{xxx} , as higher ones, including the interactions of all pairs formed by the considered set of three molecules [1, 11], will not be discussed in this paper.

Table 3 Enthalpic pair and triplet interaction coefficients for some *L*- α -amino acids in water at 298.15 K

<i>L</i> - α -amino acid	$h_{xx}/\text{J kg mol}^{-2}$	$h_{xxx}/\text{J kg}^2 \text{mol}^{-3}$	$\Delta f_t^{\text{a)}}$ /kJ mol ⁻¹
Glycine	-424	60	0
Alanine	206	-5	2.09
Valine	871	-33	6.28
Leucine	1243	-100	7.53
Serine	-709	120	-1.26
Threonine	-99	44	1.67

^{a)} Hydrophobicity scale: Δf_t for transfer of amino acid side-chain from organic solvent to water at 298.15 K [18]

The enthalpic pair interaction coefficients h_{xx} of the zwitterion of glycine have negative values (Table 3). This indicates a strongly exothermic effect of the direct interaction between the zwitterions of glycine, as compared with the endothermic effect of partial dehydration of the solvation layers of glycine molecules in water. The replacement of a hydrogen atom in the molecule of glycine by an alkyl group causes an increase in the enthalpic pair interaction coefficients h_{xx} . This can be explained by the reinforcement of the hydrogen-bonds of the water molecules in the hydrating layers of the zwitterion of the amino acid (directly combined with the alkyl group). This brings about an increase in the endothermic dehydrating effects of the interacting molecules, which increase with increasing alkyl group size. This is shown by the values of the enthalpic pair interaction coefficients for the amino acid zwitterions (Table 3): $G < A < V < L$.

It is assumed that the values of the enthalpic homogeneous pair interaction coefficients of the *L*- α -amino acids are the sums of the effects of the zwitterion and the side-chain. The side-chain of glycine is -H, of alanine is -CH₃, of valine is -C₃H₇ and that of leucine is -C₄H₉.

The dependence of h_{xx} on the number of CH₂ groups in the *L*- α -amino acid molecule is linear (Fig. 1) (as proposed by Savage and Wood [16, 17], it is accepted that the CH₃ group corresponds to 1.5CH₂ while CH corresponds to 0.5CH₂), as described by the equation $h_{xx} = -522.75 + 199.95 n_{\text{CH}_2}$ ($R^2 = 0.9828$). The constant term in this equation describes the contribution of the zwitterion-zwitterion interaction $h_{(\pm\pm)}$ to the homogeneous enthalpic pair interaction

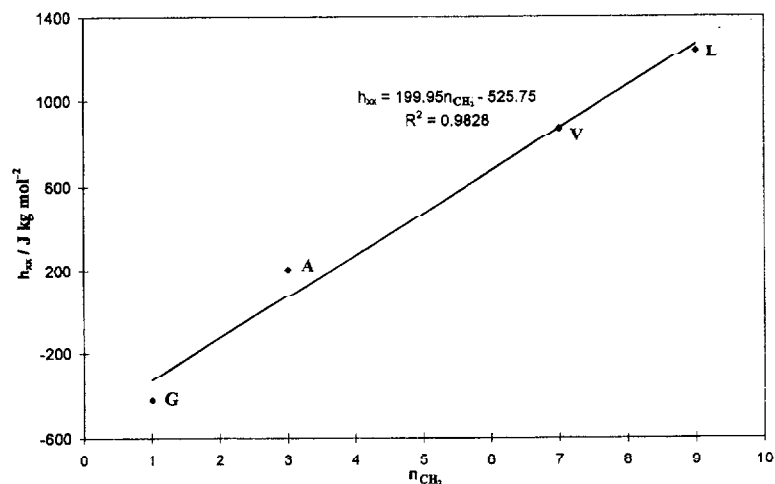


Fig. 1 Dependence of the homogeneous enthalpic pair interaction coefficients of *L*- α -amino acids in water on the number of CH_2 groups in the interacting *L*- α -amino acid molecules

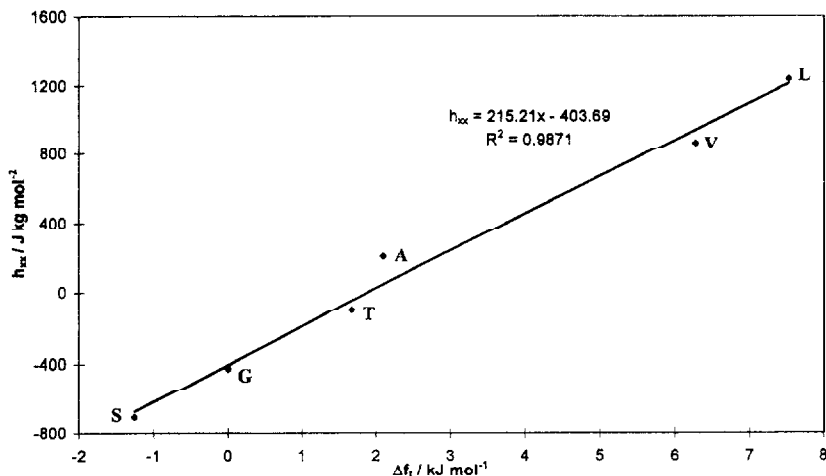


Fig. 2 Relationship between the hydrophobicity (Δ_f) and the homogeneous enthalpic pair interaction coefficients of *L*- α -amino acids in water at 298.15 K

coefficient. The negative value of $h_{(++)}$ testifies to a stronger exothermic effect of the direct zwitterion-zwitterion interaction than the dehydrating effects of the hydrating shells of the interacting polar groups. The slope of this function determines the contribution of the CH_2 group to the value of the enthalpic pair interaction coefficient h_{xx} . The presence of the CH_2 group causes a reinforcement of

the hydrogen-bonds in the shells of the interacting zwitterions of this amino acid, which is the reason for the reduction in the direct interactions between the polar groups.

Substitution of a hydroxy group by a hydrogen atom in an amino acid molecule results in an increase in the negative value of h_{xx} (Table 3: serine and threonine), which is caused by an enhancement of the exothermic contribution of the electrostatic interaction between the amino acids molecules in water.

It is interesting to consider the relationship between the enthalpic homogeneous pair interaction coefficients of the amino acids and the hydrophobicity scale (Δf) for the amino acid side-chains (Table 3) proposed by Nozaki and Tanford [18]. This parameter describes the influence of the hydrophobic side-chain of the amino acids on the water–water hydrogen-bonds in the water around this side-chain. The parameter includes the effect of an aliphatic OH group.

Figure 2 shows that both series of values correlate well. The observed relationship is described by the linear equation $h_{xx}=215.21x-403.69$ ($R^2=0.9871$).

The enthalpic homogeneous pair interaction coefficients h_{xx} , as a measure of the interactions between two solvated molecules in solution, depend to a great extent on how much the examined molecules are affected by the solvent. This can be clearly seen in the case of aqueous solutions, where all the processes reinforcing the hydrogen-bonds in the water (e.g. hydrophobic hydration) weaken the direct interactions between the polar groups of the interacting molecules (ions).

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