Amino acids in aqueous solution. Effect of molecular structure and temperature on thermodynamics of dissolution

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The enthalpies of dissolution of glycine (Gly) and L-α-alanine (Ala) in water at 288.15—318.15 K were measured. The results were compared with the earlier obtained data for L-α-phenylalanine (Phe) and L-α-histidine (His). The standard enthalpies of dissolution ($\Delta_{soln}H^0$) and differences (ΔC_p^0) between the limiting partial molar heat capacity of the amino acids in solution and the heat capacity of the amino acids in the crystalline state ($\Delta C_p^0 = \overline{C}_{p,2}^{\infty} - C_p$) were calculated in the temperature interval 273—373 K. Changes in the entropy of dissolution ($\Delta\Delta_{soln}S^0$) and reduced Gibbs energy [$\Delta(\Delta_{soln}G^0/T)$] in the temperature interval from 273 to 373 K were determined from the known thermodynamic relationships. The ΔC_p^0 value is negative for hydrophilic glycine and positive for other amino acids. The $\Delta\Delta_{soln}S^0$ values increase with an increase in the hydrophobicity of the amino acids. The $\Delta(\Delta_{soln}G^0/T)$ values become more negative in the order Ala, Phe, Gly, His.

Key words: glycine, L-α-alanine, L-α-phenylalanine, L-α-histidine, aqueous solution, calorimetry, enthalpy, heat capacity, entropy, Gibbs energy.

Temperature plays a substantial role in evolution of the structure and properties of solvents. This reflects changes in the thermodynamic characteristics of solution formation. However, published data on polythermal studies of solutions of amino acids are virtually lacking.[1] We have earlier[2—4] studied the temperature effect on the enthalpy of dissolution of Phe and His in water. The purpose of the present work is to measure by calorimetry the enthalpies of dissolution of Gly and Ala in water in the functional interval of temperatures from 288.15 to 318.15 K. The size of molecules increases and the hydrophobic properties are enhanced in the series of these amino acids.[5,6] It was of interest to reveal the temperature effect on the thermodynamic characteristics of aqueous solutions of the amino acids with variation of the above parameters.

Experimental

Bidistilled water (conductivity 10^{-5} S cm^{-1}) was used. Glycine and alanine (purity grade) (Reanal, Hungary) were twice recrystallized from an ethanol—water mixture[7] and dried *in vacuo* ($P < 10$ Pa) at 333 K.

Integral heats of dissolution were measured in an ampule-type calorimeter with an isothermic shell and a volume of the reaction flask of 60 cm^3 (see Ref. 8). A thermoresistor of Karmanov´s construction was used as a temperature sensor placed inside the titanium case filled with Wood´s alloy. The structures of the calorimeter and measuring scheme provide thermometric and heat sensitivities of 10^{-5} deg and $2 \cdot 10^{-3}$ J per 1 mm of the detector scale. To measure heat effects, a comparative method was used when the system was calibrated with electric current after each experiment. The arithmetic mean values of the heat effects of dissolution ($\Delta_{soln}H^m$) were taken as standard values of the enthalpies of dissolution ($\Delta_{soln}H^0$) of the compounds, because the difference between them lies within the experimental error, being at most 1% according to our estimates. The calorimeter was calibrated according to published recommendations.[9]

Results and Discussion

The data on the heat effects of dissolution of the amino acids in water are given in Tables 1—3. The literature data on $\Delta_{soln}H^0$ of Gly and Ala at 298.15 K are presented in Note to Table 3. It can be seen that our values agree well with published data.[10—14]

The results of our experiments show that the dissolution process of Gly becomes less endothermic with the temperature rise. For other amino acids, the endothermicity of dissolution increases in the studied interval with increasing temperature. Although, the amino acid molecules in an aqueous solution exist in the zwitterionic form, the temperature plot of their $\Delta_{soln}H^0$ (except for Gly) has a shape characteristic of nonelectrolytes. This shape in the case of aqueous solutions of nonelectrolytes containing hydrocarbon radicals in the composition of the

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Table 1. Heat effects of dissolution of L-α-alanine in water

T/K	m/mol kg^{-1}	q/J	$\Delta_{soln}H^m$/kJ mol^{-1}
288.15	0.0128	6.70	7.29
	0.0168	8.78	7.24
293.15	0.0088	4.00	7.55
	0.0104	4.69	7.52
	0.008	3.65	7.56
	0.0142	6.48	7.62
298.15	0.0228	9.41	7.79
	0.0231	9.55	7.80
	0.0365	14.97	7.74
306.15	0.0075	3.88	8.28
	0.0089	4.60	8.25
318.15	0.0174	8.07	8.75
	0.019	8.80	8.74
	0.0231	10.69	8.73

Note. Here and in Table 2, m is the molality of the amino acid, and q is the heat effect of dissolution of a given number of moles of the amino acid.

Table 2. Heat effects of dissolution of glycine in water

T/K	m/mol kg^{-1}	q/J	$\Delta_{soln}H^m$/kJ mol^{-1}
298.15	0.0285	24.26	14.17
	0.0369	31.16	14.07
	0.0256	21.82	14.22
	0.0267	22.72	14.20
	0.0333	28.36	14.18
313.15	0.0468	37.76	13.44
	0.0379	30.61	13.46
	0.0409	33.36	13.58
	0.0422	34.15	13.48
	0.0398	32.14	13.47

Table 3. Standard enthalpies of dissolution ($\Delta_{soln}H^0$)[a] of L-a-alanine and glycine in water

T/K	$\Delta_{soln}H^0$/kJ mol^{-1}	
	L-α-Alanine	Glycine
288.15	7.26±0.05	—
293.15	7.56±0.04	—
298.15	7.78±0.04[b]	14.17±0.05[c]
306.15	8.27±0.03	—
318.15	8.74±0.01	—
313.15	—	13.49±0.05

[a] $\pm 2\sigma$/kJ mol^{-1}; $\sigma = [\Sigma(x_{av} - x_i)^2/(n(n-1)]^{0.5}$.
[b] Literature data on $\Delta_{soln}H^0$ for Ala in water at 298.15 K: 7.36 (see Ref. 12), 7.54 (see Ref. 11), and 7.99 kJ mol^{-1} (see Ref. 10).
[c] $\Delta_{soln}H^0$ for Gly in water at 298.15 K: 14.16 (see Ref. 13) and 14.20 kJ mol^{-1} (see Ref. 14).

molecules is caused by the contribution of hydrophobic hydration and a change in the thermodynamic parameters with temperature variation, which characteristic of this type of hydration. Thus, the presence of the Me and Ph substituents and heterocyclic imidazole ring in the amino acid molecules determines the effect of their hydrophobic hydration. This is confirmed by the data of spectroscopic studies[15,16] indicating that water—water bonds are strengthened in the environment of hydrocarbon radicals of a series of L-α-amino acids. The absence of nonpolar groups in a Gly molecule determines different temperature dependences of $\Delta_{soln}H^0$.

The results obtained in the present work and data published earlier[2–4] made it possible to calculate the differences (ΔC_p^0) between the limiting partial molar heat capacity in solution and the heat capacity for the crystalline state of the amino acids ($\Delta C_p^0 = \overline{C}_{p,2}^{\infty} - C_p = \partial(\Delta_{soln}H^0)/\partial T$). The temperature dependence of $\Delta_{soln}H^0$ was approximated by the equations

$$\Delta_{soln}H_T^0 = \Delta_{soln}H_\Theta^0 + \Theta\Delta C_{p(\Theta)}^0(1 - \Theta/T), \quad (1)$$

$$\Delta_{soln}H_T^0 = \Delta_{soln}H_\Theta^0 + \Theta\Delta C_{p(\Theta)}^0(T/\Theta - 1), \quad (2)$$

$$\Delta_{soln}H_T^0 = \Delta_{soln}H_\Theta^0 + \Delta C_{p(\Theta)}^0(T - \Theta) + 0.5\,\delta c_p^0\,(T - \Theta)^2, \quad (3)$$

Here Θ is the unchanged temperature, and δc_p^0 is the temperature coefficient of heat capacity.

The form of equation was determined by the error of approximation close to the experimental error at the smallest number of parameters. Our analysis showed that for Gly and Ala Eq. (1)[4] satisfies there requirements, whereas for Phe and His these are Eqs (2)[4] and (3),[3] respectively. The data in Table 3 and Ref. 13 were used for Gly. The results of approximation are given in Table 4.

The hydrophobicity parameters of the studied amino acids are presented in Table 5. Hydrophobicity of amino acids can be characterized by the free energy of transfer ($\Delta_{tr}G^0$) of an amino acid from water to ethanol (or dioxane).[5] Histidine and alanine are close to each by this parameter (see Table 5). From the viewpoint of structure, hydrophobicity can be characterized by the contact surface of the side chain accessible for water (A)[6] and hydrophobicity parameter (π).[17] The A value for His exceeds A for Ala by ~3 times (see Table 5).

Analysis of the values given in Tables 4 and 5 shows that ΔC_p^0 of the amino acids become more positive with an increase in the hydrophobicity of hydrocarbon radicals of the molecules. Since ΔC_p^0 reflects the structural changes in the solvent and intensity of the solvent—solute interactions,[18] it can be assumed that the effect of hydrophobic hydration is enhanced in the order Gly—Ala—His—Phe. This is confirmed by an increase in the absolute value of the enthalpies of hydration of the amino acids in this order and an increase in the enthalpic coefficients of pair interactions[19,20] (see Table 5) in an aqueous solution. The enthalpies of hydration were calculated from the data on the enthalpies of dissolution (see Table 3

Table 4. Standard enthalpies (kJ mol^{-1}) and heat capacities (J mol^{-1} K^{-1}) of dissolution of the amino acids in water

Θ/K	Glycine		L-α-Histidine		L-α-Alanine		L-α-Phenylalanine	
	$\Delta_{soln}H_\Theta{}^0$	$\Delta C_{p(\Theta)}{}^0$	$\Delta_{soln}H_\Theta{}^0$	$\Delta C_{p(\Theta)}{}^0$	$\Delta_{soln}H_\Theta{}^0$	$\Delta C_{p(\Theta)}{}^0$	$\Delta_{soln}H_\Theta{}^0$	$\Delta C_{p(\Theta)}{}^0$
273.15	15.47±0.08	−57±3	13.42±0.08	7±6	6.41±0.06	61±2	3.52±0.08	185±2
298.15	14.16±0.02	−48±3	14.22±0.05	58±5	7.81±0.02	51±2	8.19±0.03	185±2
323.15	13.05±0.05	−41±2	16.29±0.03	108±4	8.99±0.05	44±2	12.86±0.05	185±2
348.15	12.10±0.10	−35±2	19.60±0.04	158±7	10.01±0.08	38±1	17.52±0.11	185±2
373.15	11.28±0.10	−31±2	24.23±0.50	210±14	10.89±0.10	33±1	22.19±0.17	185±2

Note. Regression parameters $R^2 > 0.99$, se $= \Sigma(y_{calc} - y_{exp})^2/(n - p) < 0.002$, n is the number of points, p is the number of parameters. For His, $\delta c_p{}^0 = 2.0 \pm 0.2$. The standard deviations are given after symbol ±.

Table 5. Surface areas of the contact surface of the side chain accessible for water (A),[6] Gibbs transfer energies ($\Delta_{tr}G^0$) from water to ethanol,[5] hydrophobicity parameters (π)[17] at 298.15 K, enthalpic coefficients of homotactic pair interactions in an aqueous solution,[19,20] and enthalpies of sublimation[21,22] and hydration of the studied amino acids

Amino acid	A/Å^2	$\Delta_{tr}G^0$	$\Delta_{sub}H^0$	$\Delta_{hydr}H^0$	h_{22} /J kg mol^{-2}	π
		kJ mol^{-1}				
Gly	0	—	136.3	−122.1	−439	0
Ala	28.5	−0.5	144.7	−136.9	203	0.31
Phe	122.0	−2.5	153.9	−144.7	1229	1.79
His	110.3	−0.5	156.7	−142.7	—	—

and published data[2,3]) and sublimation of the compounds.[21,22]

The $\Delta C_p{}^0$ values (see Table 4) and heat capacities of crystalline Gly (C_p = 95 J mol^{-1} K^{-1}) and Ala (C_p = 115 J mol^{-1} K^{-1}) borrowed from Ref. 1 allowed us to calculate their limiting partial molar heat capacities in an aqueous solution at 298.15 K: $\overline{C}{}^\infty_{p,2} = C_p + \Delta C_p{}^0$, which are equal to 47 and 165 J mol^{-1} K^{-1} for Gly and Ala, respectively. The values of $\overline{C}{}^\infty_{p,2}$ and $\Delta C_p{}^0$ obtained by us for Ala exceed the corresponding values for the racemate, being 141 and 19 J mol^{-1} K^{-1} at 298.15 K, respectively (see Ref. 13).

The temperature dependences of the entropy and reduced Gibbs energy of dissolution are described by the relationships

$$\partial(\Delta_{soln}G^0/T)/\partial T = -\Delta_{soln}H^0/T^2, \quad (4)$$

$$\partial(\Delta_{soln}S^0)/\partial T = \Delta C_p{}^0/T. \quad (5)$$

Integrating Eqs (4) and (5) with account for the data obtained in the present work, we can calculate the changes in the reduced Gibbs energy ($\Delta_{soln}G_2{}^0/T_2 - \Delta_{soln}G_1{}^0/T_1$) = $\Delta(\Delta_{soln}G^0/T)$ and entropy ($\Delta_{soln}S_2{}^0 - \Delta_{soln}S_1{}^0$) = $\Delta\Delta_{soln}S^0$ of dissolution in the temperature interval from T_1 to T_2. The temperature changes in the $\Delta\Delta_{soln}S^0$ value and dimensionless parameter $\Delta(\Delta_{soln}G^0/T)/R$ in the temperature interval 273.15—373.15 K are presented in Table 6.

Table 6. Change in the thermodynamic functions of dissolution of the amino acids in the interval 273.15—373.15 K

Amino acid	$\Delta\Delta_{soln}S^0$/J mol^{-1} K^{-1}	$\Delta(\Delta_{soln}G^0/T)/R$
Gly	−11	−1.58
Ala	14	−1.02
His	32	−1.96
Phe	58	−1.41

The data in Table 6 show that for hydrophilic glycine both $\Delta\Delta_{soln}S^0$ and $\Delta C_p{}^0$ are negative. The $\Delta\Delta_{soln}S^0$ values increase with an increase in the hydrophobicity of the amino acids. The $\Delta(\Delta_{soln}G^0/T)/R$ values become more negative in the order Ala, Phe, Gly, His.

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