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Thermochemical Characteristics of Interactions of *DL*-Alanine in Aqueous Solutions of Glycerol, Ethylene Glycol, and 1,2-Propylene Glycol

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Abstract—The method of dissolution calorimetry was used to measure the integral enthalpy of dissolution $\Delta_{sol}H^m$ of *DL*-alanine in mixtures of water with glycerol, ethylene glycol, and 1,2-propylene glycol at a concentration of organic solvent up to 0.32 mole fraction. The standard dissolution enthalpy ($\Delta_{sol}H^0$) and transport enthalpy of amino acids from water to mixed solvent ($\Delta_{tr}H^0$) were calculated. The calculated enthalpy coefficients of pair interactions of the *DL*-alanine molecules with the polyol molecules are positive and less than these values for *L*-alanine. The effect of interactions of different types in solution and the structural features of biomolecules and co-solvents on the enthalpy of dissolution characteristics of amino acids were considered.

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At the chemical synthesis of optical isomers the enantiomers are formed in 50:50 ratio. Such mixtures are commonly referred to as racemates or racemic mixtures. Sometimes the enantiomer whose properties have been studied and possibly modified should be reduced in an optically pure form, which is of particular importance for the pharmaceutical industry. Stereospecific intermolecular interactions resulting from the asymmetry of the molecular structures play an important role in biochemical enzymatic reactions [1]. It was found that at the dissolution of the enantiomers of aliphatic amino acids in water and aqueous alcohol solutions in some cases the thermodynamic characteristics significantly alter, which points to the selectivity of the interactions with the co-solvent of molecules differing by the spatial arrangement of groups [2, 3].

Table 1 shows experimental data on $\Delta_{sol}H^0$ of *DL*-alanine in the mixed solvent of water with glycerol, ethylene glycol and 1,2-propylene glycol. The figure shows the plots of transfer enthalpies $\Delta_{tr}H^0$ of *DL*-Ala from water into water–organic mixtures versus the mole fraction of the co-solvent (X_2).

As can be seen from the figure all dependences have an extreme character. The transfer enthalpies are determined by different contributions of competing interactions in the solution with opposite signs, of different nature and in different solvation processes. For the analysis of the observed dependences we used the previously proposed model approach based on the interactions of the solute and co-solvent [5]. In the three-component solutions of amino acid–organic co-solvent–water, the molecules of hydrated solutes are close enough for overlapping of their hydration shells. The resulting transfer enthalpies for the *DL*-alanine are determined by the sum of contributions with opposite signs:

$$\Delta_{tr}H^0 = -\Delta H^1 + \Delta H^2 + \Delta H^3, \qquad (1)$$

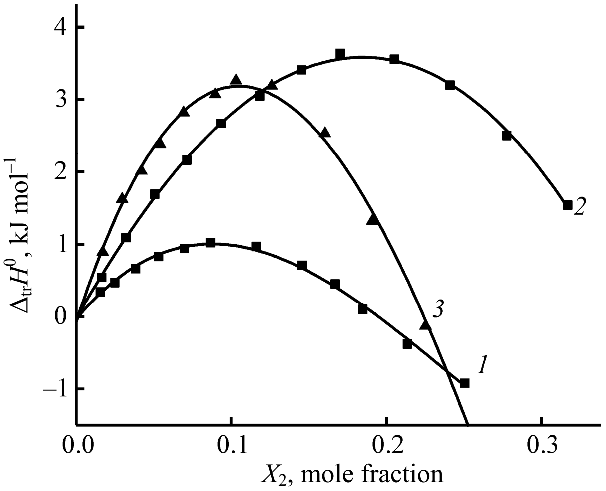
where ΔH^1 is the enthalpy of ion-bipolar interactions that occur between zwitterionic centers of amino acids and the OH groups of polyols; ΔH^2 is the enthalpy of hydrophobic–hydrophilic interactions between nonpolar part of the amino acid or organic cosolvent and the cosolvent OH group or zwitterionic *DL*-alanine center; ΔH^3 is the enthalpy of hydrophobic–hydrophobic interactions between nonpolar parts of the amino acid and the polyol. The contribution of the first of these types of interactions is negative, while the contributions of the second and third types to $\Delta_{tr}H^0$ at the transfer of amino acid from water to aqueous–

Table 1. The standard enthalpy of solution $\Delta_{sol}H^0$ (kJ mol^{-1}) of *DL*-alanine in a mixed solvent water–polyhydric alcohol at 298.15 K

H_2O–glycerol		H_2O–ethylene glycol		H_2O–1,2-propylene glycol	
m_y[a]	$\Delta_{sol}H^0$	m_y[a]	$\Delta_{sol}H^0$	m_y[a]	$\Delta_{sol}H^0$
0	9.34±0.05 [4]	0	9.34±0.05 [4]	0	9.34±0.05 [4]
0.8753	9.68±0.05	0.9335	9.88±0.05	0.9673	10.23±0.06
1.4263	9.81±0.06	1.8398	10.43±0.05	1.7020	10.96±0.05
2.2147	10.00±0.05	2.9674	11.03±0.06	2.4435	11.35±0.06
3.1164	10.17±0.06	4.2714	11.50±0.06	3.1847	11.72±0.06
4.1663	10.28±0.06	5.7249	12.01±0.06	4.1356	12.16±0.07
5.2635	10.36±0.06	7.4561	12.39±0.07	5.4662	12.41±0.07
7.2941	10.31±0.06	9.4463	12.75±0.07	6.3765	12.60±0.07
9.4638	10.05±0.05	11.3821	12.98±0.07	8.0152	12.53±0.07
11.1186	9.79±0.05	14.3317	12.90±0.07	10.6002	11.87±0.06
12.5756	9.44±0.05	17.6239	12.54±0.07	13.0939	10.66±0.07
15.0662	8.96±0.04	21.3381	11.84±0.06	16.1376	9.21±0.06
18.5677	8.42±0.04	25.7741	10.88±0.06	19.6475	7.40±0.04

[a] Cosolvent molality (mol kg^{-1}).

organic solvents are positive. Positive values of $\Delta_{tr}H^0$ for the *DL*-Ala in aqueous solutions of 1,2-propylene glycol and in the solutions of glycerol and ethylene glycol up to concentrations of 0.19 and 0.22 mole fractions, respectively, (see the figure) show a predominance of the second (ΔH^2) and the third (ΔH^3) types of interactions. After passing the maximum, the transfer enthalpies begin to decrease, which means the prevalence of ion-bipolar interactions. Apparently, with increasing concentrations of co-solvent the interactions between the polar groups of polyols and zwitterionic centers of *DL*-alanine become stronger, which leads to an increase in the proportion of exo-effects in the three-component solution. The fact that the maxima are at different mole fractions of the studied co-solvents show that the contributions from the interactions of hydrophobic–hydrophilic and hydrophobic–hydrophobic groups reach maximum at certain different concentrations of the polyols.



Transfer enthalpies ($\Delta_{tr}H^0$) of *DL*-alanine from water to its mixtures with glycerol (*1*), ethylene glycol (*2*), and 1,2-propylene glycol (*3*) vs. concentration of organic cosolvent (X_2) at 298.15 K.

The interparticle interactions in ternary aqueous systems are described in the framework of the McMillan–Mayer theory [6] by calculating the enthalpy coefficients of pair interactions (h_{xy}) of amino acids with molecules of organic solvents. For the calculation, the concentration dependence of $\Delta_{sol}H^0 = f(m_y)$ for the *DL*-alanine in aqueous–organic solutions was approximated by a polynomial of third degree:

$$\Delta_{sol}H^0 = a_0 + a_1 m_y + a_2 m_y^2 + a_3 m_y^3, \qquad (2)$$

where m_y is molal concentration of the organic cosolvent, a_0, a_1, a_2 are the coefficients of the approximation, calculated by the least-squares method.

As a result, we obtained the following equations for the *DL*-Ala in aqueous solutions of glycerol [Eq. (3)], ethylene glycol [Eq. (4)], and 1,2-propylene glycol [Eq. (5)].

$$\Delta_{sol}H^0 = (9.34\pm0.03) + (0.40\pm0.01)m_y\text{-}\ldots \quad R\ 0.999,\ SD\ 0.024,\ N\ 12; \tag{3}$$

$$\Delta_{sol}H^0 = (9.33\pm0.04) + (0.65\pm0.01)m_y\text{-}\ldots \quad R\ 0.999,\ SD\ 0.040,\ N\ 12; \tag{4}$$

$$\Delta_{sol}H^0 = (9.34\pm0.07) + (1.06\pm0.03)m_y\text{-}\ldots \quad R\ 0.998,\ SD\ 0.073,\ N\ 12. \tag{5}$$

The values of the free terms in the Eqs. (3)–(5) correspond to the standard enthalpies of dissolution of *DL*-alanine in pure water and are in good agreement with those obtained previously (Table 1) and with published data, for example $\Delta_{sol}H^0$ (*DL*-Ala) = 9.35 [7], 9.25 [8] (kJ mol^{-1}).

To calculate the enthalpy coefficients of pair interactions h_{xy} we used the coefficient a_1, which is related to h_{xy} according to the ratio $h_{xy} = a_1/2$ [9]. The values obtained for *DL*-Ala in solutions of polyols are listed in Table 2.

All the enthalpic interaction coefficients for the studied amino acids h_{xy} are positive. This means that endothermic processes related to the restructuring of three-component solution and release of the water molecules from hydration shells of *DL*-alanine and organic solvents prevail over the direct interactions of solvated polar groups of interacting molecules. The enthalpy coefficients of the pair interactions increase in the order: glycerol < ethylene glycol < 1,2-propylene glycol. Higher h_{xy} for 1,2-propylene glycol compared with ethylene glycol is due to the presence of additional methyl group in the former molecule that contributes to the hydrophobic hydration, which is manifested in the strengthening of the hydrogen bonds of water around the CH_3 groups [12]. This results in the increased restructuring of the solution at the interaction of the solvated molecules, increased endo-effects and h_{xy}. Less positive h_{xy} for glycerol compared with 1,2-propylene glycol is associated with the replacement of the hydrogen atom in the methyl group of 1,2-propylene glycol molecule by the polar OH group capable of forming donor–acceptor bond. As a result, the exothermicity of *DL*-Ala dissolution increases and the enthalpy parameter for the interaction h_{xy} in the *DL*-alanine–glycerol system decreases.

The main conditions of the chiral recognition of amino acid molecules in solution are the presence of bipolar ions and alkyl side chains [13, 14]. In addition, if the side chains of amino acids contain a polar functional group, the combined effect of hydrophilic and hydrophobic interactions determines the greater difference in the thermodynamic characteristics of dissolution [15]. As seen from Table 2, the enthalpy interaction coefficients h_{xy} for a racemic mixture of *DL*-alanine are less than those of the natural *L*-form of the amino acid. This means that the presence of D-alanine isomers in the racemic mixture creates conditions for the smaller degree of hydration of *DL*-forms of amino acids. As a result, at the dissolution of *DL*-alanine in aqueous solutions of polyols the degree of interaction with the co-solvent and the exothermicity of the dissolution are higher for the racemic mixture compared to the *L*-form of the amino acid, which is reflected in less positive h_{xy}. This is confirmed also by the observation of lower enthalpy of dissolution of *L*-alanine {$\Delta_{sol}H^0$ (*L*-Ala) = 7.66±0.05 [10]} in water compared with *DL*-alanine (Table 1), which means a higher degree of hydration of the *L*-isomer. Replacing a nonpolar alanine methyl group by the polar OH group causes an increase in the exothermic interactions between the molecules of alcohols and the *L*-serine zwitterion, which is due to the donor ability of the serine OH group to form a donor–acceptor bond with the components of the solution.

Table 2. Enthalpy coefficients of pair interactions h_{xy} (J kg mol^{-2}) of amino acids with organic solvents in aqueous solutions at 298.15 K

Substance	Glycerol	Ethylene glycol	1,2-Propylene glycol
DL-alanine	200±7	325±7	531±17
L-alanine [10]	355±7	444±13	694±19
L-serine [11]	135±7	264±7	471±16

Thus, the thermochemical characteristics of the interaction of the aliphatic amino acid *DL*-alanine with the components of the solution are affected by the structural features of molecules of the polyols, dehydration of the interacting substances, hydrophobic effects, and the spatial arrangement of the side groups of the biomolecules.

EXPERIMENTAL

Measurements of the integral dissolution enthalpies were performed in a hermetically sealed four-ampule variable temperature calorimeter of our construction with isothermal shell, which allowed to carry out a series of successive measurements of the thermal effects of dissolution of several samples of the substance in the same volume of solvent without reloading the calorimetric cell [16]. The reactive part of the calorimeter and all internal parts contacting with solution are made of titanium alloy VT-1. The calorimetric cell volume is ~110 ml. The stability of temperature control system in the calorimetric measurements was maintained to within 10^{-3} K. Thermometric and energy sensitivity of the calorimeter was 2×10^{-4} K mm^{-1} and 1×10^{-3} J mm^{-1} of the scale of recording device. Compensation of the thermal effect was carried out with electric current. To assess the accuracy and reliability of the calorimetric systems thermal effect of KCl dissolution in water was measured at 298.15 K. Ten independent measurements of the enthalpies of dissolution of KCl in H_2O and the use of the data on enthalpies of dilution [17] gave the value of the standard $\Delta_{sol}H^0$ = 17.23±0.06 kJ mol^{-1}, which agrees well with the value recommended in the literature (17.22±0.04 kJ mol^{-1}) [18, 19].

The *DL*-alanine concentration was varied in the range of 0.006–0.009 mol kg^{-1}. Enthalpies of dissolution $\Delta_{sol}H^m$ of amino acids in the investigated concentration range (up to 0.009 mol kg^{-1}) do not depend on the concentration of the biomolecules, so as the default values of $\Delta_{sol}H^0$ are taken the arithmetic mean values of the thermal effects of dissolution $\Delta_{sol}H^m$ of 3–5 measurements. *DL*-alanine (Reanal, 99%) before the experiment was recrystallized from water–ethanol mixture and dried in a vacuum at 343 K for 48 h. Deionized water was twice distilled (conductivity 10^{-5} ohm^{-1} cm^{-1}). Organic solvents (all from Aldrich): glycerol (99.5%), ethylene glycol (99%), and 1,2-propylene glycol (99%) were used without further purification. The water–organic mixed solvents were prepared gravimetrically.

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