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Thermochemical Analysis of Intermolecular Interaction of Aliphatic Amino Acids with Propanediol-1,3 in Aqueous Media

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Abstract—Integral enthalpy of dissolution of L-alanine, D,L-alanine, and D,L-valine in aqueous propanediol-1,3 (the diol molar fraction 0.26) has been determined. Standard enthalpies of the amino acids dissolution and transfer from water into the mixed solvent have been calculated. Influence of the interaction types and structural features of the amino acids and organic cosolvent on the enthalpies have been analyzed.

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In solutions in aqueous alcohols various types of interactions with solute molecules are possible due to competing processes with enthalpy and entropy effects depending on the mixed solvent composition. The processes complexity is reflected in minima in partial molar volume of the solute as well as in maxima in viscosity and dissolution enthalpy plotted as function of the mixed solvent composition [1–4]. The extrema are due to structure and energy changes in the three-component mixtures depending on their composition and orientation of hydrophilic and hydrophobic parts of the interacting molecules [5]. Furthermore, polyols can stabilize natural conformation of globular proteins [6]. In view of that, study of model smaller solutes (amino acids and oligopeptides) interactions in mixed aqueous-organic solvents is essential for deeper understanding of structural stability of complex biomolecules and their biological activity in the solutions.

Experimentally determined standard enthalpies $\Delta_{sol}H^0$ of L-alanine (L-Ala), D,L-alanine (D,L-Ala), and D,L-valine (DL-Val) dissolution in aqueous propanediol-1,3 are collected in Table 1. Enthalpies of the amino acids transfer from water into aqueous propanediol-1,3 $\Delta_{tr}H^0$ are plotted as function of the organic cosolvent fraction in the figure.

The maxima are to be seen in the $\Delta_{tr}H^0$ functions of propanediol-1,3 molar fraction; moreover, the transfer enthalpy sign was different depending on the solvent composition. The transfer enthalpy was determined by competing intermolecular interactions of various types, including solvation process, some of them of opposite sign. Detailed analysis of the experimental results was based on considering the interactions between the solute and the organic cosolvent, as described in [8–10]. In the amino acid–polyol–water three-component mixtures, molecules of hydrated solute were present at a sufficiently small distance, therefore, partial reorganization of solvation shells of the molecules could change the type of interparticle interactions. The transfer enthalpy could be expressed as a sum of the three types of interactions (1).

$$\Delta_{tr}H^0 = \Delta H_1 + \Delta H_2 + \Delta H_3, \quad (1)$$

ΔH_1 reflects the ion-bipolar interactions between amino acids zwitter-ionic sites and OH of the diol; ΔH_2 reflects the hydrophobic–hydrophilic interactions between nonpolar part of amino acids or diol and OH groups of the solvent; ΔH_3 reflects the hydrophobic–hydrophobic interactions between nonpolar parts of the molecules.

The first type of interactions gives negative contribution into the transition enthalpy. The other interaction enthalpies were positive. $\Delta_{tr}H^0$ were positive in the whole range of the studied solvent compositions in the case of D,L-Val; in the cases of L-Ala and D,L-Ala, the transition enthalpy was positive

Table 1. Standard enthalpy of dissolution $\Delta_{sol}H^0$ (kJ/mol) of amino acids in the water–propanediol-1,3 mixed solvent at 298.15 K

D,L-Alanine		L-Alanine		D,L-Valine	
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	7.66±0.05 [7]	0	5.87±0.04
0.9657	10.11±0.05	0.9673	8.77±0.05	0.9641	7.54±0.04
1.7031	10.48±0.05	1.7049	9.40±0.05	1.7022	8.72±0.05
2.4408	10.88±0.06	2.4399	9.93±0.05	2.4460	9.59±0.06
3.1839	11.20±0.06	3.1843	10.45±0.06	3.1835	10.44±0.06
4.1332	11.53±0.06	4.1357	11.07±0.05	4.1387	11.29±0.06
5.4678	11.87±0.06	5.4665	11.65±0.07	5.4653	12.22±0.07
6.3744	11.97±0.07	6.3795	11.90±0.07	6.3759	12.62±0.07
8.0165	11.88±0.06	8.0125	12.07±0.07	8.0126	12.97±0.07
10.6013	11.41±0.05	10.6021	11.87±0.07	10.5995	12.58±0.08
13.0932	10.50±0.05	13.0967	11.32±0.06	13.0962	11.68±0.06
16.1375	9.05±0.05	16.1342	9.97±0.05		
19.6477	7.09±0.04	19.6503	8.53±0.05		

[a] Molality of propanediol-1,3 solution (mol/kg).

at propanediol-1,3 molar fraction below 0.27 and below 0.22, respectively (see Figure). Therefore, ΔH_2 and/or ΔH_3 contributions in these cases prevail. The decrease in the transfer enthalpy at higher diol fraction indicates the domination of the ion-bipolar interactions. Apparently, with increasing fraction of the organic cosolvent the interaction between diol polar groups and charged groups of amino acids enhanced, thus increasing the contribution of exothermal effects in the three-component solution. The maxima of $\Delta_{tr}H^0$ in the plots mark the mixed solvent compositions at which the contributions of hydrophobic-hydrophilic and hydrophobic-hydrophobic interactions are the most pronounced.

In order to estimated quantitatively the interparticle interactions in the studied systems, we performed the McMillan–Meyer regression analysis [11] consisting in calculation of enthalpy coefficients of pairwise interactions between amino acids and propanediol-1,3 (h_{xy}). To do so, the concentration dependences $\Delta_{sol}H^0 = f(m_y)$ were fitted with the cubic polynomial by the least squares procedure (2).

$$\Delta_{sol}H^0 = a_0 + a_1m_y + a_2m_y^2 + a_3m_y^3. \quad (2)$$

The following regression equations were obtained in the cases of D,L-alanine [Eq. (3)], L-alanine [Eq. (4)], and D,L-valine [Eq. (5)].

$$\Delta_{sol}H^0 = (9.34\pm0.04) + (0.80\pm0.02)m_y\ldots, \quad (3)$$
$$R = 0.999,\ SD = 0.035,\ N = 12,$$
$$\Delta_{sol}H^0 = (7.66\pm0.07) + (1.17\pm0.03)m_y\ldots, \quad (4)$$
$$R = 0.998,\ SD = 0.061,\ N = 12,$$
$$\Delta_{sol}H^0 = (5.86\pm0.07) + (1.89\pm0.04)m_y\ldots, \quad (5)$$
$$R = 0.999,\ SD = 0.047,\ N = 10.$$

The free terms of Eqs. (3)–(5) correspond to standard enthalpy of the amino acids dissolution in pure water, coinciding with the reference data: $\Delta_{sol}H^0$(D,L-Ala) = 9.35 kJ/mol [12], $\Delta_{sol}H^0$(L-Ala) = 7.67 ± 0.04 kJ/mol [13], and $\Delta_{sol}H^0$(D,L-Val) = 5.98 ± 0.10 kJ/mol [14]. The enthalpy coefficients of pairwise interactions calculated as $h_{xy} = a_1/2$ [15] are collected in Table 2.

All calculated h_{xy} coefficients were positive thus showing that the endothermic processes connected with structural rearrangement of the three-component solution and water release from solvate shells prevailed over the direct interactions of solvated polar groups.

Hydrophobic hydration and hydrophobic interactions are known to play important part in many biologic systems [17–19]. In the complex systems, hydrophobic interactions between the nonpolar parts of

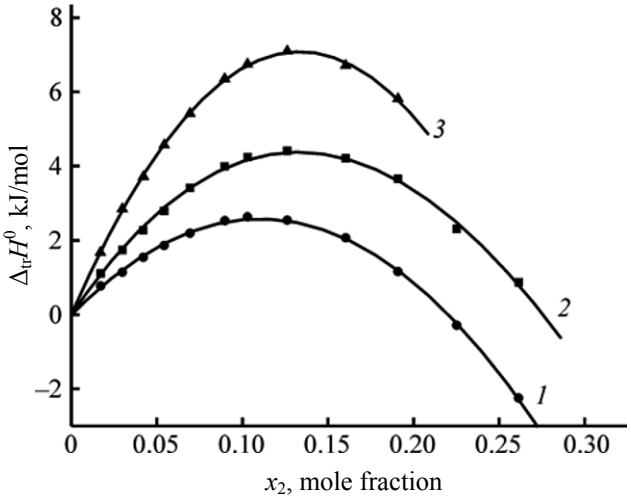
amphiphilic molecules are often additionally facilitated by electrostatic interactions and hydrogen bonding. The enthalpy coefficients of pairwise interactions in the studied systems followed the D,L-Ala < L-Ala < D,L-Val series. The higher h_{xy} value in the case of D,L-valine was likely due to the presence of additional $CH–CH_3$ group favoring hydrophobic hydration, strengthening of hydrogen bonds around methyl groups [20], and other structural rearrangements enhancing the endothermic effects. Hydroxy groups positions in propanediol significantly affected the thermodynamic parameters of interaction. In the case of propanediol-1,3, h_{xy} were lower than the corresponding values in the case of propanediol-1,2 (Table 2). The effect could be possibly due to stronger hydrophobic hydration shielding of the propanediol-1,2 hydroxy groups and thus impeding direct interaction with the amino acids. Furthermore, stronger intramolecular hydrogen bonding in the case of propanediol-1,3 could enhance the endothermic interactions in the three-component solution as well [21].

The presence of bipolar ions and alkyl-containing compounds is known to be a necessary condition of chiral recognition of amino acids in solutions [22, 23]. The enthalpy coefficient of pairwise interaction with propanediol-1,3 was lower in the case of racemic D,L-alanine as compared with L-alanine (Table 2). Hence, the presence of D-alanine decreased the hydration of the amino acid. As a result, dissolution of D,L-alanine in aqueous propanediol-1,2 was accompanied with stronger exothermic effect as compared with L-alanine.

To conclude, we revealed significant effect of the amino acids structure on their interaction with the mixed solvent and thermochemical parameters of dissolution. Effect of shielding of 2-OH group in propanediol-1,2 due to hydrophobic hydration of the methyl group on interactions in the studied systems was also found to be significant.

EXPERIMENTAL

Integral enthalpy of dissolution were measured with custom-made hermetic four-ampoule varied temperature calorimeter of our construction equipped with isothermal jacket allowing sequential experiments on dissolution of several portions of the tested compound in the same solvent volume without recharging the calorimeter cell [24]. The reactor part of calorimeter and the internal parts were made of titanium alloy VT-1. The calorimeter cell volume was about 110 mL. The



Enthalpy of transfer ($\Delta_{tr}H^0$) of (*1*) D,L-alanine, (*2*) L-alanine, and (*3*) D,L-valine from water into aqueous propanediol-1,3 as a function of the organic cosolvent fraction at 298.15 K.

unit temperature was kept constant within 10^{-3} K in the course of measurement. Temperature and energy sensitivity of the calorimeter was 2×10^{-4} K/mm and 1×10^{-3} J/mm of the recording unit, respectively. Thermal effect was compensated with electric current. Accuracy of the calorimeter was checked by measuring heat effect of KCl dissolution in water at 298.15 K. Ten independent measurements by the dilution technique [25] gave the standard dissolution enthalpy of $\Delta_{sol}H^0$ = 17.23±0.06 kJ/mol, in accordance with the reference value (17.22±0.04 kJ/mol [26, 27]).

The amino acids concentrations were in the range of 0.004–0.008 mol/kg. Enthalpy of dissolution $\Delta_{sol}H^m$ was independent of the amino acids concentration within the studied concentration range; the standard values $\Delta_{sol}H^0$ were therefore averaged from 2–3 independent measurements of the dissolution heat effect $\Delta_{sol}H^m$. L-Alanine (Aldrich, 99%), D,L-alanine (Reanal, 99%), and D,L-valine (Aldrich, 97%) were recrystallized from aqueous ethanol and dried in a vacuum at 343 K during 48 h. Deionized water was

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

Amino acid	Propanediol-1,2	Propanediol-1,3
D,L-Alanine	531±17 [16]	403±9
L-Alanine	694±19 [7]	584±16
D,L-Valine	–	944±23

twice distilled (specific conductivity of 10^{-5} S sm^{-1}). Propanediol-1,3 (Panreac, 98%) was used as received.

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