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Short communication

Enthalpies of solution of glycylglycine and diglycylglycine in aqueous alcohols at 298.15 K

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Abstract

The integral enthalpies of solution of glycylglycine and diglycylglycine in water–ethanol, water–*n*-propanol and water–*i*-propanol mixtures were measured at 298.15 K and alcohol mole fraction concentrations (x_2) ranging up to 0.3 by calorimetry. The $\Delta_{sol}H^{\circ}$ and $\Delta_{tr}H^{\circ}$ vs. x_2 were found to have extrema. Enthalpic coefficients of pairwise interactions (h_{xy}) between peptide and alcohol molecules were positive and increased in the series ethanol, *n*-propanol, *i*-propanol.

Keywords: Peptides; Aqueous and alcoholic solutions; Enthalpies of solution and transfer

1. Introduction

Many works are concerned with various physicochemical properties of amino acids and peptides and the influence of the structure and nature of solvents on their reactions [1–6]. However, the thermochemical behavior of peptides in binary mixtures of water with organic co-solvents over a wide range of compositions has been studied scarcely. And, in the overwhelming majority of these works, thermochemical characteristics have been determined in narrow concentration ranges (up to $x_2 \approx 0.1$). Substantial changes in intermolecular interactions between glycylglycine and diglycylglycine and components of the mixed aqueous–alcoholic solvent should be expected as composition changes over the whole concentration range. New data on physicochemical properties of amino acids that characterize their interactions with solvents in wide concentration ranges is therefore of importance for predicting the behavior of peptides in mixed solvents.

2. Experimental

Chromatographically homogeneous peptides (Reanal Co., Hungary) were recrystallized twice from water–ethanol mixture, dried in a vacuum chamber at 333 K for 48 h, and kept over P_2O_5 under vacuum in desiccators. The molal concentration (m) of the peptide solutions was varied in the range of $0.005 < m < 0.015$ mol kg^{-1} mixed solvent. The alcohols were purified as recommended in Refs. [7,8]. Water content determined by Karl Fisher titration [9] did not exceed 0.05, 0.03, and 0.04 wt% in EtOH, *n*-PrOH, and *i*-PrOH, respectively. Water was purified by deionization and double distillation until a specific conductivity of *ca.* 1.0×10^{-5} S m^{-1}. Mixtures were prepared by weight.

The enthalpies of solution $\Delta_{sol}H^{m}$ for glycylglycine and diglycylglycine were measured at 298.15 ± 0.005 K with an isoperibol (ampoule-type) calorimeter fitted with a 60 cm^3 reaction vessels and electrical calibration. The calorimeter setup and experimental procedure were described in detail previously [10–12]. The relative random error of measurements was less than 0.5%. The calorimeter was tested by measuring (10 experiments) the enthalpy of solution of potassium chloride (KCl) in water at 298.15 K according to Refs. [13–15]. Our values of ($\Delta_{sol}H^{m}$ ($m = 0.111$ mol kg^{-1}) $= 17.60 \pm 0.04$ kJ mol^{-1} and $\Delta_{sol}H^{\circ} = 17.23 \pm 0.07$ kJ mol^{-1}) agree with of rec-

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Table 1
Standard enthalpies (kJ mol^{-1}) of dissolution ($\Delta_{sol}H^{\circ}$) of glycylglycine and diglycylglycine in aqueous alcohols at 298.15 K

EtOH			*n*-PrOH			*i*-PrOH		
m_2[a]	Glycylglycine	Diglycylglycine	m_2[a]	Glycylglycine	Diglycylglycine	m_2[a]	Glycylglycine	Diglycylglycine
0.769	12.21 ± 0.02	18.13 ± 0,02	0.749	12.48 ± 0.02	18.48 ± 0.02	0.772	13.01 ± 0.02	18.91 ± 0.02
1.797	13.64 ± 0.02	18.69 ± 0,02	1.451	14.06 ± 0.02	19.34 ± 0.02	1.316	15.19 ± 0.02	19.87 ± 0.02
4.279	15.47 ± 0.02	20.38 ± 0,02	3.236	15.89 ± 0.03	20.95 ± 0.03	3.180	18.16 ± 0.02	21.84 ± 0.02
7.355	18.17 ± 0.03	22.82 ± 0,03	4.342	16.97 ± 0.04	21.93 ± 0.04	4.397	19.56 ± 0.04	23.09 ± 0.04
9.407	19.45 ± 0.04	24.56 ± 0,04	5.736	17.83 ± 0.03	23.24 ± 0.03	5.515	20.75 ± 0.03	24.83 ± 0.03
11.457	19.89 ± 0.03	25.41 ± 0,03	7.096	18.77 ± 0.05	24.81 ± 0.04	6.901	21.76 ± 0.03	26.12 ± 0.03
14.271	20.23 ± 0.03	26.14 ± 0,03	8.932	19.69 ± 0.03	25.77 ± 0.03	8.566	22.35 ± 0.04	27.27 ± 0.04
17.087	19.59 ± 0.03	24.45 ± 0,03	10.812	19.54 ± 0.03	26.19 ± 0.03	10.743	21.58 ± 0.04	26.50 ± 0.04
19.880	17.96 ± 0.04	22.45 ± 0,04	13.301	18.55 ± 0.02	24.64 ± 0.03	12.988	18.52 ± 0.04	24.92 ± 0.05
22.140	15.01 ± 0.04	18.16 ± 0,04	16.206	16.70 ± 0.03	22.47 ± 0.03	16.210	12.53 ± 0.04	20.48 ± 0.04

[a] The molal concentration of alcohols (mol kg^{-1}).

ommended literature values (17.56 ± 0.02 kJ mol^{-1} [11]/17.58 ± 0.02 kJ mol^{-1} [12] and 17.22 ± 0.04 kJ mol^{-1} [13,15], respectively).

3. Results

The standard enthalpies of solution $\Delta_{sol}H^{\circ}(\equiv\Delta_{sol}H^{\infty})$ were calculated by averaging the results of five measurements of $\Delta_{sol}H^{m}$ for each composition of aqueous alcohol, on dependence of $\Delta_{sol}H^{m}$ on m was observed in the mixed solvents studied. The experimental data on $\Delta_{sol}H^{\circ}$ obtained for glycylglycine and diglycylglycine in aqueous alcohols under study are summarized in Table 1 and $\Delta_{tr}H^{\circ}$ values are plotted in Figs. 1 and 2.

4. Discussion

The curves in Figs. 1 and 2 show three concentration regions, namely $0 < x_2 < 0.15$, where the endothermicity of peptide dissolution increases monotonically; $0.15 < x_2 < 0.2$, which is a transition region; $x_2 > 0.2$, where the exothermicity of peptide dissolution increases.

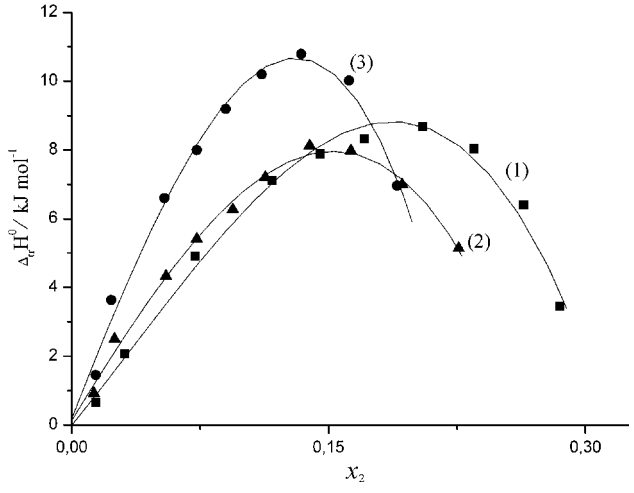

Fig. 1. Enthalpies of transfer $\Delta_{tr}H^{\circ}$ of glycylglycine from water into the water–EtOH (1); water–*n*-PrOH (2); water–*i*-PrOH (3) mixed solvent as functions of the alcohol mole fraction x_2 at 298.15 K.

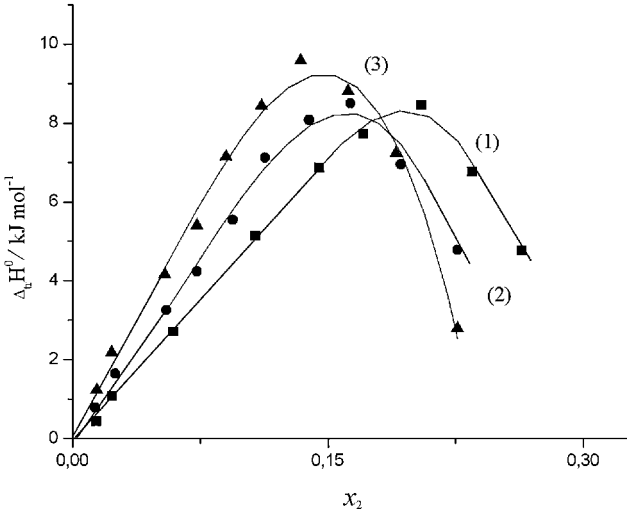

Fig. 2. Enthalpies of transfer $\Delta_{tr}H^{\circ}$ of diglycylglycine from water into the water–EtOH (1); water–*n*-PrOH (2); water–*i*-PrOH (3) mixed solvent as functions of the alcohol mole fraction x_2 at 298.15 K.

The interparticle interactions in the first region were characterized in terms of the McMillan–Mayer theory by calculating the enthalpy coefficients h_{xy} of pairwise interactions [16]. The $\Delta_{sol}H^{\circ}$ (m_2) functions were approximated by a third-degree polynomial of the form

$$\Delta_{sol}H^{\circ} = a_0 + a_1 m_2 + a_2 m_2^2 + a_3 m_2^3, \quad (1)$$

where m_2 is the molal concentration of the alcohol, and a_i are coefficients calculated by least squares. The correlation coefficient R varied from 0.986 to 0.996, and the Student criterion value from 0.228 to 0.433. The h_{xy} value was calculated from the a_1 coefficient related to the coefficient of pairwise interactions as $h_{xy} = a_1/2$ [2]. The h_{xy} values are listed in Table 2.

Table 2
Enthalpic coefficients of pairwise interactions (h_{xy}, J kg mol^{-2}) between peptide and alcohols in aqueous solutions at 298.15 K

Substance	EtOH	*n*-PrOH	*i*-PrOH
Glycylglycine	515 ± 50	795 ± 70	1245 ± 110
Diglycylglycine	260 ± 65	503 ± 110	760 ± 130

The coefficients h_{xy} reflect the preferential interactions occurring between the solutes and water. The interaction between the hydrated peptide molecules and the hydrated alcohol molecule at low alcohol concentrations is weaker. This conclusion is in agreement with the results obtained earlier [17–19]. The h_{xy} values for glycine change similarly over the same series of alcohols [17]. Glycylglycine and diglycylglycine are, however, hydrated more strongly than amino acids. This can be explained by the presence of the hydrophilic O=C–NH group of glycylglycine and O=C–N–C=O group of diglycylglycine molecules.

There is a structural rearrangement of the solvent under the influence of glycylglycine and diglycylglycine molecules, and its intensity (and, therefore, the energy consumption) increases with an increase in size of the solute molecule. This is indicated by a shift of the endothermic maxima of the functions $\Delta_{sol}H^{\circ}$ (x_2) toward lower alcohols concentrations in the EtOH < *n*-PrOH < *i*-PrOH series (see Figs. 1 and 2).

In the second range (at x_2 between 0.15 and 0.2) the endothermic effects caused by solvent structural rearrangement and the dehydration of glycylglycine and diglycylglycine as well as alcohol molecules are gradually compensated by the exothermic effects of direct interactions (via H bonds) between the solute and peptide. With the further increase of concentration of alcohol ($x_2 > 0.2$) the exothermic contribution from peptide–alcohol interactions begins to prevail in the total enthalpic effect of interactions, explained as follows.

The molecules of a peptide have a mixed solvated cover, consisting of both molecules of water and molecules of alcohol. At the small concentrations of alcohol ($x_2 < 0.25$) this is mainly water. Increasing concentration of alcohol ($x_2 > 0.25$) leads to gradual replacement of water cover of peptide by a cover of alcohol molecules that leads to the increase of $\Delta_{tr}H^{\circ}$ contributions from electrostatic, bipolar–bipolar, induction, dispersive interactions. Along with formation of hydrogen bonds, it results in growth of exothermicity of $\Delta_{sol}H^{\circ}$ for glycylglycine and diglycylglycine with the increase of concentration of alcohol.

The endothermic effect of transfer observed for *i*-PrOH is stronger than that for *n*-PrOH, probably because of steric hindrances created by two CH_3 groups when hydrated glycylglycine and diglycylglycine molecules interact with hydrated alcohol molecules and because of the stronger hydrophobic hydration effect of *i*-PrOH [20].

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