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Short communication

Transfer enthalpies of amino acids and glycine peptides from water to aqueous solutions of trimethylamine *N*-oxide at 298.15 K

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ABSTRACT

Enthalpies of solution of glycine, L-alanine, L-serine, L-threonine, L-valine, diglycine and triglycine in aqueous solutions of trimethylamine *N*-oxide (TMAO) have been measured by calorimetry at 298.15 K. The results obtained were used to calculate the heterogeneous enthalpic interaction coefficients (h_{AT}) between the amino acids or glycine peptides and the molecule of TMAO in water and the transfer enthalpies ($\Delta_{tr}H_m$) of the amino acids or glycine peptides from water to aqueous solutions of TMAO. It has been observed that the transfer enthalpies of the amino acids and glycine peptides from water to aqueous solutions of TMAO are monotonically positive over the investigated concentration ranges. The relative order of h_{AT} and $\Delta_{tr}H_m$ for amino acids are all L-serine > L-threonine > glycine > L-alanine > L-valine, whereas the sequence of glycine peptides is triglycine > diglycine > glycine. The results are discussed in terms of solute–solute and solute–solvent interactions.

1. Introduction

The function, structure and stability of native proteins show marginal changes in the co-solvent environment that can dramatically affect their properties and functional activity [1–4]. The folded conformation adapted by a protein under the given solvent environment depends on its interaction with the surrounding solvent molecules [5,6]. It is important to understand whether these added co-solutes affect protein conformation by direct binding or through solvent mediated effects. Since the protein is a large bio-macromolecule, the effect of the solvent environment on its conformational stability depends on the nature of interaction of its different functional groups with the solvent molecules. In order to understand the fine details of solute-solvent interactions, several studies have been reported on the physico-chemical properties of the constituent amino acids and peptides in water and mixed aqueous solutions [7–15].

Small naturally occurring organic molecules known as osmolytes, can affect functions and integrity of proteins significantly [1]. Osmolytes can be categorized as stabilizing and destabilizing osmolytes. Trimethylamine *N*-oxide (TMAO) is an osmolyte which is present in high concentrations in coelacanth and marine elasmobranches [16] and can enhance protein folding, ligand binding, and counteract perturbations by urea, inorganic ions, and hydrostatic pressure [2,17,18]. Understanding the interactions of TMAO and amino acids or peptides can provide insights of its role in protein stabilization as well as on its mechanism to counteract the denaturing effect of urea.

Enthalpy of transfer and the heterogeneous enthalpic interaction coefficients are important thermodynamic parameters which reflect on the nature of solute–solvent and solute–solute interactions. To assess the possible contributions of the amino acid residues and peptide bond to the thermodynamic properties of the biopolymer in solution, we studied the transfer properties of glycine, L-alanine, L-serine, L-threonine, L-valine, diglycine and triglycine from water to aqueous TMAO solutions and the heterogeneous enthalpic interaction coefficients between the amino acids or glycine peptides and the molecule of TMAO in water. The results on the interaction of TMAO with amino acids or glycine peptides have been analyzed in terms of different intermolecular interactions.

2. Experimental

Amino acids, glycine ($CH_2(NH_2)COOH$), L-alanine ($CH_3CH(NH_2)COOH$), L-serine ($HOCH_2CH(NH_2)COOH$), L-threonine (CH_3CH

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Table 1
Enthalpy of solution and enthalpy of transfer of amino acids and glycine peptides in aqueous TMAO solutions at 298.15 K.

m_{TMAO} (mol kg^{-1})	$\Delta_{sol}H$ (kJ mol^{-1})	$\Delta_{tr}H$ (kJ mol^{-1})	m_{TMAO} (mol kg^{-1})	$\Delta_{sol}H$ (kJ mol^{-1})	$\Delta_{tr}H$ (kJ mol^{-1})
Gly			Ser		
0.0000	14.20 ± 0.01	0.00	0.0000	11.30 ± 0.02	0.00
0.4962	14.76 ± 0.02	0.56	0.5465	12.23 ± 0.02	0.93
1.0034	15.38 ± 0.02	1.18	1.0034	12.81 ± 0.03	1.51
1.4971	16.01 ± 0.01	1.81	1.478.0	13.83 ± 0.03	2.53
2.0514	16.96 ± 0.03	2.76	2.0514	14.43 ± 0.02	3.13
2.5070	17.83 ± 0.01	3.63	2.5429	15.81 ± 0.01	4.51
2.9497	19.06 ± 0.02	4.86	2.9147	16.70 ± 0.02	5.40
Thr			Ala		
0.0000	10.23 ± 0.01	0.00	0.0000	7.56 ± 0.01	0.00
0.5166	10.80 ± 0.02	0.57	0.5164	7.85 ± 0.02	0.29
0.9641	11.57 ± 0.03	1.34	0.9936	8.20 ± 0.02	0.64
1.5448	12.16 ± 0.02	1.93	1.4780	9.01 ± 0.02	1.45
2.0051	13.14 ± 0.02	2.91	2.0514	9.90 ± 0.02	2.34
2.4890	14.33 ± 0.02	4.10	2.5070	10.85 ± 0.03	3.29
2.9394	15.31 ± 0.03	5.08	2.9497	12.10 ± 0.03	4.54
Val			Digly		
0.0000	3.15 ± 0.01	0.00	0.0000	11.44 ± 0.01	0.00
0.5063	3.30 ± 0.02	0.15	0.5365	13.96 ± 0.02	2.52
0.9641	3.47 ± 0.02	0.32	1.0426	14.30 ± 0.02	2.86
1.5448	4.01 ± 0.01	0.86	1.5733	16.29 ± 0.02	4.85
2.0620	5.13 ± 0.03	1.98	1.9215	17.67 ± 0.03	6.23
2.4980	6.18 ± 0.02	3.03	2.5429	20.06 ± 0.01	8.62
3.0120	7.33 ± 0.02	4.18	2.9889	21.98 ± 0.02	10.54
Trigly					
0.0000	16.87 ± 0.01	0.00			
0.5365	20.33 ± 0.02	3.46			
1.0426	23.23 ± 0.02	6.36			
1.5733	25.11 ± 0.03	8.24			
2.0883	26.22 ± 0.02	9.35			
2.5429	28.00 ± 0.02	11.13			
2.9889	30.08 ± 0.03	13.21			

(OH)CH(NH_2)COOH) and L-valine ($CH_3CH(CH_3)CH(NH_2)COOH$), were biological reagents with mass fraction >99.0% obtained from the Shanghai Chemical Co., China. They were twice recrystallized from aqueous ethanol solution and dried under vacuum at 348 K for 6 h before use. Peptides, diglycine ($H_2NCH_2CONHCH_2COOH$) and triglycine ($H_2NCH_2CONHCH_2CONHCH_2COOH$) were biological reagents with mass fraction >99.0% obtained from Fluka and Aldrich. TMAO were purchased from Sigma Chemical Co., USA, and the purity is better than 99%. They were used as received. All the solutions investigated were prepared freshly with twice-distilled water. The samples were weighed on a Mettler AE 200 balance with a sensitivity of 0.0001 g. The molality of each amino acid or glycine peptide solution was prepared at 0.05 mol kg^{-1} of water.

Measurements on the enthalpies of solution at 298.15 K were carried out with an RD496-II microcalorimeter, which was manufactured by the 2905 factory of the Nuclear Industry Department of China, as previously described [19]. Its heat-flux detectors of sample and reference are composed of 496 pairs of thermocouples, respectively. The mixing vessel of the microcalorimeter is divided into two parts by a drop partition, the lower part is ca. 4 ml and the upper part ca. 6 ml. The partition was first placed into the vessel with a special device. Then the solid sample was introduced into the lower part and the solvent into the upper part. The lower part of the reference vessel was empty, and the upper part contained the same solvent as the sample vessel. The partition is released through a pole, then the solid and solvent become mixed, and the enthalpies of solution recorded automatically by a computer. The apparatus was calibrated by the solution enthalpy of KCl in water with the mole ratio of 1:500. The calorimetric curves were recorded automatically, and the enthalpies of solution were reported on the basis of three replicates. The calorimeter had a high temperature control precision (±0.001 K), a high stability (±0.1 μV for baseline) and a high sensitivity (62.13 mV W^{-1} at 298.15 K).

3. Results

The calorimetric results of the enthalpies of solution, $\Delta_{sol}H_m$, for glycine, L*L*-alanine, L-serine, L-threonine, L-valine, diglycine and triglycine in pure water and in aqueous solutions of TMAO with different concentrations are given in Table 1. The values of $\Delta_{sol}H_m$ of amino acid in pure water are in good agreement with those found in the literature [15,20,21]. The transfer enthalpy, $\Delta_{tr}H_m$, is derived from the difference between the enthalpy of solution in each aqueous solution of TMAO, $\Delta_{sol}H_m$(s), and that in pure water, $\Delta_{sol}H_m$(w), respectively [19]. The transfer enthalpy, $\Delta_{tr}H_m$, are also presented in Table 1.

$$\Delta_{tr}H_m = \Delta_{sol}H_m\ (s) - \Delta_{sol}H_m\ (w) \quad (1)$$

The changes of $\Delta_{tr}H_m$ of the amino acids and glycine peptides against the concentrations of the TMAO solutions are shown in Figs. 1 and 2. It follows that the transfer enthalpies of the amino acids and glycine peptides from water to aqueous solutions of TMAO are monotonically positive over the investigated concentration ranges. The relative order in the positive value of $\Delta_{tr}H_m$ of amino acids in the same concentration of TMAO is L-serine > L-threonine > glycine > L-alanine > L-valine, whereas the sequence of $\Delta_{tr}H_m$ of glycine peptides is triglycine > diglycine > glycine.

The solution enthalpies of amino acids or glycine peptides in water and in aqueous solution of TMAO were used to obtain the enthalpic heterogeneous pair interaction coefficients h_{AT} for the interaction between amino acids or glycine peptides and the TMAO molecule in water [22]. The solution enthalpies of amino acids and glycine peptides in aqueous solutions of TMAO are presented as a polynomial function:

$$\Delta_{sol}H_m\ (s) = \Delta_{sol}H_m\ (w) + 2h_{AT}m_{TMAO} + 3h_{ATT}m_{TMAO}^2 + \cdots \quad (2)$$