Thermodynamics of the ethylene glycol pair interaction with some amino acids and benzene

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ABSTRACT

We have studied thermodynamics of interaction of benzene and some amino acids with ethylene glycol (Eg) which is a stabilizing agent for proteins in water using calorimetric and solubility data. Enthalpic, entropic and free energy parameters in highly diluted aqueous solutions have been computed at 298 and 313 K using the virial expansion technique and compared with available literature values. The results obtained are discussed in terms of solute–solute interactions and their relation to stability of macromolecules.

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1. Introduction

During the last decade we have been involved in the extensive and continuing study on thermodynamics of interactions between some amino acids and denaturing agents of a native structure of globular proteins [1–6]. The main objective of these investigations was to obtain the experimental information on the temperature dependence of the energetics of solute–solute interactions in diluted aqueous solutions in the hope that such studies may help to highlight some intriguing features of protein unfolding. Recently [5] we have also studied the L-histidine behavior in water–glycerol mixtures and found that enthalpies and entropies of pair and triplet amino acid–kosmotrope interactions are nearly independent of the temperature both in cold and hot water. This temperature independent behavior leads to zero heat capacity changes of the solute transfer from water to rather concentrated aqueous glycerol solutions. This phenomenon has been attributed to the existence of a delicate balance between hydrophobic and hydrophilic interactions. In contrast, for the interaction between aromatic amino acids and urea or dimethylformamide (DMF) enthalpies and entropies change gradually with the temperature.

In the present work we try to give a deeper insight into the mechanism of stabilization of proteins by polyols and studied the interaction of some amino acids and benzene with other kosmotrope, *i.e.* Eg using our calorimetric data and solubility values reported earlier by Nozaki and Tanford [7]. One more important reason to perform this work is to compare enthalpic parameters for glycine and L-alanine with the results reported earlier [8–10].

2. Experimental

Ethylene glycol (Sigma–Aldrich, spectrophotometric grade, >99%) was stored with freshly dried 4 Å molecular sieves and then used without further purification. The liquid chromatography analysis showed that the content of the basic substance exceeded 99.5 mass%. L-Histidine (Free base, MP Biomedicals Inc., >99%), L-phenylalanine (Carl Roth GmbH, >99.5%), glycine (Sigma–Aldrich, >99%) were dried in vacuum at 343 K for several days and used without further purification. 1-butanol and benzene (both from Reachem, for chromatography, >99.5%) were used as supplied. Ethylene glycol aqueous solutions were prepared by weight from deionized and freshly bidistilled water and the pure non-electrolyte.

Enthalpies of solution were measured with the automated ampoule calorimeters provided with titanium vessels of various capacities. The apparatuses and experimental procedure were described many times previously [1–6]. The measurements for benzene required special accuracy dealt with low solubility and a correct estimation of side effects which were associated with an

ampoule crushing on the vessel bottom and partial solute vaporization into a free space of the ampoule. Our results in pure water were found to be in a good agreement with most reliable values reported by the thermochemical center in Lund [11] (see Table 1).

3. Results

Standard enthalpies of solution or enthalpies of solution at an infinite dilution in water given in Table 1 represent the mean value from four or more independent measurements in the range of solute molalities of 0.002–0.03 mol kg^{-1}, where experimental quantities do not depend on the solute concentration [6,12]. These values were found to be in a very good agreement with those reported earlier [5,8,11,13]. The $\Delta_{sol}H^m \cong \Delta_{sol}H^0$ values in water–ethylene glycol mixtures listed here are the result of one experiment at the solute molality of 0.002–0.025 mol kg^{-1}. Based on the results of our previous studies [5,6], the overall uncertainty of the $\Delta_{sol}H^0$ values are estimated to be within 1% for amino acids and 2–3% for slightly soluble benzene (Table 2).

4. Discussion

The formally exact theory of diluted solutions developed by McMillan and Mayer [14] and then adapted by Kauzmann [15], Friedman [16] and Lilley [17] relates thermodynamic properties of a multicomponent system to certain integrals of the potential of mean force associated with the interaction between pairs, triplets and a high number of solute molecules. The formalism used here to extract the information about the pair interaction from thermodynamic quantities is the same as in our previous works [2,5].

Thermodynamic parameters reflecting the interaction between one amino acid molecule and one glycol molecule in water are presented in Tables 3 and 4. Our h_{AB} value for glycine is in a satisfactory agreement with the quantity recently reported by Li et al. [10], but much smaller than that given elsewhere [8] (see Table 3). The enthalpic parameter for L-alanine obtained in our laboratory [18] is seen to be in a good agreement with the h_{AB} value [10], but also smaller than the quantity reported by Mezhevoi and Badelin [9]. Since the $\Delta_{sol}H^0$ values in water are nearly equal to each other, the discrepancy observed should arise from the measurements in the mixed solvent. Thus, we have performed additional measurements in the water–Eg mixtures and compare our enthalpies of solution for 1-butanol with those reported by Nwankwo and Wadso [19]. Our results equal to −3.35 and 1.84 kJ mol^{-1} for 0.075 and 0.178 glycol mol fractions, respectively, are found to be in a good agreement with the $\Delta_{sol}H^0$ values of −3.51 and 1.99 kJ mol^{-1} given elsewhere [19].

Tables 3 and 4 compare enthalpic, entropic and free energy parameters of pair interaction. Free energies of interaction are small and positive, whereas enthalpies and entropies are much larger. The larger hydrophobicity of the solute, the larger are h_{AB} and s_{AB} values. Thus, for the amino acid–Eg interaction we have $g_{AB} > 0$ and $h_{AB} > Ts_{AB} > 0$. It is known that such a combination of parameters is usually observed for non-electrolytes stabilizing native structure of globular proteins [21]. Our results for both temperatures are in an obvious agreement with this point of view. There is also one interesting feature for g_{AB} values listed in Tables 3 and 4 which is worth noting. Free energy parameters are nearly identical for the pairs of glycine-L–alanine and L-histidine–L-phenylalanine. Since s_{AB} values for aromatic solutes are larger than those for other amino acids and the g_{AB} values are smaller, free energies of the aromatic amino acid–Eg interaction become negative at lower temperatures than corresponding quantities for glycine and L-alanine. Thus, we assume that proteins with a larger amount of aromatic residues on their surface should reveal lower thermal stability in aqueous Eg

Table 1
Enthalpies of solution ($\Delta_{sol}H^0$, kJ mol^{-1}) of amino acids and benzene in highly aqueous ethylene glycol solutions at 298.15 K.

Glycine		L-Histidine		L-Phenylalanine		Benzene	
X_{Eg}[a]	$\Delta_{sol}H^0$	X_{Eg}	$\Delta_{sol}H^0$	X_{Eg}	$\Delta_{sol}H^0$	X_{Eg}	$\Delta_{sol}H^0$
0	14.17 ± 0.05[b] 14.20 [8]	0	14.22 ± 0.06 [12]	0	8.33 ± 0.04 8.30 ± 0.03 [5] 8.28 [13]	0	2.14 ± 0.07 2.22 ± 0.01 [11]
0.0100	14.37	0.00500	14.39	0.0110	9.13	0.00500	2.62
0.0150	14.40	0.00800	14.51	0.0260	9.99	0.0100	2.79
0.0250	14.52	0.0100	14.67	0.0320	10.33	0.0150	3.06
0.0350	14.67	0.0130	14.78	0.0510	11.40	0.0200	3.73
0.0450	14.76	0.0150	14.86	0.0610	11.85	0.0300	4.38
0.0500	14.80	0.0200	15.02	0.0780	12.71	0.0400	5.09
0.0600	14.86	0.0300	15.26	0.107	13.81	0.0550	5.88
0.0800	14.96	0.0500	15.57	0.124	14.38	0.0700	6.72
0.0850	14.98	0.0700	15.83			0.0850	7.29
0.100	15.04	0.0900	15.90			0.0950	7.56
0.112	15.06	0.100	15.92			0.0980	7.62
		0.119	15.89			0.100	7.70
						0.110	8.03
						0.120	8.13
						0.130	8.14
						0.140	8.10
						0.150	8.08

[a] Eg mol fractions.
[b] Errors from here on represent the twice standard deviation.