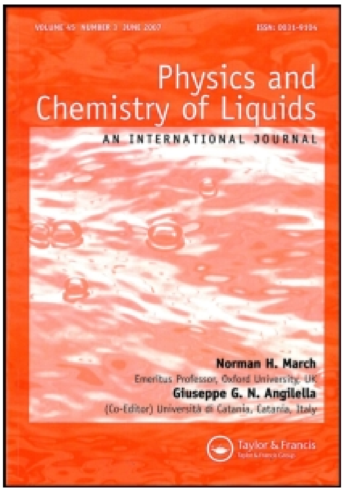

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THERMODYNAMICS OF TRANSFER OF AMINO ACIDS FROM WATER TO AQUEOUS SODIUM SULFATE

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The solubilities of amino acids at 288.15, 298.15 and 308.15 K in water and aqueous sodium sulfate have been determined as a function of electrolyte concentration (0.5, 1.0, 1.5 mol/kg of water). It has been observed that sodium sulfate renders amino acids less soluble. The free energies of transfer of amino acids from water to aqueous sodium sulfate have been calculated from the solubility data. The enthalpies and entropies of transfer have also been estimated. The solubility and the thermodynamics of transfer data manifest that sodium sulfate generates favourable interaction between nonpolar groups of amino acids. If applied to proteins, it seems to stabilize the protein native globular structure by enhancing the intramolecular nonpolar–nonpolar group interactions.

Keywords: Solubility; Amino acid; Free energy of transfer

1. INTRODUCTION

A better understanding of the effect of electrolytes on the thermodynamic properties of amino acids in aqueous solution is of vital importance because such studies give useful information regarding protein unfolding [1] and the extent of hydrophobic interactions of nonpolar side chains [2]. Biological macromolecules are physiologically active in aqueous solutions. Addition of salts modifies the

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structure of proteins by affecting properties like solubility, denaturation and activity of enzymes [3–5]. Hence there is considerable and renewed interest in this field. Thermodynamic and transport studies on amino acid-water systems in the presence of salts have been reported [6–13] in the recent past.

As a part of our systematic study of the effect of concentrated electrolytes on the thermodynamic properties of aqueous solutions of amino acids, the solubilities of some amino acids in (0.5, 1.0 and 1.5 molal) aqueous sodium sulfate at 288.15, 298.15 and 308.15 K have been measured. The free energy, entropy and enthalpy of transfer of the amino acids from water to aqueous sodium sulfate are reported in this paper. Sodium sulfate is chosen as it distinguishes itself from the usual protein denaturants and tends to stabilize the native structure of proteins [3, 4].

2. EXPERIMENTAL SECTION

Glycine (gly), DL-alanine (ala), DL-α-amino butyric acid (aba), DL-valine (val), β-alanine (β-ala) and γ-amino butyric acid (gaba), procured from Sigma, were dried at 100°C for 12 h and then at room temperature in vacuo over phosphorous pentoxide for at least 24 h. Anhydrous sodium sulfate (Sarabhai, G. R.) was dried at 110°C followed by vacuum desiccation over phosphorous pentoxide for a minimum of 24 h. Double distilled water deionized by passing through two Cole-Parmer mixed bed ion-exchange columns and of conductivity less than $6 \times 10^{-7}\,\mathrm{S\,cm^{-1}}$ was used for preparation of solutions afresh by weight.

The solvent $[H_2O/(H_2O + Na_2SO_4)]$ and an excess amount of amino acid were placed into glass tubes ($10\,\mathrm{cm}^3$ capacity) fitted with ground glass stoppers. The glass tubes were incompletely filled to facilitate good mixing. A unit consisting of rotating disc holding the glass tubes was immersed in the thermostatic bath and solutions were shaken by rotating the disc for more than 30 h to attain saturation. The temperature of the bath was controlled to ±0.01°C. A known mass of the filtered saturated solution was transferred to a conical flask. The amount of amino acid was determined by 'formal titration' method using freshly standardized NaOH solution and phenolphthalein as indicator. Formaldehyde solution was used to mask before titration. The titration was carried out by weight. Triplicate or more measurements were performed for each amino acid and solubility values agreed to within ±0.5% were taken. The reported solubility values are the average of these readings.

3. RESULTS AND DISCUSSION

Solubility of amino acids in water, s_w, and in aqueous sodium sulfate solutions, s_e, at 288.15, 298.15 and 308.15 K are presented in Table I.

TABLE I Solubility of amino acids in water, s_w (g/100 g of H_2O) and in water + sodium sulfate, s_e (g/100 g of aqueous sodium sulfate) at 288.15, 298.15 and 308.15 K

		$Solubility/g(100\,g\ of\ solvent)^{-1}$		
Amino acid	m_1*	288.15 K	298.15 K	308.15 K
glycine	0	20.19 (19.95[a], 20.20[b])	25.02 (24.99[a], 25.00[c])	30.17 (30.16[a])
	0.5	20.07	24.66	29.58
	1.0	19.86	24.38	28.37
	1.5	18.69	22.84	26.83
DL-alanine	0	15.10	16.63 (16.67[d], 16.50[e], 16.66[f])	18.74
	0.5	14.11	15.82	17.35
	1.0	12.34	13.98	15.38
	1.5	10.65	11.95	13.45
DL-α-aminobutyric acid	0	21.85	23.30	26.59
	0.5	19.92	21.72	24.80
	1.0	16.77	18.40	21.51
	1.5	13.42	14.76	17.12
DL-valine	0	6.30	8.81 (8.85[e], 8.84[f])	9.70
	0.5	5.05	7.05	8.17
	1.0	3.94	5.52	6.50
	1.5	2.93	4.47	5.12
β-alanine	0	63.21	72.36	78.85
	0.5	59.79	69.96	76.25
	1.0	55.94	64.57	73.78
	1.5	50.85	59.14	68.01
γ-aminobutyric acid	0	91.29	97.08	106.19
	0.5	86.33	93.28	101.80
	1.0	79.63	85.69	95.91
	1.5	72.54	78.48	87.87

* m_1 is concentration of Na_2SO_4 in mol (kg of $H_2O)^{-1}$.

[a] Reference [14]; [b] Reference [15]; [c] Reference [16]; [d] Reference [17]; [e] Reference [18]; [f] Reference [19].

Our solubility data in water are in excellent agreement with the data reported by the earlier workers [14–19]. The solubility of amino acids increases with the increase in temperature. DL-α-amino butyric acid is more soluble than DL-alanine, which is contrary to the prediction based on the hydrophobic nature of these two compounds. This has been attributed to the relatively low crystal lattice energy of the former [20]. The solubility of ω-amino acids increases with the increase in the number of CH_2 groups in their backbone, due to the increase in dipole moment. The solubility, s_e, of amino acids in aqueous sodium sulfate solutions increases with the increase in temperature, whereas, an increase in concentration of sodium sulfate renders amino acids less soluble.

The standard free energies, ΔG^o_{tr}, for transfer of amino acids from water to aqueous sodium sulfate solution have been calculated from the solubility data using the relation

$$\Delta G^o_{tr} = RT\,\mathrm{Ln}(m_w/m_e) \tag{1}$$

where, m_w and m_e are the solubilities expressed in mol kg^{-1} in water and aqueous sodium sulfate, respectively. The ratio of the activity coefficients has been assumed to be unity as proposed by the earlier workers [15–17]. Free energy of transfer of amino acids from water to aqueous sodium sulfate as a function of sodium sulfate concentration and temperature are listed in Table II. Our ΔG^o_{tr} values at 298.15 K for the transfer of glycine, DL-alanine and DL-valine from water to 1 molal Na_2SO_4 solution are in good agreement with those reported by Bull *et al.* [21].

The ΔG^o_{tr} for all the amino acids is positive and increases with the increase in concentration of sodium sulfate. As the temperature increases ΔG^o_{tr} for glycine increases, whereas for other amino acids it decreases. Furthermore, it increases with the increase in the hydrophobicity of the amino acids. This increase is, in all probability, due to the effect of sodium sulfate on apolar moieties of amino acids. The contribution of the CH_2 group to ΔG^o_{tr}, calculated by subtracting the ΔG^o_{tr} values of two successive amino acids of a series, decreases with the increase in chain length which is in agreement with the earlier observations of Gekko [16], Dey and Lahiri [19]. This may be due to the accommodation of Na^+ and SO_4^{2-} around the apolar

TABLE II Free energy of transfer, ΔG^o_{tr}, of amino acids from water to aqueous sodium sulfate at 288.15, 298.15 and 308.15 K

Amino acid	m_1[a]	$\Delta G^o_{tr}/cal\,mol^{-1}$		
		288.15	298.15	308.15
glycine	0.5	3.42	8.60	12.10
	1.0	9.45	15.36	37.68
	1.5	44.21	54.02	71.85
DL-alanine	0.5	38.83	29.58	47.19
	1.0	115.56	102.85	121.00
	1.5	199.92	195.80	202.67
DL-α-aminobutyric acid	0.5	52.91	41.59	42.67
	1.0	151.52	139.88	129.84
	1.5	279.16	270.51	269.63
DL-valine	0.5	126.64	132.02	101.71
	1.0	268.85	276.98	245.21
	1.5	438.44	401.92	391.37
β-alanine	0.5	31.86	19.98	20.53
	1.0	69.97	67.49	40.70
	1.5	124.60	119.54	90.57
γ-aminobutyric acid	0.5	31.99	23.66	25.86
	1.0	78.25	73.95	62.36
	1.5	131.65	126.03	115.97

[a] m_1 is concentration of Na_2SO_4 in mol (kg of H_2O)$^{-1}$.

groups with larger accessible surface area resulting in a decrease in the contribution of the CH_2 group for the higher amino acids.

The contribution of alkyl side chains to ΔG^o_{tr} of amino acids is an interesting parameter, which can give more insight into the mechanism of protein denaturation. The side chain contribution to ΔG^o_{tr} was obtained as difference in ΔG^o_{tr} between an amino acid and glycine, the first member of the series. Such subtraction does not account for the contribution due to the H atom, which is being replaced and hence is called as replacement contribution. The alkyl side chain contribution to ΔG^o_{tr} reported by the earlier workers [16, 17] are actually the replacement (of H by *R*) values, $\Delta G^o_{tr,r}$ (H → *R*). The $\Delta G^o_{tr,r}$ (H → *R*) values have been presented in Table III.

The positive $\Delta G^o_{tr,r}$ indicates that sodium sulfate has salting out effect on the apolar groups which underscore the earlier observation [3]. The positive $\Delta G^o_{tr,r}$ value, which increases with the hydrophobicity of the amino acid and sodium sulfate concentration is due to the salt-nonpolar group interactions. The Na_2SO_4–nonpolar group interactions disrupt the hydrophobic hydration sphere around the

TABLE III Replacement (H → *R*) contribution $\Delta G^o_{tr,r}$ (H → *R*) of amino acid alkyl side chain to ΔG^o_{tr} at different temperatures and sodium sulfate concentrations

			$\Delta G^o_{tr,r}/cal\ mol^{-1}$		
Alkyl chain	*Method*	m_1[a]	288.15 *K*	298.15 *K*	308.15 *K*
CH_3	ala-gly	0.5	35.41	20.98	35.09
		1.0	106.11	87.49	83.32
		1.5	155.71	141.78	130.82
CH_3CH_2	aba-gly	0.5	49.49	32.99	30.57
		1.0	142.07	124.52	92.16
		1.5	234.95	216.49	197.78
$(CH_3)_2CH$	val-gly	0.5	123.22	123.42	89.61
		1.0	259.40	261.62	207.53
		1.5	394.23	247.89	319.52

[a] m_1 is concentration of Na_2SO_4 in mol (kg of H_2O)$^{-1}$.

nonpolar moiety giving rise to the positive energy of transfer *i.e.*, salting out effect. As the sodium sulfate concentration and surface area of nonpolar group interaction increases the salt-nonpolar group interaction increases resulting in the more positive $\Delta G^o_{tr,r}$ value. The disruption of hydrophobic hydration cospheres favours the hydrophobic interactions among the nonpolar groups. It menifests that sodium sulfate may stabilize the hydrophobic interactions among the nonpolar groups within the proteins.

The entropy, ΔS^o_{tr}, and the enthalpy, ΔH^o_{tr}, of transfer at 298.15 K, calculated from the temperature dependence of ΔG^o_{tr}, are listed in Table IV. It can be seen from Table IV that, the unfavourable entropy of transfer for glycine dominates over the enthalpy of transfer to give positive free energy of transfer. The nonspontaneous transfer of remaining amino acids is caused by greater increase in enthalpy of transfer overcoming the increase in entropy of transfer. The transfer of amino acids from water to aqueous sodium sulfate is primarily enthalpic but for glycine it is entropic. Similar observations have also been reported by earlier workers [21].

To observe the effect of salt on the nonpolar groups the replacement entropy, $\Delta S^o_{tr,r}$, and enthalpy, $\Delta H^o_{tr,r}$, of transfer were calculated, following the procedure applied for the calculation of $\Delta G^o_{tr,r}$. These values are shown in Table V. The positive $\Delta S^o_{tr,r}$ and $\Delta H^o_{tr,r}$ values for the alkyl chains reveal that the hydrogen bonds around them are weaker in aqueous sodium sulfate than in water. This may be due to the disruption of the hydrophobic hydration by the

TABLE IV Entropy, ΔS^{o}_{tr}, and Enthalpy, ΔH^{o}_{tr}, of transfer of amino acids from water to aqueous sodium sulfate at 298.15 K

Amino acid	m_1[a]	$\Delta S^{o}_{tr}/cal\,mol^{-1}K^{-1}$	$\Delta H^{o}_{tr}/cal\,mol^{-1}K^{-1}$
glycine	0.5	− 0.43	− 120.80
	1.0	− 1.41	− 405.63
	1.5	− 1.38	− 358.02
DL-alanine	0.5	− 0.42	− 95.05
	1.0	− 0.27	21.75
	1.5	− 0.14	154.66
DL-α-aminobutyric acid	0.5	0.52	194.24
	1.0	1.08	463.07
	1.5	0.48	412.73
DL-valine	0.5	1.25	503.81
	1.0	1.18	629.39
	1.5	2.35	1103.76
β-alanine	0.5	0.37	189.03
	1.0	1.46	503.98
	1.5	1.70	626.99
γ-aminobutyric acid	0.5	0.31	115.19
	1.0	0.79	310.98
	1.5	0.78	359.78

[a] m_1 is concentration of Na_2SO_4 in mol (kg of H_2O)$^{-1}$.

TABLE V Replacement entropy, $\Delta S^{o}_{tr,r}$, and enthalpy, $\Delta H^{o}_{tr,r}$, of transfer of amino acid side chain from water to aqueous sodium sulfate at 298.15 K

Alkyl chain	*Method*	m_1[a]	$\Delta S^{o}_{tr,r}/cal\,mol^{-1}$	$\Delta H^{o}_{tr,r}/cal\,mol^{-1}$
CH_3	ala − gly	0.5	0.02	25.75
		1.0	1.14	427.38
		1.5	1.24	527.68
CH_3CH_2	aba − gly	0.5	0.08	315.04
		1.0	2.00	868.70
		1.5	1.86	770.75
$(CH_3)_2CH$	val − gly	0.5	1.68	624.61
		1.0	2.59	1035.02
		1.5	3.74	1461.78

[a] m_1 is concentration of Na_2SO_4 in mol (kg of H_2O)$^{-1}$.

salt-nonpolar group interactions which in turn creates favourable environment resulting enhanced association between the nonpolar moieties of the solutes [22, 23].

The free energy of transfer increases with the increase in the number of CH_2 groups but the entropy and enthalpy functions do not show such correlation [24]. This indicates that the water molecules at nonpolar-water interface do not have a particular orientation of placement but adopt different arrangements depending upon the surrounding atomic groups which may affect the entropy in different ways.

The present study shows that sodium sulfate generates favourable interaction between nonpolar groups of amino acids. If applied to macromolecules like proteins, it seems to stabilize the protein native globular structure by enhancing the intra-molecular nonpolar–nonpolar group interactions.

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