

Physicochemical Study on Solvation Behavior of Biologically Active Molecules in Aqueous 18C6 Systems

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ABSTRACT

The density (ρ), viscosity (η) and refractive index (n_D) of some biologically active molecules (glycine, L-alanine, and L-isoleucine) have been determined in different mass fractions ($w_1 = 0.001, 0.003, 0.005$) of aqueous 18-crown-6 (18C6) solutions at three different temperatures. The limiting apparent molar volumes (ϕ_V^∞), experimental slopes (S_V^∞) have been found out from the Masson equation. *A*- and *B*-coefficients have been obtained from the Jones–Dole equation. The Lorentz–Lorenz equation has been employed to measure molar refractions (R_M). The standard volumes of transfer and solvation number of the amino acids have been considered for rationalizing various molecular interactions in the ternary solutions. Group contribution from charged end groups (NH_3^+ , COO^-), $-\text{CH}_2$ and the alkyl groups of amino acids has been determined using a group additive approach. The results have been discussed in terms of ion-dipolar, hydrophilic-hydrophobic and hydrophobic-hydrophobic group interactions as well as thermodynamic parameters.

1. Introduction

In Biological systems, macromolecular globular proteins have well characteristics physicochemical properties. Various non-covalent forces viz. ionic and dipolar interactions, H-bonding and hydrophobic forces, etc. [1] play a decisive role to determine their stable structures. In aqueous solution, the process of denaturation of a globular protein involves a change from a marginally stable native state (folded conformation) to other denaturated state i.e., extended form [2, 3]. Therefore, the studies of these protein solvent interactions are difficult due to complexity in interactions of the large molecules. However, to understand these interactions we consider some simple amino acids which are treated as the model compounds for some specific purpose. Also, amino acids are commonly used in fertilizers, food technology and industry.

On the other hand, macrocyclic polyethers [4] have been extensively used as interesting model compounds for the study of molecular effect on membrane permeability [5–8], due to their many similarities to cyclic antibiotics and biological transport agents. Considerable attention has been focused on the interactions between different protonated amines and macrocyclic ligands in order to study the molecular interaction on membrane permeability [9–11]. 18C6 can give better insight into the effect of electrostatic and hydrophobic interactions on the stability of proteins as the cyclic ether contains hydrophilic ethereal oxygen and hydrophobic ethylene moiety, expected to influence macromolecular conformations. Crown ethers are very important, especially in application on thermodynamic studies [12], solvent extraction of divalent and monovalent ions [13], selective synergistic solvent-extraction [14] and competitive complexation of some alkaline earths and transition metal ions [15]. Synthesis, characterization, crystal structure of some salts with 18C6 are valuable [16] ones.

In the present study, we have attempted to ascertain the nature of solute–solvent/cosolute interactions of amino acids (glycine, L-alanine, and L-isoleucine) in $w_1 = 0.001, 0.003, 0.005$ mass fraction of aqueous 18C6 binary mixtures at 293.15K, 298.15K, and 303.15K.

2. Experimental Methods

2.1 Source and Purity of Samples

The studied amino acids (glycine, L-alanine, L-isoleucine) and cosolute 18-crown-6 of puriss grade were procured from Sigma-Aldrich, Germany and used as purchased. The amino acids were used after recrystallization from (ethanol + water) mixture and dried over P_2O_5 in a desiccator for about 72 h before use. The mass fraction purity of 18-crown-6 was ≥ 0.99 . The 18C6 was dried from moisture at 373 K for 72 h, and then cooled and stored in a desiccator [17]. Freshly distilled conductivity water was used for the preparation of the 18C6 solution. The physical properties of different mass fractions of aqueous 18C6 solution are shown in Table 1.

Table 1 Experimental values of density (ρ), viscosity (η), refractive index (n_D) different mass fractions of aqueous 18-crown-6 at different temperatures

Aqueous 18C6 mixture	$\rho \times 10^{-3} / \text{kg} \cdot \text{m}^{-3}$			$\eta / \text{mPa s}$			n_D
	293.15 K ^a	298.15 K ^a	303.15 K ^a	293.15 K ^a	298.15 K ^a	303.15 K ^a	298.15 K ^a
$W_1=0.001$	0.99832	0.99712	0.99572	1.28	1.18	0.91	1.3320
$W_2=0.003$	0.99836	0.99720	0.99581	1.30	1.20	0.93	1.3326
$W_3=0.005$	0.99843	0.99727	0.99593	1.32	1.22	0.95	1.3329

^a Standard uncertainties *u* are: $u(\rho) = 5 \times 10^{-5} \text{ g cm}^{-3}$, $u(\eta) = 0.02 \text{ mPa s}$, $u(n_D) = 0.0003$ and $u(T) = 0.01 \text{ K}$.

2.2 Apparatus and Procedure

Aqueous binary solution of 18C6 was prepared by mass (Mettler Toledo AG-285 with uncertainty $\pm 0.0003 \text{ g}$). Stock solutions of the amino acids were also prepared by mass and then working solutions were obtained by mass dilution. The conversion of molarity into molality was accomplished using experimental density values. All the solutions were prepared afresh before use. The uncertainty molality of the solutions is evaluated to $\pm 0.0001 \text{ mol kg}^{-3}$.

The densities of the solutions (ρ) were measured by means of vibrating u-tube Anton Paar digital density meter (DMA 4500 M) with a precision of $\pm 0.00005 \text{ g cm}^{-3}$ maintained at ± 0.01 . A density check or air/water adjustment was performed with triply distilled and degassed water and

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with dry air at atmospheric pressure. Before each series of measurements, the density meter was calibrated with triple distilled and degassed water in the experimental temperature range [18].

The viscosities were measured using a Brookfield DV-III Ultra Programmable Rheometer with spindle size-42 fitted to a Brookfield digital bath TC-500. The viscosities were obtained using the following equation,

$$\eta = (100 / \text{RPM}) \times \text{TK} \times \text{torque} \times \text{SMC}$$

where, *RPM*, *TK* (0.09373) and *SMC* (0.327) are the speed, viscometer torque constant and spindle multiplier constant respectively. It was calibrated against the standard viscosity samples supplied with the instrument, water and aqueous CaCl_2 solutions [19]. Temperature of the experimental solution was maintained $\pm 0.01\text{K}$ using Brookfield Digital TC-500 thermostat bath. Viscosities were measured with an accuracy of $\pm 1\%$. Each measurement reported herein is an average of triplicate reading with a precision of 0.3%.

Refractive index was measured by means of Mettler Toledo digital refractometer. The light source was LED, $\lambda = 589.3\text{ nm}$. The calibration of refractometer was done twice using triply distilled water and being checked after every few measurements. The uncertainty of refractive index measurement was ± 0.0002 units.

Table 2 Limiting apparent molar volume (ϕ_V^0) and *B*-coefficient and limiting molar refraction (R_M^0) of amino acids in different mass fractions of aqueous 18-crown-6 at different temperatures

Aq. solvent mixture	$\phi_V^0 \times 10^6$ / $\text{m}^3 \text{mol}^{-1}$			S_V^* / $\text{m}^3 \text{mol}^{-3/2} \text{kg}^{1/2}$			R_M^0 / $\text{m}^3 \text{mol}^{-1}$
T=	293.15 K ^a	298.15 K ^a	303.15 K ^a	293.15 K ^a	298.15 K ^a	303.15 K ^a	298.15 K ^a
Glycine							
$W_1=0.001$	43.41	43.42	43.89	-10.05	-10.78	-16.50	15.41
$W_1=0.003$	43.94	43.98	44.05	-13.69	-13.86	-16.89	15.44
$W_1=0.005$	44.10	44.13	44.21	-20.27	-24.18	-26.59	15.46
L-alanine							
$W_1=0.001$	60.55	60.63	60.66	-14.90	-15.22	-16.41	18.29
$W_1=0.003$	60.71	60.73	60.88	-15.53	-18.21	-16.92	18.31
$W_1=0.005$	60.93	60.96	60.97	-21.48	-24.06	-27.26	18.34
L-isoleucine							
$W_1=0.001$	107.50	107.60	107.71	-6.641	-13.24	-24.05	27.09
$W_1=0.003$	107.81	107.89	108.02	-28.89	-36.14	-43.85	27.11
$W_1=0.005$	108.11	108.20	108.31	-50.87	-57.84	-65.39	27.19

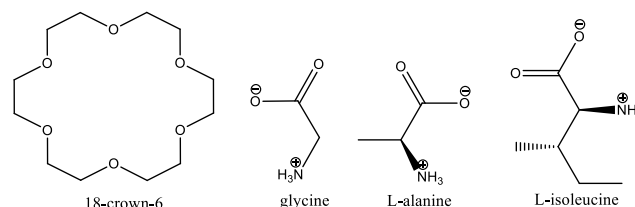
^a Standard uncertainties u are: $u(T) = 0.01\text{K}$.

3. Result and Discussion

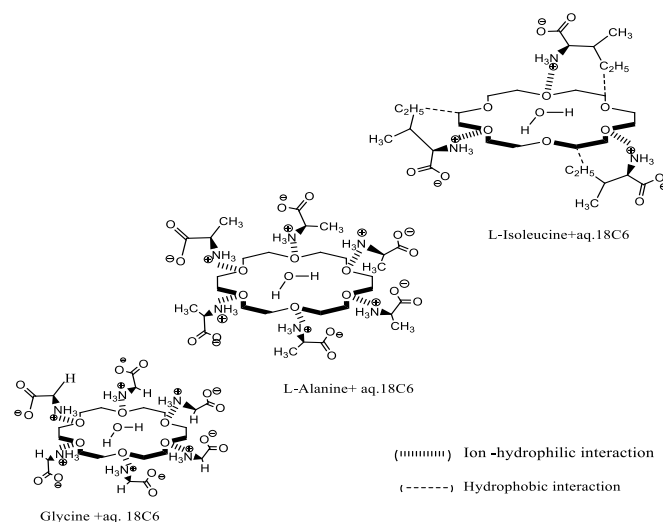
3.1 Apparent Molar Volume (ϕ_V)

Probing amino acids are highly soluble in all proportions of the aqueous 18C6 solvent mixtures (Scheme 1). The physical properties of binary mixtures in different mass fractions ($w_1 = 0.001, 0.003, 0.005$) of aqueous 18C6 solutions at 293.15, 298.15 and 303.15 K are reported in Table 1. The measured experimental values of densities of studied amino acids in different mass fractions ($w_1 = 0.001, 0.003, 0.005$) of aqueous 18-crown-6 mixture at 293.15–303.15 K as a function of concentration (molality) are measured. Volumetric properties, such as, limiting apparent molar volume (ϕ_V^0) are regarded as sensitive tools for the understanding of interactions in solutions [20]. The values of ϕ_V^0 and S_V^* are reported in Table 2. At infinite dilution, each monomer of solute is surrounded only by the solvent molecules, and being infinite distant with other ones. Therefore, that ϕ_V^0 is unaffected by solute–solute interaction and it is measure only of the solute–solvent interaction [21, 22]. The ϕ_V^0 data are often entrenched with important information of solute hydrophobicity, solvation behavior, and solute–solvent interactions [23, 24] occurred in aqueous 18C6. The inspection of Table 2 shows that values of ϕ_V^0 are large and positive for all the amino acids at all the investigated temperatures and molalities, suggesting the presence of strong solute–solvent interaction [25]. Furthermore, at each temperature, the values of ϕ_V^0 increase with increasing number of hydrophobic alkyl groups (or size of alkyl group) from L-glycine to L-isoleucine. A similar increase in ϕ_V^0 with increasing number of carbon atoms for amino acids in aqueous glycerol, at 298.15 K, was also reported by Banipal et al. 2001[26]. The behavior of ϕ_V^0 for the present systems can be explained employing the co-sphere model, proposed by Friedman and Krishnan [27]. By using this model Mishra et al. 1983 [28] observed that an overlap of co spheres of two species cause in an increase or decrease in volume. The increase ϕ_V^0 with increasing temperature may be attributed to the release of some solvation molecules

from the loose solvation layers of the solutes in solution. A plausible mechanism of interaction between 18C6 and different amino acids as evident from the experimental observation is given in Scheme 2. The required values of ϕ_V^0 and S_V^* for the amino acids in pure water are collected from the literature [29]. From Table 2, a quantitative comparison between ϕ_V^0 and S_V^* values show that the magnitude of ϕ_V^0 values is higher than S_V^* , suggesting that the solute–solvent interactions dominate over the solute–solute interactions in all solutions at the investigated temperatures. Furthermore, S_V^* values are negative at all temperatures, and the values increase with the increase of experimental temperatures which may be attributed to more violent thermal agitation at higher temperatures and the pair-wise interaction [30–32] is restricted by the non-covalent interaction of the charged functional group of one amino acid molecule to the side chain of other amino acid molecules.



Scheme 1 Molecular structures of solute and co-solute



Scheme 2 Plausible solute–solvent interaction in the studied ternary mixtures

3.1.1 Group Contributions of Amino Acids to (ϕ_V^0)

ϕ_V^0 values for amino acids containing alkyl part can be represented as follows,

$$\phi_V^0 = \phi_V^0(\text{NH}_3^+, \text{COO}^-) + n_c \phi_V^0(\text{CH}_2) \quad (1)$$

Where, n_c is the number of carbon atoms in the alkyl chain of the amino acid $\phi_V^0(\text{NH}_3^+, \text{COO}^-)$ and $\phi_V^0(\text{CH}_2)$ are the zwitter ionic end group and methylene group contribution to ϕ_V^0 , respectively. The values of $\phi_V^0(\text{NH}_3^+, \text{COO}^-)$ and $\phi_V^0(\text{CH}_2)$ estimated by regression analysis and are listed in Table 3, where required values in pure solvent are collected from the literature [33]. By obtaining above values we can calculate the mean contribution of the $\phi_V^0(\text{CH})$ and $\phi_V^0(\text{CH}_3)$ values of the amino acids (Table 3).

$$\phi_V^0(\text{CH}) = 0.5\phi_V^0(\text{CH}_2) \quad (2)$$

$$\phi_V^0(\text{CH}_3) = 1.5\phi_V^0(\text{CH}_2) \quad (3)$$

From the table it is clear that contributions of $\phi_V^0(\text{NH}_3^+, \text{COO}^-)$ to the ϕ_V^0 are higher than CH_2 -group and increases with increase in mass fraction of 18C6(cosolute) at all investigated temperatures indicates that the interaction between cosolute and polar end groups ($\text{NH}_3^+, \text{COO}^-$) of amino acids are much stronger than those between cosolute and CH_2 (hydrophobic) group [34]. The side chain contribution to the partial molar volume of the amino acids can be derived by using the following equation

$$\phi_V^0(\text{R}) = \phi_V^0(\text{amino acids}) - \phi_V^0(\text{glycine}) \quad (4)$$

Where, $\phi_v^0(R)$ defines the side chain contribution to ϕ_v^0 of the respective amino acid relative to the H-atom of glycine. For this purpose, it is assumed that the volume contribution of the H-atom in glycine is insignificant. The results are given in Table 4.

Table 3 Contributions of zwitter ionic group (NH_3^+ , COO^-), CH_2 group, and the other alkyl chains to the limiting apparent molar volume, ϕ_v^0 , and the viscosity B -coefficient for amino acids in different mass fraction of aqueous 18-crown-6

Groups	$\phi_v^0 \times 10^6$ / $\text{m}^3 \text{mol}^{-1}$	B / kgmol^{-1}				
T/ K ^a	293.15	298.15	303.15	293.15	298.15	303.15
W ₁ =0.001						
$\text{NH}_3^+, \text{COO}^-$	26.27	26.21	27.12	1.040	1.080	1.070
(CH)	8.57	8.60	8.38	0.150	0.141	0.155
Gly(CH_2)	17.14	17.21	16.77	0.301	0.283	0.310
(CH_3)	25.71	25.80	25.14	0.452	0.423	0.465
Ala($\text{CH}_3\text{CH}-$)	34.28	34.42	33.54	0.602	0.570	0.621
Isoleu(EtMeCH-)	81.23	81.39	80.59	0.885	0.847	0.862
W ₁ =0.003						
$\text{NH}_3^+, \text{COO}^-$	27.17	27.23	27.24	1.050	1.060	1.070
(CH)	8.39	8.37	8.40	0.160	0.162	0.181
Gly(CH_2)	16.77	16.75	16.82	0.321	0.324	0.363
(CH_3)	25.17	25.11	25.20	0.482	0.486	0.545
Ala($\text{CH}_3\text{CH}-$)	33.54	33.50	33.64	0.651	0.651	0.722
Isoleu(EtMeCH-)	80.84	80.66	80.78	0.892	0.950	1.010
W ₁ =0.005						
$\text{NH}_3^+, \text{COO}^-$	27.27	27.29	27.45	1.140	1.160	1.200
(CH)	8.41	8.42	8.38	0.162	0.189	0.180
Gly(CH_2)	16.83	16.84	16.76	0.325	0.359	0.360
(CH_3)	25.23	25.26	25.14	0.486	0.567	0.540
Ala($\text{CH}_3\text{CH}-$)	33.66	33.67	33.52	0.652	0.767	0.719
Isoleu(EtMeCH-)	80.84	80.31	80.26	1.032	1.104	1.111

^aStandard uncertainties u are: $u(T) = 0.01 \text{ K}$

Table 4 Contribution of the Alkyl Chain Group (R) to Standard Partial Molar Volume, $\phi_v^0(R)$ and Viscosity B -Coefficient $B(R)$ in Different Aqueous 18C6 Solutions

Mass fractions	$\phi_v^0(R) \times 10^6$ / $\text{m}^3 \text{mol}^{-1}$	$B(R)$ / kgmol^{-1}				
T=	293.15K ^a	298.15K ^a	303.15K ^a	293.15K ^a	298.15K ^a	303.15K ^a
L-alanine						
W ₁ =0.001	17.14	17.21	16.77	0.301	0.303	0.310
W ₁ =0.003	16.77	16.75	16.83	0.321	0.324	0.363
W ₁ =0.005	16.83	16.83	16.76	0.324	0.379	0.360
L-isoleucine						
W ₁ =0.001	64.09	64.18	63.82	0.584	0.590	0.591
W ₁ =0.003	63.56	63.91	66.97	0.562	0.623	0.735
W ₁ =0.005	64.01	64.07	67.10	0.704	0.716	0.752

^aStandard uncertainties u are: $u(T) = 0.01 \text{ K}$

Table 5 Contribution of Transfer Volumes, $\Delta\phi_v^0$ from $\phi_v^0 \times 10^6$ (aqueous) for amino acids in different Aqueous 18C6 solutions at 293.15 K - 303.15 K

Amino acid Groups	$\phi_v^0 \times 10^6$ (aqueous) / $\text{m}^3 \text{mol}^{-1}$	$\Delta\phi_v^0 \times 10^6$ / $\text{m}^3 \text{mol}^{-1}$			
T=	293.15K ^a	298.15K ^a	303.15K ^a		
W ₁ =0.001					
$\text{NH}_3^+, \text{COO}^-$	25.91	0.36	0.30	1.21	
(CH)	8.64	-0.07	-0.04	-0.26	
Gly(CH_2)	17.28	-0.14	-0.03	-0.51	
(CH_3)	25.92	-0.21	-0.12	-0.78	
Ala($\text{CH}_3\text{CH}-$)	34.56	-0.28	-0.14	-0.80	
Isoleu(EtMeCH-)	81.83	-0.60	-0.44	-1.30	
W ₁ =0.003					
$\text{NH}_3^+, \text{COO}^-$	25.91	1.26	1.32	1.33	
(CH)	8.64	-0.25	-0.27	-0.24	
Gly(CH_2)	17.28	-0.51	-0.53	-0.46	
(CH_3)	25.92	-0.75	-0.81	-0.72	
Ala($\text{CH}_3\text{CH}-$)	34.56	-1.02	-1.06	-0.92	
Isoleu(EtMeCH-)	81.83	-1.29	-1.40	-1.50	
W ₁ =0.005					
$\text{NH}_3^+, \text{COO}^-$	25.91	1.36	1.38	1.54	
(CH)	8.64	-0.23	-0.22	-0.30	
Gly(CH_2)	17.28	-0.45	-0.44	-0.52	
(CH_3)	25.92	-0.68	-0.65	-0.77	
Ala($\text{CH}_3\text{CH}-$)	34.56	-0.90	-1.06	-1.04	
Isoleu(EtMeCH-)	81.83	-1.39	-1.52	-1.57	

^aStandard uncertainties u are: $u(T) = 0.01 \text{ K}$

3.1.2 Group Contributions of Amino Acids to Standard Transfer Volume ($\Delta\phi_v^0$)

Partial molar transfer volume of the zwitterionic end group and other hydrophobic alkyl chain groups of amino acids from water to aqueous 18C6 have been done as follows

$$\Delta\phi_v^0(\text{NH}_3^+\text{COO}^-) = \Delta\phi_v^0(\text{NH}_3^+\text{COO}^-)[\text{inaqueous18C6}] - \Delta\phi_v^0(\text{NH}_3^+\text{COO}^-)[\text{inwater}] \quad (5a)$$

$$\text{Or, } \Delta\phi_v^0(R) = \Delta\phi_v^0(R)[\text{inaqueous18C6}] - \Delta\phi_v^0(R)[\text{inwater}] \quad (5b)$$

and reported in Table 5. The contribution of ($\text{NH}_3^+, \text{COO}^-$) is positive to $\Delta\phi_v^0$ and increases with increase in mass fraction of the cosolute. On the other hand contribution of side chain to $\Delta\phi_v^0$ is negative for all the studied amino acids and their contribution decreases with increase in the number of hydrophobic side part.

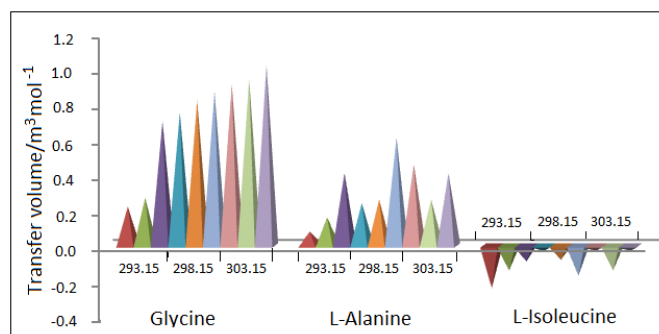


Fig. 1 Transfer volume ($\Delta\phi_v^0$) of amino acids varying with increasing temperatures (T/K) with increasing concentrations of 18C6 (0.001, 0.002 & 0.003 mass fraction)

Standard transfer volume for amino acids, $\Delta\phi_v^0$, from pure water to 18C6 is derived by using the Eq.(6) and the results are shown in Fig. 1.

$$\Delta\phi_v^0(\text{amino acid}) = \phi_v^0(\text{amino acid} + \text{aq.18C6}) - \phi_v^0(\text{water}) \quad (6)$$

Solute-solvent interactions [35] among the amino acids with co solute can be explained by the co-sphere model developed by Friedman and Krishnan. According to this model the effect of overlap of the hydration co-spheres between crown and amino acids bearing hydrophobic alkyl chain is destructive. Since amino acids exist predominantly as zwitterions in pure water and there is an overall increase in volume of water due to electrostriction, but the observed decreasing transfer volumes indicate that in the ternary solutions (amino acid and aq. 18C6), have the hydrophobic-hydrophobic group interactions (mainly repulsion) for long chain amino acids and the contribution increases with the mass fraction of 18C6. Therefore, the negative $\Delta\phi_v^0$ values for L-isoleucine point out that ion-hydrophobic and hydrophobic-hydrophobic interaction are higher in case of L-isoleucine than that of other two amino acids. The observed result can also be elucidate by the following equation [36, 37],

$$\phi_v^0 = \phi_{vw} + \phi_v - \phi_s \quad (7)$$

Where, ϕ_{vw} is the van der Waals volume, ϕ_v is the volume associated with voids or empty space, and ϕ_s is the shrinkage volume due to electrostriction. Assuming the ϕ_{vw} and ϕ_v have the same magnitudes in water and in aqueous 18C6 solutions for the same class of solutes [38], the observed positive $\Delta\phi_v^0$ values ascribed to the decrease in the volume of shrinkage, whereas negative $\Delta\phi_v^0$ values for L-isoleucine may be attributed to shrinkage in volume [26]. The introduction of a non-polar CH_3 - group in L-alanine provides an additional tendency for hydrophobic-hydrophobic group interactions, and as a result, greater electrostriction of water is produced leading to smaller changes of $\Delta\phi_v^0$. Similarly, when the H-atom of glycine is replaced by the alkyl group in L-isoleucine, the additional propensity for the hydrophobic-hydrophobic group interaction increases further and thus leads to change in $\Delta\phi_v^0$ values. The above facts are supported by the experimental observation drawn by Li et al. [39] in a study of glycine, L-alanine and L-serine in glycerol-water mixture at 298.15 K.

3.1.3 Solvation Number of Amino Acids

Number of solvent molecules associated with amino acids can be estimated from the flowing relation,

$$n_{\text{H}} = \frac{\phi_v^0(\text{elect})}{\phi_e^0 - \phi_b^0} \quad (8)$$

Where, ϕ_e^0 (elect) is electrostriction partial molar volume ϕ_e^0 is the molar volume of the electrostricted water and ϕ_b^0 is the molar volume of bulk water. The value of $(\phi_e^0 - \phi_b^0)$ is calculated [29] to be -2.9, -3.3 and -3.5 $\text{cm}^3\text{mol}^{-1}$ at 293.15, 298.15 and 303.15 K respectively. The ϕ_v^0 (elect) values can be calculated [40] from the intrinsic partial molar volumes of the amino acids, ϕ_v^0 (int) [41, 42] and experimentally determined ϕ_v^0 values, as follows,

$$\phi_v^0(a \text{ min oacid}) = \phi_v^0(\text{int}) + \phi_v^0(\text{electric}) \quad (9)$$

$$\phi_v^0(\text{int}) = \frac{0.7}{0.634} \phi_v^0(\text{cryst}) \quad (10)$$

Where, $\phi_v^0(\text{cryst})$ (= mol wt/density) is the crystal molar volume, 0.7 is the packing density for the molecules in an organic crystal, and 0.634 is the packing density for a random packing sphere. The values of n_H in table 6 for the amino acids are follows the order,

$$n_H(\text{L-isoleucine}) > n_H(\text{L-alanina}) > n_H(\text{glycine})$$

The observed decreasing tendency of n_H for glycine and L-alanine (Table 6) supports the overall solute–solvent interaction of the amino in aq. 18C6 solutions [43]. However, a slight increase of n_H for L-isoleucine indicates that the increase in the interaction of hydrophobic groups of L-isoleucine with those of the 18C6 does not reduce the electrostriction of water molecules to it, but leads to a slight increase in the solvation number, (n_H).

Table 6 Solvation number (S_n) of the amino acids at different mass fractions of aqueous 18C6

Mass fractions	Solvation Number(S_n)								
	Glycine			L-alanine			L-isoleucine		
T/ K ^a	293.15	298.15	303.15	293.15	298.15	303.15	293.15	298.15	303.15
W ₁ =0.001	2.8	2.5	2.2	3.0	2.6	2.4	3.9	3.4	3.2
W ₁ =0.003	2.6	2.3	2.2	2.9	2.5	2.3	3.8	3.3	3.1
W ₁ =0.005	2.6	2.2	2.1	2.8	2.4	2.3	3.7	3.2	3.0

3.2 Viscosity B-Coefficient

The effects of solute–solvent interactions on the solution viscosity can be inferred from the B -coefficient [21, 29]. The viscosity B -coefficient is an important tool to provide information concerning the solvation of the solutes and their effects on the structure of the solvent. It is evident that the values of the B coefficient are positive, thereby suggesting the presence of strong solute–solvent interactions, and strengthened with an increase in the number of hydrophobic groups of amino acids and with the increase of mass fraction of 18C6 in the solvent mixture. This interaction is strengthened with rise in temperature and thus the values of B -coefficient increases with increase in temperature. This observation is in a well agreement with the results obtained from apparent molar volume values discussed earlier. The B -coefficient values of amino acids follow the sequence, L-glycine < L-alanine < L-isoleucine. Thus from this trend it is obvious that the B -coefficients reflect the net structural effects of the charged groups and the hydrophobic CH_2 -groups of the amino acids. As B -coefficients vary linearly with the number of carbon atoms of the alkyl chain (n_c), these two effects can be determined as follows

$$B = B(\text{NH}_3^+, \text{COO}^-) + n_c B(\text{CH}_2) \quad (11)$$

The regression parameters, i.e., the zwitterionic group contribution $B(\text{NH}_3^+, \text{COO}^-)$, and $B(\text{CH}_2)$ group contribution, to B -coefficients are scheduled in Table 3. It shows that both the $B(\text{NH}_3^+, \text{COO}^-)$ and $B(\text{CH}_2)$ values increase with increasing molality of 18C6 in ternary solutions, indicating that the zwitterionic and CH_2 - group enhances the structure to solute–solvent interaction in the aqueous crown solutions. The hydrophobic side chain contributions to B -coefficients, $B(\text{CH}_2)$, have also been derived using the same procedure as that of $\Delta\phi_v^0(R)$ and are tabulated in Table 4, which shows that $B(R)$ values are positive and greater for L-isoleucine than L-alanine in all the experimental condition. This order is due to the greater structure-breaking tendency and these findings are in line with our volumetric results discussed earlier.

3.3 Refractive Index Measurements for Molecular Interaction

The refractive index of a molecule denotes its capability to refract light as it passes through one medium to another. According to Deetlefs et al. 2006 [44] the greater the refractive index of a molecule is, the more the light is refracted [45]. A more dense solution i.e., a more tightly packed substance has a higher refractive index. Therefore, refractive index values

increases with increase in amino acids concentration to the given solvent system [46]. Among the three amino acids, higher molar refraction values in case of L-isoleucine suggests solute cosolute (18C6) interaction is higher for L-isoleucine than that of other two amino acids and solute–solvent interaction predominates over solute–solute interaction (Fig. 2). These findings about compactness of the system in relating to the interactions are in good agreement with the results found from density and viscosity measurements.

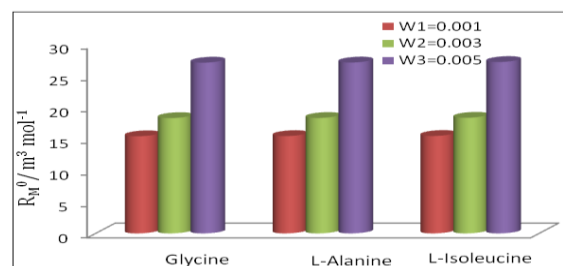


Fig. 2 Plot of limiting molar refraction (R_M^0) for glycine, L-alanine and L-isoleucine in different mass fractions (w_1) of aq. 18C6 at 298.15 K

Table 7 Thermodynamic derived parameters of the amino acids at different mass fractions of aqueous 18C6

Temp/K	ϕ_v^0 (purewater) / $\text{m}^3 \text{mol}^{-1}$	$\Delta\mu_1^{0\#}$ / KJ·mol ⁻¹	$\Delta\mu_2^{0\#}$ / KJ·mol ⁻¹	$\Delta\mu^{0\#}$ / KJ·mol ⁻¹	$\Delta S^{0\#}$ / kJ·mol ⁻¹	$\Delta H^{0\#}$ / KJ·mol ⁻¹
Glycine+ W ₁ =0.001(18C6)						
293.15	18.016	60.41	70.19	65.30	-16.28	49.02
298.15	18.039	61.24	71.57	66.40	-16.41	49.99
303.15	18.062	61.61	71.68	66.59	-16.79	49.80
Glycine+ W ₁ =0.003(18C6)						
293.15	18.016	60.44	70.91	65.69	-16.35	49.34
298.15	18.039	61.28	71.81	66.54	-16.36	50.18
303.15	18.062	61.65	71.92	66.70	-16.43	50.27
Glycine+ W ₁ =0.005(18C6)						
293.15	18.016	60.47	72.14	66.30	-16.46	49.84
298.15	18.039	61.31	72.51	66.91	-16.49	50.42
303.15	18.062	61.69	72.62	67.15	-16.57	50.58
L-alanine+ W ₁ =0.001(18C6)						
293.15	18.016	60.41	72.81	66.61	-16.74	49.87
298.15	18.039	61.24	72.87	67.05	-16.83	50.22
303.15	18.062	61.61	73.95	67.78	-16.75	51.03
L-alanine + W ₁ =0.003(18C6)						
293.15	18.016	60.44	73.29	66.86	-16.91	49.90
298.15	18.039	61.28	74.04	67.66	-17.03	50.63
303.15	18.062	61.65	74.15	67.90	-17.15	50.75
L-alanine + W ₁ =0.005(18C6)						
293.15	18.016	60.47	73.86	67.16	-17.26	49.91
298.15	18.039	61.31	74.14	67.72	-17.49	50.23
303.15	18.062	61.69	74.55	68.12	-17.63	50.49
L-isoleucine+ W ₁ =0.001(18C6)						
293.15	18.016	60.41	74.86	67.63	-17.71	49.92
298.15	18.039	61.24	74.95	68.09	-17.75	50.34
303.15	18.062	61.61	75.06	68.33	-17.81	50.52
L-isoleucine+ W ₁ =0.003(18C6)						
293.15	18.016	60.44	75.55	67.99	-17.83	50.16
298.15	18.039	61.28	75.86	68.77	-17.86	50.91
303.15	18.062	61.65	76.57	69.11	-17.94	51.17
L-isoleucine+ W ₁ =0.005(18C6)						
293.15	18.016	60.47	77.63	69.02	-17.97	51.05
298.15	18.039	61.31	77.76	69.53	-18.21	51.32
303.15	18.062	61.69	77.81	70.09	-18.28	51.81

3.4 Thermodynamic Influence

The $\Delta\mu_1^{0\#}$ (free energy of activation of viscous flow per mole of solvent) and $\Delta\mu_2^{0\#}$ (free energy of activation of viscous flow per mole of the solute) values are positive and are comparable for all the solvent composition for each amino acids and are tabulated in Table 7. This may be due to the fact that amino acids –cosolute (18C6) interactions occurs in the ground state and are almost same as in the transition state [47, 48]. In other words, the solvation of amino acids in the transition state is also favourable in terms of free energy. The $\Delta\mu_2^{0\#}$ values of the amino acids were found to increases from glycine to L-isoleucine at a given temperature (Table 7). This indicates that the solvation of the amino acids in the ground state becomes favourable for the investigated amino acids. Positive activation enthalpy

(ΔH^*) values of the mixtures are suggesting that the formation of activated species for the solution becomes difficult as the amount of 18C6 in the mixtures increases. The negative value of $T\Delta S^*$, which increase with increasing concentration of amino acids, for all the studied mixtures, suggest that the net order of the system decreases as the concentration of amino acid in the mixture increases[33]. Therefore, the possibility of the interaction is favourable with the rise in temperature as well as the molality of 18C6 for glycine to L-isoleucine. The ΔH^* and ΔS^* quantities contain contributions from the following processes: (i) non-covalent interactions between amino acids and 18C6 (H-bonding, van der Waals forces, hydrophobic and electrostatic interactions and steric effects) (ii) dehydration (release of water molecules) of the 18C6 during the molecular interactions (iii) hydration of the interacted species (amino acids and 18C6) by the surrounding water molecules.

4. Conclusion

In summary, wide study on volumetric, viscometric and refractometric investigations of three simple amino acids in aq.18C6 reveals that the overall molecular interaction of amino acids with co solutes follows the order : glycine< L-alanine< L-isoleucine. Therefore, this behavior suggests that although ion-ion or hydrophilic-hydrophilic group interactions are predominant for glycine and L-alanine, ion-hydrophobic or hydrophobic-hydrophobic group interactions are predominant for L-isoleucine in aq.18C6 solutions. The size and number of carbon atoms of the alkyl groups of the amino acids also play an important role in determining the solvation consequences on the selected solvent systems.

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