Solvation mechanism of DL-nor-valine in aqueous mixtures of protophilic dipolar aprotic Dimethylsulfoxide

¹ Roy S, ² Mahalic K and ³ Dolui BK*.

¹ Department of Chemistry, Shibpur Dinobundhoo Institution (college), Howrah, West Bengal, India.

² Department of Chemistry, University of Kalyani, Nadia, West Bengal, India.

³ Department of Chemistry, Visva-Bharati, Santiniketan, Birbhum, West Bengal, India.

* **Corresponding Author:** E-Mail: bijoy_dolui@yahoo.co.in

ABSTRACT

In this study the solubilities of α-amino acid DL-nor-Valine have been measured by 'formol titrimetry' method at five equidistant temperatures i.e. from 15 to 35 ^{0}C in aqueous mixtures of protophilic dipolar aprotic Dimethylsulfoxide (DMSO) and also the related thermodynamic parameters like standard free energies ($\Delta G_t^0(i)$) and entropies ($\Delta S_t^0(i)$) of transfer of for the species (i) i.e. solute DL-nor-Valine from water to aqueous mixture of DMSO have been evaluated at 298.15 K. The chemical effects of the transfer Gibbs energies ($\Delta G_{t,ch}^0(i)$) and entropies of transfer ($T\Delta S_{t,ch}^0(i)$) have been obtained after elimination of cavity effect and dipole-dipole interaction effects from the total transfer energies. The chemical contribution of transfer energetics of DL-nor-Valine are mainly guided by the composite effects of increased dispersion interaction, basicity effect and decreased acidity, hydrogen bonding effects, hydrophilic hydration and hydrophobic hydration of aqueous DMSO mixtures as compared to that of reference solvent, water.

Keywords: Aqua-organic solvent system, Amino acid, Transfer energetic, hydrophobic hydration, dispersion interaction.

1. INTRODUCTION

Amino acids are the primary building blocks of proteins. DL-nor-Valine [i.e. CH_3-CH_2-CH_2-CH (NH_2) (COOH)] is an α- amino acid having apolar hydrophobic side chain. This apolar aliphatic hydrophobic side chain ($CH_3CH_2CH_2$-) may impart hydrophobic hydration interaction for the stabilization of proteins and other biomolecules constituted by it. So the thermodynamic studies of such type of amino acid are very important.

Researchers have been drawn their attention [1-5] to determine the various thermodynamic properties of amino acids in different aqua-organic mixed solvent systems.

Such studies will help to gain the various aspects of protein folding-unfolding processes and protein stability in different solvent systems [7, 8]. The field of protein folding and stability has been demanded as a critically important area of research for long years. In this regard Tanford, Nozaki and other authors [9, 10] reported solubilities, transfer free energies and entropies of some amino acids from water to urea, water-glycerol [11, 14] and water to ethylene glycol [13, 17], water to *N ,N*-dimethyl formamide [27, 28, 34] and water to 2-methoxyethanol [29], water to 1, 2-dimethoxyethane [30] solvents systems. All these experiments tried to give an idea about the relative stabilization of those amino acids and other biomolecules in aqua-organic media with respect to reference solvent (water) and the complex solute-solvent and solvent-solvent interactions therein.

In such context our purposes of such type of study are to know about the nature of solvation as well as interaction of heavier amino acids or biomolecules with dipolar aprotic solvent systems compared to protic solvent, water. Recently solvation chemistry of Valine is studied in aqueous mixture of cationophilic dipolar aprotic *N, N*-Dimethyl formamide [34]. Dimethylsulphoxide is also a protophilic dipolar aprotic solvent having

two hydrophobic groups (i.e. –CH₃) as well as soft (>S=O) moiety. This solvent may also play important role in term of soft-soft, dispersion and hydrophobic interaction to influence solvation chemistry of larger amino acid DL-nor-Valine. The estimated thermodynamic parameters will also be helpful to enrich chemical, biochemical and pharmaceutical sciences in future.

2. MATERIALS AND METHOD

2.1. Chemicals and their purifications

DL-nor-Valine [> 99.5 %, E Merck] was used after drying as described in previous works [15, 26]. Dimethylsulphoxide [> 99.8 %, Aldrich] rigorously dried over fused CaCl₂ for 3-4 days, decanted and then distilled under reduced pressure. The distilled sample was preserved in a well stopper Jena battle in desiccators and redistilled before use [16, 26]. For titration standardized NaOH [E Merck] solution and phenolphthalein indicator [LR, BDH] were used. Neutral formaldehyde [E Merck] was used to mask before titration. Triple distilled water was used for whole experiment.

2.2. Experimental procedure

Aqueous mixtures of co-solvent, DMSO that have been used were 0, 20, 40, 60, 80 and 100 wt %. These were taken in well fitted stoppered glass tubes. Glass tubes were incompletely filled to facilitate good mixing. The low-cum-high temperature thermostat was used for all measurements which is capable of registering temperatures having an accuracy of ±0.1 ⁰C. A known mass of filtered saturated solution was transferred to a dry conical flask. The solubility of Valine is measured by formol titrimetry method [17, 26]. These measurements were taken at 15, 20, 25, 30 and 35 ⁰C temperatures. Five sets of measurements for all the co-solvent mixtures were made for all temperatures by equilibrating the solutions from both above and below (± 0.1⁰C) the required temperatures and the solubilities were found to agree to within ±0.5 to 1.0 %.

3. RESULTS AND DISCUSSION

3.1. Thermodynamic parameters evaluation

The important parameters of the amino acid, DL-nor-Valine and co-solvent are presented in the Table 1. The measured solubilities (mol·kg⁻¹) of DL-nor-Valine are listed in Table 2. The standard deviations, s_f are also estimated for all solubility values to know about the precision and are shown in parentheses (Table 2) only for 40, 60 and 80 wt % of DMSO at all temperatures.

As in the previous studies by Bates and coworkers on Tris [18, 35] and by Kundu and coworkers [18], [19] and B. K. Dolui et al.[26-31, 34] calculated the Gibbs energies of solutions (ΔG°s) of the solutes, amino acids on molal scale for each solvent by using Eq.1.

$$\Delta G°_s = -RT \ln a = -RT \ln m\gamma \qquad (1)$$

where a is the activity and γ is the activity coefficient of the solutes but it is taken tentatively to be unity in each solvent and 'm' is the solubility in mol·kg⁻¹ of the solute in aquo-organic co-solvent mixtures at 25 ⁰C on the molal scale.

The transfer free energetics i.e. (ΔG°t) is obtained as given by Eq. 2 [30].

$$\Delta G_t^0(i) = \Delta G_s^0(i) - \Delta G_R^0(i) \qquad (2)$$

The free energies of solutions , ΔG°s at different temperatures are fitted by the method of least squares to an equation of the form [11];

$$\Delta G_s^0 = a + bT + cT \ln T \qquad (3)$$

where T is the temperature in Kelvin scale. The values of the coefficients a, b, c are presented in Table 3. These are found to reproduce the experimental data within ±0.04 kJ·mol⁻¹. Transfer Gibbs energies ΔG_t^0 and entropies ΔS_t^0 of the amino acids from water to Dimethylsulphoxide mixtures are calculated at 298.15 K on mole fraction scale by using the following equations 4 & 5.

$$\Delta G_t^0(i) = {}_s\Delta G_s^0(i) - {}_R\Delta G_R^0(i) \qquad \text{i.e.}$$

$$\Delta G_t^0(i) = (a_s - a_R) + (b_s - b_R)T + (c_s - c_R)T\ln T - RT\ln(M_s/M_R) \qquad (4)$$

and

$$\Delta S_t^0(i) = (b_R - b_s) + (c_R - c_S)(1 + \ln T) + R\ln(M_s/M_R) \qquad (5)$$

here the subscript 's' and 'R' refer to the co-solvent (H₂O +DMSO) mixtures and reference solvent (H₂O) respectively and M_R and M_s are the molar mass of the pure and mixed solvent respectively. $\Delta G_t^0(i)$ and $T\Delta S_t^0(i)$ values of amino acid, DL-nor-Valine are thus obtained and presented in the Table 3. The involved uncertainties in $\Delta G_t^0(i)$ and $\Delta S_t^0(i)$ are about ±0.05 kJ·mol⁻¹ and 2.00 J·K⁻¹·mol⁻¹respectively.

Now $\Delta X_t^0(i)$ (where X=G or S) may be ascribed as the sum of the following terms

Table - 1: Values of solvent parameters (Mole % of DMSO, Wt % DMSO, Mole fraction of DMSO (z_s), water ((z_R), mean mol. Weight (M_S), density (d_s), hard sphere diameter of co-solvent (σ_s) (DMSO+H2O) and σ_{s-x} (= ½($\sigma_s + \sigma_x$)), Dipole moment of co-solvent (μ_s), and thermal expansibility (α) of the H₂O+DMSO system at 298.15 K

Wt % of DMSO	Mole fraction of DMSO(z_s)	Mole % of DMSO	Mole fraction of Water (z_R)	M_S	$10^3 d_s$ (kg·m⁻³)	σ_s (Å)	σ_{s-x} (Å)	Dipole moment of co-solvent (μ_s)	α (x 10⁻³)
0	0	0	1	18.015	0.997	0.274	0.483	1.831	0.257*
20	0.054	5.4	0.946	21.260	1.002	0.286	0.489	1.941	0.296
40	0.133	13.3	0.867	26.010	1.009	0.303	0.498	2.105	0.353
60	0.256	25.6	0.744	33.400	1.021	0.329	0.511	2.359	0.442
80	0.479	47.9	0.521	46.810	1.042	0.378	0.535	2.821	0.604
100	1.000	100	0	78.130	1.091	0.491	0.592	3.900	0.982

*reference [24]

Table - 2: Solubilities (mol·kg⁻¹) of DL-nor-Valine in aqueous mixtures of DMSO at different temperature (⁰C)

Wt % of DMSO	15⁰C	20⁰C	25⁰C	30⁰C	35⁰C
0	0.618 (0.618)[a]	0.650	0.683 (0.677)[a]	0.702	0.718 (0.715)[a]
20	0.337	0.441	0.517	0.583	0.616
40	0.305 (±0.002)[b]	0.351 (±0.002)[b]	0.376 (±0.001)[b]	0.416 (±0.002)[b]	0.502 (±0.001)[b]
60	0.243 (±0.001)[b]	0.269 (±0.001)[b]	0.290 (± 0.002)[b]	0.324 (±0.001)[b]	0.396 (±0.002)[b]
80	0.209 (±0.001)[b]	0.221	0.250 (±0.001)[b]	0.284 (±0.002)[b]	0.306 (±0.001)[b]
100	0.035	0.038	0.043	0.049	0.055

a= reference [12], b= standard deviation;

Table - 3: Coefficients a, b and c, Gibbs energies ΔG_t^0 and entropies $T\Delta S_t^0$ of transfer of DL-nor-Valine on mole fraction scale from H₂O to H₂O-DMSO mixture at 298.15 K

Wt% of DMSO	a (kJ·mol⁻¹)	b (kJ·mol⁻¹·K⁻¹)	c (kJ·mol⁻¹·K⁻¹)	$\Delta G_t^0(i)$ (kJ·mol⁻¹)	$T\Delta S_t^0(i)$ (kJ·mol⁻¹)
0	92.54	-1.9700	0.29185	0	0
20	564.23	-12.2552	1.81974	0.233	15.506
40	-183.61	4.4631	-0.67382	0.547	10.717
60	-301.37	7.1084	-1.06840	0.576	10.453
80	-64.69	1.7516	-0.26731	0.131	8.515
100	-108.25	2.7859	-0.42065	3.194	7.178

(assuming dipole induced dipole term to be negligibly small).

i.e. $\Delta X_t^0(i) = \Delta X_{t,cav}^0(i) + \Delta X_{t,d-d}^0(i) + \Delta X_{t,ch}^0(i)$ (6)

Here, $\Delta X_{t,cav}^0(i)$ indicates the transfer energy

contribution of the cavity effect which is involved due to creation of cavities for the species, Valine in H_2O and H_2O + DMSO mixed solvent system and $\Delta X_{t,d-d}^0(i)$ stands for the dipole-dipole interaction effect (computed by the used of Keesom-orientation) [24, 31] expression involving interaction between this dipolar-zwitter-ionic α-amino acids and the solvent molecules [20]. On the other hand, $\Delta X_{t,ch}^0(i)$ includes all other effects such as those arising from acid-base or short-range dispersion interaction, hydrophilic or hydrophobic hydration and structural effects etc.

Scaled particle theory (SPT) [1, 18, 25] has been applied for computation of $\Delta X_{t,cav}^0(i)$ as earlier [18], [25] assuming the solutes and solvent molecules as equivalent to hard-sphere models as are dictated by their respective diameters.(vide Table 4**)**. The involved equations are given as follow:

$$\Delta G_{cav}^0(i) = G_C + RT \ln(RT/V_S) \qquad (7)$$

$$G_C = RT[-\ln(1-Z) + \{3X/(1-Z)\}D + \{3Y/(1-Z)\}D^2$$
$$+ \{9X^2/4(1-Z)^2\}D^2]$$

$$Z = \pi N_A/6V_S(z_R\sigma_R^3 + z_s\sigma_s^3)$$

$$X = \pi N_A/6V_S(z_R\sigma_R^2 + z_s\sigma_s^2)$$

$$Y = \pi N_A/6V_S(z_R\sigma_R + z_s\sigma_s)$$

$$V_S = M_s/d_s$$

Where In this expression N_A is Avogadro's number, z_R and z_s are the mole fraction of water

and DMSO respectively. 'D', 'σ_R' and 'σ_s' are the hard sphere diameters of amino acid, water and hard sphere diameter of co-solvent respectively. 'M_s' for molar mass of the solvent and 'd_s' stands for molar density of the solvent, DMSO.

Therefore, the required $\Delta G_{t,cav}^0(i)$ represents the difference,

$$\Delta G_{t,cav}^0(i) =_s \Delta G_{t,cav}^0(i) -_R \Delta G_{t,cav}^0(i) =_s G_C -_R G_C$$
$$+ RT\ln(V_R/V_s) \qquad (8)$$

The values of $\Delta X_{t,d-d}^0(i)$ (where X= G or S) are calculated by means of the Keesom-orientation expression [24, 28] as follows:

$$\Delta G_{t,d-d}^0(i) = (_s\Delta G_{d-d}^0(i) -_R\Delta G_{d-d}^0(i)) \qquad (9)$$

and

$$\Delta S_{t,d-d}^0(i) = (_s\Delta S_{d-d}^0(i) -_R\Delta S_{d-d}^0(i)) \qquad (10)$$

For $_s\Delta G_{d-d}^0(i)$ in a solvent S, as given below

$$_s\Delta G_{d-d}^0(i) =-$$
$$(8\Pi/9)N^2\mu_s^2\mu_x^2\sigma_{s-x}^{-3}(kT)^{-1}v_s^{-1} = A/TV_s \qquad (11)$$

Where

$$A = -(8\Pi/9)N^2\mu_s^2\mu_x^2\sigma_{s-x}^{-3}(k)^{-1} \text{ and } V_s=M_s/d_s$$

and that of $\Delta S_{d-d}^0(i)$ as follows:

$$_s\Delta S_{d-d}^0(i) = -\{\delta_s\Delta G_{d-d}^0(i)/\delta T\}_p \qquad (12)$$

Table – 4: Gibbs energies of transfer $\Delta G_t^0(i)$, $\Delta G_{t,cav}^0(i)$, $\Delta G_{t,dd}^0(i)$, $\Delta G_{t,ch}^0(i)$ **and enthalpy of transfer,** $\Delta H_{t,cav}^0(i)$ **and entropies of transfer** $T\Delta S_t^0(i)$, $T\Delta S_{t,cav}^0(i)$, $T\Delta S_{t,dd}^0(i)$ **and** $T\Delta S_{t,ch}^0(i)$ **of DL-nor-Valine from H_2O to H_2O-DMSO at 298.15 K (on mole fraction scale) in kJ·mol⁻¹.**

Wt% of DMSO	$\Delta G_t^0(i)$ (kJ·mol⁻¹)	$\Delta G_{t,cav}^0(i)$ (J·mol⁻¹)	$\Delta G_{t,dd}^0(i)$ (kJ·mol⁻¹)	$\Delta G_{t,ch}^0(i)$ (kJ·mol⁻¹)	$T\Delta S_t^0(i)$ (kJ·mol⁻¹)	$\Delta H_{t,cav}^0(i)$ (kJ·mol⁻¹)	$T\Delta S_{t,cav}^0(i)$ (kJ·mol⁻¹)	$T\Delta S_{t,dd}^0(i)$ (kJ·mol⁻¹)	$T\Delta S_{t,ch}^0(i)$ (kJ·mol⁻¹)
0	0	0	0	0	0	0	0	0	0
20	0.233	-1.650	0.407	1.481	15.506	-1.181	0.469	0.382	14.655
40	0.547	-3.320	1.820	2.047	10.717	-1.984	1.336	1.670	7.711
60	0.576	-5.031	4.470	1.137	10.453	-2.276	2.755	3.961	3.739
80	0.131	-6.860	8.680	-1.689	8.515	-1.198	5.662	7.230	-4.377
100	3.194	-7.951	14.501	-3.356	7.178	18.263	26.214	10.500	-29.535

The required diameter and other solvent parameters of H_2O and DMSO mixtures are taken from Ref. [24].The required diameter of DL-nor-Valine is 6.92 Å as given in Ref.[6, 22, 26]. Dipole-moment value of DL-nor-Valine is 16D [31].

i.e. $T_s \Delta S_{d-d}^0(i) =_s \Delta G_{d-d}^0(i)[1+T\alpha]$, where N stands for Avogadro's number, μ_s, μ_x are the dipole moment of co-solvents and amino acid molecules respectively (Table 4).

σ_{s-x} is the distance at which the attractive and repulsive interactions between the solvent and solute molecules are equal and is generally equal to ½($\sigma_s + \sigma_x$) where σ_s and σ_x are the hard sphere diameter of co-solvent and solute molecules respectively (Table 3) and α is the isothermal expansibility of the solvent and given by $(\delta \ln V_s / \delta T)_P = -(\delta \ln d_s / \delta T)$. Following Marcus [24] and Kim *et al.* [22] in order to get this $\Delta X_{t,d-d}^0(i)$ term on mole fraction scale the quantity is again multiplied by the term Z_{s1}.

$$Z_{s1} = Z_s(\mu_s / \sigma_s^3)/(\mu_R / \sigma_R^3) \qquad (13)$$

which is the real mole fraction contribution for dipole-dipole interaction [21]. Subtraction of $\Delta X_{t,cav}^0(i)$ and $\Delta X_{t,d-d}^0(i)$ from the total we can get $\Delta X_{t,ch}^0(i)$ of amino acid, valine. The values of $\Delta X_{t,cav}^0(i)$, $\Delta X_{t,d-d}^0(i)$ and $\Delta X_{t,ch}^0(i)$ are presented in Table 4.

3.2. Analysis of solubility data

Experimental results for the solubility of DL-nor-Valine in aqueous mixtures of Dimethylsulphoxide were not previously reported in the literature but have been measured and presented in this work [Table 2]. The solubility values of DL-nor-Valine increases with increasing temperature in a particular composition of aqua-organic mixed solvent system but with the increased concentration of DMSO solubility values decreased.

3.3. Interactions involved between DL-nor-valine and solvent mixtures

In this work we have reported different types of interactions involved between solute and solvent molecules and presented these by graphically to signify more clearly. Here figure 1 represents the variation of $\Delta G_t^0(i)$ for amino acid DL-nor-Valine against the mole % of DMSO at 298.15 K.

Figure shows a complicated nature. Here, $\Delta G_t^0(i)$ is actually composed of $\Delta G_{t,cav}^0(i)$, $\Delta G_{t,d-d}^0(i)$ and $\Delta G_{t,ch}^0(i)$. [$\Delta G_{t,d-id}^0(i)$ i.e. free energy change due to dipole-induced dipole

interaction, it is considered negligible]. The positive increment of $\Delta G_t^0(i)$ values (with a slight distortion at about 30 to 40 mole % of DMSO) indicates that DL-nor-Valine will be destabilized with the increased concentration of DMSO in aqueous-DMSO system. The $\Delta G_{t,cav}^0(i)$, values are gradually decreased with DMSO concentration (Table 4) which indicates that DL-nor-Valine should easily be accommodated in DMSO than H_2O with release of concerned energy due to the greater size of DMSO (0.491Å) than H_2O (0.274 Å) [24].
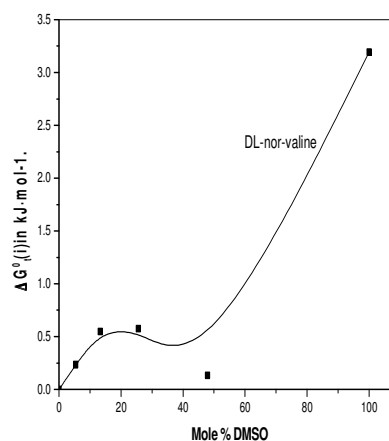

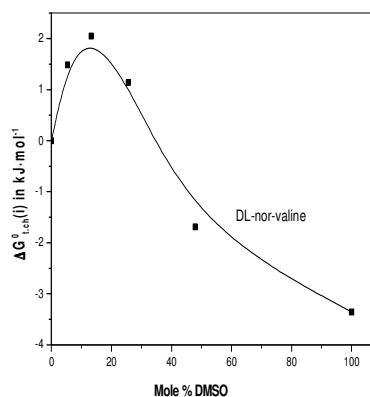Figure -1: Variation of $\Delta G_t^0(i)$ of DL-nor-valine in kJ·mol⁻¹ in aqueous mixtures of DMSO at 298.15K

Figure -2: Variation of $\Delta G_{t,ch}^0(i)$ of DL-nor-valine in in kJ·mol⁻¹ in aqueous mixtures of DMSO at 298.15K

On the other hand $\Delta G_{t,d-d}^0(i)$ (Table 4) values are increased gradually with increased mole % of DMSO. The dipole moment of DMSO (3.90D) [24, 29] is greater than H_2O (1.83D) but the involved hard sphere diameter difference of DMSO and H_2O supports such variation.

$\Delta G_{t,ch}^0(i)$ values for the solute DL-nor-Valine have computed after subtraction of $\Delta G_{t,cav}^0(i)$ (estimated by the scaled particle

theory) $\Delta G^0_{t,d-d}(i)$ from $\Delta G^0_t(i)$. $\Delta G^0_{t,ch}(i)$ involves the chemical interaction (i.e. H-bonding, acid-base, hard-soft, dispersion, hydrophilic hydration and hydrophobic hydration etc.) between solute (DL-nor-Valine) and solvent molecules in this system. Figure 2 represents the variation of $\Delta G^0_{t,ch}(i)$ with DMSO concentration.

The $\Delta G^0_{t,ch}(i)$ value increases up to around 15 mole % of DMSO in the H₂O-DMSO system. This indicates the destabilization of DL-nor-Valine. This occurs due to the breaking of extensive hydrogen bond between protic water and hydrophilic head of amino acid with the introduction of larger dipolar aprotic DMSO in water. After that the gradual stabilization of Valine occurs with the sharp decrement of $\Delta G^0_{t,ch}(i)$ values with DMSO concentration. Here hydrogen bonding capacity of DMSO is weaker than water. This factor will destabilize Valine with the increased concentration of DMSO. But the greater size of DMSO (0.491 Å) [24, 29] introduces very strongly the soft-soft as well as dispersion interaction among DMSO and larger amino acid, DL-nor-Valine [i.e. CH₃-CH₂-CH₂-CH (NH₃⁺)(COO⁻)] having larger R=-CH₂- CH₂-CH₃. Here it is important to note that in higher concentration of DMSO in aqueous co-solvent system the association of the solvents molecules (i.e. between water and DMSO molecules in 1:2 ratios) [31-33] [Diagram C] and the self association of DMSO [Diagram A] occurs extensively which may take part in dispersion interaction with larger DL-nor-Valine molecules.

The hydrophilic as well as hydrophobic hydration interactions are gradually reduced with decreased concentration of H₂O in aqueous DMSO mixtures. This factor may destabilize DL-nor-Valine in aqueous DMSO system. But the increased dispersion interaction may play more dominating role over the reduced acid-base, H-bonding, hydrophilic and hydrophobic interaction involved between amino acid and DMSO in aqueous DMSO mixtures compared to the reference solvent, H₂O.

3.4. Role of DL-nor-Valine for controlling solvent-solvent interactions in aqueous dimethylsulphoxide

Figure 3 represents the variation of $T\Delta S^0_t(i)$, of valine against mole % of DMSO in aqueous DMSO.

Like $\Delta G^0_t(i)$, $T\Delta S^0_t(i)$ is composed of cavity, dipole-dipole and chemical interaction effects i.e.

$$T\Delta S^0_t(i) = T\Delta S^0_{t,cav}(i) + T\Delta S^0_{t,d-d}(i) + T\Delta S^0_{t,ch}(i)$$

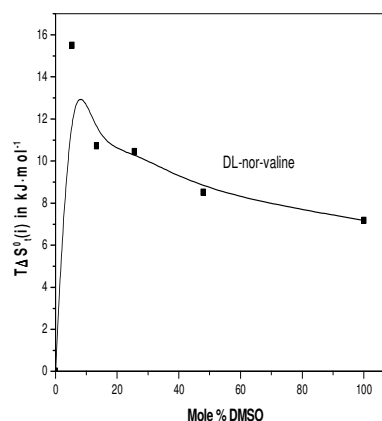Now combined effect in $T\Delta S^0_t(i)$ value may represents such behavior as shown in Figure-3.

Figure -3: Variation of TΔS⁰ₜ(i) in kJ·mol⁻¹ of DL-nor-valine in aqueous mixtures of DMSO at 298.15K

$T\Delta S^0_{t,cav}(i)$ values (Table 4) are gradually increased with the mole % DMSO. This indicates that in presence of DL-nor-valine the co-solvent (DMSO) and reference solvent (H₂O) become separated. With the increased DMSO concentrations the water molecule becomes free from amino acid to allow it to be accommodated by DMSO. $T\Delta S^0_{t,d-d}(i)$ values (Table 4) are also gradually increased with the DMSO concentration. Here with the increased concentration of DMSO the dipolar amino acid DL-nor-Valine become less associated with dipolar co-solvent due to the larger size of DMSO (0.491 Å) [24, 30] and therefore DL-nor-Valine allow water as well as DMSO molecules to be more free as the concentrations of DMSO gradually increased.

$T\Delta S^0_{t,ch}(i)$ values are determined after subtraction of $T\Delta S^0_{t,cav}(i)$ and $T\Delta S^0_{t,d-d}(i)$ from $T\Delta S^0_t(i)$. Figure 4 represents the variation of $T\Delta S^0_{t,ch}(i)$ of DL-nor-Valine with increased DMSO concentration in aqueous DMSO mixture at 298.15 K. The nature of the curve with mole % DMSO indicates that the adopted 3-D structure of water due to its extensive intermolecular hydrogen bonding (Diagram B.) is broken due to introduction of DMSO at its lower concentration.

With increase of DMSO concentration from 10 to 100 mole % the $T\Delta S^0_{t,ch}(i)$ values are decreased sharply. This indicate that the large sized amino acid DL-nor-Valine induces the

solvent molecules to be associated (i.e. between water and DMSO molecules) (Diagram C.) and dimerised of the dipolar aprotic DMSO [32-33] molecules also at its higher concentration (Diagram A.).

(A)   **(B)**
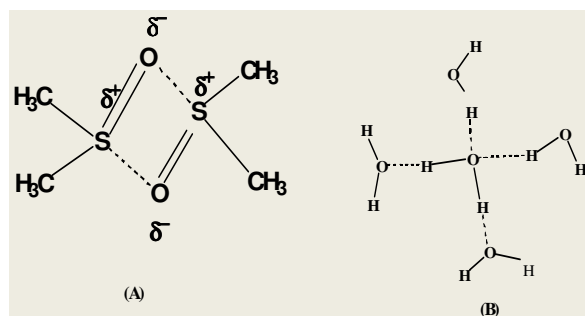
Here the α-amino acid DL-nor-Valine also induces the hydrophilic hydration and hydrophobic hydration to be decreased with the increased DMSO concentration.

(C)

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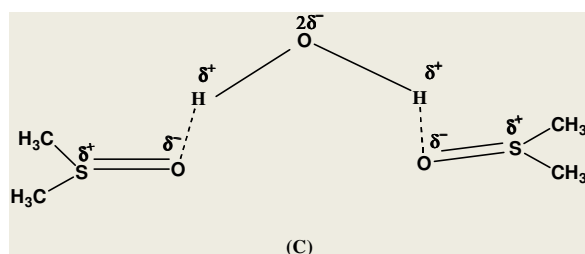
Hence the solute induced dispersion interaction among large size DMSO molecules being the predominant factor over others. The overall decrement of $T\Delta S^0_{t,ch}(i)$ values occur throughout the higher concentration of DMSO in this aqueous DMSO mixed solvent system
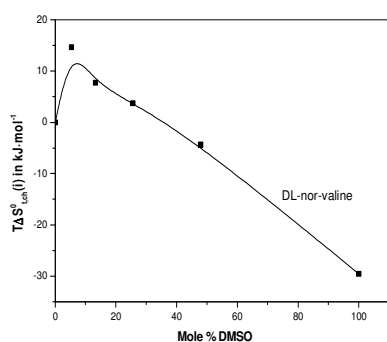

Figure -4: Variation of $T\Delta S^0_{t,ch}(i)$ in kJ·mol^{-1} of DL-nor-valine in aqueous mixtures of DMSO at 298.15K

4. CONCLUSION

Experimental results for solubility values of DL-nor-Valine decreased with the increased concentration of DMSO. Here also observed that due to chemical interactions the larger DL-nor-Valine will be stabilized in comparatively larger co-solvent DMSO, with dipolar aprotic character.

The zwitterionic amino acid valine induces to adopt 3-D-structuredness of water at water rich region in aqueous DMSO solvent system. Valine induces DMSO to be dimerised mainly through dispersion interaction in the DMSO rich region of this mixed solvent system.

5. REFERENCES

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