Electrical Conductivity Studies of 1-Butyl-3-methylimidazolium Salicylate as an Active Pharmaceutical Ingredient Ionic Liquid (API-IL) in Aqueous Amino Acids Solutions

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The molar conductivity data of 1-butyl-3-methylimidazolium salicylate, [BMIm][Sal], as an active pharmaceutical ingredient ionic liquid (API-IL) have been determined in water and aqueous solutions of amino acids, glycine and L-alanine at T = (288.15-318.15) K. The molar conductivity data were analyzed by low concentration Chemical Model (lcCM) and limiting molar conductivities (Λ_0), ion association constants (K_A) and standard Gibbs energies (ΔG_A°) of the ion association process were calculated. The obtained values of Λ_0 and K_A decrease with increase in the amino acid concentration. Moreover, the values of Λ_0 increase from glycine to L-alanine solutions due to the stronger solvation of the [BMIm][Sal] ions by (COO$^-$/NH$_3^+$) zwitterionic centers of glycine compared to L-alanine but this trend is vice versa for K_A. The more negative values of (ΔG_A°) for [BMIm][Sal] in glycine compared to L-alanine solutions is indicative of the high degree of spontaneity and more feasibility of the association process in this amino acid.

Keywords: 1-Butyl-3-methylimidazolium salicylate, Molar conductivity, Low concentration Chemical Model, Amino acids

INTRODUCTION

The ionic liquids (ILs) are much considered in various sciences due to their unique properties such as low vapor pressure, thermal stability, inflammability, high ion conductivity, and wide liquid range. The properties of this class of electrolytes can be modulated by appropriate selection of cation and anion [1,2]. Salicylic acid is one of the active pharmaceutical ingredients with poor water solubility (2 g l^{-1} at 20 °C) and many applications in skin care products for the treatment of acne and food preservative and antiseptic in toothpaste.

Recently, third generation of ionic liquids or active pharmaceutical ingredients in the ionic liquids forms (API-ILs) have been prepared by the combination of conventional ionic liquid and active pharmaceutical ingredient (API). These API-ILs present excellent properties, such as improved stability, high solubility, and enhanced

permeability compared to the corresponding solid pharmaceutical forms [3]. Pinto et al. [4] reported several API-ILs containing salicylate anion (especially 1-ethyl-3-methyl-imidazolium salicylate) strongly bound to human albumin serum which have the ability to form micelle (increased bioavailability). The information about the thermodynamic and transport properties of this class of ionic liquids in the presence of biomolecules (protein, enzyme, and hormone) are required in optimization and controlling of biotechnological processes [5,6]. Direct study of proteins is difficult due to their complex structure, so, the simple models such as amino acids is a useful approach.

In recent years, some references reported the thermodynamic properties of the mixtures containing amino acid (or drug) and the first generation of ionic liquid in aqueous media at different temperatures through the volumetric, viscometric, compressibility and conductrometric properties [7-10]. For the first time, Shekaari *et al.* [11-15] have examined the effect of the

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active pharmaceutical ingredients in the ionic liquids form (API-ILs), 1-butyl (or 1-hexyl or 1-octyl)-3-methylimidazolium salicylate and 1-butyl (or 1-octyl)-3-methyl-imidazolium ibuprofenate on the thermodynamic properties of aqueous mixtures of amino acids, glycine, and L-alanine. Results show that the ion-polar and polar-polar interactions between the amino acid and API-IL are predominant.

The present work is a continuation of our systematic thermodynamic studies of the ternary mixtures of (amino acid + API-IL + water) [11-15] and (drug + ionic liquid + water) [16]. In this study, the molar conductivities of 1-butyl-3-methylimidazolium salicylate, [BMIm][Sal] in water and aqueous solutions of glycine and L-alanine are determined at T = 288.15-318.15 K. Initial estimation of molar conductivities (Λ_0) and ion association constants (K_A) are estimated using Onsager equation. Low concentration Chemical Model (lcCM) is applied to calculate the limiting molar conductivities (Λ_0) and ion association constants (K_A). The estimated K_A values have been used to calculate the evaluate thermodynamic functions (ΔG_A°, ΔS_A° and ΔH_A°).

EXPERIMENTAL TECHNIQUES

Materials

Table 1 presents the origin, CAS number, purity, and analysis methods used in the purity determination. The double distilled deionized water had the specific conductivity less than (1 μs cm^{-1}) at T = 298.15.

Synthesis of Ionic Liquid

The [BMIm][Sal] was synthesized and purified according to standard procedures described in our previous work [13]. The ionic liquid was analyzed by ^{1}H NMR spectra (see Fig. 1) verifying the absence of any significant impurity [17,18].

Apparatus and Procedure

The values of density, viscosity and relative permittivity used in the calculations were taken from our previous work [12,13]. The conductivity meter (Metrohm model 712, Switzerland) was used to measure the specific electrical conductivities, κ and evaluated repeatability by this apparatus is approximately 0.1 μs cm^{-1}. Calibration of the cell constant was performed by repeated measurements of

KCl solution in 0.01 mol kg^{-1}. After calibration of the instrument, 60 ml of solvent was filled into the conductivity cell and argon was blown through the solution and κ value was recorded. Then one drop of API-IL weighted by an analytical balance (AND, GR202, Japan) with a precision of $\pm 1 \times 10^{-8}$ kg was added to the solvent present in the conductivity cell. The resulting solution was stirred continuously with a magnetic stirrer. Then the κ value was recorded again and next weighted drop was added and κ was read and this process was continued. The temperature was controlled by water circulated around the cell with double walls and temperature uncertainty was ±0.02 K.

Data Analysis

Low concentration Chemical Model (lcCM). The Onsager model was used to evaluate the limiting molar conductivity Λ_0 and ion association constant K_A. Then, the low concentration Chemical Model (lcCM) equation was used to calculate the limiting molar conductivity (Λ_0) and ion association constant K_A of the studied solutions containing the API-IL using the following set equations [12,16,24]:

$$\Lambda = \alpha[\Lambda_0 - S(c\alpha)^{1/2} + Ec\alpha \ln(c\alpha) + J_1 c\alpha + J_2(c\alpha)^{3/2}] \quad (1)$$

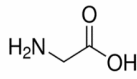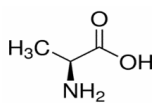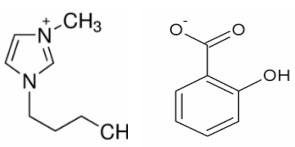$$K_A = \frac{1-\alpha}{\alpha^2 c \gamma_\pm^2} \quad (2)$$

$$\ln \gamma_\pm = \frac{\kappa q}{1+\kappa R} \quad (3)$$

$$\kappa^2 = \frac{16000 N_A z^2 e^2 \alpha c}{\varepsilon_0 \varepsilon k_B T} \quad (4)$$

$$q = \frac{z_+ z_- e^2}{8\pi\varepsilon_0 \varepsilon kT} \quad (5)$$

in which, Λ_0 is the molar conductivity at infinite dilution, $(1 - \alpha)$ is the fraction of oppositely charged ions acting as ion pairs, $\gamma_\pm$ is the corresponding mean activity coefficient of the free ions, κ is the Debye parameter, e is the electronic charge, z is the ionic charge, ε_0 is the permittivity of vacuum, ε is the dielectric constant of the solvent, and the other symbols have their usual meanings. The required

Table 1. Descriptions of the Chemicals Used

Chemical name	CAS No.	Supplier	Mass fraction purity	Structure	Purification method	Analysis method
Glycine	56-40-6	Loba-Chemie	0.99		None	
L-Alanine	56-41-7	Merck	>0.99		None	
[BMIm][Sal]	This work	Synthesized	0.98		Rotary/ evaporator and vacuum	^{1}H NMR
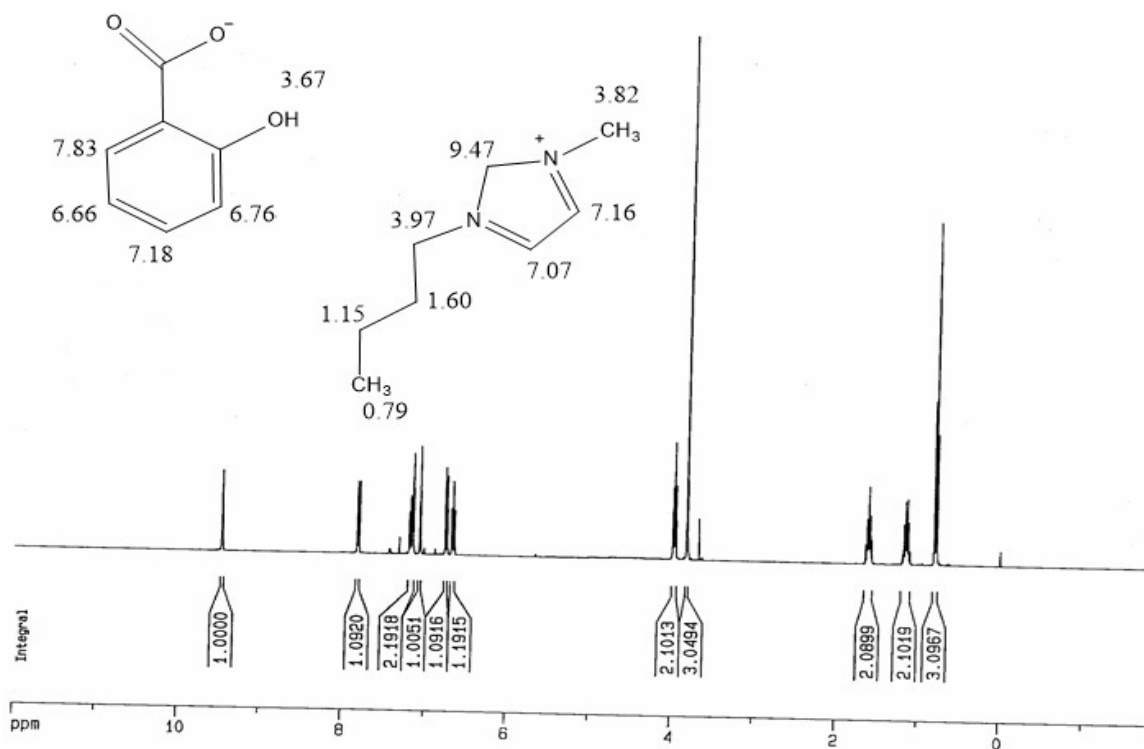
Fig. 1. ^{1}H NMR spectrum (CDCl$_3$, 400 MHz) of [BMIm][Sal].

Table 2. The Molar Conductivity (Λ) Values of [BMIm][Sal] in Water and Aqueous Solutions of Glycine as a Function of [BMIm][Sal] Concentration at T = (288.15-318.15) K and 0.087 MPa[a]

c (mol m^{-3})[b]	$10^4\Lambda$ (s m^2 mol^{-1})	c (mol m^{-3})	$10^4\Lambda$ (s m^2 mol^{-1})	c (mol m^{-3})	$10^4\Lambda$ (s m^2 mol^{-1})	c (mol m^{-3})	$10^4\Lambda$ (s m^2 mol^{-1})
T = 288.15 K		T = 298.15 K		T = 308.15 K		T = 318.15 K	
[BMIm][Sal] in water							
0.2367	66.85	0.1799	83.48	0.1599	102.44	0.1800	119.26
0.5043	65.67	0.3751	82.22	0.3405	100.77	0.4577	116.82
0.6998	65.11	0.5807	81.02	0.5623	98.69	0.7251	114.36
0.9365	64.45	0.7760	79.89	0.7274	97.52	0.9462	112.69
1.2093	63.64	0.9764	79.02	0.9286	96.22	1.1931	111.02
1.4511	63.12	1.2025	78.01	1.1143	95.14	1.4399	109.12
1.6467	62.65	1.5314	76.53	1.3052	94.22	1.6970	107.32
1.8782	62.07	1.7318	75.79	1.5270	93.10	1.9182	105.97
2.1150	61.50	1.9014	75.15	1.7024	92.20	2.1753	104.51
2.3362	61.08			1.9345	91.45	2.4221	103.21
2.6038	60.54					2.6638	101.89
2.8302	60.11						
$^c m_{Gly}$ = 0.1001 mol kg^{-1}							
0.1812	64.29	0.2544	77.05	0.2639	96.65	0.2384	114.76
0.3727	63.49	0.5190	76.24	0.5431	95.45	0.4819	113.10
0.6729	62.15	0.8040	75.22	0.7816	94.35	0.7051	111.68
0.8851	61.33	1.0534	74.49	0.9897	93.69	0.9689	110.06
1.1439	60.34	1.3383	73.60	1.2283	92.75	1.1972	108.70
1.3820	59.52	1.5928	72.85	1.4771	91.87	1.4153	107.88
1.6045	58.77	1.8593	72.24	1.7460	90.90	1.5675	107.28
1.8737	58.01	2.0501	71.73	2.0123	90.21	1.7044	106.78
2.1324	57.32	2.2462	71.37	2.3120	89.38	1.8523	106.09
2.3188	56.80						

Table 2. Continued

$m_{Gly} = 0.3026$ mol kg^{-1}							
0.2034	60.67	0.2129	72.83	0.2521	87.17	0.2380	100.52
0.4628	60.17	0.4614	71.93	0.4789	86.33	0.4406	99.23
0.7120	59.73	0.6540	71.27	0.6957	85.50	0.6381	97.91
0.9968	59.31	0.9481	70.49	0.9327	84.80	0.8863	96.54
1.2103	59.01	1.2675	69.70	1.1646	84.13	1.0838	95.52
1.4290	58.70	1.5160	69.11	1.3965	83.50	1.3067	94.19
1.6630	58.36	1.7644	68.45	1.6284	82.80	1.6541	92.58
1.9020	58.02	2.0077	67.86	1.9284	82.02	1.9263	91.53
2.1257	57.74	2.2562	67.35	2.2284	81.30	2.1212	90.95
2.3292	57.48						
2.5580	57.26						
$m_{Gly} = 0.5011$ mol kg^{-1}							
0.2312	56.67	0.2021	68.88	0.2421	84.21	0.2144	96.32
0.4875	56.17	0.4684	67.49	0.4595	82.99	0.4488	95.00
0.7338	55.73	0.6903	66.47	0.6621	82.16	0.6582	93.73
0.9851	55.41	0.9171	65.45	0.8844	81.40	0.8626	92.83
1.2163	55.03	1.1389	64.49	1.0722	80.69	1.0421	92.12
1.4626	54.70	1.4249	63.43	1.3192	79.95	1.2421	91.18
1.6887	54.42	1.6270	62.79	1.5613	79.07	1.4431	90.38
1.8747	54.16	1.8440	62.09	1.8034	78.33	1.6411	89.65
2.1562	53.86			2.0405	77.68		
2.4276	53.58						

[a]Standard uncertainties u are: u (Λ) = 1 × 10^{-6} s m^2 mol^{-1} and u (T) = 0.01 K. [b]Relative standard uncertainties u$_r$ for molarities of AP-IL is u$_r$ (c) = 0.004 and amino acid is u$_r$ (m) = 0.005.

coefficients E, J_1 and J_2 for calculations were taken from the literature [19]. The parameter R represents the center-to-center distance between the ions in the ion pairs formed in the solutions. To calculate the Λ_0, K_A and R the evaluated parameters from Onsager equation as well as initial guess for R were considered as input correlation coefficients and the output obtained was used as input value. This process was repeated until the input and output coefficients become equal and minimum standard deviation was obtained.

RESULTS AND DISCUSSION

Limiting Molar Conductivity

The values of molar conductivity, Λ_0 of [BMIm][Sal] in (0.0, 0.1, 0.3 and 0.5) mol kg^{-1} of aqueous solutions of amino acid over the temperature range of (288.15-318.15) K were calculated by the relation $\Lambda = 1000\kappa/c$, as presented in Tables 2 and 3.

Moreover, dependency of the molar conductivities, Λ, to the square root of the concentration, $\sqrt{c}$, of [BMIm][Sal] in several molalities of amino acids in water is shown in Fig. 2. The limiting values of molar conductivities, Λ_0, for the studied solutions estimated by the lcCM model, Λ_0, are listed in Table 4.

It is evident that the Λ and Λ_0 values of [BMIm][Sal] decrease with increase in the amino acid concentration. These lower values indicate the low mobility of the solvated ions by (COO$^-$/NH$_3^+$) zwitterionic centers with large radii and increase the viscosity of medium with addition of the amino acid. The lower values of Λ and Λ_0 in the solutions of glycine relative to L-alanine suggest the strong solvation of the ions of [BMIm][Sal] by (COO$^-$/NH$_3^+$) zwitterions centers of amino acid due to the less hydrophobicity of this amino acid [14,15]. Figure 3 presents the values of the molar conductivity for [BMIm][Sal] in aqueous solutions of L-alanine with 0.30 molality at experimental temperatures. Moreover, Fig. 4 shows the molar conductivities, Λ, of [BMIm][Sal] in the aqueous solutions of glycine and L-alanine with 0.1 molality at 298.15 K.

The possible reasons are that (i) the solvent viscosities reduce with increase in temperature, and (ii) the solvated ions move faster in higher temperature [20]. Comparison of the Λ and Λ_0 with similar API-IL, [BMIm][Ibu] in the reference [12] shows that these values for [BMIm][Sal] are larger than [BMIm][Ibu] which may be due to the low mobility of the salicylate anion relative to the ibuprofenate.

To exclude the influence of the viscosity on the ionic mobility, Walden product, as a helpful tool to explain the ionic interactions, have been estimated. The conductivity of the ions at infinite dilution depends only on their mobility. Therefore, it is supposed that the product of ion conductivity by the viscosity of the medium is independent of the solvent nature. A constant Walden product of solutions with several concentrations shows that the radius

of the ions remains unchanged and variation in the values of $\Lambda_0\eta_0$ suggests the change in the ionic radii and ions mobility [21]. The smaller amounts of $\Lambda_0\eta_0$ in the aqueous solutions of amino acid may be related to large effective radius (due to the high association of API-IL) compared to this value in water [12]. The calculated values of Walden product ($\Lambda_0\eta_0$) for [BMIm][Sal] in the aqueous solutions of amino acid are listed in Table 4. Besides, the obtained values of ($\Lambda_0\eta_0$) for [BMIm][Sal] in water and aqueous solutions of glycine and L-alanine with 0.5 molalities were compared in Fig. 5. It is clear that at a fixed temperature, the values of Walden product decrease with amino acid concentration. It explains the preferential solvation of the ions by zwitterions of amino acids and low mobility of the ions with large hydrodynamic radii.

In addition, the $\Lambda_0\eta$ values of [BMIm][Sal] in water and aqueous solutions of amino acid compared to those of [BMIm][Ibu] in the reference [12] are lower which may be due to the high mobility of salicylate anion compared to the ibuprofenate.

The standard deviations of the calculated molar conductivities (Λ) and the experimental ones (Λ_{cal}) were calculated as follows:

$$\sigma(\Lambda) = \left[\frac{\sum (\Lambda - \Lambda_{cal})^2}{n - p} \right]^{\frac{1}{2}}$$

where n and p show the number of experimental data and parameters, respectively. The calculated standard deviations of electrical conductivity using lcCM are presented in Table 4.

Ion Association Constant

The ion association constant (K_A) values of [BMIm][Sal] in water and aqueous solutions of glycine and L-alanine estimated using the lcCM model are listed in Table 4. As observed in this table, the K_A values of [BMIm][Sal] decrease by the amino acid concentration increment. In the concentrated solutions, the powerful interactions between the ions and zwitterions reduce the ion-pair formation. The important hydration of the ions originated from dissociation of API-IL induces the release of water molecules from hydration shell of amino acid. The
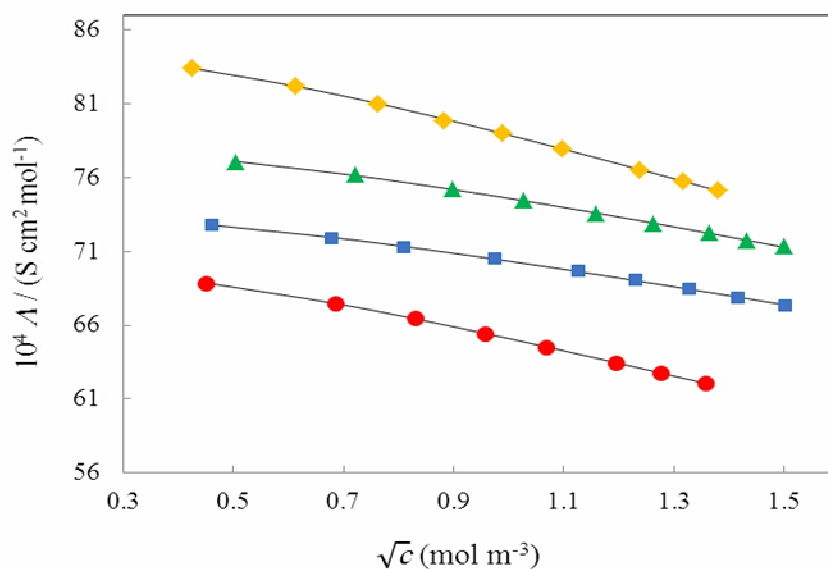
Table 3. The Molar Conductivities (Λ) of [BMIm][Sal] in Water and Aqueous Solutions of L-Alanine as a Function of [BMIm][Sal] Concentration at $T = (288.15\text{-}318.15)$ K and 0.087 MPa[a]

c[b] (mol m^{-3})	$10^4\Lambda$ (s m^2 mol^{-1})	c (mol m^{-3})	$10^4\Lambda$ (s m^2 mol^{-1})	c (mol m^{-3})	$10^4\Lambda$ (s m^2 mol^{-1})	c (mol m^{-3})	$10^4\Lambda$ (s m^2 mol^{-1})
$T = 288.15$ K		$T = 298.15$ K		$T = 308.15$ K		$T = 318.15$ K	
			$^{c}m_{Ala} = 0.9998$ mol kg^{-1}				
0.2906	64.03	0.2189	80.89	0.2289	98.84	0.2286	117.47
0.5812	62.21	0.4328	79.64	0.4883	96.93	0.4878	115.00
0.8819	60.56	0.6721	78.12	0.7426	95.50	0.6961	113.26
1.1266	59.22	0.9368	76.90	0.9715	94.40	0.9755	111.50
1.3611	58.16	1.1710	75.95	1.2513	93.23	1.2092	110.07
1.6721	57.14	1.4154	74.99	1.5311	92.08	1.4480	108.65
1.9219	56.53	1.6649	74.12	1.8108	90.80	1.7021	107.16
2.2125	55.63	1.8991	73.13	2.1567	89.52	2.0342	105.59
2.4419	55.10	2.0925	72.49	2.4619	88.56	2.3123	104.33
2.7579	54.09	2.3675	71.55				
3.0077	53.63						
3.2728	53.01						
			$m_{Ala} = 0.3021$ mol kg^{-1}				
0.1823	60.57	0.2094	75.38	0.2680	87.62	0.2142	101.72
0.4103	59.47	0.4437	73.88	0.5411	85.64	0.4184	99.52
0.5926	58.68	0.6830	72.34	0.8192	84.23	0.6077	97.52
0.7800	57.78	0.9422	71.12	1.0771	82.97	0.8319	95.43
0.9877	56.93	1.2115	69.93	1.3704	81.73	1.0560	93.59
1.1751	56.14	1.4458	69.12	1.6435	80.60	1.2603	91.89
1.3524	55.46	1.6751	68.15	1.9267	79.50	1.4496	90.52
1.5347	54.89	1.9493	67.21	2.2048	78.42	1.6534	89.11
1.7123	54.33	2.2185	66.39	2.4521	77.65	1.8736	88.09
		2.4329	65.78				

Table 3. Continued

				$m_{Ala} = 0.4996$ mol kg^{-1}				
0.2634	55.67	0.2457	70.00	0.2421	86.80	0.2328	101.33
0.5317	54.00	0.4864	68.50	0.4595	85.89	0.4805	99.52
0.7504	52.89	0.7472	66.91	0.6621	85.01	0.7530	98.13
0.9789	52.00	1.0431	65.22	0.8844	84.20	1.0057	96.86
1.2274	51.00	1.3389	63.80	1.0722	83.59	1.2385	95.71
1.5007	50.18	1.5847	62.75	1.3192	82.75	1.4713	94.68
1.8038	49.29	1.8454	61.99	1.5613	82.01	1.7587	93.47
2.1020	48.64	2.1714	60.89	1.8034	81.33	1.9453	92.89
2.3405	48.14	2.4071	60.22	2.0405	80.74	2.2134	91.91
2.6089	47.55	2.6528	59.65				

[a]Standard uncertainties u are: u $(\Lambda) = 1 \times 10^{-6}$ s m^2 mol^{-1} and u $(T) = 0.01$ K. [b]Relative standard uncertainties u$_r$ for molarities of AP-IL is u$_r$ $(c) = 0.004$ and amino acid is u$_r$ $(m) = 0.005$. [c]m_{Ala} is the molal concentration of L-alanine in water.

Fig. 2. The molar conductivities, Λ, against the square root of the molarities, $\sqrt{c}$, for [BMIm][Sal] in water (♦) and (glycine + water) with 0.1 (▲), 0.3 (■) and 0.5 (●) molality at 298.15 K.

Table 4. The Limiting Molar Conductivities (Λ_0), Walden Products ($\Lambda_0\eta$), Ion Association Constants (K_A), Distance Parameters (R), and Standard Deviations ($\sigma(\Lambda)$) of [BMIm][Sal] in Water and (Glycine + Water) and (L-Alanine + Water) Solutions at $T = (288.15\text{-}318.15)$ K and 0.087 MPa[a]

T	K_A	$10^4\Lambda$	$10^{104}R$	σ	$10^4\lambda_0^{ion}\eta$
(K)	(dm^3 mol^{-1})[a]	(s m^2 mol^{-1})[a]	m	(Λ)	(s m^2 mol^{-1} mPa s)
		[BMIm] [Sal] in water			
288.15	36.35	67.72 ± 0.04	33.14	0.04	76.53
298.15	61.54	84.76 ± 0.03	33.10	0.06	75.26
308.15	70.76	103.68 ± 0.16	32.77	0.27	74.64
318.15	91.12	121.83 ± 0.12	27.20	0.20	73.95
		[b]$m_{Gly} = 0.1001$ mol kg^{-1}			
288.15	36.83	65.40 ± 0.03	40.23	0.04	72.82
298.15	51.12	78.20 ± 0.04	12.74	0.07	72.26
308.15	51.42	98.15 ± 0.04	20.79	0.07	71.65
318.15	54.93	116.75 ± 0.08	31.78	0.14	71.57
		$m_{Gly} = 0.3026$ mol kg^{-1}			
288.15	29.81	61.13 ± 0.01	19.59	0.02	71.95
298.15	43.28	73.68 ± 0.04	26.38	0.06	69.99
308.15	45.53	88.28 ± 0.02	17.59	0.04	66.12
318.15	53.22	102.62 ± 0.07	36.08	0.11	65.47
		$m_{Gly} = 0.5001$ mol kg^{-1}			
288.15	17.01	57.21 ± 0.01	31.98	0.02	69.11
298.15	38.60	70.15 ± 0.02	40.74	0.04	69.03
308.15	39.87	85.48 ± 0.05	34.15	0.08	65.82
318.15	42.92	97.87 ± 0.04	35.96	0.07	64.89
		[c]$m_{Ala} = 0.9998$ mol kg^{-1}			
288.15	34.87	65.44 ± 0.18	43.89	0.03	75.91
298.15	47.69	82.39 ± 0.06	38.06	0.10	74.97
308.15	48.67	100.48 ± 0.07	35.53	0.12	74.16
318.15	51.52	119.86 ± 0.07	39.51	0.11	73.49

Table 4. Continued

		$m_{Ala} = 0.3021$ mol kg^{-1}			
28.15	29.41	61.71 ± 0.03	43.62	0.06	75.41
298.15	38.67	76.64 ± 0.09	41.19	0.14	73.19
308.15	42.07	89.50 ± 0.06	39.56	0.10	60.33
318.15	49.89	104.60 ± 0.08	47.38	0.13	67.89
		$m_{Ala} = 0.4996$ mol kg^{-1}			
288.15	16.42	56.58 ± 0.18	45.91	0.29	72.76
298.15	31.14	71.57 ± 0.15	44.97	0.24	71.64
308.15	35.73	88.12 ± 0.02	33.81	0.29	71.29
318.15	40.22	103.12 ± 0.05	38.16	0.08	70.64

[a]The estimated uncertainties for u $(K_A) = 0.2$ dm^3 mol^{-1}, u $(10^4 \Lambda_0) = 0.04$ s m^2 mol^{-1} and u $(T) = 0.01$ K.
[b]m_{Gly} is the molal concentration of glycine in water. [c]m_{Ala} is the molal concentration of L-alanine in water.
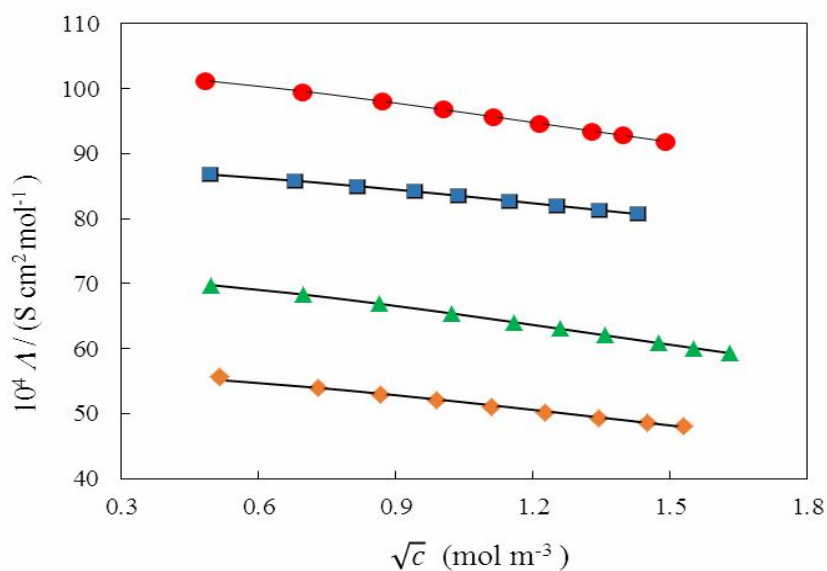
Fig. 3. The molar conductivities, Λ, against the square root of the molarities, $\sqrt{c}$, for [BMIm][Sal] in the (L-alanine + water) solutions with 0.5 molality at $T = 288.15$ K (●), 298.15 K (■), 308.15 K (▲) and 318.15 K (♦).
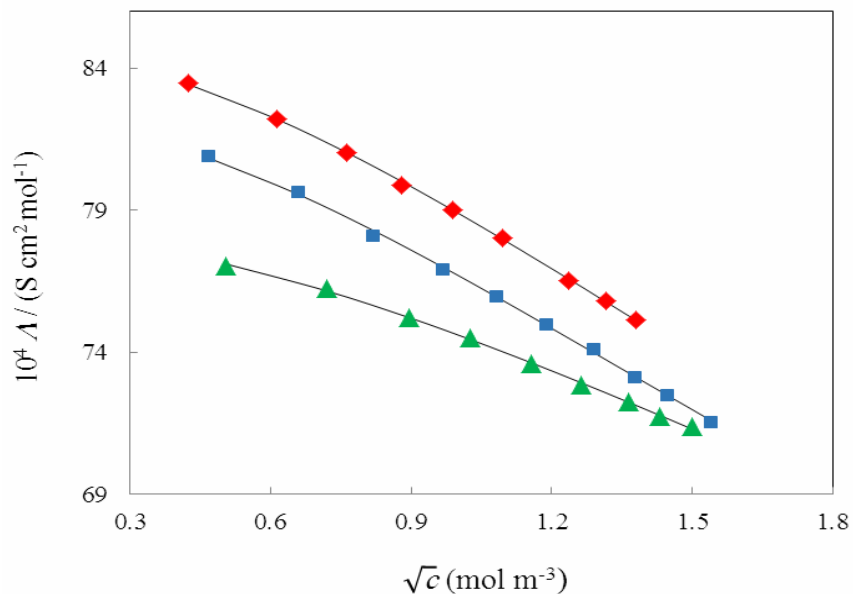
Fig. 4. The molar conductivities, Λ, against the square root of the molarities, $\sqrt{c}$, for [BMIm][Sal] in water (♦) (glycine + water) (▲) and (L-alanine + water) (■) solutions with 0.1 molality at 298.15 K.
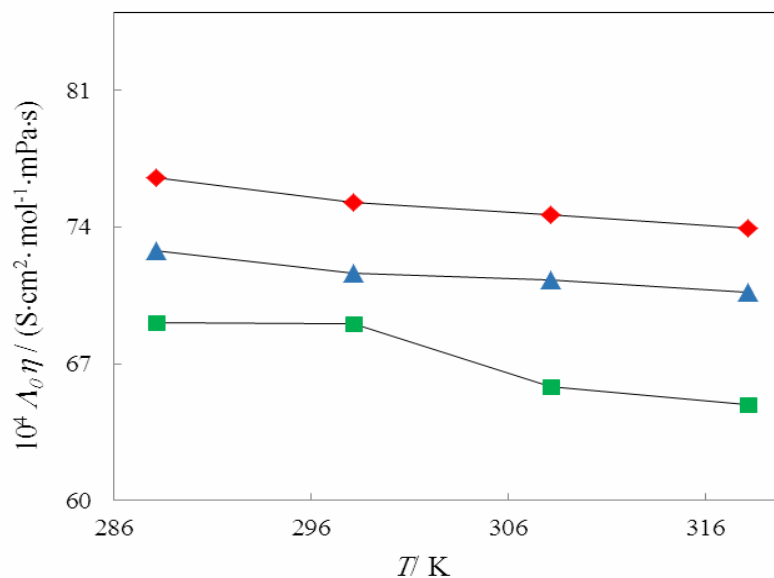
Fig. 5. The plot of Walden product ($\Lambda_0\eta$) against temperature for [BMIm][Sal] in water (♦), (glycine + water) (■) and (L-alanine + water) (▲) with 0.5 molalities at experimental temperatures.

electrostriction interactions between amino acid and water molecules are suppressed due to the ion pair formation between the ions of API-IL and zwitterions of amino acids [22]. The higher values of K_A in the solutions of glycine relative to L-alanine suggest the stronger interactions between (COO^-/NH_3^+) of the zwitterions and ions of [BMIm][Sal] in this amino acid due to its low hydrophobicity. Dehydration of the ions at the high temperatures could be attributed to the increase in the K_A values with increase in temperature.

The K_A values of [BMIm][Sal] were also compared to those of the [BMIm][Ibu] in the reference [12] indicating that the electrostatic interactions between cation and anion of [BMIm][Sal] are stronger than those of [BMIm][Ibu]. The large size of ibuprofene with more hydrophobic groups relative to salicylate anion can be the cause of this phenomenon.

Distance Parameter

Table 4 presents the values of distance parameter, *R,* for [BMIm][Sal] in the studied solutions. The parameter *R* is the maximum distance between cation and anion in the ion pair isolated by solvent ([BMIm]$^+\cdots\cdots$O-H$_2\cdots\cdots$[Sal]$^-$). The stronger interactions between the ions of API-IL and zwitterions of amino acid with addition of [BMIm][Sal] decrease the distance parameter (*R*) [23,24].

Diffusion Coefficients and Walden Products of Ions

The values of ionic limiting molar conductivity of individual ions can be calculated from the following relation:

$$\lambda_\pm^\circ = z_+\lambda_+^0 + z_-\lambda_-^0 \tag{8}$$

The ionic limiting molar conductivities λ_+^0 of [BMIm]$^+$ in water at experimental temperatures were taken from the literature [25] and the limiting molar conductivities of the anion λ_-^0 were obtained from Eq. (8) using the known λ_+^0 values. The collected values of λ_0^+ as well as the calculated values of λ_-^0 are given in Table 5 which are in agreement with those reported in the literature [25]. Moreover, the λ_-^0 of ibuprofenate in [BMIm][Ibu] [12] is lower than that of salicylate in [BMm][Sal] which is directly attributed to the

mobility of the anions.

The diffusion coefficients of particular ions are also calculated using the following equation [24,12]:

$$D_{ion}^0 = \frac{RT\lambda_\pm^0}{|z_\pm|F^2} \tag{9}$$

The obtained values of the diffusion coefficient of the ions (D_{ion}^0) are recorded in Table 5. The more participation of cation in the D_{ion}^0 value suggests that these ion diffuses more easily through the solvent (see Table 5). Diffusion coefficients of [Bmim]$^+$ and [Sal]$^-$ which are close to the reported values for [Bmim]$^+$ and [Sal]$^-$ are in agreement with those reported in our previous works [12,26].

The calculated values of D_{ion}^0 are used to evaluate the Stoke's radius (r_s) or effective hydrodynamic radius of the ions as follows:

$$r_s = \frac{kT}{6\pi\eta D_{ion}^0} \tag{10}$$

where η is the viscosity of pure water. The calculated values of r_s for [BMIm]$^+$ and [Sal]$^-$ are listed in Table 5. Stoke's radius is almost related to mobility, size of ions and solvent effects. Larger values of r_s for anion at higher temperature suggest the stronger hydration of the ions while this trend is opposite trend for cation [26,27].

Replacement of Eq. (10) in Eq. (9) and its rearrangement will yield the following relation:

$$\lambda_\pm^0\eta = \frac{k|z_\pm|F^2}{6\pi R r_s} \tag{11}$$

This equation gives the reverse relationship between the effective hydrodynamic radius of an ion and its Walden product ($\lambda_\pm^0\eta$). Since all the parameters in the right hand of Eq. (11) except r_s are constant, the Walden product varies only if r_s changes. Table 5 also shows that the Walden products of [BMIm]$^+$ and [Sal]$^-$ increase and decrease with increase in temperature, respectively [12].

Ion transport number, called the transference number, is the contribution of an ion to the total molar conductivity of the solution. The ion transport number can be computed as

Table 5. The Values of Ionic Limiting Molar Conductivity ($\lambda_{\pm}^0$), Walden Product ($\lambda_{\pm}^0 \eta$), Stoke's Radius (r_s), Diffusion Coefficient (D_{ion}^0), and Transport Number (t_+) of [BMIm]$^+$ and [Sal]$^-$ in Water at $T = (288.15\text{-}318.15)$ K and 0.087 MPa[a]

T (K)	$10^4 \lambda_{\pm}^0$ (s m^2 mol^{-1})	$10^4 \lambda_{\pm}^0 \eta$ (s m^2 mol^{-1} mPa s)	$10^{10} r_s$ (m)	D_{ion}^0 (m^2 s^{-1})	t
[BMIm][Sal] in water
[BMIm]$^+$					
288.15	32.1[a]	36.27	2.26	8.26	0.474
298.15	43.4[a]	38.54	2.13	11.56	0.512
308.15	54.2[a]	39.02	2.10	14.92	0.523
318.15	65.7[a]	39.80	2.06	18.67	0.539
[Sal]$^-$					
288.15	33.69	40.26	2.04	9.17	0.526
298.15	40.65	36.72	2.23	11.01	0.488
308.15	51.29	35.62	2.30	13.62	0.477
318.15	60.16	34.07	2.41	15.95	0.461

[a]The λ_{ion}^0 values of the cation ([BMIm]$^+$ in for $T = 308.15$ and $T = 318.15$ K were taken directly from Ref. [25] and at other temperatures were calculated from the extrapolation of the existing data.

Table 6. Diffusion Coefficients (D_{AB}^0) and Thermodynamic Functions, ΔG_A°, ΔH_A° and ΔS_A^0 of [BMIm][Sal] in Water at $T = (288.15\text{-}318.15)$ K and 0.087 MPa[a]

T (K)	ΔH_A° (kJ mol^{-1})	ΔS_A^0 (J mol^{-1})	ΔG_A° (kJ mol^{-1})	$10^{10} D_{AB}^0$ (m^2 s^{-1})
[BMIm][Sal] in water
288.15	34.64	150.29	-8.61	8.69
298.15	26.14	121.30	-10.21	11.28
308.15	17.35	92.31	-10.91	14.24
318.15	8.27	63.31	-11.94	17.20

follows:

$$t_{\pm} = \frac{\lambda_0}{\Lambda_0} \qquad (12)$$

The symbols t_+ and t_- are the transport numbers of cation and anion, separately. The calculated values of t_+ and t_- are given in Table 5 showing that the t_- values decrease with increase in temperature.

The evaluated molar conductivities at infinite dilution were employed to calculate the diffusion coefficients of the API-IL using the Nernst–Haskell equation as follows [24,25]:

$$D_{AB}^0 = \frac{RT}{F^2} \frac{|z_+||z_-|}{|z_+ z_-|} \frac{\lambda_+^\circ \lambda_-^\circ}{\lambda_+^\circ + \lambda_-^\circ} \qquad (7)$$

where D_{AB}^0 is the diffusion coefficient of API-IL (A) in water (B) at infinite dilution, z_+, z_-, λ_+^0 and λ_-^0 are the charge numbers and limiting molar conductivities of the cation and anion, respectively. The computed values of D_{AB}^0 for [BMIm][Sal] in water are given in Table 5. The enhanced values of D_{AB}^0 at higher temperature are attributed to the increase in the ionic mobility of the [BMIm][Sal] ions.

Thermodynamics of Ion Association

The ion association constants were employed to calculate the standard Gibbs free energy (ΔG_A°) of the ion-association process using the following equation:

$$\Delta G_A^\circ = -RT \ln K_A(T) \qquad (13)$$

Temperature dependency of ΔG_A° was displayed with the help of the following polynomial:

$$\Delta G_A^\circ = A_0 + A_1(298.15 - T) + A_2(298.15 - T)^2 \qquad (14)$$

Enthalpy and entropy of the ion association have been calculated as follows:

$$\Delta S_A^\circ = -\left(\frac{\partial \Delta G_A^\circ}{\partial T}\right)_P = A_1 + 2A_2(298.15 - T) \qquad (15)$$

$$\Delta H_A^\circ = \Delta G_A^\circ(T) + T\Delta S_A^\circ(T) = A_0 + 298.15A_1 + \left(298.15^2 - T^2\right)A_2 \qquad (16)$$

The calculated values of standard thermodynamic functions, Gibbs free energy (ΔG_A°), enthalpy (ΔS_A°) and entropy (ΔH_A°) of the ion association process of [BMIm][Sal] in water and aqueous solutions of amino acid (0.1, 0.3 and 0.5) mol kg^{-1} at experimental temperatures are given in Tables 6 and 7.

The obtained values of ΔG_A° for [BMIm][Sal] in the several molalities of glycine and L-alanine have been compared in Fig. 6.

As seen in Fig. 6, the values of ΔG_A° for ion association process in the solutions of glycine and L-alanine solutions are negative. The more negative values are observed in the solutions of glycine which indicated the more spontaneity and the feasibility of the ion association process in this amino acid. The ΔG_A° of [BMIm][Sal] in water and the solutions of amino acid was compared with that of [BMIm][Ibu] in the reference [12] and the more negative of the ΔG_A° values are observed for [BMIM][Sal] in the studied solutions. This trend is completely consistent with the observed values for [BMIm][Sal] and [BMIm][Ibu]. This means that the ion association process for [BMIm][Sal] in the aqueous solution is more preferable relative to [BMIm][Ibu].

The positive values of ΔH_A° also indicate that the ion pair formation process is endothermic and decrease with increase in temperature as far as become negative at $T = 318.15$ K: The ΔH_A° is the enthalpy exchanged in the ion association process. Trends of ΔH_A°, ΔG_A° and K_A are similar. This suggests the ion association process becomes more spontaneous and the ions tend to forms the ion pair formation easily. In the higher temperatures, the interactions between ion pairs and amino acid may be prevalent relative to the ions-amino acid interactions.

Moreover, the positive ΔS_A° values may be ascribed to the increase in the number of degrees of freedom due to the release of water molecules from the hydration shells as a result of interactions between ions of [BMIm][Sal] with (COO$^-$/NH$_3^+$) zwitterionic centers [24]. The higher values of ΔS_A° in the aqueous solutions of glycine relative to L-alanine indicate the high tendency of glycine for

Table 7. The Thermodynamic Functions of the Ion-pairing Formation, ΔG_A°, ΔH_A° and ΔS_A° of ([BMIm][Sal] in (Glycine + Water) and (L-Alanine + Water) Solutions at T = (288.15-318.15) K and 0.087 MPa[a]

T (K)	ΔH_A° (kJ mol^{-1})	ΔS_A° (J mol^{-1})	ΔG_A° (kJ mol^{-1})	ΔH_A° (kJ mol^{-1})	ΔS_A° (J mol^{-1})	ΔG_A° (kJ mol^{-1})
	[BMIm][Sal] in (glycine + water)			[BMIm][Sal] in (L-alanine + water)		
	[b]m_{Gly} = 0.1001 mol kg^{-1}			[c]m_{Ala} = 0.9998 mol kg^{-1}		
288.15	23.39	107.84	-8.64	12.80	75.07	-8.80
298.15	13.41	77.20	-9.75	8.39	60.00	-9.58
308.15	4.12	46.56	-10.09	3.82	449.40	-9.95
318.15	-5.48	15.93	-10.59	-0.90	298.60	-10.43
	m_{Gly} = 0.3026 mol kg^{-1}			m_{Ala} = 0.3021 mol kg^{-1}		
288.15	27.71	124.75	-8.13	17.01	87.28	-8.10
298.15	17.53	90.00	-9.61	14.20	77.40	-9.06
308.15	6.99	55.25	-9.73	11.13	67.53	-9.58
318.15	-3.89	20.05	-10.51	8.033	57.65	-10.34
	m_{Gly} = 0.5011 mol kg^{-1}			m_{Ala} = 0.4996 mol kg^{-1}		
288.15	59.68	231.00	-6.79	40.39	163.79	-6.70
298.15	33.79	142.70	-9.06	27.02	118.20	-8.52
308.15	7.02	54.40	-9.44	13.21	72.61	-8.86
318.15	-20.63	33.91	-9.94	-1.07	27.03	-9.77

[a]The estimated uncertainties for u (ΔH_A°) = 0.12 kJ mol^{-1}, u (ΔG_A°) = 0.15 kJ mol^{-1} and (ΔS_A°) = 0.05 J mol^{-1}.
[b]m_{Gly} is the molal concentration of glycine in water. [c]m_{Ala} is the molal concentration of L-alanine in water.

dehydration. The amounts of ΔH_A° and ΔS_A° implies that the ion-pair formation is entropy-driven at low temperatures, while it switches to enthalpy-driven process with increase in temperature [12].

CONCLUSIONS

Electrical conductivities of 1-butyl-3-methyl-imidazolium salicylate, [BMIm][Sal], were determined in water and aqueous solutions of glycine and L-alanine with 0.1, 0.3 and 0.5 molalities over the temperature range of 288.15-318.15 K. Results show that the values of Λ_0 become lower with the addition of amino acid to the solutions of [BMIm][Sal]. This trend indicates the low mobility of the solvated ions by (COO$^-$/NH$_3^+$) zwitterionic centers with large radii and increase in the viscosity of medium with an increase in the amino acid concentration. Moreover, dehydration of the ions with an increase in the temperature led to increase in the Λ_0 increment at high temperatures. The positive values of dK_A/dT imply that the
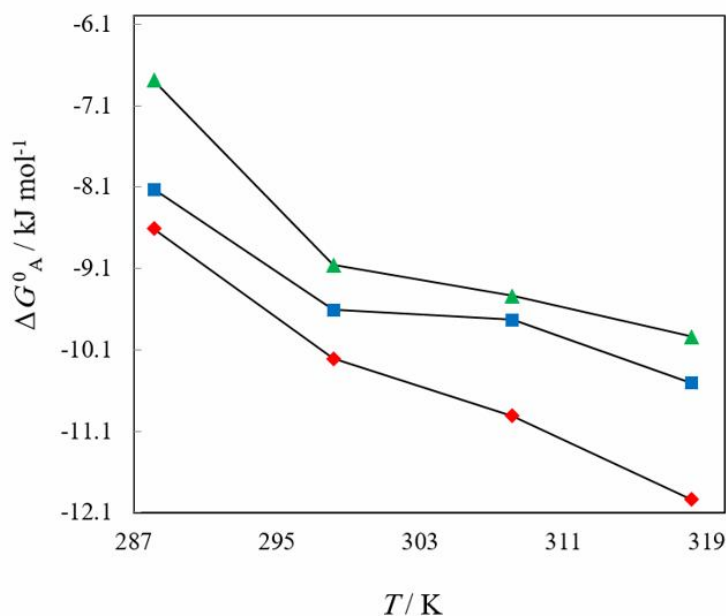
Fig. 6. The standard Gibbs energy (ΔG_A°) against temperature for [BMIm][Sal] in water (♦), (glycine + water) (■) and (L-alanine + water) (▲) with 0.3 molality at different temperatures.

ion-pair formation is an endothermic process. Based on the thermodynamic data analysis, the entropy manages the ion association process for [BMIm][Sal] in the studied solutions at all temperatures. The more negative values of ΔG_A° for [BMIm][Sal] in the aqueous solution of glycine relative to L-alanine solutions is indicative of the more spontaneity of the ion association process.

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