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Volumetric, Acoustic and Conductometric Studies of Acetaminophen in Aqueous Ionic Liquid, 1-Octyl-3-methylimidazolium Bromide at *T* = 293.15-308.15 K

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The density (*d*), speed of sound (*u*) and electrolytic conductivity (Λ) for systems containing acetaminophen, ionic liquid {1-octyl-3-methyl imidazolium bromide, [OMIm] Br} and water have been measured at *T* = 293.15-308.15 K. The measured data have been applied to calculate, standard partial molar volume (V_φ^0), Hepler's constant $(\partial^2 V_\varphi^0 / \partial T^2)_P$, apparent molar isentropic compressibility (K_φ), transfer volume ($\Delta_{tr}K_\varphi^0$), transfer compressibility ($\Delta_{tr}K_\varphi^0$) and hydration number (n_H), and used to discuss various solute-solvent interactions. The transfer quantities are positive and increase with molalities of ionic liquid and decrease with temperature, indicating the dominance of hydrophilic-hydrophilic interactions between the ionic liquid and acetaminophen, and dehydration effect of ionic liquid on the solutions. The limiting molar conductivities (Λ_0) and ion association constants (K_a) for [OMIm]Br in aqueous acetaminophen solutions have been estimated using low concentration Chemical Model (lcCM). The Ka values were also used to obtain the thermodynamic functions of association process. Thermodynamic results show that the formation process of ion association of the ionic liquid has endothermic nature and is driven by the change in entropy.

Keywords: Acetaminophen, Ionic liquid, Apparent molar volume, Molar conductivity

INTRODUCTION

In last two decades, ionic liquids (ILs) have been used in many academic areas and industrial processes. This is mainly due to the unusual physical and chemical properties of ILs. In particular, ILs have negligible vapor pressure due to ionic inherent characteristics with good thermal stability which make them as "green" alternatives to conventional hazardous organic solvents and echo-friendly as rules of green chemistry in a range of synthesis, catalysis, electrochemistry, liquid-liquid extraction, chromatography, gas capture and nanoscience. The other physicochemical properties of ionic liquids are high solvation ability for organic and inorganic compounds, recyclability, non-flammability, wide liquid range, wide electrochemical window in the range of 4.0-5.7 V, and high ionic conductivity [1-3]. Moreover, their properties can be significantly tuned by appropriate modifications of the cation, anion, or both for a specific application. They usually comprise bulky and asymmetric organic cations (*e.g.*, imidazolium, pyrrolidinium, pyridinium, ammonium and phosphonium) and small inorganic anions (especially halogen-based anions, *e.g.*, $[Cl^-]$, $[Br^-]$, $[I^-]$, $[BF_4^-]$, $[AlCl_4^-]$, $[PF_6^-]$). The low lattice energies of ILs due to the asymmetry of the cation are caused their liquid state at ambient conditions. Currently, the most widely used ionic liquids are based on the alkyl-substituted methyl-imidazolium cation as prototype organic cation, which can be synthesized relatively easy from commercial chemicals [4-5].

Due to these favorable properties, ionic liquids have been recently proposed as solvent for a variety of pharmaceutical applications. They have been found to be particularly useful for the solubilization of poorly soluble drugs, to synthesize active pharmaceutical ingredients (APIs) with modified solubility, increased thermal stability,

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as additives in formulations for typical drug delivery and a significant enhancement in the efficiency of topical analgesia compared to their starting materials. Furthermore, many ionic liquids exhibit antimicrobial activity which can make them useful as APIs or formulation preservatives. Based on the studies in this area, the use of ILs often leads to higher yields, better selectivity, high dissolution power and simple product isolation. Poor water solubility of drug candidates is a major problem in the pharmaceutical industry and it has been estimated that 40% of all newly developed drugs are poorly soluble or insoluble in water [6-11]. For the potential use of these compounds in various chemical processes, it is of immense importance to understand their behavior in the presence of other regular chemical compounds. In spite of their extensive applications a very little information on their thermodynamic behavior is available.

Acetaminophen, *N*-acetyl-*p*-amino phenol (NAPAP), more commonly known as paracetamol is a popular analgesic drug used widely in current therapeutics for the treatment of pain and reducing fever. Acetaminophen, a white odorless crystalline powder, poorly solute in water is also used as an API and has been detected in wastewaters and surface water [12-14]. Its solubility is a key parameter during the processes associated with the design and development of new liquid pharmaceutical dosage forms. Extraction of NAPAP by the use of volatile solvents is also the most used method for their recovery. One of the main approaches in recent years proposed to overcome the extraction and solubility of APIs in aqueous media has been the use of ionic liquid. Mizuuchi *et al*. have reported that the solubility of albendazole, for example, increased by more than 10000 times by dissolution in [BMIm][PF_6] compared to water [15]. Furthermore, this compound contains both hydrophilic and hydrophobic groups which are responsible to its much thermodynamic behavior in aqueous media.

In such studies, drug interactions with ionic liquids at molecular level can be understood through the thermodynamic properties. Systematic information of the thermodynamic properties relating to the drug behavior in such solutions can be therefore of great significance for understanding their physiological action, solute-solvent interactions, and structure making or breaking ability of the added components. Thus, to achieve a better understanding of the API-solvent and API-ionic liquid interactions and development of ionic liquids in this field, it is essential to have knowledge of certain physical and thermodynamic properties of such systems including density, viscosity and speed of sound.

To date, a number of papers have measured some of the thermophysical properties of binary systems containing a drug in aqueous and nonaqueous solutions such as density, viscosity, speed of sound, surface tension, conductivity and liquid-liquid equilibria. Several volumetric and viscometric studies have been conducted on salicyl amide, salicylic acid and acetyl salicylic acid in alcohols[16], phenyl salicylate in aprotic solvents [17], antidepressant drugs in aqueous medium [18], acetyl salicylic acid a (2-acetoxy benzoic acid) solutions in higher alcohols[19], diclofenac sodium, cetrizine and doxycycline in aqueous medium[20], salicyl amide, salicylic acid and acetyl salicylic acid (non-steroidal antiflammatory drugs) in two aprotic solvents namely, dimethyl sulfoxide and acetonitrile [21] by Muhammad J. Iqbal and co-workers. Recent studies by other authors have been also focused on the volumetric and transport properties of a drug in the presence of aqueous amino acids or saccharides solutions [22-29]. However, there is no report on the thermophysical and thermodynamic properties of any drug in the presence of aqueous or non-aqueous ionic liquid solutions.

The aim of this work is to present new thermodynamic properties of ternary {acetaminophen + 1-octyl-3-methylimidazolium bromide ([OMIm]Br) + H_2O} solutions, as a model to study the solvation (hydration) behavior of acetaminophen in aqueous ionic liquid solutions. This IL has been well-characterized in the literature and is known to be good solvent for a wide range of organic and inorganic compounds. To do so, the densities and speeds of sound of the solutions containing acetaminophen in the presence of aqueous [OMIm]Br solutions were measured at T = 293.15-308.15 K and used to calculate the apparent molar volumes (V_φ), standard partial molar volumes (V_φ^0), transfer volumes ($\Delta_{tr}V_\varphi^0$), apparent molar isentropic compressibility (K_φ), limiting apparent molar isentropic compressibility (K_φ^0) and transfer compressibility (ΔK_φ^0) of acetaminophen from water to aqueous [OMIm]Br solutions. Electrical conductivity measurements for [OMIm]Br in aqueous

acetaminophen solutions were also carried out at 293.15-308.15 K. The molar conductivities were correlated with low concentration Chemical Model (lcCM). The limiting molar conductivity (Λ_0) along with association constant (K_A) of the ionic liquid were computed. The results were utilized to investigate the effect of the ionic liquid on the solute-solvent interactions in aqueous solution of acetaminophen and its dehydration effect.

EXPERIMENTAL

Materials

N-Methylimidazole (> 99%), 1-bromooctane (> 99%) and ethyl acetate (> 99%) were obtained from Merck, and acetaminophen with mass fraction purity (> 995%) was obtained from Temad Co. (Iran). All chemicals were used without further purification. Double distilled deionized water with specific conductivities less than 1.0 μS $cm^{-1}$was used for the preparation of all the solutions. The characteristic of the used chemical in this work are given in Table 1.

Synthesis of Ionic Liquid

The ionic liquid [OMIm]Br was synthesized and purified by using the procedure described in literature [30,31]. Briefly, [OMIm]Br was synthesized by direct alkylation of *N*-methylimidazole with an 10% excess in mole of 1-bromooctane in a round bottom flask with continuous stirring at T = 353 K for 48 h and refluxed under nitrogen atmosphere. The crude product was separated from the unreacted reagents and then washed with fresh ethyl acetate three times, each time with 30 ml ethyl acetate. The removal of residual volatile compounds in the ionic liquid was performed in high vacuum at about T = 333 K using a rotary evaporator for at least 3 h under reduced pressure. This ionic liquid was used after vacuum desiccated for at least 48 h to remove trace amount of moisture. The obtained ionic liquid has no major impurity verified by ^{1}H NMR spectrum. Water content found in the ionic liquid by Karl Fischer method using a Karl Fischer titrator (751 GPD Titrino-Metrohm, Herisau, Switzerland) was less than 0.2% and has been taken into account and the apparent molality corrections have been applied. The ionic liquid was analyzed by ^{1}H NMR (Brucker Av-300) and FTIR (PerkinElmer, Spectrum RXI) to confirm the absence of any major impurities and they were found to be in good agreement with those reported in the literature [32].

Apparatus and Procedure

The solutions were prepared in mass basis (by Shimadzu, 321-34553, Shimadzu Co., Japan) with precision 1×10^{-4} g.

The experimental densities, *d*, and speed of sound, *u*, of the studied solutions were measured by an automated vibrating tube densimeter (DSA5000 Anton Paar, Austria). The apparatus was calibrated with doubly distilled deionized and degassed water and with dry air at atmospheric pressure. Before each series of measurements, the densimeter was calibrated in the experimental temperature. The density and speed of sound are extremely sensitive to temperature, so it was kept constant within $\pm 1.0 \times 10^{-3}$ K by an internal temperature controller built in peltier device. The standard uncertainty of density and speed of sound measurements were found to be within 5.0×10^{-6} g

Table 1. Sample Provenance of the Chemicals and Purity

Chemical name	Source	Initial massfraction purity	Purification method	Final purity	Analysis method
Acetaminophen	Temad	GR > 0.995	None	GR > 0.995	
[OMIm]Br	Synthetic	Not measured	Extraction and distillation	>0.998	Karl Fischer titration and ^{1}H NMR

cm^{-3} and 0.5 m s^{-1}, respectively. The sensitivity at the instrument corresponds to repeatability in density and speed of sound, which according to the manufacturer manual are 1 × 10^{-6} g cm^{-3}, 0.1 m s^{-1}, respectively.

Electrical conductance measurements were carried out on a digital conductivity meter (Metrohm model 712, Switzerland) and a dipping-type conductivity cell with platinized electrodes and cell constant of 0.867 cm^{-1}. The cell constant was obtained by 0.01 mol kg^{-1} aqueous KCl solution. The precise mass of doubly distilled deionized and degassed water and acetaminophen was placed in a sample holder. The conductivity electrode was inserted and the cell was tightly closed. The defined weighed pure ionic liquid was added with a syringe to the sample holder containing water solution and stirred continuously. Circulating water from a thermostatically regulated bath (Julabo ED Germany having a temperature stability with in 0.01 K), around the sample holder with double wall was carried out to maintain the temperature with a precision of 0.02 K. The uncertainty in the measured specific conductivity was estimated to be less than 0.5%.

RESULTS AND DISCUSSION

Volumetric Results

The experimental density (d) values of acetaminophen in water and (0.1, 0.2, 0.3 and 0.4) mol kg^{-1} aqueous solutions of [OMIm]Br as a function of acetaminophen molality (m) were measured at temperatures T = 293.15-308.15 K and listed in Table 2. The densities of investigated solutions {acetaminophen + water/aqueous ionic liquid solutions} decrease with temperature and increase with increasing the ionic liquid concentration. The apparent molar volumes (V_φ) of acetaminophen in the investigated solutions were determined from the experimentally measured densities using the equation:

$$V_\varphi = \frac{M}{d} - \frac{(d - d_0)}{m d d_0} \quad (1)$$

where M is the molar mass of acetaminophen, m is the molality of acetaminophen in aqueous [OMIm]Br solutions, d and d_0 are the densities of the solutions containing (acetaminophen + [OMIm]Br + H_2O) and ([OMIm]Br + H_2O) solutions, respectively. The calculated V_φ values of this drug as a function of molality, m and the experimental temperatures are given in Table 2. Figure 1 is representative of the apparent molar volume (V_φ) values of acetaminophen versus acetaminophen molality in ionic liquid. The V_φ values increase with the increase in the concentration of [OMIm]Br at all experimental temperatures. There is a good linear correlation between V_φ values and acetaminophen molality (m). Therefore, the values of apparent molar volumes at infinite dilution (standard partial molar volume) (V_φ^0) are estimated by least-squares fitting to Masson's equation [33]:

$$V_\varphi = V_\varphi^0 + S_v m \quad (2)$$

Where S_v is the experimental slope indicating solute-solute interactions occurring between acetaminophen molecules. The V_φ^0 values are independent of solute-solute interactions at infinite dilution and only reflect the presence of solute-solvent interactions between acetaminophen and ionic liquid, [OMIm] Br. The values of V_φ^0 and S_v along with their corresponding standard errors and standard deviations are shown in Table 3. It is observed that the values of S_v are negative for all the investigated solutions and all experimental temperatures and become more negative with the increase in concentration of the ionic liquid. The negative values of S_v indicates weak solute-solute interactions between acetaminophen molecules in the presence of ionic liquid solutions. The less values of S_v compared to V_φ^0 suggest the weak solute-solute interactions compared to stronger solute-solvent interactions.

As seen in Table 3, the V_φ^0 values are positive and increase as the ionic liquid concentration increases. The V_φ^0 values for this compound in water are in well agreement with those in our previous work [34] at T = 29315, 298.15, 303.15 and 308.15 K.

The transfer volumes ($\Delta_{tr}V_\varphi^0$) of acetaminophen at infinite dilution from water to aqueous [OMIm]Br solutions have been calculated as:

$$\Delta_{tr}V_\varphi^0 = V_\varphi^0(\text{in[OMIm] + } H_2O) - V_\varphi^0(H_2O) \quad (3)$$

The calculated values of the transfer volume ($\Delta_{tr}V_\varphi^0$) at

Table 2. Densities (d) and Apparent Molar Volumes ($V_{\downarrow}\varphi$) of Acetaminophen in Water and Aqueous [OMIm]Br Solutions as a Function of Acetaminophen Molality (m) at T = (293.15, 298.15, 303.15 and 308.15) K and p = 101.3 kPa.$V_{\varphi}(cm^3.mol^{-1})$

m (mo kg^{-1})	T (K)							
	293.15		298.15		303.15		308.15	
	$10^3 d/(kgm^3)$	$10^6 V_\varphi/(m^3.mol^{-1})$	$10^3 d/(kgm^3)$	$10^6 V_\varphi/(m^3.mol^{-1})$	$10^3 d/(kgm^3)$	$10^6 V_\varphi/(m^3.mol^{-1})$	$10^3 d/(kgm^3)$	$10^6 V_\varphi/(m^3.mol^{-1})$
				m_{IL} = 0.0000				
0.0000	0.998200		0.997041		0.995642		0.994022	
0.0312	0.999038	123.26	0.997858	124.08	0.996447	124.62	0.994812	125.28
0.0323	0.999103	123.19	0.997923	123.96	0.996513	124.44	0.994876	125.13
0.0361	0.999216	123.10	0.998034	123.85	0.996623	124.32	0.994984	125.02
0.0390	0.999299	123.08	0.998117	123.78	0.996706	124.23	0.995065	124.93
0.0432	0.999429	122.92	0.998244	123.63	0.996829	124.14	0.995189	124.77
0.0474	0.999546	122.73	0.998356	123.51	0.996938	124.04	0.995299	124.61
0.0492	0.999612	122.60	0.998417	123.45	0.997699	123.97	0.995358	124.56
0.0531	0.999726	122.49	0.998528	123.34	0.997113	123.78	0.995466	124.45
0.0563	0.999796	122.44	0.998595	123.31	0.997179	123.75	0.995533	124.39
m_{IL} = 0.1004								
0.0000	1.003367		1.002087		1.000568		0.998832	
0.0295	1.004153	124.10	1.002859	124.70	1.001332	125.12	0.999583	125.74
0.0325	1.004245	123.75	1.002943	124.55	1.001415	124.97	0.999667	125.51
0.0360	1.004344	123.62	1.003045	124.26	1.001511	124.83	0.999763	125.34
0.0390	1.004433	123.41	1.003128	124.17	1.001599	124.57	0.999843	125.26
0.0435	1.004561	123.23	1.003256	123.93	1.001718	124.51	0.999971	124.94
0.0475	1.004676	123.14	1.003369	123.83	1.001834	124.32	1.000081	124.84
0.0494	1.004731	123.05	1.003422	123.76	1.001892	124.13	1.000136	124.71
0.0531	1.004843	122.87	1.003529	123.63	1.001992	124.12	1.000235	124.68
0.0553	1.004908	122.81	1.003595	123.52	1.002055	124.05	1.000296	124.64

Table 2. Continued

$m_{IL} = 0.1995$								
0.0000	1.006678		1.005298		1.003700		1.001869	
0.0300	1.007464	124.24	1.006069	124.88	1.004462	125.33	1.002623	125.78
0.0329	1.007541	124.15	1.006145	124.77	1.004541	125.11	1.002698	125.66
0.0358	1.007626	123.91	1.006225	124.62	1.004622	124.92	1.002776	125.52
0.0394	1.007729	123.73	1.006325	124.47	1.004721	124.78	1.002873	125.39
0.0436	1.007847	123.54	1.006444	124.20	1.004835	124.61	1.002984	125.25
0.0467	1.007939	123.36	1.006535	124.00	1.004924	124.44	1.003071	125.09
0.0493	1.008015	123.24	1.006608	123.92	1.004997	124.34	1.003149	124.86
0.0528	1.008119	123.07	1.006707	123.80	1.005094	124.24	1.003244	124.78
0.0561	1.008214	122.96	1.006795	123.77	1.005186	124.13	1.003333	124.70
$m_{IL} = 0.2995$								
0.0000	1.010289		1.008859		1.007178		1.005249	
0.0297	1.011047	124.51	1.009603	125.11	1.007917	125.45	1.005978	125.97
0.0330	1.011139	124.28	1.009687	125.10	1.008007	125.21	1.006066	125.76
0.0359	1.011222	124.06	1.009768	124.85	1.008085	125.08	1.006142	125.65
0.0393	1.011317	123.91	1.009863	124.64	1.008179	124.88	1.006236	125.42
0.0437	1.011440	123.69	1.009982	124.45	1.008298	124.69	1.006351	125.28
0.0472	1.011542	123.47	1.010082	124.23	1.008397	124.48	1.006447	125.11
0.0497	1.011611	123.42	1.010151	124.16	1.008469	124.34	1.006519	124.95
0.0529	1.011706	123.22	1.010239	124.05	1.008557	124.23	1.006607	124.81
0.0566	1.011813	123.06	1.010340	123.95	1.008656	124.17	1.006709	124.67
$m_{IL} = 0.4009$								
0.0000	1.013713		1.012267		1.010407		1.008514	
0.0301	1.014464	124.76	1.013004	125.36	1.011142	125.61	1.009240	126.09
0.0334	1.014551	124.57	1.013089	125.18	1.011226	125.46	1.009324	125.91
0.0357	1.014615	124.42	1.013153	125.00	1.011285	125.40	1.009388	125.71
0.0389	1.014703	124.25	1.013242	124.77	1.011370	125.25	1.009474	125.52
0.0435	1.014827	124.04	1.013363	124.59	1.011489	125.09	1.009595	125.30
0.0460	1.014895	123.95	1.013433	124.47	1.011564	124.85	1.009667	125.12
0.0488	1.014973	123.80	1.013510	124.32	1.011645	124.60	1.009746	124.91
0.0534	1.015107	123.54	1.013636	124.14	1.011779	124.26	1.009877	124.62
0.0558	1.015179	123.38	1.013702	124.07	1.011846	124.18	1.009951	124.40

m_{IL} is the molality of ionic liquid in aqueous ionic liquid solutions.Uncertainties: u (p) = ± 0.05 kpa; u (T) = ± 0.01 K; u (m) = 1 × 10^{-4} mol kg^{-1}; u (d) = ± 5 10^{-6} g cm^{-1}; u (u) = ± 0.5 m s^{-1}.

Table 3. Standard Partial Molar Volumes V_φ^0, Transfer Volumes, $\Delta_{tr}V_\varphi^0$, Experimental Slopes S_v, Standard Deviations $\sigma(V_\varphi)$ and Solvation Number, n_H, of Acetaminophen in Aqueous [OMIm]Br Solutions at T = (293.15, 298.15, 303.15, 308.15) K

m_{IL} (mol kg^{-1})	T (K)	$S_v \times 10^6$ (m^{-3} kg mol^{-2})	$V_\varphi^0 \times 10^6$ (m^3 mol^{-1})	$\Delta_{tr}V_\varphi^0 \times 10^6$ (m^3 mol^{-1})	$\sigma(V_\varphi)$	n_H
0.0000						
	293.15	-33.45 ± 1.60	124.30 ± 0.08		0.029	2.52
	298.15	-29.97 ± 0.81	124.94 ± 0.06		0.020	2.19
	303.15	-31.95 ± 0.70	125.59 ± 0.09		0.038	1.83
	308.15	-34.29 ± 0.83	126.26 ± 0.07		0.025	1.47
0.1004						
	293.15	-46.08 ± 1.77	125.31 ± 0.12	1.03	0.072	2.32
	298.15	-46.82 ± 1.82	125.93 ± 0.15	0.99	0.079	1.84
	303.15	-42.52 ± 1.57	126.34 ± 0.11	0.75	0.059	1.59
	308.15	-43.07 ± 1.62	126.92 ± 0.09	0.66	0.069	1.31
0.1994						
	293.15	-50.59 ± 1.57	125.76 ± 0.07	1.47	0.035	2.17
	298.15	-46.36 ± 2.70	126.26 ± 0.11	1.32	0.061	1.76
	303.15	-44.97 ± 1.61	126.58 ± 0.07	0.99	0.036	1.55
	308.15	-43.15 ± 1.21	127.08 ± 0.07	0.82	0.039	1.27
0.2995						
	293.15	-51.29 ± 2.02	125.94 ± 0.11	1.65	0.058	2.11
	298.15	-48.73 ± 1.99	126.53 ± 0.11	1.59	0.041	1.68
	303.15	-48.91 ± 1.94	126.83 ± 0.09	1.24	0.028	1.46
	308.15	-48.12 ± 1.17	127.37 ± 0.05	1.11	0.034	1.19
0.4009						
	293.15	-51.05 ± 1.71	126.28 ± 0.07	1.99	0.038	1.99
	298.15	-50.50 ± 2.15	126.82 ± 0.09	1.88	0.048	1.62
	303.15	-57.70 ± 1.98	127.44 ± 0.15	1.85	0.080	1.29
	308.15	-64.34 ± 1.53	128.04 ± 0.07	1.78	0.034	1.03

m_{IL} is the molality of ionic liquid in aqueous ionic liquid solutions.

infinite dilution are given in Table 3. It is clear that the $\Delta_{tr}V_\varphi^0$ values are positive and increase with increasing the ionic liquid molality. According to cosphere overlap model of ternary mixtures [35,36], the following types of interactions are possible between acetaminophen and [OMIm]Br molecules in water: (a) the hydrophilic-ionic group interactions, (b) hydrophilic-hydrophilic group interactions, (c) hydrophilic-hydrophobic group interactions and (d) hydrophobic-hydrophobic group interactions. Taking this model as the guideline, (a, and b) type interactions would lead to positive $\Delta_{tr}V_\varphi^0$ values and the remaining types of interactions have negative $\Delta_{tr}V_\varphi^0$ values. In this case, $\Delta_{tr}V_\varphi^0$ values show that the (a) and (b) types of interactions between the hydrophilic -OH and -CO groups of acetaminophen molecules and the ions and polar groups

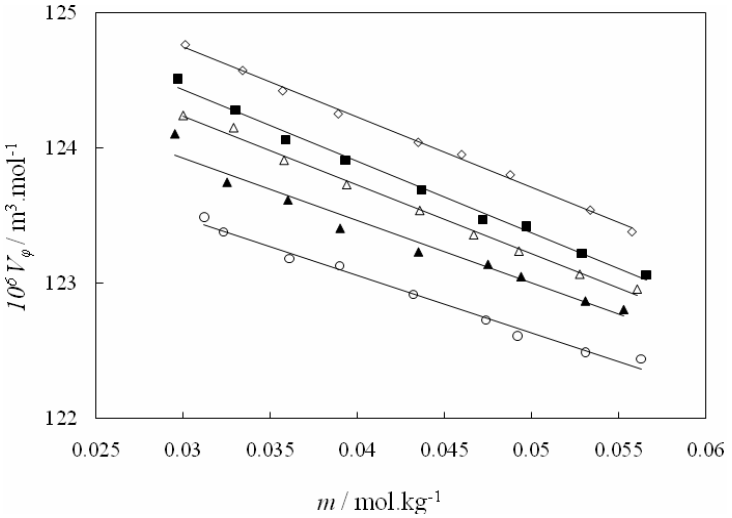

Fig. 1. Apparent molar volumes (V_ϕ) of acetaminophen *vs.* its molality (m) in aqueous [OMIm]Br solutions with different molalities of [OMIm]Br, at T = 293.15 K: ○, 0.000; ▲, 0.1004; △, 0.1995; ■, 0.2995; ◇, 0.4009.

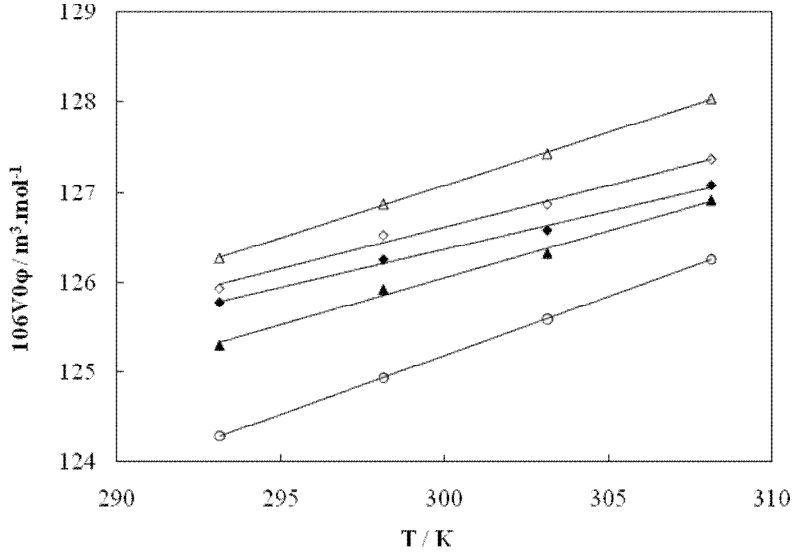

Fig. 2. The variation ofstandard partial molar volumes (V_φ^0) of acetaminophen in aqueous (○, 0.000; ▲, 0.1004; ◆, 0.1995; ◇, 0.2995; △, 0.4009 mol kg^{-1}) of [OMIm]Br solutions at different temperatures.

of ionic liquid are dominant between [OMIm]Br and acetaminophen. Furthermore, the increase in their values at high concentration of ionic liquid indicates strengthening of these types of interactions in the concentration range studied. So, there is a competition among various interactions occurring among solute (acetaminophen) and co-solute (ionic liquid) molecules.

Shahidi *et al.*'s [37] model also shows that the positive $\Delta_{tr}V_{\varphi}^{0}$ values may be due to the decrease in the shrinkage volume. Transfer volumes of solute may be also expressed by the McMillar Mayer theory [38] of solutions, which permits the formal separation of the effects due to interactions between the pairs of the solute molecules and those due to interactions between three or more solute molecules by the following equation:

$$\Delta_{tr}V_{\varphi}^{0} = 2V_{AI}.m_{I} + 3V_{AII}.m_{I}^{2} + \ldots \quad (4)$$

where A stands for the acetaminophen and I stands for the ionic liquid and V_{AI} and V_{AII} are the paired and triplet volumetric interaction parameters, respectively. The volumetric interaction parameters were obtained by fitting the $\Delta_{tr}V_{\varphi}^{0}$ values to the above equation which are given in Table 4. The pair interaction coefficients, V_{AI} are positive for all investigated solutions, whereas the triplet interaction coefficients V_{AII} are negative at all experimental temperatures. The magnitude of both interaction coefficients decreases with the increase in temperature. Furthermore, the magnitude of V_{AI} is greater than V_{AII}, suggesting that interactions between acetaminophen and IL are mainly pair wise.

The slope temperature dependence of standard apparent molar volumes is positive for acetaminophen in the studied solutions as shown in Fig. 2 and can be expressed as the following equation:

$$V_{\varphi}^{0} = A + BT + CT^{2} \quad (5)$$

where *A*, *B* and C are empirical parameters and *T* is the absolute temperature. The values of *A*, *B* and *C* could be obtained by the least-square fittings of the V_{φ}^{0} values at the experimental temperatures. The parameter that measures the variation of volume with temperature is the partial molar isobaric expansion $E_{P,\varphi}^{o}$ which can be obtained by differentiating equation (5) with respect to the temperature [39]:

$$E_{P,\varphi}^{o} = \left(\frac{\partial V_{\varphi}^{0}}{\partial T}\right) = B + 2CT \quad (6)$$

The calculated values of $E_{P,\varphi}^{o}$ for acetaminophen in the studied solutions are reported in Table 5. The $E_{P,\varphi}^{o}$ values provide us important information about solute–solvent interactions and structure-making or breaking tendency of solute [40]. The values of $E_{P,\varphi}^{o}$ are positive for the solute studied which indicates while heating some solvent molecules may be released from the solvation layers. Positive expansibility is a characteristic property of aqueous solutions of hydrophobic hydration. This would increase the solution volume a little more rapidly than that of the pure water and so $E_{P,\varphi}^{o}$ would be positive [41]. These observations again support the presence of competitive hydrophilic and hydrophobic interactions.

It has been shown that the sign of $(\partial^{2}V_{\varphi}^{0}/\partial T^{2})_{P}$ is a better criterion in characterizing the long-range structure-making and breaking capacity of solute in solution which is called Hepler's constant [40]. The general thermodynamic expression has been used by Hepleras:

$$\left(\frac{\partial C_{P}^{0}}{\partial P}\right)_{P} = -T\left(\frac{\partial^{2}V_{\varphi}^{0}}{\partial^{2}T}\right) = -2CT \quad (7)$$

where C_{P}^{0} is the partial molar heat capacity.

If the sign of $(\partial^{2}V_{\varphi}^{0}/\partial T^{2})_{P}$ is small or negative, the solute is a structure breaker, otherwise is structure maker [40]. The values of $(\partial^{2}V_{\varphi}^{0}/\partial T^{2})_{P}$ for acetaminophen in water and aqueous ionic liquid have small and negative values and decrease with increasing of ionic liquid concentration. Therefore, the acetaminophen is predominantly regarded as structure breaker but with addition of the ionic liquid this behavior decreases. This means that ionic liquid has the strong interaction with acetaminophen rather than water.

The change in volume due to electrostriction can be related to the number of water molecules hydrated to acetaminophen, named hydration number, n_{H}. Despite the

Table 4. The Pair and Triplet Interaction Coefficients V_{AI}, V_{AII} and Correlation Coefficient (R^2), Obtained from Eq. (4) for Acetaminophen in Aqueous [OMIm]Br Solutions at T = (293.15, 298.15, 303.15 and 308.15) K

T (K)	$10^6 VAI$ (m^{-3} mol^{-2} kg)	$10^6 V_{AII}$ (m^{-3} mol^{-2} kg)	R^2
293.15	4.943	-4.263	0.97
298.15	4.603	-3.978	0.99
303.15	2.788	-0.973	0.95
308.15	2.198	-0.145	0.97

Table 5. Partial Molar Isobaric Expansions ($E^0_{p,\varphi}$) and Hepler's Constants ($\partial^2 V^0_\varphi / \partial T^2$) for Acetaminophen Inaqueous [OMIm]Br Solutions at T = (293.15,298.15, 303.15 and 308.15) K

m_{IL}	T (K)				$\partial^2 V^0_\varphi / \partial T^2 \times 10^{-3}$
	293.15	298.15	303.15	308.15	(m^3 mol^{-1} K^{-1})
$E^0_{p,\varphi} \times 10^{-6}$ (m^3 mol^{-1} K^{-1})					
0.0000	0.118	0.107	0.097	0.086	-2.102
0.1004	0.121	0.110	0.099	0.089	-2.086
0.1994	0.122	0.111	0.101	0.094	-2.006
0.2995	0.129	0.118	0.107	0.097	-1.890
0.4009	0.134	0.124	0.114	0.104	-1.522

m_{IL} is molality of ionic liquid [OMIm]Br in water.

various numerous structural studies and attempts at molecular modeling to account for water-acetaminophen interactions, it remains difficult to accurately quantify the number of water molecules that hydrate solute molecules. As a general rule, the hydration numbers given in the literature for a solute greatly varies with the technique used to determine it. In the current paper, the values of hydration number are obtained by the following equation [42]:

$$n_H = \frac{V^0_\varphi(elect.)}{V^0_E - V^0_B} \tag{8}$$

where $V^0_\varphi(elect.)$ is the electrostriction partial molar volume due to the hydration of acetaminophen and can be estimated from the values of V^0_φ for acetaminophen and its intrinsic partial molar volume as follows:

$$V^0_\varphi(elect.) = V^0_\varphi - V^0_\varphi(\text{int.}) \tag{9}$$

$$V^0_\varphi(\text{int.}) = \left(\frac{0.7}{0.634}\right).V^0_\varphi(cryst.) \tag{10}$$

in which $V^0_\varphi(cryst.) = \left(M \big/ d_{cryst.}\right)$ is the crystal molar

volume of acetaminophen and *M* is its molar mass, 0.7 is the packing density for molecules in organic crystals, and 0.634 is the packing density for random packed spheres. The crystal density ($d_{cryst.}$) of acetaminophen is 1.263 g cm^{-3}. The suggested values of ($V_E^0 - V_B^0$) are -2.6, -3.3 and -4.0 cm^3 mol^{-1}, respectively, at 288.15, 298.15 K and 308.15 K [43]. In reference [43], no values have been reported for ($V_E^0 - V_B^0$) at temperatures 293.15 K and 303.15 K, so we extracted them through fitting to a linear equation. The character of V_E^0 is the molar volume of electrostricted water and V_B^0 is the molar volume of bulk water. Based on the Eq. (8), and values of ($V_E^0 - V_B^0$) and $V_\varphi^0(elect.)$, hydration number of acetaminophen was calculated at different temperatures. It can be inferred from Table 3 that the values of hydration number decrease at higher temperatures. This observation indicates that dehydration effect of ionic liquid on acetaminophen increases as the temperature increases.

Acoustic Properties

The apparent molar isentropic compression ($K_\downarrow(m,\varphi)$) for acetaminophen in aqueous [OMIm]Br solutions at different temperatures was determined by using the following equation

$$K_{m,\varphi} = \left(\frac{M\kappa_s}{d}\right) - \left[\frac{\kappa_{s,0}d - \kappa_s d_0}{m d d_0}\right] \tag{11}$$

where *m* is the molality of acetaminophen in water and aqueous [OMIm]Br solutions, *M* is the molar mass of acetaminophen and *d* and d_0 are the densities of the solutions containing (acetaminophen + [OMIm]Br + H_2O) and ([OMIm]Br + H_2O) solutions, respectively. The $k_{s,0}$ and k_s are the isentropic compressibility of pure solvent and solution, respectively, calculated as,

$$\kappa_s = \frac{1}{u^2 d} \tag{12}$$

where *u* is the speed of sound and *d* is the density of solution. The calculated values of $k_{m,\varphi}$ for acetaminophen in (0.1, 0.2, 0.3 and 0.4) mol kg^{-1} of aqueous [OMIm]Br solutions at the experimental temperatures are reported in Table 6. As indicated in this table, $k_{m,\varphi}$ values are positive at all experimental temperatures expect for acetaminophen in water and increase with increasing in temperature and concentration of IL. It has been reported that $k_{m,\varphi}$ values are in aqueous solutions (a) large and negative for ionic compounds, (b) positive for mainly hydrophobic solutes, and (c) intermediate, small, and negative, for uncharged hydrophilic solutes such as sugars [44-46]. In the present investigation the positive values of $k_{m,\varphi}$ indicate that the ionic liquid molecules around the acetaminophen molecules are more compressible than water molecules in the bulk solution, [46] indicating strong interaction between acetaminophen and IL.

The variation of apparent molar isentropic compressibility $k_{m,\varphi}$ with molal concentration can be adequately represented by the following equation

$$K_{m,\varphi} = K_{m,\varphi}^0 + S_K.m \tag{13}$$

where $K_{m,\varphi}^0$ is the limiting value of apparent molar isentropic compressibility, S_k is an experimental slope the indicative of the solute-solute interactions. The value of $K_{m,\varphi}^0$ and S_k, in addition to the standard deviation obtained by the least square fittings are reported in Table 7. The values of $K_{m,\varphi}^0$ for acetaminophen in different concentration of aqueous IL solutions are graphically presented in Fig. 3. The positive values of $K_{m,\varphi}^0$ for drug at different temperatures are attributed to the strong attractive interactions between drug and IL molecules [47]. The values of $K_{m,\varphi}^0$ are also increased with the increase in temperature which may be due to the release of water molecules from the second solvation layer of solute in water as well as in aqueous ionic liquid solutions. Therefore, there is a strong attractive interaction between acetaminophen molecules and ionic liquid.

The transfer partial molar isotropic compressibility, $\Delta_{tr}K_{m,\varphi}^0$ of acetaminophen from water to aqueous IL solutions at infinite dilution was calculated by using the following equation:

$$\Delta_{tr}K_{m,\varphi}^0 = K_{m,\varphi}^0(\text{in aq. IL solution}) - K_{m,\varphi}^0(\text{in water}) \tag{14}$$

These values of $\Delta_{tr}K_{m,\varphi}^0$ are reported in Table 7 which

Table 6. Experimental Speed of Sound, u, and Apparent Molar Isentropic Compressibility, K_φ, Data for Acetaminophen + [OMIm]Br + water at T = (293.15, 298.15, 303.15, 308.15) K

m (mol kg^{-1})	T (K)							
	293.15		298.15		303.15		308.15	
	u (m s^{-1})	K_φ.10^{14} (m^3 mol^{-1} Pa^{-1})	u (m s^{-1})	K_φ.10^{14} (m^3 mol^{-1} Pa^{-1})	u (m s^{-1})	K_φ.10^{14} (m^3 mol^{-1} Pa^{-1})	u (m s^{-1})	K_φ.10^{14} (m^3 mol^{-1} Pa^{-1})
				$m_{IL} = 0.0000$				
0.0000	1481.87		1496.68		1508.88		1519.37	
0.0312	1484.61	-1.28	1498.52	0.63	1510.58	0.96	1520.89	1.36
0.0323	1484.78	-1.22	1498.59	0.75	1510.69	0.98	1521.00	1.36
0.0361	1484.99	-0.99	1498.78	0.81	1510.90	0.99	1521.18	1.38
0.0390	1485.21	-0.95	1498.95	0.81	1511.04	1.01	1521.28	1.44
0.0432	1485.52	-0.87	1499.10	0.94	1511.26	1.04	1521.47	1.46
0.0474	1485.70	-0.70	1499.28	0.97	1511.37	1.15	1521.64	1.46
0.0492	1485.80	-0.63	1499.39	0.97	1511.45	1.18	1521.73	1.47
0.0531	1486.05	-0.57	1499.55	1.02	1511.63	1.19	1521.87	1.51
0.0563	1486.20	-0.54	1499.65	1.04	1511.72	1.22	1521.97	1.51
$m_{IL} = 0.1004$								
0.0000	1502.47		1514.59		1525.05		1533.97	
0.0295	1503.69	1.88	1515.72	2.10	1526.12	2.21	1534.99	2.34
0.0325	1503.79	1.90	1515.80	2.14	1526.21	2.23	1535.07	2.36
0.0360	1503.92	1.90	1515.90	2.16	1526.31	2.26	1535.17	2.37
0.0390	1504.01	1.93	1515.99	2.18	1526.39	2.27	1535.26	2.38
0.0435	1504.15	1.96	1516.10	2.23	1526.50	2.32	1535.37	2.40
0.0475	1504.29	1.97	1516.22	2.24	1526.62	2.32	1535.47	2.43
0.0494	1504.35	1.98	1516.26	2.26	1526.66	2.33	1535.51	2.44
0.0531	1504.46	2.00	1516.36	2.28	1526.76	2.35	1535.62	2.44
0.0553	1504.52	2.02	1516.40	2.30	1526.82	2.36	1535.67	2.46

Table 6. Continued

$m_{IL} = 0.1995$								
0.0000	1512.88		1523.72		1533.02		1540.91	
0.0300	1513.83	2.42	1524.65	2.53	1533.85	2.71	1541.70	2.78
0.0329	1513.89	2.51	1524.71	2.56	1533.91	2.73	1541.76	2.81
0.0358	1513.94	2.56	1524.78	2.58	1533.97	2.74	1541.81	2.84
0.0394	1514.02	2.58	1524.86	2.60	1534.05	2.75	1541.88	2.86
0.0436	1514.11	2.60	1524.93	2.64	1534.14	2.76	1541.97	2.86
0.0467	1514.17	2.61	1524.99	2.66	1534.20	2.77	1542.03	2.86
0.0493	1514.22	2.62	1525.05	2.66	1534.25	2.78	1542.07	2.87
0.0528	1514.30	2.63	1525.12	2.68	1534.32	2.79	1542.15	2.87
0.0561	1514.37	2.64	1525.20	2.68	1534.38	2.80	1542.20	2.88
$m_{IL} = 0.2995$								
0.0000	1517.75		1527.86		1536.61		1543.79	
0.0297	1518.68	2.51	1528.70	2.71	1537.37	2.85	1544.50	2.95
0.0330	1518.76	2.53	1528.78	2.72	1537.43	2.87	1544.56	2.96
0.0359	1518.82	2.56	1528.83	2.75	1537.48	2.89	1544.62	2.97
0.0393	1518.89	2.59	1528.90	2.76	1537.54	2.90	1544.68	2.97
0.0437	1518.98	2.61	1528.99	2.78	1537.61	2.93	1544.76	2.99
0.0472	1519.05	2.63	1529.05	2.80	1537.66	2.95	1544.81	3.00
0.0497	1519.10	2.64	1529.09	2.82	1537.70	2.95	1544.85	3.00
0.0529	1519.16	2.66	1529.15	2.83	1537.75	2.96	1544.90	3.01
0.0566	1519.23	2.68	1529.21	2.85	1537.81	2.98	1544.95	3.03
$m_{IL} = 0.4009$								
0.0000	1520.56		1529.91		1538.07		1544.89	
0.0301	1521.41	2.72	1530.71	2.82	1538.81	2.93	1545.59	3.02
0.0334	1521.48	2.74	1530.78	2.83	1538.87	2.95	1545.64	3.04
0.0357	1521.52	2.76	1530.83	2.83	1538.92	2.95	1545.67	3.06
0.0389	1521.59	2.77	1530.89	2.85	1538.98	2.96	1545.72	3.07
0.0435	1521.68	2.79	1530.98	2.86	1539.06	2.98	1545.79	3.09
0.0460	1521.73	2.80	1531.03	2.87	1539.09	3.00	1545.82	3.10
0.0488	1521.78	2.81	1531.08	2.88	1539.13	3.00	1545.86	3.10
0.0534	1521.86	2.83	1531.15	2.90	1539.18	3.02	1545.91	3.11
0.0558	1521.89	2.84	1531.20	2.90	1539.22	3.02	1545.94	3.11

m_{IL} is the molality of ionic liquid in aqueous ionic liquid solutions. Uncertainties: u (P) = ±0.05 kpa; u (T) = ±0.01 K; u (m) = 1×10^{-4} mol kg^{-1}; u (d) = $\pm 5.10^{-6}$ g cm^{-1}; u (u) = ±0.5 m s^{-1}.

Table 7. The Values of S_K, K_φ^0, $\Delta_{tr}K_\varphi^0$ and Standard Deviations $\sigma(K_\varphi)$ for Acetaminophen+ [OMIm]Br + Water at T = (293.15, 298.15, 303.15 and 308.15) K

m_{IL} (mol kg^{-1})	T (K)	$S_K.10^{13}$ (kg m^3 mol^{2-} Pa^{-1})	$K_\varphi^0.10^{15}$ (m^3 mol^{-1} Pa^{-1})	$\Delta_{tr}K_\varphi^0$ (m^3 mol^{-1} Pa^{-1})	$\sigma(K_\varphi)$
0.0000					
	293.15	2.94 ± 0.12	-21.4 ± 0.08		0.041
	298.15	1.46 ± 0.13	2.56 ± 0.06		0.031
	303.15	1.09 ± 0.18	6.14 ± 0.05		0.025
	308.15	0.63 ± 0.06	11.67 ± 0.03		0.013
0.1004					
	293.15	0.50 ± 0.02	17.28 ± 0.01	38.68	0.005
	298.15	0.75 ± 0.03	18.91 ± 0.01	16.35	0.006
	303.15	0.57 ± 0.04	20.56 ± 0.02	14.42	0.009
	308.15	0.44 ± 0.04	22.13 ± 0.01	10.40	0.005
0.1994					
	293.15	0.62 ± 0.05	22.65 ± 0.03	44.05	0.019
	298.15	0.60 ± 0.04	23.56 ± 0.02	20.96	0.011
	303.15	0.31 ± 0.01	26.29 ± 0.01	19.99	0.003
	308.15	0.33 ± 0.05	27.07 ± 0.03	15.40	0.014
0.2995					
	293.15	0.64 ± 0.03	23.31 ± 0.01	44.71	0.006
	298.15	0.51 ± 0.02	25.52 ± 0.01	22.96	0.004
	303.15	0.49 ± 0.03	27.09 ± 0.01	20.95	0.006
	308.15	0.27 ± 0.01	28.71 ± 0.01	17.04	0.003
0.4009					
	293.15	0.45 ± 0.03	25.88 ± 0.01	47.28	0.006
	298.15	0.32 ± 0.02	27.32 ± 0.01	24.76	0.003
	303.15	0.36 ± 0.01	28.20 ± 0.01	22.06	0.003
	308.15	0.35 ± 0.03	29.16 ± 0.01	17.49	0.008

m_{IL} is the molality of ionic liquid in aqueous ionic liquid solutions.

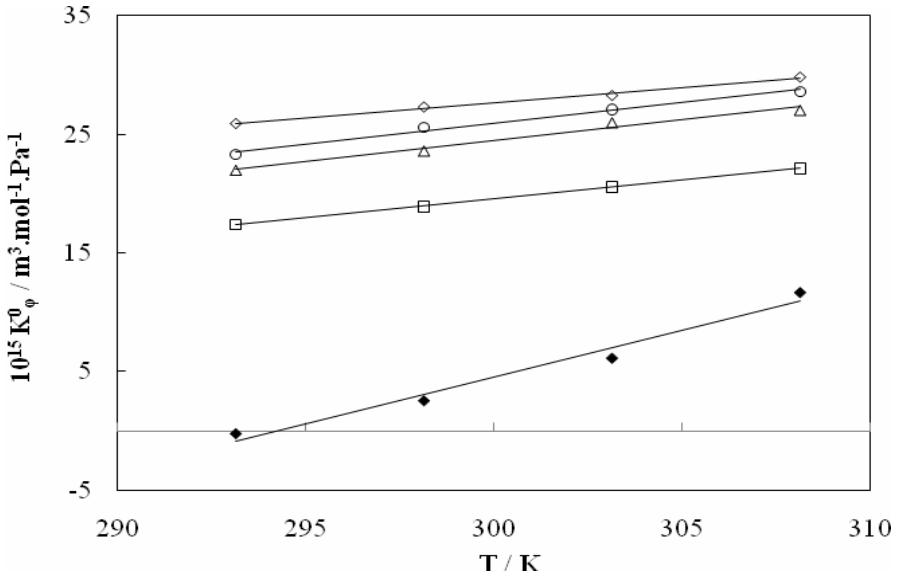

Fig. 3. The variation of limiting value of isentropic compressibility (K_φ^0) in aqueous [OMIm]Br solutions with different temperatures: ◆, 0.000; □, 0.1004; △, 0.1995; ○, 0.2995; ♢, 0.4009.

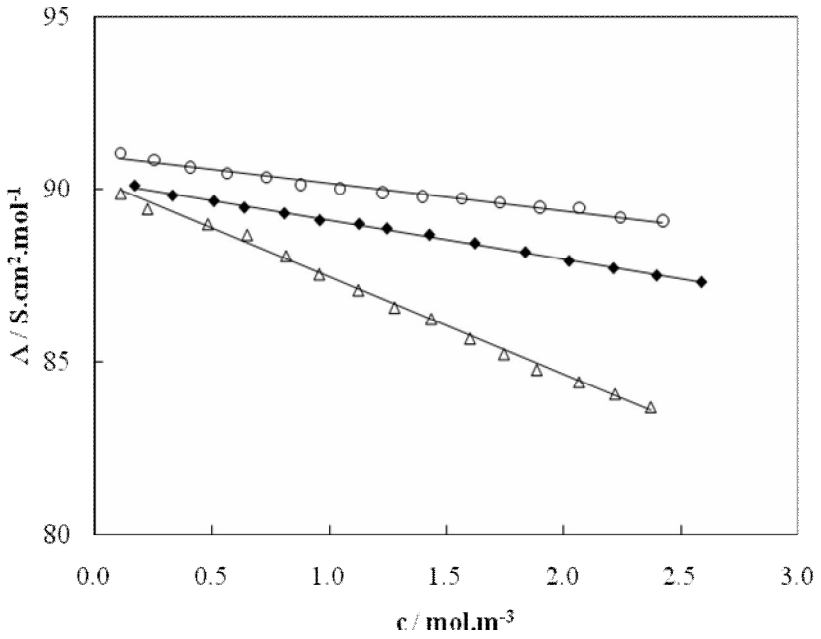

Fig. 4. Molar conductivities (Λ) of [OMIm]Br in aqueous acetaminophen solutions with different molalities of acetaminophen at T = 293.15 K: ○, 0.000; ◆, 0.0301; △, 0.0605.

have positive values at all concentration range of [OMIm] Br. According to co-sphere overlap model, the positive values of $\Delta_{tr}K^0_{m,\varphi}$ show the presence of type (a) and (b) interactions.

Conductometric Results

The values of molar conductivity, Λ of [OMIm] Br in acetaminophen + H_2O solutions are listed in Table 8. These values are also demonstrated graphically against the ionic liquid concentration at several molalities of acetaminophen in Fig. 4. It is clear that the molar conductivities decrease with the increase of both ionic liquid and acetaminophen concentrations. The experimental data were analyzed using the low concentration Chemical Model (lcCM) [48] by the following set of equations:

$$\Lambda = \alpha\left[\Lambda_0 - S(c\alpha)^{1/2} + Ec\alpha\ln(c\alpha) + J_1 c\alpha + J_2(c\alpha)^{3/2}\right] \quad (15)$$

$$K_A = \frac{1-\alpha}{\alpha^2 c\gamma_{\pm}^2} \quad (16)$$

$$\ln\gamma_{\pm} = -\frac{kq}{1+kR} \quad (17)$$

$$k^2 = \frac{16000N_A z^2 e^2 \alpha c}{\varepsilon_0 \varepsilon k_B T} \quad (18)$$

$$q = \frac{z^2 e^2}{8\pi\varepsilon_0 \varepsilon k_B T} \quad (19)$$

where Λ and Λ_0 are the molar conductivity and the limiting molar conductivity, respectively, (1 - α) is the fraction of oppositely charged ions acting as ion pairs, *R* is a distance parameter, and $\gamma_{\pm}$ is the corresponding mean activity coefficient of the free ions. The quantities required for the calculations of the coefficients *E*, J_1 and J_2 were taken from Ref. [48]. In this equation, *c* is molar concentration of the ionic liquid calculated through its molality and density data of the solution. The rest of the parameters have the usual meanings. Three-parameter fitting of the molar conductivity data yield the ion-association constant (K_A), the limiting molar conductivity, (Λ_0) and the distance parameter (*R*) by nonlinear least-squares iteration. The values of K_A, Λ_0 and *R* are given in Table 9. In this table, the values of limiting molar conductivity (Λ_0) and association constant (K_A), respectively, decrease and increase with increasing the concentration of acetaminophen. This can be explained by the fact that with the increase of acetaminophen concentration (i) the interactions of the ions of ionic liquid and acetaminophen get strength leading to increase in the radii of solvated ions, thereby the mobility and (ii) the mobility of ions decrease due to the increase in the viscosity of the solutions [49]. This extent of ion association in ionic liquid solutions increases with increasing temperature and thus ion-solvent interactions decreases. The obtained results from this work show the stronger ion-solvation at low temperature than high temperature. Also, the Λ_0 values measured for the studied ionic liquid increase as a function of increasing temperature; since the mobility of free ions is increased. The ion association constant $K_A(T)$ value was used to calculate Gibbs free energy of ion pair formation, $\Delta G^0_A(T)$,

$$\Delta G^0_A(T) = -RT\ln K_A(T) \quad (20)$$

Temperature dependence of $\Delta G^0_A(T)$ was expressed with the help of a polynomial,

$$\Delta G^0_A(T) = A_0 + A_1(298.15 - T) + A_2(298.15 - T)^2 \quad (21)$$

Enthalpy and entropy of ion association have been obtained as follows

$$\Delta S^0_A(T) = -\left(\frac{\partial \Delta G^0_A(T)}{\partial T}\right)_P = A_1 + 2A_2(298.15 - T) \quad (22)$$

$$\Delta H^0_A(T) = \Delta G^0_A(T) + T\Delta S^0_A(T) = A_0 + 298.15A_1 + (298.15^2 - T^2)A_2 \quad (23)$$

The values of the coefficients A_0, A_1 and A_2 at different molalities of acetaminophen are given in Table 10. The calculated thermodynamic functions are also listed in Table 9 and depicted by Fig. 5.This trend indicates that the ion association process exhibits a negative value of ΔG^0_A and

Table 8. Molar Conductivities, Λ , of [OMIm]Br in Aqueous Acetaminophen Solutions as a Function of Ionic Liquid Molarity (c) at Different Temperatures

T (K)							
293.15		298.15		303.15		308.15	
C (mol m^{-3})	$\Lambda \times 10^{-4}$ (S m^2 mol^{-1})	C (mol m^{-3})	$\Lambda \times 10^{-4}$ (S m^2 mol^{-1})	C (mol m^{-3})	$\Lambda \times 10^{-4}$ (S m^2 mol^{-1})	C (mol m^{-3})	$\Lambda \times 10^{-4}$ (S m^2 mol^{-1})
$m_A = 0.0000$ (mol kg^{-1})							
0.1101	91.050	0.115	99.738	0.130	109.348	0.128	116.998
0.2533	90.877	0.235	98.920	0.295	108.314	0.263	115.545
0.4092	90.648	0.336	98.323	0.395	107.637	0.423	113.862
0.5652	90.465	0.460	97.551	0.571	106.414	0.597	112.252
0.7331	90.367	0.591	96.656	0.714	105.498	0.757	110.664
0.8773	90.147	0.723	95.921	0.859	104.501	0.866	109.508
1.0441	90.033	0.858	94.884	1.007	103.699	1.059	108.110
1.2271	89.911	0.997	94.158	1.159	102.827	1.235	106.579
1.3990	89.799	1.130	93.388	1.324	102.030	1.412	105.299
1.5663	89.741	1.286	92.850	1.483	101.256	1.585	104.093
1.7272	89.606	1.431	92.271	1.625	100.556	1.749	103.122
1.8993	89.485	1.571	91.868	1.788	99.702	1.914	102.258
2.0661	89.449	1.711	91.370	1.962	98.884		
2.2404	89.376	1.864	91.026	2.120	98.071		
2.4222	89.296	1.992	90.705	2.239	97.434		
		2.130	90.288				
		2.285	89.943				
$m_A = 0.0301$ (mol kg^{-1})							
0.1682	90.105	0.131	98.248	0.161	105.206	0.101	117.664
0.3302	89.815	0.225	97.494	0.318	104.450	0.314	114.984
0.5061	89.651	0.353	96.495	0.474	103.526	0.506	112.895
0.6363	89.465	0.469	95.548	0.620	102.896	0.585	111.933
0.8072	89.300	0.572	94.748	0.785	102.077	0.766	110.253
0.9594	89.100	0.678	94.110	0.920	101.500	0.925	108.896
1.1273	88.996	0.860	93.122	1.072	100.824	1.084	107.577
1.2452	88.864	1.023	92.247	1.222	100.242	1.244	106.048
1.4271	88.684	1.161	91.606	1.366	99.676	1.388	105.312
1.6213	88.438	1.324	90.770	1.515	99.194	1.521	103.922
1.8362	88.181	1.483	90.130	1.661	98.596	1.659	103.030
2.0234	87.927	1.654	89.500	1.828	98.076	1.828	101.831
2.2131	87.718	1.817	89.051	1.969	97.650	1.985	100.798
2.3971	87.508	1.982	88.668	2.133	97.090	2.132	99.895
2.5882	87.319			2.278	96.672	2.279	99.002

Table 8. Continued

$m_A = 0.0605$ (mol kg^{-1})							
0.1123	89.640	0.137	96.674	0.046	100.779	0.092	105.455
0.2261	89.405	0.253	95.569	0.166	100.495	0.183	104.949
0.4833	88.756	0.385	94.807	0.202	100.346	0.322	104.314
0.6512	88.309	0.517	94.047	0.302	100.174	0.444	103.889
0.8162	87.891	0.633	93.421	0.503	99.635	0.623	103.168
0.9584	87.562	0.764	92.712	0.654	99.249	0.751	102.744
1.1245	87.101	0.852	92.275	0.797	98.891	0.902	102.078
1.2784	86.604	1.011	91.523	0.982	98.543	1.023	101.736
1.4341	86.274	1.133	90.911	1.142	98.163	1.153	101.215
1.5990	85.907	1.269	90.438	1.296	97.700	1.273	100.802
1.7444	85.556	1.411	89.946	1.476	97.381	1.421	100.385
1.8843	85.204	1.537	89.498	1.631	97.083	1.576	99.909
2.0642	84.842	1.698	88.819	1.795	96.840	1.704	99.509
2.2173	84.494	1.853	88.327	1.952	96.600	1.838	99.174
2.3693	84.191	1.997	87.827	2.120	96.386		

m_A *is* molality of acetaminophen in water.

Table 9. The Association Constants (K_A), Limiting Molar Monductivities (Λ_0), the Distance of Closest Approach of Ions (R), Standard Deviations ($\sigma(\Lambda)$) and Thermodynamic Functions (ΔG^0, ΔS^0 and ΔH^0) of [OMIm]Br in Aqueous Acetaminophen Solutions at Different Temperatures

T (K)	K_A (dm^3 mol^{-1})	$\Lambda_0 \times 10^{-4}$ (S m^2 mol^{-1})	$10^{10} R$ (m)	$\sigma(\Lambda)$	ΔG^0 (kJ mol^{-1})	ΔS^0 (J mol^{-1} K^{-1})	ΔH^0 (kJ mol^{-1})
$m_A = 0.0000$ mol kg^{-1}							
293.15	5.29 ± 0.67	91.39 ± 0.33	24.41		-4.06	576.4	164.79
298.15	12.41 ± 0.67	100.99 ± 0.31	43.92	0.03	-6.24	460.4	130.91
303.15	31.69 ± 0.77	110.97 ± 0.33	44.74	0.11	-8.87	344.4	104.28
308.15	36.03 ± 1.41	118.86 ± 0.35	44.84	0.11	-9.89	228.4	60.39
				0.09			

Table 9. Continued

m_A = 0.0301 mol kg^{-1}							
293.15	7.56 ±0.71	90.48±0.33	0.001	0.04	-4.93	678.2	193.83
298.15	15.53 ±0.81	99.14 ±0.32	45.80	0.27	-7.58	436.2	121.41
303.15	33.68 ± 0.79	106.46 ±0.33	32.68	0.04	-8.86	194.2	49.95
308.15	51.27 ±0.85	114.65 ±0.33	40.73	0.14	-10.09	-47.8	-24.82
m_A = 0.0605 mol kg^{-1}							
293.15	9.31 ± 0.75	90.38 ± 0.33	0.18	0.07	-5.44	516.4	145.83
298.15	22.36 ± 1.05	97.51 ± 0.33	41.04	0.09	-7.93	388.4	107.75
303.15	38.64 ± 0.73	101.14 ± 0.33	13.96	0.07	-9.21	260.4	69.61
308.15	52.26 ± 0.77	106.10 ± 0.33	16.45	0.04	-10.42	132.4	30.26

m_A *is* molality of acetaminophen in water.

Table 10. The Values of Coefficients in Eq. (21) A_0, A_1, A_2 and Correlation Coefficient (R^2) at Different Molality of Acetaminophen

m_A (mol kg^{-1})	$10^{-3} A_0$ (J mol^{-1})	A_1 (J mol^{-1} K^{-1})	A_2 (J mol^{-1} K^{-2})	R^2
0.0000	-6.549	460.4	11.6	0.97
0.0301	-7.932	406.2	14.2	0.96
0.0605	-7.759	388.4	12.8	0.97

m_A *is* molality of acetaminophen in water.

becomes more negative with increasing temperature proposing the spontaneity and feasibility of the association process at high temperatures. In the majority of cases, the ΔS_A^0 values are positive over the whole temperature range. The positive ΔS_A^0 values may be attributed to the increasing number of degrees of freedom due to the release of solvent molecules from hydration shells as association takes place. In other words, the solvation of the individual ions is weakened as soon as these ion pairs are formed. The positive contribution of entropy results from the dehydration of ions which is dominant over the negative contribution from the formation ion pairs. It should be noted that the entropy term, $T\Delta S_A^0$, is sufficiently positive to exceed the positive contribution of the enthalpy, ΔH_A^0. Consequently, the ion-association process exhibits negative values of ΔG_A^0 and the process is driven by the change in entropy.

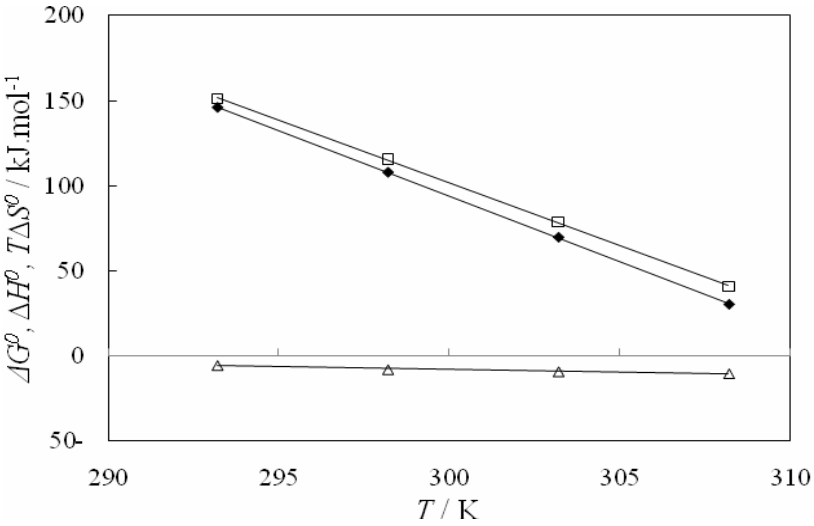

Fig. 5. Thermodynamic functions of association process for [OMIm]Br in 0.06 mol kg^{-1} aqueous acetaminophen solution at different temperatures: △, ΔG_A^0; ◆, ΔH_A^0; □, $T\Delta S_A^0$.

Inspection of Table 9 indicates that the ΔH_A^0 values for [OMIm]Br in aqueous acetaminophen solutions are positive at all experimental temperatures suggesting an endothermic process for the ion pair formation.

CONCLUSIONS

In the present work, volumetric, compressibility and conductometric measurements have been used to study the interactions between a drug, acetaminophen, and the ionic liquid in aqueous medium. The apparent molar volume, V_φ, apparent molar isontropic compressibility, $K_{m,\varphi}$, of acetaminophen in the aqueous ionic liquid, 1-octyl-3-methyl-imidazolium bromide ([OMIm]Br), solutions calculated from density and speed of sound measurements are used to obtain the standard partial molar properties, transfer partial molar properties, hydration number. It was found that the calculated quantities decrease with the [OMIm]Br concentration. This observation indicates that the interactions of the ionic liquid with acetaminophen become stronger with the increase of the ionic liquid concentration. The derived transfer properties, $\Delta_{tr}V_\varphi^0$ and $\Delta_{tr}K_{m,\varphi}^0$ indicated the dominance of hydrophilic-ionic hydrophilic-hydrophilic interactions between acetaminophen and ions of the ionic liquid. Generally, the calculated Hepler's constant suggest that acetaminophen would be acting as a structure breaker and this behavior will be weakened with increasing ionic liquid concentration. The conductometric results show that the values of association constant (K_A) and limiting molar conductivity (Λ_0) of [OMIm]Br in aqueous acetaminophen solutions, respectively, increase and decrease by increasing the concentration of acetaminophen. This can be explained by the fact that an increase in the molality of acetaminophen causes the strong interactions between ions of the ionic liquid and acetaminophen. The spontaneity of the association formation process was confirmed by the Gibbs free energy changes accompanied by these processes.

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