Salting-Out Effect, Preferential Exclusion, and Phase Separation in Aqueous Solutions of Chaotropic Water-Miscible Ionic Liquids and Kosmotropic Salts: Effects of Temperature, Anions, and Cations

Mohammed Taghi Zafarani-Moattar* and Sholeh Hamzehzadeh

Physical Chemistry Department, Faculty of Chemistry (Excellence of Science for New Materials and Clean Chemistry), University of Tabriz, Tabriz, Iran

The phase diagrams and the liquid−liquid equilibrium (LLE) data of 1-butyl-3-methylimidazolium chloride ([C_4mim]Cl) + tripotassium citrate and 1-butyl-3-methylimidazolium bromide ([C_4mim]Br) + trisodium citrate aqueous two-phase systems (ATPS's) were determined experimentally at T = (278.15, 298.15, and 318.15) K. The Merchuk equation with three dependent-temperature adjustable parameters was used for reproducing the binodal curves. In the studied systems, the salting-out effect caused by the addition of the inorganic salts to the aqueous solutions of the water-miscible ionic liquids (ILs) was investigated. The effects were analyzed using the corresponding composition phase diagrams. The effect of temperature on the phase-forming ability in the investigated systems was also evaluated based on a salting-out coefficient obtained from fitting the tie-line data to a Setschenow-type equation. The values of the salting-out coefficients may reflect the extent of the preferential hydration of the IL. Furthermore, the salting-out effect and the consequent phase separation in the investigated ATPS's were interpreted taking into account the complex and competing nature of the interactions between the solutes and water. Finally, the intensity of the phase-forming ability in the [C_4mim]X (X = Cl^- or Br^-) + salt ATPS's was also examined on the basis of the ionic viscosity B-coefficients of the Jones−Dole equation.

Introduction

Liquid−liquid extraction utilizing aqueous two-phase systems (ATPS's) has often been a favored choice in both industry and academia for the development of separation processes because these systems are considered to be environmentally safe and benign due to the lack of use of traditional volatile organic compounds (VOCs) in the whole process. Recently, systems based on polymers or ionic liquids (ILs: a new type of ionic solvents which have melting points less than 100 °C) have received more attention since both can exhibit negligible vapor pressures. ATPS's usually form when an aqueous solution exceeds specific threshold concentrations of two water-soluble, but mutually incompatible (e.g., a polymer vs a polymer, a polymer vs a salt, or an IL vs a salt), components.[1−4]

Polymer-based (i.e., polymer−polymer or polymer−salt) ATPS's have been widely used to separate and purify various biological products,[1−3,5] metal ions,[6,7] dyes, drug molecules and small organic species,[8,9] and nano- and microsolid particles[10,11] from the complex mixtures in which they are produced. For large-scale extractions, the polymer−salt ATPS's are more attractive because of their greater selectivity, lower viscosity, lower cost, rapid phase disengagement, and availability of commercial separators, which allow a faster and continuous separation. Poly(ethylene glycol) (PEG), which is a hydrophilic polymer, is the most common polymer used with a water-structuring salt to form the polymer−salt ATPS's. Such salts are known as promoters of the water structure and are therefore referred to as kosmotropes ("kosmo-trope" = order maker). These salts would give rise to salting-out effects, tending to precipitate proteins and prevent unfolding. The PEG is "salted-out" through the use of a kosmotropic salt because of its solubility to be decreased.[8,12,13] The applications of the polymer-based ATPS's have been well-documented.[1−15]

In recent years, IL-based (i.e., hydrophobic IL−water or hydrophilic IL−salt) ATPS's have been gaining great exposure because of their potential use in the design of new "green" separation technologies for the development of clean manufacturing processes. Hydrophobic ILs usually contain expensive fluorinated ions, which raises the cost of the IL and causes environmental concerns. There are many more inexpensive, hydrophilic ILs; however, these hydrophilic ILs cannot be used directly in a liquid−liquid extraction with water because of their complete mutual solubility. In this respect, the hydrophilic ILs have been investigated in mixtures with aqueous solutions of kosmotropic salts in recent years.[4,16−31] These new ATPS's have many advantages shared by ILs and ATPS's, such as low viscosity, little emulsion formation, no need of using volatile organic solvent, quick phase separation, high extraction efficiency, and gentle biocompatible environment, and have been successfully used to separate testosterone,[25] epitestosterone,[25] opium alkaloids,[26] bovine serum albumin,[27,28] and amino acids.[30,31]

The most common kosmotropic salts employed by different research groups[4,16−28] on the IL-based aqueous two-phase extraction technique consist of selective cations (ammonium, potassium, or sodium) and anions (phosphate, sulfate, hydroxide, or carbonate). The high concentrations of each of these salts required to form the two-phase systems cause environmental concerns. For this purpose, different biodegradable solutes such as amino acids[32] and carbohydrates[33−35] have been examined in recent years as replacements for inorganic salts in hydrophilic

---

* Corresponding author. Fax: +98 411 3340191. E-mail: zafarani47@yahoo.com.

10.1021/je900681b

IL−salt ATPS's. However, these solutes failed to form an ATPS with some hydrophilic ILs such as [C_4mim]Cl[32−35] or [C_4mim]-Br.[33−35] Previous studies on the polymer-based ATPS's[36] have demonstrated that replacing the inorganic salts by other biodegradable and nontoxic ones such as citrates could be considered a good alternative, because citrates can be discharged into biological wastewater treatment plants. Recently, we[29] have used citrate as a substitute for inorganic salts in [C_4mim]Br−salt ATPS's. In continuation of our previous work on the phase equilibrium properties of aqueous IL−citrate salt two-phase systems,[29] here we report the phase diagrams and the compositions of coexisting phases for the [C_4mim]Cl + tripotassium citrate and the [C_4mim]Br + trisodium citrate ATPS's at T = (278.15, 298.15, and 318.15) K that have not been previously published. The obtained results are necessary for the design and optimization of extraction processes, understanding the general factors determining the partition of solutes and particles in such ATPS's, and the development and testing of both thermodynamic and mass transfer models of ATPS's.

In the studied systems, the salting-out effect arising from the addition of tripotassium citrate or trisodium citrate to the aqueous solutions of the water-miscible [C_4mim]Cl or [C_4mim]Br ILs was investigated. The effects were analyzed using the corresponding composition phase diagrams. It is now better to review previous works on the salting-out effects in the systems involving ILs. The first attempt to promote IL salting-out in aqueous solutions made use of supercritical carbon dioxide.[37−43] This fluid has shown antisolvent effects inducing liquid−liquid phase separation between ILs and organic or water liquid mixtures as well as the precipitation of solid solutes dissolved in ILs.[37−43] Scurto et al.[38] showed that the phase separation of water and ILs in the presence of CO_2 can partly result from the formation of carbonate in solution. In addition, the enhancement of liquid−liquid phase separation in systems involving ILs and aqueous phases using inorganic salts was first qualitatively studied by Dupont et al.[44] followed by Gutowski et al.[4] who confirmed those results quantitatively. Trindade et al.[45] described the entire liquid−liquid temperature−composition phase diagram between aqueous salt solutions and an hydrophilic IL, [C_4mim][BF_4], where significant upward shifts of the liquid−liquid demixing temperatures of those systems were observed. On the other hand, Najdanovic-Visak et al.[46] presented ternary phase diagrams describing the large salting-out effect produced by the addition of potassium phosphate to aqueous solutions of water-miscible ILs. Moreover, recently, Canongia Lopes and Rebelo[47] reviewed the salt effects of hydrophilic IL-containing systems and some of their applications. On the other part, in more recent years, in connection with the salting in/out effects in the systems involving hydrophobic ILs a thorough investigation on the effects of inorganic or organic ions on the mutual solubilities of water and hydrophobic ILs has also been carried out by Coutinho group.[48,49]

In this work, the effect of temperature on the phase-forming ability in the investigated systems has also been evaluated in the shape of the salting-out effect using a Setschenow-type equation,[50] because the capability of a certain amount of a given kosmotropic salt to motivate the formation of the two phases in a given water-miscible IL solution at different temperatures may also be related to the salting-out strength of the kosmotropic salt.[45,46] More recently, we have been successfully applied the Setschenow-type equation[50] to introduce a quantitative measure for the salting-out effects of the tripotassium citrate salt on [C_4mim]Br in the investigated [C_4mim]Br + tripotassium citrate ATPS at different temperatures.[29] The work described in this paper was undertaken to further explore the relationship between Setschenow-type behavior and the phase diagrams in IL−salt ATPS's.

Using the hydration theories,[51−54] we may also correlate the salting-out effect and the consequent phase separation in the investigated IL−salt ATPS's to the hydration strength of the IL or salt constituent ions. From this point of view the values of the obtained salting-out coefficients for the used Setschenow-type equation may be related to the extent of the preferential hydration (or the preferential exclusion of the salt from the solvation shell) of the IL. Previously, the Setschenow-type equation along with the preferential hydration theory has been used by Hey et al. to describe the salting-out effects in polymer−salt ATPS's.[50] Finally, under the label of hydration theories, the intensity of the phase-forming ability in the investigated systems has also been examined in comparison with the previously studied imidazolium-based IL−salt ATPS's based on the ionic viscosity B-coefficients of the Jones−Dole equation as a criterion for the ion kosmotropicity (water-structuring effects) of the IL or salt constituent ions.

Experimental Section

Materials. [C_4mim]Cl and [C_4mim]Br were obtained from Merck with a quoted purity greater than w (mass fraction) = 0.98 and used without further purification. The water content in the [C_4mim]Cl and [C_4mim]Br was determined by the use of the Karl Fischer method to be respectively w = 0.0080 and 0.0095 in mass fraction, which were in good agreement with the values quoted by the suppliers, approximately less than w = 0.01. This water content in the ILs was taken into account during the preparation of the aqueous solutions for the treatment of the experimental data. Tripotassium citrate and trisodium citrate with purity of minimum w = 0.99 by mass were supplied by Fluka and used without further purification. Double-distilled deionized water was used for preparation of the solutions.

Experimental Procedure. The experimental apparatus employed is essentially similar to the one used previously.[22,29,55] The temperature was controlled to within ± 0.05 K. The binodal curves were determined by the cloud-point method. A salt solution of known concentration was titrated with the IL solution or vise versa, until the solution turned turbid, which indicated the formation of two liquid phases. In accordance with the amount of titrant added until turbidity was observed, the composition of the mixture for each point on the binodal curve was calculated by mass using an analytical balance (model: 321-34553, Shimatzu Co., Japan) with an uncertainty of $\pm 1 \cdot 10^{-7}$ kg. For the determination of the tie-lines, feed samples (about $1 \cdot 10^{-5}$ m^3) were prepared by mixing appropriate amounts of IL, salt, and water in the vessel. After sufficient mixing, the samples were placed in a water bath at the desired temperature and allowed to settle overnight to separate into two clear phases. After separation of the two phases, the concentrations of salts in the top and bottom phases were determined by potassium or sodium analysis using flame photometry. Following Cheluget et al.,[56] the concentration of IL in both phases was also determined by refractive index measurements performed at 298.15 K using a refractometer (model: DR-A1, Atago Co., Ltd., Japan) with a precision of ± 0.0001. The uncertainties in refractive index measurements are within ± 0.0002. For dilute aqueous solutions containing an IL and a salt, the relation between the refractive index, n_D, and the mass fractions of IL, w_1, and salt, w_2, is given by[56]

$$n_D = n_0 + a_1w_1 + a_2w_2 \tag{1}$$

where n_0 is the refractive index of pure water which is set to 1.3325 at 298.15 K. This equation has been used for the phase analysis of the PEG + NaCl + H_2O system by Cheluget et al.[56]

In regards with the validity of the above procedure in the determination of the tie-line compositions, a mass balance check was performed between the amounts of salt and IL used to create the feed sample and the amounts in the top and bottom phases on the basis of equilibrium compositions. It was found that our procedure in determination of the concentrations of salt in both phases using potassium or sodium analysis and those of ILs by refractive index measurements is consistent with the mass balance calculations within ± 1 %. Therefore we concluded that the same method of calibration plots and evaluation of parameters given by Cheluget et al.[56] can also be used for analysis of [C_4mim]Cl + tripotassium + water and [C_4mim]Br + trisodium citrate + water systems. Thus, the value of coefficient a_1 in eq 1 was obtained as 0.1728 ± 0.0002 and 0.1536 ± 0.0002, and the value of coefficient a_2 was also obtained as 0.1537 ± 0.0001 and 0.1785 ± 0.0001, for the [C_4mim]Cl + tripotassium + water and [C_4mim]Br + trisodium citrate + water systems, respectively. The standard uncertainties in the a_1 and a_2 values were evaluated using the method of least-squares to fit a linear curve to the refractive index calibration plots to estimate the parameters of the curve and their standard deviations.[57] However, it should be noted that this equation is only valid for dilute solutions ($w_1 \leq 0.1$ and $w_2 \leq 0.05$) for which linear calibration plots of the refractive index of ternary solutions with a fixed mass fraction of salt or IL against IL or salt are obtained. Therefore, before the refractive index measurements, it was necessary to dilute the samples to the above mass fraction ranges. The results of the refractive index measurements for the diluted samples along with the corresponding dilution factors for the [C_4mim]Cl + tri- potassium + water and [C_4mim]Br + trisodium citrate + water systems are respectively presented in the Tables 1S and 2S in the Supporting Information of this manuscript.

Furthermore, to see more closely the reliability of the above procedure employed in the determination of the tie-line compositions of the investigated systems, the water contents in some phases were arbitrarily determined by the Karl Fischer method using a Karl Fischer titrator (model: 751 GPD Titrino- Metrohm, Herisau, Switzerland). The obtained results were in good agreement with the results obtained using the method given by Cheluget et al.[56]

The tie-line length, TLL, and the slope of the tie-line, S, at different compositions and temperatures were also calculated respectively using eqs 2 and 3 as follows[3]

$$\mathrm{TLL} = [(w_1^{\mathrm{t}} - w_1^{\mathrm{b}})^2 + (w_2^{\mathrm{t}} - w_2^{\mathrm{b}})^2]^{0.5} \tag{2}$$

$$S = (w_1^{\mathrm{t}} - w_1^{\mathrm{b}})/(w_2^{\mathrm{t}} - w_2^{\mathrm{b}}) \tag{3}$$

where w_1^{t}, w_1^{b}, w_2^{t}, and w_2^{b} represent the equilibrium compositions (in weight percent) of IL (1) and salt (2), in the top, t, and bottom, b, phases, respectively.

Results and Discussion

Table 1. Binodal Data for {IL (1) + Salt (2) + H_2O (3)} Systems at T = (278.15, 298.15, and 318.15) K

T/K = 278.15		T/K = 298.15		T/K = 318.15	
100 w_1	100 w_2	100 w_1	100 w_2	100 w_1	100 w_2
[C_4mim]Cl + Tripotassium Citrate + H_2O					
63.12	1.56	48.50	8.82	59.35	4.47
59.49	2.40	47.23	9.64	56.67	5.89
53.56	4.76	46.39	10.22	51.32	8.50
47.86	7.71	45.29	10.91	48.52	10.19
42.80	11.02	44.54	11.53	46.60	11.37
40.14	13.30	43.81	12.19	44.04	13.22
38.94	14.13	42.91	12.65	41.61	15.15
36.71	15.81	40.92	14.15	39.45	16.87
34.59	17.74	40.08	14.84	37.78	18.31
32.75	19.41	38.98	15.84	35.71	20.18
30.78	21.25	37.44	17.04	34.01	21.79
28.73	23.35	35.90	18.49	31.73	23.91
26.69	25.45	34.92	19.37		
24.09	28.14	33.74	20.48		
		32.31	21.82		
		30.93	23.11		
		28.30	25.79		
		25.35	28.39		
[C_4mim]Br + Trisodium Citrate + H_2O					
51.94	3.12	44.34	6.72	53.81	3.93
46.32	4.82	43.56	7.11	50.57	4.94
43.33	5.95	39.55	9.11	48.40	5.70
39.76	7.18	35.95	10.93	46.55	6.44
37.66	8.53	34.85	11.62	44.94	7.14
36.35	9.33	33.64	12.40	43.66	7.83
35.63	9.69	31.48	13.77	42.34	8.47
34.86	10.18	27.83	16.16	41.09	9.07
		22.81	19.69	40.00	9.66
				39.00	10.21
				37.71	10.95
				35.69	12.14

Phase Diagrams. For the aqueous [C_4mim]Cl + tripotassium citrate and [C_4mim]Br + trisodium citrate systems the binodal data at T = (278.15, 298.15, and 318.15) K are given in Table 1, and the compositions of coexisting phases determined experimentally at T = (278.15, 298.15, and 318.15) K are also given in Tables 2 and 3, respectively. For the studied systems the experimental binodal data were fitted by least-squares regression method to the following empirical nonlinear expression developed by Merchuk[58]

$$w_1 = a \exp(bw_2^{0.5} - cw_2^{3}) \tag{4}$$

where a, b, and c represent fit parameters and w_1 and w_2 represent the concentrations (in weight percent) of IL and salt, respectively. Recently, the above equation has been used for the correlation of binodal data of some aqueous IL−salt systems.[4,22−24] More recently, we[29] have successfully used the Merchuk equation with temperature-dependent fitting parameters to reproduce the binodal data of the [C_4mim]Br + tripotassium citrate ATPS at T = (278.15, 298.15, and 318.15) K. The used Merchuk equation could also be applied accurately to predict the characteristics of the binodal curves for the [C_4mim]Br + tripotassium citrate ATPS at the temperature where no experimental data were available.[29]

The temperature dependence for the fitting parameters of Merchuk equation, a, b, and c, is expressed in a linear form with $(T - T_0)$ K as a variable, as follows:[29]

$$a = a^0 + a^1(T - T_0) \tag{4a}$$

$$b = b^0 + b^1(T - T_0) \tag{4b}$$

$$c = c^0 + c^1(T - T_0) \tag{4c}$$

In eqs 4a, 4b, and 4c, T_0 is assumed to be the reference temperature, T_0 = 273.15 K, and a^0, a^1, b^0, b^1, c^0, and c^1 are independent-temperature adjustable parameters. These fitting parameters obtained from the correlation of the experimental binodal data along with the corresponding absolute average deviations (AAD) are given in Table 4. The binodals reproduced from eq 4 at different temperatures are also shown in Figures 1 and 2. On the basis of

Table 2. Experimental Phase Equilibrium Compositions, Tie-Line Lengths, TLL, and Slope of Tie-Lines, *S*, for {[C_4mim]Cl (1) + Tripotassium Citrate (2) + H_2O (3)} System at *T* = (278.15, 298.15, and 318.15) K

	total composition		top phase: IL-rich phase			bottom phase: salt-rich phase				
	100 w_1	100 w_2	100 w_1	100 w_2	100 w_3	100 w_1	100 w_2	100 w_3	TLL	*S*
					T = 278.15 K					
tie1	30.03	32.90	59.13 ± 0.22	3.23 ± 0.16	37.64,[a] 37.47[b]	2.13 ± 0.36	61.40 ± 0.36	36.47,[a] 36.91[b]	81.44	−0.98
tie2	29.93	30.79	56.54 ± 0.27	4.34 ± 0.23	39.11,[a] 39.54[b]	3.33 ± 0.36	57.16 ± 0.36	39.51,[a] 40.25[b]	74.97	−1.01
tie3	30.41	28.43	53.74 ± 0.36	5.66 ± 0.33	40.61,[a] 40.44[b]	4.30 ± 0.34	54.41 ± 0.34	41.29,[a] 41.58[b]	69.44	−1.01
tie4	29.94	26.03	48.41 ± 0.10	8.20 ± 0.05	43.38,[a] 43.09[b]	5.58 ± 0.32	49.49 ± 0.31	44.93,[a] 45.07[b]	59.50	−1.04
					T = 298.15 K					
tie1	29.01	35.64	61.14 ± 0.09	3.63 ± 0.02	35.22[a]	3.98 ± 0.31	62.33 ± 0.31	33.69[a]	81.93	−0.97
tie2	29.27	33.39	58.88 ± 0.09	4.57 ± 0.02	36.55[a]	5.47 ± 0.27	58.21 ± 0.25	36.32[a]	75.69	−1.00
tie3	29.76	30.45	53.73 ± 0.10	6.84 ± 0.04	39.43[a]	5.99 ± 0.28	55.67 ± 0.27	38.34[a]	68.29	−0.98
tie4	29.76	28.55	49.86 ± 0.10	8.76 ± 0.04	41.38[a]	6.87 ± 0.26	52.50 ± 0.25	40.63[a]	61.34	−0.98
tie5	29.68	26.93	45.02 ± 0.10	11.52 ± 0.06	43.45[a]	8.24 ± 0.24	48.86 ± 0.23	42.90[a]	52.41	−0.99
					T = 318.15 K					
tie1	29.68	35.35	60.05 ± 0.10	4.40 ± 0.03	35.55,[a] 35.62[b]	2.97 ± 0.36	61.76 ± 0.36	35.27,[a] 35.15[b]	80.92	−1.00
tie2	30.07	32.86	57.26 ± 0.11	5.68 ± 0.04	37.06,[a] 37.11[b]	3.46 ± 0.36	59.12 ± 0.35	37.42,[a] 37.22[b]	75.82	−1.01
tie3	29.91	30.70	52.59 ± 0.50	7.76 ± 0.48	39.65,[a] 39.40[b]	3.96 ± 0.35	55.36 ± 0.34	40.68,[a] 40.35[b]	68.04	−1.02
tie4	30.42	28.47	49.91 ± 0.08	9.12 ± 0.02	40.97,[a] 40.65[b]	5.34 ± 0.34	52.24 ± 0.35	42.41,[a] 43.07[b]	62.01	−1.03

[a] Calculated using the equation $\sum_i w_i^t = \sum_i w_i^b = 1$ (i = 1, 2, 3), where w_i^t and w_i^b represent the weight fraction of the component i [i.e., IL (1), salt (2), or water (3)] in the top, t, and bottom, b, phases, respectively. [b] Determined experimentally by the Karl Fischer method.

Table 3. Experimental Phase Equilibrium Compositions, Tie-Line Lengths, TLL, and Slope of Tie-Lines, *S*, for {[C_4mim]Br (1) + Trisodium Citrate (2) + H_2O (3)} System at *T* = (278.15, 298.15, and 318.15) K

	total composition		top phase: IL-rich phase			bottom phase: salt-rich phase				
	100 w_1	100 w_2	100 w_1	100 w_2	100 w_3	100 w_1	100 w_2	100 w_3	TLL	*S*
					T = 278.15 K					
tie 1	27.88	21.15	54.31 ± 0.25	2.46 ± 0.15	43.23,[a] 43.22[b]	3.43 ± 0.58	38.55 ± 0.46	58.02,[a] 57.99[b]	62.38	−1.41
tie 2	27.41	20.38	51.83 ± 0.12	3.03 ± 0.04	45.14[a]	4.16 ± 0.82	36.72 ± 0.66	59.12[a]	58.38	−1.41
tie 3	27.54	19.46	50.13 ± 0.12	3.48 ± 0.05	46.38,[a] 46.58[b]	4.56 ± 0.82	35.69 ± 0.66	59.75,[a] 59.37[b]	55.80	−1.42
tie 4	27.91	18.52	48.65 ± 0.12	3.97 ± 0.06	47.37,[a] 47.32[b]	5.93 ± 0.85	33.71 ± 0.69	60.35,[a] 59.95[b]	52.05	−1.44
tie 5	27.10	17.43	43.88 ± 0.21	5.77 ± 0.12	50.35[a]	8.37 ± 0.77	30.37 ± 0.63	61.25[a]	43.20	−1.44
tie 6	27.54	16.17	40.33 ± 0.15	7.07 ± 0.08	52.60,[a] 52.58[b]	9.92 ± 0.75	28.35 ± 0.60	61.74,[a] 61.52[b]	37.12	−1.43
					T = 298.15 K					
tie 1	27.33	20.45	50.79 ± 0.11	4.19 ± 0.03	45.02[a]	5.76 ± 0.38	35.83 ± 0.29	58.40[a]	55.04	−1.42
tie 2	27.68	19.48	49.02 ± 0.11	4.83 ± 0.03	46.15[a]	6.96 ± 0.33	34.09 ± 0.24	58.95[a]	51.24	−1.44
tie 3	27.69	18.58	46.26 ± 0.12	6.11 ± 0.05	47.63[a]	8.69 ± 0.39	31.90 ± 0.28	59.42[a]	45.56	−1.46
tie 4	27.28	17.68	42.15 ± 0.12	7.86 ± 0.05	49.99[a]	10.9 ± 0.28	29.27 ± 0.20	59.83[a]	37.89	−1.46
					T = 318.15 K					
tie 1	27.98	21.55	52.16 ± 0.16	4.20 ± 0.07	43.64,[a] 43.59[b]	6.18 ± 0.70	37.28 ± 0.55	56.54,[a] 56.73[b]	56.65	−1.39
tie 2	28.00	20.50	49.95 ± 0.14	4.79 ± 0.06	45.26,[a] 45.22[b]	7.60 ± 0.45	35.29 ± 0.34	57.11,[a] 57.79[b]	52.19	−1.39
tie 3	28.12	19.53	47.21 ± 0.15	5.85 ± 0.07	46.94,[a] 46.85[b]	8.71 ± 0.52	33.13 ± 0.40	58.16,[a] 57.81[b]	47.18	−1.41
tie 4	27.89	18.45	42.42 ± 0.16	8.04 ± 0.09	49.54,[a] 49.71[b]	10.69 ± 0.66	30.95 ± 0.53	58.36,[a] 58.73[b]	39.14	−1.38
tie 5	28.08	17.53	38.79 ± 0.18	9.98 ± 0.10	51.23,[a] 51.26[b]	12.54 ± 0.58	28.26 ± 0.46	59.19,[a] 59.25[b]	31.99	−1.44

[a] Calculated using the equation $\sum_i w_i^t = \sum_i w_i^b = 1$ (i = 1, 2, 3), where w_i^t and w_i^b represent the weight fraction of the component i [i.e., IL (1), salt (2), or water (3)] in the top, t, and bottom, b, phases, respectively. [b] Determined experimentally by the Karl Fischer method.

Table 4. Values of the Parameters of Equation 4 for {IL (1) + Salt (2) + H_2O (3)} at *T* = (278.15, 298.15, and 318.15) K

T/K	a^0	a^1	b^0	$b^1 \cdot 10^4$	$c^0 \cdot 10^6$	$c^1 \cdot 10^8$	AAD[a]
			[C_4mim]Cl + Tripotassium Citrate + H_2O				
278.15	77.76	0.2490	−0.1790	−1.897	10.24	−3.447	0.27, 1.22[b]
298.15							0.10, 1.58[b]
318.15							0.12, 0.45[b]
			[C_4mim]Br + Trisodium Citrate + H_2O				
278.15	78.88	0.2163	−0.2479	−0.5526	26.68	−7.683	0.39, 0.60[b]
298.15							0.30, 0.57[b]
318.15							0.13, 0.67[b]

[a] AAD = $(1/N)\sum_{i=1}^{N}|w_{1,i}^{\text{calcd}} - w_{1,i}^{\text{exptl}}|$, where w_1 and N represent the concentration (in weight percent) of the IL and the number of binodal data, respectively. [b] Obtained from comparison of the experimental IL phase equilibrium compositions, w_1, for the investigated aqueous IL + salt systems at *T* = (278.15, 298.15, and 318.15) K reported in Tables 1 and 2 with those predicted using eq 4 at the corresponding temperatures.

the obtained AAD, we conclude that eq 4 can be satisfactorily used to reproduce the binodal curves of the investigated systems.

Furthermore, to examine the performance of eq 4 in extrapolating the locus of the phase diagrams for the investigated systems, we attempted to compare the experimental IL phase equilibrium compositions, w_1, for the investigated aqueous IL−salt systems at *T* = (278.15, 298.15, and 318.15) K reported in Tables 2 and 3 with those predicted using eq 4 at the corresponding temperatures. The AAD obtained from this comparison is also given in Table 4. As can be seen, eq 4 can also predict satisfactorily the characteristics of the phase diagrams for the investigated systems where no experimental data are available. The binodals extrapolated using eq 4 for the investigated IL−salt ATPS's at *T* = 298.15 K are also illustrated in Figures 6 and 7, as examples.

The effect of temperature on the phase-forming ability for the aqueous [C_4mim]Cl + tripotassium citrate and [C_4mim]Br + trisodium citrate systems is also illustrated in Figures 1 and 2, respectively. Figures 1 and 2 show the binodal boundaries obtained from turbidimetric titrations at different temperatures. In Figures 1 and 2, all mixtures of the compositions represented by points under the binodal line at each temperature give rise to phase separation, and the mixtures represented by points

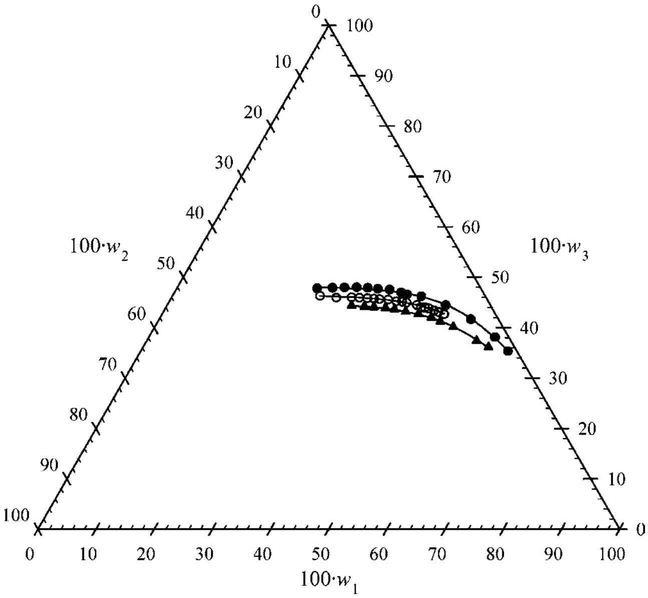


Figure 1. Binodal curves for the {[C_4mim]Cl (1) + tripotassium citrate (2) + H_2O (3)} two-phase system at different temperatures. ●, 278.15 K; ○, 298.15 K; ▲, 318.15 K; —, calculated from eq 4.

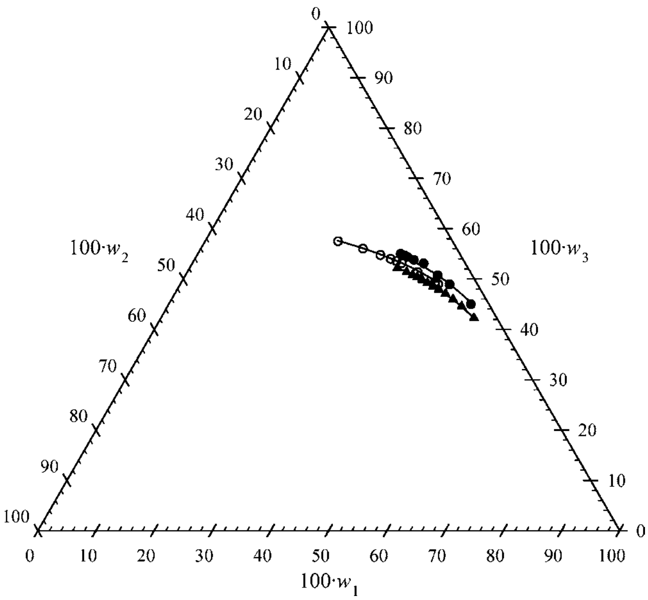


Figure 2. Binodal curves for the {[C_4mim]Br (1) + trisodium citrate (2) + H_2O (3)} two-phase system at different temperatures. ●, 278.15 K; ○, 298.15 K; ▲, 318.15 K; —, calculated from eq 4.

above the binodal lines give an apparently homogeneous one-phase system. The locus for the experimental binodals shown in Figures 1 and 2 demonstrates that the two-phase area is expanded with a decrease in temperature which may be attributed to the increase in the phase-forming ability in the studied systems. In other words, if we take a sample on the binodal with a known composition, this mixture becomes two-phase by a decrease in temperature as we observed experimentally, similarly to the one observed in our previous work for the aqueous [C_4mim]Br + tripotassium citrate system.[29] A possible reason is that the effect of a decrease in temperature on the structure of water is qualitatively similar to that of a kosmotropic (structure-making) ion[3] and therefore can promote the phase-forming ability in the investigated systems, as a favorable factor for the exclusion of the IL.

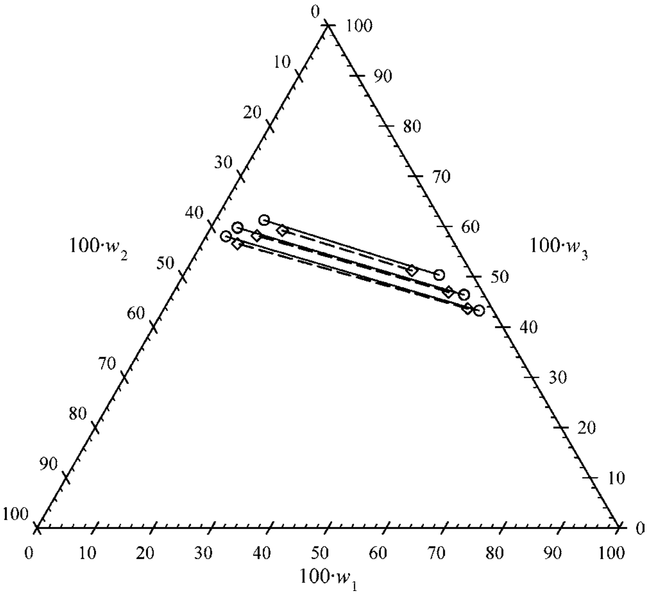


Figure 3. Effect of temperature on the equilibrium phase compositions for the {[C_4mim]Br (1) + trisodium citrate (2) + H_2O (3)} system. ○, 278.15 K; ◊, 318.15 K; —, tie-lines at 278.15 K; ---, tie-lines at 318.15 K. These tie-lines were obtained by connecting the experimental equilibrium phase composition data.

An investigation of the temperature influence on the equilibrium phase compositions for the studied systems provides results which are also collected in the two last columns of Tables 2 and 3. A comparison between the tie-lines which have nearly the same total compositions in Table 2 or 3 shows that for both of the investigated systems the working temperatures have no significant effect upon the slope, *S*, of the tie-lines. However, the length of the tie-lines decreases with an increase in temperature. To illustrate the effect of temperature on the tie-lines of the investigated systems, the experimental tie-lines of the aqueous [C_4mim]Br + trisodium citrate system are compared in Figure 3, for the temperatures T = (278.15 and 318.15) K, as an example. In simple terms, this trend means that by decreasing temperature the mutually liquid−liquid demixing in the studied aqueous IL−salt systems is promoted, leading to an increase in concentration of the phase-forming component (i.e., IL or salt) which is predominant in each phase. Actually, what appears to happen is that the interaction of the hydrophilic IL with surrounding water molecules which is weakened in the presence of a kosmotropic inorganic salt (with the relatively strong affinity for water) is further diminished due to a decrease in temperature. Decreasing the temperature may be effective as a factor to enhance the formation of the water structure (i.e., like that of a kosmotrope), and therefore the ability of the system for the mutually liquid−liquid demixing increases with decreasing temperature. This means that according to the hydration theories, in the presence of a given kosmotropic salt (here, tripotassium citrate or trisodium citrate), the effect of temperature on the solubility of the studied hydrophilic ILs ([C_4mim]Cl or [C_4mim]Br, respectively) in water may also be directly correlated to the salting-out phenomenon. A decrease in the solubility of [C_4mim]Cl or [C_4mim]Br in water with a decrease in temperature, as shown respectively in Figures 1 and 2, is reflected by a decrease in the critical concentration of a salt required to form a two-phase system which in turn indicates the capability of the salt in inducing the formation of the two phases (i.e., the salting-out strength of the salt). Salting-out effects are usually quantified by fitting solubility data to the empirical equation of Setschenow[59]

$$\ln \frac{S_0}{S} = k_S c_S \qquad (5)$$

where S_0 and S refer to the solubility of a given nonelectrolyte in pure water and in a salt solution of concentration c_S, respectively, and k_S, defined as the salting-out coefficient specific for a particular nonelectrolyte−salt pair. In earlier studies, on the basis of eq 5 or the salting-out concept, the Setschenow-type behavior of the phase diagrams for a number of PEG−salt ATPS's have been substantiated by some authors,[60,61] but with only limited success. In this regard, Hey et al.[50] have proposed a new derivation of Setschenow-type equations from which a characteristic parameter, k_S, for the salting-out effect of an electrolyte on ethylene oxide (EO) groups in PEG + salt ATPS's can be satisfactorily determined. Recently, we have also successfully applied this equation to introduce a quantitative measure for the salting-out effects of the tripotassium citrate salt on propylene oxide (PO) units in the investigated PPG + tripotassium citrate ATPS at different temperatures.[62]

In our previous work,[29] we have demonstrated that the same Setschenow-type equation derived by Hey et al.[50] to characterize the phase diagrams for the typical nonelectrolyte−salt ATPS's can be successfully applied to the [C$_4$mim]Br + tripotassium citrate ATPS. This is because, in the aqueous solutions of the hydrophilic ILs, the extent of the water-structure-enforced hydrophobic ion associations for ILs is remarkable.[63−65] Using statistical mechanical theories,[63,66] these extensive water-structure-enforced hydrophobic ion associations may reflect the considerable nonelectrolyte contributions in the aqueous IL solutions. This means that, as stated by Grover and Ryall,[67] for all practical purposes, the electrolytes and nonelectrolytes usually used in the definition of the salting-out phenomenon may be considered as the salts that have respectively high and low solubilities (or as ions with a relatively strong and less affinity for the solvent). In recent years, for the aqueous solutions of some hydrophilic ILs such as [C$_2$mim][Br] and [C$_4$mim][Cl] the formation of the extensive water-structure-enforced hydrophobic ion pairs which, in turn, shows that in these solutions the solute−solute interactions have a greater contribution than solute−solvent interactions has been verified by some thermodynamic studies.[63] The overall picture of this thermodynamic analysis[63] reveals that the low charge density of constituent ions and their hydrophobic nature is responsible for the formation of the water-structure-enforced ion pairs in the studied IL[63] solutions. From these studies[63] we may conclude that the extent of the ion association and thus the nonelectrolyte contribution in aqueous [C$_4$mim][Br] solution is higher than in [C$_2$mim][Br] or [C$_4$mim][Cl] aqueous solutions due to a lower charge density of [C$_4$mim][Br] constituent ions. In this respect, in continuation of our previous research,[29] we decided to further examine this Setschenow-type equation to describe the salting-out affects in the [C$_4$mim]Cl + tripotassium citrate and the [C$_4$mim]Br + trisodium citrate ATPS's at different temperatures. The equation[50] used has the following form

$$\ln\left(\frac{c'_I}{c''_I}\right) = k_I(c''_I - c'_I) + k_S(c''_S - c'_S) \qquad (6)$$

where c_I, c_S, k_I, and k_S, represent the molality of IL, the molality of the salt, a parameter relating the activity coefficient of IL to its concentration, and the salting-out coefficient, respectively. Single and double primes also refer to the upper and lower phases, respectively. If the first term on the right-hand side of this equation is small compared to the second term, a Setschenow-type equation is obtained. This would imply that $k_I \ll k_S$ since the absolute values of $(c''_I - c'_I)$ exceed the $(c''_S - c'_S)$ values.[50]

Table 5. Values of Parameters from Least-Squares Linear Fits to the Setschenow-Type Equation, Equation 6, for {IL (1) + Salt (2) + H$_2$O (3)} at T = (278.15, 298.15, and 318.15) K

T/K	k_S/kg·mol^{-1}	intercept	R^2	dev^a·10^4
	[C$_4$mim]Cl + Tripotassium Citrate + H$_2$O			
278.15	0.4949	0.6893	0.994	0.02
298.15	0.3446	0.7217	0.998	0.01
318.15	0.3395	1.2259	0.947	0.12
	[C$_4$mim]Br + Trisodium Citrate + H$_2$O			
278.15	1.3824	−0.1805	0.999	0.00_4
298.15	1.2341	−0.0590	1.000	0.00_1
318.15	1.0228	0.1248	0.993	0.02
	[C$_4$mim]Br + Tripotassium Citrate + H$_2$O^b			
278.15	1.2384	−0.3729	0.996	0.06
298.15	0.9222	0.4123	0.995	0.11
318.15	0.6489	0.7986	0.988	0.12

[a] dev = $(\sum_p\sum_l\sum_j(w_{p,l,j}^{\text{calcd}} - w_{p,l,j}^{\text{exptl}})^2/6N)$, where $w_{p,l,j}$ is the weight fraction of the component j (i.e., IL, salt or water) in the phase p for lth tie-line and the superscripts "calcd" and "exptl" refer to the calculated and experimental values, respectively. N is the number of tie-line data. [b] Data from ref 29.

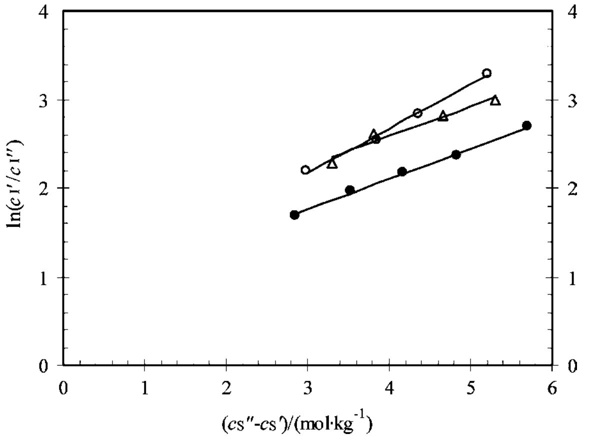


Figure 4. Setschenow-type plots for the tie-line data of the {[C$_4$mim]Cl (1) + tripotassium citrate (2) + H$_2$O (3)} system. Upper and lower phase concentrations are denoted by single and double primes, respectively. ○, 278.15 K; ●, 298.15 K; △, 318.15 K.

The experimental tie-line compositions for the studied IL−salt ATPS's given in Tables 2 and 3 were fitted by a least-squares linear regression method to eq 6 (i.e., the logarithm of the ratio between the molality of IL for the top phase to the one for the bottom phase, ln (c'_I/c''_I), were considered as a linear function of $(c''_S - c'_S)$, the differences in the salt concentrations between the bottom and top phases, respectively), and the obtained slopes which give the salting-out coefficients, k_S, together with the corresponding intercepts and correlation coefficients, R, are listed in Table 5 for each working temperature. In Table 5, the corresponding values for the [C$_4$mim]Br + tripotassium citrate ATPS taken from ref 29 have also been given for comparison. To examine more closely the relation between the Setschenow-type behavior and the phase diagrams, the Setschenow-type plots of the tie-line data for the studied systems have also been shown in Figures 4 and 5. On the basis of the correlation coefficient, R, given in Table 5 and Setschenow-type plots shown in Figures 4 and 5, we conclude that the equilibrium compositions of the investigated systems at the studied temperatures can be satisfactorily characterized by Setschenow-type behavior. In the further analysis, the comparison between the obtained param-

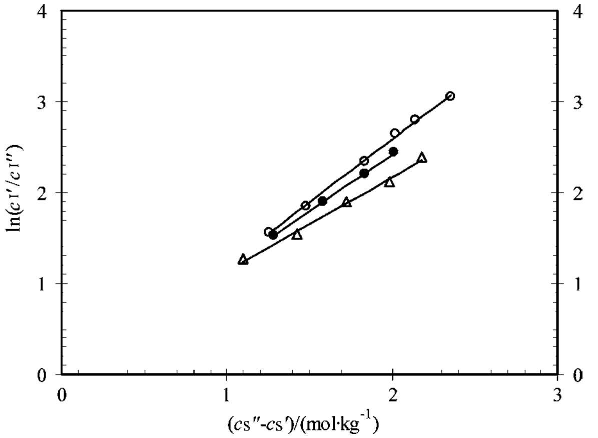


Figure 5. Setschenow-type plots for the tie-line data of the {[C_4mim]Br (1) + trisodium citrate (2) + H_2O (3)} system. Upper and lower phase concentrations are denoted by single and double primes, respectively. ○, 278.15 K; ●, 298.15 K; △, 318.15 K.

eters, k_S and intercepts, and the correlation coefficients, R, for the studied IL−salt ATPS's (Table 5) implies that the systems containing [C_4mim]Br exhibit preferably the Setschenow-type behavior. It seems that the smaller charge density of anion, Br^-, its relatively high hydrophobic nature,[63−65] and as a consequence the relatively higher tendency to form the water-structure-enforced ion pairs in [C_4mim]Br may be responsible for these observations.

For the studied systems, as shown in Table 5, the values of k_S increase with decreasing temperature, similarly to the one observed in our previous work for the aqueous [C_4mim]Br + tripotassium citrate system. The increase of k_S is reflected in the phase diagram by a shift in the position of the binodal curve to the top corresponding to a decrease in the area representing the single-phase mixture as shown in Figures 1 and 2, indicating an increasing phase-forming ability.

Furthermore, using the parameters given in Table 5 the performance of eq 6 in representing the tie-line data of the investigated systems has been examined, and the corresponding deviations are also given in Table 5. The results show that eq 6 can be satisfactorily used to correlate the tie-line data of the investigated systems. To show the reliability of the model, as examples, the comparison between the experimental and the reproduced tie-lines for the [C_4mim]Cl + tripotassium citrate and the [C_4mim]Br + trisodium citrate ATPS's at $T = 298.15$ K is also shown in Figures 6 and 7, respectively.

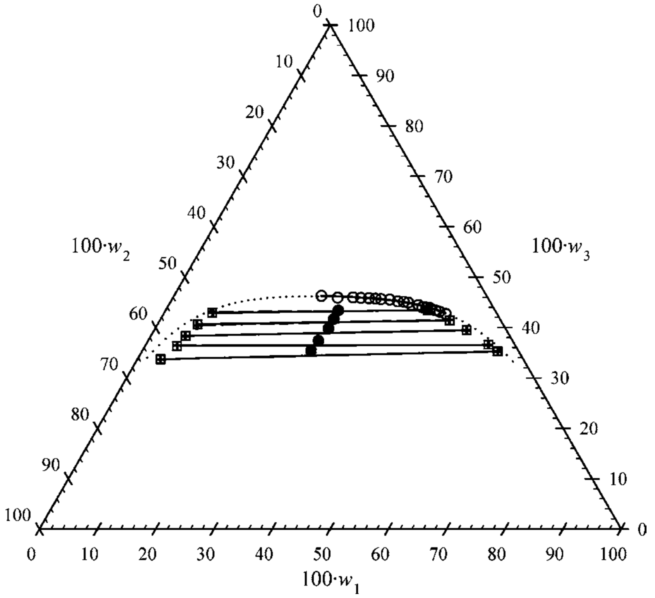


Figure 6. Phase diagram of the {[C_4mim]Cl (1) + tripotassium citrate (2) + H_2O (3)} two-phase system at 298.15 K. ○, experimental binodal; −, calculated binodal from eq 4; •••, extrapolated binodal from eq 4; ●, total composition of tie-lines; −□−, experimental tie-lines; ---+---, calculated tie-lines using eq 6.

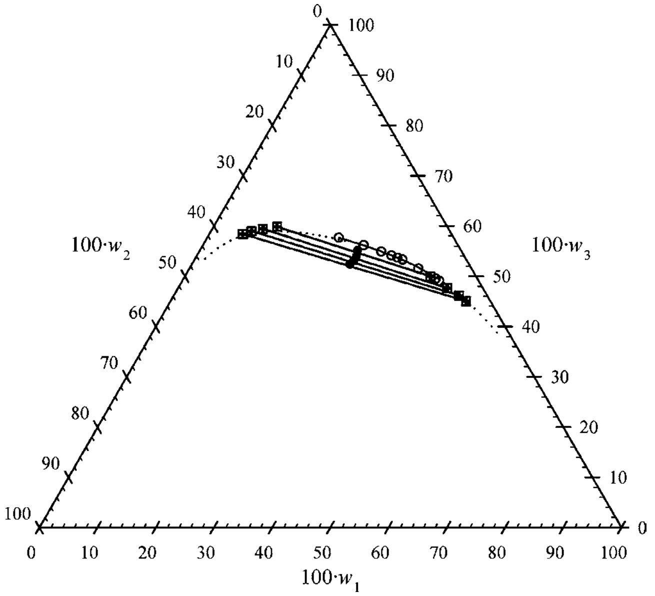


Figure 7. Phase diagram of the {[C_4mim]Br (1) + trisodium citrate (2) + H_2O (3)} two-phase system at 298.15 K. ○, experimental binodal; −, calculated binodal from eq 4; •••, extrapolated binodal from eq 4; ●, total composition of tie-lines; −□−, experimental tie-lines; ---+---, calculated tie-lines using eq 6.

Effect of Temperature on the Exclusion of ILs. In the beginning, it is better to illustrate a picture of the two-phase forming phenomenon in a typical ternary IL−salt aqueous system as well as the role of the used hydrophilic ILs as a phase-forming component. From the foregoing discussion, it is easily seen that the phenomenon of the two-phase forming in a typical ternary "chaotropic" water-miscible IL/kosmotropic salt/water system clearly indicates the mutual exclusion of the kosmotropic salt and the chaotropic IL which in turn results from their competition for the water. Hydrophilic ILs such as [C_4mim]Cl or [C_4mim]Br, because of their low symmetry ions which contain charge delocalization and weak directional intermolecular interactions, tend to behave as chaotropes[24] ("chao-trope" = order breaker, a type of solute which breaks hydrogen bonds between water molecules and thus suppresses water-structure formation, originates salting-in effects, and destabilizes folded macromolecules). This fact is confirmed by some preliminary thermodynamic results based on interactions of ILs with water molecules[63,68−70] as well as thermodynamic analysis of extensive experimental data on enzyme stability in the presence of several hydrophilic ILs.[71−77] From the later studies,[71−77] it has been known that the enzyme stabilization and activation in aqueous solutions of hydrophilic ILs follows the well-known Hofmeister series (i.e., kosmotropic anions and chaotropic cations stabilize enzymes, while chaotropic anions and kosmotropic cations destabilize them). Therefore, a combination of a high chaotropic anion and a high kosmotropic cation in designing a hydrophilic IL seems beneficial to induce the enzyme inactivation in aqueous solutions. The whole picture of this thermodynamic analysis reveals that the overall IL kosmotropicity or chaotropicity may be quantified by the δ parameter[76] (defined as the difference in the Jones−Dole viscosity *B*-coefficients of the IL anion and cation) or similarly by the δ' parameter[77] (defined as the difference in the NMR B'-coefficients of the IL anion and cation). In general, a high enzyme stability is observed in IL solutions possessing a high δ or δ' value. As the Jones−Dole viscosity *B*-coefficients of imidazolium cations are not yet available,[75−78] using the NMR B'-coefficients,[77] we estimated the δ' values for the $[C_4mim]Cl$ and $[C_4mim]Br$ ILs as $(-0.347$ and $-0.370)$ $dm^3 \cdot mol^{-1}$, respectively. Comparing the obtained δ' values for the $[C_4mim]Cl$ and $[C_4mim]Br$ with the corresponding value estimated as[77] -0.570 $dm^3 \cdot mol^{-1}$ for the strong chaotropic IL (i.e., $[BuPy]BF_4$ which induces high enzyme instability[76,77]), it is clear that the $[C_4mim]Cl$ and $[C_4mim]Br$ tend to behave as a chaotrope species. Furthermore, from these values one can conclude that $[C_4mim]Br$ with $\delta' = -0.370$ $dm^3 \cdot mol^{-1}$ has a higher chaotropicity than $[C_4mim]Cl$ with $\delta' = -0.347$ $dm^3 \cdot mol^{-1}$. Thus, compared to $[C_4mim]Cl$, the IL, $[C_4mim]Br$, can be more easily salted-out by a kosmotropic salt to form the IL-based ATPS's (the relative chaotropicity of the $[C_4mim]Br$ and $[C_4mim]Cl$ ILs is discussed in detail in the last section).

According to the above explanations the salting-out effect and the consequent phase separation in the investigated IL−salt ATPS's may be accounted for in terms of the complex and competing nature of the interactions between the solutes (i.e., ions from the inorganic salt and IL) and water as follows: Kosmotropic inorganic salt ions are entropically favorably hydrated in solution and interact with water molecules rather than with less favorably hydrated chaotropic IL ion pairs, leading to an effective preferential exclusion of the kosmotropic species from the solvation shell of the ILs. This causes increasing local water densities near chaotropic ILs (i.e., preferential hydration) and exclusion of the ILs from the solution as a separated phase. This means that the preferential exclusion of one solute from the hydration shell of another solute can be described in terms of a local excess of water molecules, in analogy with the Gibbs surface excess defined in connection with macroscopic interfaces.[79] Therefore, we decided here to estimate the excess number of water molecules adjacent to the studied chaotropic IL pairs, $[C_4mim]Cl$ or $[C_4mim]Br$, to get some information in regards to the effect of temperature on the exclusion of the $[C_4mim]Cl$ or $[C_4mim]Br$ pairs in the investigated IL-based ATPS's. As stated by Hey et al.,[50] the excess number of water molecules can be related to the magnitude of the salting-out coefficient, k_S, for a given electrolyte as follows

$$\frac{k_S}{\upsilon} = 0.018 N_{ew} \frac{d(\phi c_S)}{dc_S} \tag{7}$$

where k_S represents the salting-out coefficient, υ is the number of moles of ions in the fully dissociated mole of kosmotropic electrolyte, ϕ and c_s are respectively the molal osmotic coefficient and the molality of the salt, and N_{ew} is the excess number of water molecule per IL particles in the salt-depleted region.

The necessary molal osmotic coefficients, ϕ, for tripotassium citrate[80] or trisodium citrate[81] have been calculated from the corresponding water activity data[80,81] using the following equation

$$\phi = -\frac{\ln(a_w)}{\upsilon m M_w} \tag{8}$$

where a_w and M_w represent the activity and molecular weight of water, respectively. For the temperatures where no water activity data are available, the necessary molal osmotic coefficients, ϕ, for tripotassium citrate or trisodium citrate were predicted employing the Wilson model used successfully by Sadeghi and Ziamajidi[80] or Sadeghi[81] to correlate the water activity data of the corresponding binary aqueous systems at different temperatures.[80,81] Using the obtained molal osmotic coefficients and the same procedure outlined in our previous work,[29] N_{ew} values were estimated at different temperatures. The estimated values for N_{ew} are listed in Table 6. The obtained N_{ew} values, which may give a quantitative measure for the preferential hydration of $[C_4mim]Cl$ or $[C_4mim]Br$, show that the increasing number of water molecules around $[C_4mim]Cl$ or $[C_4mim]Br$ pairs with a decrease in the temperature may be related to the enhancement of the exclusion both of the kosmotropic salts from the solvation shell of ILs and of ILs from the solution in the investigated ATPS's (Figures 1 to 3). It seems that, because of the hydration sheath increment per IL ion pairs by decreasing temperature, the near-surface region of the IL ion pairs may be less accessible to structure-making ions, and hence the extent of exclusion will increase. In a further analysis, what appears to happen is that the interactions of the chaotropic $[C_4mim]Cl$ or $[C_4mim]Br$ pairs with surrounding water molecules weakened due to the formation of water structure (which in turn resulted from the presence of the studied kosmotropic salts) are further diminished as a result of a decrease in temperature. Thus, for a given concentration of the investigated water-structure making salts, the water-structuring forces dominate preferably the interaction between structure-making electrolyte and IL ion pairs leading to the hydration sheath increment around IL ion pairs, and therefore the ability of the system to produce a IL-rich, salt-deficient local composition increases as the temperature is decreased.

Table 6. Excess Number of Water Molecules per IL Constituent Ion Pairs

T/K	(k_S/υ)/$kg \cdot mol^{-1}$	$d(\phi c_S)/dc_S$	N_{ew}
	$[C_4mim]Cl$ + Tripotassium Citrate + H_2O		
278.15	0.12	0.75	9
298.15	0.09	0.73	7
318.15	0.08	0.74	6
	$[C_4mim]Br$ + Trisodium Citrate + H_2O		
278.15	0.35	0.75	26
298.15	0.31	0.68	25
318.15	0.26	0.64	22
	$[C_4mim]Br$ + Tripotassium Citrate + H_2O[a]		
278.15	0.31	0.75	23
298.15	0.23	0.73	18
318.15	0.16	0.74	12

[a] Data from ref 29.

Effect of Salt on the Exclusion of ILs. The phase diagrams for the aqueous $[C_4mim]Cl + K_3PO_4$,[23,31] $[C_4mim]Cl + K_2HPO_4$, $[C_4mim]Cl + K_2CO_3$,[23] and $[C_4mim]Cl$ + K_3-citrate (this work) systems at $T = 298.15$ K in which respectively the kosmotropic K_3PO_4, K_2HPO_4, K_2CO_3, or K_3-citrate salts are used to salt-out the same chaotropic $[C_4mim]Cl$ pair in an aqueous solution are shown in Figure 8a, as a criterion by which the differences in kosmotropicity of the used salts may be illustrated. As far as we know, at room temperature there are some reports on the binodal curve for the system containing K_2HPO_4 as figures without any experimental data.[25,27] The necessary data for this system along with the complementary binodal data used for the systems containing K_3PO_4 and K_2CO_3 have also been obtained in this work, and the results are presented in the Table 3S in the Supporting Information of this manuscript. In Figure 8b the relative kosmotropicity of the same salts against a single chaotropic $[C_4mim]Br$ pair discussed exhaustively in our recent work[29] is also illustrated for comparison. As mentioned in the

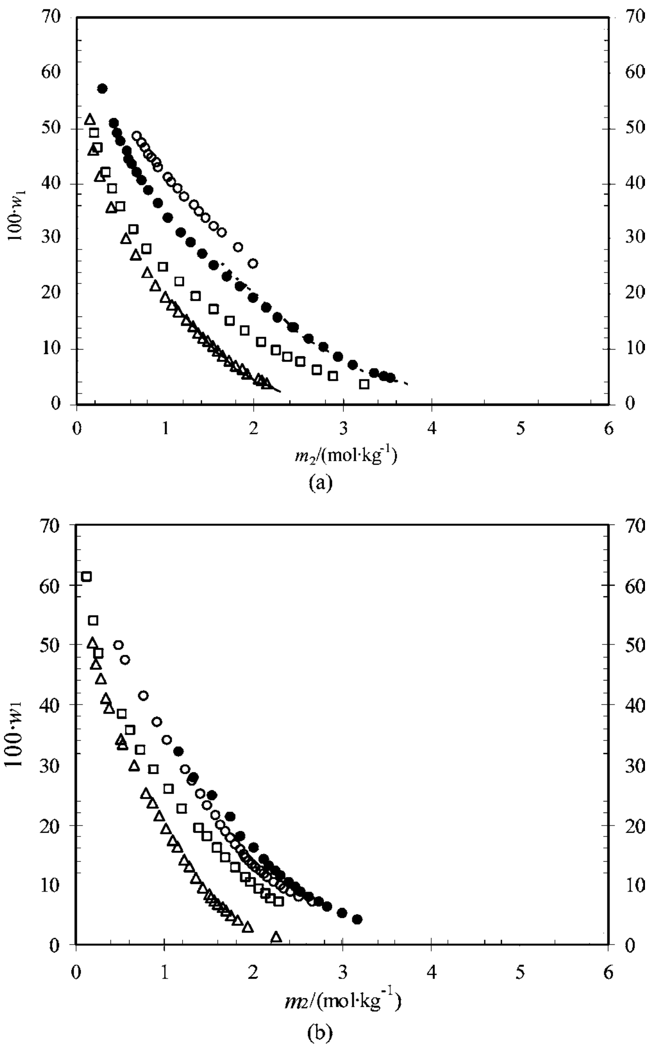
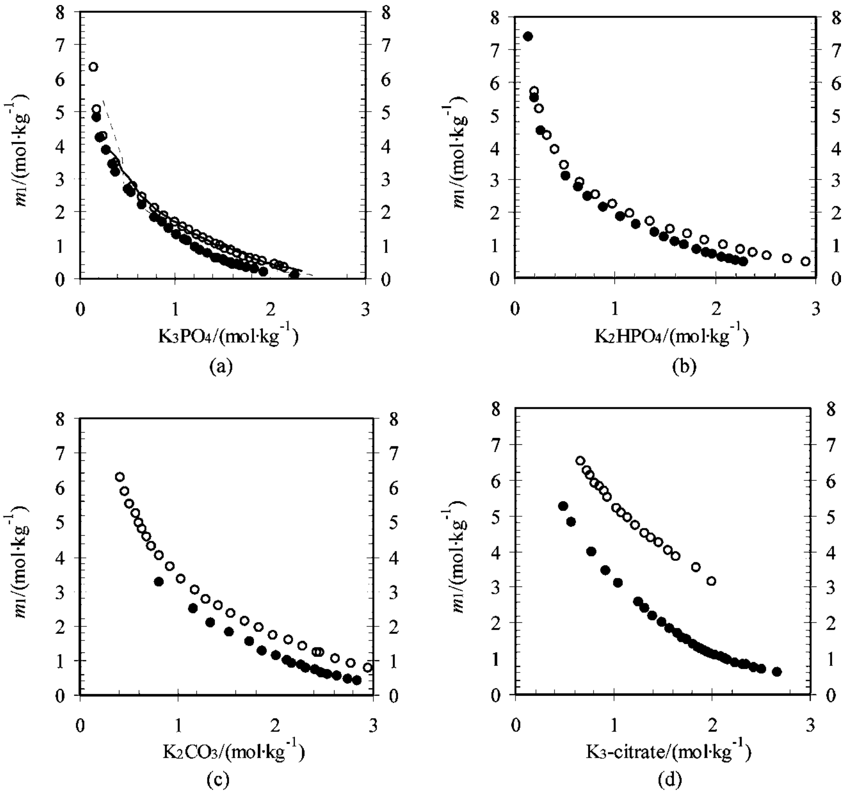


Figure 8. a. Effect of the type of salt on the binodal curves for the [C_4mim]Cl (1) + salt (2) ATPS at T = 298.15 K. △, K_3PO_4; —, K_3PO_4;[23] □, K_2HPO_4; ●, K_2CO_3; ---, K_2CO_3;[23] ○, K_3Cite (this work). b. Effect of the type of salt on the binodal curves for the [C_4mim]Br (1) + salt (2) ATPS at T = 298.15 K.[29] △, K_3PO_4;[22] □, K_2HPO_4;[22] ●, K_2CO_3;[21] ○, K_3Cite.[29]

preceding section, the salt kosmotropicity can also be reflected by viscosity *B*-coefficients of its constituent ions. The ionic viscosity *B*-coefficients in aqueous solutions allow us to understand the interactions involved in the hydration of the ions and their effects on the structure of the water in the near environment of the solute particles.[82] For inorganic ions, positive *B*-values typically suggest ions as kosmotropes since strongly hydrated ions exhibit a larger change in viscosity with concentration, while negative *B*-coefficients suggest chaotropes for weakly hydrated ions.[83] Our previous investigation[29] on the position of binodals (Figure 8b) for [C_4mim]Br with the aforementioned kosmotropic salts which share a common cation (K^+) but contain different anions indicated that the higher kosmotropicity of the salt for the exclusion of [C_4mim]Br is observed when the anion of the salt have more positive *B*-coefficient values as follows: PO_4^{3-} (0.495 $dm^3 \cdot mol^{-1}$)[83] > HPO_4^{2-} (0.382 $dm^3 \cdot mol^{-1}$)[83] > citrate^{3-} (0.333 $dm^3 \cdot mol^{-1}$)[76,77] > CO_3^{2-} (0.294 $dm^3 \cdot mol^{-1}$).[83] As discussed earlier,[29] this is because the anion with a more positive *B*-coefficient value hydrates more water than the anion with a less positive *B*-coefficient value, thus decreasing to a higher extent the amount of water available to hydrate [C_4mim]Br. This means that in the presence of a more kosmotropic anion the chaotropic [C_4mim]Br preferably excludes from the aqueous solution and transfers to the upper phase. So, the use of the more kosmotropic salt should be expected to result in a binodal closest to the origin, meaning less salt is needed to form an ATPS. This fact is confirmed by some thermodynamic results based on the preferential hydration of the [C_4mim][Br].[29] However, from Figure 8a the following trend is observed with the kosmotropicity of the anion for the exclusion of [C_4mim]Cl decreasing in the order: PO_4^{3-} (0.495 $dm^3 \cdot mol^{-1}$)[83] > HPO_4^{2-} (0.382 $dm^3 \cdot mol^{-1}$)[83]> CO_3^{2-} (0.294 $dm^3 \cdot mol^{-1}$)[83] > citrate^{3-} (0.333 $dm^3 \cdot mol^{-1}$)[76,77] (the CO_3^{2-} and citrate^{3-} are displaced). Also, comparing the depicted ordering in Figure 8a with the one in Figure 8b, it can be easily seen that there is little overall difference in the relative kosmotropicity of the same salts used for the exclusion of a single imidazolium-based IL, [C_4mim]Cl or [C_4mim]Br, except for citrate^{3-}. In other words, the distance between different binodal curves shown in Figure 8a,b are very similar, except for citrate^{3-}. It seems that the smaller chaotropicity of the [C_4mim]Cl (confirmed by the δ' parameter in the previous section) may be accountable for this observation. In Figure 9a two imidazolium-based ILs, [C_4mim]Cl and [C_4mim]Br, which have a common cation, are compared versus the strongest kosmotropic salt, K_3PO_4, to illustrate the relative chaotropicity of the ILs. As can be seen, [C_4mim]Br for which the locus of the binodal curve is closer to the origin has a higher chaotropicity than [C_4mim]Cl. This fact is also substantiated by several thermodynamic parameters taken from the literature which are based on the structural hydration entropies,[78] viscosity (*B*-coefficients of the Jones−Dole equation),[83] or NMR (*B′*-coefficients)[77] measurements. The data show that the bromide anion is more chaotropic than the chloride anion. Hence, the IL associated anion seems to play a key role in these systems. Recent studies show that there is strong hydrogen bonding between the anion, Cl^-, of the [C_4mim]Cl and water and also the hydrogens of alkyl chain, the C2−H, C4−H, and C5−H of the imidazolium ring forming an H···Cl chain.[84] The hydrogen bonding between the C2−H and Cl^- is stronger than the others as substantiated by quantum chemical calculations.[85,86] This may be due to the presence of the two N atoms and the positive charge in the imidazolium ring that make an acidic H in the C2−H bond.[84] Moreover, NMR spectroscopy reveals that the water molecule could form hydrogen bonds with the hydrogens of the C2−H, C4−H, and C5−H of the imidazolium ring,[87] and the strongest bond forms between the oxygen of water and the C2−H of the imidazolium ring, [C2−H···O−H], as found by quantum chemical calculations.[84] We expect that the hydrogen bonding between water and the acidic hydrogen of the imidazolium cation should have a large influence in the liquid−liquid phase behavior in the investigated systems. It was found that the interaction of Br^- with water[77,78,83,84] and the hydrogens of the imidazolium ring are weaker than that of Cl^-.[86] The possible reason is that the radius of Cl^- is smaller than that of Br^-. Therefore, for the Br^- associated imidazolium cation, the tendency for the interaction between the C2−H and water, [C2−H···O−H], where the acidic H2 proton comes loose somewhat, may be greater than that of Cl^-. Our pH values of 3.18 and 5.74 measured respectively at T = 298.15 K for the aqueous solutions of [C_4mim]Br and [C_4mim]Cl with mass fraction (w_{IL} = 0.23) are consistent with this viewpoint. As a result, [C_4mim]$^+$ in the presence of more chaotropic Br^- becomes apparently more kosmotropic than in the presence of less chaotropic Cl^-. This fact promotes the chaotropicity of the [C_4mim]Br. As can be seen in Figure 9a the biphasic regions



(a) (b) (c) (d)

Figure 9. Effect of IL anion chaotropicity on the binodal curves for the IL(1) + salt (2) ATPS at $T = 298.15$ K. ○, [C_4mim]Cl; ●, [C_4mim]Br; —, [C_4mim]Cl;[31] ---, [C_4mim]Br.[31]

of the systems containing [C_4mim]Br are rather greater than systems containing [C_4mim]Cl. This observation which is in good agreement with literature[31] (Figure 9a) is consistent with the more chaotropicity of [C_4mim]Br. Further investigation of the phase diagrams for [C_4mim]Cl and [C_4mim]Br against K_2HPO_4 or K_2CO_3 shown respectively in Figure 9b,c gives a similar result with chaotropicity increasing [C_4mim]Br > [C_4mim]Cl, as expected. From the comparisons of the Figures 9a−c we may conclude that the relative differences in the chaotropicities of [C_4mim]Cl and [C_4mim]Br are suppressed as the kosmotropicity of the anion for the exclusion of IL is increased. It is reasonable that as the kosmotropicity of the anion is increased, the anion hydrates more water, thus rather decreasing the amount of water available to hydrate [C_4mim]Cl or [C_4mim]Br; thereby Cl^- anions could not exhibit their ability to form hydrogen bonds with water as much as possible. An exception was observed for the citrate^{3-} anion which has a higher kosmotropicity than the CO_3^{2-} anion based on viscosity *B*-coefficients;[76,77,83] however, the binodals for [C_4mim]Cl and [C_4mim]Br versus K_3-citrate show a higher degree of separation with the chaotropicity increasing [C_4mim]Br > [C_4mim]Cl compared to the one observed with K_2CO_3. A possible reason may be due to the salting-in effects caused by the direct binding of the carboxylate groups ($-COO^-$) of the citrate^{3-} anion to the acidic C2−H of the [C_4mim]$^+$. In the aqueous solution of less chaotropic [C_4mim]Cl, this binding is stronger, thus requiring more salt than the amount predicted by the corresponding ionic viscosity *B*-coefficient. In fact, the citrate anion functions as a pure H-bond acceptor because the hydrogens of the backbone carbons are hydrophobic and that of the −OH group forms an intramolecular H-bond with one of the oxygens of the carboxylate groups and plays no active role in intermolecular H-bonding.[88]

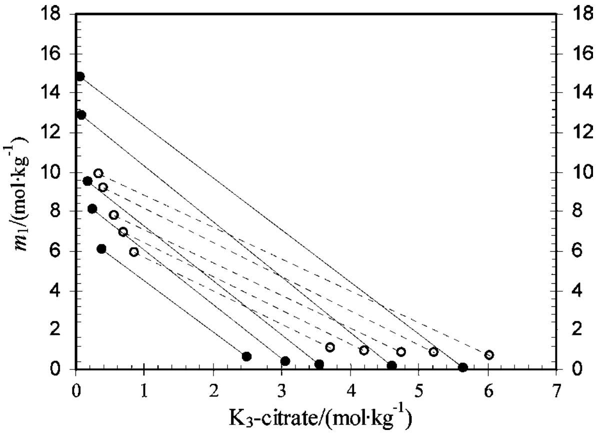


Figure 10. Effect of IL anion chaotropicity on the tie-lines for the IL (1) + K3-citrate (2) ATPS at $T = 298.15$ K. ○---○, [C_4mim]Cl; ●—●, [C_4mim]Br.

Additionally, to show the effects of IL anion chaotropicity on the phase compositions, the tie-lines for the {[C_4mim]Cl or [C_4mim]Br + K_3-citrate} ATPS's at $T = 298.15$ K are compared and depicted in Figure 10. As can be seen, the slope and the length of the tie-lines increase for the system containing [C_4mim]Br. The possible reason is that an increased anion chaotropicity (i.e., weakly hydrated anion) for the system containing [C_4mim]Br causes the water to drive preferably from the IL-rich phase to the salt-rich phase, so the IL concentration at the IL-rich phase increases, while the salt-rich phase will be somewhat more diluted (i.e., the required salt will be decreased). Furthermore, comparing the obtained N_{ew} values (Table 6) for the [C_4mim]Br + K_3-citrate and [C_4mim]Cl + K_3-citrate ATPS's at $T = 298.15$ K as a criterion for the preferential hydration of the used ILs, [C_4mim]Cl, or [C_4mim]Br shows that the [C_4mim]Br pairs have a higher N_{ew} value (= 18) than the [C_4mim]Cl pairs (= 7). An increased number of water molecules per [C_4mim]Br pairs may be responsible for the enhancement

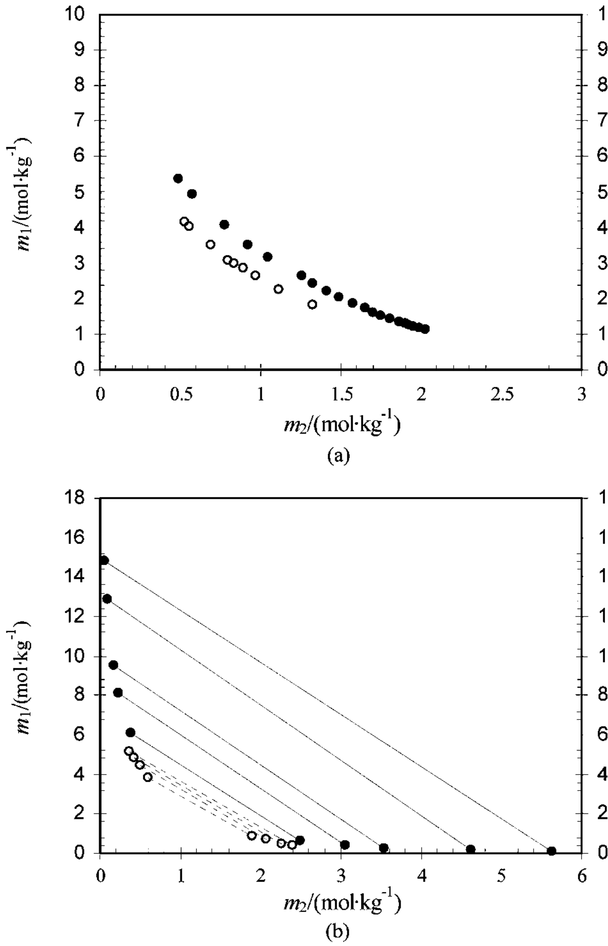


Figure 11. Effect of salt cation on the phase-forming ability for the [C$_4$mim]Br (1) + salt (2) ATPS at T = 298.15 K. a. Binodals; ○, trisodium citrate; ●, tripotassium citrate. b. Tie-lines; ○---○, trisodium citrate; ●—●, tripotassium citrate.

of the exclusion of the IL in the investigated [C$_4$mim]Br + K$_3$-citrate ATPS. It seems that, because of the hydration sheath increment per [C$_4$mim]Br pairs compared with that per [C$_4$mim]Cl pairs, the near-surface region of the IL ion pairs may be less accessible to the same structure-making ions, K$_3$-citrate, and hence the extent of exclusion will increase.

Furthermore, to demonstrate the cation effect on the mutual solubilities, the binodals and also the tie-lines of the [C$_4$mim]Br + K$_3$-citrate ATPS are compared with those for the [C$_4$mim]Br + Na$_3$-citrate ATPS at T = 298.15 K and are shown in Figure 11a,b, respectively. As can be seen, the phase-forming ability of Na$_3$-citrate is higher than that of K$_3$-citrate. This is because Na$^+$ with a positive viscosity *B*-coefficient (0.085 dm^3·mol^{-1})[81] is more kosmotropic than K$^+$ with a negative viscosity *B*-coefficient (−0.009 dm^3·mol^{-1}).[83] This fact is also substantiated by some other thermodynamic parameters based on the structural hydration entropies[78] and NMR (*B*′-coefficients)[78] measurements. These observations are consistent with the obtained N_{ew} values for the investigated systems (Table 6). A reasonable explanation may be that the interactions between Na$^+$ and water molecules are stronger than K$^+$, leading to an enhanced preferential exclusion of the Na$^+$ from the solvation shell of the same chaotropic [C$_4$mim]Br pairs, and thereby the local water densities near the chaotropic [C$_4$mim]Br pairs increase to a greater extent, as can be seen in Table 6. However, Figure 11b indicates that K$_3$-citrate has an extended effective concentration region to form an ATPS with a given IL due to its higher solubility, although it has less ability than Na$_3$-citrate.

In addition, trisodium citrate is not effective in forming a stable ATPS with less chaotropic [C$_4$mim]Cl in the whole concentration range, as after a few minutes the primary turbid solution which is expected to separate into two clear phases converted to a clear solution and a “solid” mass, as we observed experimentally. Moreover, the primary unstable turbidity which is observed in the mixed state may be due to the “solid” precipitation. This observation, however, shows that there is no liquid−liquid phase region for the aqueous [C$_4$mim]Cl + Na$_3$-citrate system under the working circumstances. To provide a reasonable explanation for this behavior, further investigation is needed which could not be taken into account within the framework of this work.

Conclusions

Liquid−liquid equilibrium data for the aqueous [C$_4$mim]Cl + tripotassium citrate and the aqueous [C$_4$mim]Br + trisodium citrate two-phase systems have been determined experimentally at T = (278.15, 298.15, and 318.15) K. The experimental binodal data were satisfactorily correlated with the Merchuk equation for which the three fitting parameters, *a*, *b*, and *c*, are further expressed as a function of temperature in the linear form with $(T - T_0)$ K as a variable. The effect of temperature on the phase-forming ability for the studied systems was also successfully explained on the basis of the salting-out coefficient of the salt, k_S, obtained from fitting the tie-line data to a Setschenow-type equation. It was shown that, for the studied systems, the value of k_S increases with decreasing temperature and the temperature with the higher phase-forming ability has a larger value of k_S. Further, these studies show that the systems containing [C$_4$mim]Br exhibit preferably the Setschenow-type behavior due to the existence of higher nonelectrolyte contributions in the [C$_4$mim]Br aqueous solutions. Additionally, the tie-line data for the investigated systems can be successfully represented by the Setschenow-type equation. Furthermore, using the k_S values obtained for the studied electrolytes, the number of water molecules adjacent to [C$_4$mim]Cl or [C$_4$mim]Br was estimated, and it was shown that the enhancement of the exclusion of the used ILs in the investigated ATPS’s may be related to the increasing number of water molecules around the [C$_4$mim]Cl or [C$_4$mim]Br, as the temperature is decreased. Finally, the intensity of the phase-forming ability in the investigated systems together with the previously studied imidazolium-based IL + salt ATPS’s was also explained on the basis of the complex and competing nature of the interactions between the solutes (i.e., ions from the inorganic salt and IL) and water, the preferential hydration (or the preferential exclusion of the salt from the environs) of the ILs, and the ionic viscosity *B*-coefficients of the Jones−Dole equation.

Supporting Information Available:

Experimental binodal data. This material is available free of charge via the Internet at http://pubs.acs.org.

Literature Cited

(1) Albertsson, P. A. *Partition of Cell Particles and Macromolecules*, 3rd ed.; Wiley-Interscience: New York, 1986; p 22.
(2) Walter, H.; Brooks, D. E.; Fisher, D. *Partitioning in Aqueous Two-Phase Systems*; Academic Press: New York, 1985.
(3) Zaslavsky, B. Y. *Aqueous Two-Phase Partitioning, Physical Chemistry and Bioanalytical Applications*; Marcel Dekker: New York, 1995.
(4) Gutowski, K. E.; Broker, G. A.; Willauer, H. D.; Huddleston, J. G.; Swatloski, R. P.; Holbrey, J. D.; Rogers, R. D. Controlling the Aqueous Miscibility of Ionic Liquids: Aqueous Biphasic Systems of Water-Miscible Ionic Liquids and Water-Structuring Salts for Recycle, Metathesis, and Separations. *J. Am. Chem. Soc.* **2003**, *125*, 6632–6633.

(5) Chen, J.; Ma, G. X.; Li, D. Q. HPCPC Separation of Proteins Using Polyethylene Glycol-Potassium Phosphate Aqueous Two-Phase. *Prep. Biochem. Biotechnol.* **1999**, *29*, 371–383.

(6) Rogers, R. D.; Zhang, J. New Technologies for Metal Ion Separations Polyethylene Glycol Based-Aqueous Biphasic Systems and Aqueous Biphasic Extraction Chromatography. In *Ion Exchange and Solvent Extraction*; Marinsky, J. A., Marcus Y., Eds.; Marcel Dekker: New York, 1997; Vol. 13, Chapter 4, pp 141−193.

(7) Rogers, R. D.; Bauer, C. B. Partitioning Behavior of Group 1 and 2 Cations in Poly(ethylene glycol)-Based Aqueous Biphasic Systems. *J. Chromatogr., B* **1996**, *680*, 237–241.

(8) Rogers, R. D.; Willauer, H. D.; Griffin, S. T.; Huddleston, J. G. Partitioning of Small Organic Molecules in Aqueous Biphasic Systems. *J. Chromatogr., B* **1998**, *711*, 255–263.

(9) Willauer, H. D.; Huddleston, J. G.; Rogers, R. D. Solute Partitioning in Aqueous Biphasic Systems Composed of Polyethylene Glycol and Salt: The Partitioning of Small Neutral Organic Species. *Ind. Eng. Chem. Res.* **2002**, *41*, 1892–1904.

(10) Baxter, S. M.; Sperry, P. R.; Fu, Z. W. Partitioning of Polymer and Inorganic Colloids in Two-Phase Aqueous Polymer Systems. *Langmuir* **1997**, *13*, 3948–3952.

(11) Helfrich, M. R.; El-Kouedi, M.; Etherton, M. R.; Keating, C. D. Partitioning and Assembly of Metal Particles and Their Bioconjugates in Aqueous Two-Phase Systems. *Langmuir* **2005**, *21*, 8478–8486.

(12) Bailey, F. E., Jr. *Poly(Ethylene Oxide)*; Academic Press: New York, 1976.

(13) Huddleston, J. G.; Willauer, H. D.; Griffin, S. T.; Rogers, R. D. Aqueous Polymeric Solutions as Environmentally Benign Liquid/Liquid Extraction Media. *Ind. Eng. Chem. Res.* **1999**, *38*, 2523–2539.

(14) Willauer, H. D.; Huddleston, J. G.; Rogers, R. D. Solvent Properties of Aqueous Biphasic Systems Composed of Polyethylene Glycol and Salt Characterized by the Free Energy of Transfer of a Methylene Group Between the Phases and by a Linear Solvation Energy Relationship. *Ind. Eng. Chem. Res.* **2002**, *41*, 2591–2601.

(15) Pan, I. H.; Chiu, H. H.; Lu, C. H.; Lee, L. T.; Li, Y. K. Aqueous Two-Phase Extraction as an Effective Tool for Isolation of Geniposide from Gardenia Fruit. *J. Chromatogr., A* **2002**, *977*, 239–246.

(16) Lucas, M. Coefficients de Partage d'un Certain Nombre d'ions Entre deux Melanges eau-sels non Miscibles I-1. Le Système eau Bromure de Tétrabutylammonium/eau Sulfate d'ammonium à 30°. *J. Inorg. Nucl. Chem.* **1970**, *32*, 3692–3693.

(17) Anzai, Y.; Akama, Y. Aqueous Two-Phase Extraction of Au (III) and Pd (II). *Bunseki Kagaku* **2003**, *52*, 337–340.

(18) Akama, Y.; Ito, M.; Tanaka, S. Selective Separation of Cadmium from Cobalt, Copper, Iron (III) and Zinc by Water-Based Two-Phase System of Tetrabutylammonium Bromide. *Talanta* **2000**, *53*, 645–650.

(19) Akama, Y.; Sali, A. Extraction Mechanism of Cr (VI) on the Aqueous Two-Phase System of Tetrabutylammonium Bromide and $(NH_4)_2SO_4$ Mixture. *Talanta* **2002**, *57*, 681–686.

(20) Franklin, T. C.; Benson, S. B. A Demonstration of the Transformation of a Hydrophobic Liquid to a Partially Hydrophilic Semisolid. *J. Chem. Educ.* **1986**, *63*, 82–83.

(21) Pei, Y.; Wang, J.; Liu, L.; Wu, K.; Zhao, Y. Liquid-Liquid Equilibria of Aqueous Biphasic Systems Containing Selected Imidazolium Ionic Liquids and Salts. *J. Chem. Eng. Data* **2007**, *52*, 2026–2031.

(22) Zafarani-Moattar, M. T.; Hamzehzadeh, S. Liquid-Liquid Equilibria of Aqueous Two-Phase Systems Containing 1-Butyl-3-methylimidazolium Bromide and Potassium Phosphate or Dipotassium Hydrogen Phosphate at 298.15 K. *J. Chem. Eng. Data* **2007**, *52*, 1686–1692.

(23) Deng, Y.; Chen, J.; Zhang, D. Phase Diagram Data for Several Salt + Salt Aqueous Biphasic Systems at 298.1 K. *J. Chem. Eng. Data* **2007**, *52*, 1332–1335.

(24) Bridges, N. J.; Gutowski, K. E.; Rogers, R. D. Investigation of Aqueous Biphasic Systems Formed from Solutions of Chaotropic Salts with Kosmotropic Salts (Salt-Salt ABS). *Green Chem.* **2007**, *9*, 177–183.

(25) He, C.; Li, S.; Liu, H.; Li, K.; Liu, F. Extraction of Testosterone and Epitestosterone in Human Urine Using Aqueous Two-Phase Systems of Ionic Liquid and Salt. *J. Chromatogr., A* **2005**, *1082*, 143–149.

(26) Li, S.; He, C.; Liu, H.; Li, K.; Liu, F. Ionic Liquid-Based Aqueous Two-Phase System, a Sample Pretreatment Procedure Prior to High-Performance Liquid Chromatography of Opium Alkaloids. *J. Chromatogr., B* **2005**, *826*, 58–62.

(27) Du, Z.; Yu, Y.; Wang, J. Extraction of Proteins from Biological Fluids by Use of an Ionic Liquid/Aqueous Two-Phase System. *Chem.—Eur. J.* **2007**, *13*, 2130–2137.

(28) Pei, Y.; Wang, J.; Wu, K.; Xuan, X.; Lu, X. Ionic Liquid-Based Aqueous Two-Phase Extraction of Selected Proteins. *Sep. Purif. Technol.* **2009**, *64*, 288–295.

(29) Zafarani-Moattar, M. T.; Hamzehzadeh, S. Diagrams for the Aqueous Two-Phase Ternary System Containing the Ionic Liquid 1-Butyl-3-Methylimidazolium Bromide and Tri-potassium Citrate at T = (278.15, 298.15, and 318.15) K. *J. Chem. Eng. Data* **2009**, *54*, 833–841.

(30) Neves, C. M. S. S.; Ventura, S. P. M.; Freire, M. G.; Marrucho, I. M.; Coutinho, J. A. P. Evaluation of Cation Influence on the Formation and Extraction Capability of Ionic-Liquid-Based Aqueous Biphasic Systems. *J. Phys. Chem. B* **2009**, *113*, 5194–5199.

(31) Ventura, S. P. M.; Neves, C. M. S. S.; Freire, M. G.; Marrucho, I. M.; Oliveira, J.; Coutinho, J. A. P. Evaluation of Anion Influence on the Formation and Extraction Capacity of Ionic-Liquid-Based Aqueous Biphasic Systems. *J. Phys. Chem. B* **2009**, *113*, 9304–9310.

(32) Zhang, J.; Zhang, Y.; Chen, Y.; Zhang, S. Mutual Coexistence Curve Measurement of Aqueous Biphasic Systems Composed of [bmim][BF4] and Glycine, L-Serine, and L-Proline, Respectively. *J. Chem. Eng. Data* **2007**, *52*, 2488–2490.

(33) Wu, B.; Zhang, Y.; Wang, H. Phase Behavior for Ternary Systems Composed of Ionic Liquid + Saccharides + Water. *J. Phys. Chem. B* **2008**, *112*, 6426–6429.

(34) Wu, B.; Zhang, Y.; Wang, H.; Yang, L. Temperature Dependence of Phase Behavior for Ternary Systems Composed of Ionic Liquid + Sucrose + Water. *J. Phys. Chem. B* **2008**, *112*, 13163–13165.

(35) Chen, Y.; Wang, Y.; Cheng, Q.; Liu, X.; Zhang, S. Carbohydrates-Tailored Phase Tunable Systems Composed of Ionic Liquids and Water. *J. Chem. Thermodyn.* **2009**, *41*, 1056–1059.

(36) Vernau, J.; Kula, M. R. Extraction of Proteins from Biological Raw Material Using Aqueous PEG/Citrate Phase Systems. *Biotechnol. Appl. Biochem.* **1990**, *12*, 397–404.

(37) Scurto, A. M.; Aki, S. N. V. K.; Brennecke, J. F. CO_2 as a Separation Switch for Ionic Liquid/Organic Mixtures. *J. Am. Chem. Soc.* **2002**, *124*, 10276–10277.

(38) Scurto, A. M.; Aki, S. N. V. K.; Brennecke, J. F. Carbon Dioxide Induced Separation of Ionic Liquids and Water. *Chem. Commun.* **2003**, *5*, 572–573.

(39) Aki, S. N. V. K.; Scurto, A. M.; Brennecke, J. F. Ternary Phase Behavior of Ionic Liquid (IL)-Organic-CO_2 Systems. *Ind. Eng. Chem. Res.* **2006**, *45*, 5574–5585.

(40) Mellein, B. R.; Brennecke, J. F. Characterization of the Ability of CO2 to Act as an Antisolvent for Ionic Liquid/Organic Mixtures. *J. Phys. Chem. B* **2007**, *111*, 4837–4843.

(41) Najdanovic-Visak, V.; Serbanovic, A.; Esperança, J. M. S. S.; Guedes, H. J. R.; Rebelo, L. P. N.; Nunes da Ponte, M. Supercritical Carbon Dioxide-Induced Phase Changes in (Ionic Liquid, Water and Ethanol Mixture) Solutions: Application to Biphasic Catalysis. *ChemPhysChem* **2003**, *4*, 520–522.

(42) Kroon, M. C.; van Spronsen, J.; Peters, C. J.; Sheldon, R. A.; Witkamp, G. J. Recovery of Pure Products from Ionic Liquids Using Supercritical Carbon Dioxide as a Co-Solvent in Extractions or as an Anti-Solvent in Precipitations. *Green Chem.* **2006**, *8*, 246–249.

(43) Saurer, E. M.; Aki, S. N. V. K.; Brennecke, J. F. Removal of Ammonium Bromide, Ammonium Chloride, and Zinc Acetate from Ionic Liquid/Organic Mixtures Using Carbon Dioxide. *Green Chem.* **2006**, *2*, 141–143.

(44) Dupont, J.; Consorti, C. S.; Suarez, P. A. Z.; de Souza, R. F. In *Organic Syntheses*; Hegedus, L. S., Ed.; John Wiley: Chichester, U.K., 2002.

(45) Trindade, J. R.; Visak, Z. P.; Blesic, M.; Marrucho, I. M.; Coutinho, J. A. P.; Canongia Lopes, J. N.; Rebelo, L. P. N. Salting-Out Effects in Aqueous Ionic Liquid Solutions: Cloud-Point Temperature Shifts. *J. Phys. Chem. B* **2007**, *111*, 4737–4741.

(46) Najdanovic-Visak, V.; Canongia Lopes, J. N.; Visak, Z. P.; Trindade, J.; Rebelo, L. P. N. Salting-Out in Aqueous Solutions of Ionic Liquids and K_3PO_4: Aqueous Biphasic Systems and Salt Precipitation. *Int. J. Mol. Sci.* **2007**, *8*, 736–748.

(47) Canongia Lopes, J. N.; Rebelo, L. P. N. From Aqueous Biphasic System Formation to Salting Agent Precipitation. *Chim. Oggi* **2007**, *25*, 37–39.

(48) Freire, M. G.; Carvalho, P. J.; Silva, A. M. S.; Santos, L. M. N. B. F.; Rebelo, L. P. N.; Marrucho, I. M.; Coutinho, J. A. P. Ion Specific Effects on the Mutual Solubilities of Water and Hydrophobic Ionic Liquids. *J. Phys. Chem. B* **2009**, *113*, 202–211.

(49) Tomé, L. I. N.; Varanda, F. R.; Freire, M. G.; Marrucho, I. M.; Coutinho, J. A. P. Towards an Understanding of the Mutual Solubilities of Water and Hydrophobic Ionic Liquids in the Presence of Salts: The Anion Effect. *J. Phys. Chem. B* **2009**, *113*, 2815–2825.

(50) Hey, M. J.; Jackson, D. P.; Yan, H. The Salting-Out Effect and Phase Separation in Aqueous Solutions of Electrolytes and Poly(ethylene glycol). *Polymer* **2005**, *46*, 2567–2572.

(51) Philip, J. C. Influence of Non-Electrolytes and Electrolytes on the Solubility of Sparingly Soluble Gases in Water. The Question of Hydrates in Solution. *J. Chem. Soc.* **1907**, *91*, 711–717.

(52) Glasstone, S.; Dimond, D. A.; Jones, E. C. Solubility Influences. Part II. The Effect of Various Salts on the Solubility of Ethyl Acetate in Water. *J. Chem. Soc.* **1926**, *129*, 2935–2939.

(53) Glasstone, S.; Bridgman, J.; Hodgson, W. R. P. Solubility Influences. Part IV. The Salting-Out of Aniline from Aqueous Solutions. *J. Chem. Soc.* **1927**, *63*, 5–640.

(54) Eucken, A.; Hertzberg, G. Aussalzeffekt und Ionenhydratation (Salt Effects and Ion Hydration). *Z. Phys. Chem.* **1950**, *195*, 1–23.

(55) Andrew, M. T.; Lynn, S.; Prausnitz, J. M. Liquid-liquid Equilibria for Aqueous Systems Containing *N*,*N*-Diethylmethylamine and Sodium Chloride or Sodium Sulfate. *J. Chem. Eng. Data* **1992**, *37*, 252–259.

(56) Cheluget, E. L.; Gelinas, S.; Vera, J. H.; Weber, M. E. Liquid-liquid Equilibrium of Aqueous Mixtures Poly(propylene glycol) with NaCl. *J. Chem. Eng. Data* **1994**, *39*, 127–130.

(57) Taylor, B. N.; Kuyatt, C. E. *Guidelines for the Evaluation and Expression of Uncertainty in NIST Measurement Results*, Technical Note 1297; NIST: Gaithersburg, MD, 1994.

(58) Merchuk, J. C.; Andrews, B. A.; Asenjo, J. A. Aqueous Two-Phase Systems for Protein Separation: Studies on Phase Inversion. *J. Chromatogr., B* **1998**, *711*, 285–293.

(59) Setschenow, J. Über die Konstitution der Salzlösungen auf Grund ihres Verhaltens zu Kohlensäure. *Z. Phys. Chem.* **1889**, *4*, 117–125.

(60) Ananthapadmanabhan, K. P.; Goddard, E. D. Aqueous Biphasic Formation in Polyethylene Oxide-Inorganic Salt Systems. *Langmuir* **1987**, *3*, 25–31.

(61) Zaslavsky, B. Y.; Gulaeva, N. D.; Djafarov, S.; Masimov, E. A.; Miheeva, L. M. Phase Separation in Aqueous Poly(ethylene glycol)-$(NH_4)_2SO_4$ Systems and Some Physicochemical Properties of the Phases. *J. Colloid Interface Sci.* **1990**, *137*, 147–156.

(62) Zafarani-Moattar, M. T.; Emamian, S.; Hamzehzadeh, S. Effect of Temperature on the Phase Equilibrium of the Aqueous Two-Phase Poly(propylene glycol) + Tripotassium Citrate System. *J. Chem. Eng. Data* **2008**, *53*, 456–461.

(63) Gardas, R. L.; Dagade, D. H.; Coutinho, J. A. P.; Patil, K. J. Thermodynamic Studies of Ionic Interactions in Aqueous Solutions of Imidazolium-Based Ionic Liquids [Emim][Br] and [Bmim][Cl]. *J. Phys. Chem. B* **2008**, *112*, 3380–3389.

(64) Shekaari, H.; Mansoori, Y.; Sadeghi, R. Density, Speed of Sound, and Electrical Conductance of Ionic Liquid 1-Hexyl-3-Methyl-Imidazolium Bromide in Water at Different Temperatures. *J. Chem. Thermodyn.* **2008**, *40*, 852–859.

(65) Shekaari, H.; Mousavi, S. S. Influence of Alkyl Chain on the Thermodynamic Properties of Aqueous Solutions of Ionic Liquids 1-Alkyl-3-Methylimidazolium Bromide at Different Temperatures. *J. Chem. Thermodyn.* **2009**, *41*, 90–96.

(66) Herrington, T. M.; Mole, E. L. Apparent Molar Volumes, Temperatures of Maximum Density and Osmotic Coefficients of Dilute Aqueous Hexamethylenetetraamine Solutions. *J. Chem. Soc., Faraday Trans. 1* **1982**, *78*, 213–223.

(67) Grover, P. K.; Ryall, R. L. Critical Appraisal of Salting-Out and Its Implications for Chemical and Biological Sciences. *Chem. Rev.* **2005**, *105*, 1–10.

(68) Pandey, S.; Fletcher, K. A.; Baker, S. N.; Baker, G. A. Correlation Between the Fluorescent Response of Microfluidity Probes and the Water Content and Viscosity of Ionic Liquid and Water Mixtures. *Analyst* **2004**, *129*, 569–573.

(69) Katayanagi, H.; Nishikawa, K.; Shimozaki, H.; Miki, K.; Westh, P.; Koga, Y. Mixing Schemes in Ionic Liquid-H_2O Systems: A Thermodynamic Study. *J. Phys. Chem. B* **2004**, *108*, 19451–19457.

(70) Miki, K.; Westh, P.; Nishikawa, K.; Koga, K. Effect of an "Ionic Liquid" Cation, 1-Butyl-3-Methylimidazolium, on the Molecular Organization of H2O. *J. Phys. Chem. B* **2005**, *109*, 9014–9019.

(71) Zhao, H. Effect of Ions and Other Compatible Solutes on Enzyme Activity, and Its Implication for Biocatalysis Using Ionic Liquids. *J. Mol. Catal. B: Enzym.* **2005**, *37*, 16–25.

(72) Zhao, H.; Campbell, S.; Solomon, J.; Song, Z.; Olubajo, O. Improving the Enzyme Catalytic Efficiency Using Ionic Liquids with Kosmotropic Anions. *Chin. J. Chem.* **2006**, *24*, 580–584.

(73) Zhao, H.; Jackson, L.; Song, Z.; Olubajo, O. Enhancing Protease Enantioselectivity by Ionic Liquids Based on Chiral- or ω-Amino Acids. *Tetrahedron: Asymmetry* **2006**, *17*, 1549–1553.

(74) Zhao, H.; Jackson, L.; Song, Z.; Olubajo, O. Using Ionic Liquid [EMIM][CH_3COO] as an Enzyme-'Friendly' Co-Solvent for Resolution of Amino Acids. *Tetrahedron: Asymmetry* **2006**, *17*, 2491–2498.

(75) Zhao, H.; Olubajo, O.; Song, Z.; Sims, A. L.; Person, T. E.; Lawal, R. A.; Holley, L. A. Effect of Kosmotropicity of Ionic Liquids on the Enzyme Stability in Aqueous Solutions. *Bioorg. Chem.* **2006**, *34*, 15–25.

(76) Zhao, H.; Campbell, S. M.; Jackson, L.; Song, Z.; Olubajo, O. Hofmeister Series of Ionic Liquids: Kosmotropic Effect of Ionic Liquids on the Enzymatic Hydrolysis of Enantiomeric Phenylalanine Methyl Ester. *Tetrahedron: Asymmetry* **2006**, *17*, 377–383.

(77) Zhao, H.; Song, Z. Nuclear Magnetic Relaxation of Water in Ionic-Liquid Solutions: Determining the Kosmotropicity of Ionic Liquids and Its Relationship with the Enzyme Enantioselectivity. *J. Chem. Technol. Biotechnol.* **2007**, *82*, 304–312.

(78) Zhao, H. Are Ionic Liquids Kosmotropic or Chaotropic? An Evaluation of Available Thermodynamic Parameters for Quantifying the Ion Kosmotropicity of Ionic Liquids. *J. Chem. Technol. Biotechnol.* **2006**, *81*, 877–891.

(79) Parsegian, V. A.; Rand, R. P.; Rau, D. C. Osmotic Stress, Crowding, Preferential Hydration, and Binding: A Comparison of Perspectives. *Proc. Natl. Acad. Sci. U.S.A.* **2000**, *97*, 3987–3992.

(80) Sadeghi, R.; Ziamajidi, F. Vapor-Liquid Equilibria of Binary Tripotassium Citrate + Water and Ternary Polypropylene Oxide 400 + Tri-potassium citrate + Water Systems from Isopiestic Measurements over a Range of Temperatures. *Fluid Phase Equilib.* **2007**, *255*, 46–54.

(81) Sadeghi, R. Vapor-Liquid Equilibrium in Aqueous Systems Containing Poly(vinylpyrrolidone) and Sodium Citrate at Different Temperatures—Experimental and Modeling. *Fluid Phase Equilib.* **2006**, *249*, 33–41.

(82) Jones, G.; Dole, M. The Viscosity of Aqueous Solutions of Strong Electrolytes with Special Reference to Barium Chloride. *J. Am. Chem. Soc.* **1929**, *51*, 2950–2964.

(83) Jenkins, H. D. B.; Marcus, Y. Viscosity B-Coefficients of Ions in Solution. *Chem. Rev.* **1995**, *95*, 2695–2724.

(84) Wang, Y.; Li, H.; Han, S. A Theoretical Investigation of the Interactions between Water Molecules and Ionic Liquids. *J. Phys. Chem. B* **2006**, *110*, 24646–24651.

(85) Wang, Y.; Li, H.; Han, S. Structure and Conformation Properties of 1-Alkyl-3-Methylimidazolium Halide Ionic Liquids: A Density-Functional Theory Study. *J. Chem. Phys.* **2005**, *123*, 174501.

(86) Wang, Y.; Li, H.; Han, S. The Chemical Nature of the $^{\oplus}$C-H···X^- (X = Cl or Br) Interaction in Imidazolium Halide Ionic Liquids. *J. Chem. Phys.* **2006**, *124*, 044504.

(87) Mele, A.; Tran, C. D.; Lacerda, S. H. The Structure of a Room-Temperature Ionic Liquid with and without Trace Amounts of Water: The Role of C-H···O and C-H···F Interactions in 1-*n*-Butyl-3-Methylimidazolium Tetrafluoroborate. *Angew. Chem., Int. Ed.* **2003**, *42*, 4364–4366.

(88) Collins, K. D. Ion Hydration: Implications for Cellular Function, Polyelectrolytes, and Protein Crystallization. *Biophys. Chem.* **2006**, *119*, 271–281.

Received for review August 22, 2009. Accepted February 25, 2010.

JE900681B