



Binary Mixtures of Ionic Liquids in Aqueous Solution: Towards an Understanding of Their Salting-In/Salting-Out Phenomena

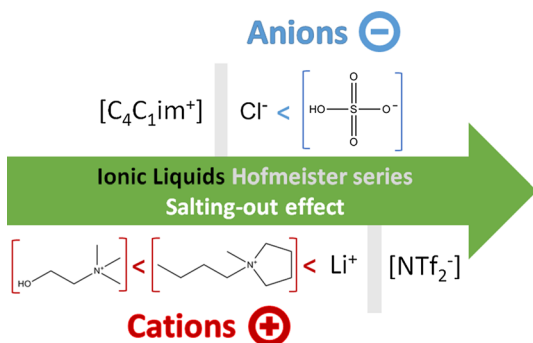
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Abstract

The order of the salting-in or salting-out inducing ability of ions on the aqueous solubility of macromolecules in aqueous solutions is known as the Hofmeister series. Taking into account that ionic liquids (ILs) are constituted by ions, they can exert similar effects on the solubility of other ILs in aqueous media. To expand the knowledge of the salting-in/-out ability of ILs, experimental studies on the solubility of 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonylimide) in water and in the presence of other IL/salts, were conducted at 298.15 K and atmospheric pressure. Both the impact of the anion and cation of the IL were evaluated with the following ILs/salts: 1-butyl-3-methylimidazolium chloride, 1-butyl-3-methylimidazolium hydrogensulfate, cholinium bis(trifluoromethylsulfonyl) imide, 1-butyl-1-methylpyrrolidinium bis(trifluoromethylsulfonyl)imide and lithium bis(trifluoromethylsulfonyl)imide, over a wide composition range. As happens with common salts, both salting-in and salting-out effects exerted by ILs were observed, with a higher impact exerted by the IL anion on the salting-out phenomenon. These data allow better understanding of the ILs impact when designing liquid–liquid separation processes.

Graphical Abstract



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Keywords Ionic liquids · Solubility · Water · Salting-in effect · Salting-out effect · Hofmeister series

1 Introduction

Ionic liquids (ILs) belong to the molten salts group and are usually formed by a large organic cation and a smaller organic or inorganic anion, allowing them to remain liquid below 373 K at atmospheric pressure [1]. One of the most interesting feature of ILs is their design ability for a specific task, by a particular combination of cations and anions [2].

The use of ILs as alternative solvents for a range of applications has attracted large interest [3–5]. Hydrophobic ILs have been used in the creation of liquid–liquid extraction systems with aqueous media [6], whereas hydrophilic ones have been used in the creation of aqueous biphasic systems (ABS) by the addition of a salting-out species [7]. In both types of systems, the manipulation of the IL's solubility in water by adding specific compounds could lead to the development of efficient extraction and purification systems to be used in separation processes [8–13]. Over the years, ILs mutual solubilities with water have been studied and different IL structural effects have been addressed, namely the cation core [14–16], the alkyl chain length [17–20], the cation isomerism [18, 21, 22] and the anion's nature [14]. However, when dealing with real aqueous matrices that contain, for instance, metabolites and salts, significant changes in the ILs solubility can occur. Freire et al. [23, 24] showed that the presence of salts in aqueous media has a significant influence on the mutual solubilities of water and ILs, following the salting-in/salting-out trends of the Hofmeister series [25]. The authors found that salting-out inducing ions (high charge density) and salting-in inducing ions (low charge density) act by different mechanisms [23, 24]. While the former act mainly through an entropic effect resulting from the formation of hydration complexes, the salting-in results from a direct ion binding of the low charge density ions to the hydrophobic moieties of the IL [23]. Additionally, Shahriari et al. showed the effect of salts on promoting the phase separation in ABS, i.e. in phase separation of mixtures comprising an hydrophilic IL and water [26]. The results gathered showed that the salts ability to form two phases follows the Hofmeister series, and that the salt ions molar entropy of hydration closely correlates with the salting-out effect [26].

Although the Hofmeister series is a well-known qualitative approach ranking the ions influence on the solubility of charged molecules, further research in order to rank IL ions in this series is still scarce [27–29]. Yang [28] and Zhao et al. [27] showed that ILs, which follow the Hofmeister series in the stability and activity of enzymes, composed of chaotropic cations and kosmotropic anions can be valuable for the application of ILs in bio-transformations. On the other hand, Constantinescu and Weingärtner [29] ranked the cations and anions of ILs in the Hofmeister series by evaluating the stability of ribonuclease A in different ILs aqueous solutions.

Since ILs are composed of ions, they may exert similar (salting-in/salting-out) effects to traditional salts on the solubility of other ILs in aqueous media. The aim of this work is to expand the knowledge of the salting-in/-out ability of ILs by evaluating their effect on the aqueous solubility of a given hydrophobic IL. For that purpose, experimental data on the solubility of 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide, $[\text{C}_4\text{C}_1\text{im}][\text{NTf}_2]$, in aqueous solutions containing other ILs were determined at 298.15 K at atmospheric pressure. Both the influence of the cation core and anion of the IL added to the system on the solubility of $[\text{C}_4\text{C}_1\text{im}][\text{NTf}_2]$ in water were evaluated.

2 Experimental Section

2.1 Chemicals

The study of solubility of 1-butyl-3-methylimidazolium bis(trifluoromethanesulfonyl) imide, $[\text{C}_4\text{C}_1\text{im}][\text{NTf}_2]$ (99% purity, halides < 100 ppm), in water was carried out in presence of the following ILs and salt: 1-butyl-3-methylimidazolium hydrogen-sulphate, $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ (> 98% purity, halides < 100 ppm), 1-butyl-3-methylimidazolium chloride, $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ (99% purity), 1-butyl-1-methylpyrrolidinium bis(trifluoromethanesulfonyl)imide, $[\text{C}_4\text{C}_1\text{pyr}][\text{NTf}_2]$ (99% purity, halides < 100 ppm), cholinium bis(trifluoromethanesulfonyl)imide, $[\text{N}_{1112\text{OH}}][\text{NTf}_2]$ (99% purity, halides < 100 ppm), and lithium bis(trifluoromethanesulfonyl)imide, $\text{Li}[\text{NTf}_2]$ (99% purity, halides < 100 ppm). With the exception of $\text{Li}[\text{NTf}_2]$, which has a melting temperature between 507 and 511 K [30], all remaining compounds fall in the IL class according to their general characterization of melting temperatures below 373 K. Figure 1 shows the chemical structures of the ILs/salts investigated. To avoid any ambiguity, all these ILs will be hereafter referred as salts. All of these salts were supplied by Iolitec. Before their use, they were purified (to reduce the content of water and other volatile components) by drying individual samples at circa 353 K for at least 48 h under constant stirring and moderate vacuum conditions (≈ 0.1 Pa). After this procedure, ^1H , ^{13}C , and ^{19}F NMR analyses confirmed the purity of the samples used; the respective spectra are given in the Supplementary Information. Doubly distilled water, passed through a reverse osmosis system and further treated with a MilliQ plus 185 water purification apparatus, was used in the preparation of all ($[\text{C}_4\text{C}_1\text{im}][\text{NTf}_2]$ + salt + water) ternary mixtures. Purity analyses of water

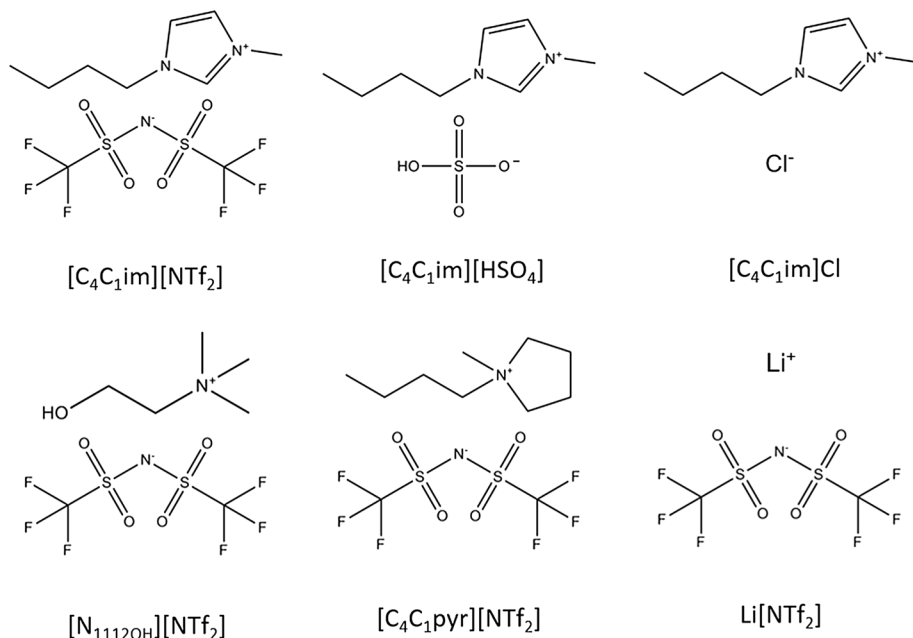


Fig. 1 Chemical structures of the ILs and salt used in this work

revealed resistivity values of 18.2 M Ω -cm and a TOC (Total Organic Carbon content) lower than 5 $\mu\text{g}\cdot\text{dm}^{-3}$.

2.2 Experimental Procedure

The solubility of $[\text{C}_4\text{C}_1\text{im}][\text{NTf}_2]$ in aqueous solutions of salts was determined at 298.15 K at atmospheric pressure. The solubility of pure $[\text{C}_4\text{C}_1\text{im}][\text{NTf}_2]$ in water at 298 K was taken from the literature, corresponding to a value of $1.72 \times 10^{-2} \text{ mol}\cdot\text{kg}^{-1}$ [17]. Mixtures of $[\text{C}_4\text{C}_1\text{im}][\text{NTf}_2]$ + salt were gravimetrically prepared within $\pm 10^{-4} \text{ g}$, with the salt present at a concentration ranging between 500 and 100,000 ppm, followed by the addition of 15 mL of doubly distilled water (the mass of each component is given in Table S1). The ternary mixtures were vigorously agitated and allowed to reach complete phase separation and equilibrium for at least 48 h. This period proved to be the time sufficient to guarantee a complete separation of the two phases and that no further variations in mole fraction solubilities occurred [18]. The phases in equilibrium, kept in the glass vials, were stabilized for 24 h in an aluminum block designed for the purpose, which was further placed in an isolated air bath capable of maintaining the temperature within $\pm 0.01 \text{ K}$. The temperature control was achieved with a PID temperature controller driven by a calibrated Pt100 (class 1/10) temperature sensor inserted in the aluminum block. The solubility of $[\text{C}_4\text{C}_1\text{im}][\text{NTf}_2]$ in water was determined by UV spectroscopy, using a SHIMADZU UV-1700 Pharma-Spec Spectrometer, at a wavelength of 211 nm, and using a calibration curve established before measuring the IL solubility (given in Fig. S6 in the Supplementary Information). For that, and according to the detection limits of the equipment (given in Table S1 in the Supplementary Information), the dilution factor was circa 1:500 (w/w) times. The solubility results are an average of at least five independent measurements. The detailed values and respective associated uncertainty at the 95% of confidence level are given in Table S1 in the Supplementary Information. A scheme of this procedure is depicted in Fig. 2. Since the mixtures with $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ and $[\text{C}_4\text{C}_1\text{im}][\text{HSO}_4]$ have a common cation, ionic chromatography (IC) was used to quantify SO_4^{2-} and Cl^- in the water-rich phase. The quantitative analyses of SO_4^{2-} and Cl^- in the water-rich phase were carried out using a Dionex ionic chromatography system (Model: Series 2000/SP, using the anion IC column Model IonPac AS12A with background conductivity suppression technology). The aqueous phase was diluted immediately after sampling in order to avoid further phase separation and finally diluted to the ionic chromatography concentration level of the calibration range (10^{-3} to $10^{-5} \text{ mol}\cdot\text{dm}^{-3}$) of the IC analytical system. The molality of each IL in the water phase is given in Table S1 in the Supplementary Information.

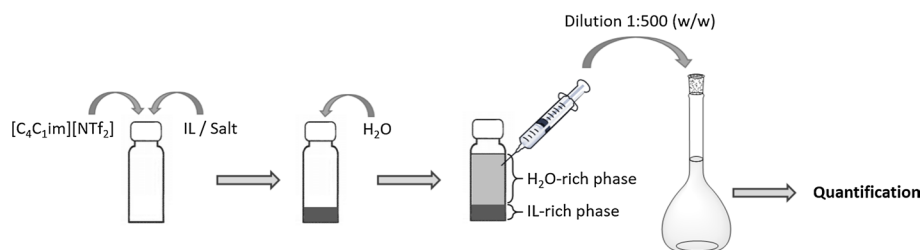


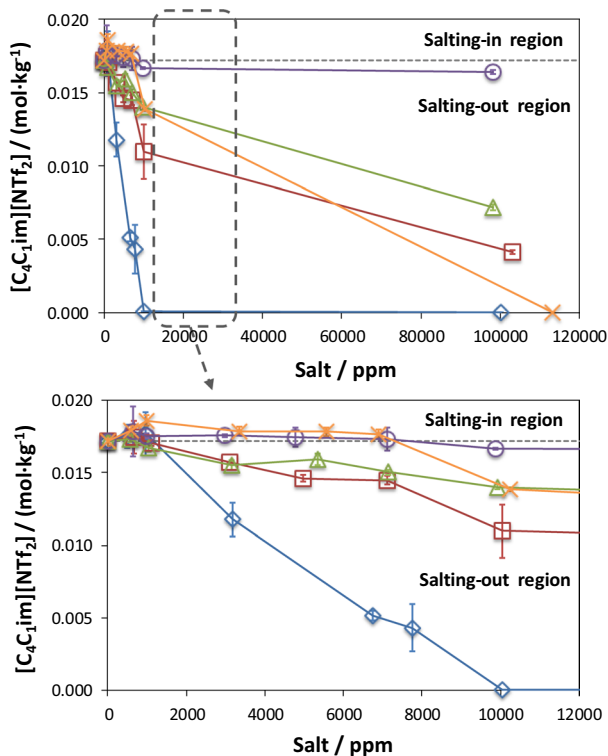
Fig. 2 Scheme of the experimental procedure for sample preparation and quantification used in this work

3 Results and Discussion

The impact of the addition of a second IL or salt in the $[C_4C_1mim][NTf_2]$ solubility in water was investigated. This IL was chosen for being one of the “standard” hydrophobic ILs, with a high temperature and chemical stability, and because its solubility was previously widely studied in the presence of a large diversity of salts [23, 24, 31]. In this work, each salt was added to $[C_4C_1im][NTf_2]$ in the concentration range of (500–100,000) ppm for the IL–salt binary mixture, and the solubility of $[C_4C_1mim][NTf_2]$ in water was measured at 298.15 K and atmospheric pressure. All systems here studied are comprised always of a similar cation or anion, thus avoiding ion exchange. The experimental results obtained are shown in Fig. 3 and presented in Table S1 in the Supplementary Information.

The influence of ILs/salts, e.g. at $\approx 10,000$ ppm, in the $[C_4C_1im][NTf_2]$ solubility in water follows the order $[C_4C_1im][H_2SO_4] > [C_4C_1im]Cl > Li[NTf_2] > [N_{1112OH}][NTf_2] > [C_4C_1pyrr][NTf_2]$. These results clearly establish that the change of the salt anion has a major impact on decreasing the solubility of $[C_4C_1im][NTf_2]$, or on inducing the salting-out effect, in good agreement with previous works [23, 24, 31]. Although all salts lead to $[C_4C_1im][NTf_2]$ salting-out at higher concentrations, at lower concentrations of salt, mainly below 1000 ppm, an increase in the $[C_4C_1im][NTf_2]$ solubility is observed for some salts. This inversion in behavior, i.e. a salting-in effect at low concentrations of salt followed by a salting-out at higher concentrations was also observed by Freire et al. [23], when evaluating the effect of traditional salts on the $[C_4C_1im][NTf_2]$ solubility [32]. This type of effect was also reported when ILs were added to poly(ethylene glycol)/water

Fig. 3 Solubility, and respective associated uncertainties at the 95% of confidence level, of $[C_4C_1im][NTf_2]$ in aqueous solutions at different concentrations: square, $Li[NTf_2]$; triangle, $[N_{1112OH}][NTf_2]$; circle, $[C_4C_1pyrr][NTf_2]$; diamond, $[C_4C_1im][H_2SO_4]$; asterisk, $[C_4C_1im]Cl$, at 298.15 K and atmospheric pressure; ($u(T) = 0.1$ K and $u(p) = 0.05$). The lines have no physical meaning are only guides for the eye



mixtures [33]. The authors explained that ILs with shorter alkyl chain can produce some water-structuring (salting-out) effect through the polar parts of the cation and anion, while the non-polar parts are responsible for the water-structure-breaking (salting-in) effect [33].

In the salting-out regions, the higher the ability of each salt ion to be hydrated, the higher is its impact on decreasing the $[C_4C_1im][NTf_2]$ solubility in water, as indicated by the differentiation of their hydrogen-bond basicity's ($[C_4C_1im][HSO_4]$, 0.95 [34] > $[C_4C_1im]Cl$, 0.70 [34]) and hydrogen-bond acidity's ($[N_{1112OH}][NTf_2]$, 1.491 [35]) > $[C_4C_1pyrr][NTf_2]$, 0.433 [35]). The solubility of $[C_4C_1im][NTf_2]$ in water decreases in the order $[C_4C_1pyrr]^+ > [N_{1112OH}]^+ > Li^+$, the lithium salt being the one that promotes a strong salting-out effect, while the pyrrolidinium ion almost does not affect the solubility of the IL, even up to concentrations of 100,000 ppm. The cholinium-based salt has a similar behavior to the lithium salt at lower concentrations; however, at the highest concentration studied its salting-out effect is less pronounced. This behavior follows the Hofmeister series [25, 36] generally applied to common salts, because ammonium-based cations are weaker salting-out species than Li^+ . In general, organic cations have a lower effect on inducing salting-out than inorganic ones, mainly because of their low-charge density and lower ability to be hydrated. In what concerns the anion effect, ILs containing the common cation $[C_4C_1im]^+$ were used combined with the anions SO_4^{2-} and Cl^- . These salts ability to salt-out $[C_4C_1im][NTf_2]$ follows the order: $SO_4^{2-} > Cl^-$. The anion SO_4^{2-} is a stronger salting-out agent than Cl^- , although, at the highest concentration studied, both compounds are able to completely exclude $[C_4C_1im][NTf_2]$ from the aqueous medium. The IL with the halogen anion induces the $[C_4C_1im][NTf_2]$ salting-in at concentrations up to 7000 ppm, having thus a behavior similar to that previously observed and discussed with NaCl [23].

According to the results of Fig. 3, the IL/salt effects on the $[C_4C_1im][NTf_2]$ solubility in water closely follow the Hofmeister series [37]. Furthermore, IL/salt anions induce a more significant salting-out effect than the corresponding cations, in agreement with previous studies on the effect of traditional salts on the IL's solubility in water [23], which is due to their higher hydration capability and polarization [38]. Like with the common salts, ILs affect the solubility of charged molecules, such as other ILs. The experimental data obtained in this work reveal that IL ions seem to follow the Hofmeister series towards their ability to promote salting-in/-out effects through other ILs, and with IL anions presenting a more significant contribution in the salting-out effect. However, a more complex framework, particularly at the molecular-level, is still required in order to better understand IL ions specific effects.

This study contributes to the understanding of the solubility of a hydrophobic IL in water in the presence of additional ILs/salts, allowing the design of ILs for a given application and with a predicted solubility in water, as well as in the design of the solubility of a panoply of charged compounds in water by the addition of ILs.

4 Conclusions

The influence of ILs/salts ions on the aqueous solubility of another IL was here determined and discussed in terms of salting-in/salting-out phenomena. The results obtained show that the solubility of $[C_4C_1im][NTf_2]$ in water at 298.15 K displays a salting-in region at low concentrations of the salt added, followed by a salting-out region at higher concentrations. These effects depend on the IL/salt nature and its concentration, although the anion plays the main role on defining the salting-out regions due to its higher hydration capability

and polarizability. The strength of the salting-in/-out phenomena allow classifying IL ions according to the Hofmeister series. The understanding of these phenomena helps in the design of solvents with a predicted solubility in water, and therefore on the tailoring of liquid–liquid processes involving ILs.








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