Overview of the Effect of Salts on Biphasic Ionic Liquid/Water Solvent Extraction Systems: Anion Exchange, Mutual Solubility, and Thermomorphic Properties

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Ⓢ Supporting Information

ABSTRACT: Hydrophobic (water-immiscible) ionic liquids (ILs) are frequently used as organic phase in solvent extraction studies. These biphasic IL/water extraction systems often also contain metal salts or mineral acids, which can significantly affect the IL trough (un)wanted anion exchange and changes in the solubility of IL in the aqueous phase. In the case of thermomorphic systems, variations in the cloud point temperature are also observed. All these effects have important repercussions on the choice of IL, suitable for a certain extraction system. In this paper, a complete overview of the implications of metal salts on biphasic IL/water systems is given. Using the Hofmeister series as a starting point, a range of intuitive prediction models are introduced, supported by experimental evidence for several hydrophobic ILs, relevant to solvent extraction. Particular emphasis is placed on the IL betainium bis(trifluoromethylsulfonyl)imide $[Hbet][Tf_2N]$. The aim of this work is to provide a comprehensive interpretation of the observed effects of metal salts, so that it can be used to predict the effect on any given biphasic IL/water system instead of relying on case-by-case reports. These prediction tools for the impact of metal salts can be useful to optimize IL synthesis procedures, extraction systems and thermomorphic properties. Some new insights are also provided for the rational design of ILs with UCST or LCST behavior based on the choice of IL anion.
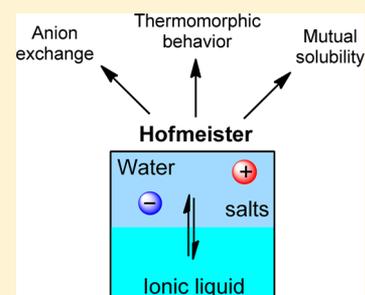
■ INTRODUCTION

The study of the effect of metal salts on the behavior of compounds in solution starts with Franz Hofmeister in 1888. He described the effect of salt cations and anions on the stability and solubility of the protein ovalbumin in aqueous solutions, and ranked the ions in the so-called Hofmeister series.[1] His observations were later transposed to explain the effect of metal salts and organic salts on the behavior of other proteins, colloids, and polymers in solution.[2−22] Ions that promote the dissolution of a compound in solution are called *salting-in ions*, while ions that exclude a solute from solution are called *salting-out ions*.[2−22] Despite the apparent simplicity of this theory, it still continues to puzzle scientists to this day.[23,24] The importance of this complicated solvation science is becoming ever more apparent as the study of interfacial phenomena and solvent structure on a molecular level is the key to understanding many areas of chemistry.[22−33] Due to their strongly ionic character, ionic liquids (ILs) have received particular attention lately in this area of solvation science.[34] Under the influence of salts, some water-miscible ILs can form IL-based aqueous biphasic systems (ABS).[34−49] More importantly, the properties of biphasic IL/water systems formed by water-immiscible ILs are also greatly affected by the addition of metals and mineral acids.[50−56] These water-immiscible ILs have shown great promise as organic phase in solvent extraction studies. The ILs can be used as diluents for extractants, or task-specific ILs can be prepared in which a functional (extracting) group is incorporated in the structure of the IL.[57] Due to the

infinite number of possible anion and cation combinations, ILs are often considered designer or task-specific solvents.[58] A well-known example is the carboxyl-functionalized IL betainium bis(trifluorosulfonyl)imide $[Hbet][Tf_2N]$, which can be used for the extraction of a range of metal ions.[59−64] In traditional solvent extraction, which uses apolar solvents such as toluene or kerosene as organic phase, the effect of metal salts is mostly visible in the mutual solubility of the organic phase and aqueous phase.[65] The solubility of uncharged hydrophobic molecules such as benzene or toluene in the aqueous phase can be increased by the adsorption of ions which counters the van der Waals attraction between the hydrophobic solutes.[10,66] Both anions and cations are effective at increasing the surface charge and improving their solubility by countering the van der Waals attraction. The effect of ions is therefore only related to their hydrophobicity since this will determine if they can adsorb on the hydrophobic surface and contribute to its surface charge. The charge density of an ion determines its level of hydration and therefore also its hydrophobicity (Figure 1). It was shown experimentally that the rank order of effectiveness of the anions in salting-out benzene is indeed $SO_4^{2-} > Cl^- > Br^- > NO_3^- > I^-$, and the rank order of the cations is $Ca^{2+} > Na^+ > K^+ > NH_4^+ > Cs^+$, which is in agreement with the series in Figure 1.[2,10,66] This corresponds to the Hofmeister series with a reversed
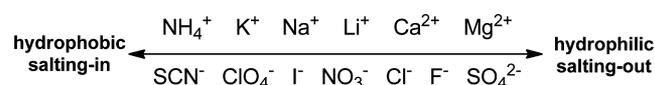
Figure 1. Salting-in/salting-out series for uncharged molecular solvents and ionic liquids. This ranking of anions and cations follows the hydrophobicity which is a consequence of the charge density and the resulting size of their hydration mantle.

cation series because the Hofmeister series was established for the negatively charged hydrophobic protein ovalbumin. Therefore, adsorbed cations diminish the surface charge of the protein and lower its solubility. Schwiertz et al., used this to predict the order of the salting-in/salting-out series depending on the surface charge and the hydrophobicity of a protein or colloid surface.[5,6]

The same order also applies to the solubility of ionic liquids in the water phase.[47,50−54,67,68] However, ILs are more complicated than the above-mentioned organic solvents in the sense that they consist of ions themselves. Therefore, salts can also cause other effects such as anion exchange, which can negatively affect the ionic liquid. This paper gives and overview of all the effects of metal salts and mineral acids on a selection of biphasic IL/water systems, relevant to solvent extraction. These effects include anion exchange, changes in mutual solubility and effects on the cloud point temperature of thermomorphic systems. The countless different combinations of anions and cations to form ILs, increases the need for a general prediction model that is applicable for all ILs, regardless of the structural characteristics of their anions and cations. Rationalizations and prediction models are therefore provided, which are generally applicable to all water-immiscible ILs. Understanding these aspects is important for the design of stable solvent extraction systems and to minimize the loss of IL to the water phase.[37,46,61,69−77] Particular emphasis was placed on water-immiscible ILs used as organic phase in solvent extraction of metal ions, such as the alkylated ammonium and phosphonium ILs and the functionalized ILs like [Hbet]-[Tf$_2$N].[59−62,73,76,78,79]

■ EXPERIMENTAL SECTION

Chemicals. MgCl$_2$·6H$_2$O (98%), NaCl (98%), NaClO$_4$·H$_2$O (98%), NaF (99%), Mg(NO$_3$)$_2$·6H$_2$O, KSCN (99%), LiNO$_3$ (99%) and D$_2$O (99.9 atom % D) were obtained from Sigma-Aldrich (Diegem, Belgium). CaCl$_2$·2H$_2$O (99.5%), NaNO$_3$ (99%), Na$_2$SO$_4$ (99%), Ca(NO$_3$)$_2$·4H$_2$O (99%), KNO$_3$ (99%), NH$_4$NO$_3$ (99%) and HNO$_3$ (65%) were purchased from Chem-Lab (Zedelgem, Belgium). KCl (99.5%) and NaI (99.5%) were purchased from AppliChem (Darmstadt, Germany) and LiCl (99%) from Fisher Chemical (Loughborough, UK). CsCl (99%), NaBr (99.5%), NH$_4$Cl (99.5%), H$_2$SO$_4$ (96%), HClO$_4$ (70%), HCl (37%) and 1,4-dioxane (99.9%) were obtained from Acros Organics (Geel, Belgium). The silicone solution in isopropanol was purchased from SERVA Electrophoresis GmbH (Heidelberg, Germany). All chemicals were used as received without further purification.

Ionic Liquids. Table 1 shows the ILs used in this work. An overview of the chemical structure of all the ILs is provided in the Supporting Information (Figure S2). The ILs [N$_{4111}$]-[Tf$_2$N] (99%), [S$_{222}$][Tf$_2$N] (99%), [Chol][Tf$_2$N] (99%), [emim][Tf$_2$N] (99%) and [mppip][Tf$_2$N] (99%) were purchased from IoLiTec (HeilBronn, Germany). The ILs [P$_{8444}$][Cl] (Cyphos 253), [P$_{66614}$][Cl] (Cyphos 101) and [P$_{66614}$][Br] (Cyphos 102) were purchased from Cytec

Table 1. Overview of the Ionic Liquids Used in This Work

formula	full name	origin
[P$_{8444}$][Cl]	tributyl(octyl)phosphonium chloride	purchased
[P$_{8444}$][Br]	tributyl(octyl)phosphonium bromide	synthesized
[P$_{8444}$][NO$_3$]	tributyl(octyl)phosphonium nitrate	synthesized
[P$_{8444}$][ClO$_4$]	tributyl(octyl)phosphonium perchlorate	synthesized
[P$_{8444}$][Tf$_2$N]	tributyl(octyl)phosphonium bistriflimide[a]	synthesized
[P$_{66614}$][Cl]	trihexyl(tetradecyl)phosphonium chloride	purchased
[P$_{66614}$][Br]	trihexyl(tetradecyl)phosphonium bromide	purchased
[P$_{66614}$][NO$_3$]	trihexyl(tetradecyl)phosphonium nitrate	synthesized
[P$_{66614}$][Tf$_2$N]	trihexyl(tetradecyl)phosphonium bistriflimide	synthesized
[N$_{8881}$][Cl]	trioctyl(methyl)ammonium chloride	purchased
[N$_{4111}$][Tf$_2$N]	trimethyl(butyl)ammonium bistriflimide	purchased
[S$_{222}$][Tf$_2$N]	triethylsulfonium bistriflimide	purchased
[Hbet][Tf$_2$N]	betainium bistriflimide	synthesized
[Chol][Tf$_2$N]	choline bistriflimide	purchased
[P$_{444}$E$_3$][DEHP]	tributyl(2-[2-(2-methoxyethoxy)ethoxy] ethyl) phosphonium bis(2-ethylhexyl) phosphate	synthesized
[P$_{4441}$COOH][Cl]	tributyl(carboxymethyl)phosphonium chloride	synthesized
[emim][Tf$_2$N]	1-ethyl-3-methylimidazolium bistriflimide	purchased
[mppip][Tf$_2$N]	1-methyl-1-propylpiperidinium bistriflimide	purchased

[a]bistriflimide = bis(trifluoromethylsulfonyl)imide.

(Vlaardingen, Netherlands), and [N$_{8881}$][Cl] (Aliquat 336) was obtained from Sigma-Aldrich (Diegem, Belgium). The commercially available ILs were used as received without further purification. For the synthesized ILs, a detailed overview of the synthesis procedures and required chemicals is given in the Supporting Information.

Equipment and Characterization. ^{1}H and ^{13}C spectra were recorded on a Bruker Avance 300 spectrometer, operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C. A TMS-200 thermoshaker (Nemus Life) was used to shake the samples and a Heraeus Megafuge 1.0 centrifuge was used to accelerate phase separation. Total reflection X-ray fluorescence (TXRF) analysis was performed with a Bruker S2 Picofox TXRF spectrometer equipped with a molybdenum source. For the sample preparation, plastic microtubes were filled with a small amount of IL sample (10−50 mg) and ethanol/water (700 μL). The microtubes were then vigorously shaken on a vibrating plate (IKA MS 3 basic). Finally, a 1 μL drop of this solution was put on a quartz glass plate, previously treated with a silicone/isopropanol solution (Serva) to avoid spreading of the sample droplet on the quartz glass plate. The quartz glass plates were then dried for 30 min at 60 °C prior to analysis. Each sample was measured for 5 min.

Determination of the IL Solubility in the Water Phase with Quantitative ^{1}H NMR. The IL (1 g) was contacted with a water phase (1 g) and shaken for 1 h (25 °C, 2000 rpm) to guarantee equilibrium. The samples were then centrifuged (5000 rpm, 10 min) to accelerate phase separation. A sample of the water phase was taken (100 mg) and mixed with a known amount of 1,4-dioxane (5 mg) and diluted with deuterated water (500 mg). This mixture was then shaken on a vibrating plate (IKA MS 3 basic) and measured with ^{1}H NMR. The integrated intensity of the 1,4-dioxane signal (δ = 3.6) was compared with the IL signals (and corrected for the amount of protons) in order to quantify the concentration of IL in the water phase. The water peak did not cause problematic interferences. This analytical technique was validated using

Table 2. Degree of Anion Exchange (%) after Contacting Several ILs with Salt-Containing Aqueous Solutions (2 equiv)^a

	Tf_2N^-	SCN^-	ClO_4^-	I^-	NO_3^-	Br^-	Cl^-	SO_4^{2-}
$[P_{66614}][Tf_2N]$	^{b}	^{b}	2.9	0.4	0.1	0.04	0.01	<DL^c
$[P_{66614}][NO_3]$	98.7	98.1	97.3	96.9	^{b}	51.2	16.4	0.5
$[P_{66614}][Br]$	99.7	99.5	99.4	99.1	84	^{b}	27.1	1.8
$[P_{66614}][Cl]$	100	100	^{b}	99.9	97.6	96.1	^{b}	2.5

^{a}Sodium salts were used except for LiTf$_2$N and KSCN. The mixtures were shaken (2000 rpm) for 1 h at 50 °C. The anion exchange was quantified by TXRF. ^{b}Not quantifiable because the same element is present after exchange. ^{c}Below the detection limit for TXRF (1 ppm).

known amounts of betaine in solution (Figure S1) and has an average uncertainty of ±0.1 wt %.

Determination of the Cloud Point Temperature. The cloud point temperature (T_{CP}) of thermomorphic IL/water systems was determined visually. An oil bath setup was used to control the temperature of the IL-containing vial (4 mL) and a temperature probe was present in the mixture. The IL−water solvent mixtures were prepared in a 1:1 wt/wt ratio. The temperature of the sample was gradually increased or decreased (in steps of 0.1 °C) and allowed to equilibrate at every step until phase separation was observed. At every step the sample was shortly agitated (1 s) to overcome a possible metastable state. The determination of the cloud point temperature was repeated three times to guarantee its accuracy.

Studying Anion Exchange with TXRF Analysis. ILs of the type $[P_{66614}][X_A]$ (X_A = different anion) (1 g) were contacted with aqueous solutions (1 g) containing 2 equiv of sodium salts with the desired anion X_B. The mixtures were shaken (2000 rpm) at 50 °C for 1 h. Then, the samples were centrifuged (5000 rpm) to accelerate phase separation. A sample of the IL phase was then taken to determine the degree of anion exchange. This was quantified by measuring the P/X (phosphor/anion) ratio before and after the exchange, using total reflection X-ray fluorescence (TXRF). These relative measurements did not require an internal standard.

■ RESULTS AND DISCUSSION

1. Ionic Liquid Anion Exchange. When a hydrophobic (water-immiscible) IL is contacted with a water phase, a biphasic system is created. If salts are present in the aqueous phase, the salt anions can exchange with the anions of the IL depending on their affinity for the water phase and the IL phase. In some cases anion exchange is intended, for example, to synthesize an IL with a different anion than the anion present in the commercial IL.[73] In other cases, anion exchange can be an unwanted effect, for example, in metal extraction processes with different anions in the IL phase and the water phase. In such processes anion exchange can significantly pollute the IL phase and change its properties. Fortunately, the occurrence of anion exchange can be predicted based on the Hofmeister series. Hydrophobic anions (with low charge density) such as Tf_2N^-, SCN^-, ClO_4^- and I^- prefer to be in the IL, while more hydrophilic anions such as Cl^- and SO_4^{2-} prefer to be in the water phase where they are better solvated (Figure 1). The exact order of anion exchange was tested using trihexyl(tetradecyl)phosphonium ILs with the formula $[P_{66614}][X]$ (X = Tf_2N^-, NO_3^-, Br^-, and Cl^-). This IL has been used successfully for the extraction of various metal ions.[75,76,78−80] These very hydrophobic ILs were contacted with an aqueous phase (1:1 ratio wt/wt) containing 2 equiv of a salt (LiTf$_2$N, NaSCN, NaClO$_4$, NaI, NaNO$_3$, NaBr, NaCl, Na$_2$SO$_4$). The mixtures were shaken (2000 rpm) for 1 h at 50 °C. The P/X ratio (phosphor/anion) in the IL phase was

analyzed by TXRF and compared with the initial P/X ratio to obtain the degree of anion exchange (%) (Table 2). The aim was not to obtain full equilibrium, but to measure the relative tendency of salt anions to exchange with IL anions.

Anion exchange is increasingly efficient from right to left (Table 2): SO_4^{2-} < Cl^- < Br^- < NO_3^- < I^- < ClO_4^- < SCN^- < Tf_2N^-, which corresponds to a decrease in charge density (Figure 1). Ions with a lower charge density are less well hydrated and have a higher affinity for the IL phase. The efficiency of anion exchange is also dependent on the IL anion (in the opposite direction). ILs containing Tf_2N^- anions are very difficult to exchange, while chloride ILs are very easy to exchange (Table 2). This is summarized in a graphical overview (Figure 2). The anions considered in this work are derived
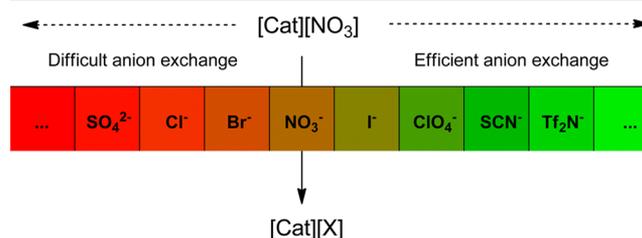
Figure 2. Prediction tool for the occurrence of anion exchange when a hydrophobic IL is contacted with a salt-containing water phase. The tendency of an IL $[Cat][X_A]$ toward anion exchange with a salt MX_B is shown. For example for an IL $[Cat][NO_3]$, the exchange will be efficient with the anions to the right, and difficult with the anions to the left of the position of NO_3^- in the series. This should be considered when designing IL synthesis routes and extraction systems.

from strong acids and are therefore fully deprotonated at neutral pH. Note, however, that for anions derived from weak acids, their speciation will be pH dependent. This has to be taken into account as it will also influence their tendency for anion exchange.

This scheme can be used as a prediction tool for anion exchange, which is relevant both for the synthesis of ILs and the design of stable IL/water extraction systems. It is, for instance, possible to synthesize $[P_{66614}][Tf_2N]$ in one step starting from $[P_{66614}][Cl]$ and contacting it with an aqueous LiTf$_2$N solution. The anion exchange reaction is fast and complete. On the other hand, the synthesis of $[P_{66614}][NO_3]$ starting from $[P_{66614}][Cl]$ requires three steps to obtain more than 99.9% purity.[73] For extraction experiments, this is also important when a different anion is present in the water phase and the organic or IL phase.[59,61,62,81,82] For example, Vander Hoogerstraete et al. and Onghena et al. have reported on metal extraction systems from chloride aqueous solutions using the IL [Hbet][Tf$_2$N].[60−62] No chloride ions were detected in the IL since the exchange of Tf_2N^- by Cl^- ions does not occur (Table 2).[59] However, other extraction systems such as the extraction of metal ions from an aqueous phase with $[P_{66614}][Cl]$ must be done from chloride

solutions to avoid contamination of the IL.[78] Many more examples could be cited, but the conclusion is that due to the endless variety of ILs it is most important to understand the trends in anion exchange (Figure 2), so that an appropriate and stable extraction system can be designed for any given IL. Cation exchange is not observed since small inorganic cations do not form ILs and are always more hydrophilic than the bulky organic IL cations.

2. Water-Miscibility of Ionic Liquids: Structure Dependence.

An important parameter in solvent extraction is the solubility of the organic phase in the aqueous phase. This can cause pollution of the water and loss of (valuable) organic solvent. In the case of IL/water extraction systems, this is particularly important due to their high cost. Recovery of ILs from water with physical methods such as nanofiltration or electrodialysis is still relatively cumbersome.[83−86] Therefore, it is more practical to limit the loss of IL to the aqueous phase in the first place by altering the structure of the IL or by the addition of metal salts to the aqueous phase.[69] The inherent solubility of the IL in the aqueous phase can vary a lot depending on the IL structure and the polarity of its anions and cations.[87] The long-chain tetraalkylphosphonium IL $[P_{66614}][Cl]$ for example, has a very low water solubility of 20−80 ppm (0.002−0.008 wt %), while the carboxyl-functionalized IL $[Hbet][Tf_2N]$ has a water solubility of 14 wt %.[59,80] A straightforward way to alter the water-miscibility of a certain IL, is by changing the IL cation or IL anion. The effect of the anion (X) on the water solubility is shown for the IL $[P_{8444}][X]$ (Table 3) and the effect of cation (Cat) is shown for the IL $[Cat][Tf_2N]$ (Table 4). The trends can be of interest when choosing an IL for solvent extraction.

Table 3. Solubility of the IL $[P_{8444}][X]$ in the Water Phase at 25 °C, for Increasingly Hydrophobic Anions X. A 1:1 Ratio (w/w) of IL/Water Was Used

	ionic liquid content in the water phase (wt %)[a]
$[P_{8444}][Cl]$	Homogeneous system
$[P_{8444}][Br]$	2.14
$[P_{8444}][NO_3]$	0.91
$[P_{8444}][ClO_4]$	0.04
$[P_{8444}][Tf_2N]$	<DL[b]

[a]All IL/water systems were biphasic, except for $[P_{8444}][Cl]$. $[P_{8444}][Br]$ has thermomorphic behavior with a LCST (24 °C) but is biphasic at 25 °C.[88] [b]Below detection limit using quantitative ^{1}H NMR.

Table 4. Solubility (25 °C) of the ILs $[Cat][Tf_2N]$ in the Water Phase for Increasingly Hydrophobic Cations (Cat) and 1:1 IL/Water Ratio (wt/wt)

	ionic liquid content in the water phase (wt %)[a]
$[Hbet][Tf_2N]$	14.0
$[Chol][Tf_2N]$	10.7
$[N_{4111}][Tf_2N]$	1.1
$[S_{222}][Tf_2N]$	0.81
$[emim][Tf_2N]$	0.72
$[mppip][Tf_2N]$	0.14
$[N_{8881}][Tf_2N]$	< DL[b]
$[P_{66614}][Tf_2N]$	< DL[b] (literature value: 0.002−0.008 wt %)[80]

[a]All IL/water systems were biphasic at 25 °C. [b]Below detection limit using quantitative ^{1}H NMR.

For the IL anions (Table 3), the hydrophobicity of the ILs follows the charge density series (Figure 1). Anions can alter the hydrophobicity of the IL very much: $[P_{8444}][Cl]$ is water-soluble, while $[P_{8444}][Br]$ forms a biphasic system with only around 2 wt % of IL in the aqueous phase. These large differences can be used to change the properties of known ILs by simply exchanging the IL anion (Figure 2). For cations, the differences are smaller between structurally similar aliphatic cations. However, when functional groups are incorporated in the cation (e.g., $[Hbet]^+$ or $[Chol]^+$), significantly higher solubilities are observed due to the formation of hydrogen bonds (Table 4). Water can also dissolve in the IL phase, but this is not problematic since it does not pollute the system nor cause loss of valuable reagents. Note, however, that for very hydrophobic ILs such as $[C_8mim][Tf_2N]$ or $[P_{66614}][Tf_2N]$, the solubility of water in the IL is significant, while the solubility of IL in the aqueous phase is almost negligible.[67,80]

3. Effect of Metal Salts on the Mutual Solubility if Biphasic IL/Water Systems.

Instead of changing the structure of the IL to influence its water solubility, it is also possible to add metal salts to the aqueous phase. Salts can influence the solubility ILs in the aqueous phase and improve the process design and recovery of IL in solvent extraction processes.[69] It is therefore important to understand the effect that the presence of metal salts in aqueous phase can have on the solubility of ILs. The effect of metal salts has been studied for some specific ILs such as $[C_4mim][CF_3SO_3]$ and $[C_4mim][Tf_2N]$, but there is no general prediction model.[47,50−54,67,68] An intuitive model is therefore proposed here to rationalize the effect of metal salts on the solubility of any hydrophobic IL. In the liquid-precipitate model (Figure 3),
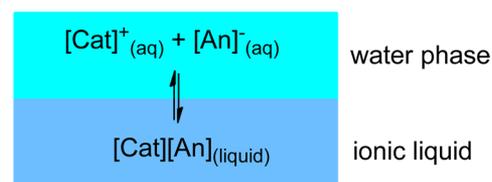
Figure 3. Schematic overview of the liquid-precipitate model described in this work. The model is based on the assumption that when a hydrophobic IL is contacted with water it behaves like a liquid-precipitate that is in equilibrium with an amount of dissolved IL in the water phase, just like salt precipitates.

biphasic IL/water systems are thought of as liquid organic salts (the IL) precipitating out of solution, while maintaining a certain equilibrium concentration in the aqueous phase, similar to the behavior of solid salt precipitates. Note that nano-aggregates of IL can exist in the aqueous phase, but this does not change the conclusions derived from this model.

As a consequence, the solubility of the hydrophobic IL is governed by the ability of the aqueous phase to solvate the IL cations and anions and counter the electrostatic attraction between the IL cations and anions. More polar IL anions and cations result in a better solvation by water molecules and therefore a higher water solubility. In the presence of salts, charge-neutralizing ion pairs can be formed between the IL ions and salt counterions.[31] Salts ions that are more effective at neutralizing the IL ion charge than water molecules, decrease the IL solubility (salting-out). Salt ions that are less effective at neutralizing the IL ions charge than water molecules, increase the IL solubility (salting-in). Therefore, the effect of salts on the

solubility of ILs follows the charge-density series (Figure 1) because a higher charge density results in stronger charge-neutralizing ion pairs.[31] This salting-out series based on the charge density (Figure 1) is valid for every IL regardless of its structure, but its best visible for hydrophobic ILs with a large water solubility (e.g., [Chol][Tf$_2$N] and [Hbet][Tf$_2$N]). The ILs were contacted with water to form biphasic systems and a range of inorganic salts was then added to the water to reveal the effect of salt cations (Figure 4) and anions (Figure 5) on

on the IL solubility, by increasing the salting-in or salting-out effects compared to pure water. This concentration effect was observed for all investigated ILs but is shown here for [Hbet][Tf$_2$N] (Figure 6 and 7). The reason that some data
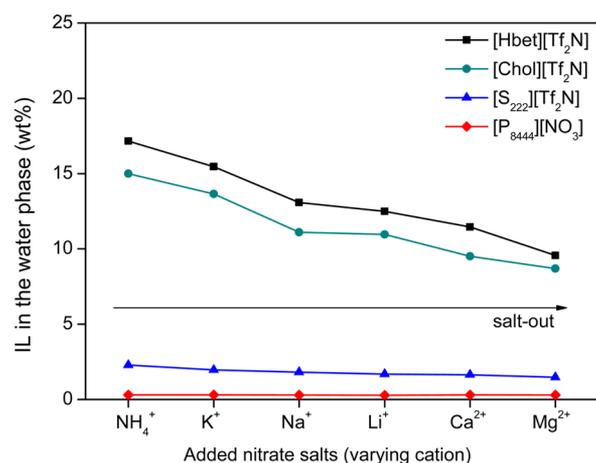
Figure 4. Influence of salt cations (added as nitrate salts, 0.5 mol.kg^{-1}) on the solubility of different ILs in the water phase (1:1 wt/wt ratio of IL/H$_2$O).
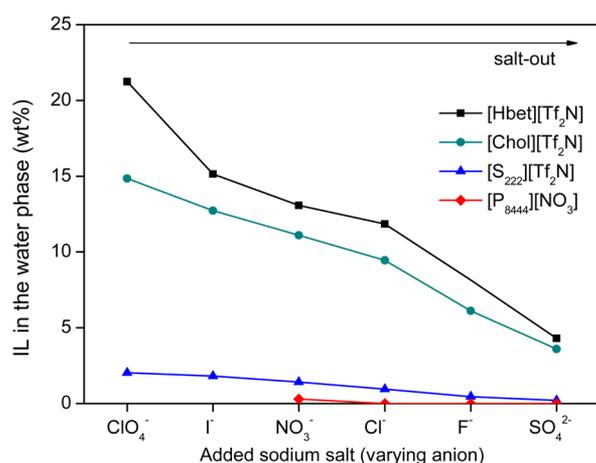
Figure 5. Influence of salt anions (added as sodium salts, 0.5 mol.kg^{-1}) on the solubility of different ILs in the water phase (1:1 ratio wt/wt of IL/H$_2$O). For [P$_{8444}$][NO$_3$], the anions I$^-$ and ClO$_4^-$ could not be tested due to anion exchange.

the solubility of these different ILs. The IL content in the water phase was determined by quantitative ^{1}H NMR. The results are in agreement with previously published results for ILs such as [C$_4$mim][CF$_3$SO$_3$] and [C$_4$mim][Tf$_2$N].[47,51] Note that this salting-out series for ILs (Figure 1) is different from the behavior of proteins, colloidal surfaces and polymers, where the effect of salts on the solubility is determined by the ability of adsorbed ions to increase the surface charge and improve the solubility by countering the van der Waals interactions.[5−8]

The influence of the salt concentration on the salting-in and salting-out effect was also investigated. A higher salt concentration simply reinforces the above-mentioned effects

Figure 6. [Hbet][Tf$_2$N] content (wt %) in the water phase when adding different chloride salts and concentrations. A 1:1 wt/wt ratio of IL/H$_2$O was used.
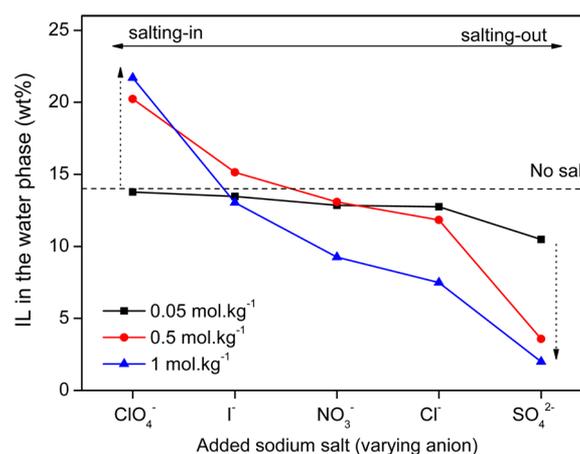
Figure 7. [Hbet][Tf$_2$N] content (wt %) in the water phase when adding different sodium salts and concentrations. A 1:1 wt/wt ratio of IL/H$_2$O was used.

points seem illogical is that the effect of the counterion has to be taken into account. For example for NH$_4^+$ ions (Figure 6), the salting-in effect does increase with the concentration at first, but the increasing Cl$^-$ concentration counters this effects at high salt concentrations, due to its salting-out effect (Figure 5). The dominant salting-out effect of salts at high concentrations is a direct consequence of the above-mentioned model. At high salt concentrations the charge neutralizing effect of the salt ions on the IL ions will become more predominant, even for the ions with low charge densities, resulting in a lower IL solubility. This predominant salting-out effect at high salt concentrations was previously also observed by Freire et al.[51] Strong salting-out agents have been used previously to successfully recover spent IL from aqueous waste streams.[69,89] For example, [Hbet][Tf$_2$N] can be recovered efficiently by addition of Na$_2$SO$_4$ to the IL-containing aqueous phase. A concentration of 3 M Na$_2$SO$_4$ can reduce the [Hbet][Tf$_2$N] content in the

aqeuous phase to less than 0.15 wt %, compared to 14 wt % without salts.[59,89]

4. Effect of Mineral Acids on the Mutual Solubility of Biphasic IL/Water Systems. Extraction systems with acidic extractants require acids to strip the extracted metals. For ILs this is the case when the extracting IL is functionalized with an acidic group such as the carboxyl-functionalized $[Hbet][Tf_2N]$ or when the IL is used as a diluent for an acidic extractant such as the $[Chol][Tf_2N]/[Chol][hfac]$ extraction system (Figure 8).[59-62] In both cases, stripping with acids is required to

Figure 8. Structure of choline bis(trifluoromethylsulfonyl)imide $[Chol][Tf_2N]$ (left) and betainium bis(trifluoromethylsulfonyl)imide $[Hbet][Tf_2N]$ (right).

remove the metals from the IL phase after extraction.[59-62] The addition of concentrated mineral acids can significantly affect the solubility of the IL in the water phase, which can be an issue due to unwanted loss of IL.

The ILs were contacted with an aqueous phase containing different mineral acids to investigate the effect on the IL solubility (Figure 9). The results are compared with the effect
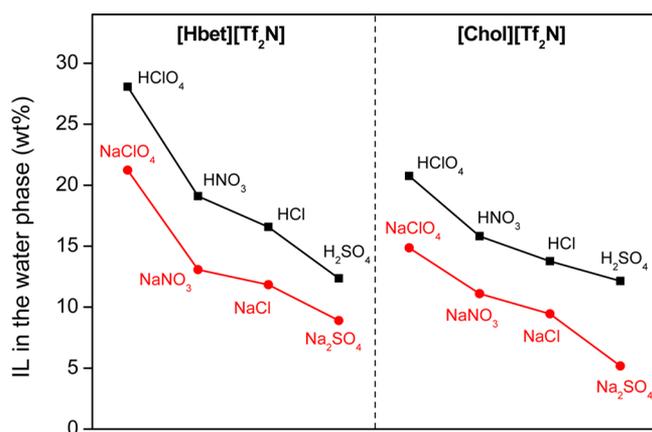
Figure 9. IL solubility (wt %) in the aqueous phase (1:1 wt/wt phase ratio) when adding mineral acids (1 N) or sodium salts (1 M). Without additives, $[Hbet][Tf_2N]$ has a solubility of 14 wt %, and $[Chol][Tf_2N]$ 10.7 wt %.

of equivalent sodium salts. It is clear that mineral acids follow the same salting-out trend (H_2SO_4 > HCl > HNO_3 > $HClO_4$) as their salt analogues. However, protons appear to be stronger salting-in agents than expected based on their charge density. This anomaly has been reported previously by Freire et al. for other ILs such as $[C_4mim][Tf_2N]$ and was attributed to the basic character of the Tf_2N^- anion.[51] The fact that no significant difference was observed between the Brønsted acid functionalized $[Hbet][Tf_2N]$ and the alcohol functionalized $[Chol][Tf_2N]$ (Figure 9), supports that hypothesis. Although, the exact origin of the salting-in by acidic protons may not be fully understood yet, it is important to know that it exists because it influences the loss of IL during the stripping process.

5. Effect of Metal Salts and Mineral Acids on the Cloud Point Temperature of Thermomorphic IL/Water Systems. A lot of research has been done on the design of ILs

with thermomorphic properties.[55,68,88,90−96] Thermomorphic systems change between a homogeneous system and a biphasic system by crossing the cloud point temperature (T_{CP}). This can be useful for biphasic extraction systems since a homogeneous phase guarantees very fast extraction equilibrium by removing the phase boundary.[60−62] This is especially true for ILs due to their high viscosity and relatively slow extraction kinetics.[60−62] Two types of thermomorphic systems can be distinguished based on the shape of the phase diagram (Figure 10): systems
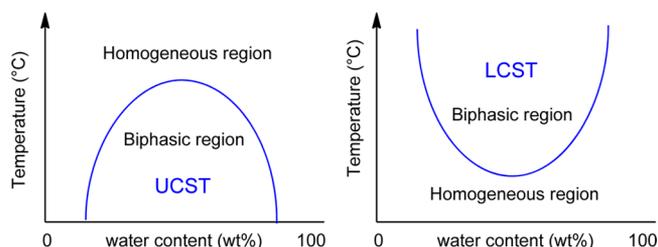
Figure 10. Schematic overview of the phase diagram of IL/water systems with a UCST and LCST.

with an upper critical solution temperature (UCST) and systems with a lower critical solution temperature (LCST). For UCST systems, the mixture is biphasic below the cloud point temperature ($T < T_{CP}$) and homogeneous above the cloud point temperature ($T > T_{CP}$), and for LCST systems the opposite is observed. The cloud point temperature and thermomorphic properties of an IL/water system can be controlled by altering the composition of the two phases (e.g., add salts) or by changing the phase ratio (Figure 10).[55]

It is well-known that for thermomorphic behavior to occur in IL/water systems, the IL must have the right balance between hydrophobic and hydrophilic character.[55,68,88,90−96] However, to the best of our knowledge, no general rules exist to predict whether the IL will have UCST or LCST behavior. Some guidelines are introduced here for the rational design of ILs with UCST or LCST behavior, based on the choice of IL anion. Thermodynamically, mixing of two components occurs when the Gibbs free energy of mixing is negative (eq 1).

$$\Delta G_{mix} = \Delta H_{mix} - T\Delta S_{mix} \tag{1}$$

For thermomorphic systems this means that UCST behavior is observed when the entropy of mixing (ΔS_{mix}) is positive and LCST behavior when ΔS_{mix} is negative. UCST behavior is more common since mixing two components is most likely to increase the entropy of the system ($\Delta S_{mix} > 0$).[68] LCST is less common than UCST but can occur when ΔS_{mix} is negative. Despite the large variety of anions and cations in ILs, some trends can be observed. Using lists of known thermomorphic IL/water systems such as the one provided by Kohno et al.,[88] we derived a general guideline for the rational design of systems with UCST or LCST behavior. It is our observation that generally ILs with weakly hydrated (low charge density) anions (e.g., Tf_2N^-, BF_4^-, I^-) show UCST behavior, while ILs with more strongly hydrated (high charge density) anions (e.g., Cl^-, Br^-, CF_3COO^-) show LCST behavior.[88] This is in agreement with the currently known thermomorphic IL/water systems.[68,88,90−95] The explanation is that ions with a higher charge density, structure a lot of water molecules around them to solvate their charge when dissolved in water. This reduces the entropy of mixing, which can become negative, resulting in LCST behavior. Low charge density ions on the other hand, do

not structure much water molecules around them which is why the entropy of mixing is generally positive (UCST behavior). Note how this is again related to the charge density (Hofmeister) series (Figure 1). A striking example is the contrast between the IL $[P_{4444}]$[maleate] (LCST) and $[P_{4444}]$[fumarate] (UCST).[91] Fumaric and maleic acid have the same molecular formula but due to their conformation, maleic acid is a hundred times more soluble in water than fumaric acid. This means the hydration of maleic acid is much stronger, which explains the LCST behavior according to the above-mentioned hypothesis. For biphasic systems consisting of ILs and apolar organic solvents, the affinity of the solvent for the IL anions is opposite to the situation for water. This results in a reversal of the above-mentioned rules, because the hydrophobic anions now have a higher affinity for the apolar solvent then hydrophilic anions. An interesting example is the fact that $[C_4mim][PF_6]$ and $[C_4mim][Tf_2N]$ have UCST behavior in polar solvents and LCST behavior in apolar solvents.[88] An overview of the above-mentioned rules for the rational design of ILs with UCST or LCST behavior is shown in Figure 11.

Figure 12. Effect of metal salts on the solubility of IL (wt %) in the water phase of the UCST system $[Hbet][Tf_2N]-H_2O$ (1:1 wt/wt) and the LCST system $[P_{444}E_3][DEHP]-H_2O$ (1:1 wt/wt). The salt concentration was 0.5 mol·kg^{-1} for the UCST system and 0.1 mol·kg^{-1} for the LCST system.

	weakly-hydrated IL anion (e.g. Tf_2N^-, PF_6^-, BF_4^-)	highly-hydrated IL anion (e.g. Cl^-, Br^-, CF_3COO^-)
polar solvent	UCST	LCST
apolar solvent	LCST	UCST

Figure 11. Prediction model for the rational design of ILs with UCST or LCST behavior. The UCST or LCST behavior of a biphasic IL/solvent system is determined by the charge density (hydration) of the IL anion (Figure 1).

It can be useful to tune the cloud point temperature of a thermomorphic IL/water system, so that the phase transition occurs at the desired temperature. The cloud point temperature is influenced by the IL/water ratio (Figure 10) and by the addition of metal salts.[55,96] The effect of metal salts on the cloud point temperature is different for UCST and LCST systems, but can be rationalized by linking it to the solubility of the IL in the aqueous phase. The addition of salting-in salts improves the mutual solubility of both phases and therefore favors the mixed (homogeneous) state. For UCST systems this means a decrease in the cloud point temperature while for LCST systems this means an increase in the cloud point temperature (Figure 10). Salting-out salts on the other hand, decrease the mutual solubility and therefore promote demixing of the phases which results in an increase of the cloud point temperature for UCST systems and a decrease for LCST systems.[55,97] This is shown here for the LCST system $[P_{444}E_3][DEHP]-H_2O$ and the UCST system $[Hbet]-[Tf_2N]-H_2O$. Both ILs are very relevant for solvent extraction.[60,98,99] These systems have a T_{CP} of 55 and 51 °C respectively, when no salts are added. This opposite effect on the cloud point temperature is clearly visible by comparing the effect of metal salts on the solubility of these two ILs in the water phase (Figure 12), with the change in cloud point temperature (Figure 13) caused by these same salts. It is evident that salt anions have a larger effect than salt cations. This is in agreement with previous observations (Figure 4 and 5) and is due to the poorer solvation of anions in water compared to cations.[100]

Finally, the impact of some mineral acids on the cloud point temperature of $[Hbet][Tf_2N]-H_2O$ is shown (Table 5). For
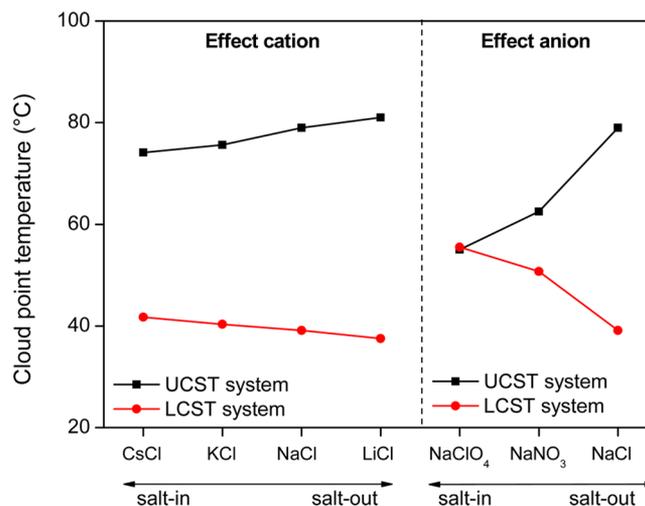
Figure 13. Effect of metal salts on the cloud point temperature of thermomorphic IL/water systems (1:1 wt/wt) with an UCST ($[Hbet][Tf_2N]-H_2O$) and an LCST ($[P_{444}E3][DEHP]-H_2O$). A salt concentration of 0.5 mol·kg^{-1} was used for the UCST system and 0.1 mol·kg^{-1} for the LCST system. Without salt, the UCST system has a cloud point of 55 °C and the LCST system of 51 °C.

Table 5. Cloud Point Temperature of a $[Hbet][Tf_2N]-H_2O$ System (1:1 wt/wt) When Adding Different Mineral Acids (1 N)

	cloud point temperature (°C)
$HClO_4$	24.2
HNO_3	49.4
No acid	55.0
HCl	67.5
H_2SO_4	66.5[a]

[a]The cloud point for H_2SO_4 (1 N) is lower than for HCl (1 N) because the concentration of sulfate ions is only half that of chloride ions.

acidic extractants such as $[Hbet][Tf_2N]$, acids are required to strip extracted metal ions back to the water phase. It is therefore useful to understand the impact of acids on the cloud

point temperature of the system. The trend in TCP is in agreement with the effect of the various acids on the solubility of IL in the water phase (Figure 9).

6. Effect of Metal Salts on Water-Soluble ILs. So far we have discussed hydrophobic (water immiscible) ionic liquids that form biphasic IL/water systems. However, certain hydrophilic (water miscible) ILs can also form biphasic IL/water systems in the presence of large amounts of salt. These so-called Aqueous Biphasic Systems (ABS) are salt-induced biphasic systems that consist of two components (a hydrophilic IL and water) that are fully miscible in the absence of salts.[34−49] This field has grown very rapidly and is not discussed here in detail as it has been reviewed previously by Freire et al.[34] It is, however, interesting to note that the salting-out effect follows the same trend as the previously discussed IL/water systems and is often even more pronounced due to the large salt concentrations and high water solubility of the ILs used in ABS. We will restrict the discussion to a new carboxyl-functionalized ABS system with LCST behavior that was recently developed in our lab: $[P_{444}C_1COOH][Cl]$. This ionic liquid is very relevant due to its ability to extract metal ions. As mentioned before, carboxyl-functionalized ILs have been used successfully for metal ion extractions.[59−62] Note that the LCST behavior of this ABS system is also in agreement with our rational design model, which predicts LCST behavior for thermomorphic ILs with chloride anions. The large effect of salts on the cloud point temperature of this thermomorphic IL is shown in Figure 14.
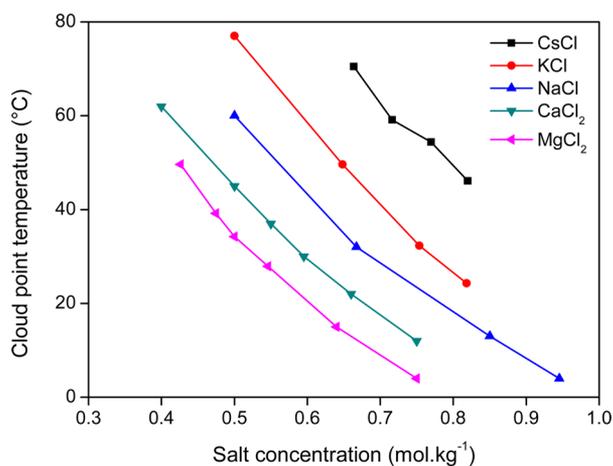
Figure 14. Effect of salt concentration on the cloud point temperature (LCST) of the aqueous biphasic system $[P_{444}C_1COOH][Cl]-H_2O$ (1:1 ratio wt/wt).

CONCLUSIONS

Biphasic IL/water systems show a lot of potential for solvent extraction. However, the presence of metal salts can affect these systems in many different ways such as (un)wanted anion exchange, changes in mutual solubility and changes in cloud point temperature in the case of thermomorphic. Due to the endless variety of ILs, it is important to find general trends instead of relying on case-by-case reports. Here, an overview is given of all the effects and intuitive guidelines and models are introduced to predict the effects of metal salts on any given IL/water system. Anion exchange was investigated and translated into guidelines for stable solvent extraction systems and synthetic strategies for ILs. The salting-in/salting-out effect of salts on the miscibility of ILs in water was also discussed and

rationalized based on the charge density series (Hofmeister series). Salting-out salts can be used to recover lost IL in the aqueous phase and thus avoid pollution of the water. The effect of metal salts on the cloud point temperature of thermomorphic systems was also investigated. Thermomorphic systems with an upper critical solution temperature (UCST) are affected differently by salts than systems with a lower critical solution temperature (LCST). Finally, new insights were introduced for the rational design of thermomorphic ILs with UCST or LCST behavior. This paper is intended as a tool for the rational design of ILs and (thermomorphic) IL/water extraction systems as well as an overview of the general rules to find the most suitable salt additives. These insights will hopefully give an additional boost to this promising field of IL solvent extraction systems.

ASSOCIATED CONTENT

Ⓢ Supporting Information

Overview of the synthesis procedures, characterization, chemicals and equipment for the synthesized ionic liquids. Chemical structures of all ionic liquids discussed in this paper. Validation of quantitative ^{1}H NMR as analytical technique. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpcb.5b02980.

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Notes
The authors declare no competing financial interest.

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