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Temperature dependency of aqueous biphasic systems: an alternative approach for exploring the differences between Coulombic-dominated salts and ionic liquids†

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Herein we propose an alternative way to distinguish ionic liquids from Coulombic-dominated salts, based not on their upper limit melting temperature (100 °C), but on the trend of their phase-forming abilities to create aqueous biphasic systems as a function of temperature, in which a wider plethora of interactions can be appraised.

Currently, the boundary between high melting temperature salts (mainly comprising high-charge density ions dominated by Coulombic interactions) and ionic liquids (ILs) is generally drawn on the basis of their melting temperatures, where ILs are defined as "salts with melting temperatures below 100 °C".[1–5] The low melting temperatures of ILs are a result of the lack of symmetry in their ions and their low-charge density, which lead to weaker Coulombic interactions and weaker cohesive energies in the solid phase when compared to conventional, *i.e.* Coulombic-dominated, salts.[1–5] Being made up of ions, electrostatic interactions play an important role in ILs; however, ILs also display a strong melting entropy resulting from hydrogen-bonding interactions. Moreover, ILs are nanostructured materials in which the non-polar moieties aggregate on non-polar domains while the charged groups and polar parts form a continuous network,[6] in contrast to the classical isotropic structure of molten inorganic salts. These features provide ILs with a dual (polar/non-polar) nature which results in specific properties and phase behaviours, and that may differ from that of a Coulombic-dominated salt and

regardless of the melting point. In this context, the common definition of ILs based on their melting temperature, although useful, may underestimate the ILs' dual nature and the complexity of interactions that these fluids can establish. The melting temperature only considers IL–IL interactions, and these can be quite different in the presence of other solutes/solvents.

Efforts have been carried out aiming at elucidating what makes an IL different from a Coulombic-dominated salt.[3,7,8] Zahn *et al.*,[3] using computational simulation studies, showed that the interaction energies in ILs result mainly from dispersion and induction forces, contrarily to Coulombic-dominated salts. Based on the dual ionic-organic nature of ILs, Shi and Wang[7] showed that the interactions observed in ILs are closer to those taking place in organic solvents than those found in inorganic salts. Watanabe and co-workers[8] revealed that the ionic nature of ILs is controlled by the magnitude of the interactive forces, including the ions' donor and acceptor abilities, and by inductive and dispersive forces. Recently, Shi and Wang[7] compared the ion/molecule cage structures obtained from molecular dynamics simulations for molten inorganic salts, ILs and organic solvents, and elucidated the dual organic-ionic nature of ILs by demonstrating that: (i) the electrostatic interactions dominate the cage energy (ionic nature) and (ii) the van der Waals interactions are attractive and with a similar strength as in organic solvents (organic nature), while in inorganic salts the electrostatic interactions dominate the cage energy (ionic nature) and the van der Waals interactions are repulsive.

Based on the variety and strength of interactions that ILs can establish with other solutes/solvents, in addition to the interactions that occur in their pure state, this work aims at proposing an alternative way to distinguish between ILs and Coulombic-dominated salts. For this purpose, the temperature-dependency of the solubility curves of aqueous biphasic systems (ABS) composed of poly(ethylene) glycol (PEG 2000 g mol^{-1}) and various quaternary ammonium chlorides was evaluated. The chemical structures of the studied compounds are depicted in Fig. 1.

The criterion behind the selection of the investigated ammonium chlorides was based both on their melting temperatures

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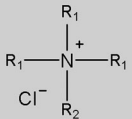
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† Electronic supplementary information (ESI) available: Experimental and computational details, experimental weight fraction data, partial molar excess enthalpies, and ^{1}H NMR chemical shift deviations. See DOI: 10.1039/c7cc02294h

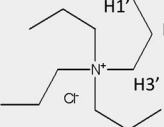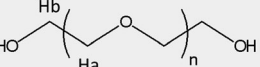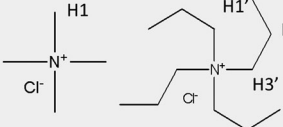| A	Acronym	R$_1$	R$_2$	T$_m$ (°C)
	[N$_{1111}$]Cl	CH$_3$	CH$_3$	339.72
	[N$_{1112(OH)}$]Cl	CH$_3$	(CH$_2$)$_2$OH	302 – 305 [a]*
	[N$_{2222}$]Cl	CH$_2$CH$_3$	CH$_2$CH$_3$	253.63
	[N$_{3333}$]Cl	(CH$_2$)$_2$CH$_3$	(CH$_2$)$_2$CH$_3$	229.92
	[N$_{4441}$]Cl	(CH$_2$)$_3$CH$_3$	CH$_3$	114.61
	[N$_{4444}$]Cl	(CH$_2$)$_3$CH$_3$	(CH$_2$)$_3$CH$_3$	71.19
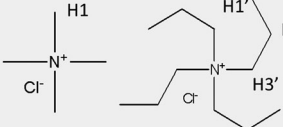
Fig. 1 Chemical structure, acronym, melting temperature (T$_m$) (A) and atom numbering (B) of the quaternary ammonium chlorides and PEG investigated. [a] Value retrieved from the MSDS provided by Sigma-Aldrich®. *Decomposition temperature.

(herein determined by differential scanning calorimetry, DSC – further details given in the ESI†) and on the ability to continuously change from compounds that are unquestionably Coulombic-dominated, high-melting temperature and high-charge density salts, such as [N$_{1111}$]Cl and [N$_{1112(OH)}$]Cl (cholinium chloride), to others that fit within the current IL definition (e.g. [N$_{4444}$]Cl), simply by increasing their alkyl side chains. The study of ternary systems, i.e. ABS, and their dependence with temperature, allows one to ascertain the main interactions that ILs or salts can establish (or not) with water (mainly hydrogen-bonding) and with a polymer (hydrogen-bonding, ion-induced dipole and dispersive-type interactions), and on their relative relevance and magnitude.

It was previously shown that the formation of ABS constituted by high-charge density salts and polymers is dominated by a salting-out phenomenon, where the phases separation is favoured by a temperature increase,[9–13] whilst the liquid–liquid demixing in some polymer–polymer ABS[14–17] follows an opposite trend with temperature. However, for ABS composed of polymers and ILs, the molecular-level mechanisms behind the two-phase formation is by far more intricate and depends on a delicate balance between polymer–IL, polymer–water, and IL–water interactions.[18–22] These differences in preferential interactions translate into different temperature dependencies of the ABS solubility curves. While for imidazolium-based ILs + PEG combinations in aqueous media the phase separation ability decreases with an increase in temperature, similar to what is observed in some polymer–polymer ABS,[18] the opposite pattern is observed in cholinium-based or protic ILs + polymers systems.[20,23] These results suggest that imidazolium-based ILs resemble polymers in their phase separation ability when combined with PEG in aqueous media, certainly a result of the dispersive-type interactions occurring between the IL and the polymer. On the other hand, cholinium-based or protic-based ILs display a behaviour similar to that of Coulombic-dominated or traditional salts, and where the salting-out of the IL over the polymer seems to be the driven force for phase separation. These previously reported results reveal that ILs and Coulombic-dominated salts present

different trends in their ABS temperature dependency, thus motivating us to carry out the present investigation.

In this work, the ternary phase diagrams of the ABS were determined by the cloud point[24,25] and the turbidimetric titration methods[19,26] at different temperatures (30, 40, 50, and 60 °C). The detailed experimental procedure and all data obtained are provided in the ESI.† Fig. 2 depicts two examples of the ABS phase diagrams at different temperatures. The binodal curves shown in Fig. 2 separate the monophasic and the biphasic regimes, where mixtures with compositions above the curve are biphasic and those below are monophasic. In general, the larger the biphasic region, the better the ABS formation ability. Remarkably, within the studied series of ammonium halides, different trends as a function of temperature are observed for Coulombic-dominated-salts and ILs, and these behaviours are not aligned with the conventional ILs definition based on their melting point. Moreover, the phase diagrams for heavier ammonium halides display a stronger dependence on temperature, an indication of stronger temperature-dependent interactions taking place in these systems.

In ABS composed of lighter ammonium halides ([N$_{1111}$]Cl, [N$_{2222}$]Cl and [N$_{1112(OH)}$]Cl) the temperature increase enlarges the immiscibility domain, similar to the polymer + salt ABS behaviour previously described in the literature.[9–13] On the other hand, in ABS formed by ammonium halides with longer alkyl side chains or of lower symmetry ([N$_{3333}$]Cl, [N$_{1444}$]Cl and [N$_{4444}$]Cl) the immiscibility region decreases with an increase in temperature, following the polymer + polymer ABS behaviour.[15–17] This resemblance of the former systems with the polymer–polymer ABS temperature dependency behaviour results from the capability of ILs to establish dispersive-type interactions, not possible to occur in high-charge density salts.

Due to its longer alkyl side chains, [N$_{4444}$]Cl has a high propensity to establish dispersive-type interactions with the polymer, and thus behaves like an IL (actually being an IL within the melting temperature definition – Fig. 1). [N$_{3333}$]Cl and [N$_{1444}$]Cl display a similar behaviour to that found with [N$_{4444}$]Cl. The temperature dependency of their ABS formation is evidence of their ability to establish dispersive-type interactions with PEG, in spite of their melting temperatures that are above 100 °C and that according to the conventional definition would prevent them of being classified as ILs. The remaining quaternary ammonium counterparts, namely [N$_{1111}$]Cl, [N$_{1112(OH)}$]Cl, and [N$_{2222}$]Cl, with shorter alkyl side chains, higher charge-density, lower ability to establish dispersive-type interactions, follow the temperature dependency trend of polymer–salt ABS,[9–13] in which they are preferentially hydrated and act as salting-out agents. In summary, all of these results suggest that there is a difference between Coulombic-dominated salts and ILs that goes beyond their melting temperature threshold of 100 °C. To further understand the nature of the molecular interactions which dominate the formation of ABS composed of ILs or Coulombic-dominated salts, ^{1}H NMR measurements were carried out for different ternary mixtures (composed of IL/salt + water + PEG).

For this purpose, two compounds with opposite behaviours, namely [N$_{1111}$]Cl and [N$_{3333}$]Cl corresponding respectively to
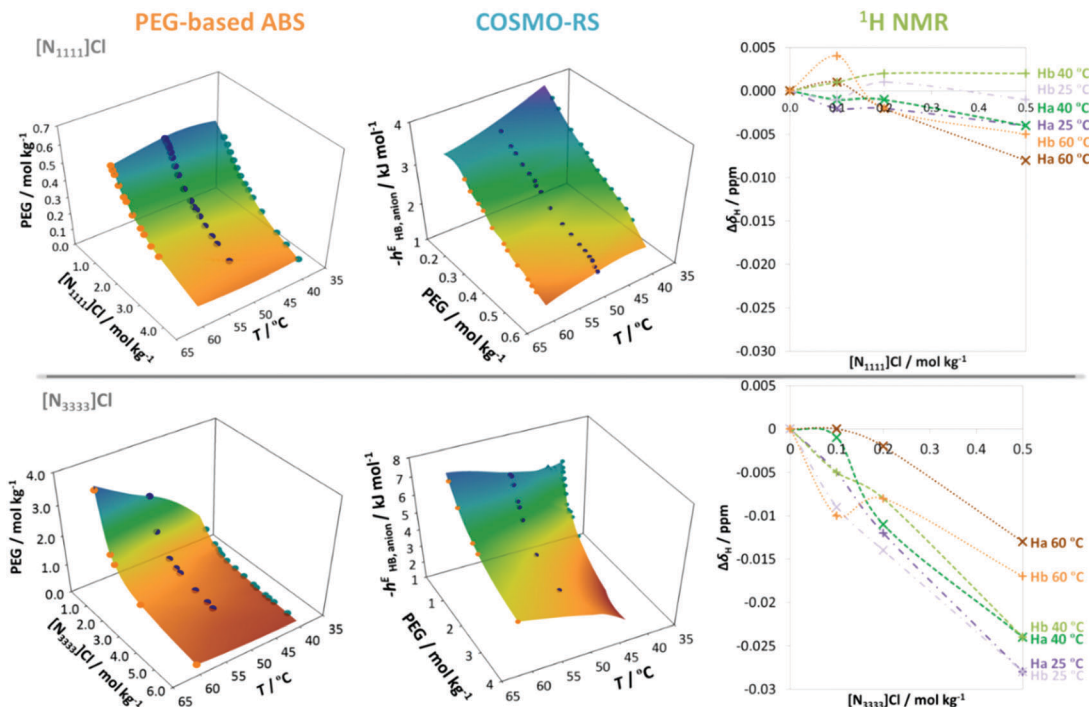
Fig. 2 Phase diagrams of the ternary systems composed of $[N_{1111}]Cl$ or $[N_{3333}]Cl$ + PEG + water at 40, 50, and 60 °C; partial molar excess enthalpies of the IL/salt anion in the ternary mixture predicted by COSMO-RS as a function of PEG molality at 40, 50, and 60 °C; and ^{1}H NMR chemical shift deviations of PEG protons relative to those of the initial PEG/water binary mixture as a function of ammonium molality at 25, 40, and 60 °C.

salt-like and IL-like behaviours, were used. Three series of experiments were conducted, each changing the concentration of one of the species while keeping the two other constant. A detailed description of the experimental approach and results is given in the ESI.† The atom numbering of each compound is described in Fig. 1.

The deviations in the chemical shifts while changing the salt/IL concentrations (Fig. 2) reveal negligible changes (within ±0.005 ppm) for the PEG methylene protons, Ha and Hb, over the entire concentration range of $[N_{1111}]Cl$, therefore supporting preferential and stronger hydrogen-bonding interactions of the salt with water and with the –OH terminal groups of the polymer. Remarkably, different trends are observed in the $[N_{3333}]Cl$ mixture, in which a larger dependence of the interactions strength between the $[N_{3333}]Cl$ and the hydrogens of the PEG aliphatic chain is observed, and where less favourable interactions are perceived with a decrease in temperature (negative deviations > −0.01 ppm). This stronger dependency on temperature also corroborates the larger dependency observed in the solubility curves with temperature for the $[N_{3333}]Cl$ system when compared with the $[N_{1111}]Cl$-based one (Fig. 2). The two other series of ^{1}H NMR assays, carried out varying the water and the PEG concentration (shown in the ESI†), reveal a similar behaviour for both $[N_{1111}]Cl$ and $[N_{3333}]Cl$, where: (i) an increase in both the PEG concentration and temperature lead to an increase of the interactions between the IL/salt aliphatic moieties and the PEG methylene protons; and (ii) an increase in the water content and a decrease in temperature result in less favourable interactions between water and the hydrogens of the aliphatic chains of

the IL or salt (following the expected decrease of hydrogen-bonding interactions by increasing temperature). Still, the ^{1}H NMR chemical shift deviations only allow one to infer dispersive-type and ion-induced dipole interactions over the PEG or salt/IL alkyl side chains, and therefore it was not possible to address the interactions taking place between the terminal –OH groups of PEG and Cl⁻ by ^{1}H NMR (these are discussed below based on a different approach). In summary, the main differences observed in the solubility curves dependency with temperature for the IL-like phase behaviour are a main result of the weaker dispersive-type interactions occurring between PEG and the IL at lower temperatures, which are favourable for the two-phase separation.

The COnductor-like Screening Model for Real Solvents (COSMO-RS)[20,27] was used to predict the partial molar excess enthalpies in the studied ternary mixtures to better understand the temperature dependency of ABS formation, and in particular to address the hydrogen-bonding interactions established between the chloride anion and the –OH terminal groups of PEG or water. The hydrogen bonding component of the estimated partial molar excess enthalpies, h_i^E, of the chloride anion, displayed in Fig. 2, shows favourable interactions between the $[N_{1111}]Cl$ or $[N_{3333}]Cl$ and the media as the concentration of PEG increases. However, $[N_{1111}]Cl$ displays the weakest interactions with the polymer in aqueous media, as reflected by the least negative h_i^E values. Conversely, $[N_{3333}]Cl$ has more negative h_i^E, revealing stronger interactions with the polymer. Since the only difference between the various systems studied are the cations, the stronger interactions in the $[N_{3333}]Cl$ system are a result of the cation

chemical structure, although weaker cation–anion interactions in longer alkyl side chain ILs cannot be discarded[28,29] since these will allow stronger interactions of the IL anion with the polymer. The excess enthalpies in the $[N_{3333}]$Cl-based ABS, and the respective interactions, increase with temperature making it less prone to phase separate as experimentally observed. A similar behaviour is observed for $[N_{1444}]$Cl – *cf.* the ESI.† On the other hand, the excess enthalpies for the $[N_{1111}]$Cl-based ABS decrease with an increase in temperature, which translates into the experimentally observed expansion of the two-phase region. The same behaviour is observed for the $[N_{2222}]$Cl and $[N_{1112(OH)}]$Cl (ESI†). In summary, the results obtained from COSMO-RS also reveal a difference in the interactions strength dependency with temperature when moving from a Coulombic-dominated salt to an IL.

All approaches used in this work (temperature dependency of ABS solubility curves, ^{1}H NMR chemical shifts deviations, and COSMO-RS calculations) reveal a shift in behaviour occurring between $[N_{2222}]$Cl and $[N_{3333}]$Cl, clearly evidencing a change from a Coulombic-dominated-salt-like to an IL-like behaviour. Although some controversy still exists on the differences between ILs and Coulombic-dominated molten salts,[30–32] the gathered results suggest that the complex nature of ILs and the richness of interactions that can occur between their ions and with other solutes/solvents should be taken into account.

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