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## Introduction

Aqueous biphasic systems (ABS) composed of ionic liquids (ILs) offer several advantages over typical polymer-based ABS,<sup>1</sup> and as such have been largely investigated for alternative liquid–liquid separation techniques. These advantages include low viscosity, high thermal stability, and a wide hydrophilic/hydrophobic range that can lead to enhanced selectivities and tailored extraction efficiencies. Moreover, these systems provide higher density differences between the coexisting phases, enabling a faster and easier phase separation than that observed in more traditional polymer-based ABS.<sup>2</sup>

Gutowski *et al.*<sup>3</sup> reported the first of the ABS composed of an hydrophilic IL – 1-butyl-3-methylimidazolium chloride,  $[C_4C_1im]Cl$  – combined with  $K_3PO_4$ , after which a large array of ILs and conventional salts have been used in order to form novel IL-based ABS.<sup>1</sup> In these studies, their ternary phase diagrams have been determined and their extraction ability for a wide variety of biomolecules appraised. Most studies have focused on imidazolium-based ILs.<sup>1</sup> However, given the large number of ILs that can be prepared and their high structural versatility, their full characterization by experimental approaches

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† Electronic supplementary information (ESI) available: IL/salt molality at saturation of each of the ABS and respective references, and detailed experimental data of determined binodal curves. See DOI: 10.1039/c8cp01401a

## Hydrogen bond basicity of ionic liquids and molar entropy of hydration of salts as major descriptors in the formation of aqueous biphasic systems<sup>†</sup>

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Aqueous biphasic systems (ABS) composed of ionic liquids (ILs) and conventional salts have been largely investigated and successfully used in separation processes, for which the determination of the corresponding ternary phase diagrams is a prerequisite. However, due the large number of ILs that can be prepared and their high structural versatility, it is impossible to experimentally cover and characterize all possible combinations of ILs and salts that may form ABS. The development of tools for the prediction and design of IL-based ABS is thus a crucial requirement. Based on a large compilation of experimental data, a correlation describing the formation of IL-based ABS is shown here, based on the hydrogen-bonding interaction energies of ILs ( $E_{HB}$ ) obtained by the COnductor-like Screening MOdel for Real Solvents (COSMO-RS) and the molar entropy of hydration of the salt ions. The ability of the proposed model to predict the formation of novel IL-based ABS is further ascertained.

is an extensive task. Therefore, tools for the *a priori* design of IL-based ABS are a crucial requirement while envisaging the development of more selective extraction processes.

From the many studies available on IL-based ABS,<sup>1,4,5</sup> a molecular-level model for their formation has been previously proposed, suggesting that it is driven by the competition between the IL and the salt ions for the formation of hydration complexes. This competition is dominated by ions that have a higher charge density and, consequently, are capable of stronger interactions with water,<sup>1,4,5</sup> corresponding thus to salt ions. ILs, with a more diffuse charge, are thus usually salted-out by highcharge density salts. Previously, Coutinho and co-workers<sup>6–8</sup> suggested the existence of a relationship between the hydrogen bond basicity ( $\beta$ ) of ILs and their ability to form ABS. However, they failed at quantitatively describing this dependence.<sup>6–8</sup>

The hydrogen bond basicity parameter, describing the ability of a given species to accept protons, is actually one of the most important descriptors of the IL solvation capability for a wide variety of compounds,<sup>9–12</sup> and great efforts have been made to establish polarity scales for ranking ILs. Furthermore, it was already shown that the polarity of ILs reflects also their own solvation in water, which is intrinsically associated with their capability to form ABS.<sup>1</sup> A polarity-scale of ILs is thus of high importance as it allows the development of a framework to, at least qualitatively, predict the solubility of a given solute in ILs and also of ILs in a set of solvents.

Several dyes have been used as solvatochromic probes to experimentally determine the polarity of several solvents,

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including ILs.<sup>13–23</sup> The multiparametric approach proposed by Kamlet-Taft<sup>24-27</sup> is able to characterize a given fluid in terms of polarity, by determining specific parameters, namely the hydrogen bond (acceptor) basicity ( $\beta$ ), the hydrogen-bond (donor) acidity ( $\alpha$ ), and the dipolarity/polarizability ( $\pi^*$ ), and is one of the best established and accepted polarity scales in the literature. Several researchers have determined these parameters in neat ILs.<sup>14-23</sup> However, the determination of the solvatochromic parameters contributing to the measurement of specific solute-solvent interactions is probe dependent, meaning that different solvatochromic probes will result in different values for the same parameter, but at least it can be used to rank ILs in terms of polarity if performed using the same probe and under the same conditions. Lungwitz et al.<sup>17-19</sup> and Welton and coworkers<sup>15,20-23</sup> are the two research groups that extensively determined solvatochromic parameters of pure ILs. For the  $\beta$ determination, Lungwitz et al.<sup>18</sup> used 3-(4-amino-3-methylphenyl)-7-phenyl-benzo-[1,2-b:4,5-b']-difuran-2,6-di-one dye (1) as a solvatochromic probe, while Welton and co-workers<sup>21-25</sup> employed the N,N-diethyl-4-nitroaniline (2) and 4-nitroaniline (3) probe pair -Fig. 1. Although the IL tendencies observed by both research groups are similar, the obtained absolute values of solvatochromic parameters are distinct. For example, for the ILs  $[C_4C_1im]$  [CH<sub>3</sub>CO<sub>2</sub>] and  $[C_4C_1im]$  [CF<sub>3</sub>SO<sub>3</sub>], the  $\beta$  values obtained are, respectively, 0.85 and 0.5718 when 3-(4-amino-3-methylphenyl)-7-phenyl-benzo-[1,2-b:4,5-b']-difuran-2,6-di-one is used, and 1.20 and 0.49<sup>20</sup> when the probe pair N,N-diethyl-4-nitroaniline/4-nitroaniline is employed. Furthermore, the Kamlet-Taft parameters are highly sensitive to impurities and water content,<sup>24-29</sup> and require the use of liquid samples. Some probes also do not allow the determination of solvatochromic parameters of aqueous solutions of ILs, for which alternative probes have been suggested.<sup>30</sup> These are significant experimental drawbacks in the determination of the IL solvatochromic parameters.

Based on the above, the development of a generalized and coherent polarity  $\beta$ -scale for ILs is thus a major challenge. Furthermore, with continuous reports on the synthesis of new ILs,



**Fig. 1** Chemical structures of the solvatochromic probes used by Lungwitz *et al.*<sup>18</sup> and Tom Welton and co-workers:<sup>20</sup> (1) 3-(4-amino-3-methylphenyl)-7-phenyl-benzo-[1,2-*b*:4,5-*b*']-difuran-2,6-di-one dye; (2) *N*,*N*-diethyl-4-nitroaniline; (3) 4-nitroaniline.

finding simple computational tools that can provide this assessment, based only on the cation and anion structures of the ILs, is of utmost importance. To overcome the drawbacks described above with experimental approaches, several attempts have been made to develop predictive methods for solvatochromic parameters.<sup>31-34</sup> Hunt et al.<sup>33</sup> used computational simulations for predicting the Kamlet-Taft parameters a and  $\beta$  in neat ILs. However, this approach has a high computational cost and requires expert knowledge, being unfeasible for a routine screening. A simpler, alternative, computational method, based on the COnductor-like Screening MOdel for Real Solvents (COSMO-RS), has been successfully applied for predicting the solvatochromic parameters of pure ILs.<sup>35,36</sup> Other authors demonstrated the ability of COSMO-RS to evaluate and correlate the polarity of ILs.<sup>37,38</sup> COSMO-RS is a computational approach well established in the literature, and commonly applied to describe the properties and phase equilibria of systems involving ILs.<sup>39-41</sup> Of particular relevance is the work of Freire and coworkers35,36 that reported the successful correlation of the experimental  $\beta$  and  $\alpha$  parameters with the IL equimolar cation-anion hydrogen-bonding interaction energies,  $E_{\rm HB}$ , the electrostatic-misfit interactions, E<sub>MF</sub>, and the van der Waals forces, E<sub>vdw</sub>, determined using COSMO-RS. The authors proposed new and extended scales of polarities based on the COSMO-RS parameters for a variety of ILs composed of a large number of anions and cations.35,36

In this work, the most extended experimental solvatochromic parameter scales available for the hydrogen-bond basicity of ILs – the Lungwitz *et al.*<sup>18</sup> and Welton and co-workers<sup>20</sup> scales – are used to correlate with the ILs' ability to form ABS. Due to the reduced amount of experimental data reported in the literature, and aiming to find a predictive model, the COSMO-RS hydrogenbonding interaction energies were then evaluated as potential substitutes for  $\beta$ , allowing the development of a model to predict the formation of IL-based ABS.

### Experimental

#### Phase diagrams

Most IL-based ABS experimental data (solubility curves of the respective ternary phase diagrams at 25 °C and atmospheric pressure) considered in this work were previously reported.<sup>2,4,6-8,42-55</sup> Nevertheless, to fill gaps in the literature data, some binodal curves were additionally determined in this work through the cloud point titration method<sup>8,50</sup> at 25 °C and atmospheric pressure. To this end, aqueous solutions of each salt and IL under study were prepared and used for the determination of the binodal curves. Repetitive dropwise addition of the aqueous salt solution to the aqueous solutions of IL was carried out until the detection of a cloudy (biphasic) solution, followed by the dropwise addition of ultrapure water until the finding of a monophasic region (clear and limpid solution). The ternary system compositions were determined by weight quantification within  $\pm 10^{-4}$  g. These novel results are shown in the ESI.† Due to the size of the database used, the values of IL molality at

saturation for each of the ABS and the respective reference are given in the ESI.†

#### COSMO-RS

The IL hydrogen-bonding interaction energies,  $E_{\rm HB}$ , were calculated using the COSMO-RS (COnductor-like Screening MOdel for Real Solvents) thermodynamic model that combines quantum chemistry, based on the dielectric continuum model known as COSMO, with statistical thermodynamic calculations. The standard process of COSMO-RS calculations employed in this work was previously described in depth by Cláudio *et al.*<sup>35</sup> and Kurnia *et al.*<sup>36</sup>

COSMO calculations are performed in an ideal conductor medium, taking into account the electrostatic screening and the back-polarization of the solutes. COSMO gives a discrete surface around each solute, characterized by its geometry and screening charge density ( $\sigma$ ) which iteratively corresponds to a minimum energetic state at the conductor. In the second step, COSMO-RS treats the surface around the solute molecule as segments, and the screening charge density of the respective segment,  $\sigma'$ , in a similar way.

One of the most significant molecular interaction energy modes in COSMO-RS is the hydrogen-bonding energy,  $E_{\text{HB}}$ , defined according to the following equation:

$$E_{\rm HB} = a_{\rm eff} c_{\rm HB} \min(0; \min(0; \sigma_{\rm donor} + \sigma_{\rm HB}) \times \max(0; \sigma_{\rm acceptor} + \sigma_{\rm HB}))$$
(1)

which is described as a function of the polarization charges of the two interacting segments ( $\sigma_{donor}$ ,  $\sigma_{acceptor}$ ), where  $a_{eff}$  is the effective contact area between two surface segments,  $c_{HB}$  is the hydrogen-bond strength and  $\sigma_{HB}$  is the threshold for hydrogenbonding.<sup>40,56</sup> The quantum chemical COSMO calculations were performed with the TURBOMOLE 6.1 program package at the density functional theory (DFT) level, applying the BP functional B88-P86 with a triple- $\zeta$  valence polarized basis set (TZVP) and the resolution of the identity standard (RI) approximation.<sup>57</sup> The COSMO*thermX* program using the parameter file BP\_TZVP\_ C20\_0111 (COSMOlogic GmbH & Co KG, Leverkusen, Germany) was used in all calculations.<sup>58</sup> The calculated  $E_{\rm HB}$  values are presented in the ESI.†

### Results and discussion

Taking into account that ABS (ILs + salts) formation results from competition from all ions for hydration, the system composition at each binodal curve where the molality of the IL equals the molality of the salt, hereafter named "saturation solubility" as proposed by Shahriari *et al.*,<sup>4</sup> was used in this work as a relative measure of the formation ability of ABS. By using all the published data<sup>2,4,6–8,42–55</sup> and the new data determined in this work, shown in the ESI,† the IL molality at saturation solubility, [IL]<sub>SS</sub>, was plotted as a function of the hydrogen bond basicity ability of pure ILs, depicted in Fig. 2. A linear correlation was found, represented by the following equation:

$$[IL]_{SS} = A \cdot \beta + B \tag{2}$$

where *A* and *B* are constants that depend on the salt used in the preparation of ABS.

Fig. 2 presents the correlations obtained for ABS composed of  $[C_4C_1im]$ -based ILs and the following salts:  $K_3PO_4$ ,  $K_3C_6H_5O_7$ ,  $K_2HPO_4$ ,  $Na_2CO_3$ ,  $Na_2SO_4$ , and  $KNaC_4H_4O_6$ . Two different correlations for each salt are obtained, which depend on the



**Fig. 2** Relationship between the molality of the IL/salt at saturation solubility ( $[IL]_{SS}$ ) and the hydrogen-bond basicity ( $\beta$ ) of [C<sub>4</sub>C<sub>1</sub>im]-based ILs determined with the solvatochromic probes: (1) by Lungwitz *et al.*<sup>18</sup> ( $\beta_{Lung}$ , blue circles) and the pair (2)/(3) by Welton and co-workers<sup>20</sup> ( $\beta_{TW}$ , green triangles) for IL-based ABS composed of: (A) K<sub>3</sub>PO<sub>4</sub>; (B) K<sub>3</sub>C<sub>6</sub>H<sub>5</sub>O<sub>7</sub>; (C) K<sub>2</sub>HPO<sub>4</sub>; (D) Na<sub>2</sub>CO<sub>3</sub>; (E) Na<sub>2</sub>SO<sub>4</sub>; (F) KNaC<sub>4</sub>H<sub>4</sub>O<sub>6</sub>.

set of  $\beta$  values used –  $\beta$  values determined with the solvatochromic probe (1) by Lungwitz *et al.*<sup>18</sup> ( $\beta_{\text{Lung}}$ ), or with the pair (2)/(3) by Welton and co-workers<sup>20</sup> ( $\beta_{\text{TW}}$ ).

As previously described, the formation of IL + salt ABS is driven by the competition between the IL and the salt ions for the formation of hydration complexes, in which the IL hydrogenbond basicity<sup>6-8</sup> and the salt's molar entropy of hydration<sup>4</sup> play a major role. In salt + IL ABS, the salt jons display a higher charge density and more easily form hydration complexes, leading therefore to the IL salting-out from the aqueous media.59 Regarding the IL, the higher the hydrogen-bond basicity, the higher the ability of the IL to accept protons and thus to interact with water, and the more difficult to induce its salting-out. It is also well-known that the hydrogen bond accepting ability of an IL is highly dependent on the anion nature of the IL.<sup>35</sup> Thus, and as shown in Fig. 2, IL anions with lower  $\beta$  values have a lower capacity to interact with water, are more prone to be salted-out by the salt ions, and thus an easier liquid-liquid demixing is achieved at lower [IL]<sub>ss</sub> values.

Independent of the set of  $\beta$  values used ( $\beta_{\text{Lung}}$  or  $\beta_{\text{TW}}$ ), correlations presenting  $R^2 > 0.70$  are obtained. It is however important to recall that both the hydrogen bond basicity and the [IL]<sub>SS</sub> were experimentally determined, taken from the literature,<sup>2,4,6-8,18,20,42-55</sup> and therefore have an experimental associated error that is further increased by the fact of using different literature sources. Although the trends found here are based on a specific IL cation, namely  $[C_4C_1\text{im}]^+$ , this is also valid for other ILs classes, since it was previously shown that the anion rank is maintained even if the cation is changed.<sup>1</sup>

Despite the correlations found between the hydrogen bond acceptor ability of the ILs and the saturation solubility in the ABS evaluated (Fig. 2), the drawbacks associated with the experimental solvatochromic parameters' determination, such as the required experimental efforts given the large number of possible ILs, their sensitivity to the impurities and color of the ILs, and the fact of it only being possible to carry out measurements in liquid samples, make the convenience of  $\beta$  values highly limited.<sup>35</sup> Furthermore, most ABS studies are focused on [C<sub>4</sub>C<sub>1</sub>im]-based ILs, and there is almost no data for other types of cations, which makes the use of experimental  $\beta$  parameters in the development of a model that can be used to predict the formation of IL-based ABS unfeasible.

It was previously shown by Cláudio *et al.*<sup>35</sup> that COSMO-RS hydrogen-bonding interaction energies,  $E_{\rm HB}$ , correlate with the  $\beta$ solvatochromic parameter. The authors demonstrated a linear correlation between both parameters, and that the estimated  $E_{\rm HB}$ could be used instead of the  $\beta$  values in the development of correlations with this property, allowing the drawbacks associated with the experimental determination of this parameter to be overcome.<sup>35</sup> As previously described by eqn (1), the  $E_{\rm HB}$  values estimated by COSMO-RS comprise the contribution of the effective contact area between two surface segments with donor and acceptor contributions, the hydrogen-bond strength, and a threshold for hydrogen-bonding, being thus representative of the hydrogen bond basicity of ILs. Katsyuba *et al.*<sup>60,61</sup> proposed a method to quantitatively estimate the hydrogen-bond energy of ILs based on quantum-chemical modelling of bulk ILs in combination with experimental structural and spectroscopic methods. Despite most of the data reported being for hydrophobic ILs, considering the structural similarity between  $[OHC_2C_1im][CH_3CO_2]$  and  $[C_2C_1im][CH_3CO_2]$ , and comparing the parameter determined by COSMO-RS with the estimated H-bond energy, the  $E_{HB}$  of  $[C_2C_1im][CH_3CO_2]$  (4.8 kcal mol<sup>-1</sup>) is similar to the value of the H-bond energy estimated for  $[OHC_2C_1im][CH_3CO_2]$  (3.8 kcal mol<sup>-1</sup>),<sup>60</sup> demonstrating that COSMO-RS provides an adequate estimation of the hydrogenbond energy of ILs. Unfortunately, the lack of sufficient data does not allow more extensive analysis.

Taking into account the importance of the parameter  $\beta$  in the description of the polarity of ILs, its relation with the ILs ability to form ABS, and the previously reported correlation,<sup>35</sup>  $E_{\text{HB}}$  (kJ mol<sup>-1</sup>) was further used to correlate the formation ability of ABS, according to eqn (3):

$$[IL]_{SS} = C \cdot E_{HB} + D \tag{3}$$

with C and D as constants that depend on the salt employed.

The set of available data for  $E_{\rm HB}$  from COSMO-RS can be as large as desired since this approach only requires computational information based on the chemical structure of ILs, without restrictions on the IL cation–anion combinations. This overcomes the drawbacks associated with the use of solvatochromic probes, not only by avoiding an extensive experimental determination of the  $\beta$  values, but also by eliminating the limitations to establish a coherent and complete polarity scale for any IL structure caused by the presence of impurities and water, or by the IL physical state. For that purpose, in Fig. 3,  $\beta$  values were replaced by the COSMO-RS  $E_{\rm HB}$  values and a very diversified set of ILs included. The ILs included in the correlations shown in Fig. 3 are described in Table 1.

When replacing  $\beta$  by  $E_{\rm HB}$  values, and by introducing different types of IL cations, such as pyridinium, tetraalkylammonium- and phosphonium-based, similar linear dependencies were observed for IL-based ABS composed of the salts K<sub>3</sub>PO<sub>4</sub>, K<sub>3</sub>C<sub>6</sub>H<sub>5</sub>O<sub>7</sub>, K<sub>2</sub>HPO<sub>4</sub>, Na<sub>2</sub>CO<sub>3</sub>, Na<sub>2</sub>SO<sub>4</sub> and KNaC<sub>4</sub>H<sub>4</sub>O<sub>6</sub>, with correlation coefficients ranging between 0.74 and 0.89 (*cf.* Fig. 3). As reported by Cláudio *et al.*,<sup>35</sup> ILs with more negative values of  $E_{\rm HB}$  present higher hydrogen bond basicities, and for these, formation of ABS is only attained at higher [IL]<sub>SS</sub>.

The ILs used in these correlations, as well as their ability to form ( $\checkmark$ ) or not ( $\varkappa$ ) ABS with each salt, are summarized in Table 1. Some ABS composed of a given IL and salt were considered as outsiders (within a 95% confidence interval) to the tendency generated with the  $E_{\rm HB}$  values. Despite some particular cases that may be related to higher experimental errors, there are two ILs, namely  $[C_4C_1pip]Cl$  and  $[C_4C_1pyr]Cl$ that, independent of the salt used, were always identified as outsiders. This suggests that the  $E_{\rm HB}$  values for these two ILs could be wrongly estimated by COSMO-RS. It is important to keep in mind that COSMO-RS is a thermodynamic model that combines quantum chemistry with statistical thermodynamic calculations, and this tool is in constant upgrade trying to enhance its ability to estimate more accurate properties of ILs.

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**Fig. 3** Relationship between the molality of the IL/salt at saturation solubility ( $[IL]_{SS}$ ) and the hydrogen-bonding interaction energy in the equimolar cation–anion mixture ( $E_{HB}$ ) of ILs, estimated by COSMO-RS, for the IL-based ABS composed of (A) K<sub>3</sub>PO<sub>4</sub>, (B) K<sub>3</sub>C<sub>6</sub>H<sub>5</sub>O<sub>7</sub>, (C) K<sub>2</sub>HPO<sub>4</sub>, (D) Na<sub>2</sub>CO<sub>3</sub>, (E) Na<sub>2</sub>SO<sub>4</sub>, and (F) KNaC<sub>4</sub>H<sub>4</sub>O<sub>6</sub>. The ILs used in each correlation (blue circles) and outsiders (orange circles) are identified in Table 1.

Table 1 ABS used to evaluate the correlation between  $[IL]_{SS}$  and  $E_{HB}$ : ( $\checkmark$ ) formation of ABS; ( $\bigstar$ ) no formation of ABS. ABS identified as outsiders are colored in grey

		SALTs					
	ILS	(A) K <sub>3</sub> PO <sub>4</sub>	(B) K <sub>3</sub> C <sub>6</sub> H <sub>5</sub> O <sub>7</sub>	(C) K <sub>2</sub> HPO <sub>4</sub>	(D) Na <sub>2</sub> CO <sub>3</sub>	(E) Na <sub>2</sub> SO <sub>4</sub>	(F) KNaC <sub>4</sub> H <sub>4</sub> O <sub>6</sub>
(1)	[C <sub>2</sub> C <sub>1</sub> im]Cl	$\checkmark$	Х	$\checkmark$	$\checkmark$	Х	Х
(2)	$[C_4C_1im][CF_3SO_3]$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
(3)	[C <sub>4</sub> C <sub>1</sub> im][SCN]	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
(4)	$[C_4C_1im][N(CN)_2]$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
(5)	[C₄C₁im]Br	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
(6)	[C <sub>4</sub> C <sub>1</sub> im]Cl	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	Х	Х
(7)	[C <sub>4</sub> C <sub>1</sub> im][DMP]	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	Х	Х
(8)	$[C_4C_1im][CH_3CO_2]$	$\checkmark$	$\checkmark$	$\checkmark$	Х	Х	Х
(9)	[C <sub>4</sub> C <sub>1</sub> py]Cl	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	Х
(10)	[C <sub>4</sub> C <sub>1</sub> pip]Cl	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
(11)	[C <sub>4</sub> C <sub>1</sub> pyr]Cl	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
(12)	[C <sub>6</sub> C₁im]Cl	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	Х	$\checkmark$
(13)	[N <sub>111(20H)</sub> ]Cl	$\checkmark$	Х	$\checkmark$	Х	Х	Х
(14)	[N <sub>4444</sub> ]Cl	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
(15)	[P <sub>4444</sub> ]Cl	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$

However, taking into account the chemical structure of these two ILs, both cyclic amines with non-aromatic rings, the determined  $E_{\rm HB}$  parameters are in good agreement with what is expected. Although some limitations have been identified, the obtained results demonstrate the potential of COSMO-RS hydrogen-bonding interaction energies,  $E_{\rm HB}$ , to predict the formation of IL + salt ABS.

After identifying the correlations between  $[IL]_{SS}$  and  $E_{HB}$ , their ability to predict the formation of ABS constituted of other ILs, which were not considered in the establishment of these correlations, was further evaluated. The obtained results are shown in Fig. 4. Experimental data used in these correlations and an example comparing the experimental binodal curves with the predicted  $[IL]_{SS}$  for some  $K_3PO_4$ -based ABS are given in

the ESI.<sup>†</sup> The respective average relative deviations (ARD) were determined through eqn (4),

$$ARD = 100 \frac{1}{NP} \sum_{k=1}^{NP} \left| \left( 1 - \frac{z_k^{\text{pred}}}{z_k^{\text{exp}}} \right) \right|$$
(4)

where NP is the number of experimental data points and  $z^{\text{pred}}$  and  $z^{\text{exp}}$  are the predited results and experimental data, respectively. ARD values between 11.21 and 24.17% were obtained, indicating that the correlations for each salt can be used to predict the formation of new ABS. Predicted results for [C<sub>4</sub>C<sub>1</sub>pyr]Cl- and [C<sub>4</sub>C<sub>1</sub>pip]Cl-based ABS were also represented in Fig. 4 (orange circles). Since they behave as outsiders in the correlation between the [IL]<sub>SS</sub> and

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**Fig. 4** Correlation between experimental (Exp.  $[IL]_{SS}$ ) and predicted (Pred.  $[IL]_{SS}$ ) values of IL/salt molality at saturation solubility in ABS composed of: (A) K<sub>3</sub>PO<sub>4</sub>, (B) K<sub>3</sub>C<sub>6</sub>H<sub>5</sub>O<sub>7</sub>, (C) K<sub>2</sub>HPO<sub>4</sub>, (D) Na<sub>2</sub>CO<sub>3</sub>, (E) Na<sub>2</sub>SO<sub>4</sub>, and (F) KNaC<sub>4</sub>H<sub>4</sub>O<sub>6</sub> (blue circles).  $[C_4C_1pyr]Cl$ - and  $[C_4C_1pip]Cl$ -based ABS (orange circles). Legend: N – number of ABS considered; ARD – average relative deviation.

 $E_{\rm HB}$  parameters (*cf.* Fig. 3), they were not considered in the ARD calculation; even so it is possible to observe quite good results for these systems in some of the salt-based ABS considered.

It was demonstrated that for a common salt and using the IL  $E_{\rm HB}$  values estimated by COSMO-RS, it is possible to predict the amount of IL/salt required to form a two-phase system, without the need for experimental data. This type of data is valuable for researchers who aim to address the possibility of using specific ABS, *i.e.* to carry out a preliminary screening, for separation purposes. The ability/non-ability of an IL to form ABS is possible to determine in a qualitative way. For a specific given salt, all ILs that present  $E_{\rm HB}$  values belonging to the range of  $E_{\rm HB}$  values of the experimental data presented in Fig. 3 will be able to induce the demixing of the phases, while those that are out of the range are expected to not induce ABS. However, the correlations proposed are salt dependent, and it is relevant to derive generic correlations that could account for both the nature of the salt and the IL.

Since each correlation presented in Fig. 3 was determined for a fixed salt, the constants *C* and *D* of eqn (3) are salt dependent. Shahriari *et al.*<sup>4</sup> demonstrated that the ability of the salt cation and the anion to induce the formation of IL-based ABS follows the Hofmeister series, and that the driving force connected to the salt corresponds to the molar entropy of hydration of the salt ions ( $\Delta_{hyd}S$ ). The  $\Delta_{hyd}S$  values for the cations and anions that make up the salts evaluated in this work are reported in Table 2. In fact, it was possible to find a linear dependence of the constants *C* and *D* determined for each salt and the salt ions' molar entropy of hydration. These correlations are described by eqn (5) and (6) below.

$$C = (2.41 \times 10^{-4} \pm 4.35 \times 10^{-5}) \cdot \Delta_{\text{hyd}} S_{\text{anion}} - 0.134 \pm 0.013$$
(5)

Table 2 Molar entropy of hydration ( $\Delta_{hyd}S$ ) for the ions that make up the salts under study  $^{62-64}$ 

	$\Delta_{\rm hyd} S \left( { m J \ K}^{-1} \ { m mol}^{-1}  ight)$
Anions	
$PO_4^{3-}$	-421
$C_6H_5O_7^{3-}$	n.a.
$HPO_4^{2-}$	-272
$\mathrm{CO_3}^{2-}$	-245
$\mathrm{SO_4}^{2-}$	-200
$C_4 H_4 O_6^{-2-}$	n.a.
Cations	
$\mathbf{K}^{+}$	-74
Na <sup>+</sup>	-111

 $R^2 = 0.94; F = 31; N = 4$ 

$$D = (8.08 \times 10^{-4} \pm 2.64 \times 10^{-5}) \cdot \Delta_{\text{hyd}} S_{\text{anion}} + (3.51 \times 10^{-3} \pm 1.18 \times 10^{-4}) \cdot \Delta_{\text{hyd}} S_{\text{cation}} + 0.346 \pm 0.017$$
$$R^2 = 1.0; F = 3584; N = 4.$$
(6)

Through eqn (5) and (6), it is possible to conclude that the parameter *C* is dominated by the molar entropy of hydration of the salt anion, while parameter *D* depends on both the salt anion and cation  $\Delta_{\text{hyd}}S$ . Unfortunately, there is no available data for the molar entropy of hydration of the citrate and tartrate anions, and thus eqn (5) and (6) were estimated only with N = 4.

Constants *C* and *D* for ABS containing the salt  $K_2CO_3$ ,<sup>65</sup> not used in the establishment of eqn (5) and (6), were here adopted to evaluate the predictive capability of these equations for the formation of IL-based ABS. By their direct application, the following values were calculated for  $K_2CO_3$ -based ABS:  $C = -0.075 \text{ mol}^2 (\text{kg kJ})^{-1}$  and  $D = 0.28 \text{ mol kg}^{-1}$ . With these



**Fig. 5** Correlation between experimental and predicted values of IL/salt molality at saturation solubility ( $[IL]_{SS}$ ) for K<sub>2</sub>CO<sub>3</sub>-based ABS. Legend: N – number of ABS considered; ARD – average relative deviation.

parameters and ILs  $E_{\rm HB}$  values, it was possible to predict the [IL]<sub>SS</sub> for ABS containing K<sub>2</sub>CO<sub>3</sub>. In Fig. 5 the values predicted by eqn (3) are represented as a function of experimental data. An ARD of 19.68% was obtained. This result demonstrates that [IL]<sub>SS</sub> values of K<sub>2</sub>CO<sub>3</sub>-based ABS can be predicted only using the ILs  $E_{\rm HB}$  parameters estimated by COSMO-RS and the molar entropy of hydration of both the cation and anion of the salt.

## Conclusions

It was demonstrated that the IL saturation solubility of ABS presents a linear dependence with the hydrogen-bond basicity of the ILs and COSMO-RS hydrogen-bonding interaction energies, allowing the ability of the ILs to form ABS with a specific salt to be predicted. The correlation constants obtained are shown to be intrinsically related to the salt ions' molar entropy of hydration, allowing a predictive model of the formation of IL-based ABS which considers both the nature of the IL and salt used to be further established. This type of correlation is particularly relevant due the large number of ILs that can be prepared, making it impossible to experimentally characterize all possible combinations of ILs and salts that may form ABS. The established predictive model is highly relevant for researchers dealing with the use of ABS composed of ILs and conventional salts applied in separation processes, for which the assessment of the formation ability of given ABS could be previously carried out.

## Conflicts of interest

There are no conflicts to declare.

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