Do ion tethered functional groups affect IL solvent properties? The case of sulfoxides and sulfones†

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The covalent incorporation of functional groups—specifically sulfoxide and sulfone—into the cation of imidazolium ionic liquids leads to significant, quantifiable changes in solvent parameters which in turn have important effects on the bulk properties of the materials.

The dictum *like dissolves like* neatly sums up the multitude of factors that account for the ability of a molecular solvent to dissolve a given substrate. In contrast, we cannot yet so concisely summarize the solvent behavior of ionic liquids. In fact, the interplay of forces contributing to the properties of ILs remains a focus of ongoing study.[1] The emergence of functionalized ILs ("task-specific" ionic liquids – TSILs) further complicates the issue, and the rapid growth of interest in them makes studies illuminating their properties especially timely.[2]

The impact of IL-bound functional groups is clear-cut in situations where a TSIL *reacts* with a substrate.[3] However, the impact of these groups on the *solvent properties* of ILs has scarcely been addressed. To our knowledge only one study has heretofore done so, a solvatochromic probe having been used to assess the impact of alcohol-groups on a single TSIL solvent parameter, polarity.[4] Here we report the first application of the solvation parameter model (*i.e.*, Abraham equation) to imidazolium TSILs using data derived from inverse gas chromatography.[5] This approach has been used previously to good effect in elucidating a *range* of solvent properties involving "conventional" ionic liquids.[5] Using as substrates a new family of TSILs, our results clearly show that cation-tethered functional groups are capable of making meaningful, quantifiable contributions not only to polarity but also H-bond basicity, H-bond acidity and dispersion forces in an imidazolium IL medium. The increased H-bonding effects *versus* conventional ILs are further validated spectroscopically. Overall these contributions result in salts with behaviors distinct from otherwise similar "conventional" ILs; one example has even proven to be a suitable medium for the first CLEC (cross-lined enzyme crystal) catalyzed reaction in an IL.[6]

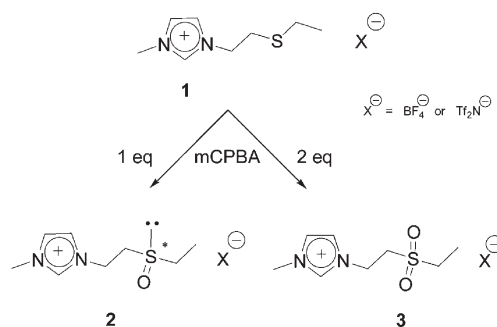Sulfoxides and sulfones—typified by dmso and sulfolane—are used in a phenomenal variety of applications and are counted among the most valuable polar aprotic molecular solvents.[7] As a consequence, we deemed it to be particularly useful to prepare and study TSILs that incorporate the two functional group types and to probe the effects of their incorporation on the resulting liquids. Beginning with the BF_4^- and Tf_2N^- salts of an imidazolium thioether cation (**1**),[8a,b] the products—**2·Tf₂N**, **2·BF₄**, **3·Tf₂N**, and **3·BF₄**—are readily isolated as pale yellow liquids after oxidation using *m*-chloroperoxybenzoic acid (Scheme 1).[8c] Each of the new TSILs is conceptually the result of the formal insertion of an SO_x fragment into the side chain of a conventional [bmim]⁺ (1-butyl-3-methyl imidazolium) cation.

Characterization data are consistent with the isolation of compounds of the proposed structures and compositions.[9]† Interestingly, salts of cations **2** and **3** are readily differentiated by means of ¹H- and ¹³C-NMR, in which the diastereotopism of the three methylene proton sets of **2** are evident.

The solvation parameter model (eqn (1)) proposed by Abraham is a linear free energy relationship that describes the liquid or gas phase interactions between solute molecules and liquid phases.[5a] In previous work structure–property relationships were developed for a series of "conventional" ionic liquids (mostly [bmim]⁺ salts) to identify the influence of the cation and anion on specific solvation interactions.[5b]

$$\log k = c + rR_2 + s\pi_2^H + a\alpha_2^H + b\beta_2^H + l \log L^{16} \quad (1)$$

By performing multiple linear regression analysis on the GC-derived data (k = chromatographic retention factor), interaction parameters—r, s, a, b, and l—can be obtained. Of these, the ability of the IL to interact with π- and n-electrons of the solute is described by r, while s is a measure of the IL dipolarity/polarizability, a defines the IL hydrogen bond basicity, b is a

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Scheme 1 Syntheses and structures of the sulfoxide and sulfone TSIL cations.

measure of the hydrogen bond acidity, and l describes dispersion forces.

As observed in our earlier study the s, a, and b terms are strongly anion (*e.g.*, BF_4^- and Tf_2N^-) influenced.[5] However, a comparison of the parameters from the same-anion salts of **2**, **3**, and [bmim]$^+$ also shows a *pronounced* cation dependence (Table 1). The variations clearly originate from the SO_x groups since there are no other differences between these ILs.

The most dramatic effect is seen in H-bond basicity, where the a values of the sulfoxide and sulfone TSILs are quite different from those of the [bmim]$^+$ salts. While earlier results[5b] indicated that imidazolium cation contributions to IL H-bond basicity are quite small, the present data indicate that in these TSILs the cations make meaningful contributions to the a term. Indeed, save for [bmim]Cl, the salts **2·Tf₂N**, **2·BF₄**, **3·Tf₂N**, and **3·BF₄** appear to have the greatest IL a values reported thus far.[5] It also bears noting that the sulfoxide TSILs are *systematically* more H-bond basic than the corresponding sulfones, a trend consistent with that observed in molecular SO_x solvents by Joesten and Drago.[10] And, while the mechanism remains to be elucidated, a synergistic effect between the anions and the functional cations appears to be operative; for example, at all temperatures the Δa values for Tf_2N^- salts of **2** and **3** versus [bmim]Tf₂N are lower than those for BF_4^- salts of **2** and **3** versus [bmim]BF₄.

Functional group based variations in these ILs extend to other measures as well. Our data indicate that sulfones repeatedly produce TSILs that have higher H-bond acidity (b-term) than do the corresponding sulfoxides or [bmim]$^+$ salts. This is consistent with a greater inductive effect on the α-hydrogens by the more electron-withdrawing SO_2 group. Their capacity to interact via π–π and n-interactions (r-term) is also marginally greater than either the sulfoxides or [bmim]$^+$ ILs. Dispersion forces (l-term) are consistently lower for all the TSILs *versus* their [bmim]$^+$ counterparts, and a significant increase in dipolar interactions (s term; "polarity") is observed for **2·BF₄**, **3·BF₄** and **3·Tf₂N**. As was the case with a values, the s values for these salts indicate them to be among the most polar ILs characterized to date.[5] The basis of the deviation of **2·Tf₂N** from the s trend is not clear; it, like the

cation–anion synergy implied by the Δa values (*vide supra*), merits additional study.

Functional group contributions to TSIL properties—specifically H-bonding—are further supported by the sulfoxide IR spectra. In the two-peak (*ca.* 3120 and 3160 cm^{-1}) imidazolium ring C–H fingerprint region, the TSILs and their [bmim]$^+$ counterparts exhibit clear differences in the relative intensities of the absorptions as well as in their absolute absorption frequencies (Fig. 1). The $\Delta(\%T)$ in **2·BF₄** for these peaks is 0.63 while being 1.36 for [bmim]BF₄. In turn, **2·Tf₂N** has a $\Delta(\%T)$ value of -0.10 *versus* 0.95 for [bmim]Tf₂N. Indeed, in each of these TSILs, the $\sim$3120 peak is relatively more intense, is shifted to lower wavenumbers and is broadened relative to that in the same-anion [bmim]$^+$ counterpart. Each of these observations is generally consistent[11a] with an increase in hydrogen bonding interactions and the first two have been shown to be *specific* indicators of the degree of H-bonding in imidazolium salts.[11b]

Unfortunately, the S–O stretch in **2·Tf₂N** and **2·BF₄** is not readily assigned due to the superimposition of S–O and B–F stretches from the respective anions. However, the BPh_4^- salt of the same cation exhibits a strong S–O stretch at 1053 cm^{-1}, four wavenumbers lower than in structurally similar diethyl sulfoxide (1058 cm^{-1}) and almost identical to that in dmso (1052 cm^{-1}). In those molecular sulfoxides the S–O stretch values are known to reflect significant H-bonding and S–O/S–O dipolar interactions in the bulk solvent.[7c,12] The similarity of the TSIL S–O values to those of the molecular sulfoxides is then strongly suggestive of functional group participation in the overall cohesive interactions within the IL, this also being fully consistent with the inverse GC data.

Overall, the forgoing data indicate that TSIL cations and anions act *in concert* to create unique sets of solvent parameters. These in turn would be expected to govern IL interactions with other materials, an expectation borne out in practice. For example, each of the TSIL BF_4^- salts are water miscible while the Tf_2N^- salts are not; the latter behavior is highly atypical of small molecules containing sulfoxide and sulfone groups.[7] Interesting biphasic behaviors are also seen with a number of organic solvents, especially aromatics and halogenated hydrocarbons. In these cases,

Table 1 A comparison of the solvent interaction parameters for conventional [bmim]$^+$ ILs[8] and those containing sulfoxide (**1**) and sulfone (**2**) functionalities

	r	s	a	b	l
[bmim]BF₄					
40 °C	0	1.647	2.219	−0.102	0.644
70 °C	0	1.456	1.967	−0.127	0.569
2·BF₄					
30 °C	0	2.23	4.13	0	0.56
70 °C	0	1.90	3.36	0	0.45
3·BF₄					
30 °C	0.22	2.43	3.79	0.50	0.56
70 °C	0.17	1.83	3.21	0.21	0.42
[bmim]Tf₂N					
40 °C	0	1.889	2.016	0.362	0.634
70 °C	0	1.671	1.752	0.378	0.557
2·Tf₂N					
30 °C	0	1.78	2.61	0.41	0.58
70 °C	0	1.49	1.95	0.36	0.45
3·Tf₂N					
30 °C	0.08	2.24	2.35	0.55	0.56
70 °C	0.10	2.01	1.93	0.49	0.44
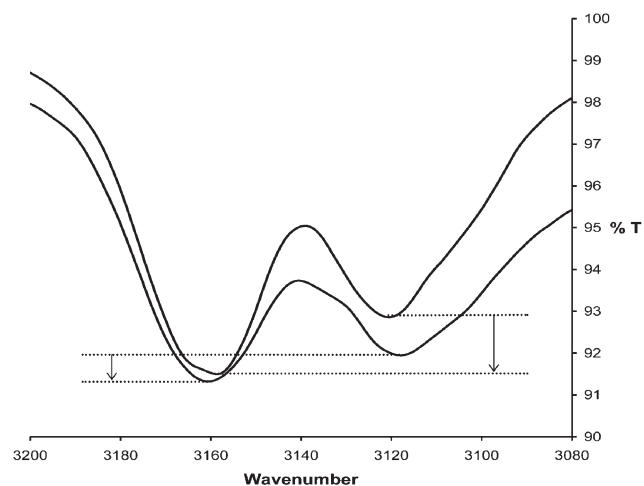
Fig. 1 Imidazolium IR C–H fingerprint region of [bmim]BF₄ (upper) *versus* **2·BF₄** (lower).

two-phase systems are formed in which the IL (dense) phase absorbs organic solvent without itself dissolving into the less dense organic phase. Such responses to aromatic solvents by "conventional" imidazolium ILs have been reported and ascribed to the formation of liquid clathrates.[13] It is also behavior that is highly evocative of the solvent swelling of polymers—analogies between polymers and ionic liquids having been previously drawn.[14] Indeed, this model has been invoked to describe the swelling of ionic liquids by sc-CO$_2$.[14c] In the present case, the interactions of [bmim]Tf$_2$N, **2·Tf$_2$N** and **3·Tf$_2$N** with benzene are illustrative. The swelling ratios Q_v for these are 2.35, 1.50 and 1.29, respectively. These numbers indicate that the IL phase is less effectively swollen by benzene as the nature of the cation side chain is varied in nature from hydrocarbon to sulfoxide to sulfone, a trend mirroring that in polymers containing comparable functionalities.

Given the differences in properties between these TSILs and more conventional ILs, we decided to screen one of the former in a process in which one widely-used conventional IL—[bmim]PF$_6$—has proven particularly useful, that being as the solvent for transesterification reactions catalyzed by the enzyme *Candida rugosa* lipase. The latter is one of several enzymes with which we have extensive experience using in conjunction with ILs.[15]

Choosing **3·Tf$_2$N** as our test bed, we evaluated the aforementioned lipase in the transesterification of methyl methacrylate with 2-ethylhexanol. Under conditions similar to those used successfully with [bmim]PF$_6$, we observed no reaction. This was also the case at higher enzyme concentrations. After a series of unsuccessful screenings† involving other enzymes, we were gratified to find that a cross-linked enzyme, Lipase PC 'CLEC', shows significant transesterification activity in **3Tf$_2$N**. In this TSIL, the Lipase PC (*Pseudomonas cepacia*) CLEC catalyzed the alcoholysis of methyl methacrylate by 2-ethylhexanol at an initial rate of 95.4 μM h^{-1} mg^{-1}. While the enzyme loses 40% of its initial activity over a 10 hour period, it is notable that it is *wholly inactive* in [bmim]PF$_6$, normally the IL of choice for biocatalysis studies.

To date TSILs have been used largely in applications in which the desired outcome depended on a reaction between the substrate and the ion-appended functional group.[2,3] However, the use of functionalized ILs in more clearly "solvent" applications[16] is of growing interest and is likely to be facilitated by a better understanding of functional group contributions to global IL solvent properties. Here, the incorporation of functionality into imidazolium IL cations—specifically the tethering of sulfone and sulfoxide groups to them—has been plainly shown to induce meaningful, quantifiable, individually distinctive changes in an array of IL solvent attributes, with attendant ramifications for utility. Further, the nature of these changes (increases in polarity, H-bonding, *etc.*) is consistent with those which would be logically expected from the addition of SO or SO$_2$ groups to an existing molecular structure, and renders them distinctive from otherwise similar conventional ILs. These results thus constitute a powerful affirmation that the solvent properties of imidazolium ILs are rightly regarded as being amenable to tuning by functional group incorporation as well as ion choice.

Notes and references

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9 By appropriate choices of synthetic approach and purification procedures, products are isolated which give negative silver ion tests for chloride as well as giving contacted aqueous solutions with chloride levels below ISE detection limits. Water contents (Karl Fischer) of 350–500 ppm may be obtained after azeotropic drying with benzene and prolonged storage under high vacuum with P$_2$O$_5$ in a vacuum dessicator. See references in 1*b* for further information on techniques for assessing IL purities.

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