

# The “non-nucleophilic” anion $[\text{Tf}_2\text{N}]^-$ competes with the nucleophilic $\text{Br}^-$ : an unexpected trapping in the dediazonation reaction in ionic liquids†

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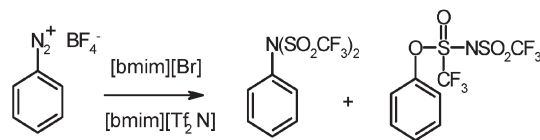
Imidazolium ionic liquids containing  $[\text{Tf}_2\text{N}]^-$  anion are not as innocent as they are often considered;  $[\text{Tf}_2\text{N}]^-$  is more reactive than  $\text{Br}^-$  in heterolytic dediazonation reactions.

Ionic liquids (ILs) resulting from the association of a large and asymmetric organic cation with weakly coordinating anions have recently gained much attention in the ongoing search for green solvents for synthesis, catalysis and separations.<sup>1</sup> In particular, the hydrophobic salts based on bis(trifluoromethanesulfonyl)amide anion ( $[\text{Tf}_2\text{N}]^-$ ) have been considered a promising alternative to the widely investigated tetrafluoroborates and hexafluorophosphates, being much more stable in the presence of water. Furthermore, they have lower melting points, lower viscosities and higher conductivities.<sup>2</sup> The positive properties of  $[\text{Tf}_2\text{N}]^-$  based ILs have stimulated our interest in using them as non-coordinating and non-nucleophilic solvents in a study which is underway on the ability of ILs to affect the reactivity of arenediazonium salts,  $\text{ArN}_2^+$ . Arenediazonium salts are versatile compounds that have found widespread use in organic synthesis.<sup>3</sup> Whereas the diazo group is maintained in coupling reactions, replacement processes (dediazonation reactions) are characterized by the loss of the group. These latter reactions may involve both heterolytic and homolytic pathways, depending on which reagents (apart from the diazonium salts) are used. Data on heterolytic fluorodediazoniation in ionic liquids have been recently reported<sup>4</sup> by Laali. Moreover, a patent<sup>5</sup> on the preparation of aryl diazonium salts and their reactions with nucleophiles in hydrophobic ionic liquids appeared this year.

With the aim of investigating ILs' solvent properties, we have performed some typical dediazonation reactions in several ILs. Much to our surprise, we found that the presumed “innocent”  $[\text{Tf}_2\text{N}]^-$  anion was able to react with benzenediazonium salt,  $\text{PhN}_2^+$  in the presence of other nucleophiles. Here, we report the first data showing that the nucleophilicity of some anions in ILs may be significantly different from that characterizing the same anions in common molecular solvents. The “innocent”  $[\text{Tf}_2\text{N}]^-$  may be more reactive than  $\text{Br}^-$  or  $\text{Cl}^-$  when associated with 1-butyl-3-methylimidazolium cation,  $[\text{bmim}]^+$ .

Benzenediazonium tetrafluoroborate,  $\text{PhN}_2^+\text{BF}_4^-$ , reacts with water in  $[\text{bmim}][\text{BF}_4]$  to give pure phenol. A first order rate

constant,  $k_1 = 8.3 (0.2) \times 10^{-5} \text{ s}^{-1}$  at 25 °C, has been evaluated for this reaction following at 260 nm the disappearance of  $\text{PhN}_2^+$ . Dissolution of  $\text{PhN}_2^+\text{BF}_4^-$  in  $[\text{bmim}][\text{Br}]$  gives instead bromobenzene as sole product arising from the formal “dissociation” of the ion pair  $\text{PhN}_2^+\text{BF}_4^-$  and subsequent nucleophile quenching by the ionic liquid counter-ion. The dissolution of the salt in the ionic medium probably leads to an immediate metathesis reaction;<sup>4</sup> diazonium cation becomes surrounded by one or more IL anions. Since the high viscosity of  $[\text{bmim}][\text{Br}]$  prevented the determination of a kinetic constant for the bromodediazoniation reaction, we tried to perform the reaction in mixtures of  $[\text{bmim}][\text{Br}]$  and  $[\text{bmim}][\text{Tf}_2\text{N}]$ . A first order rate constant,  $k_1 = 2.0 (0.2) \times 10^{-5} \text{ s}^{-1}$  at 25 °C, was evaluated for the reaction carried out in a 1 : 1 mixture  $[\text{bmim}][\text{Br}]$ – $[\text{bmim}][\text{Tf}_2\text{N}]$ . However, to our surprise when we performed some preparative experiments<sup>6</sup> to corroborate the reaction pathway, only traces of the expected bromobenzene (< 1%)<sup>7</sup> were detected in the ethereal extracts of all the examined  $[\text{bmim}][\text{Br}]$ – $[\text{bmim}][\text{Tf}_2\text{N}]$  mixtures (ranging from 1 : 2 to 3 : 1). NMR and GC-MS analysis of the reaction mixtures evidenced the formation of two products both arising from the exclusive nucleophilic trapping of the intermediate by  $[\text{Tf}_2\text{N}]^-$  anion (Scheme 1).<sup>8</sup> The same products were obtained also on dissolving  $\text{PhN}_2^+\text{BF}_4^-$  in pure  $[\text{bmim}][\text{Tf}_2\text{N}]$ . For this reaction again a first order rate constant,  $k_1 = 2.2 (0.2) \times 10^{-5} \text{ s}^{-1}$  at 25 °C, was evaluated following spectrophotometrically the disappearance of the salt at 260 nm. These observations show that imidazolium ionic liquids containing  $[\text{Tf}_2\text{N}]^-$  are not as innocent as they are often considered.



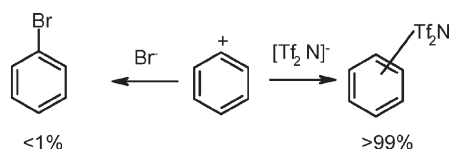
Scheme 1 Dediazonation of  $\text{PhN}_2^+\text{BF}_4^-$  in  $[\text{bmim}][\text{Br}]$ – $[\text{bmim}][\text{Tf}_2\text{N}]$ .

In contrast, hexafluorophosphate ILs are much more innocent in this process. When the reaction of  $\text{PhN}_2^+\text{BF}_4^-$  with  $[\text{bmim}][\text{Br}]$  was performed in a 1 : 1 mixture of  $[\text{bmim}][\text{Br}]$ – $[\text{bmim}][\text{PF}_6]$  only bromobenzene was obtained. The ability of  $[\text{Tf}_2\text{N}]^-$  anion to compete with nucleophilic  $\text{Br}^-$  is however strictly related to the situation characterizing these species when they are the anions of ILs used as solvents. In water, the reaction of  $\text{PhN}_2^+\text{BF}_4^-$  with  $[\text{bmim}][\text{Br}]$  and  $[\text{bmim}][\text{Tf}_2\text{N}]$  (1 : 1 mixture) gives mainly bromobenzene and phenol (*ca.* 1 : 1 ratio).<sup>9</sup>

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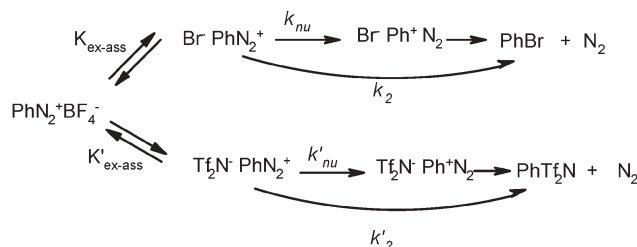
† Electronic supplementary information (ESI) available: ESI-MS spectra of pure  $[\text{bmim}][\text{Br}]$ ,  $[\text{bmim}][\text{BF}_4]$ ,  $[\text{bmim}][\text{Tf}_2\text{N}]$ ,  $[\text{emim}][\text{I}]$ ,  $[\text{emim}][\text{Tf}_2\text{N}]$  and of the 1 : 1 mixture  $[\text{emim}][\text{I}]$ – $[\text{emim}][\text{Br}]$ . See DOI: 10.1039/b514988f

To rationalize these results it is necessary to consider the mechanism of heterolytic decomposition of aryl diazonium cations. In molecular solvents, reaction is regarded to occur through an  $S_N1$  or  $S_N2$  mechanism,<sup>3</sup> although pathways at the boundary between  $S_N2Ar$  and  $S_N1$  have been invoked.<sup>10</sup> If the reaction of  $\text{PhN}_2^+\text{BF}_4^-$  occurs also in ILs through a pure  $S_N1$  mechanism (involving an aryl cation as steady-state intermediate), the observed product selectivity should suggest a surprising increase in nucleophilicity on going from  $\text{Br}^-$  to  $[\text{Tf}_2\text{N}]^-$ ,  $N_{+}(\text{Tf}_2\text{N}) > 100 N_{+}(\text{Br})$  (Scheme 2).



**Scheme 2** Nucleophilic trapping of  $\text{Ph}^+$ .

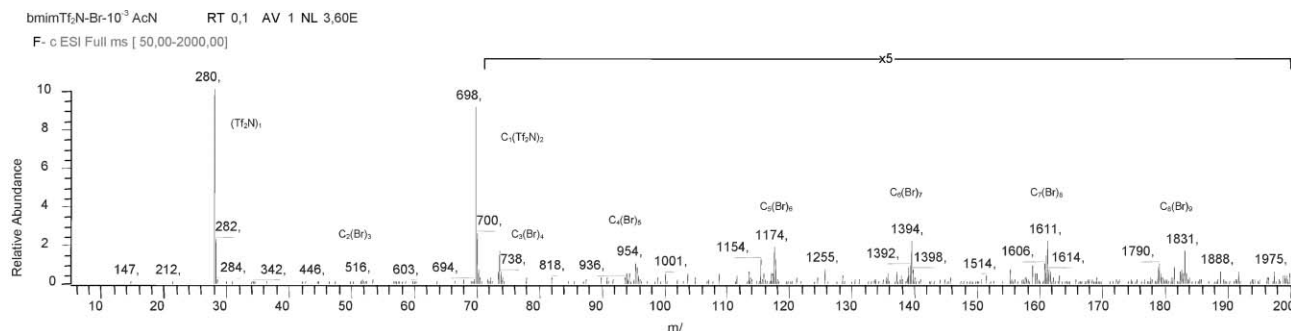
The possibility of having free cations in ILs is however quite remote. Phenyl diazonium cations are present in the ILs as ion pairs or more complex ion-aggregates. The reaction of our substrate, a positively charged species, with the anionic nucleophile may therefore be considered in terms of a multistep mechanism (Scheme 3). The first step, implying the anion exchange and the formation of a new ion pair (this step has been defined here as “exchange and preassociation”), is followed by the product formation through one or two steps depending on the more or less synchronous C–N bond cleavage and C–Nu bond formation. The different abilities of the two competing anions ( $\text{Br}^-$  and  $[\text{Tf}_2\text{N}]^-$ ) to give metathesis and to interact with  $\text{PhN}_2^+$  species,  $K'_{\text{ex-ass}} > K_{\text{ex-ass}}$ , may be chiefly responsible for the product selectivity.<sup>11</sup>



**Scheme 3** Proposed reaction pathway.

The situation of anionic nucleophiles in ILs is different from that characterizing these species in molecular solvents. In ionic liquids, each anion is part of a network of charged species and the ability of each anion to interact with substrates or intermediates is a competitive process, depending on the entity of the interaction of the anion with the ionic liquid cation(s). As previously evidenced in Diels–Alder reactions,<sup>12</sup> a strong anion–cation interaction drastically reduces the possibility for anion and cation to interact with other electrophilic or nucleophilic species. In contrast, loosely interacting anions may become more prone to react with substrates and intermediates. In other words, inside of the 1,3-dialkylimidazolium ILs the higher nucleophilicity of  $[\text{Tf}_2\text{N}]^-$  anion might be a consequence of its reduced interaction with the cations  $[\text{bmim}]^+$ . The  $\text{Br}^-$  anion is strongly associated with the ionic liquid cation through hydrogen bonding: it, therefore, is less prone to exchange with the  $[\text{BF}_4]^-$  anion, which is a weaker hydrogen bonding anion. In contrast, the  $[\text{Tf}_2\text{N}]^-$  anion replaces the  $[\text{BF}_4]^-$  and the  $[\text{BF}_4]^-$  anion associates with the ionic liquid cations. The  $[\text{Tf}_2\text{N}]^-$ , favoured by the higher  $K'_{\text{ex-ass}}$ , reacts with the carbocation being the only ion in place to do so.

In order to assess this hypothesis, electrospray ionization (ESI-MS) has been applied to measure the *intrinsic* “solvent-free” strength of the anion–cation interaction in the case of  $[\text{bmim}][\text{BF}_4]$ ,  $[\text{bmim}][\text{Tf}_2\text{N}]$  and  $[\text{bmim}][\text{Br}]$ . The extremely high difference in the relative abundance of the peaks of the two latter anions hampered the possibility of isolating the heterogeneous cluster  $([\text{Br}][\text{bmim}][\text{Tf}_2\text{N}])^-$ , thus preventing the assessment of anion–cation interaction by fragmentation of the latter.<sup>13</sup> However, an estimation of the ion pairing strength might be obtained by analysing the shape of the spectrum of both the pure ILs and the 1 : 1 mixture  $[\text{bmim}][\text{Tf}_2\text{N}]-[\text{bmim}][\text{Br}]$ . Indeed, the ESI-MS spectra (supplementary material) of pure  $[\text{bmim}][\text{Br}]$  when operating in negative ion mode are characterized by the almost exclusive presence of clusters  $[(\text{bmim})^+(\text{Br})_{n+1}]^-$ , whereas those of  $[\text{bmim}][\text{Tf}_2\text{N}]$  show the intense peak of the anion. An intermediate situation is represented by  $[\text{bmim}][\text{BF}_4]$ . In the same way, the ESI-MS spectrum of 1 : 1 mixture of  $[\text{bmim}][\text{Br}]-[\text{bmim}][\text{Tf}_2\text{N}]$  (Fig. 1) is characterized by an intense peak, due to  $[\text{Tf}_2\text{N}]^-$  anion, whereas the peak of  $\text{Br}^-$  is not visible even after scale expansion. Clearly, the anion more loosely bonded gives the main ionic fragment, whereas the stronger interacting species is preferentially present as clusters  $[(\text{Cat}^1)_{n+1}(\text{An})_n]^{+1}$  or  $[(\text{Cat}^1)_n(\text{An})_{n+1}]^{-1}$ . The shape of the ESI-mass spectra therefore evidences, without any doubt, that  $\text{Br}^-$  anion is much more strongly bound to the  $[\text{bmim}]^+$  cation than  $[\text{Tf}_2\text{N}]^-$ . This fact supports the hypothesis that the



**Fig. 1** Full ESI-MS spectrum of a 1 : 1  $[\text{bmim}][\text{Br}]-[\text{bmim}][\text{Tf}_2\text{N}]$  mixture in acetonitrile.

nucleophilicity of  $\text{Br}^-$ , but not of  $[\text{Tf}_2\text{N}]^-$ , is drastically reduced by the interaction with  $[\text{bmim}]^+$  cation.

Finally, to obtain information on the ability of other nucleophiles to compete with  $[\text{Tf}_2\text{N}]^-$ , we performed the reaction of  $\text{PhN}_2^+\text{BF}_4^-$  in 1 : 1 mixtures  $[\text{bmim}][\text{Cl}]-[\text{bmim}][\text{Tf}_2\text{N}]$  and  $[\text{emim}][\text{I}]-[\text{emim}][\text{Tf}_2\text{N}]$ . The two adducts incorporating the bis(trifluoromethanesulfonyl)amide anion were the main products of the reaction in  $[\text{bmim}][\text{Cl}]-[\text{bmim}][\text{Tf}_2\text{N}]$ , the amount of chlorobenzene being around 20%, whereas only iodobenzene was detected in the reaction carried out in the presence of  $[\text{emim}][\text{I}]$ . Iodide is therefore the sole halide able to compete significantly with  $[\text{Tf}_2\text{N}]^-$ . The behaviour of iodide is in agreement with the ESI-MS data showing a reduced ability of this anion with respect to bromide to interact with the imidazolium cation.

In conclusion, it is evident from these preliminary data that the nucleophilicity scale of common ions in ILs *towards highly reactive short lived-intermediates*, such as those characterizing the dediazonation reaction, is significantly different from those determined in molecular solvents. The reaction presently investigated may become a probe to develop nucleophilicity scales in ILs. Finally, the fact that bis(trifluoromethanesulfonyl)amide anion may compete with other nucleophiles in substitution processes may be important, because many reactions carried out in ionic liquids might be crucially influenced by the choice of IL counteranion.

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## Notes and references

- 1 *Ionic Liquids in Synthesis*, P. Wasserscheid and T. Welton (Eds), Wiley-VCH, Weinheim, 2003; *Ionic Liquids as Green Solvents: progress and prospects*, R. D. Rogers and K. R. Seddon (Eds), ACS Symposium Series, Washington, 2003; *Ionic Liquids IIIA: Fundamentals, Progress, Challenges, and Opportunities*, R. D. Rogers and K. R. Seddon (Eds), ACS Symposium Series, Washington, 2005.
- 2 C. Chiappe and D. Pieraccini, *J. Phys. Org. Chem.*, 2005, **18**, 275.
- 3 H. Zollinger, *Diazo Chemistry I: Aromatic and Heteroaromatic Compounds*; VCH: Weinheim, Germany, 1994; H. Zollinger, *The Chemistry of Triple Bonded Functional Groups*; S. Patai and Z. Rappoport (Eds), Wiley: Chichester, UK, 1983; C. Galli, *Chem. Rev.*, 1988, **88**, 765.
- 4 K. K. Laali and V. J. Gettewert, *J. Fluorine Chem.*, 2001, **107**, 31.
- 5 D. J. Moody and A. Noel, *PCT Int. Appl.* (2004). WO 2004-GB2339 20040603.
- 6 In a typical experiment  $3 \cdot 10^{-3}$  mol of  $[\text{bmim}][\text{Tf}_2\text{N}]$  or  $[\text{bmim}][\text{PF}_6]$  and the same amount of  $[\text{bmim}][\text{X}]$  ( $\text{X} = \text{Cl}, \text{Br}$ ) were mixed in a Schlenk tube under nitrogen atmosphere and gently warmed until the solubilization of the halogenide. To these mixtures  $3 \cdot 10^{-4}$  mol of diazonium salt were then added at room temperature. The mixtures were stirred for 24 hours at 298 K. The same procedure was followed also in the case of the mixture  $[\text{emim}][\text{Tf}_2\text{N}]/[\text{emim}][\text{I}]$ . The products were extracted with ethyl ether ( $4 \times 3$  ml), the organic layers were dried over  $\text{MgSO}_4$  and evaporated at reduced pressure. The residues were analyzed by NMR and GC (using a 30 m ECONOCAP EC-5 column) after resolubilization in  $\text{CH}_2\text{Cl}_2$  and addition of an appropriate amount of  $\text{PhCH}_2\text{Br}$  as internal standard. GC-MS spectra were carried out on a 30 m DB5 capillary column using an instrument equipped with an ion trap detector. Some reaction mixtures were also analyzed directly, avoiding the extraction procedure. In this case small quantities (50  $\mu\text{l}$ ) of the raw reaction mixtures were dissolved in 0.5 ml of  $\text{CH}_2\text{Cl}_2$  and immediately analysed by GC after addition of the internal standard.
- 7 Slightly higher amounts of bromobenzene (around 10%) were detected analysing directly the reaction mixture. In this case however we cannot exclude the formation of this product after the dilution with the organic solvent ( $\text{CH}_2\text{Cl}_2$ ) or inside the ionization chamber.
- 8 S.-Z. Zhu and D. D. DesMarteau, *Inorg. Chem.*, 1993, **32**, 223.
- 9 In a typical experiment  $3 \cdot 10^{-4}$  mol of diazonium salt were dissolved in 0.6 mL ( $3 \times 10^{-2}$  mol) of water containing  $3 \cdot 10^{-3}$  mol of  $[\text{bmim}][\text{Tf}_2\text{N}]$  and the same amount of  $[\text{bmim}][\text{Br}]$ . The mixture was stirred for 24 hours at 298 K then extracted with ethyl ether ( $4 \times 3$  ml). The organic phase was analyzed by GC after addition of  $\text{PhCH}_2\text{Br}$  as internal standard.
- 10 I. M. Cuccovia, M. A. da Silva, H. M. C. Ferraz, J. R. Pliego, J. M. Riveros and J. Chaimovic, *J. Chem. Soc., Perkin Trans. 2*, 2000, 1896; R. U. Bryson and D. A. Singleton, *J. Am. Chem. Soc.*, 2005, **127**, 2888.
- 11 This peculiarity of the dediazonation process might explain the fact that the unusual nucleophilicity of  $[\text{Tf}_2\text{N}]^-$  was not previously observed in other nucleophilic substitution reactions in ILs. L. Crowhurst, N. L. Lancaster, J. M. P. Arlandis and T. Welton, *J. Am. Chem. Soc.*, 2004, **126**, 11549; N. L. Lancaster, T. Welton and G. B. Young, *J. Chem. Soc., Perkin Trans. 2*, 2001, 2267; N. L. Lancaster, P. A. Salter, T. Welton and G. B. Young, *J. Org. Chem.*, 2002, **67**, 8855; N. L. Lancaster and T. Welton, *J. Org. Chem.*, 2004, **69**, 5986; C. Chiappe and D. Pieraccini, *J. Org. Chem.*, 2004, **69**, 6059; R. Bini, C. Chiappe, D. Pieraccini, P. Piccioli and C. S. Pomelli, *Tetrahedron Lett.*, 2005, **46**, 6675.
- 12 A. Aggarwal, N. L. Lancaster, A. R. Sethi and T. Welton, *Green Chem.*, 2002, **4**, 517–520.
- 13 F. G. Gozzo, L. S. Santos, R. Augusti, C. S. Consorti, J. Dupont and M. N. Eberlin, *Chem. Eur. J.*, 2004, **10**, 6187.