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# A study of halide nucleophilicity in ionic liquids

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The relative nucleophilicity of chloride, bromide and iodide anions in [bmim][$BF_4$] ionic liquid has been measured by studying their reaction with methyl *p*-nitrobenzenesulfonate ([bmim] = 1-butyl-3-methylimidazolium cation). It has been found that iodide is the most nucleophilic halide, and that chloride and bromide have approximately equal nucleophilicities ($Cl^-$ is slightly more nucleophilic than $Br^-$) in [bmim][$BF_4$]. Activation energies for the reaction of chloride and bromide with methyl *p*-nitrobenzenesulfonate have been calculated. The relative nucleophilicity of the halides has been compared with that observed in molecular solvents and in a tetraalkylammonium tetraalkylboride ionic liquid.

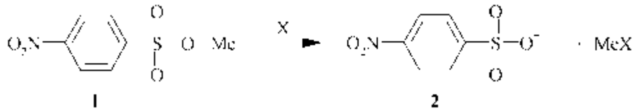
## Introduction

As concern about the environmental impact of the chemical industries has increased, the search for alternative solvents has become an important area for investigation. As part of this drive, room-temperature ionic liquids are being applied to a wide range of syntheses[1] and their usefulness in a number of reactions, both catalytic and stoichiometric, has been demonstrated. However, there is little understanding of how the ionic liquids might affect reactivity within them.

In order to achieve such an understanding it is necessary to gain quantitative comparisons of reactivities in molecular solvent systems and ionic liquid systems. To date there have been few quantitative investigations of reactions in ionic liquids[2,3] and even simple questions remain unanswered. In this paper we report a quantitative measure of anion nucleophilicity in a 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]-[$BF_4$]) ionic liquid.

Recently a study of nucleophilic substitution of chloride by cyanide in [bmim][$PF_6$] has been reported,[4] in which the effect of temperature on the rate of reaction of potassium cyanide with benzyl chloride was described. We, however, chose to study the substitution of halides for *p*-nitrobenzenesulfonate anion in methyl *p*-nitrobenzenesulfonate.

The use of methyl toluene-*p*-sulfonate and its analogues as probes of anion nucleophilicity is well established.[5] A recent study by Alluni, Pero and Reichenbach[6] made use of methyl *p*-nitrobenzenesulfonate (**1**). This was chosen because both it and the *p*-nitrobenzenesulfonate (**2**) anion product have convenient $\lambda_{max}$ values for study of this reaction by UV spectroscopy, at 253 and 275 nm respectively. The reaction is illustrated in Scheme 1.



**Scheme 1**

This reaction has been observed to be first order both in substrate concentration and in reagent concentration. However, analysis can become less straightforward in molecular solvents because the reaction can occur through either or both of the discrete anion [eqn. (1)] and the ion pair [eqn. (2)], where X is halide and M is a cation. It should be noted that both the "free" anion and the ion pair are solvated, *i.e.* coordinated by solvent molecules.

$$X^- + \mathbf{1} \longrightarrow \mathbf{2} + MeX \qquad (1)$$

$$M^{\delta+}X^{\delta-} + \mathbf{1} \longrightarrow \mathbf{2} + MeX \qquad (2)$$

In ionic liquids the anions are always coordinated by cations. Whilst this could not be properly described as an ion pair (which suggests a discrete cation and anion surrounded by molecular solvent), it is not thought likely that reaction could occur *via* the uncoordinated anion. Hence, it was anticipated that only one reaction route would be operating, particularly if the anion is added as the salt with a common cation to the ionic liquid.

## Results and discussion

A recent study by Gordon *et al.* in which ionic liquid polarities were estimated also made use of "spectroscopic grade" ionic liquids.[7] Using a similar preparative route, it was possible to prepare ionic liquids that were colourless and free-flowing, and of sufficient purity and optical clarity to allow study of substances dissolved within them by UV/vis spectroscopy. The ionic liquid used was prepared by a method that minimised the amount of residual halide.

A study of the reaction of **1** with [bmim]Cl, [bmim]Br and [emim]I ([emim] = 1-ethyl-3-methylimidazolium cation) in [bmim][$BF_4$] was conducted. The halide source used was [bmim]X (X = Cl or Br) where possible so that the same cation would be present throughout. However, [emim]I was used instead of [bmim]I as the latter compound was only obtained as a yellow–brown oil that could not be further purified. Once it had been demonstrated that a small amount of dichloromethane did not significantly affect the reaction (see below), the substrate was added as a solution in dichloromethane by microlitre syringe as attempts to prepare standard solutions of **1** in the ionic liquids had proved unsatisfactory. The reactions were initiated by adding the substrate to the UV cuvette containing a solution of the halide salt in the ionic liquid.

A run was performed in which the substrate was added (at known time), then the solution was maintained at 25 °C *in vacuo* until all of the dichloromethane had been removed. A sample was withdrawn to a UV cuvette and spectra were recorded, against a reference cell, at regular time intervals. The

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**Table 1** Observed rates of reaction of halides with methyl *p*-nitrobenzenesulfonate in [bmim][BF$_4$] ionic liquid at 25 °C

| [Halide]/M | [**1**]$_0$/mM | $10^3\ k_{obs}/s^{-1}$ | $k_2/M^{-1}\ s^{-1}$ |
|---|---|---|---|
| | 0.324 | 0.0125 (0.0003) | |
| [bmim]Cl | | | |
| 0.0318[a] | 0.289 | 1.58 (0.05) | |
| 0.0297 | 0.289 | 1.48 (0.01) | |
| 0.118 | 0.307 | 3.32 (0.15) | 0.0403 (0.0050) |
| 0.213 | 0.286 | 9.42 (0.31) | |
| 0.357 | 0.291 | 13.97 (1.08) | |
| [bmim]Br | | | |
| 0.0301 | 0.296 | 1.70 (0.03) | |
| 0.118 | 0.299 | 3.00 (0.04) | 0.0381 (0.0051) |
| 0.241 | 0.282 | 9.90 (0.24) | |
| 0.355 | 0.287 | 13.20 (0.97) | |
| [emim]I | | | |
| 0.0301 | 0.296 | 2.19 (0.04) | |
| 0.0592 | 0.287 | 3.50 (0.11) | 0.0538 (0.0019) |
| 0.0905 | 0.282 | 5.49 (0.07) | |
| 0.149 | 0.289 | 8.49 (0.14) | |

[a] Dichloromethane removed *in vacuo*. Standard deviations in parentheses.

result is shown (Table 1, entry 2). The $k_{obs}$ value recorded was similar to that expected from the same initial reagent and substrate concentrations in the ionic liquid–dichloromethane system described later. However, the fact that approximately two half-lives had passed before the first spectrum could be recorded shows this method to be inappropriate for study of this reaction.

### Analysis of results

All runs were performed using an excess of the halide. Pseudo first order rate constants ($k_{obs}/s^{-1}$) were calculated for the reaction of **1** with chloride, bromide and iodide anions in [bmim][BF$_4$]. It was found that the UV cut off point of this ionic liquid occurred at approximately 240 nm. Where chloride was the nucleophile, it was possible to record the absorbances of both the substrate (253 nm) and product (275 nm) as functions of time; an isosbestic point was observed at around 263 nm. This feature was also observed where bromide was the nucleophile, although it was only possible to measure the absorbance of the product when using this reagent. In reactions using iodide as nucleophile, it was necessary to record the absorbance at 295 nm and an isosbestic point was not observed.

The absorbances as a function of time were fitted with a first order kinetic model using the *SCIENTIST*[8] package. In the examples where chloride was the nucleophile the product and substrate were fitted simultaneously using the same estimated value of $k_{obs}$, calculated by using a least squares iterative procedure. Given that this is an example of an "A to B" reaction [eqn. (3)], this was achieved by fitting eqns. (4) and (5).

$$A \longrightarrow B \tag{3}$$

$$A = A_0 \times \exp^{-kt} + \text{const1} \tag{4}$$

$$B = B_{inf} \times (1 - \exp^{-kt}) + \text{const2} \tag{5}$$

Where $A_0$ is the initial amount of substrate and $B_{inf}$ is the final amount of product; A and B are the amounts of substrate and product respectively at given time, *t*.

The constants "const1" and "const2" are required to correct for the fact that the UV absorbance does not equal zero when the concentration of **1** or of **2** is equal to zero.

Typical sequential UV spectra for the reaction of [bmim]Cl with **1** in [bmim][BF$_4$] are shown in Fig. 1. The absorbance values of the substrate and of the product as functions of time are plotted in Fig. 2.

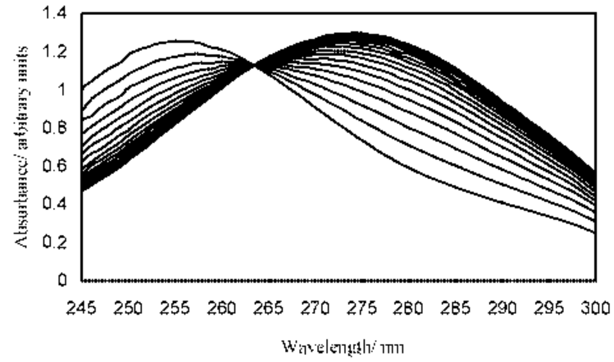

**Fig. 1** Reaction of [bmim]Cl (0.0297 mol dm$^{-3}$) with **1** in [bmim][BF$_4$] at 25 °C. The spectra were recorded at 120 s intervals.

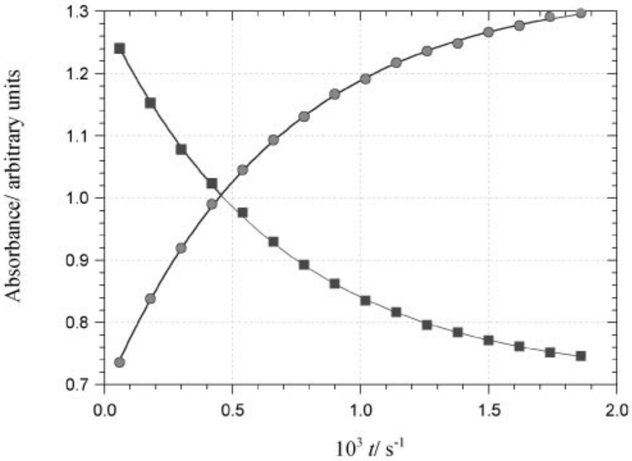

**Fig. 2** Absorbance against time in the reaction shown in Fig. 1 Squares: **1**. Circles: **2**. The curves are first order fits of eqns. (4) and (5).

### Dependence of rate upon nucleophile concentration

A run in which no halide was added showed that a slow reaction occurred in the [bmim][BF$_4$] ionic liquid, but was somewhat slower than the reactions being studied (see below), with $k_{obs}$ of *ca.* $0.013 \times 10^{-3}\ s^{-1}$. The identity of the reagent in this system is not clear, it could be residual $Cl^-$ from the preparation of the ionic liquid or possibly $F^-$ from the hydrolysis of the $[BF_4]^-$ anion.

It is known that in molecular solvents, the reaction of **1** with halides proceeds *via* an $S_N2$ mechanism and shows a first order dependence upon the concentrations of both **1** and halide. The reactions of the imidazolium halides with **1** are outlined (Table 1). That this reaction remained first order in halide concentration when performed in ionic liquids was verified by the study of [bmim]Cl in [bmim][BF$_4$]. It was found that there was a linear dependence of $k_{obs}$ on initial concentration of chloride, confirming that this reaction was first order in halide concentration when carried out in ionic liquids.

Use of [bmim]Br as the source of bromide again showed a linear dependence of $k_{obs}$ on initial concentration of nucleophile. Finally, use was made of [emim]I as the source of iodide. Iodide was a difficult anion to study because it interfered significantly with the UV spectra. It was observed that good fits of the data to the expression in eqn. (5) could be obtained (as shown by the values of standard deviation in the $k_{obs}$ values). However, comparison of the individual runs at different initial concentrations of iodide showed that although there was a linear relationship between initial concentration of nucleophile and $k_{obs}$, the value of $k_2$ could not be determined to the same precision as that for the bromide or chloride.

By evaluating the slope of the plots of $k_{obs}$ against [nucleophile]$_0$, it is possible to compare the relative rates of reaction of the halides with **1**. The values of $k_2$ recorded suggest that the

**Table 2** Arrhenius activation energies for the reaction of methyl *p*-nitrobenzenesulfonate with chloride or bromide in [bmim][$BF_4$]

| [Halide]/M | [**1**]$_0$/mM | $10^3\ k_{obs}$/s$^{-1}$ | $T$/K | $\Delta E_a$/kJ mol$^{-1}$ | ln $A$ |
|---|---|---|---|---|---|
| [bmim]Cl | | | | | |
| 0.118 | 0.307 | 3.32 (0.15) | 297.6 | | |
| 0.118 | 0.299 | 3.99 (0.07) | 301.2 | 58.2 | 17.8 |
| 0.120 | 0.303 | 6.53 (0.04) | 306.8 | (3.5) | (1.4) |
| 0.119 | 0.294 | 9.20 (0.15) | 311.5 | | |
| [bmim]Br | | | | | |
| 0.118 | 0.299 | 3.00 (0.04) | 297.6 | | |
| 0.119 | 0.294 | 3.73 (0.04) | 301.2 | 60.0 | 18.4 |
| 0.119 | 0.305 | 4.72 (0.03) | 305.8 | (8.4) | (3.3) |
| 0.120 | 0.299 | 9.69 (0.06) | 312.5 | | |

Standard deviations in parentheses.

relative reactivity is of the order chloride (1.06) : bromide (1) : iodide (1.41). It would appear that chloride and bromide are of approximately equal nucleophilicity in [bmim][$BF_4$], with iodide being the most nucleophilic of the halides in this system.

The normal order of nucleophilicities in protic solvents (*e.g.* water or methanol) is $I^- > Br^- > Cl^-$. The observed relative nucleophilicity of the halides is dependent upon a number of factors including the polarisability of the anion, and solvation of the halide[9] (including such factors as ion–dipole, dipole–dipole and H-bonding interactions). Which of these factors is most important in the observation made in this study is not clear from study of just one ionic liquid.

The only literature comparison available to halide nucleophilicity in ionic liquids shows that the relative nucleophilicities of the chloride, bromide and iodide anions is that found by Ford *et al.*[3] (2.1 : 1.2 : 1 respectively) for reactions in a trimethylhexylammonium trimethylhexylboride ionic liquid. This is not the same as the trend that was determined in [bmim][$BF_4$]. Clearly, different ionic liquids do not show the same behaviours and cannot be treated as if the same. Although it is not possible at this stage of the investigation to be certain of the reason for this difference, it is notable that 1,3-dialkylimidazolium cations form strong hydrogen bonds to halide ions,[10] whereas this interaction is not possible for simple tetraalkylammonium salts.

### Arrhenius activation energies

The reactions of [bmim]Cl and [bmim]Br with **1** were studied in [bmim][$BF_4$] over a range of temperatures (the reaction of [emim]I was not studied because of difficulties in obtaining reproducible data). The data obtained were analysed using Arrhenius plots, allowing calculation of activation energies and the results are shown (Table 2).

The Arrhenius activation energy for the reaction of chloride ion with **1** was measured to be 58.2 kJ mol$^{-1}$. This value was somewhat lower than the value of activation energy determined for reaction of the ion pair ($\Delta E_a = 83.3$ kJ mol$^{-1}$) and similar to the activation energy determined for reaction of the naked anion ($\Delta E_a = 57.4$ kJ mol$^{-1}$) with the same substrate in dichloromethane.[6] The activation energy for the reaction of [bmim]Br in [bmim][$BF_4$] was almost identical at 60.0 kJ mol$^{-1}$. Although one would expect the solvation energies of the chloride and bromide ions in [bmim][$BF_4$] to be different to each other, the Arrhenius activation energy arises from the difference between the initial and transition states. The values of the pre-exponential $A$ term found in this work are significantly lower than those found for the same reaction by the ion (ln $A = 23.4$) or ion pair (ln $A = 31.9$) in dichloromethane.[6]

## Conclusions

This work has demonstrated that it is possible to carry out kinetic measurements by using *in situ* techniques in ionic liquids. The relative reactivities of chloride, bromide and iodide ion towards methyl *p*-nitrobenzenesulfonate have been determined and show a trend different to that observed in another class of ionic liquid. Activation energies for the reaction of chloride and of bromide with the substrate have been found to be near identical to each other, and similar to the activation energy for the reaction of the free solvated ion with the same substrate in dichloromethane.

This work will be continued by the investigation of the effect of ionic liquid anion (both coordinating and non-coordinating); the effect of the imidazolium cation; and the use of neutral nucleophiles.

## Experimental

### Materials

Methyl *p*-nitrobenzenesulfonate was purchased from Fisher and used as received; 1-methylimidazole was purchased from Avocado and distilled from potassium hydroxide; iodoethane, 1-chlorobutane and 1-bromobutane were purchased from Lancaster and distilled from phosphorus pentoxide. Tetrafluoroboric acid was purchased from Lancaster and used as received.

### Spectroscopy

Proton NMR spectra were recorded on a JEOL 270 MHz spectrometer. FAB Mass spectra were recorded on a VG AutoSpec-Q mass spectrometer. UV/vis spectra were recorded using a Perkin Elmer Lambda 2 spectrophotometer with a thermostatted sample holder.

### Synthesis

The salts [bmim]Cl, [bmim]Br and [emim]I were prepared by reaction of 1-methylimidazole with the appropriate haloalkane[10] and recrystallised from acetonitrile.

**1-Butyl-3-methylimidazolium tetrafluoroborate.** In a Schlenck flask [bmim]Cl (158 g, 0.905 mol) and water (50 cm$^3$) were combined and stirred at room temperature until dissolved. Then tetrafluoroboric acid (113 cm$^3$ of 50% w/w aqueous solution, 1 equivalent) was added slowly with stirring. The mixture was stirred for 24 hours, after which the resulting [bmim][$BF_4$] was extracted with dichloromethane (4 × 50 cm$^3$). The combined dichloromethane fraction was washed with water (3 × 10 cm$^3$) until the aqueous fraction was pH neutral, and observed to be free of chloride ($AgNO_3$). The dichloromethane was removed by rotary evaporation. After isolating the crude ionic liquid, it was further purified by mixing with activated charcoal then filtered through a plug of acidic alumina into a Schlenck tube, dried by heating *in vacuo* and stored under nitrogen. The ionic liquid thus obtained (140 g, 0.620 mol, 69%) was a colourless, viscous liquid.

$\delta_H$ (ppm) (DMSO): 9.04 (1H, s, C*H*-2), 7.69 (2H, 2 s, C*H*-4,5), 4.14 (2H, t, N-C*H*$_2$), 3.83 (3H, s, N-C*H*$_3$), 1.75 (2H, t, N-CH$_2$-C*H*$_2$-), 1.25 (2H, q, N-CH$_2$-CH$_2$-C*H*$_2$), 0.88 (3H, m, N-CH$_2$-CH$_2$-CH$_2$-C*H*$_3$).

FAB+ MS: 365 ([(bmim)$_2$BF$_4$]$^+$, 1%), 139 ([bmim]$^+$, 100%). FAB− MS: 313 ([(bmim)(BF$_4$)$_2$]$^-$, 8%), 87 ([BF$_4$]$^+$, 92%), 19 (F$^-$, 100%). No peaks due to chloride containing species were observed in the mass spectra. The UV cut off point of this solvent was found to be approximately 240 nm.

### General method for studying reactions by UV spectroscopy

A solution of [bmim]Cl (0.2 mmol) in [bmim][$BF_4$] (1.5 cm$^3$, freshly outgassed *in vacuo*) was weighed into a 0.5 cm path length UV/vis quartz cuvette under anaerobic conditions. At known time, an aliquot of methyl *p*-nitrobenzenesulfonate (5 × 10$^{-7}$ mol) in dichloromethane (0.1 cm$^3$) was added and spectra were recorded at regular time intervals.

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