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Nucleophilicity in Ionic Liquids. 2.[1] Cation Effects on Halide Nucleophilicity in a Series of Bis(trifluoromethylsulfonyl)imide Ionic Liquids

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In this work, the nucleophilicities of chloride, bromide, and iodide have been determined in the ionic liquids [bmim][N(Tf)$_2$], [bm$_2$im][N(Tf)$_2$], and [bmpy][N(Tf)$_2$] (where bmim = 1-butyl-3-methylimidazolium, bm$_2$im = 1-butyl-2,3-dimethylimidazolium, bmpy = 1-butyl-1-methylpyrrolidinium, and N(Tf)$_2$ = bis(trifluoromethylsulfonyl)imide). It was found that in the [bmim]$^+$ ionic liquid, chloride was the least nucleophilic halide, but that changing the cation of the ionic liquid affected the relative nucleophilicities of the halides. The activation parameters $\Delta H^‡$, $\Delta S^‡$, and $\Delta G^‡$ have been estimated for the reaction of chloride in each ionic liquid, and compared to a similar reaction in dichloromethane, where these parameters were found for reaction by both the free ion and the ion pair.

Introduction

In the search for alternative, environmentally benign solvents, ionic liquids have become one of the key focuses.[2] They have been used as solvents for a wide range of chemical processes, both stoichiometric and catalytic. However, there has been little work directed at what effect ionic liquids might have upon solute reactivity.

It is well-known that the microenvironment generated by a solvent can change the outcome of a reaction, in terms of both equilibria and rates.[3] Since ionic liquids have the potential to provide reaction media that are quite unlike any other available at room temperature, it is possible that they will have dramatic effects on reactions in them. Indeed, there have been many claims of great improvements in reaction yields and rates when using ionic liquids.[4] To understand how such effects may arise, we have chosen to study a range of relatively simple and well-understood reactions in a variety of ionic liquids. The work described in this paper forms part of this study.

Ionic liquids are composed of anions and cations, either of which may interact with solutes and therefore affect the outcome of a reaction. In this work we have investigated the effect of altering the cation upon halide nucleophilicity. Our methodology to determine the nucleophilicity of halides in ionic liquids has been previously reported for [bmim][BF$_4$].[5] A similar substrate has also been used to determine halide nucleophilicity in a tetraalkylammonium tetraalkylboride ionic liquid.[6] The only other quantitative study of nucleophilic substitution reported in an ionic liquid is that of chloride by cyanide in [bmim][PF$_6$],[7] in which the effect of temperature on the rate of reaction of potassium cyanide with benzyl chloride was described.

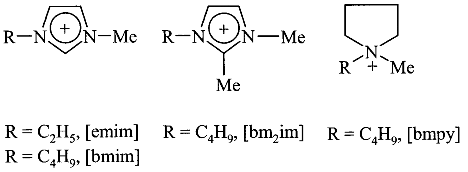

FIGURE 1. Cations from which the ionic liquids were derived.

The cations used to prepare the ionic liquids used in this study are shown, with their adopted abbreviations, in Figure 1.

The reaction chosen for study is that of methyl *p*-nitrobenzenesulfonate, **1**, with halide to give methyl halide and the *p*-nitrobenzenesulfonate anion, **2** (Scheme 1). This system was chosen because both the substrate and the anion product have convenient λ_{max} values to study this reaction by UV spectroscopy, at 253 and 275 nm, respectively. This substrate has been used in some

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[1] Part 1: see ref 5.

[2] (a) Welton, T. *Chem. Rev.* **1999**, *99*, 2071−2083. (b) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772−3789. (c) Sheldon, R. *Chem. Commun.* **2001**, 2399−2407. (d) Gordon, C. M. *Appl. Catal., A* **2001**, *222*, 101−117. (e) Olivier-Bourbigou, H.; Magna, L. *J. Mol. Catal. A* **2002**, *182*, 419−437. (f) Zhao, D.; Wu, M.; Kou, Y.; Min, E. *Catal. Today* **2002**, *74*, 157−189.

[3] Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; VCH (UK) Ltd.: Cambridge, U.K., 1998.

[4] *Ionic Liquids in Synthesis*; Wasserscheid, P., Welton, T., Eds.; VCH Wiley: Weinheim, Germany, 2002; see also references therein.

[5] Lancaster, N. L.; Welton, T.; Young, G. B. *J. Chem. Soc., Perkin Trans. 2* **2001**, 2267−2270.

[6] Ford, W. T.; Hauri, R. J.; Smith, S. G. *J. Am. Chem. Soc.* **1974**, *96*, 4316−4318.

[7] Wheeler, C.; West, K. N.; Liotta, C. L.; Eckert, C. A. *Chem. Commun.* **2001**, 887−888.

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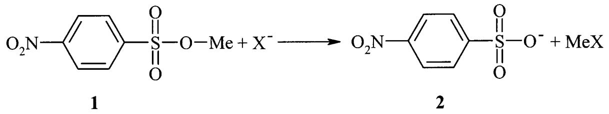
SCHEME 1



studies in molecular solvents to determine and compare the nucleophilicities of anions and neutral species within those solvents.[8-12] The use of alkyl sulfonates as probes of nucleophilicity in molecular solvents and in ionic liquids is well established.[13]

In molecular solvents, the reaction can proceed either through the discrete anion (eq 1) or through an ion pair (eq 2), where X is a halide and M is a cation.

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

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

In the ionic liquid, we would expect the anion to be coordinated by cations (which is not necessarily the same as an ion pair), and the discrete anion would not be expected to be available to react in an ionic liquid. Hence, only one reaction path is expected. To avoid the confusion that might arise if mixtures of cations were present, the halide was usually introduced as the salt of the cation under study. However, [emim]I was used to study iodide in [bmim][N(Tf)$_2$] because [bmim]I was obtained only as a yellow oil which could not be further purified.

Results and Discussion

Preliminary Findings and Methodology. The first thing to note is the UV cutoff point of the ionic liquids: Both [bmim][N(Tf)$_2$] and [bm$_2$im][N(Tf)$_2$] have a UV cutoff of approximately 240 nm, and [bmpy][N(Tf)$_2$] has a UV cutoff of 200 nm, which is to be expected as this ionic liquid's cation does not have a delocalized π-system. These values indicate that it is possible to study the chosen reaction by UV spectroscopy in ionic liquids.

To each pure ionic liquid was added an aliquot of the substrate, and spectra were recorded over 24 h. In no case was reaction of the substrate with the ionic liquid observed. This shows both the low nucleophilicity of the [N(Tf)$_2$]$^-$ ion in these ionic liquids and that any Cl$^-$ contamination that may have been left after the synthesis, as either unreacted [cation]Cl or dissolved LiCl, had been successfully removed by the purification procedure. Once the quality of the ionic liquids was established, it was possible to study the reaction of **1** with halides.

Typical UV spectra for the reaction of [bmim]Cl with **1** in [bmim][N(Tf)$_2$] are shown in Figure 2. The figure shows the λ_{max} values for **1** (at 253 nm) and for **2** (at 275 nm), as well as an isosbestic point at 263 nm. The isosbestic point shows that this reaction is an example of an "A to B" reaction, and that no other spectroscopically significant species are formed during this reaction. When the halide was bromide, the wavelength of the substrate could not be studied, though the isosbestic point was observed. When iodide was used, it was necessary to take values of absorbance from the shoulder of the product peak (ca. 300 nm); the isosbestic point was not observed.

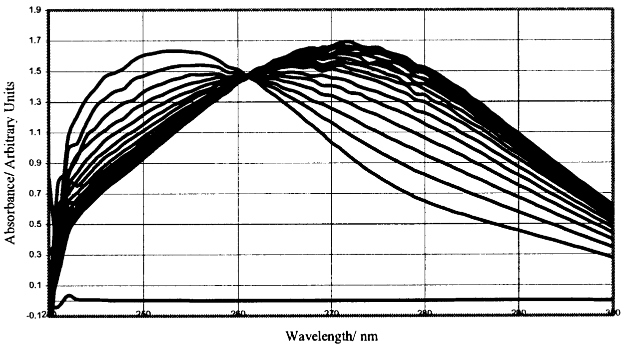


FIGURE 2. UV spectra of [bmim]Cl (0.125 M) with **1** in [bmim][N(Tf)$_2$] at 25 °C taken at 150 s intervals.

Two sets of experiments were performed in each ionic liquid. The first was to use a range of concentrations of each halide at 25 °C to determine the second-order rate constant for a given halide in a given ionic liquid at this temperature. In the second set of reactions, the concentration of chloride was kept constant while the temperature was varied, allowing determination of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$.

Determination of Halide Nucleophilicity. The observed rate constants, k_{obs}, were found in the same way as described previously,[5] by a least-squares fitting procedure. In all of the reactions shown, the standard deviation in the fit was always less than 5% of the quoted value, and was more usually between 1% and 2% of the quoted value. Values of k_2 were determined by plotting k_{obs} against [halide]$_0$ and finding the gradient. In each case the intercept was allowed to float, but was always close to zero (as expected). Comparison of these values of k_2 allows direct comparison of the relative nucleophilicities of the halides in a given ionic liquid. Note that standard deviations in the values of k_2 quoted (in parentheses) are the standard deviations in the fit of the absolute values of k_{obs} against halide concentrations.

The results for the reactions of [bmim]Cl, [bmim]Br, and [emim]I with **1** in [bmim][N(Tf)$_2$] are shown in Table 1.

In each case there was a linear (first-order) relationship between the initial concentration of halide and k_{obs}, allowing assessment of k_2 values. These data show that iodide is the most nucleophilic of the halides in the [bmim]$^+$ ionic liquid, followed by bromide, with chloride being the least nucleophilic.

The results for the reactions of [bm$_2$im]Cl, [bm$_2$im]Br, and [bm$_2$im]I with **1** in [bm$_2$im] [N(Tf)$_2$] are shown in Table 2.

As in the [bmim]$^+$ ionic liquid, a linear dependence of k_{obs} upon halide concentration was observed with each of the halides, allowing the value of k_2 to be determined. However, these k_2 values reveal that chloride is now the most nucleophilic of the halides, with iodide being slightly more nucleophilic than bromide. These results showing a change in relative k_2 values might appear surprising,

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[8] Alluni, S.; Pero, A.; Reichenbach, G. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1747–1750.

[9] Alluni, S.; Pica, M.; Reichenbach, G. *J. Phys. Org. Chem.* **2001**, *14*, 265–270.

[10] Bunting, J. W.; Mason, J. M.; Heo, C. K. M. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2291–2300.

[11] Kurz, J. L.; Lu, J. Y.-W. *J. Phys. Chem.* **1983**, *87*, 1444–1448.

[12] Dietze, P. E.; Hariri, R.; Khattak, J. *J. Org. Chem.* **1989**, *54*, 3317–3320.

[13] Reference 3, Table 5–15, p 215 and references therein.

TABLE 1. Observed Rates of Reaction of Halides with 1 in [bmim][N(Tf)$_2$] at 25 °C

[halide]$_0$/M	[**1**]$_0$/mM	$10^3k_{\mathrm{obs}}{}^a$/s^{-1}	k_2/M^{-1} s^{-1}
		[bmim]Cl	
0.0304	0.282	0.664	
0.125	0.281	1.30	0.0124(0.0014)
0.253	0.282	2.87	
0.372	0.282	4.85	
		[bmim]Br	
0.0317	0.281	0.446	
0.127	0.284	1.66	0.0195(0.0027)
0.253	0.291	3.65	
0.378	0.288	7.30	
		[emim]I	
0.0122	0.281	0.332	
0.0303	0.284	0.776	
0.0607	0.281	1.41	0.0232(0.0040)
0.0901	0.284	2.16	
0.120	0.288	2.84	

[a] The standard deviations in the values of k_{obs} were less than 5%.

TABLE 2. Observed Rates of Reaction of Halides with 1 in [bm$_2$im][N(Tf)$_2$] at 25 °C

[halide]$_0$/M	[**1**]$_0$/mM	$10^3k_{\mathrm{obs}}{}^a$/s^{-1}	k_2/M^{-1} s^{-1}
		[bm$_2$im]Cl	
0.0309	0.296	0.277	
0.0306	0.296	0.271	
0.123	0.303	2.38	0.0296(0.0012)
0.243	0.313	6.15	
0.365	0.309	12.04	
		[bm$_2$im]Br	
0.0298	0.301	0.422	
0.122	0.298	1.97	0.0221(0.0011)
0.245	0.301	5.12	
0.360	0.299	7.66	
		[bm$_2$im]I	
0.0119	0.296	0.352	
0.0300	0.292	0.731	
0.0592	0.301	1.44	0.0238(0.0004)
0.0899	0.301	2.23	
0.120	0.301	2.88	

[a] The standard deviations in the values of k_{obs} were less than 2%.

given that the cations of the two ionic liquids considered thus far are imidazolium based. Clearly the structure of the cation has had an effect upon organic reactivity within the ionic liquid.

The results for the reactions of [bmpy]Cl, [bmpy]Br, and [bmpy]I with **1** in [bmpy][N(Tf)$_2$] are shown in Table 3.

As before, a linear dependence of k_{obs} upon initial halide concentration was observed. In this ionic liquid, the chloride ion is by far the most nucleophilic of the halides, but we now observe a further change in relative nucleophilicities. The iodide anion is now less nucleophilic than the bromide anion.

Summary of Nucleophilicity Data. A summary of the relative nucleophilicities of the halides in the ionic liquids studied in this work is shown in Table 4. Comparison of the data for reactions of the same substrate with different sources of halide in dichloromethane and hexafluoropropan-2-ol is also made. The conditions used for the study of nucleophilicity in the molecular solvents are not identical to ours, but are similar enough to allow meaningful comparisons to be made.

TABLE 3. Observed Rates of Reaction of Halides with 1 in [bmpy][N(Tf)$_2$] at 25 °C

[halide]$_0$/M	[**1**]$_0$/mM	$10^3k_{\mathrm{obs}}{}^a$/s^{-1}	k_2/M^{-1} s^{-1}
		[bmpy]Cl	
0.0312	0.296	0.958	
0.124	0.311	4.04	0.0391(0.0026)
0.248	0.303	8.36	
0.373	0.307	14.43	
		[bmpy]Br	
0.0307	0.297	0.589	
0.123	0.296	2.31	0.0226(0.0013)
0.244	0.294	4.90	
0.366	0.291	8.18	
		[bmpy]I	
0.0120	0.293	0.209	
0.0304	0.287	0.514	
0.0607	0.291	1.00	0.0188(0.0008)
0.0919	0.296	1.62	
0.121	0.287	2.27	

[a] The standard deviations in the values of k_{obs} were less than 2% when the nucleophile was Cl$^-$ or Br$^-$ and less than 3% when the nucleophile was I$^-$.

TABLE 4. Second-Order Rate Constants for the Reaction of Halides with 1 in Ionic Liquids at 25 °C, Relative Rate Constants, and a Comparison with Two Polar Molecular Solvents

	k_2/M^{-1} s^{-1}			relative k_2 values		
solvent	Cl$^-$	Br$^-$	I$^-$	Cl$^-$	Br$^-$	I$^-$
[bmim][N(Tf)$_2$]	0.0124	0.0195	0.0232	0.64	1	1.19
[bm$_2$im][N(Tf)$_2$]	0.0296	0.0221	0.0238	1.34	1	1.08
[bmpy][N(Tf)$_2$]	0.0391	0.0226	0.0188	1.73	1	0.83
CH$_2$Cl$_2$, ion pair^a	0.51	0.42		1.21	1	
CH$_2$Cl$_2$, free ion^a	1.04	0.46		2.26	1	
(CF$_3$)$_2$CHOH^b	0.00011	0.00045	0.00039	0.24	1	8.67

[a] Values obtained at 22 °C, using bis(triphenylphosphoranylidene)ammonium chloride or bromide.[8] [b] Values obtained at 50 °C, using tetramethylammonium halide.[12]

The first point of note is that the difference between the slowest reaction in an ionic liquid and the fastest is approximately a factor of 3. However, the reactions in the ionic liquids are greatly (orders of magnitude) decelerated in comparison to the reaction in dichloromethane, whether this is by the free ion or the ion pair, and much faster than in the hexafluoropropan-2-ol. All of the solvents considered here are considered polar, with (CF$_3$)$_2$CHOH being regarded as highly ionizing and hydrogen bond donating but weakly nucleophilic.[12]

In comparing the relative rates of reaction by chloride, for example, in the ionic liquids, one might consider that in these related solvents the differences are due to viscosities. Recently the viscosities of the ionic liquids used in this work have been determined;[14] at 25 °C the order of increasing viscosity is [bmim][N(Tf)$_2$] < [bmpy][N(Tf)$_2$] < [bm2im][N(Tf)$_2$]. The data clearly show that the reaction rates are not dependent on the viscosity of the ionic liquid alone. This observation is in agreement with other studies that we have made in ionic liquids whose viscosities are known.[15] Additionally, it is noted that while these reactions are slower than in the less viscous dichloromethane, they are also much faster than

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(14) Okoturo, O. O.; Pell, T.; VanderNoot, T. J. Private communication.

(15) Lancaster, N. L.; Welton, T.; Young, G. B. Unpublished data.

in less viscous hexafluoropropan-2-ol. Therefore, it would appear that the activation parameters are shown to influence the rate of reaction. These will be considered later in the text.

It is well-known that the rates of nucleophilic substitutions are solvent dependent. This dependence has been interpreted with reference to the nature of the charge distributions in the ground state and the activated complex in the rate-determining step by Hughes and Ingold.[16,17] In the studied reaction, the nucleophiles used can be approximated as point charges which then combine with the substrate **1** to give an activated complex with a single negative charge distributed over several atoms. Transferring the reaction from a nonpolar to a polar solvent is expected to stabilize the ground state with respect to the activated complex, thus slowing the reaction. The energy differences between the ground and excited states can also be influenced by other interactions, such as H-bonding.

It then remains to discuss the differences between the ionic liquids. In the ionic liquids studied bromide nucleophilicity, k_2, was approximately constant, while iodide showed a little variation and chloride showed more. Therefore, we used the Br^- nucleophilicity as our benchmark and compared the Cl^- and I^- values to that (Table 4).

In [bmpy][N(Tf)$_2$] chloride is the most nucleophilic halide followed by bromide and finally iodide. This is in very good agreement with Ford et al.,[6] who used triethylhexylammonium triethylhexylboride ionic liquid and found that the relative nucleophilicities of Cl^-:Br^-:I^- were 1.8:1:0.83, respectively. It is also in agreement with the known gas-phase nucleophilicities, which follow the order chloride > bromide.[18] This suggests that any interactions between the ionic liquids and the reagents act equally on all three halides in the two different ionic liquids.

In [bmim][N(Tf)$_2$] chloride is the least nucleophilic of the halides and iodide the most nucleophilic, a complete reversal of the previously observed trend. This clearly indicates that some influence of the ionic liquid is acting differentially on the three halides, making the chloride less reactive and the iodide more so. The [bm$_2$im][N(Tf)$_2$] ionic liquid is in some way intermediate in character, with the nucleophilicities changing in the order $Cl^- > I^- > Br^-$.

An alternative way to view the data is by how the nucleophilicities of the different halides change in going from one ionic liquid to another. As noted above, the k_2 values for bromide in the three ionic liquids are similar, though not identical. The k_2 values for iodide are the same in the two imidazolium-based ionic liquids and only marginally lower in the [bmpy][N(Tf)$_2$] ionic liquid. However, the rate of reaction of the chloride shows a great deal more variation. For the reaction of Cl^- in [bmim][N(Tf)$_2$] the value of k_2 is less than half the value in [bm$_2$im][N(Tf)$_2$] and less than one-third the value in [bmpy][N(Tf)$_2$]. Clearly there is some interaction between the ionic liquid and the Cl^- ion that is lowering its nucleophilicity in [bm$_2$im][N(Tf)$_2$] and yet more so in [bmim][N(Tf)$_2$].

It is well established that a strong hydrogen bond is formed between halide ions and [bmim]$^+$ and to a lesser extent [bm$_2$im]$^+$.[19] The [bmpy]$^+$ cation, on the other hand, would not be expected to act as such a strong hydrogen bond donor. However, studies have shown that strong hydrogen bonds can be formed via the hydrogen atom on a carbon α to a quaternary nitrogen (specifically $R_3N^+{-}C{-}H\cdots$, a cation to which [bmpy]$^+$ is analogous).[20] Chloride is the best hydrogen bond acceptor of the halides (hardest, most charge dense, and most coordinating). The change in observed nucleophilicities can therefore be explained by the degree of stabilization of the chloride ion via hydrogen bonding to the cation of the ionic liquid. The similarity of nucleophilicities in the tetraalkylammonium tetraalkylboride ionic liquid to that observed in [bmpy]$^+$ can also be understood by the argument that these cations coordinate anions more poorly. Recently the effect of hydrogen bonding in ionic liquids upon organic reactions (specifically the Diels−Alder reaction) have been speculated upon.[21,22]

Determination of Activation Parameters. The activation enthalpy ($\Delta H^‡$) and activation entropy ($\Delta S^‡$) were both determined using the Eyring equation (eq 3).

$$\ln\left(\frac{k_2 h}{k_B T}\right) = \frac{\Delta S}{R} - \frac{\Delta H}{RT} \tag{3}$$

Given that we had shown that there was a linear dependence of k_{obs} upon [chloride]$_0$ at 25 °C, with negligible intercept, the values of k_2 were determined using one value of [chloride]$_0$ only at each temperature. From these data, we can evaluate the influence of activation enthalpy and entropy upon the reactions studied.

Although we might expect the reaction to be promoted by a polar solvent because the transition complex will be stabilized, the Hughes−Ingold approach to solvent effects on the rates of nucleophilic substitutions[16,17] states that such reactions will be slightly slowed by polar solvents because the point charge nucleophiles are stabilized even more.

There are two good experimental reasons for studying only the reaction of chloride in this work. The first is that the quality of spectra for chloride were better than those achieved for bromide or iodide. The second is that, in other work, we found that the activation parameters were

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(16) Ingold, C. K. *Structure and Mechanism in Organic Chemistry*, 2nd ed.; Bell: London, 1969.

(17) (a) Hughes, E. D.; Ingold, C. K. *J. Chem. Soc.* **1935**, 244−255. (b) Hughes, E. D. *Trans. Faraday Soc.* **1941**, *37*, 603−632. (c) Hughes, E. D.; Ingold, C. K. *Trans. Faraday Soc.* **1941**, **37**, 657−686. (d) Cooper, K. A.; Dhar, M. L.; Hughes, E. D.; Ingold, C. K.; MacNulty, B. J.; Woolf, L. I. *J. Chem. Soc.* **1948**, 2043−2049.

(18) (a) Brauman, J. I.; Olmstead, W. N.; Lieder, C. A. *J. Am. Chem. Soc.* **1974**, *96*, 4030−4031. (b) Lieder, C. A.; Brauman, J. I. *J. Am. Chem. Soc.* **1977**, *99*, 4219−4228. (c) Tanaka, K.; Mackay, G. I.; Payzant, J. D.; Bohme, D. K. *Can. J. Chem.* **1976**, *54*, 1643−1659.

(19) (a) Avent, A. G.; Chaloner, P. A.; Day, M. P.; Seddon, K. R.; Welton, T. *J. Chem. Soc., Dalton Trans.* **1994**, 3405−3413. (b) Abdul-Sada, A. K.; Al-Juaid, S.; Greenway, A. M.; Hitchcock, P. B.; Howells, M. J.; Seddon, K. R.; Welton, T. *Struct. Chem.* **1990**, *1*, 391−394. (c) Elaiwi, A.; Hitchcock, P. B.; Seddon, K. R.; Srinivasan, N.; Tan, Y.-M.; Welton, T.; Zora, J. A. *J. Chem. Soc., Dalton Trans.* **1995**, 3467−3472.

(20) Cannizzaro, C. E.; Houk, K. N. *J. Am. Chem. Soc.* **2002**, *124*, 7163−7169.

(21) (a) Sethi, A. R.; Welton, T. In *Ionic Liquids: Industrial Applications to Green Chemistry*; Rogers, R. D., Seddon, K. R., Eds.; ACS Symposium Series No. 818; American Chemical Society, Washington, DC, 2002; pp 241−246. (b) Aggarwal, A.; Lancaster, N. L.; Sethi, A. R.; Welton, T. *Green Chem.* **2002**, *4*, 517−520.

(22) Dzyuba, S. V.; Bartsch, R. A. *Tetrahedron Lett.* **2002**, *43*, 4657−4659.

TABLE 5. Activation Enthalpies, Entropies, and Free Energies for the Reaction of Chloride with 1

$[\text{chloride}]_0$/M	k_2/M^{-1} s^{-1}	T/K	$\Delta H^‡$/kJ mol^{-1}	$\Delta S^‡$/J K^{-1} mol^{-1}	$\Delta G^‡_{298\text{ K}}$/kJ mol^{-1}
[bmim][N(Tf)$_2$]					
0.116	0.00381	288.15			
0.125	0.0104	198.15	71.8(1.6)	−42.2(5.4)	84.4(3.2)
0.125	0.0273	308.15			
[bm$_2$im][N(Tf)$_2$]					
0.122	0.00696	288.15			
0.123	0.0194	198.15	71.8(1.6)	−37.3(5.3)	82.9(3.2)
0.121	0.0500	308.15			
[bmpy][N(Tf)$_2$]					
0.122	0.0117	288.15			
0.122	0.0202	293.15			
0.124	0.0326	298.15	68.5(1.8)	−43.9(6.0)	81.6(3.6)
0.123	0.0498	303.15			
0.123	0.0799	308.15			
CH_2Cl_2, ion-pair[8]			79.5(2.9)	7.9(10)	77.2(5.9)
CH_2Cl_2, free ion[8]			54.4(2.5)	−58.6(8.4)	71.9(5.0)

[a] The values of k_{obs} from which the k_2 values were derived show standard deviations of 2% or less.

the same for both chloride and bromide.[5] Values for iodide have not been determined by us for any ionic liquid system. The data are shown in Table 5. Note that the standard deviations for the values of $\Delta H^‡$ and $\Delta S^‡$ (given in parentheses) represent the quality of the fit of the data to eq 3, and contain no allowance for the quality of k_2. The values of k_{obs} from which k_2 is derived typically had a standard deviation of less than 2% of the value derived from the fit of absorbance/time data to the first-order kinetic model. Additionally, $\Delta G^‡_{298\text{ K}}$ values have been determined for each system (eq 4); standard deviations are given, and the same caveats apply as stated previously.

$$\Delta G^‡ = \Delta H^‡ - T\Delta S^‡ \tag{4}$$

Also given in the table are values for the chloride ion and for the chloride ion pair in dichloromethane for the reaction of the same substrate with chloride, where the cation was tetrabutylammonium ion.[8] It should be noted that there is very little comparative data available in the literature, as most studies have been more concerned with determining the relative nucleophilicities of reagents in given solvents or else determining the substituent effects on the substrate.

Values of $\Delta H^‡$ are similar to those for the ion pair in dichloromethane. Therefore, the effect of the ionic liquid on the activation enthalpy does not arise from general "polarity" differences between the ionic liquids and dichloromethane, but rather the association of the chloride with a cation or cations. This suggests that the same process is occurring in the rate-limiting step in both cases, i.e., as the chlorine−carbon bond is being formed in the activated complex, a cation−chloride association is being broken with an associated enthalpic cost. This is opposed to the "free ion" case where the chlorine−carbon bond is formed without the concomitant breaking of another interaction, giving a lower activation enthalpy.

In an ionic liquid, where there is no molecular solvent present to separate the ionic species, a free (molecular solvent solvated) ion cannot occur. An ionic species would always be expected to be coordinated by one or more counterions of the ionic liquid, and we would expect that the chloride will always have its first coordination sphere dominated by cations. In fact recent structural studies in a related system confirm this expectation, and this is discussed later.[23] It is noteworthy that our data suggest $\Delta H^‡$ to be more similar to that for the ion pair in dichloromethane than that for the free ion in dichloromethane. An ion pair is a cation and anion that are coordinated to some extent and contained within a solvent shell; in our system that solvent shell is ionic, but is still more analogous to an ion pair than a free anion.

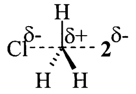

FIGURE 3. Activated complex.

That the ion-pair-like behavior should be observed is not without precedent. Similar behavior is seen in the influence of molecular solvation of ions in the gas phase, where a single molecule of the "solvent" can interact with the reagent and convert the reactivity to give a solution-like behavior. In this system, the coordination of a solvent molecule (the cation) is giving ion-pair-like behavior. It might be argued that the number of additional cations around the anion is not important, since our system that contains several cations about each halide anion behaves in an analogous mode to that for an ion pair in a molecular solvent.

The $\Delta S^‡$ values, however, are more similar to those for the reaction by the free ion in dichloromethane than for the reaction by the ion pair in dichloromethane.[8] Since the activation enthalpies are so similar to those for the ion pair in dichloromethane, this needs to be explained. This reaction follows an S_N2 reaction pathway and will form an activated complex as shown in Figure 3.

The activation step of an S_N2 reaction is an associative process, and one would expect it to have a negative entropy. In dichloromethane the reaction by the ion pair has a small positive activation entropy because, as the

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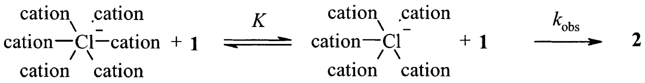
[23] Hardacre, C.; Holbrey, J. D.; McMath, S. E. J.; Bowron, D. T.; Sopev, A. K. In *Ionic Liquids: Industrial Applications to Green Chemistry*; Rogers, R. D., Seddon, K. R., Eds.; ACS Symposium Series No. 818; American Chemical Society: Washington, DC, 2002; pp 400−412.

SCHEME 2



activated complex is formed, the cation of the ion pair is liberated as a free solvated cation. This process counterbalances the loss of entropy associated with the formation of the activated complex. When performed in dichloromethane, the anionic leaving group **2** does not form an ion pair in dichloromethane but becomes a free solvated anion. In the ionic liquid **2** does associate with the cations of the ionic liquid. It is proposed that the entropy gained by liberating a cation from its association with the chloride ion is cancelled out by the association of another cation with **2**. Hence, the activation entropy for the reaction was what might be expected for an S_N2 process, with a value similar to that for reaction by the free ion in dichloromethane.

Finally, the $\Delta G^{\ddagger}_{298\,K}$ values have been compared, and a slight trend emerges. It appears that the highest $\Delta G^{\ddagger}$ value is observed in the [bmim]$^+$ ionic liquid, and that it falls a little for [bm$_2$im]$^+$, and still more for [bmpy]$^+$. This trend is to be expected, given that these values should follow the same relationship as the k_2 values. These $\Delta G^{\ddagger}$ values are higher than those observed for reaction by either the free ion or the ion pair in dichloromethane, suggesting, as one would expect, that in fact this reaction (with its charged reagent and its transition state with a delocalized charge) is slightly less favored in ionic liquids than in dichloromethane. However, the activation parameters alone are not sufficient to explain the observed differences in the nucleophilicities of the halides in the different ionic liquids.

These parameters reveal the size of the entropy and enthalpy barriers on going from the ground state of the *available reactive forms* of the reagents and the activated complex. The ground state for the reaction has first to be achieved to give such an available chloride ion before the reaction can occur. The evidence shows that the chloride is not always available to react with the substrate when dissolved in the ionic liquids, though there is still a linear relationship between the concentration of chloride and k_{obs}. It is likely that this relationship will break at higher concentrations where the ratio of chloride to [bmim]$^+$ approaches unity. There was no evidence of that in the concentration range studied. So, it seems that there is an equilibrium (Scheme 2) that must be accounted for.

The left-hand side of the equilibrium represents a fully coordinated, "unavailable" chloride, whereas on the right-hand side one face of the chloride ion is exposed to the substrate following the dissociation of one [bmim]$^+$ cation, giving an "available" chloride. This loose association of available chloride with the substrate represents the ground state for the reaction in this system. It should be noted that UV/vis spectroscopy showed that there is no significant interaction between available chloride and the substrate to give rise to a formal intermediate. The extent to which the nucleophile is coordinated by the cation will affect K, and thus k_{obs} and k_2. This is consistent with our results.

Although the nature of the complexes proposed above, and of the equilibrium constant, has not been determined in this work, some initial proposals can be made. Hardacre et al.[23] have demonstrated by neutron diffraction that a Cl$^-$ ion is surrounded by six cations within 6.5 Å of the halide in the related [mmim]Cl ([mmim]$^+$ = 1,3-dimethylimidazolium cation). For the reaction to occur, the Cl$^-$ ion must first come into close proximity with the substrate **1**. To do this, the Cl$^-$ ion must dissociate from at least one cation. Our data suggest that the order of availability of chloride to react is [bmim][N(Tf)$_2$] < [bm$_2$im][N(Tf)$_2$] < [bmpy][N(Tf)$_2$], which is in the reverse order of the strength of the cation–chloride interaction.

Conclusions

The first thing that becomes obvious in this work is that not all ionic liquids are the same. This work begins to show that one cannot simply take a conventional organic reaction and replace the solvent with a single ionic liquid and then expect the result to be the same as would be achieved in all other ionic liquids. However, by the same token this work reveals that the claims made,[24] that ionic liquids can be tailor-made for a given reaction, are true. It is possible to imagine that ionic liquids can be made to have the ideal combination of cation and anion for a given reaction. Although this study only concentrates on S_N2 reactions, we can generalize to say that, when using ionic liquids for reactions of highly associating anions such as halides, reaction rates will probably be greater in ionic liquids composed of the least coordinating (poor hydrogen bond acids) cations.

What we cannot say is that there is an "ionic liquid effect" on this reaction, rather that the reaction rates for this reaction of halides with methyl *p*-nitrobenzenesulfonate are found to be within the range observed for the same reaction in molecular solvents. In fact the relative rates of reaction can be explained (and predicted) by the classical Hughes–Ingold approach to examining solvent effects on organic reactions.

We have shown that the nucleophilicity of the halides is ionic liquid specific, just as nucleophilicity is solvent specific in molecular solvents, with the ability of the cation to act as a hydrogen bond donor being a key feature of this dependence in this reaction. We have published elsewhere the relative nucleophilicities of the halides in [bmim][BF$_4$][5] and found them to be (Cl$^-$) 1.06:(Br$^-$) 1:(I$^-$) 1.41. The trend of halide nucleophilicity in [bmim][N(Tf)$_2$] is not the same as in [bmim][BF$_4$], and shows that the nucleophilicity is determined by a combination of cation and anion properties, and that the explanation of nucleophilicities given above in this work is only part of the answer. We will report the details of the effect of the ionic liquid anions on these reactions at a later date.

Experimental Section

Materials. All syntheses were performed under anaerobic conditions using standard Schlenk techniques. All heterocycles were distilled from potassium hydroxide, alkyl halides from phosphorus pentoxide, and solvents from standard drying agents before use. Methyl *p*-nitrobenzenesulfonate and lithium

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[24] See, for example: Freemantle, M. *Chem. Eng. News* **1998**, *76* (34, Aug 24), 12.

bis(trifluoromethylsulfonyl)imide were purchased from commercial sources and used as received.

^{1}H NMR spectra (270 MHz) were recorded in deuterated DMSO, and chemical shifts are expressed in parts per million. Mass spectra were recorded using FAB ionization. UV/vis spectra were recorded using a PC-controlled spectrophotometer, fitted with a thermostatted sample holder.

The preparations and spectral data of the compounds [bmim]Cl, [bm$_2$im]Cl, [bmim][N(Tf)$_2$], and [bm$_2$im][N(Tf)$_2$] are described elsewhere.[25] The ionic liquids [bmim][N(Tf)$_2$] and [bm$_2$im][N(Tf)$_2$] both had UV cutoffs of ca. 240 nm. It should be noted that the yields of crude products were near quantitative for all compounds listed below, and that low reported final yields occurred only where material was lost during recrystallization.

Kinetic Studies. The reactions were studied by adding methyl *p*-nitrobenzenesulfonate in dichloromethane (4.7×10^{-7} mol in 0.1 cm^3) to a solution of halide in ionic liquid (1.5 cm^3) at known time. The complete experimental method used for the study of these reactions by UV spectroscopy and the subsequent data analysis are described elsewhere.[5] Most of the reactions were monitored for 6 half-lives or more.

1-Butyl-3-methylimidazolium Bromide, [bmim]Br. A solution of 1-methylimidazole (16 cm^3, 0.20 mol) in toluene (25 cm^3) was prepared and cooled in an ice/water bath. To this was added slowly 1-bromobutane (25 cm^3, 0.23 mol) with stirring. After addition, the mixture was allowed to warm to room temperature, then heated at reflux for 24 h, and then crystallized. The solid was purified by recrystallization from acetonitrile to give a colorless, crystalline solid (38 g, 0.17 mol, 86%). ^{1}H NMR:

δ_H (ppm) 9.23 (s, 1H), 7.77 (d, 1H, $J = 1.2$ Hz), 7.70 (d, 1H, $J = 1.2$ Hz), 4.13 (t, 2H, $J = 7.4$ Hz), 3.81 (s, 3H), 1.70 (quintet, 2H, $J = 7.4$ Hz), 1.19 (sextet, 2H, $J = 7.4$ Hz), 0.82 (t, 3H, $J = 7.4$ Hz). MS (FAB$^+$): *m/z* 357 ([(bmim)$_2$Br]$^+$, 10), 139 ([bmim]$^+$, 100). MS (FAB$^-$): *m/z* 299 ([(bmim)Br$_2$]$^-$, 100), 81 ([^{81}Br]$^-$, 92), 79 ([^{79}Br]$^-$, 92).

1-Ethyl-3-methylimidazolium Iodide, [emim]I. [emim]I was prepared from 1-methylimidazole (1.7 cm^3, 40 mmol) and iodoethane (5.0 cm^3, 44 mmol) by the same method as [bmim]-Br and purified by recrystallization from ethyl acetate to give a colorless, crystalline solid (9.8 g, 35 mmol, 87%). ^{1}H NMR:

δ_H (ppm) 9.08 (s, 1H), 7.73 (s, 1H), 7.64 (s, 1H), 4.13 (t, 2H, $J = 7.4$ Hz), 3.78 (s, 3H), 1.34 (t, 3H, $J = 7.4$ Hz). MS (FAB$^+$): *m/z* 349 ([(emim)$_2$I]$^+$, 15), 111 ([emim]$^+$, 100). MS (FAB$^-$): *m/z* 840 ([emim)$_3$I$_4$]$^-$, 5), 603 ([(emim)$_2$I$_3$]$^-$, 25), 365 ([(emim)I$_2$]$^-$, 100), 127 ([I]$^-$, 55).

1-Butyl-2,3-dimethylimidazolium Bromide, [bm$_2$im]Br. A solution of 1,2-dimethylimidazole (4.1 g, 42 mmol) in toluene (5 cm^3) was prepared and cooled in ice/water. To this was added 1-bromobutane (5.5 cm^3, 51 mmol) with stirring. After addition was complete the solution was allowed to warm to room temperature and then heated to reflux for 24 h. After cooling, a solid formed which was purified by recrystallization from ethyl acetate to give a colorless, crystalline solid (3.7 g, 16 mmol, 38%). ^{1}H NMR:

δ_H (ppm) 7.62 (s, 1H), 7.60 (s, 1H), 4.05 (t, 2H, $J = 7.4$ Hz), 3.69 (s, 3H), 2.52 (s, 3H), 1.62 (quintet, 2H, $J = 7.4$ Hz), 1.20 (sextet, 2H, $J = 7.4$ Hz), 0.82 (t, 3H, $J = 7.4$ Hz). MS (FAB$^+$): *m/z* 385 ([(bm$_2$im)$_2$Br]$^+$, 10), 153 ([bm$_2$im]$^+$, 100). MS (FAB$^-$): *m/z* 313 ([(bm$_2$im)Br$_2$]$^-$, 90), 79 ([Br]$^-$, 100).

1-Butyl-2,3-dimethylimidazolium Iodide, [bm$_2$im]I. [bm$_2$im]I was prepared from 1,2-dimethylimidazole (3.8 g, 40 mmol) and 1-iodobutane (5.0 cm^3, 44 mmol) by the same method as [bm$_2$im]Br and obtained as a colorless, crystalline solid (9.8 g, 35 mmol, 87%) after recrystallization from ethyl acetate. ^{1}H NMR:

δ_H (ppm) 7.64 (s, 1H), 7.61 (s, 1H), 4.08 (t, 2H, $J = 7.4$ Hz), 3.72 (s, 3H), 2.56 (s, 3H), 1.64 (quintet, 2H, $J = 7.4$ Hz), 1.23 (sextet, 2H, $J = 7.4$ Hz), 0.84 (t, 3H, $J = 7.4$ Hz). MS (FAB$^+$): *m/z* 433 ([(bm$_2$im)$_2$I]$^+$, 10), 153 ([bm$_2$im]$^+$, 100). MS (FAB$^-$): *m/z* 407 ([(bm$_2$im)I$_2$]$^-$, 60), 127 ([I]$^-$, 100).

1-Butyl-1-methylpyrrolidinium Chloride, [bmpy]Cl. In a Schlenk flask, 1-chlorobutane (221 cm^3, 2.05 mol) was added slowly with cooling to 1-methylpyrrolidine (200 cm^3, 1.92 mol) in propan-2-ol (200 cm^3). The mixture was then brought to reflux for 24 h. After cooling, the solvent was decanted to leave transparent crystals, which were recrystallized with propan-2-ol, washed with ethyl acetate, and then dried under vacuum, giving colorless crystals (314 g, 1.76 mol, 92%). ^{1}H NMR: δ_H (ppm) 3.49−3.42 (m, 4H), 3.42−3.34 (m, 2H), 3.02 (s, 3H), 2.06 (br. s, 4H), 1.66 (quintet, 2H, $J = 7.8$ Hz), 1.29 (sextet, 2H, $J = 7.8$ Hz), 0.91 (3, t, 3H, $J = 7.8$ Hz). MS (FAB$^+$): *m/z* 319 ([(bmpy)$_2$Cl]$^+$, 15), 142 ([bmpy]$^+$, 100). MS (FAB$^-$): *m/z* 212 ([(bmpy)Cl$_2$]$^-$, 100), 37 ([^{37}Cl]$^-$, 34), 35 ([^{35}Cl]$^-$, 40).

1-Butyl-1-methylpyrrolidinium Bromide, [bmpy]Br. [bmpy]Br was prepared from 1-methylpyrrolidine (4.5 cm^3, 43 mmol) and 1-bromobutane (5.5 cm^3, 51 mmol) by the same method as [bmpy]Cl and obtained as a colorless, crystalline solid (2.5 g, 11 mmol, 27%) after recrystallization from propan-2-ol and ethyl acetate. ^{1}H NMR:

δ_H (ppm) 3.54−3.34 (m, 4H), 3.32 (t, 2H, $J = 7.8$ Hz), 2.99 (s, 3H), 2.07 (br. s, 4H), 1.68 (quintet, 2H, $J = 7.8$ Hz), 1.31 (sextet, 2H, $J = 7.4$ Hz), 0.93 (t, 3H, $J = 7.4$ Hz). MS (FAB$^+$): *m/z* 363 ([(bmpy)$_2$Br]$^+$, 10), 142 ([bmpy]$^+$, 100). MS (FAB$^-$): *m/z* 302 ([(bmpy)Br$_2$]$^-$, 100), 81 ([^{81}Br]$^-$, 27), 79, ([^{79}Br]$^-$, 40).

1-Butyl-1-methylpyrrolidinium Iodide, [bmpy]I. [bmpy]I was prepared from 1-methylpyrrolidine (3.8 cm^3, 37 mmol) and 1-iodobutane (5.0 cm^3, 44 mmol) by the same method as [bmpy]-Cl and obtained as a colorless, crystalline solid (4.5 g, 17 mmol, 38%) after recrystallization from propan-2-ol and ethyl acetate. ^{1}H NMR:

δ_H (ppm) 3.58−3.40 (m, 4H), 3.40−3.28 (m, 2H), 3.00 (s, 3H), 2.08 (br. s, 4H), 1.68 (quintet, 2H, $J = 7.4$ Hz), 1.31 (sextet, 2H, $J = 7.4$ Hz), 0.92 (t, 3H, $J = 7.4$ Hz). MS (FAB$^+$): *m/z* 411 ([(bmpy)$_2$I]$^+$, 15), 142 ([bmpy]$^+$, 100). MS (FAB$^-$): *m/z* 396 ([(bmpy)I$_2$]$^-$, 100), 127 ([I]$^-$, 75).

1-Butyl-1-methylpyrrolidinium Bis(trifluoromethylsulfonyl)imide, [bmpy][N(Tf)$_2$]. In a Schlenk flask, a solution of [bmpy]Cl (35.8 g, 0.202 mol) in dichloromethane (50 cm^3) was added to lithium bis(trifluoromethylsulfonyl)imide (57.4 g, 0.200 mol). The resulting suspension was stirred for 72 h and then filtered. The residual salt was washed with further aliquots of dichloromethane, and the combined organic extracts were washed with water until the aqueous phase was halide free (by silver nitrate test), after which the solvent was removed in vacuo. The resulting liquid was treated with activated charcoal and filtered through a pad of acidic alumina to give a colorless liquid (73 g, 0.17 mol, 86%). ^{1}H NMR:

δ_H (ppm) 3.65−3.32 (m, 4H), 3.30−3.24 (m, 2H), 2.96 (s, 3H), 2.08 (br. s, 4H), 1.65 (quintet, 2H, $J = 7.4$ Hz), 1.30 (sextet, 2H, $J = 7.4$ Hz), 0.93 (3, t, 3H, $J = 7.4$ Hz). MS (FAB$^+$): *m/z* 564 ([(bmpy)$_2$(N(Tf)$_2$)]$^+$, 1), 142 ([bmpy]$^+$, 100). MS (FAB$^-$): *m/z* 702 ([(bmpy)(N(Tf)$_2$)$_2$]$^-$, 5), 280 ([N(Tf)$_2$]$^-$, 100).

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(25) Cammarata, L.; Kazarian, S. G.; Salter, P. A.; Welton, T. *Phys. Chem. Chem. Phys.* **2001**, *3*, 5192−5200.