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Nucleophilicity in Ionic Liquids. 3.[1] Anion Effects on Halide Nucleophilicity in a Series of 1-Butyl-3-methylimidazolium Ionic Liquids

N. Llewellyn Lancaster and Tom Welton*

Department of Chemistry, Imperial College London, South Kensington Campus,
London SW7 2AZ, United Kingdom

t.welton@imperial.ac.uk

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We have continued the study of halide nucleophilicity in ionic liquids, concentrating on the effect of changing the anion ($[BF_4]^-$, $[PF_6]^-$, $[SbF_6]^-$, $[OTf]^-$, and $[N(Tf)_2]^-$) when the cation is $[bmim]^+$ (where bmim = 1-butyl-3-methylimidazolium). It was found that the nucleophilicities of all the halides were lower in all of the ionic liquids than in dichloromethane. Changing the anion affected the order of halide nucleophilicity, e.g., in $[bmim][BF_4]$ the order of nucleophilicity was $Cl^- > Br^- > I^-$ while in $[bmim][N(Tf)_2]$ the order was $Cl^- < Br^- < I^-$. It was also found that the nucleophilicity of each halide was different in each ionic liquid, with chloride being almost four times as nucleophilic in $[bmim][BF_4]$ as in $[bmim][SbF_6]$. Similarly bromide was more than four times as nucleophilic in $[bmim][BF_4]$ as in $[bmim][PF_6]$. The activation parameters $\Delta G^\ddagger$, $\Delta H^\ddagger$, and $\Delta S^\ddagger$ have been measured for the reaction of chloride in each of the ionic liquids, plus the reaction of bromide in $[bmim][BF_4]$ and $[bmim][PF_6]$. These data were also compared to each other as well as to a similar reaction in dichloromethane (where these parameters have been estimated for both the free ion and the ion-pair). These studies show that the reaction in the ionic liquids has a high activation free energy barrier, due to the solvent−solute interactions within the ionic liquids. These interactions are described and discussed.

Introduction

Ionic liquids continue to be of interest as environmentally benign solvents.[2] They have various useful properties, being nonflammable, noncorrosive, and apparently nonvolatile. They have been used as solvents for a range of organic reactions.[3] Furthermore, there are wide ranges of cations and anions that have been used in the preparation of ionic liquids, giving a great potential for synthetic variation. It is even possible now to buy a wide range of ionic liquids in a range of qualities from several different suppliers. The study of the effects that the cation or, as in this work, the anion can have on reactions, and the eventual application of this knowledge, will make the description of ionic liquids as "designer solvents" a fair one. Hence, the study of the physical and chemical properties of ionic liquids is still an intensely active area of research.[4]

One important class of organic reaction is nucleophilic substitution. It has already attracted synthetic interest in ionic liquids,[5] while we[1,6] and others[7] have made kinetic and mechanistic studies. Other groups have made detailed studies of the effects of ionic liquids upon electrophilic[8] and other[9] reactions within them. These investigations should eventually help chemists to choose, or design, the appropriate ionic liquid for any given reaction.

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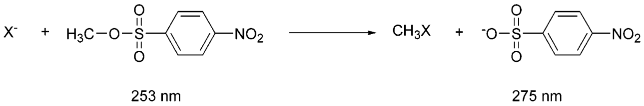
SCHEME 1



Ionic liquids are by definition liquids which are composed entirely of cations and anions. All of the ionic liquids used in this work melt at or below room temperature and so can be described as “ambient-temperature ionic liquids”. It is to be expected that both the cations and anions might interact with the reagents and the intermediate (or activated complex) of a reaction performed within the ionic liquid, thus affecting the studied reaction. In this work, we would expect the rate of the reaction to be affected. In molecular solvents, the effects of solvent polarity on the rates of nucleophilic substitutions have been established through the classic work of Hughes and Ingold[10] and others.[11] This work allows us to compare ionic liquid properties to those of molecular solvents.

In the project reported herein we have studied the effect of the ionic liquid anion on the nucleophilicity of chloride, bromide, and iodide. In all cases, the ionic liquid cation was $[bmim]^+$ (bmim = 1-butyl-3-methylimidazolium). The reaction studied was that of methyl *p*-nitrobenzenesulfonate with the halide to give methyl halide and *p*-nitrobenzenesulfonate anion (Scheme 1). The substrate (λ_{max} = 253 nm) and anionic product (λ_{max} = 275 nm) both have convenient absorbances in the UV region. In our hands, the ionic liquids used do not absorb significantly above 240 nm. The use of alkylsulfonates as substrates for studies of nucleophilicity is well established,[11] and this substrate has been used in some studies of nucleophilicity in molecular solvents[12−15] as well as in ionic liquids.[1,6]

In molecular solvents, the reaction can proceed either through the discrete anion or through the ion-pair. In the ionic liquids the halides are coordinated by the ionic liquid cations;[1] studies of the structurally related compound [mmim]Cl (where $[mmim]^+$ is 1,3-dimethylimidazolium) by neutron diffraction showed that the anion is coordinated by 6 cations within 6.5 Å.[16] This is not the same as an ion-pair, but is certainly not a free ion. Therefore, it was assumed that there is only one kinetically significant reaction path in the ionic liquids. Since there is a significant cation effect on the nucleophilicity of the halides,[1] the halides were introduced as the $[bmim]^+$ salts, except for I^-, which was introduced as [emim]I (emim = 1-ethyl-3-methylimidazolium). In our hands, [bmim]I was only obtained as a yellow oil; all of the halide salts used were white crystalline solids.

Results and Discussion

In our earlier work we reported the reaction of the halides with methyl *p*-nitrobenzenesulfonate in [bmim]-$[BF_4]$.[6] In that work we found that adding the substrate in a small volume of dichloromethane to a solution of the halide in the ionic liquid was satisfactory, and that the dichloromethane did not significantly affect the reaction rate. Therefore the same methodology was employed throughout this work. As observed before, when the chloride was used, it was possible to see the disappearance of the substrate, the appearance of the product, and an isosbestic point. Where bromide was the reagent, it was not possible to measure the absorbance due to the substrate although the isosbestic point was normally observed. Where the nucleophile was iodide, it was necessary to record the absorbance due to the product at between 295 and 305 nm. No isosbestic point was observed with this reagent.

As in the earlier work, the absorbance against time data were treated with a first-order kinetic model by using an iterative least-squares fitting procedure. Full details of the fitting procedure and representative figures for the reactions of halides with methyl *p*-nitrobenzenesulfonate are given elsewhere.[1,6]

Halide Nucleophilicity. The nucleophilicity of each halide was compared by determining the k_2 values. These were found by plotting k_{obs} against initial halide concentration.

It was observed that in neat [bmim]$[PF_6]$, a reaction of the substrate occurred. The degradation of the substrate (which took many hours to reach completion) was very slow when compared to the reactions studied and no adjustment was made in the treatment of the data. This degradation led to reduced absorbance at 253 nm, but without increased absorbance at 275 nm or formation of any other peak. It is not likely that this reaction was due to residual chloride (which would be expected to give a new peak at 275 nm). Instead it could be due to HF formed through partial hydrolysis of the ionic liquid (although care was taken throughout to avoid adventitious water). Other studies within our laboratory have shown that fluoride itself reacts with methyl *p*-nitrobenzenesulfonate to give the *p*-nitrobenzenesulfonate anion as expected, giving a peak at 275 nm. The degradation was not studied further and we did not attempt to characterize the product.

The substrate was also observed to react in the other ionic liquids. Again these reactions were very slow in comparison with the reactions that we were attempting to study, and so could be discounted when analyzing the reaction data. In each of these ionic liquids there was an increased absorbance at 275 nm with a concomitant decreased absorbance at 253 nm and an isosbestic point at around 262 nm. This suggested that this was a substitution reaction either by the ionic liquid anion or by residual chloride from the synthesis of the ionic liquid. All of the ionic liquids used in this work were prepared by the salt metathesis method (starting with [bmim]Cl), then washed with water until the aqueous phase was halide free.

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TABLE 1. The Reaction of Methyl *p*-Nitrobenzenesulfonate with Cl^-, Br^-, and I^- in [bmim][PF_6] at 25 °C[a]

[substrate]/ mM	[halide]/ M	10^3k_{obs}/ s^{-1}	k_2/ $M^{-1}\ s^{-1}$
	chloride		
0.317	0.00622	0.59^c	
0.313	0.0307	1.05	0.0144
0.313	0.0619	1.50	(0.0009)
0.309	0.124	2.73^c	
0.309	0.249	4.62	
0.319	0.371	5.69	
	bromide		
0.317	0.0307	1.71^c	
0.303	0.124	2.78	0.0086
0.315	0.237	3.50	(0.0015)
	iodide		
0.315	0.121	2.64	
0.309^b	0.0305	1.70	0.0278
0.299^b	0.0596	0.406^c	(0.0088)
0.311^b	0.156	1.08	
0.288^b	0.301	8.73	

[a] n_0(substrate) = 4.88 × 10^{-7} mol except as noted. Standard deviations in parentheses; standard deviations of k_{obs} are <5% except as noted. [b] n_0(substrate) = 4.70 × 10^{-7} mol. [c] Standard deviate <10%.

TABLE 2. The Reaction of Methyl *p*-Nitrobenzenesulfonate with Cl^-, Br^-, and I^- in [bmim][SbF_6] at 25 °C[a]

Vol_{IL+DCM}/ cm^3	[substrate]/ mM	[halide]/ M	10^3k_{obs}/ s^{-1}	k_2/ $M^{-1}\ s^{-1}$
1.62	0.290		0.0169	
		chloride		
1.57	0.299	0.0311	0.246	
1.55	0.303	0.123	1.13	0.0115
1.64	0.287	0.236	2.51	(0.0004)
1.56	0.301	0.362	4.02	
		bromide		
1.63	0.288	0.0314	0.355^b	
1.64	0.287	0.124	1.37	0.0123
1.59	0.296	0.252	2.79	(0.0007)
1.60	0.294	0.376	4.63	
		iodide		
1.64	0.287	0.0302	0.575	
1.60	0.294	0.0598	1.15	0.0180
1.62	0.290	0.0907	1.61	(0.0009)
1.64	0.287	0.0126	0.213	

[a] n_0(substrate) = 4.70 × 10^{-7} mol. Standard deviations in parentheses; standard deviations of k_{obs} are <5% except as noted. [b] Standard deviation 8%.

TABLE 3. The Reaction of Methyl *p*-Nitrobenzenesulfonate with Cl^-, Br^-, and I^- in [bmim][OTf] at 25 °C[a]

Vol_{IL+DCM}/ cm^3	[substrate]/ mM	[halide]/ M	10^3k_{obs}/ s^{-1}	k_2/ $M^{-1}\ s^{-1}$
1.62	0.284^b		0.198	
		chloride		
1.64	0.292	0.0310	1.47	
1.65	0.290	0.123	4.23	0.0197
1.62	0.296	0.246	5.63	(0.0023)
1.61	0.298	0.367	8.49	
		bromide		
1.63	0.294	0.0316	1.08	
1.63	0.294	0.126	4.29	0.0314
1.56	0.307	0.252	7.76	(0.0010)
1.58	0.303	0.381	12.2^c	
		iodide		
1.60	0.299	0.0123	0.874	
1.54	0.311	0.0296	1.74	
1.59	0.301	0.0594	3.46^c	0.0619
1.62	0.296	0.0914	5.90	(0.0024)
1.57	0.305	0.121	7.40	

[a] n_0(substrate) = 4.79 × 10^{-7} mol except as noted. Standard deviations in parentheses; standard deviations of k_{obs} are <3% except as noted. [b] n_0(substrate) = 4.60 × 10^{-7} mol. [c] Standard deviation <10%.

Assuming that the reactions were due to residual chloride only, the data would suggest that [Cl^-] is 3.1 × 10^{-4} M (or 9.4 ppm) in [BF_4]$^-$, 9.5 × 10^{-4} M (or 24 ppm) in [$N(Tf)_2$]$^-$, 1.5 × 10^{-3} M (or 32 ppm) in [SbF_6]$^-$, and 1.0 × 10^{-2} M (or 280 ppm) in [OTf]$^-$. The concentration of Cl^- calculated in this way for [bmim][OTf] is over 100 times higher than that measured by ion chromatography, suggesting that background reactivity for this ionic liquid is largely due to the triflate anion being slightly nucleophilic. A simple calculation shows that, if the reaction in [bmim][OTf] is entirely due to the anion of the ionic liquid, then the value of k_2 for [OTf]$^-$ is 4.0 × 10^{-5} M^{-1} s^{-1}. This is 3 orders of magnitude less than the reactions of the halides.

The reaction of chloride, bromide, and iodide with methyl *p*-nitrobenzenesulfonate in [bmim][PF_6] was studied and the results are shown in Table 1. The ionic liquid [bmim][SbF_6] was found to be a colorless liquid of sufficient purity that studies of nucleophilicity could be made in it. The data for the reaction of the halides with methyl *p*-nitrobenzenesulfonate in [bmim][SbF_6] are shown in Table 2. Finally [bmim][OTf] was prepared and studies of chloride, bromide, and iodide nucleophilicity were made in it. The data for the reaction of the halides with methyl *p*-nitrobenzenesulfonate in this ionic liquid are shown in Table 3. The data for the reactions of the halides with methyl *p*-nitrobenzenesulfonate in [bmim][BF_4][6] and [bmim][$N(Tf)_2$][1] are presented elsewhere.

Comparisons of the rates of the reactions of Cl^- and Br^- in the ionic liquids with those in dichloromethane show that they are slower in the ionic liquids. This is entirely consistent with predictions based on the Hughes−Ingold approach to the rates of nucleophilic substitutions, with the ionic liquids being more “polar” solvents than dichloromethane, as seen by the higher value for the Kamlet−Taft parameter π^*.[4,10] The charge on the activated complex for the reaction is distributed over several atoms (Figure 1), whereas in the starting materials it is firmly located on the halide ion. The Huhes−Ingold interpretation is that the more polar solvent preferentially stabilizes the halide ion, increasing the activation energy of the reaction and so reducing the rate. However, this interpretation fails to explain the differences seen between the ionic liquids.

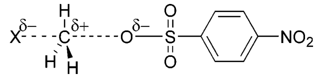

FIGURE 1. A schematic representation of the activated complex for the reaction.

When we studied the effect of the ionic liquid cation in a series of [$N(Tf)_2$]$^-$ ionic liquids, we found that the order of halide nucleophilicity was affected by the ionic liquid cation. However, there was not a lot of variation

TABLE 4. Second-Order Rate Constants for the Reaction of Halides with Methyl *p*-nitrobenzenesulfonate in Ionic Liquids at 25 °C, in Dichloromethane, and a Comparison of Halide Nucleophilicities toward Other Alkyl Tosylates in Some Polar Molecular Solvents

	k_2/M^{-1} s^{-1}			Kamlett−Taft parameters[4]		
solvent	Cl^-	Br^-	I^-	α	β	π*
[bmim][BF_4]	0.0403	0.0381	0.0538	0.627	0.146	1.047
[bmim][PF_6]	0.0144	0.0086	0.0278	0.634	0.207	1.032
[bmim][SbF_6]	0.0115	0.0123	0.0180	0.639	0.146	1.039
[bmim][OTf]	0.0197	0.0314	0.0619	0.625	0.464	1.006
[bmim][$N(Tf)_2$]	0.0124	0.0195	0.0232	0.617	0.243	0.984
CH_2Cl_2, ion-pair 22 °C[12]	0.51	0.42		0.042	−0.014	0.791
CH_2Cl_2, free ion 22 °C[12]	1.04	0.46		0.042	−0.014	0.791
$(CF_3)_2CHOH$ 50 °C[15]	0.00011	0.00045	0.00039	1.96	0	0.65
CH_3CN 30 °C[17]	1[a]	1[a]	0.87[a]	0.350	0.370	0.799
CH_3OH 25 °C[18]	0.15[a]	1[a]	7.7[a]	0.105	0.61	0.73
DMSO 50 °C[19]	1.6	1[a]	0.3[a]	0	0.76	1

[a] k_2 values relative to bromide for the reactions of the halides with alkyl tosylates.

in absolute halide nucleophilicity from one ionic liquid to the next, except where the halide was chloride.

In this work, we have shown that the nature of the anion affects reactivity in ionic liquids, as shown in Table 4. For example, the nucleophilicities and even the order of halide nucleophilicities can be changed by the ionic liquid anion. Changes in the anion of the ionic liquids are most associated with changes in the Kamlet−Taft hydrogen bond acceptor parameter, β.[4] In this study using $[bmim]^+$ ionic liquids, we have found that the nucleophilicity of all the halides is affected. The range of values of k_2 for the reaction of chloride in these ionic liquids (0.01 to 0.04 M^{-1} s^{-1}) is the same as that in the $[N(Tf)_2]^-$ ionic liquids.[1] However, the range of k_2 values for the reactions of bromide and iodide is much greater in the $[bmim]^+$ ionic liquids with a range of anions than in the $[N(Tf)_2]^-$ ionic liquids with a range of cations (where they both had k_2 values of about 0.02 M^{-1} s^{-1} regardless of the cation). That is for chloride as a nucleophile the anion and cation effects are of the same order, but for bromide and iodide the effect of changing the anion of the ionic liquid is greater than the effect of changing the cation.

Comparison of the relative nucleophilicities of the halides in ionic liquids and molecular solvents with similar E_T^N values shows that in [bmim][PF_6], chloride is more nucleophilic than bromide (as in DMSO). In the $[BF_4]^-$ and $[SbF_6]^-$ ionic liquids, the chloride and bromide ions are almost equally nucleophilic (as in acetonitrile). When the ionic liquids have $[OTf]^-$ or $[N(Tf)_2]^-$ anions, the chloride is less nucleophilic than bromide (as it is in methanol). In most of these ionic liquids, iodide is significantly more nucleophilic than bromide, again as it is in methanol and other protic solvents (though there has to be some doubt in the case of [bmim][PF_6], where there is a fairly large uncertainty in k_2 for I^-). However, in [bmim][$N(Tf)_2$] bromide and iodide have similar nucleophilicities.

The fastest reactions of Cl^- and Br^- occur in [bmim][BF_4] (I^- in $[OTf]^-$); the slowest reactions of Cl^- and I^- occur in [bmim][SbF_6] (Br^- in $[PF_6]^-$). This contrasts with our earlier work[1] where we showed that cation choice affects Cl^- nucleophilicity, but had little effect on the nucleophilicity of Br^- or I^-.

As well as being evaluated by measuring Kamlet−Taft parameters,[4b] the ionic liquids have been probed by Armstrong, using Abraham parameters.[4c] The "*a*" value of the ionic liquid in the latter study is related to β straightforwardly, and "*b*" to α, in a more complex manner, as reported.[4] There is not perfect agreement between the two scales as to which is the best (or worst) H-bond donor or acceptor ionic liquid. For example, using the Kamlet−Taft method, it appeared that the ionic liquid anion has only a minor affect on α, while the Abraham method suggests that the identity of the anion has a significant effect on the related parameter "*b*".[4]

When considering the H-bond acidity, α, of the solvent[4] we showed that the value was primarily controlled by the cation with $[bmim]^+$ based salts having values in the range 0.62−0.69. There was a "secondary" (or induced) anion effect, presumably because the probe molecule was a better H-bond acceptor than the ionic liquid anion. Any effect seen arises from the competition of cation−anion and cation−probe interactions. We can expect a similar situation in the nucleophilic substitutions reported here. The halides should be better H-bond acceptors than the ionic liquid anions, with chloride being the best of all. If there is a strong cation−anion (ionic liquid) interaction then the halide will be less strongly coordinated by the ionic liquid and will therefore be more nucleophilic.[1] On this basis we would predict that the reaction will be fastest (see Table 4) in the solvent with lowest α (which was [bmim][OTf]), which is an inverse relationship between H-bond acidity and k_2. This trend is generally followed, but only imperfectly.

It was found that the H-bond basicities, β or "*a*", of the ionic liquids were affected by the identity of the anion; the cation had only a negligible effect on either β or "*a*". It is reasonable to predict that if the ionic liquid anion is a good H-bond acceptor, it will compete with the halide to form H-bonds to the cation, thus altering the nucleophilicity of the halide, as described above. However, there is not a complete correlation. For example, the ionic liquids with the highest values of β are [bmim][BF_4] and [bmim][OTf] and it is in these ionic liquids that the reaction of the halides are fastest, as we would predict. Yet if we compare the relative chloride and bromide nucleophilicity in [bmim][OTf] and [bmim][$N(Tf)_2$] we find that the values of k_2 are essentially the same despite the fact that the anion in the former ionic liquid is a much better H-bond acceptor (higher β) than the latter. The least basic ionic liquid, [bmim][SbF_6], is the one in which the reactions of chloride and iodide are slowest. These observations again suggest that the binding of the anion to the cation affects the halide–cation interaction and thus the halide nucleophilicity. Structural investigations of the ionic liquids clearly show that the *N*,*N*-dialkylimidazolium based ionic liquids can self-associate to a greater or lesser extent through hydrogen bonding.[16,20] For any given cation the degree of hydrogen bonding is controlled by the hydrogen bond acceptor properties of the anion.

A comparison of k_2 against the Abraham parameter "*a*" did not reveal a direct correlation between the basicity of the ionic liquid and halide nucleophilicity.

This leads us to consider other possible factors that would affect the halide nucleophilicities, such as solvent viscosity. Yet, although [bmim][N(Tf)$_2$] is less viscous than [bmim][BF$_4$], the reaction of each halide is faster in the latter ionic liquid than in the former.

In Table 4 we have also made comparison against some molecular solvents, where halide nucleophilicity was measured by nucleophilic substitution on alkylsulfonates. Ionic liquids are often compared to acetonitrile or methanol by virtue of them all having similar empirical solvent properties. As is clear in the table, halide nucleophilicity is affected by these molecular solvents. In the polar protic solvent, chloride is less nucleophilic than bromide than iodide. However, in the polar aprotic solvent the trend is approximately reversed. The example of $(CF_3)_2CHOH$ is included as an example of a very strong hydrogen bond donating molecular solvent where the reactions of the halides (introduced as the tetramethylammonium salts) are even slower than those that we observe in the ionic liquids.

In summary, as in molecular solvents, using different ionic liquids results in different nucleophilicities of the halides (both relative and absolute). There is strong evidence of hydrogen bonding related effects but, perhaps not surprisingly, this is not the only contribution to the changes observed.

Activation Parameters. To gain further insight into the processes affecting these reactions, the activation parameters were determined. Given that we had shown that there was a linear dependence of k_{obs} upon initial halide concentration at 25 °C with negligible intercept, the values of k_2 were determined using one value of [halide]$_0$ only at each temperature. From these data we can evaluate the influence of activation enthalpy and entropy upon the reactions studied.

The effect of temperature on the rate of reaction in [bmim][BF$_4$] has been published.[6] At that time the activation parameters were determined by use of the Arrhenius equation. This gives an activation energy (similar to $\Delta H^{\ddagger}$), but the determination of the activation entropy from this expression is less straightforward. Here we have used the Eyring equation, which allows direct determination of both $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$. Therefore, these data are reproduced here, along with the data for the effect of temperature on the reaction in [bmim][N(Tf)$_2$].

Originally the reactions of both bromide and chloride were studied at varied temperatures. Iodide was not studied because of the lower quality of the spectra generated in these reactions. When the studies of the reaction of both anions in [bmim][BF$_4$] and [bmim][PF$_6$] revealed that the activation parameters for each anion were approximately the same in each ionic liquid, subsequent studies made use of chloride ion only as the nucleophile, chloride being a more satisfactory nucleophile to study in these experiments. The results for all of the reactions studied are given in Table 5.

The activation free energy follows the trend of k_2 values already recorded, as expected. It is noted that in the ionic liquids, the values of $\Delta G^{\ddagger}_{298\ K}$ are in the range of 82 to 84 kJ mol^{-1}. This contrasts to the reaction in dichloromethane, where the value of $\Delta G^{\ddagger}_{298\ K}$ is significantly lower, whether the reaction is by free chloride ion or by the ion-pair. The values of $\Delta G^{\ddagger}_{298\ K}$ are very similar to those observed when we studied the effect of the cation.[1]

The quantity $\Delta G^{\ddagger}_{298\ K}$ is calculated from the changes in enthalpy and entropy of activation, and it is the values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ that are most revealing. In most of the ionic liquids, $\Delta H^{\ddagger}$ is large, with values in the range of 70 to 80 kJ mol^{-1}. These are comparable to the value observed for the reaction by the ion-pair in dichloromethane. This is perhaps to be expected because the picture of the halide ion in the ionic liquid, while not a true ion-pair, is of the anion surrounded by cations. When the ionic liquid is [bmim][BF$_4$], the values of $\Delta H^{\ddagger}$ for the reactions of chloride and bromide are much lower, being in the range 53–56 kJ mol^{-1}. These values are more similar to the activation enthalpy for the reaction of the free ion in dichloromethane.

In considering $\Delta S^{\ddagger}$ for this reaction, we note that as it proceeds via an S_N2 mechanism, we would expect a negative activation entropy. This was observed in all cases in the ionic liquids, although there is considerable variation in the value in different ionic liquids and it is noted that the reactions in [bmim][BF$_4$] were accompanied by a particularly large entropy barrier.

In earlier work, we have proposed a reaction mechanism as shown in Scheme 2, where initially the halide is fully coordinated by a number of ionic liquid cations.[1] There is an equilibrium by which one face of the halide becomes uncoordinated, making it able to act as a nucleophile and giving rise to the observed reaction.

During the activation process the remaining cations bound to the halide become less associated as the negative charge becomes distributed over many atoms. This dissociation of the hydrogen-bonded cations from the halide to a greater or lesser degree compensates for the loss of entropy arising from the S_N2 reaction being an associative process. However, the data from the reaction in [bmim][BF$_4$] show that this compensation is not occurring. This can be interpreted as the halide dissolved into the [bmim][BF$_4$] being much less completely coordinated, giving a system of lower entropy than solutions of halide in the other ionic liquids. Therefore the activation entropy is much larger in [bmim][BF$_4$] than in the other ionic liquids. This suggestion also makes sense of

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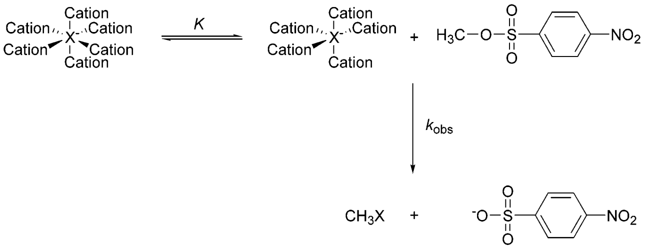
TABLE 5. Activation Enthalpies, Entropies, and Free Energies for the Reaction of Chloride and Bromide with Methyl *p*-Nitrobenzenesulfonate[a]

[chloride]$_0$/ M	k_2/ $M^{-1}s^{-1}$	T/ K	$\Delta H^‡$/ kJ mol^{-1}	$\Delta S^‡$/ J K^{-1} mol^{-1}	$T\Delta S^‡_{298K}$/ kJ mol^{-1}	$\Delta G^‡_{298K}$/ kJ mol^{-1}
			[bmim][BF_4]			
0.118	0.0281[c]	297.75				
0.118	0.0338	301.65	52.8	−97.3	−29.0	81.8
0.120	0.0544	306.45	(5.9)	(19.8)	(5.9)	(11.8)
0.119	0.0773	311.25				
0.118[b]	0.0254	297.65				
0.119[b]	0.0314	301.15	56.4	−86.5	−25.8	82.2
0.119[b]	0.0397	305.55	(8.8)	(29.3)	(8.7)	(17.5)
0.120[b]	0.0808	310.55				
			[bmim][PF_6]			
0.123	0.0222[c]	298.35				
0.123	0.0233	297.75	74.2	−27.3	−8.2	82.4
0.122	0.0324	301.65	(9.4)	(31.2)	(9.4)	(18.8)
0.124	0.0578	307.55				
0.124[b]	0.0224	298.65				
0.122[b]	0.0292	302.25	79.4	−11.0	−3.3	82.7
0.123[b]	0.0473	306.05	(4.6)	(15.2)	(4.5)	(9.1)
0.123[b]	0.0890	312.95				
			[bmim][SbF_6]			
0.123[d]	0.00384	288.15	78.6	−19.2	−5.7	84.3
0.123[d]	0.00919	298.15	(15.1)	(50.5)	(15.1)	(30.2)
0.123[d]	0.0262	308.15				
			[mim][OTf]			
0.122[e]	0.00902[c]	288.15				
0.121[e]	0.0170	293.15	71.8	−33.8	−10.1	81.9
0.123[e]	0.0344	298.15	(6.9)	(6.9)	(2.1)	(9.0)
0.121[e]	0.0474	303.15				
0.122[e]	0.0660	308.15				
			[bmim][$N(Tf)_2$]			
0.116[d]	0.00381	288.15	71.8	−42.2	−12.6	84.4
0.125[d]	0.0104	298.15	(1.6)	(5.4)	(1.6)	(3.2)
0.125[d]	0.0273	308.15				
CH_2Cl_2	ion-pair		79.5	7.9	2.3	77.2
			(2.9)	(10)	(3.0)	(5.9)
CH_2Cl_2	free ion		54.4	−58.6	−17.5	71.9
			(2.5)	(8.4)	(2.5)	(5.0)

[a] Standard deviation in k_{obs} from which k_2 is calculated is <2% except as noted. n_0(substrate) = 4.88 × 10^{-7} mol except as noted. [b] Nucleophile was bromide. [c] Standard deviation <8%. [d] n_0(substrate) = 4.70 × 10^{-7} mol. [e] n_0(substrate) = 4.79 × 10^{-7} mol.

SCHEME 2



the lower enthalpy barrier. If the halide is only poorly coordinated, the energy cost in breaking the halide−cation interactions will be lower, reducing the overall activation enthalpy.

The apparent reduction in halide−cation interactions in [bmim][BF_4] might arise from a number of factors. Included would be the strength of the interaction between the cation and anion of the ionic liquid. It is noted that [bmim][BF_4] has a high value of β compared to most of the other ionic liquids, so it is reasonable to expect strong cation−anion interactions within this system. This can only be a partial explanation, as the ionic liquid with the highest value of β ([bmim][OTf]) and that with the lowest value ([bmim][SbF_6]) show very similar values of activation parameters to each other. Another consideration could be the relative size of the anions and thus the degree to which the cations and anions can pack around each other in the liquid phase. Certainly $[BF_4]^-$, being a relatively small, approximately spherical anion, might be expected to pack better than $[N(Tf)_2]^-$, but again if this were a full explanation we would expect to see other changes. For example, when comparing the reactions in ionic liquids based on larger, spherical anions (e.g., $[PF_6]^-$ or $[SbF_6]^-$) or to those with less symmetrical or more bulky anions, there should be a change in $\Delta S^‡$ and/or $\Delta H^‡$. Such a trend is not obvious from our data.

Conclusions

We have demonstrated, in all cases studied, that the nucleophilicities of chloride, bromide, and iodide ions are lower in ionic liquids than in non-hydrogen bond donor molecular solvents. This is in direct contradiction to the assertion that bromide nucleophilicity is enhanced in ether cleavage reactions ionic liquids,[5a] but entirely in accord with predictions based on the Hughes–Ingold rules, with the ionic liquids being considered as polar solvents.[10,11] However, in the study of halide nucleophilicity in a range of $[N(Tf)_2]^-$ ionic liquids, it was clear that the major influence was the ability of the cation to interact through hydrogen bonding with the halide. The stronger that interaction was, the weaker the nucleophilicity of the halide became. Here we have shown that the hydrogen bond acceptor ability of the ionic liquids also plays a significant role in determining the nucleophilicity of the halides.

We have shown that the order of halide nucleophilicity can be altered when we change from one ionic liquid to another, just as it is when changing between various molecular solvents. We have compared the nucleophilicity data with the solvent properties of ionic liquids as described in the literature studies. At this time, these data do not make it possible to give a full explanation of why the nucleophilicity should be affected in the way observed in the $[bmim]^+$ ionic liquids. On the basis of the data collected, it is reasonable to suggest that increasing the cation hydrogen bonding donor effect decreases the nucleophilicity of the halides through a direct interaction with the nucleophile. It is clear that the effect of changing the anion is more complex than that of changing the cation. The anion exerts its effects through both self-association of the ionic liquid ions and other generalized polarity effects.

We have also demonstrated that the values of the activation parameters are comprehensible (at least in terms of their sign and approximate magnitude) when we consider that this is an example of an S_N2 reaction, and when we consider how the reagents will be coordinated within the ionic liquid. We have shown that in general our results are consistent with our understanding of solvent effects on reaction mechanism, rather than having to invoke a new understanding that is specific to ionic liquids. Thus we are able to continue to compare reactions in ionic liquids to reactions in molecular solvents, as has been the goal in this work.

Experimental Section

The syntheses of all of the ionic liquids and imidazolium salts used in this work have been reported elsewhere,[1,21] as have the data acquisition methods.[1,6]

Kinetc 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 to study these reactions and the subsequent data analysis are described elsewhere.[6] The reactions were all studied over 6 half-lives or more.

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