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Using Kamlet−Taft Solvent Descriptors To Explain the Reactivity of Anionic Nucleophiles in Ionic Liquids

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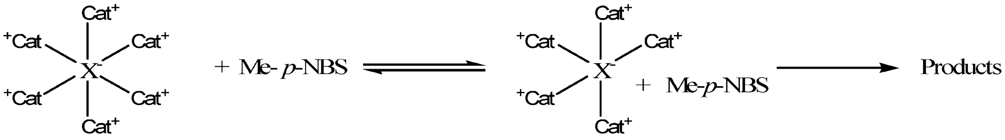

In this paper, we report the effect of ionic liquids on substitution reactions using a variety of anionic nucleophiles. We have combined new studies of the reactivity of polyatomic anions, acetate, trifuoroacetate, cyanide, and thiocyanide, with our previous studies of the halides in $[C_4C_1py][Tf_2N]$, $[C_4C_1py][TfO]$, and $[C_4C_1im][Tf_2N]$ (where $[C_4C_1im]^+$ is 1-butyl-3-methylimidazolium and $[C_4C_1py]^+$ is 1-butyl-1-methylpyrrolidinium) and compared their reactivities, k_2, to the same reactions in the molecular solvents dichloromethane, dimethylsulfoxide, and methanol. The Kamlet−Taft solvent descriptors (α, β, π^*) have been used to analyze the rates of the reactions, which were found to have a strong inverse dependency on the α value of the solvent. This result is attributed to the ability of the solvent to hydrogen bond to the nucleophile, so reducing its reactivity. The Eyring activation parameters ($\Delta H^‡$ and $\Delta S^‡$), while confirming the reaction mechanism, do not offer obvious correlations with the Kamlet−Taft solvent descriptors.

Introduction

Interest in the use of ionic liquids as solvents for synthesis continues unabated.[1,2] Ionic liquids have various useful properties, being often nonflammable, noncorrosive, and nonvolatile under atmospheric conditions. They have been used as solvents for a wide range of organic reactions. Much of the attracted interest has been based on the possibility that they might offer an environmentally benign alternative to conventional VOC solvents. However, it should be noted that this is a matter of some current contention.[3] Another point of interest in ionic liquids is their potential to act as "designer solvents".[4]

There have been a great variety of cations and anions used in the preparation of ionic liquids, showing their considerable synthetic flexibility. However, this offers potential difficulties as well as opportunities. Although the large number of component ions promises ionic liquids to be adaptable solvents, either by careful selection from those ionic liquids already available or through the possibility of designing new ionic liquids, it raises the question of how to identify the optimum combination of cation and anion for any given process. Hence, the study of how altering physicochemical properties of ionic liquids affects solute species and their reactions is becoming an increasingly active area of research.[5] It is in this area that much of our recent efforts have been focused. We are attempting to answer a number of questions, primarily, which reactions can be predicted to be accelerated or decelerated when using an ionic liquid rather than a molecular solvent and thence in which of these cases is the identity of the ions of the particular ionic liquid used important. There have been many studies published that, often on the basis of at best semiquantitative data, claim that special "ionic liquid effects" are responsible for changes in reactivities observed when ionic liquids are used as solvents. We are also seeking to show that when a sufficiently

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sophisticated description of solvent−solute interactions is used, no such special effects need to be invoked.

Historically, nucleophilic substitutions have been used to investigate the effects of solvents on chemical reactions, and these effects have been rationalized as the Hughes−Ingold rules.[6,7] These predict that if charge separation increases as the reaction system passes through the activated complex (e.g., an S_N2 reaction of neutral reagents), the effect of increased solvent polarity is to increase the rate of reaction. Conversely, if charge is destroyed (e.g., an S_N2 reaction of oppositely charged reagents) during the activation process, the effect of increased solvent polarity is to reduce the rate of reaction. Finally, if the charge becomes distributed over more atoms (e.g., an S_N2 reaction of one charged with one neutral reagent) during the activation process, the effect of increased solvent polarity is also to reduce the rate of reaction. It should be noted that the Hughes−Ingold rules are based upon an entirely electrostatic model of solvation, with liquids being viewed as simple dielectric media, and the effects of specific interactions, such as hydrogen bonding, are ignored.

We have previously reported quantitative kinetic studies of nucleophilic substitutions by both halides[8] and amines[9] in a range of ionic liquids, showing the effect of both cation and anion variation. Chiappe has also made kinetic and mechanistic studies of nucleophilic substitutions[10] as well as other reactions.[11] Other investigators[5,12] have studied reactions in ionic liquids in depth, thus allowing quantitative comparison against the same reactions in molecular solvents. This body of work generally shows that, on one level, the general predictions of reaction rates arising from the classical Hughes−Ingold rules can be applied to ionic liquids, if they are treated as polar solvents. However, closer inspection of the results reveals the importance of specific ionic liquid ion−solute hydrogen-bonding interactions on the reaction rates. For this reason, a study of the nucleophilicity of polyatomic anions, that have been deliberately selected to show different degrees of hydrogen bonding, was made in both ionic liquids and molecular solvents, using the same neutral substrate as in our previous work. It is the results of this investigation that we report here.

Ionic liquids are by definition liquids that are composed entirely of cations and anions. For experimental convenience, all of the ionic liquids used in this work (see Figure 1) melt below room temperature and so can be described as "ambient-temperature ionic liquids", or ATIL's. The reaction studied was that of methyl-*p*-nitrobenzenesulfonate (Me-*p*-NBS) with the appropriate nucleophile (Scheme 1). The use of alkylsulfonates as substrates for studies of nucleophilicity is well established,[7] and this substrate has been used in studies of nucleophilicity in molecular solvents[13] as well as by us in ionic liquids.

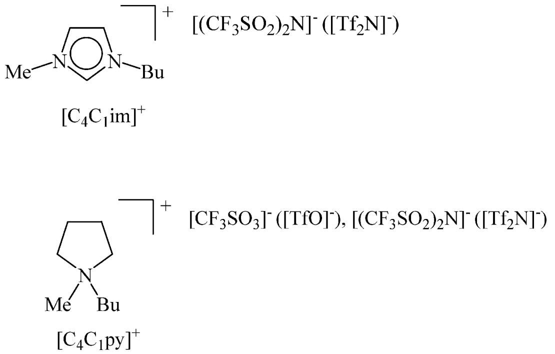
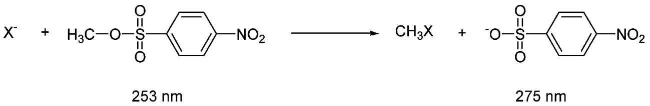


FIGURE 1. The ionic liquids used in this work (where $[C_4C_1im]^+$ is 1-butyl-3-methylimidazolium and $[C_4C_1py]^+$ is 1-butyl-1-methylpyrrolidinium).

SCHEME 1. Reaction of Methyl-*p*-nitrobenzenesulfonate with an Anionic Nucleophile



Results and Discussion

The rates of the reactions of the polyatomic anions acetate ($[Ac]^-$), trifluoroacetate ($[TFA]^-$), cyanide ($[CN]^-$), and thiocyanide ($[SCN]^-$) with methyl-*p*-nitrobenzenesulfonate were measured in the ATIL's $[C_4C_1im][Tf_2N]$, $[C_4C_1py][Tf_2N]$, and $[C_4C_1py][TfO]$ (see ESI), using the methodology previously described.[8] From these the bimolecular rate constants, k_2, have been determined. In addition, the reaction was performed in the molecular solvents methanol (MeOH), dimethylsulfoxide (DMSO), and dichloromethane (DCM). These results are compared to halide nucleophilicity[8] in the same reaction in Table 1.

Referring first to the results in terms of the Hughes−Ingold rules, it can be seen that although we would expect the reaction to be slowed by increasing polarity, we actually see no straightforward correlation between the dielectric constant of the solvent and rate of reaction in the same medium. The dielectric constants of the molecular solvents increase in the order DCM, MeOH, and DMSO (8.93, 32.66, and 46.45, respectively). Microwave dielectric spectroscopy has recently been used to estimate static dielectric constants for some ionic liquids.[14] Although none of the ionic liquids for which values are available were used in the study reported here, all of the estimates available are in the range 11−15. Assuming that the dielectric constants of our ionic liquids fall either within or close to this range, then the polarity of the ionic liquids, as described

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TABLE 1. Second-Order Rate Constants k_2/M^{-1} s^{-1} for the Reaction of Anions with Methyl-*p*-nitrobenzenesulfonate in Ionic Liquids and Molecular Solvents at 25 °C[a]

solvent	k_2/M^{-1} s^{-1}						
	$[CN]^-$	$[Ac]^-$	Cl^-	Br^-	I^-	$[TFA]^-$	$[SCN]^-$
DMSO	17.7 (0.4)	4.40 (0.1)	9.0×10^{-1} (1×10^{-2})	3.91×10^{-1} (8×10^{-3})	1.92×10^{-1} (3×10^{-3})	4.85×10^{-2} (6×10^{-4})	2.90×10^{-2} (1×10^{-3})
DCM	2.69 (5×10^{-2})	2.71×10^{-1} (3×10^{-3})	1.07 (7×10^{-2})	4.6×10^{-1} (1×10^{-1})	6.6×10^{-2} (2×10^{-3})	6.4×10^{-3} (1×10^{-4})	2.27×10^{-2} (3×10^{-4})
$[C_4C_1py][TfO]$	1.91 (6×10^{-2})	9.0×10^{-2} (1×10^{-3})	9.9×10^{-2} (5×10^{-3})	6.0×10^{-2} (1×10^{-3})	4.1×10^{-2} (2×10^{-3})	6.9×10^{-3} (1×10^{-4})	6.1×10^{-3} (6×10^{-4})
$[C_4C_1py][Tf_2N]$	1.56 (5×10^{-2})	5.40×10^{-2} (6×10^{-4})	3.9×10^{-2} (2×10^{-3})	2.2×10^{-2} (1×10^{-3})	1.88×10^{-2} (8×10^{-4})	2.50×10^{-3} (3×10^{-5})	4.61×10^{-3} (1×10^{-4})
$[C_4C_1im][Tf_2N]$	3.86×10^{-1} (8×10^{-3})	9.3×10^{-3} (8×10^{-5})	1.2×10^{-2} (1×10^{-3})	1.9×10^{-2} (2×10^{-3})	2.3×10^{-2} (4×10^{-3})	8.6×10^{-4} (5×10^{-5})	3.97×10^{-3} (8×10^{-5})
MeOH	1.62×10^{-2} (5×10^{-4})	6.8×10^{-4} (2×10^{-5})	4.0×10^{-4} (1×10^{-5})	1.62×10^{-3} (6×10^{-5})	6×10^{-3} (1×10^{-4})	5.14×10^{-5} (9×10^{-7})	2.29×10^{-3} (4×10^{-5})

[a] Standard deviations for the values are given in parentheses.

TABLE 2. Second-Order Rate Constants Relative to Those in MeOH k_2/k_2(MeOH) for the Reaction of Anions with Me-*p*-NBS in Ionic Liquids and Molecular Solvents at 25 °C

solvent	k_2/k_2(MeOH)						
	$[CN]^-$	$[Ac]^-$	Cl^-	Br^-	I^-	$[TFA]^-$	$[SCN]^-$
DMSO	1093	6471	2250	241	32.0	944	12.7
DCM	166	399	2675	284	11.0	125	9.91
$[C_4C_1py][TfO]$	118	132	248	37.0	6.83	134	2.66
$[C_4C_1py][Tf_2N]$	96.3	79.4	97.5	13.6	3.13	48.6	2.01
$[C_4C_1im][Tf_2N]$	23.8	13.7	30.0	11.7	3.83	16.7	1.73
MeOH	1	1	1	1	1	1	1

by dielectric constant, lies between that of DCM and MeOH. Hence, it is expected that the rates of the reactions should decrease in that order (DCM > ATIL's > MeOH > DMSO). However, for no reaction studied is this true. Indeed, the reactions are usually fastest in DMSO. This failure of the Hughes−Ingold approach is because it assumes an entirely electrostatic model of solvent−solute interactions and does not take into account the effect of specific interactions such as hydrogen bonding. Clearly, such specific interactions are dominating solvent effects in these reactions. It can be seen that not only do the absolute rates of the reactions change, but the relative nucleophilicities and the ordering of the nucleophilicities of the different anions in the various solvents also changes.

Viewing the data as a whole, the general trend in k_2 values is DMSO > DCM > $[C_4C_1py][TfO]$ > $[C_4C_1py][Tf_2N]$ > $[C_4C_1im][Tf_2N]$ > MeOH. However, it is clear that this trend is not adhered to by all nucleophiles. Two examples of this can be seen with the Cl^- and I^- data; the chloride reaction is faster in DCM than in DMSO, and when using iodide as a nucleophile $[C_4C_1im][Tf_2N]$ gives a greater k_2 value than $[C_4C_1py][TfO]$, both being contrary to the general trend.

Another way of viewing the data is that the relative nucleophilicity of each anion differs, depending on the solvent used. In fact, a different order of nucleophilicity is found in each of the solvents investigated. These are:

DMSO	$[CN]^- > [Ac]^- > Cl^- > Br^- > I^- > [TFA]^- > [SCN]^-$
DCM	$[CN]^- > Cl^- > Br^- > [Ac]^- > I^- > [SCN]^- > [TFA]^-$
$[C_4C_1py][TfO]$	$[CN]^- > Cl^- > [Ac]^- > Br^- > I^- > [TFA]^- > [SCN]^-$
$[C_4C_1py][Tf_2N]$	$[CN]^- > [Ac]^- > Cl^- > Br^- > I^- > [SCN]^- > [TFA]^-$
$[C_4C_1im][Tf_2N]$	$[CN]^- > I^- > Br^- > Cl^- > [Ac]^- > [SCN]^- > [TFA]^-$
MeOH	$[CN]^- > I^- > [SCN]^- > Br^- > [Ac]^- > Cl^- > [TFA]^-$

From this it can be seen that in all of the solvents studied $[CN]^-$ is the strongest nucleophile, while $[TFA]^-$ is the poorest in MeOH, DCM, $[C_4C_1im][Tf_2N]$, and $[C_4C_1py][Tf_2N]$, and $[SCN]^-$ is the weakest nucleophile in DMSO and $[C_4C_1py][TfO]$.

Finally, the range in solvent dependency of the reaction, and therefore the effective nucleophilicity, varies dramatically between the different nucleophiles, with $[Ac]^-$ k_2 values varying dramatically between the different solvents, whereas $[SCN]^-$ k_2 values show very little change. It is informative, therefore, to compare the variation in k_2 values for each nucleophile upon changing solvents (Table 2). From Table 1, it can be seen that the lowest k_2 values for all of the nucleophiles are found in methanol. Consequently, all k_2 values are shown relative to MeOH.

Table 2 clearly shows that there is little solvent dependency in k_2 when using either $[SCN]^-$ or I^- as the nucleophile, with only 13- and 32-fold increases in rate, respectively, on going from the slowest to the fastest solvent. In contrast to this, a 6471-fold increase is seen when using $[Ac]^-$ as the nucleophile.

To understand these effects, it is necessary to consider how the different solvents might interact with each of the nucleophiles. A particularly successful approach when attempting to quantitatively understand solvent-dependent data is the linear solvation energy relationship (LSER).[7] The equation, developed by Kamlet and Taft, explains the variation of any solute property in terms of three microscopic properties (α, β, and π^*). α is a quantitative scale of the hydrogen-bond acidity of a solvent, or

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TABLE 3. Kamlet−Taft Parameters for the Solvents Used in This Investigation[a]

solvent	α	β	π*
DMSO	0.00	0.76	1.00
DCM	0.04	−0.01	0.79
[C_4C_1py][TfO]	0.40	0.46	1.02
[C_4C_1py][Tf_2N]	0.42	0.25	0.95
[C_4C_1im][Tf_2N]	0.61	0.24	0.98
MeOH	1.05	0.61	0.73

[a] All values were obtained using procedures previously described in the literature, using only Reichardt's dye, *N*,*N*-diethyl-4-nitroaniline, and 4-nitroaniline.[16]

its ability to donate a hydrogen bond; β is a scale of the hydrogen-bond basicity of a solvent, or its ability to accept a hydrogen bond; and π* is the solvent dipolarity/polarizability, which is a scale of the ability of the solvent to stabilize a charge or dipole. Each of the parameters is empirically obtained and has been measured for a wide range of solvents,[15] including ionic liquids.[16] These scales have been used in multi-parameter equations to fit a number of different solvent-dependent observations, with the most useful form shown in eq 1.

$$XYZ = XYZ_0 + s\pi^* + a\alpha + b\beta \qquad (1)$$

XYZ represents the solvent-dependent property under study (e.g., the logarithm of a rate or equilibrium constant, or a λ_{max} value in a UV−vis or IR spectrum), and *a*, *b*, and *s* are solvent-independent coefficients characteristic of the process and are indicative of the sensitivity of the property under study to the associated solvent property. This has been used in the analysis of numerous reaction rates and equilibria, spectroscopic data, and various other solvent-dependent processes.[17] Here, we are using the LSER model to quantify solvent effects on the rate constant of a reaction. Since the relationship between the activation energy, E_a, and *k* is natural logarithmic in the Arrehnius equation, ln *k*, rather than log *k*, must be used in LSER correlations for the outcome to be physically meaningful (see Table 4).

We have previously reported α, β, and π* values for a number of ionic liquids,[16] including those used here {with the exception of [C_4C_1py][TfO]}. These values and those of the molecular solvents investigated are given in Table 3.

To apply the Kamlet−Taft LSER (eq 1), data obtained with each of the nucleophiles were first separated, and the solvent dependency of each process was analyzed by correlating ln k_2 with eq 1 in Minitab.[18] The error associated with each parameter was appraised in terms of the *F*-test, and the deviation associated with the equation and unnecessary terms in the correlation were eliminated. The results of these fits, along with the associated statistical data, are shown in Table 4.

TABLE 4. LSER Correlations for ln k_2 Obtained for the Nucleophiles Used[a]

nucleophile used	R^2	correlation obtained
Cl^- ($\beta = 1.00$)	0.99	$\ln k_2 = 0.21 - 7.56\alpha$ ($S = 0.34$; $F = 369$)[b]
Br^- ($\beta = 0.67$)	0.97	$\ln k_2 = -0.87 - 5.38\alpha$ ($S = 0.41$; $F = 131$)
I^- ($\beta = 0.30$)	0.88	$\ln k_2 = -2.21 - 2.85\alpha$ ($S = 0.46$; $F = 29$)
	0.95	$\ln k_2 = -2.57 - 3.05\alpha + 1.16\beta$ ($S = 0.33$; $F = 30$)
Ac^- ($\beta = 1.49$)	1.00	$\ln k_2 = -0.69 - 7.79\alpha + 2.90\beta$ ($S = 0.26$; $F = 325$)
	1.00	$\ln k_2 = -2.37 - 7.60\alpha + 2.65\beta + 1.83\pi^*$ ($S = 0.20$; $F = 373$)
TFA^- (no β available)	0.90	$\ln k_2 = -3.62 - 5.66\alpha$ ($S = 0.82$; $F = 36$)
	0.97	$\ln k_2 = -9.18 - 4.94\alpha + 5.76\pi^*$ ($S = 0.48$; $F = 57$)
SCN^- ($\beta = 0.33$)	0.89	$\ln k_2 = -3.87 - 2.46\alpha$ ($S = 0.89$; $F = 31$)
CN^- ($\beta = 1.37$)	0.86	$\ln k_2 = -2.03 - 5.75\alpha$ ($S = 1.00$; $F = 25$)
	0.99	$\ln k_2 = -3.16 - 5.07\alpha + 5.78\pi^*$ ($S = 0.99$; $F = 128$)

[a] Where the best correlation was not obtained using α alone, the better equation is shown beneath. The β values for the nucleophiles, shown in brackets, are estimates taken from the literature.[15] [b] Where R^2 is the proportion of variation in the response data explained by the descriptors; *F* is a ratio of the mean square of the factor and the mean square of the error, that is, the greater is the *F* value, the better is the fit; and *S* is an estimate of the standard deviation in the model, that is, the smaller is the value, the better is the fit.

The first point is that acceptable correlations were achieved using eq 1 with all of the nucleophiles, using data sets from both ionic liquids and molecular solvents. Hence, the data clearly demonstrate that, in this reaction at least, there is no special "ionic liquid effect" and that all significant interactions between the ionic liquids and these solutes are adequately described by an appropriate combination of their Kamlet−Taft parameters.

α appears in all of the LSER's generated and always has a negative value. For three of the nucleophiles, Cl^-, Br^-, and $[SCN]^-$, LSER's based on α alone provide the best fit. Two of the nucleophiles, I^- and $[Ac]^-$, have best fit LSER's with β in the correlations. π* appears in the best-fit LSER's for three of the nucleophiles, $[CN]^-$, $[Ac]^-$, and $[TFA]^-$.

The Hughes−Ingold interpretation of polarity effects on this reaction would lead us to expect a significant π* effect. Linear solvation energy relationships based on the Kamlet−Taft parameters have been applied extensively to the solvolysis of tertiary chlorides,[19] but seldom to S_N2 processes. An analysis of the reaction of benzyl chloride and aniline showed a strong positive correlations of log k_2 with both π* and α.[20] More recent studies of the cyclization of 4-hydroxy-4-methyl-1-pentyl-*p*-toluenesulfonate (also an S_N2 process) also showed positive π* effects.[21] We only find π* effects in the LSER's for $[CN]^-$, $[Ac]^-$, and $[TFA]^-$. However, ionic liquids have a very narrow range of π*. It was not possible to extend the range of π* values by the selection of molecular solvents, because attempts to do so led to failure due to lack of solubility of the ionic starting materials. The consequence of this restriction is that the narrow range of π* values may make this experiment unable to determine any effect that might otherwise have been seen. However, in all of the cases where a correlation was seen, the *s* value is positive, as expected from the Hughes−Ingold interpretation.

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For all of the nucleophiles, *a* is negative, meaning that an increase in the hydrogen-bond donating ability of the solvent leads to a decrease in the rate of reaction. This can be attributed to slowing of the reaction by the solvent hydrogen bonding to the nucleophile, stabilizing it with respect to the activated complex, which is a less strong hydrogen-bond acceptor than is the reagent. It can be seen that the stronger the hydrogen-bond acceptor character of the nucleophile (represented by the nucleophile β values listed in Table 4), the larger this effect. This is particularly emphasized when anions of similar structure are compared {*i.e.*, $Cl^- > Br^- > I^-$; $[Ac]^- > [TFA]^-$; $[CN]^- > [SCN]^-$}.

When comparing all of the nucleophiles, the effect of changing the α value of the solvent on the reaction, as described in eq 1, broadly splits into three groups: $Cl^- \approx [Ac]^- > [CN]^- \approx [TFA]^- \approx Br^- > I^- \approx [SCN]^-$. This again fits with the qualitative order that would be predicted from the β values of the anionic nucleophiles alone, with the exception of $[CN]^-$ (see below). This is an excellent demonstration of the intimacy of the solvent−solute relationship. While a solvent may have the potential to behave as a hydrogen-bond donor to a solute species, this potential is only realized when the solute is a good hydrogen-bond acceptor.

The apparent anomaly of the $[CN]^-$ result, for which a higher *a* would be expected on the basis of its β value alone, is consistent with the need to consider the hard/soft nature of the bases in addition to a simple strong/weak interpretation. While $[CN]^-$ can be considered to be a strong base ($\beta = 1.37$), it is a significantly softer base than Cl^-, Br^-, or either of the acetate ions. Consequently, its nucleophilicity toward carbon centers should be more difficult to reduce through hydrogen-bond donation, which can be considered to be a hard interaction. Hence, the ionic liquids used here are acting as hard solvents. Both I^- and $[SCN]^-$ are soft bases as well as weak bases. Consequently, they show the lowest ranges of solvent effects in these reactions, with significantly lower *a* values than the other nucleophiles used. As far as we are aware, this is the first time that such a hard/soft classification of ionic liquids has been made, and it is certainly worthy of further study.

In the two cases where the use of β leads to an improvement in the LSER correlations, *b* has a positive value. The value of *b* is significantly lower than *a*, suggesting that it is a secondary effect. We have previously shown that the hydrogen-bond donation of ionic liquids of a particular cation can be moderated by the hydrogen-bond acceptor ability of the ionic liquid anion.[16] Stronger hydrogen-bond acceptor anions hydrogen bond to the ionic liquid cation more strongly and reduce the availability of the cation hydrogen bond to the solute. This competition for the hydrogen-bond donor site is probably the effect that is seen in these results.

TABLE 5. Eyring Activation Parameters for the Reaction of Chloride with Methyl-*p*-nitrobenzenesulfonate in Ionic Liquids and Molecular Solvents

solvent	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J K^{-1} mol^{-1})	$T\Delta S_{298K}{}^{\ddagger}$ (kJ mol^{-1})	$\Delta G_{298K}{}^{\ddagger}$ (kJ mol^{-1})
DMSO	65.75	−25.48	−7.6	73.35
DCM (free ion)	54.4	−58.6	−17.5	71.9
DCM (ion pair)	79.5	7.9	2.35	77.2
$[C_4C_1py][TfO]$	70.62	−25.92	−7.73	78.35
$[C_4C_1py][Tf_2N]$	68.5	−43.9	−13.1	81.6
$[C_4C_1im][Tf_2N]$	71.8	−42.2	−12.6	84.4
MeOH	83.94	−27.85	−8.31	92.25

TABLE 6. Eyring Activation Parameters for the Reaction of $[CN]^-$ with Methyl-*p*-nitrobenzenesulfonate in Ionic Liquids and Molecular Solvents

solvent	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J K^{-1} mol^{-1})	$T\Delta S_{298K}{}^{\ddagger}$ (kJ mol^{-1})	$\Delta G_{298K}{}^{\ddagger}$ (kJ mol^{-1})
DMSO	28.89	−125.27	−37.35	66.24
DCM	49.15	−73.25	−21.82	70.97
$[C_4C_1py][TfO]$	66.47	−20.24	−6.03	72.50
$[C_4C_1py][Tf_2N]$	58.03	−47.44	−14.13	72.16
$[C_4C_1im][Tf_2N]$	39.23	−121.85	−36.33	75.56
MeOH	58.68	−82.02	−24.45	83.13

TABLE 7. Eyring Activation Parameters for the Reaction of $[SCN]^-$ with Methyl-*p*-nitrobenzenesulfonate in Ionic Liquids and Molecular Solvents

solvent	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J K^{-1} mol^{-1})	$T\Delta S_{298K}{}^{\ddagger}$ (kJ mol^{-1})	$\Delta G_{298K}{}^{\ddagger}$ (kJ mol^{-1})
DMSO	69.54	−41.86	−12.48	82.02
DCM	66.77	−51.83	−15.45	82.22
$[C_4C_1py][TfO]$	58.57	−89.62	−26.71	85.29
$[C_4C_1py][Tf_2N]$	45.34	−137.47	−40.97	86.31
$[C_4C_1im][Tf_2N]$	65.51	−71.22	−21.23	86.74
MeOH	67.94	−68.05	−20.29	88.23

TABLE 8. Eyring Activation Parameters for the Reaction of Acetate with Methyl-*p*-nitrobenzenesulfonate in Ionic Liquids and Molecular Solvents

solvent	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J K^{-1} mol^{-1})	$T\Delta S_{298K}{}^{\ddagger}$ (kJ mol^{-1})	$\Delta G_{298K}{}^{\ddagger}$ (kJ mol^{-1})
DMSO	42.40	−89.65	−26.73	69.13
DCM	52.80	−79.48	−23.68	76.48
$[C_4C_1py][TfO]$	62.15	−55.21	−16.46	78.61
$[C_4C_1py][Tf_2N]$	48.31	−107.22	−31.95	80.26
$[C_4C_1im][Tf_2N]$	25.23	−199.14	−59.35	84.58
MeOH	83.57	−25.33	−7.55	91.12

TABLE 9. Eyring Activation Parameters for the Reaction of Trifluoroacetate with Methyl-*p*-nitrobenzenesulfonate in Ionic Liquids and Molecular Solvents

solvent	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J K^{-1} mol^{-1})	$T\Delta S_{298K}{}^{\ddagger}$ (kJ mol^{-1})	$\Delta G_{298K}{}^{\ddagger}$ (kJ mol^{-1})
DMSO	65.20	−51.65	−15.4	80.60
DCM	72.82	−41.57	−12.39	85.21
$[C_4C_1py][TfO]$	72.93	−41.13	−12.26	85.19
$[C_4C_1py][Tf_2N]$	68.08	−66.04	−19.68	87.76
$[C_4C_1im][Tf_2N]$	73.89	−56.65	−16.88	90.78
MeOH	65.10	−107.62	−32.09	97.19

In our previous studies of halide nucleophilicity in ionic liquids, we noted that a clear effect of changing the cation could be seen, but no systematic effect of changing anion could be elucidated.[8] This can now be explained. The hydrogen-bond donor ability, α, of ionic liquids to anionic hydrogen-bond acceptors has been shown to be largely a property of the cation.[9,22] Consequently, changing the cation will affect the rate of the reaction. The principal effect of changing the anion of the ionic liquid on the Kamlet−Taft parameters is to change β. Because β is not found to correlate with the reaction rates of Cl^- and Br^- and only has a small effect on the reaction rate of I^-, changing the anion does not have a noticeable systematic effect on the nucleophilicities of the halides.

Eyring Activation Parameters

To gain greater insight into the reaction process, the activation enthalpy ($\Delta H^{\ddagger}$) and entropy ($\Delta S^{\ddagger}$) were both determined using

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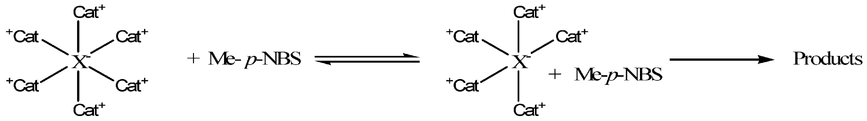
SCHEME 2



the Eyring equation. These values are reproduced in Tables 5−9. In our previous studies of the halides,[8] we did not study the activation parameters for iodide, because the data were not of the same high quality as those for chloride. Furthermore, in [C_4C_1im][BF_4] and in [C_4C_1im][PF_6] the activation parameters for bromide and chloride were largely similar. Hence, only the reactions of chloride were studied in detail.

S_N2 reactions are associative, and negative activation entropies are expected. However, in DCM, the reaction of Cl^- has been shown to proceed through both the discrete anion and the ion pair.[13] $\Delta S^{\ddagger}$ for the ion-paired chloride is slightly positive and, therefore, atypical for this reaction. When studying the chloride reaction in ionic liquids, it was noted that $\Delta S^{\ddagger}$ for the reaction was more similar to the reaction of free solvated ions, but $\Delta H^{\ddagger}$ was more similar to that of the ion-paired chloride nucleophile. This led us to consider the nature of ion pairing in ionic liquids. In a pure ionic liquid, there are no molecules available to separate ions, and the ions of the solute will be repelled by the ions of the ionic liquid bearing the same charge (cation−cation or anion−anion). Hence, in an ionic liquid, a solute ion will always be closely associated with ions of opposite charge. Studies of the compound [C_1C_1im]Cl (where [C_1C_1im]$^+$ is 1,3-dimethylimidazolium) by neutron diffraction showed that the anion is coordinated by 6 cations within 6.5 Å.[23] This is not the same as an ion pair, but it is certainly not a free ion. We used this to propose a mechanism for the reaction, which included the need to remove a cation from the nucleophile to liberate an active site for reaction before the activation process itself occurred, which also involved the reduction hydrogen bonding (see Scheme 2). Although the number of cations surrounding the other anions used as nucleophiles in this study may be different, it is likely that they are still maximally solvated by cations. The activation parameters for all of the other nucleophiles used in this project are also consistent with reaction by the same mechanism.

To understand more about the effects of changing solvent on these reactions, LSER's of these reactions were attempted. However, all attempts to achieve statistically reliable LSER correlations failed. Subtle differences in ostensibly similar reactions can have significant effects on the balance of the activation parameters. It is likely that this is preventing a successful LSER analysis for $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ of these reactions.

$\Delta G^{\ddagger}$ for the reactions was calculated from $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$. $\Delta G^{\ddagger}$ is directly proportional to ln k, and the LSER correlations for $\Delta G^{\ddagger}$ might be expected to be almost identical to those seen with ln k_2. These are reproduced in Table 10.

The best fit LSER's for $\Delta G^{\ddagger}$ are superficially similar to those for ln k_2, but very different in detail. For $\Delta G^{\ddagger}$, the best correlations are achieved with α alone for Cl^- and [SCN]$^-$, as they were for ln k_2. Ac^- has best fit LSER's, for both $\Delta G^{\ddagger}$ and ln k_2 include both α and β. Finally, the best fit $\Delta G^{\ddagger}$ LSER's for [Ac]$^-$, [TFA]$^-$, and [CN]$^-$ include π*, again as they do for ln k_2. Given the relationship between $\Delta G^{\ddagger}$ and ln k_2, their LSER's should, at least, have the same form, as is seen to be the case. That $\Delta G^{\ddagger}$ was derived from $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ and still gives LSER's of the same form as those for ln k_2, also confirms that the forms of these LSER's are not arising as artifacts of the calculations. Because the values for $\Delta G^{\ddagger}$ and ln k_2 cover very different ranges (66−97 kJ mol^{-1} and 4 × 10^{-4} to 17.7, respectively), the values of the coefficients in the LSER's are, of course, expected to be different.

TABLE 10. LSER Correlations for $\Delta G_{298K}{}^{\ddagger}$ Obtained for the Nucleophiles Used in This Investigation[a]

nucleophile used	R^2	correlation obtained
Cl^- ($\beta = 1.00$)	0.98	$\Delta G_{298K}{}^{\ddagger} = 72.3 + 19.2\alpha$ ($S = 1.38$; $F = 164$)
[Ac]$^-$ ($\beta = 1.49$)	0.95	$\Delta G_{298K}{}^{\ddagger} = 71.4025 + 19.9\alpha$ ($S = 1.86$; $F = 70$)
	1.00	$\Delta G_{298K}{}^{\ddagger} = 90.0 + 21.6\alpha - 3.2\beta - 18.5\pi^*$ ($S = 0.44$; $F = 767$)
[TFA]$^-$ (no β available)	0.97	$\Delta G_{298K}{}^{\ddagger} = 94.2 + 12.4\alpha - 12.8\pi^*$ ($S = 1.29$; $F = 47$)
[SCN]$^-$ ($\beta = 0.33$)	0.91	$\Delta G_{298K}{}^{\ddagger} = 82.5 + 6.19\alpha$ ($S = 0.85$; $F = 40$)
[CN]$^-$ ($\beta = 1.37$)	0.95	$\Delta G_{298K}{}^{\ddagger} = 66.8 + 15.7\alpha$ ($S = 1.437$; $F = 72.91$)
	0.98	$\Delta G_{298K}{}^{\ddagger} = 79.9 + 12.3\alpha - 12.8\pi^*$ ($S = 0.99$; $F = 80$)

[a] Where the best correlation was not obtained using α alone, the better equation is shown beneath. The β values for the nucleophiles, shown in brackets, are estimates taken from the literature.[15]

It can be seen that, as for ln k_2, changes in $\Delta G^{\ddagger}$ with solvent can primarily be attributed to the changing ability of the solvent to act as a hydrogen-bond donor, α, with the other Kamlet−Taft parameters only occasionally being used in the LSER. This again confirms the proposed mechanism (Scheme 2), in which the nucleophile becomes a poorer hydrogen-bond acceptor as it enters the activated complex.

Conclusion

It was found that applying the Kamlet−Taft LSER approach to kinetic data from several anionic nucleophilic substitution reactions of methyl-*p*-nitrobenzenesulfonate in both molecular and ionic liquids yielded consistent results. This approach shows that this reaction does not display an "ionic liquid effect". The correlations can be explained mainly in terms of the solvent donating a hydrogen bond to the nucleophilic anion and thus reducing its capacity as a nucleophile. The effect of using a range of multi-atom nucleophiles, rather than just the simple halides that had been studied previously, was also demonstrated. It was shown that the degree of correlation between the rate constant and α was dependent on the nucleophile itself, with more basic anions showing a higher degree of solvent dependency in their reaction with methyl-*p*-nitrobenzenesulfonate. Furthermore, the hard/soft nature of the nucleophile was also shown to be significant, with ionic liquids with the [C_1C_4im]$^+$ cation being shown to act as hard solvents, which therefore interact more strongly with hard solutes (e.g., Cl^-) rather than soft solutes (e.g., [CN]$^-$).

Experimental Section

Materials. All syntheses were performed under anaerobic conditions using standard Schlenk techniques. All heterocycles were

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distilled from potassium hydroxide, alkyl halides from phosphorus pentoxide, and solvents from standard drying agents before use. Methyl *p*-nitrobenzenesulfonate and lithium bis(trifluoromethylsulfonyl)imide were purchased from commercial sources and used as received. The preparations and spectral data of the ionic liquids have been described elsewhere.[24]

Kinetic Procedure. To the ionic liquid (1.5 cm^3, freshly outgassed *in vacuo*) was weighed a solution of [cat][nucleophile] (0.2 mmol, where cat = the cation of the ionic liquid) 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. UV/vis spectra were recorded using a spectrophotometer fitted with a thermostated sample holder.

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Supporting Information Available: Tables containing the observed rates of reactions of the nucleophiles discussed in all of the solvents used at various temperatures. This material is available free of charge via the Internet at http://pubs.acs.org.

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