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The nucleophilic aromatic substitution reaction between 1-fluoro-2,4-dinitrobenzene and ethanol was examined in a series of ionic liquids across a range of mole fractions. Temperature-dependent kinetics analyses were undertaken to determine the activation parameters for this reaction at the highest mole fraction. As the mole fraction of ionic liquid was increased, the rate constant of the reaction also increased, however the microscopic origin of the rate enhancement was shown to be different between different ionic liquids and also between different solvent compositions. These results indicate a balance between microscopic interactions that result in the observed solvent effects and a qualitative method for analysing such interactions is introduced.

Rationalising the effects of ionic liquids on a nucleophilic aromatic

Introduction

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An ionic liquid is defined as a salt which has a normal melting point below 100 °C.¹ Having a range of interesting properties; including low vapour pressure² and high thermal stability;³ ionic liquids are potential alternatives to molecular solvents.⁴ As the properties of ionic liquids are tuneable through variation of the ionic components, they are used in a range of applications including as electrolytes,⁵ catalysts,⁶ and also as solvents in a number of organic and inorganic processes.^{3, 7} For effective use as solvents, it is necessary to be able to predict any effects that an ionic liquid solvent will have on reaction outcome.

Through examination of ionic liquids as solvents in a range of reactions, identification of important interactions (with starting materials⁸⁻¹³ and/or transition states¹⁴⁻²¹) provides the potential for control of reaction outcome using known ionic liquids^{12, 13} or the design of novel ionic liquids to beneficially affect a given process.²² An example of a type of reaction considered to some extent previously is the nucleophilic aromatic substitution (S_NAr) reaction. This reaction type has been studied in ionic liquid solvents through examining the reactions of different electrophiles (including activated benzenes²³⁻²⁶ and nitrothiophenes²⁷⁻³⁰) with a variety of

liquids enhanced the rate of the reaction however in another case,³⁰ ionic liquids gave smaller rate constants than in a molecular solvent. $_{,3}$ The work of Welton *et al.*²⁵ used knowledge of the Gibbs

ne work of weiton *et al.* used knowledge of the Gibbs energy change and the hydrogen bond basicity to design ionic liquids to give increased yields compared with molecular solvents. Campodónico *et al.*²⁴ proved that the effect of ionic liquids on this kind of reaction could be correlated with either the hydrogen bond basicity or the Gutmann's donor number for the ionic liquids examined. The work of D'Anna *et al.*²⁷ used temperature dependent studies, to show that the ionic liquid was stabilising and organising around the transition state, resulting in a decrease in the enthalpy and entropy of activation compared with the molecular solvent; this interpretation was supported by computational studies.²⁸

nitrogen-based nucleophiles. In some cases, 23, 24, 27, 29 ionic

The examples above employed nitrogen-based nucleophiles. Previously we have examined an S_NAr reaction with an oxygen nucleophile; the reaction of 1-fluoro-2,4-dinitrobenzene **1** and ethanol to form 2,4-dinitrophenetole **2** (Scheme 1).



 $[\]label{eq:Scheme 1.} Scheme 1. The nucleophilic aromatic substitution (S_NAr) reaction between 1-fluoro-2,4-dinitrobenzene 1 and ethanol to gain the 2,4-dinitrophenetole 2. i) EtOH, NEt_3.$

This reaction has been examined in a series of ionic liquids with rate constant enhancements observed compared with the molecular solvent, ethanol.^{9, 15, 22} Initially,⁹ the increase in rate constant was proposed to be due to the interaction between

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Electronic Supplementary Information (ESI) available: Details of the synthesis of the ionic liquids; the corresponding ¹H NMR spectra for the ionic liquids; experimental details of the kinetic analyses; the exact composition of standard solutions and rate constants for the mole fraction dependence graphs (Figure 2 and 3); the Eyring plot from which the activation parameters in Table 1 and 2 have been calculated; the exact composition of standard solutions and rate constants for the temperature dependent kinetic analyses from which the activation parameters in Table 1 and 2 have been calculated; the change in the activation parameters from differing compositions of ionic liquid. See DOI: 10.1039/x0xx00000x

the ionic liquid anion and the π -system of the fluorodinitrobenzene **1**. An entropic benefit (a increase in the activation entropy) is consistent with organisation of the solvent around the starting materials (considered more likely than less organisation about the charge development in the transition state) and was supported by molecular dynamics simulations. When the components of the ionic liquid were varied^{15, 22} a general ionic liquid effect was observed (*i.e.* the same outcome was observed for all ionic liquids examined), with rate constant enhancement relative to ethanol again noted. Generally the same basis for rate enhancement (in terms of activation parameters) was seen.

Importantly, in these earlier studies only one composition of the reaction mixture was considered for each ionic liquid. Previous work has shown that the solvent effect of an ionic liquid can vary significantly with the proportion of the salt in the reaction mixture and that this trend differs greatly between different reaction types.^{7, 11, 16, 17, 20, 21} As such, it is clearly relevant to consider the mixture composition for this system.

In this study we markedly extend our understanding of the solvent effects of ionic liquids on this reaction through considering a range of proportions of salts in the reaction mixture. As well as demonstrating a dependence of reaction outcome on the amount of ionic liquid present not seen for previous systems, by extending the range of mixtures considered, this work elucidates the different microscopic origins for the observed solvent effects, further developing the predictive framework for the effects of ionic liquid solvents on reaction outcome.

Results and Discussion

The ionic liquids **3-7** considered in this study are shown in Figure 1. These salts are consistent with those used previously¹⁵ and represent a series containing ionic liquids with cations with varying charge localisation and accessibility.



 Figure 1. The ionic liquids examined in this study: 1-butyl-1-methylpyrrolidinium

 bis(trifluoromethanesulfonyl)imide
 ([bmpyr][N(SO2CF3)2], 3), 1-butyl-3

 methylimidazolium
 bis(trifluoromethanesulfonyl)imide
 ([bmim][N(SO2CF3)2], 4),

 1-butyl-2,3-dimethylimidazolium
 bis(trifluoromethanesulfonyl)imide
 ([bmim][N(SO2CF3)2], 4),

 1-butyl-2,3-dimethylimidazolium
 bis(trifluoromethanesulfonyl)imide
 ([bm2im][N(SO2CF3)2], 5),
 1-butyl-2,3,4,5-tetramethylimidazolium

 bis(trifluoromethanesulfonyl)imide
 ([bm4im][N(SO2CF3)2], 6), and tetraoctylammonium
 bis(trifluoromethanesulfonyl)imide

The reaction was re-examined with ethanol as the molecular solvent; previously⁹ the molecular solvent contained d_3 -acetonitrile (χ_{CD3CN} *ca*. 0.2).[‡] It had been considered that any differences in the nature of the two solvents would be small relative to any effect of the ionic liquid; such similarity in solvent effects has been seen previously for a different process with the same dependence of rate constant on mole fraction of salt in different molecular solvents.¹⁶ The reaction shown in Scheme 1 was monitored as previously⁹, ^{15, 22} using ¹⁹F NMR spectroscopy over a range of temperatures and the activation parameters determined here and previously for the molecular solvent mixtures are shown in Table 1.

Table 1 The activation parameters for the reaction between the fluorobenzene 1 and various mixtures of ethanol.

Solvent	$\chi_{ ext{etoh}}$	ΔH^{\dagger} / kJ mol ^{-1 a}	ΔS^{\dagger} / J K ⁻¹ mol ⁻¹ a
ethanol	0.98	49.0 ± 0.5	-259.0 ± 1.6
ethanol/acetonitrile ^b	0.77	48.7 ± 2.1	-249 ± 7

 a Uncertainties quoted are from the fit of the linear regression. b Data reproduced from Jones $et\,al.^9$

The activation parameters for the ethanol case (in the absence of d_3 -acetonitrile) are similar to the system containing ethanol and d_3 -acetonitrile, however, the slight differences warrant discussion. The enthalpy of activation for both molecular solvent mixtures are the same within uncertainty, suggesting that there is no difference in the relative stabilisation of the starting material and transition state between the two systems. The entropy of activation differs between the two cases, though the change is not large given the error bounds; the ethanol case has a lower (more negative) entropy of activation when compared with the ethanol and d_3 -acetonitrile case. This can be considered in two different ways; either a) with a lower (more negative) entropy of activation, there is greater ordering of the solvent around the transition state, or b) there could be less ordering of the solvent around the starting materials. Given that ethanol is more polar than acetonitrile³¹ and can readily interact with both positive and negative charges, the former seems more likely, though the difference in entropies of activation are small and the interaction is not reflected in the activation enthalpies.

Irrespective, these differences in the activation parameters for the different molecular solvent compositions make little difference to the previous arguments for the microscopic origins of the rate constant enhancements.^{9, 15, 22} In fact, the differences (including the smaller uncertainties) make the entropic origins of the solvent effects more prominent! Subsequent comparisons will be to the molecular solvent case containing only ethanol.

As introduced above, it was of interest to examine the solvent effects of ionic liquids across a wider range of solvent mixtures than previously measured. The ionic liquid [bmim][N(SO₂CF₃)₂] **4** was initially considered given the extensive work on the solvent effects of mixtures containing this salt;^{8, 9, 11, 13, 19} the kinetic analyses of the reaction shown in Scheme 1 were performed as per previous studies,^{9, 15, 22} and

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the results can be seen in the mole fraction dependence plot below (Figure 2).



Figure 2. The bimolecular rate constants for the reaction between fluorodinitrobenzene 1 and ethanol in different mole fractions of $[bmim][N(SO_2CF_3)_2]$ 4 in ethanol at 324 K. Uncertainties are reported as the standard deviation of three replicates; some fall within the size of the markers used.

As the amount of the ionic liquid [bmim][N(SO₂CF₃)₂] **4** was increased in the reaction mixture, the rate constant of the reaction shown in Scheme 1 also increased, up to a factor of 60 at the highest proportion of the salt used (χ_{IL} *ca.* 0.8). This is a large increase in rate constant on addition of an ionic liquid, compared to (for example) the 2-4-fold increase seen for bimolecular substitution reactions⁸, ¹¹ and the 8-fold enhancement observed in the case of an imine formation.¹³

Interestingly, the extent to which the rate constant changed with solvent composition becomes greater at higher proportions of the salt **4** in the reaction mixture. That is, the plot curves upward so for this S_NAr process a greater proportion of ionic liquid gives a greater rate enhancement (*i.e.* 'more is better'). This dependence on the proportion of the salt **4** in the reaction is different to what has been seen previously for other systems. For $S_N 1^{19, 21}$ and $S_N 2@P^{16, 18}$ processes the rate constant decreases on moving to high χ_{IL} in the reaction mixture while for $S_N 2^{11, 20}$ and bimolecular condensation¹³ processes the majority of the rate enhancement happens at $\chi_{IL} < 0.3$, with little effect as the amount of ionic liquid increases further.

The effect of changing the proportion of the ionic liquid in the reaction mixture on the rate constant of the reaction was then considered using the ionic liquids **3** and **5-7**, to see if changing the nature of the ionic liquid cation (charge localisation and accessibility) affected the solvent effects observed. The results are summarised in Figure 3, noting that a 'traditional' salt with a coordinating cation (lithium *bis*(trifluoromethanesulfonyl)imide), Li[N(SO₂CF₃)₂]) is included for a comparison.

All of the ionic liquids **3**, **5-7** follow the same general trend as [bmim][N(SO₂CF₃)₂] **4**; the rate constant increases with increasing proportion of the ionic liquid solvent. The relative rate constants for each of the ionic liquids at the highest mole fractions used§ are in the order [TOA][N(SO₂CF₃)₂] **7** > [bm₂im][N(SO₂CF₃)₂] **5** \approx [bm₄im][N(SO₂CF₃)₂] **6** >



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Figure 3. The bimolecular rate constants for the reaction between fluorodinitrobenzene **1** and ethanol in different mole fractions of the salts $Li[N(SO_2CF_3)_2]$ (\blacklozenge), $[bmpyr][N(SO_2CF_3)_2]$ **3** (\diamondsuit), $[bmim][N(SO_2CF_3)_2]$ **4** (\diamondsuit), $[bm_2im][N(SO_2CF_3)_2]$ **5** (\diamondsuit), $[bm_4im][N(SO_2CF_3)_2]$ **6** (\diamondsuit), $[TOA][N(SO_2CF_3)_2]$ **7** (\diamondsuit) in ethanol at 324 K. Uncertainties are reported as the standard deviation of three replicates; some fall within the size of the markers used.

 $[bmim][N(SO_2CF_3)_2] \mathbf{4} \approx [bmpyr][N(SO_2CF_3)_2] \mathbf{3}.$ It is difficult to ascertain a trend simply from these rate data; this contrasts with studies of $S_N 2^{,11, 20}_{, 20} S_N 2@P^{16, 18}$ and condensation¹³ processes where the effectiveness of the ionic liquid varied directly with the accessibility and localisation of the positive charge on the cation. Whilst in this case the ionic liquid with least coordinating cation gives the greatest rate constant change and that with the most coordinating cation gives the smallest change in the rate constant, the origin of the order of effects of the remaining salts is less clear. In the case of the lithium salt, the trend is the same as for the ionic liquids 3-7; the rate constant increases with increasing proportions of salt. The rate constant for Li[N(SO₂CF₃)₂]) at its highest mole fraction ($\chi_{\rm IL}$ *ca*. 0.15) is significantly faster than any of the ionic liquids 3-7 at similar mole fraction (over 3 times as fast as $[TOA][N(SO_2CF_3)_2]$ **7**). This effect is consistent with observations for substitution $^{\rm 14, \ 32}$ and cycloaddition processes.^{32, 33} A principle advantage of ionic liquids over 'traditional' salts remains; the proportion of salt that can be achieved in the reaction mixture is larger.

Given the above, it is clearly of interest to determine the microscopic origins of the rate constant enhancement at these higher mole fractions (χ_{1L} *ca*. 0.8§) and compare them with those obtained previously as previously (χ_{1L} *ca*. 0.5⁹). To this end, temperature dependent kinetic analyses were carried out and the activation parameters determined (Table 2).

Immediately apparent from these new data is that there is a change in the activation parameters on moving from the lower proportions of ionic liquid in the reaction mixture to the higher proportions considered here. Further, while previously the differences in activation parameters between the cases involving different ionic liquids at the lower mole fraction were small (if even measurable, given uncertainties), with the exception of the TOA salt **7**, at the higher proportions of ionic liquids the differences between their effects are more marked. These different effects can be best isolated by considering the changes in activation parameters in three categories;§ $\chi_{1L} = 0 \rightarrow 0.5$, $\chi_{1L} = 0.5 \rightarrow 0.8$.

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Table 2. The activation parameters for the reaction between the fluorobenzene 1 and ethanol in either ethanol, $Li[N(SO_2CF_3)_2]$ or one of the ionic liquids 3-7, at the specified mole fractions.

Solvent	$\chi_{\rm salt}$	ΔH^{\dagger} / kJ mol ^{-1 a}	ΔS^{\dagger} / J K ⁻¹ mol ⁻¹ a
ethanol	0	49.0 ± 0.5	-259.0 ± 1.6
$Li[N(SO_2CF_3)_2]$	0.16	54.7 ± 3.5	-208 ± 11
$[bmpyr][N(SO_2CF_3)_2]$ 3 ^b	0.51	45.7 ± 1.9	-240 ± 6
[bmim][N(SO ₂ CF ₃) ₂] 4 ^c	0.54	49.6 ± 0.5	-229 ± 2
[bm ₂ im][N(SO ₂ CF ₃) ₂] 5 ^b	0.52	49.0 ± 3.9	-223 ± 12
[bm ₄ im][N(SO ₂ CF ₃) ₂] 6 ^b	0.51	50.5 ± 1.7	-221 ± 5
[TOA][N(SO ₂ CF ₃) ₂] 7 ^b	0.32	41.0 ± 2.6	-252 ± 8
[bmpyr][N(SO ₂ CF ₃) ₂] 3	0.78	43.0 ± 2.3	-242 ± 7
[bmim][N(SO ₂ CF ₃) ₂] 4	0.79	44.6 ± 1.8	-238 ± 6
[bm ₂ im][N(SO ₂ CF ₃) ₂] 5	0.80	38.4 ± 1.9	-253 ± 6
[bm₄im][N(SO₂CF₃)₂] 6	0.79	41.0 ± 1.5	-245 ± 5
[TOA][N(SO ₂ CF ₃) ₂] 7	0.66	32.4 ± 1.0	-270 ± 3

^aUncertainties quoted are from the fit of the linear regression, ^bData reproduced from Tanner *et al*.¹² ^cData reproduced from Jones *et al*.⁹

Comparison of activation parameters from $\chi_{IL} 0 \Rightarrow 0.5$

Some of these data have been interpreted previously^{9, 15} but are summarised here to highlight changes due to using ethanol (rather than ethanol containing d_3 -acetonitrile) as the molecular solvent. Further, these arguments form the basis for understanding changes in rate constant seen at higher proportions of the salts **3-7** in the reaction mixture.

Considering the ethanol and the $[bmim][N(SO_2CF_3)_2]$ 4 cases, the enthalpies of activation are the same, which is consistent with similar interactions between the solvent and the transition state in each solvent system. The entropy of activation for the ionic liquid **4** (χ_{IL} ca. 0.5) is higher (less negative) than the ethanol case ($\chi_{IL} = 0$); suggesting that there is either less order around (more degrees of freedom about) the transition state, or more order around the starting materials compared to when ethanol was the solvent. The latter was considered more likely due to the charged nature of the components of the ionic liquid (which would be expected to order more around the charge-separated transition state) and was supported by molecular dynamics simulations⁵ showing organisation of the solvent about the benzene 1. The dominant interaction involves ordering of the ionic liquid 4 about the starting material 1; this is responsible for the observed increase in the rate constant.

The ionic liquids $[bm_2im][N(SO_2CF_3)_2]$ **5** and $[bm_4im][N(SO_2CF_3)_2]$ **6** (χ_{IL} *ca*. 0.5) behave similarly to $[bmim][N(SO_2CF_3)_2]$ **4** as solvents for the reaction shown in Scheme 1; relative to the case in ethanol, the enthalpy of activation is the same and the entropy of activation increases. The same arguments presented above suggest that organisation of the solvent about the fluorodinitrobenzene **1** is responsible for the greater rate constants seen.

For the $[bmpyr][N(SO_2CF_3)_2]$ **3** case at χ_{IL} *ca*. 0.5, both the activation parameters are different from those in ethanol. There is a decrease in the enthalpy of activation consistent with more interaction with the transition state relative to the starting material, when compared with the ethanol case; this argument is considered more likely than a decrease in

interaction with the starting materials, given the charged nature of both the solvent and the transition state. The difference between this case and the parent imidazolium system **4** is likely the extent of charge localisation on, and hence interaction with, the cation; this will be discussed further below. As above, the increase in the entropy of activation is likely due to organisation about the starting material. It is interesting to note that both enthalpic and entropic effects contribute to rate enhancement in this case.

For the ionic liquid $[TOA][N(SO_2CF_3)_2]$ 7, containing a very sterically hindered cation, the activation parameters are markedly different to the other cases. There is a large decrease in the enthalpy of activation in the [TOA][N(SO₂CF₃)₂] **7** (χ_{IL} ca. 0.3) case relative to the molecular solvent. This might be due to either less interaction with the starting materials, or greater interaction with the transition state, compared with the ethanol case. Given the extremely hindered nature of the cation, there is the potential for either or both of these effects to contribute, depending on the whether the cation or the anion is more involved in the interactions; this will be discussed further later. The entropy of activation compared to the ethanol case is the same within uncertainty.€ This similarity indicates a similar change in ordering on moving to the transition state in each of these solvent systems, in contrast to the other cases.

At this point it is worth discussing the lithium salt $Li[N(SO_2CF_3)_2]$ (χ_{salt} ca. 0.15). The activation parameters are different to those in mixtures containing one of the ionic liquids **3-7**; there is an increase in both the enthalpy and entropy of activation compared with the ethanol case. The increase in the enthalpy of activation suggests that there is greater interaction with the starting materials and the increase in the entropy of activation suggests a greater degree of ordering around the starting materials; both of these are considered more likely than the alternative involving decreased interaction with the charge separated transition state in a system containing the salt. As the lithium cation coordinates to oxygen readily³⁴ it is likely the cation is interacting with, and ordering around, the ethanol contributing markedly to the activation parameters observed.

Comparison of activation parameters from $\chi_{IL} 0 \rightarrow 0.8$

It is worthwhile comparing the activation parameters in each of the ionic liquids **3-7** at the highest mole fraction used to the ethanol case; this comparison will lead into a discussion as to the effects of changing from a 'dilute' to a 'more concentrated' ionic liquid solution.

For the cases of the ionic liquids **3**, **4** and **6** very similar trends in the activation parameters are observed. The enthalpy of activation is lower at χ_{IL} *ca*. 0.8 than the ethanol case, suggesting greater interaction with the transition state for these ionic liquids when compared with ethanol. The entropy of activation increases on moving from $\chi_{IL} = 0 \rightarrow 0.8$, likely due to ordering around the fluorodinitrobenzene **1**. Whilst theses entropic effects are smaller than between $\chi_{IL} = 0$

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and 0.5, it is interesting to note that both enthalpic and entropic effects contribute to rate enhancement.

For the ionic liquid **5** there is a decrease in the enthalpy of activation at χ_{IL} *ca*. 0.8 compared to the χ_{IL} = 0 case, while the entropy of activation is the same. These data suggest increased interactions of the solvent with the transition state compared to the ethanol case, with similar organisational changes on moving between the starting material **1** and the transition state in each solvent system. This is different to what was observed between χ_{IL} = 0 and 0.5 for the same salt.

For the $[TOA][N(SO_2CF_3)_2]$ **7** system, the enthalpy of activation is lower in the high mole fraction case than in the ethanol case ($\chi_{1L} = 0$). This change is the same direction though of greater magnitude to that observed on moving from ethanol to the case with the lower proportion of ionic liquid present, likely with similar origins. The entropy of activation is lower in the high mole fraction case than in the ethanol case ($\chi_{1L} = 0$). This entropic cost differs from the lower mole fraction case, although in both examples it is an enthalpic effect that is responsible for rate enhancement.

It is important to compare these results with the effects of ionic liquids on other S_NAr reactions. The results presented here are consistent with the outcomes of reaction of thiophene electrophiles and nitrogen nucleophiles.^{27, 28} In those cases activation parameter data indicate that at the highest mole fraction the dominant interaction is between the ionic liquid and the transition state.¥

Comparison of activation parameters from $\chi_{\rm IL}$ 0.5 \Rightarrow 0.8

In the above comparisons, for some ionic liquids, their effects do not change significantly based on the amount of ionic liquid present. In other cases, the origins of the rate enhancements are different at the two different mole fractions – this suggests that the effects of adding more ionic liquid are different depending on how much salt is already present! This is best illustrated by considering the changes in activation parameters on moving from mixtures containing $\chi_{\rm IL}$ *ca*. 0.5 to those containing $\chi_{\rm IL}$ *ca*. 0.8.

In the case of $[bmpyr][N(SO_2CF_3)_2]$ **3**; both the enthalpy and entropy of activation are the same in each of the solvent mixtures considered. While there is a difference in observed rate constants, the origin of such is not discernable given uncertainties in the activation parameters derived. Importantly however, these data show that there is little change in the behaviour of ionic liquid **3** from χ_{IL} 0.5 **+** 0.8, and the rate constant increase is due to both enthalpic and entropic considerations in each case.

The ionic liquids **4-7** all follow the same trend in activation parameters; both the enthalpy and entropy of activation decrease when moving from $\chi_{IL} ca$. 0.5 to $\chi_{IL} ca$. 0.8. These data suggest that when a greater proportion of ionic liquid is present there are more interactions with, and greater organisation about the transition state; this is considered most likely given the charged species involved. Of particular interest is that the change in the rate constant between $\chi_{IL} 0.5 \Rightarrow 0.8$ for each of the salts **4-6** is due to a decrease in the enthalpy of

activation; this is the opposite to what was observed on moving from $\chi_{\rm IL} = 0 \Rightarrow 0.5!$ Importantly, this indicates a change in the balance of the interactions responsible for the solvent effects of the ionic liquid.

Such a comparison for ionic liquid **7**, is different as initial addition of salt results in a decrease in the enthalpy of activation and no change in the entropy of activation. This suggests that the microscopic origin of this entropic cost - be it either greater ordering in the transition state or decreased ordering about the starting materials – is only significant at high proportions of the ionic liquid. Notably, a difference in the relative importance of microscopic interactions is noted and a reduction in activation enthalpy is responsible for the changes in rate constants between the two systems.

Towards predicting solvent effects - Can a trend be identified?

The above comparisons highlight that the dominant interactions resulting in the rate constant changes observed vary not only with the ionic liquid but also with the mole fraction change being considered; this is shown in Table 3. For numerical and graphical comparisons of changes in activation parameters, see ESI Table S14 and Figures S2-7.

Table 3. The activation parameters responsible for the rate constant enhancement for the reaction between the fluorobenzene 1 and ethanol in each of the ionic liquids 3-7, for the given change in mole fractions.

	χ _{IL} 0 → 0.5	χ _{IL} 0.5 → 0.8	$\chi_{\rm IL}0 \twoheadrightarrow 0.8$
[bmpyr][N(SO ₂ CF ₃) ₂] 3	ΔH^{\dagger} and ΔS^{\dagger}	- 2	ΔH^{\ddagger} and ΔS^{\ddagger}
[bmim][N(SO ₂ CF ₃) ₂] 4	ΔS^{\dagger}	ΔH^{\dagger}	ΔH^{\dagger} and ΔS^{\dagger}
[bm ₂ im][N(SO ₂ CF ₃) ₂] 5	ΔS^{\dagger}	ΔH^{\dagger}	ΔH^{\dagger}
[bm ₄ im][N(SO ₂ CF ₃) ₂] 6	ΔS^{\dagger}	ΔH^{\dagger}	ΔH^{\ddagger} and $\Delta S^{\ddagger b}$
[TOA][N(SO ₂ CF ₃) ₂] 7 §	ΔH^{\dagger}	ΔH^{\dagger}	ΔH^{\dagger}
^a There are no differences in	the activation param	neters from $\chi_{\rm IL}$ 0.5 •	→ 0.8.
^b See footnote ¢			

It is important to note that the magnitudes of the differences in activation parameters are not discussed here; a difference simply indicates whether a parameter is responsible for a rate constant enhancement. Clearly the size of these differences (and hence contributions to rate enhancements) vary; uncertainties in the activation parameter data make detailed discussion problematic.¢ However, the key point is that this analysis highlights some key trends that have the potential to be used predictively.

When interpreting Table 3 it is important to consider any organisation and interactions involving (i) components of the ionic liquid and the starting materials, and (ii) components of the ionic liquid and the transition state. the Where the change in the enthalpy of activation is responsible for the rate constant enhancement, the key interactions involve the components of the ionic liquid and the transition state. In cases where the change in the entropy of activation causes the rate constant enhancement, the principal organisation is of solvent about the starting materials. In cases where both activation parameters are listed, solvation of the transition state and the starting materials contribute to the observed rate constant changes.c

For ionic liquids **3-6**, from χ_{1L} 0 \Rightarrow 0.5, entropic contributions lead to the rate constant enhancement; the ionic liquids order around the starting materials. For salt **3**, there is also an enthalpic component leading to the rate change, suggesting the ionic liquid **3** is also interacting with the transition state. The differences between these salts suggest that interaction with the transition state is cation-dependent with a more accessible, localised charge (such as present on the cation of ionic liquid **3**) more able to interact with the transition state.

In contrast to the other cases, for ionic liquid **7** it is the enthalpy of activation that is results in the rate constant enhancement. This suggests that ionic liquid **7** has a greater interaction with the transition state than ionic liquids **3-6**. This indicates that transition state interactions cannot only involve the cation of the added salt; the sterically hindered $[TOA]^+$ cation would not be expected to interact with the transition state well but would also not be able to interact strongly with the $[N(SO_2CF_3)_2]^-$ anion, leaving it more available to interact with the transition state. As such, the interaction of the ionic liquid with the transition state must involve both the cation and the anion; there is clearly a balance between all of the interactions in solution.

As a greater proportion of ionic liquid is added to the solutions (column 3, Table 3), the enthalpy of activation is shown to be responsible for the change in rate constant for ionic liquids **4-6**. This origin is in contrast to the $\chi_{IL} \ 0 \rightarrow 0.5$ cases, and suggests that interaction with the transition state becomes more dominant for the imidazolium-based **4-6** at higher mole fractions; this change is likely due simply to the greater concentration of the ions in solution. Such interactions dominate at lower concentrations of ionic liquid **3** given the relative charge localisation and accessibility for the cation. Ionic liquid **7** with the sterically hindered $[TOA]^+$ cation has greater interaction with the transition state at higher mole fractions due to an increased concentration of the comparatively available anions present in solution.

For the ionic liquids 3-6, the overall effects on moving from $\chi_{\rm IL}$ 0 \rightarrow 0.8, are due to a balance between enthalpic and entropic contributions. This suggests that, although there are significant interactions with the transition state at higher mole fractions of these salts, any ordering about the transition state is no more than that about the starting materials. The balance between these interactions is delicate and care should be taken in interpretation given the small differences between, and the uncertainties in, the activation parameters.¢. In the case of the ionic liquid $[TOA][N(SO_2CF_3)_2]$ 7 on moving to the highest proportion used, only enthalpic effects are significant. It is interesting to note that this ionic liquid never shows significant entropic contributions to changes in rate constant. This is likely due to the sterically hindered nature of the [TOA]⁺ cation; salt 7 is unlikely to organise well around the starting materials.

From the presentation of Table 3 and the discussion above, general trends in the solvent effects of ionic liquids for this reaction are clear; at low mole fractions of salt, entropic contributions from the ionic liquid organising around the starting materials dominate and at higher mole fractions enthalpic contributions from the ionic liquid interacting with the transition state dominate. The slight deviations from the more general trends are not anomalies, rather they inform (and support!) the argument.

Organisation around the starting materials is favoured by ionic liquids with comparatively accessible and localised charges. Interactions with the transition state are both cation and anion dependent. That means that a more chargelocalised and accessible cation will interact with the transition state more than one that is sterically hindered. However at the same time, the more accessible an anion is, the greater extent to which it will interact with the transition state. This again results in a delicate balance; the more sterically hindered a cation of the ionic liquid is, the less the cation will interact with the transition state but the more the anion will interact with the transition state and *vice versa*.

Experimental

1-Fluoro-2,4-dinitrobenzene 1 was commercially available and was used without further purification. Ethanol and triethylamine were purified according to literature procedures³⁵ and stored over activated molecular sieves until use. The ionic liquids 3-6 were prepared with reference to literature methods,^{36, 37} alkylation of the corresponding imidazole or pyrrolidine formed the intermediate halide salt, then anion metathesis with lithium bis(trifluoromethanesulfonyl)imide formed the required ionic liquids. The ionic liquid 7 was prepared from the corresponding commercially available bromide.³⁸ All ionic liquids were dried under reduced pressure (<0.1 mbar) for at least 3 hours and were found to have <100 ppm water using Karl Fischer titration methodology and contained <0.4 mol% residual halide by ion chromatography. For full details of the preparation, see ESI.

¹⁹F NMR kinetic experiments were carried out on either a Bruker Avance III 400, or Bruker Avance 600 spectrometer with a BBFO probe using *ca*. 0.5 mL of reaction mixture in a 5 mm NMR tube. Results were shown to be reproducible between the spectrometers.

Kinetic analyses for the reaction were carried out in two different ways. For studies investigating the mole fraction dependence of the ionic liquids **3-7** on reaction outcome, the reaction was carried out in solutions containing fluorodinitrobenzene **1** (*ca.* 0.03 mol L⁻¹), triethylamine (*ca.* 0.35 mol L⁻¹) and ethanol (0.5 to 16 mol L⁻¹ depending on the reaction mixture) at 324 K; see ESI (Tables S1-6) for more details. For the temperature dependence studies the reaction was carried out in solutions containing fluorodinitrobenzene **1** (*ca.* 0.35 mol L⁻¹); triethylamine (*ca.* 0.35 mol L⁻¹); the temperature dapendence studies the reaction was carried out in solutions containing fluorodinitrobenzene **1** (*ca.* 0.03 mol L⁻¹); the temperature range used was 304-334 K; see ESI (Tables S7-13) for more details. In all cases the reaction was monitored *in situ* with the spectrometer set to the desired temperature for the duration of the reaction.

All reactions were followed until more than 95% of the starting material **1** was consumed, and all kinetic analyses were performed in triplicate. NMR spectra were processed

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using either MestReNova 10.0.2 or Bruker Topspin 3.5pl5 software. The pseudo-first order rate constants for the reactions were calculated using the integration of the signal due to the starting material **1** at δ ca. -110, by linear fitting of the natural logarithm of the integrations using the Microsoft Excel 14.4.3 LINEST function. Bimolecular rate constants were obtained from the pseudo-first order constants by dividing by the initial nucleophile concentration in the reaction mixture. The activation parameters were then determined through fitting the obtained data using the Microsoft Excel 14.7.0 LINEST function to the bimolecular Eyring equation.^{8, 39} Tables containing the kinetic data for all of the systems described can be found in the ESI, as can the plot from which the activation parameters were obtained.

Conclusions

The effect of a series of ionic liquids on a nucleophilic aromatic substitution reaction was investigated and the microscopic origins of these effects were deduced. The dependence of the rate constant on the proportion of ionic liquid in the mixture was determined and a novel motif was discovered; the more ionic liquid present in the reaction mixture, the larger the rate constant. At the highest mole fraction for all ionic liquids the rate constant enhancement for this reaction was at least 60 times that in the molecular solvent, the largest enhancement observed for reactions with a similar mechanism. This mole fraction dependence is important as it demonstrates the first case where addition of the maximum amount of ionic liquid is advantageous for reaction outcome.

The microscopic origins for the rate enhancement were determined for this reaction at the highest mole fraction of each of the ionic liquids used and these data were compared to previous results at a lower mole fraction. At higher mole fractions there is a change in the microscopic origins of the rate constant enhancements; at lower proportions of salt present entropic contributions dominate whilst at higher proportions the rate enhancement is the result of enthalpic effects. It is the balance between these two effects that determines how effective an ionic liquid will be as a solvent for this reaction.

A method of analysis for the activation parameters was presented in a way that allows for easy prediction of an ionic liquid's effect as a solvent for this type of reaction. This allows for ionic liquid solvents to be designed and rationally chosen for this type of nucleophilic aromatic substitution reaction. The general trends presented here allow for greater understanding and predictability of the effect of using an ionic liquid solvent on this S_NAr reaction. This understanding will allow ionic liquids to be designed for this reaction to exploit the favourable interactions and lead to ionic liquid solvents being rationally selected for this reaction.

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Notes and references

‡ A small amount of deuterated solvent was added to facilitate acquisition of NMR spectra.

§ The largest proportion of the salt **7** used was less than for the others; this TOA derivative has a large molecular weight and solutions containing $\chi_{IL} > 0.65$ could not be prepared. Similarly, in the case of the lithium *bis*(trifluoromethanesulfonyl)imide, the highest proportion of salt that could be reached was $\chi_{salt} = 0.20$. All comparisons with the other systems (where greater proportions of the ionic liquids can be put in the reaction mixture) are made with this in mind. Given the trend in all mole fraction dependencies of rate constant, this is considered reasonable.

€ Whilst the large uncertainty in the entropy for the TOA derivative 7 contributes to this, even taking this into account, the activation entropy is markedly different to the ionic liquid cases **4-6**.

 \pm Only the thiophene cases are commented upon here as activation parameter data is not reported in the other cases. $^{23-26}$

¢ Given the uncertainties in the observed activation parameters, generally the contributions to the activation energy $(T\Delta S^{\dagger} \text{ and } \Delta H^{\dagger})$ were the same. The exception was the salt **6** from $\chi_{IL} \ 0 \rightarrow 0.8$, where the enthalpic contribution dominated.

\$ In these discussions, it is the dominant interaction/organisation that is being mentioned. The ionic liquid will interact with and order around all the species along the reaction coordinate, however the rate enhancements come from the dominant interactions.

£ Also necessary to note are the interactions between components of the ionic liquids.

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