

A GENUINELY MULTIDISCIPLINARY JOURNAL

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Accepted Article

Title: Ionic liquids as solvents for SN2 processes. Demonstration of the complex interplay of interactions resulting in the observed solvent effects

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This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: ChemPlusChem 10.1002/cplu.201800510

Link to VoR: http://dx.doi.org/10.1002/cplu.201800510



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lonic liquids as solvents for $S_N 2$ processes. Demonstration of the complex interplay of interactions resulting in the observed solvent effects

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Abstract: Bimolecular nucleophilic substitution reactions between triphenylphosphine and benzylic electrophiles have been examined in an ionic liquid to probe interactions with species along the reaction coordinate. Trends in the rate constant were found on both varying the leaving group and the electronic nature of the aromatic ring. In all of the cases considered, interactions between the components of the ionic liquid and the transition state were shown to be more significant in determining reaction outcome than previously observed for this class of reaction. This demonstrates the importance of considering interactions of the ionic liquid components with all species along the reaction coordinate when investigating the origin of ionic liquid solvent effects, along with how such effects might be exploited.

Introduction

lonic liquids are defined as salts with melting points below 100 °C,^[1] with their low melting points frequently due to the bulky, asymmetric and charge diffuse nature of the constituent ions. Being a solvent composed of charged species, ionic liquids have negligible vapour pressures and low flammability, compared to organic solvents,^[1a, 1c, 2] thus making them 'safer'^[3] and 'greener'.^[2, 4] There are a plethora of cation and anion combinations possible, resulting in ionic liquids with a wide range of physicochemical properties,^[2, 4b, 5] for this reason, they are often described as 'designer solvents'.^[2, 4b, 6]

Given the potential benefits, ionic liquids have been considered for a broad variety of applications; these range from biomass pretreatment^[7] through energy storage^[8] and batteries^[9] to biomedical applications^[10] and separation technologies.^[11] In all of these cases, along with analyses of potential impacts of these salts on the environment,^[12] a key feature is the ability to choose an ionic liquid with the properties appropriate for the application. If ionic liquids are to be used as solvents for preparative chemistry, the equivalent understanding is required in terms of choosing the appropriate ionic liquid to get the desired reaction outcome.

lonic liquids have been considered as solvents for a wide variety of reaction types and the potential extension of 'solvent design' has been shown in some cases where reaction outcome can be manipulated depending upon the ionic liquid used.^[13] However, such reaction control is typically observed rather than planned on a rational basis; the application of ionic liquids as

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solvents for synthetic purposes is hindered by the lack of a general understanding as to how ionic liquids affect reaction outcome compared to conventional organic solvents.^[14]

Given this current limitation to the application of these solvents, there has been a recent focus on quantitatively analysing ionic liquid solvent effects on well-known reactions. Particularly, detailed kinetic analyses and determination of the microscopic interactions that are responsible for ionic liquid solvent effects^[15] have paved the way for initial design of solvents in efforts to control reaction outcome.^[16] An example of the latter was a study focussing on the bimolecular nucleophilic substitution reaction $(S_N 2)$ between pyridine 1 and benzyl bromide 2d (Scheme 1).^[17] For this process, the bimolecular rate constant (k_2) increased with the amount of the representative ionic 1-butyl-3-methylimidazolium liquid bis(trifluoromethanesulfonyl)imide ([Bmim][N(SO₂CF₃)₂], 4) present in the reaction mixture, with the rate constant enhancement due to an entropically favourable interaction between the cation of the ionic liquid 4 and the lone pair of pyridine 1.^[17-18] Understanding this interaction allowed a degree of control of reaction outcome through rational selection of the components of the ionic liquid for this^[19] and related nucleophilic processes.^[20] It should be noted that in related systems involving an imidazole as the nucleophile, there the authors focused primarily on ionic liquid-transition state interactions being responsible for the ionic liquid solvent effect observed, though no activation parameter data was presented.^[21]



Scheme 1. The bimolecular nucleophilic substitution reaction between pyridine 1 and benzyl bromide **2d** to give the pyridinium salt **3**, which has been examined in reaction mixtures containing the ionic liquid **4**.^[17-18]

It is of interest to extend this understanding to other nucleophilic centres. For the reaction between triphenylphosphine **5** and each of the benzyl halides **2d** and **6d** (Scheme 2), it was shown that there was a markedly different effect of the salt **4** on reaction outcome depending on the nature of the leaving group; in the case of the bromide **2d**, there was an initial increase in the rate constant on addition of ionic liquid **4**, followed by a decrease and subsequent increase as more salt was added.^[18b] This effect of the leaving group was not observed for the equivalent reactions involving pyridine **1**. Importantly, these studies suggest that there are additional interactions between the ionic liquid **4** and species along the reaction coordinate in cases involving phosphorus nucleophiles that are not present in the



Scheme 2. The bimolecular nucleophilic substitution reaction between triphenylphosphine **5** and each of the benzyl derivatives **2**, **6-8** to give the corresponding salts **9-12**, which have been examined in reaction mixtures containing the ionic liquid **4** (**a** R = 3,5-Me-4-MeO, **b** R = MeO, **c** R = Me, **d** R = H, **e** R = Br, **f** R = CF₃, **g** R = NO₂).

pyridine **1** case. These additional interactions compete with the previously noted interaction between the cation of the ionic liquid **4** and the nucleophile,^[18a] resulting in the difference in mole fraction dependence of reaction outcome.

The work described herein focuses on elucidating these additional interactions, through investigating further how varying the electrophile varies the ionic liquid solvent effect observed in these S_N2 processes. The reactions considered are between triphenylphosphine **5** and each of a range of benzyl derivatives with different substituents and differing substituents on the aromatic ring (Scheme 2) in the well described ionic liquid **4**. The use of this ionic liquid allows direct comparison to previous work, though it is noted that changing the components of the ionic liquid would also affect the interactions being considered; for example, related studies on the reaction in Scheme 1 have suggested increased interactions with the transition state in salts containing more coordinating anions.^[22]

Results and Discussion

Effect of varying the leaving group on the electrophile

Initial focus was on extending the series that began with the reactions of triphenylphosphine 5 with each of the halides 2d and 6d.[18b] To do so, the iodide 7d and the acetate 8d were considered. The iodide 7d forms a series with the halides 2d and 6d, whilst the acetate 8d has a poor, though charge diffuse, leaving group compared to, say, chloride.^[14] The solvent effects of the salt 4 on the reaction of triphenylphosphine 5 with electrophiles 7d and 8d were initially examined by determining the bimolecular rate constant (k_2) for the reaction over a range of solvent compositions of [Bmim][N(SO₂CF₃)₂] 4 in acetonitrile. These rate data are presented in Figure 1, having been normalized to the value for the rate constant in acetonitrile to allow comparison (equivalent plots for the absolute rate data are available in the Supporting Information). It should be noted that the order of the reactivity in acetonitrile is as would be expected (8d < 6d < 2d < 7d).

Immediately apparent is that the effect of the salt **4** on the reactions of species **7d** and **8d** is different to that observed previously with the same nucleophile.^[18b] There is a general decrease in the bimolecular rate constant (k_2) for the reaction of both these electrophiles with triphenylphosphine **5** as the amount of the ionic liquid **4** in the reaction mixture increases.



Figure 1. The normalised bimolecular rate constants (k_2), relative to the acetonitrile, for the reactions between triphenylphosphine **5** and either benzyl iodide **7d** (purple) or benzyl acetate **8d** (green) in different proportions of the ionic liquid [Bmim][N(SO₂CF₃)₂] **4** in acetonitrile. Reported uncertainties are the standard deviation of triplicate results compounded by division, some uncertainties fall within the size of the markers used.

While the shape of the plots are slightly different (the greatest change occurs at low proportions of salt 4 in the acetate 8d case, compared to a more linear trend for the iodide 7d) and the extent of the rate constant decrease also varies (ca. 30% for the iodide 7d and ca. 90% for the acetate 8d), these differences are small when compared to the equivalent solvent effects for reactions involving the halides 2d and 6d; in those cases, only rate constant enhancements were observed.^[23] (A normalized plot showing the effects of the salt on reactions of all of the benzyl derivatives 2d, 6d, 7d and 8d is given in the Supporting Information, Figure S1.) This trend in the ionic liquid solvent effect on related S_N2 processes involving nitrogen nucleophiles has been observed with different benzyl halides used as the electrophiles.^[17, 21a] In those studies, in the presence of an ionic liquid reaction with benzyl iodide generally led to a decrease in the rate constant of the reaction, the benzyl chlorides always resulted in a rate enhancement and benzyl bromides yielded comparable (if slightly higher) rate constants relative to the molecular solvent, though it should be noted that only one solvent composition was considered in these cases.

it is worth noting the Before continuing, that physicochemical properties of the mixture will change dramatically across the range of solvent compositions used, and such changes must be considered. For example, while the viscosity of the mixture will change, and as a result diffusion of solutes will change,^[24] the reactions are not under diffusion control so this does not affect the rate constants. Likewise, the apparent polarity (based on interactions with a given probe molecule) of the mixture would be expected to change, though not greatly given the similar polarity measurements of acetonitrile and the salt 4;[25] importantly, other solute-solvent interactions would be expected to change and might be expected to dominate in terms of solvent effects.^[26] As such, it is perhaps not surprising that it is difficult to ascribe the observed rate constant changes here (and $earlier^{[18b]}\!)$ to changes in polarity of the medium and that interactions between the solute and the species along the reaction coordinate need to

Table 1. Activation parameters for the reaction between triphenylphosphine 5 and each of the benzyl	derivatives 2d, 6d, 7d and 8d in mixtures of
[Bmim][N(SO ₂ CF ₃) ₂] 4 in acetonitrile at the mole fraction specified	

Electrophile	Acetonitrile ($\chi_4 = 0$)		Intermediate proportion of salt 4			High proportion of salt 4		
	ΔH^{\ddagger} / kJ mol ^{-1 [a]}	$\Delta \text{S}^{\ddagger}$ / J K $^{-1}$ mol $^{-1}$ $^{[a]}$	X4	ΔH^{\ddagger} / kJ mol ^{-1 [a]}	$\Delta \textbf{S}^{\ddagger}$ / J \textbf{K}^{-1} mol $^{-1}$ [a]	χ4	ΔH^{\ddagger} / kJ mol ^{-1 [a]}	$\Delta S^{\ddagger} / J K^{-1} mol^{-1} [a]$
6d ^{ib}	51.7 ± 1.9	-237.9 ± 5.5	0.20	59.7 ±1.5	-201.3 ± 4.4	0.78	60.3 ± 1.9	-197.2 ± 5.8
$2d^{[b]}$	44.8 ± 3.7	-210 ± 13	0.36	57.1 ±1.5	-163.1 ± 5.1	0.93	57.2 ± 1.5	-162.8 ± 5.3
7d	52.5 ± 1.1	-160.3 ± 3.9	0.30	41.9 ±1.7	-203.2 ± 6.1	0.96	47.0 ± 2.0	-189.6 ± 6.9
8d	71.7 ± 2.6	-206.4 ± 7.9	0.29	43.4 ± 3.7	-300 ± 11	0.90	38.0 ± 2.9	-325.2 ± 8.7

[a] Errors reported are from the fit of the linear regression. [b] Data reproduced from Schaffarczyk McHale et al.[186]

be considered. Further, whilst changes in the nanostructure of these solvent have been reported on changing solvent composition, in related bimolecular condensation reactions nanodomains of the solvent did not significantly affect reaction outcome and consideration of interactions involving components of the ionic liquid are more important.^[27]

Whilst previously the interactions of the cation of the salt **4** with the nucleophile has been used to explain (at least in part) changes in rate constant for reactions involving both pyridine $\mathbf{1}^{[17-18]}$ and triphenylphosphine $\mathbf{5}$,^[18b] these interactions cannot be dominant in the work described here since the observed rate constant effect is different. The leaving group ability of the benzyl substituent also cannot be solely responsible; the best (iodide) and worst (acetate) give the same effect. It is perhaps useful rather to consider the nature of the charge development in the transition state (Figure 2); chloride would be the 'hardest' or most charge dense leaving group, iodide and acetate being the 'softest' or most charge diffuse, and bromide sits somewhere in between.^[14] Such differences might be expected to affect interactions with the components of the ionic liquid **4**, and hence affect reaction outcome.



Figure 2. The transition state for the reaction shown in Scheme 2 – sites of charge development represent key sites for potential interaction with the ionic liquid **4**. Note that this representation is general; the extent of charge development along with the extent to which bond breakage and bond cleavage occur (and whether it is symmetrical) will depend on the nature of the reacting species.

In order to further elucidate the trends in rate constant seen on changing solvent composition, temperature dependent kinetic studies were undertaken and rate constants determined at key solvent compositions; acetonitrile ($\chi_4 = 0$), an intermediate solvent composition by which the majority of the rate decrease had occurred (χ_4 *ca.* 0.3), and 'neat' ionic liquid (χ_4 *ca.* 0.9, where the ionic liquid is diluted by reagents only). Using an Eyring plot (see Figures S15 and S17, Supporting Information) the activation parameters for the reactions of triphenylphosphine **5** with each of the electrophiles **7d** and **8d** were determined for each solvent system specified; these data are presented in Table 1, with previously reported data for reactions involving the halides **2d** and **6d** included for comparison.^[18b]

The activation parameters for reaction of each of the species **7d** and **8d** with triphenylphosphine in acetonitrile were as would be expected. The values for case **7d** are similar to the other halide cases considered, with a balance of enthalpic and entropic effects being responsible for the order of rate constants observed in molecular solvent. The enthalpy of activation for reaction of the acetate **8d** with nucleophile **5** is notably larger than the other cases considered, accounting for the significant rate constant decrease observed in that case.

For both the iodide **7d** and the acetate **8d** cases, addition of the ionic liquid **4** results in a decrease in both of the activation parameters of the reaction with triphenylphosphine **5** compared to the acetonitrile case (irrespective of the amount of salt **4** added). That is, the rate constant for the reaction decreases on addition of the ionic liquid **4** are the result of an entropic cost outweighing an enthalpic benefit. This outcome is different to that observed in the cases of the chloride **6d** and the bromide **2d**, where rate constant increases were the result of a dominant beneficial entropic effect;^[18b] these data were consistent with the pyridine **1** case^[17] and suggest interactions between reagents and the salt **4**.^[18a]

A decrease in both activation parameters for reactions involving the iodide **7d** and the acetate **8d** could be due to the dominant interactions involving either stabilisation of, and organisation about, the transition state complex or a destabilisation of, and lesser organisation about, the reagents, in the ionic liquid **4** than in the acetonitrile. The former argument is considered more likely given the charge development in the

transition state (Figure 2) and the potential for either the cation or the anion of the ionic liquid to interact with that charge development.[28] Considering the interactions implicit from activation parameters for the bromide 2d and chloride 6d cases^[18b] adds further weight to this argument. Significantly, the dominance of these interactions (which have been demonstrated by the difference in effects of the salt in the bromide 2d and chloride **6d** cases) is novel for an $S_N 2$ process with a neutral nucleophile, though some previous studies have suggested similar interactions result in rate constant enhancement.[21] Rather, such activation parameter changes have been seen before for S_N1 processes where a greater degree of charge development in the transition state would be expected.^[29] For the reactions studied here these results demonstrate that such transition state-ionic liquid interactions must be taken into account when considering solvent effects in these systems before using ionic liquids to promote the rate of reaction in a synthetic scenario.

The changes in activation parameters on moving from a low proportion of salt **4** in the reaction mixture to $[Bmim][N(SO_2CF_3)_2]$ **4** diluted only by reagents are small (if measurable) for the electrophiles **7d** and **8d**. This small change suggests only a slight change in the balance of the interactions responsible for the solvent effect of the ionic liquid **4** once a given proportion of salt had been added, despite the changes in rate constant that are observed.^[30]

It is worth briefly returning to a comment earlier regards the nature of the leaving group; differences in the degree of change density on the leaving group, might be expected to affect interactions with the components of the ionic liquid 4, and hence affect reaction outcome. The trends observed in the activation parameters support this argument, with the most charge diffuse systems (the iodide 7d and acetate 8d cases) showing the proposed transition state - ionic liquid interaction dominating, the comparatively charge dense chloride 6d case being dominated by ionic liquid - nucleophile interactions and the benzyl bromide case 2d being the intermediate example where both interactions contribute significantly. Importantly, this suggests that a charge diffuse transition state is beneficial for ionic liquid - transition state interactions, though these interactions might not necessarily result in an improvement in reaction outcome. In fact, ionic liquid solvents should only be considered in cases where such interactions might be expected to be limited.

Effect of varying the sigma donating ability on the electrophile

In order to further understand how variation of the electronics of the electrophile affects ionic liquid solvent effects, the reactions of triphenylphosphine **5** with each of the benzyl bromides **2a-c,eg** across a range of solvent compositions of the salt **4** were considered. The substituents on the phenyl ring in the electrophiles **2a-g** cover a wide range of electronic properties (as assessed by, for example, Hammett σ values^[31]) and thus might be expected to systematically vary the extent of charge development in the transition state of these reactions. The plots of rate constant against the proportion of the salt **4** in the reaction mixture for the substrates **2a-c,e-g** are presented as Figures S8-S13, Supporting Informattion. In order to allow viewing of all of the rate data together, they are presented in Figure 3 having been normalized to the value for the rate constant in acetonitrile.



Figure 3. The normalised bimolecular rate constants (k_2) for the reaction between triphenylphosphine **5** and each of the benzyl bromides **2a-g** (light blue **2a**, red **2b**, blue **2c**, green **2d**, orange **2e** and purple **2f**, pink **2g**) in different proportions of the ionic liquid [Bmim][N(SO₂CF₃)₂] **4** in acetonitrile at 24.4 °C. Reported uncertainties are propagated from the standard deviation of triplicate results and some fall within the size of the markers used.

While the shapes of these plots varied slightly with the substrate 2, there was typically a rate constant increase for each of the reactions considered except the nitro case 2g (discussed further below) with the amount of the ionic liquid 4 present. Further, in general, the magnitude of the rate constant enhancement varied with the electronic nature of the substituent; it was greater for electron donating substituents and less for electron withdrawing substituents.^[32] The exception is the bromide 2a, which has three electron donating groups but shows rate constant enhancements comparable to the protio 2d and bromide 2e cases across the range of mole fractions of the salt 4 considered. This comparison, along with the relative rate constants for the reactions in acetonitrile, suggests that the effects of the substituents are not simply additive in this case.^[33] Irrespective, in this case, practical use of an ionic liquid might be evaluated simply in terms of the electronic nature of the phenyl group with electron rich systems gaining the most benefit.

These changes in rate constant enhancement are consistent with what has been observed previously in reactions of pyridine **1** with substituted benzyl bromides (albeit studied at only one proportion of ionic liquid in the reaction mixture); the greatest rate constant enhancements were seen with electron donating groups.^[17] The same trends have been seen in the reaction of *N*-methylimidazole with benzyl chlorides, once again studied at only one proportion of ionic liquid in the reaction mixture.^[21a] Each of these reports also used Hammett analysis to compare the nature of the transition state for different substrates. Equivalent analyses were carried out for each composition of the reaction mixture (see Figures S23-S31, Supporting Information) at the two solvation extremes shown in Figure 4.

The curved nature of the plots shown in Figure 4 (and in Figures S23-S31) is consistent with that seen previously^[17, 21a]





Figure 4. Hammett plots constructed from the relative rate data obtained for the bimolecular nucleophilic substitution reaction between triphenylphosphine **5** and each of the benzyl bromides **2b-g** carried out in acetonitrile (blue, $\chi_x 0$) and [Bmim][N(SO₂CF₃] **4** (red, χ_4 ca. 0.95). Uncertainties are propagated from the standard deviation of triplicate results for the k_2 values obtained. Some uncertainties fall within the size of the markers.

and can be ascribed to the change from an 'open' or 'loose' transition state for electron donating groups to a 'closed' or 'tight' transition state for electron withdrawing groups. In general, on increasing the proportion of the ionic liquid **4** in the reaction mixture, the proportion of the plot that has a large slope increases, consistent with a greater degree of charge development being favoured by the salt **4**. This is exemplified in Figure **4**, noting the large uncertainties as a result of compounding errors and the logarithmic scale.^[34]

It should be noted that during this analysis, the nitro case **2g** was a particular outlier, being faster than might be expected at low proportions of the salt **4** in the reaction mixture. It was considered that alternative mechanisms may also be contributing, likely a radical mechanism based on literature precedent^[35] as well as EPR studies (Figure S34).^[36] As such, it was not considered during subsequent analysis.

All of the above analyses indicate that changing the nature of the substituent on the phenyl ring changes the ionic liquid effects on the substitution process. Once again, in order to determine the microscopic origins of these effects, temperature dependent kinetic studies were undertaken at the same compositions of the reaction mixture considered above ($\chi_4 = 0$, ca. 0.3 and ca. 0.9, where the ionic liquid is diluted by reagents only). From these studies Eyring plots were constructed (Figures S19-S22) and the activation parameters determined for each solvent system (Table S25); while the absolute activation parameters are necessary, it is the changes in these parameters on changing the solvent composition that requires discussion and these are presented in Table 2. Importantly, the activation parameter responsible for the rate constant change has been highlighted where it is clear. It should be noted that the given the similarity in rate constants observed across the range of solvent compositions for reactions involving species 2e,f, activation parameters were determined only at the extreme solvent compositions (and these were found to be virtually identical).^[37] Immediately apparent from the data in Table 2 is

Table 2. Changes in activation parameters for the reaction between triphenylphosphine **5** and each of the benzyl derivatives **2b-f** in mixtures of [Bmim][N(SO₂CF₃)₂] **4** in acetonitrile between the mole fractions specified. Changes in activation enthalpy are given in kJ mol⁻¹, changes in activation entropy are given in J K⁻¹ mol⁻¹. Parameters highlighted in red are responsible for the rate constant changes seen.

Reagent	Change in <i>χ</i> ₄ 0 → 0.3	Change in <i>χ</i> ₄ 0.3 → 0.9	Change in χ_4 0 \rightarrow 0.9
2b	$\Delta(\Delta H^{\ddagger}) = -2.4 \pm 3.2$ $\Delta(\Delta S^{\ddagger}) = -1 \pm 10$	$\Delta(\Delta H^{\ddagger}) = 9.8 \pm 2.9$ $\Delta(\Delta S^{\ddagger}) = 31 \pm 9$	$\Delta(\Delta H^{\ddagger}) = 7.4 \pm 3.5$ $\Delta(\Delta S^{\ddagger}) = 30 \pm 12$
2c	$\Delta(\Delta H^{\ddagger}) = 5.2 \pm 1.3$ $\Delta(\Delta S^{\ddagger}) = 23 \pm 4$	$\Delta(\Delta H^{\ddagger}) = -2.6 \pm 1.9$ $\Delta(\Delta S^{\ddagger}) = -9.4 \pm 5.9$	$\Delta(\Delta H^{\ddagger}) = 2.6 \pm 1.8$ $\Delta(\Delta S^{\ddagger}) = 14 \pm 6$
2d ^[b]	$\Delta(\Delta H^{\ddagger}) = 12 \pm 4$ $\Delta(\Delta S^{\ddagger}) = 47 \pm 14$	$\Delta(\Delta H^{\ddagger}) = 0.1 \pm 2.1$ $\Delta(\Delta S^{\ddagger}) = 0.3 \pm 7.9$	$\Delta(\Delta H^{\ddagger}) = 12 \pm 4$ $\Delta(\Delta S^{\ddagger}) = 47 \pm 14$
2e	_(c)	_[c]	$ \Delta(\Delta H^{\ddagger}) = -2.1 \pm 3.2 \Delta(\Delta S^{\ddagger}) = -9 \pm 11 $
2f	_[C]	_[c]	$\Delta(\Delta H^{\ddagger}) = 1.9 \pm 2.1$ $\Delta(\Delta S^{\ddagger}) = 8.3 \pm 7.1$

[a] Errors reported are compounded from the fit of the linear regression. [b] Calculated based on data from Schaffarczyk McHale *et al.*^[160] [c] As discussed in text, activation parameters were not determined at intermediate proportions of the salt **4** in the reaction mixture.

that the rate constant change seen for the reaction of triphenylphosphine **5** with each of the species **2b-f** is, where measurable, due to an increase in the entropy of activation. This outcome suggests that the dominant interaction involving the ionic liquid is with a starting material, likely the nucleophile **5** based on previous studies. Several things must be noted however.

The proportion of the ionic liquid 4 in the reaction mixture required to see the dominant interaction varies; it is clearly observable by χ_4 ca. 0.3 in the case of substrates **2c,d** but not in the case of substrate 2b. This result suggests that other interactions, likely with the transition state, are significant at low proportions of salt 4 in the reaction mixture in the latter case, consistent with a greater degree of charge development in (and perhaps the more 'open' nature of) the transition state in that Immediately related to this is that ionic liquid example. transition state interactions are more significant at the higher proportions of the salt 4 in the reaction mixture for cases 2c and 2d. The former case is shown here with negative changes in the activation parameters on going from $\chi_4 = 0.3 \Rightarrow \chi_4 = 0.9$; the case of the protio example 2d is more complex though has been discussed extensively previously.^[18b] Irrespective, the presence of ionic liquid - transition state interactions, their balance with ionic liquid - starting material interactions and the importance of the amount of salt 4 required for them to be observed, is highlighted.

Unlike the changes seen when the leaving group on the electrophile was changed, no case is seen where interactions between the transition state and the ionic liquid dominate (as interpreted by decreases in the activation parameters). It is worth noting that changes in these parameters are very small (if

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measurable) in the cases of the electron withdrawing substituents bromo and trifluoromethyl on the phenyl ring (reagents **2e** and **2f**, respectively), suggesting that transition state interactions might be more significant in these cases though it is not clear how these cases (which are the 'closed' or 'tight' transition state) necessarily correlate with the charge diffuse nature of the leaving group in the iodide **7d** and acetate **7d** cases. Once again though, the importance of interactions involving the components of the ionic liquid **4** and the transition state is demonstrated and merits consideration when using ionic liquids as solvents for this reaction and others where these types of interactions are also present.

Conclusions

The work described has shown that on varying the nature of the electrophile in a bimolecular substitution process, that the solvent effects of an ionic liquid change. All of the kinetic analyses presented show that these changes in ionic liquid solvent effects are due to the extent of interaction of the components of the ionic liquid with the transition state of the process. While suggested previously for related systems, this work represents the first time for bimolecular substitution processes that such interactions have been shown to be dominant (for example, in the iodide **7d** and acetate **8d** cases) and in which the proportion of the salt **4** present could be related to the balance of interactions.

This observation^[38] of the importance of ionic liquid – transition state interactions is significant as any design of ionic liquids to control reaction outcome in cases such as those demonstrated must take these interactions into account; this is in contrast to previous examples where only the interaction of the cation of the ionic liquid with the nucleophile was considered.^[16b] Rather, studies need to consider both components of the ionic liquid and both interactions, akin to studies on the S_NAr reaction reported recently.^[16a, 39] This being said, there remains ample opportunity for the design of ionic liquids to control these interactions and hence reaction outcome.

Experimental Section

Triphenylphosphine **5** was recrystallized from acetonitrile.^[40] Benzyl bromides **2c-g** were commercially available and were used without further purification. Benzyl bromides **2a**^[41],**b**^[42], benzyl iodides **7c**, **7d** and **7g**,^[43] and benzyl acetate **8d**^[44] were synthesised through modified literature procedures, details of which can be found in the Supporting Information. The ionic liquid [Bmim][N(SO₂CF₃)₂] **4** was prepared according to literature methods;^[45] 1-bromobutane was added to 1-methylimidazole to yield the bromide salt precursor which was then treated with lithium *bis*(trifluoromethanesulfonyl)imide through a salt metathesis reaction to yield [Bmim][N(SO₂CF₃)] **4**. Before use, the ionic liquid **4** was dried under reduced pressure (< 0.1 mbar) at room temperature and was found to contain < 200 ppm water using Karl Fischer titrimetry. Ion chromatography showed < 1% bromide content, confirming the absence of the bromide salt precursor. Full details for this preparation can be found in the Supporting Information.

Reaction mixtures for the kinetic studies contained triphenylphosphine 5 and at least a ten-fold excess of the electrophile at a given proportion of the ionic liquid 4, with the remainder of the solvent being acetonitrile. The reaction progress was monitored using $^{31}\text{P}\{^{1}\text{H}\}$ NMR spectroscopy following the signal corresponding to the starting material, triphenylphosphine 5 at δ ca. -5. This allowed determination of k_{obs} for the reaction, with k_2 obtained using the known concentration of the reagent in excess, the electrophile. These reactions were either monitored in situ whereby the reaction was followed until > 95% completion or by initial rates methodology where signals corresponding to both reagent and product are monitored, with appropriate t₁ times, until 7-10% completion. The reactions were monitored using either a Burker Avance III 400 or Burker Avance III 500 spectrometer equipped with either a TBI or BBFO probe using ca. 0.5 mL of the reaction mixture in a 5 mm NMR tube. Results were shown to be reproducible between different probes and spectrometers. Activation parameters, where they appear, were determined in a similar manner to that described above except that the bimolecular rate constants were determined at four temperatures across a range of at least 30 °C and then fitted to the bimolecular Eyring equation.[46

Further details for all of the kinetic analyses as well as the temperatures, rate constants, and compositions of the stock solutions (masses, concentrations of electrophile, mole fraction of ionic liquid) for each system studied can be found in the Supporting Information.

Acknowledgements

JBH acknowledges financial support from the Australian Research Council Discovery Project Funding Scheme (Projects DP130102331, DP180103682). KSSM acknowledges the support of the Australian government through the receipt of an Research Training Programme Stipend. The authors would like to acknowledge the NMR Facility within the Mark Wainwright Analytical Centre at the University of New South Wales for NMR support.

Keywords: bimolecular substitution • Hammett plot • ionic liquids • kinetics • solvent effects

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Entry for the Table of Contents

FULL PAPER

The interactions responsible for ionic liquid effects vary with the amount of ionic liquid in the reaction mixture, as does the microscopic origin of the effects observed.



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lonic liquids as solvents for $S_N 2$ processes. Demonstration of the complex interplay of interactions resulting in the observed solvent effects