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Controlling Hydrolysis Reaction Rates with Binary Ionic Liquid Mixtures by Tuning Hydrogen-Bonding Interactions

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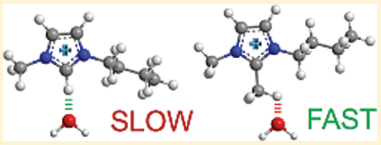
Supporting Information

ABSTRACT: The ability of a binary ionic liquid (IL) system consisting of a phosphonium transition state analogue (TSA) and 1-butyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide ([BMIM][NTf_2]) to accelerate the rate of the well-studied hydrolysis of a *tert*-alkyl picolinium salt by influencing the solvent structure was investigated. A significant rate enhancement was observed in the presence of the TSA; however, comparison with other cations illustrated that this enhancement was not unique to the chosen TSA. Instead, the rate enhancements were correlated with the dilution of hydrogen bonding by the added cations. This phenomenon was further examined by the use of 1-butyl-2,3-dimethylimidazolium bis(trifluoromethanesulfonyl)imide ([BMMIM][NTf_2]) as a cosolvent and the use of Reichardt's dye to measure the extent of hydrogen bonding on solutes in these systems. The rate increases are rationalized in terms of weaker hydrogen bonding from the solvent system to water.



INTRODUCTION

Ionic liquids (ILs) have been defined as salts that melt below 100 °C.[1,2] They have been extensively investigated as replacements for volatile organic compounds (VOCs) due to their negligible vapor pressure.[3,4] While some issues have been raised subsequently regarding the green credentials of ILs, particularly in terms of their syntheses and potential toxicity, they have continued to attract interest due to the flexibility of physical and chemical properties available through the judicious variation of the cation and anion.[5−7] Given that the potential number of ionic liquids has been estimated at $>10^{14}$, which does not account for the possibility of forming binary mixtures of varying composition, it would be valuable to possess both a thorough understanding of ionic liquid structures and their effect on reactivity, in addition to developing methods of rationally manipulating those structures toward desirable outcomes.[8]

Attention has been drawn to the supramolecular nature of IL solvents, particularly those based on 1,3-dialkylimidazolium cations, which results from their vast array of intermolecular interactions and the extent of their structural organization.[2,9,10] Experimental and theoretical studies have demonstrated that for 1-alkyl-3-methylimidazolium ILs, polar and nonpolar nanostructured domains form in ILs possessing an alkyl chain containing at least 4 carbons.[11−14] The intermolecular forces, which give rise to these domains, such as hydrogen bonding, $\pi-\pi$ stacking, and ion pairing, have also been found to lead to inclusion compounds.[10,15−18] The effects of this supramolecular behavior can be found in changes to reaction rates and outcomes for a range of processes including Diels−Alder cycloadditions,[19] hydroformylation,[20] the Baylis−Hillman reaction,[21] and the Tsuji−Trost reaction.[22] Despite these findings, the successful use of inclusion compounds to influence reactions has been largely serendipitous.

Transition state analogues (TSAs) are stable mimics of high energy transition state structures.[23] TSAs have been successfully employed in the synthesis of structured materials for separations and catalysis,[24] the generation of catalytic antibodies,[25] and to probe and/or inhibit enzyme active sites.[26] To the best of our knowledge, no investigation has been conducted into whether these structures are able to affect a reaction in an ordered solvent, such as an IL.

Here, we investigate the effect of using a binary IL system involving a TSA and [BMIM][NTf_2], to determine whether any evidence of structural reorganization to facilitate an increase in reaction rate can be observed. The idea is that the reported mesoscopic ordering of ILs would be affected by the TSA resulting in transient solvent reorganization. This would most likely require a charged TSA, as the predominant mechanism for ordering in ILs is based on electrostatics. Our hypothesis is that the use of a charged TSA would preorganize proximate solvent molecules toward solvation of the transition state, yielding a reaction rate enhancement.

In choosing a model reaction to test this hypothesis, several criteria must be satisfied. The reaction must be well studied and understood. It should also yield a simple product distribution and be amenable to study in IL (i.e., desirable criteria include solubility of reagents and products, and convenient experimental and analytical protocols resulting in high quality data) and involve relatively accessible materials. The hydrolysis of trityl chloride in the presence of pyridine in nitromethane was originally studied by Ingold and co-workers and determined to proceed via the formation of the pyridinium cation ([Ph_3CPyr][Cl]).[27] The rate limiting step was proposed to be the unimolecular dissociation of the pyridine, aided by a cosolvent effect from the added substituting agent.[27] A mechanism change was observed in benzene, where pyridine was not found

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to complex the trityl chloride, most likely due to benzene's low polarity and hence an inability to solvate ionic species.[28] However, the apparent polarity of [BMIM][NTf_2], as measured by solvatochromic dyes, lies between those of protic and polar aprotic solvents based on single parameter polarity scales such as Kosower's Z-value[29] or Reichardt's E_T^N.[30] Thus, it would be anticipated that the pyridinium mechanism would operate within this IL. The hydrolysis of a 4-picoline complexed trityl chloride derivative was selected as a model reaction as this enabled the monitoring of the reaction on a more convenient time scale near room temperature relative to the corresponding pyridine derivative.

EXPERIMENTAL SECTION

Materials. [BMMIM][NTf_2], [BMIM][NTf_2], *p*-fluorophenyldiphenylmethyl chloride (FDMC), and (*p*-fluorophenyl)diphenyl(*p*-tolyl)phosphonium iodide were prepared according to literature procedures or modifications thereof[31−33] and characterized by NMR, ESI-MS, and melting point where appropriate. Tetramethylammonium bis(trifluoromethanesulfonyl)imide ([NMe_4][NTf_2]), tetrabutylphosphonium bis(trifluoromethanesulfonyl)imide ([PBu_4][NTf_2]), tetraphenylphosphonium bis(trifluoromethanesulfonyl)imide ([PPh_4][NTf_2]), and (*p*-fluorophenyl)diphenyl(*p*-tolyl)phosphonium bis(trifluoromethanesulfonyl)imide (the TSA) were all prepared by precipitation from aqueous solution using $LiNTf_2$ and the relevant precursors and were characterized by NMR, ESI-MS, melting point, and elemental analysis (see Supporting Information for all experimental details and characterization). 4-Picoline (Fluka) was purified by passage through a column of neutral activated alumina and stored under nitrogen on activated 4 Å molecular sieves. Nitromethane, benzene, and chloroform were all distilled from drying agents and stored under nitrogen over 4 Å molecular sieves. IL samples to be used for kinetics experiments were dried at 80 °C in vacuo for a minimum of 24 h before the addition of the required amount of water using a microliter syringe. The drying procedure afforded ILs with water contents consistently below 200 ppm, as ascertained by Karl Fischer titration (c.f., ∼7000 ppm for 0.55 M solution), while the microliter syringe was found to be accurate and reproducible to within 1% through the use of gravimetric methods. The IL/water solution was stirred for at least 4 h before the experiment to ensure thorough mixing.

Hydrolysis Experiments. Kinetics experiments were conducted using an NMR tube equipped with a Young's valve. The tube was charged with FDMC (15−25 mg; 0.05−0.08 mmol) under a flow of nitrogen. 4-Picoline (50 or 100 μL) was added to dissolve the substrate. Approximately 5 min before the reaction was to be monitored, the solution was diluted with ionic liquid containing H_2O (0.98 mL of 0.55 M H_2O) and cooled on ice. The sample was mixed using a Vortex mixer and a reference capillary (1-bromo-4-fluorobenzene in acetone-d_6 (0.50 M)) inserted coaxially before monitoring the reaction using a Bruker Avance 300 NMR spectrometer (300 MHz), maintained at 294.3 K, with ^{19}F NMR spectra (total acquisition time of 60 s) obtained every 65 s. Experiments were performed in triplicate. Experimental details for the reactions conducted in nitromethane are outlined in the Supporting Information.

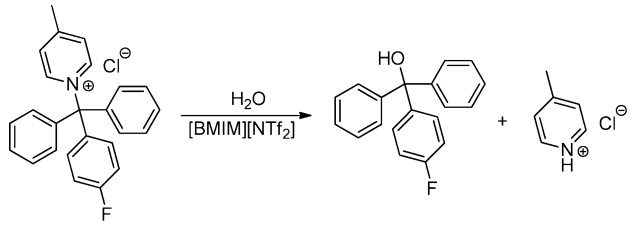
Dimerization Experiments. The dimerization experiments were conducted using the following procedure adapted from the literature.[34] Deuterated chloroform containing 0.03% (v/v) TMS (500 μL) was added to an NMR tube equipped with a Young's valve. A 1 mL solution of either [BMIM][NTf_2] (0.1 M) or 1:1 [BMIM][NTf_2] and the TSA, [PPh_4][NTf_2], or [PBu_4][NTf_2] (0.1 M in each electrolyte) was independently prepared in deuterated chloroform containing 0.03% (v/v) TMS. The IL solution was added in known aliquots using a microliter syringe to the NMR tube and a ^1H NMR spectrum recorded. The chemical shifts of peaks assigned to [BMIM]-[NTf_2] were then recorded and fitted to a dimerization isotherm (see Supporting Information for fitting details).

Solvatochromic Dye Measurements. Solvatochromic dye measurements were obtained as follows. A 250 μL aliquot of an ethanolic stock solution of Reichardt's dye (8.1×10^{-4} M) was added to a 2 mL vial, and the bulk solvent was removed under nitrogen flow. Residual solvent was removed by drying the vial contents in vacuo. The IL solution to be examined (500 μL), previously dried in vacuo at 80 °C for several hours, was added to the vial and the dye dissolved. The solution was transferred to a minimum volume cuvette (1 cm path length) and a UV−vis spectrum obtained at 25.0 °C, with the sample maintained at this temperature by means of a Peltier cooling system. E_T^N values were calculated from the wavelength of the lowest energy absorbance maximum (see Supporting Information for calculation details).

RESULTS

To enable facile reaction monitoring, *N*-(*p*-fluorophenyldiphenylmethyl)-4-picolinium chloride ([Ar_3CPic][Cl]), generated in situ from the reaction of 4-picoline with *p*-fluorophenyldiphenylmethyl chloride (FDMC), was employed to allow the use of ^{19}F NMR to follow the reaction, which is illustrated in Scheme 1.

Scheme 1. Hydrolysis of [Ar_3CPic][Cl] in [BMIM][NTf_2], the Model Reaction Employed in This Investigation



It was first necessary to confirm that 4-picoline dissociation was indeed rate-limiting, and the results of these experiments are summarized in Table 1. Excellent fits to first order rate laws

Table 1. Variation of the Observed First Order Rate Constant with Water and 4-Picoline Concentrations for the Hydrolysis of [Ar_3CPic][Cl] in [BMIM][NTf_2] at 294.3 K[a]

water concentration (M)	4-picoline concentration (M)	rate constant ($\times 10^{-4}$ s^{-1})
0.51	0.49	10.6 ± 0.2
0.51	0.94	10.5 ± 0.1
1.02	0.49	19.3 ± 0.5

[a]Reported errors are standard deviations from replicate experiments.

were observed in all cases and no dependence on 4-picoline concentration was found, while a positive dependence on the amount of water existed. These results are consistent with those of Ingold et al. and form the basis of the proposed reaction transition state and TSA, depicted in Figure 1.

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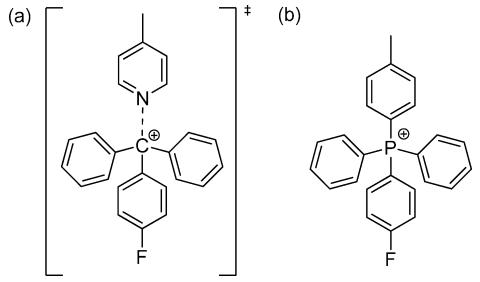

Figure 1. Structure of (a) the proposed reaction transition state and (b) the TSA.

To ascertain whether any potential rate increase was specific to the TSA, alternative templates were also examined. The templates chosen were $[PPh_4][NTf_2]$ to determine the effect of aryl substitution, $[PBu_4][NTf_2]$ to examine the necessity of a charge delocalized aromatic structure, and $[NMe_4][NTf_2]$ to probe the importance of the cation's size. The molecular structures of all templates and ILs used in this study are depicted in Figure 2.

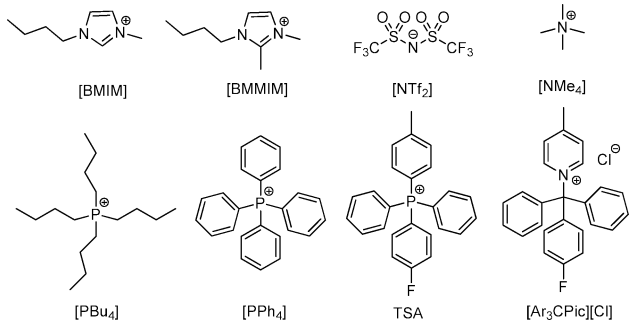

Figure 2. Structure and acronyms of IL ions, the substrate, and templates used in this investigation.

Prior to conducting the hydrolysis experiments, the potential of each of these materials to induce solvent reorganization was probed through a series of ^{1}H NMR dilution experiments. These experiments were conducted in $CDCl_3$ utilizing 1:1 mixtures of the relevant template and $[BMIM][NTf_2]$. Data were fitted to a dimerization isotherm, which yielded both the association constant (K_a) and limiting chemical shift values for the ion-pair and dimer (δ_{ip}, δ_d) (see Supporting Information for model details). Values of K_a listed are weighted averages across a minimum of 7 proton environments. As Table 2 illustrates, all templates investigated resulted in a more favorable ΔG_a when compared to that of $[BMIM][NTf_2]$ self-dimerization. Unfortunately, $[NMe_4][NTf_2]$ was unable to be examined due to its poor solubility in $CDCl_3$.

Table 2. ^{1}H NMR Titration Data in $CDCl_3$ at 300 K

template	K_a	ΔG_a (kJ mol^{-1})	$\Delta\delta_{2H}$ (ppm)[a]
N/A[b]	45 ± 9	−9.5 ± 0.5	0.49
$[PBu_4][NTf_2]$	72 ± 5	−10.7 ± 0.2	0.39
$[PPh_4][NTf_2]$	131 ± 8	−12.2 ± 0.1	0.36
TSA	143 ± 9	−12.4 ± 0.2	0.37

[a]Limiting chemical shift variation for the C2 proton on dimerization. [b]Modeled as 1:1 $[BMIM][NTf_2]$ to ensure a comparable ionic strength with the templated solutions.

The values of $\Delta\delta_{2H}$ imply that the structure of the aggregate formed is different when the template molecule is added. Unfortunately, NOESY contacts could not be observed between cations, so no direct evidence for heterodimers was obtained. The apparent preferential association with aromatic cations is an interesting result. The interaction of imidazolium cations with neutral aromatic substrates has been well-documented[10,16,18,35] as has the formation of ionic cocrystals involving cation substitution.[15] However, to the best of our knowledge, no preferential association for aromatic cations with imidazolium ILs has ever been shown.

Theoretical studies regarding the solubility of aromatic compounds in ILs have suggested that the predominant interactions between the IL and an aromatic solute are electrostatic, arising from the strong quadrupole moment of aromatic compounds.[36] It was also discovered that for benzene, the interaction with the anion dominated, while the addition of electronegative substituents, for example, in hexafluorobenzene, resulted in stronger interactions with the cation.[37] Therefore, the presence of a delocalized positive charge across the aromatic group, as in the TSA and $[PPh_4][NTf_2]$, would probably lead to an anion-dominated interaction with the aromatic solute. The stronger anion/solute rather than cation/solute interaction would account for the lack of any observable NOE interactions between different cations as the upper limit for detecting NOEs is approximately 4 Å,[38] considerably less than a cation−cation distance when the NTf_2 anion is present. The preferential formation of dimers, therefore, indicates a favorable association between the IL and the added template molecules. This would be a prerequisite if any structural reorganization around the TSA was to occur.

In order to determine whether any rate increase could be observed in the presence of the TSA, the NTf_2 salt of the TSA was dissolved in $[BMIM][NTf_2]$ in concentrations ranging from 0.5 mol % to 15 mol % of the IL solution. As depicted in Figure 3, the rate constant observed increases with TSA concentration; however, to determine the specificity of this rate increase, the other templates (i.e., the NTf_2 salts of the PPh_4, PBu_4, and NMe_4 cations) were also examined at 1 and 10 mol % concentrations. The results are shown in Figure 4.

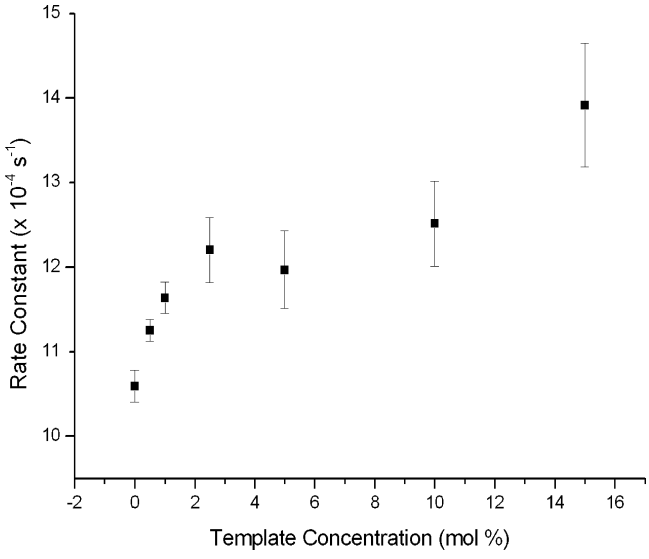

Figure 3. Variation of the observed rate constant with TSA loading. Reported errors are the standard deviations of replicate experiments.

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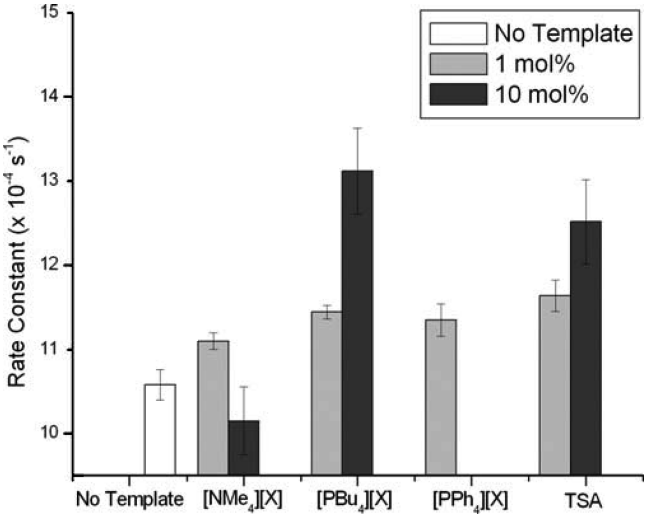

Figure 4. Observed first order hydrolysis rate constants using different templates in [BMIM][NTf_2] at 1 (light gray) and 10 (dark gray) mol % loadings (X = NTf_2). The untemplated result is depicted for comparison. Reported errors are standard deviations of replicate experiments.

From Figure 4, at 1 mol %, it appears that all templates gave a slightly faster rate although some values, in particular those for [NMe_4][NTf_2], lie only marginally outside the observed experimental error. At the 10 mol % loading, it was found that [NMe_4][NTf_2] yielded a rate consistent with that in the untemplated IL, while the other templates resulted in a significantly faster reaction. Unfortunately, because of its poor solubility, [PPh_4][NTf_2] could not be investigated at 10 mol %.

The similar results obtained for both [PBu_4][NTf_2] and the TSA, with no rate increase relative to the untemplated solution observed for the [NMe_4] cation, indicates that the rate enhancement could be a result of the size of the template and is not a result of the template's precise electronic structure. Further experiments were conducted with [PBu_4][NTf_2] and at each concentration, the observed rate constant was similar to with those obtained in the presence of the TSA at the same concentration (see Supporting Information).

One factor that cannot be ignored when examining the concept of molecular templating is that of the apparent solvent polarity, as the addition of the template molecule may vary the composition of the solvent cage surrounding the substrate. Solvent polarity has been shown to be of limited importance when pyridine and its derivatives form the leaving group for tertiary carbocations in neutral solvents due to the lack of charge development between the reactants and the transition state.[39] It should be noted, however, that these reactions utilized the solvent as the nucleophile. Therefore, the solvent−nucleophile interactions that may be experienced in the present system would have been inherently unobservable in the literature study. When nitromethane was used as a solvent for the nucleophilic substitution of [Ph_3CPyr][Cl], it was found that the rate of substitution increased in the order phenol < water < ethanol, an effect ascribed to the increasing order of nucleophilicity.[27] In light of the lack of participation of pyridine in the rate determining step, it can be concluded that it is the ability of the substituting agent to solvate the forming carbocation which is important, i.e., its hydrogen bond basicity rather than its nucleophilicity.

An alternative hypothesis for the observed reaction rate increase is, therefore, not that the templates participate in the geometric rearrangement of the solvent but that they dilute the more hydrogen bond acidic [BMIM] cation. As the hydrogen bond acidity of the medium is reduced, it would be expected that water would interact less strongly with the solvent and hence be better able to solvate the cationic transition state. To ascertain whether this hypothesis was valid, the hydrolysis was conducted both in neat [BMMIM][NTf_2], to determine the effect of definitively lowering the hydrogen bond acidity of the medium, and in 15 mol % [BMMIM][NTf_2] in [BMIM][NTf_2], to see if a low concentration of a more weakly hydrogen-bonding cation could give rise to the rate enhancements observed. As the [BMMIM] cations are comparable in size to [BMIM], this would also remove the geometric considerations. Any increase in rate can, therefore, be attributed solely to reducing the hydrogen bond acidity and not to templating through a molecular size effect. These results are illustrated in Table 3, with comparisons to the corresponding rates obtained in [BMIM][NTf_2], 15 mol % TSA and 15 mol % [PBu_4][NTf_2].

Table 3. Comparison of the Observed First Order Rate Constants for Hydrolysis in Different Ionic Liquid Solvent Systems[a]

ionic liquid solution	rate constant ($\times 10^{-4}$ s^{-1})
[BMIM][NTf_2]	10.6 ± 0.2
15% TSA[b]	13.9 ± 0.7
15% [PBu_4][NTf_2][b]	14.5 ± 0.6
15% [BMMIM][NTf_2][b]	12.6 ± 0.7
[BMMIM][NTf_2]	18.8 ± 0.4

[a]Reported errors are standard deviations of replicate experiments. [b]Mol % in [BMIM][NTf_2].

As Table 3 illustrates, the observed rate constant increases quite considerably when the reaction is conducted in [BMMIM][NTf_2] rather than [BMIM][NTf_2]. Further, when only 15 mol % [BMMIM][NTf_2] is used in [BMIM][NTf_2], a rate enhancement of similar magnitude to that for similar concentrations of the TSA and of [PBu_4][NTf_2] is observed. These observations strongly suggest that the rate enhancements do not arise from molecular size but from polarity effects.

In order to quantify the relevant change in apparent polarity resulting from the addition of a nonpolar template, Reichardt's dye was used to investigate the ILs and templated solutions, with the results summarized in Table 4 (see Supporting Information for calculation details). Reichardt's dye has been used extensively to quantify the polarity of solvents and has been widely used in the IL literature due to its large solvatochromic range (357 nm spectroscopic shift from water to diphenyl ether).[40] The wavelength of the lowest energy absorbance maximum has been shown to correlate with the hydrogen bond acidity, Lewis acidity, and dipolarity of the solvent, with the hydrogen bond acidity representing the most important contribution.[41]

As is evident from Table 4, no significant change in the E_T^N polarity parameter can be observed in the templated solutions using the solvatochromic probe, except for the 10 mol % [NMe_4][NTf_2] solution, which exhibited an increase. The lack of a discernible E_T^N decrease for the other templates could be due to preferential solvation of Reichardt's dye by the more strongly hydrogen-bonding [BMIM] cation, a phenomenon that has been shown for ILs in binary mixtures with neutral solvents such as dichloromethane.[42] Unfortunately, this could

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Table 4. Comparison of E_T^N Values Obtained in Templated Solutions with Those of the Neat ILs at 25.0 °C[a]

sample	E_T^N (lit.)
[BMIM][NTf$_2$]	0.647 (0.644)[50]
[BMMIM][NTf$_2$]	0.547 (0.541)[50]
10% [NMe$_4$][NTf$_2$][b]	0.706
10% TSA[b]	0.657
10% [PBu$_4$][NTf$_2$][b]	0.645
15% TSA[b]	0.658
15% [PBu$_4$][NTf$_2$][b]	0.658
15% [BMMIM][NTf$_2$][b]	0.639

[a]Literature values are provided for comparison, where available. [b]Mol % in [BMIM][NTf$_2$].

not be confirmed for the TSA nor for [PBu$_4$][NTf$_2$], as both are solids, and therefore, the concentrations amenable to examination at 25.0 °C are limited by their solubilities. The apparent polarity of [BMMIM][NTf$_2$], however, could be examined in [BMIM][NTf$_2$] in compositions from 0 mol % to 100 mol % to investigate this proposition, and these measurements are depicted in Figure 5.

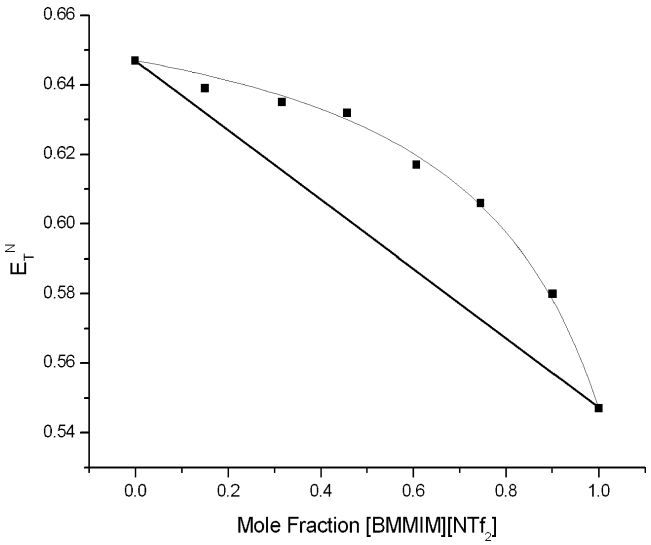

Figure 5. Variation of E_T^N with the mole fraction of [BMMIM][NTf$_2$] in [BMIM][NTf$_2$] at 25.0 °C. The bold line represents the ideal polarity curve, and the thin line represents the fitted curve to the preferential solvation model.

As illustrated in Figure 5, preferential solvation of Reichardt's dye occurs in mixtures of [BMMIM][NTf$_2$] and [BMIM][NTf$_2$]. The shape of the curve suggests, as would be expected, that the stronger hydrogen bond donor ([BMIM]) is interacting more strongly with the dye than [BMMIM] is. Models for the preferential solvation of Reichardt's dye have been proposed and fitted to a wide variety of binary solvent mixtures involving neutral solvents and binary mixtures of ILs and neutral solvents.[42−44] The simplest of these is illustrated in eq 1, which models the process as a one step solvent exchange, where RS$_i$ is Reichardt's dye solvated by solvent i, and S$_i$ indicates free solvent i.

$$RS_1 + S_2 \rightleftharpoons RS_2 + S_1 \quad (1)$$

From the above equilibrium, an expression can be derived for the corresponding constant of solvent exchange (K), in terms of the mole fraction of one solvent (x_2) and the E_T^N values for each neat solvent ($E_T^N(1)$ and $E_T^N(2)$, respectively) as shown in eq 2.[43]

$$E_T^N = \frac{Kx_2(E_T^N(2) - E_T^N(1))}{1 - x_2 + Kx_2} + E_T^N(1) \quad (2)$$

As shown in Figure 5, this model for the solvent exchange process gave an excellent fit to the experimental data (R^2 = 0.996), which indicates that a more complicated model is not necessary. Table 5 summarizes the results obtained from the fit.

Table 5. Parameters Obtained from Fitting the E_T^N Isotherm to the One-Step Preferential Solvation Model[a]

binary solvent system	K	ΔG (kJ mol^{-1})
[BMIM][NTf$_2$]:[BMMIM][NTf$_2$]	0.243 ± 0.013	3.5 ± 0.2

[a][BMMIM][NTf$_2$] was used as solvent 2 in the model.

As many recent publications[42,45−47] report preferential solvation data in terms of the more comprehensive, albeit more complex, two-step model proposed by Buhvestov et al.,[48] these data were also fitted to that model, which yielded good fits although no additional insight (see Supporting Information for details and fitting parameters).

The preferential solvation of Reichardt's dye within the binary IL mixture would appear to suggest that a polar solute capable of accepting hydrogen bonds would be primarily solvated by [BMIM] cations at low mole fractions of added template. Given that statistically significant rate increases are observed at low template loadings (<10 mol %), it would seem unlikely that preferential solvation of water is occurring. To examine this more thoroughly, the hydrolysis reaction was conducted at a variety of mole fractions of [BMMIM][NTf$_2$] in [BMIM][NTf$_2$]. The results of this investigation are illustrated in Figure 6.

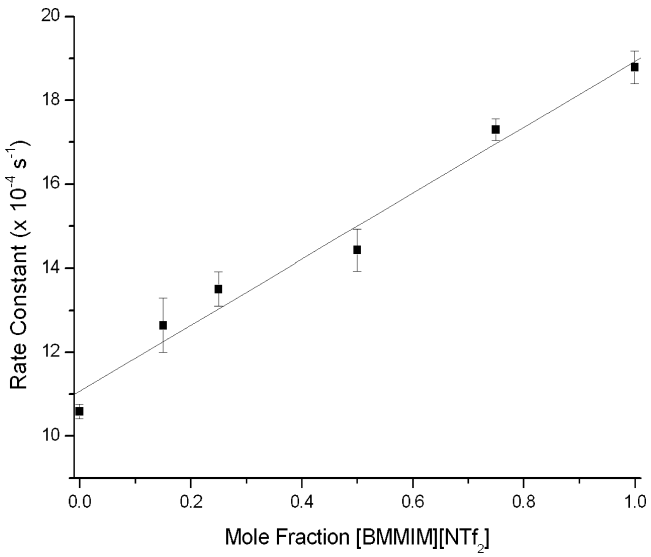

Figure 6. Variation of the observed rate constant with the mole fraction of [BMMIM][NTf$_2$] in [BMIM][NTf$_2$] with fitted regression line. Reported errors are the standard deviations of replicate experiments.

As can be observed from Figure 6, a good linear fit is found upon varying the proportion of [BMMIM][NTf$_2$] in [BMIM][NTf$_2$]. The linearity is in stark contrast with the preferential

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solvation exhibited by Reichardt's dye and indicates that the composition of the solvation sphere of water is representative of the proportions present in the bulk solvent, unlike the cybotactic sphere of Reichardt's dye, which differs significantly from that of the bulk.

DISCUSSION

On the basis of the data obtained, it is apparent that the rate enhancement observed upon the addition of the TSA to the IL can be ascribed to polarity effects. This accounts for the similar apparent behavior, both in terms of observed E_T^N value and rate enhancement, of 15 mol % $[PBu_4][NTf_2]$, TSA, and $[BMMIM][NTf_2]$. The inability to observe these polarity shifts using Reichardt's dye as a probe can be rationalized from the perspective of preferential solvation, which has been shown to occur for $[BMMIM][NTf_2]$ and would account for the lack of any detectable variation in E_T^N for the $[PBu_4][NTf_2]$ and TSA solutions.

Furthermore, the slightly larger magnitude of the rate enhancement for $[PBu_4][NTf_2]$ with respect to $[BMMIM][NTf_2]$ can also be rationalized in terms of polarity effects as the E_T^N value for $[PBu_4][Cl]$ has been measured as 0.38[49] (c.f., 0.54[50] for $[BMMIM][NTf_2]$). Although the former value was measured at elevated temperature (125 °C vs 25 °C) and using a different anion (making direct comparisons complicated), the values are sufficiently different to suggest that at 15 mol % of each template, the average hydrogen bond acidity of the medium would be lower for the $[PBu_4]$ cation.

$[NMe_4][NTf_2]$ was the only template not to yield a significantly faster rate at the 10 mol % concentration and also yielded a higher observed value of E_T^N. It can be concluded, in light of the other evidence, that the polarity increase results from preferential solvation of Reichardt's dye by $[NMe_4]$, which presumably is more capable of hydrogen bonding than the [BMIM] cation is, due to the short alkyl chains of the $[NMe_4]$ cation. Therefore, $[NMe_4]$ does not dilute the [BMIM] cation's ability to hydrogen bond, if anything, it enhances it, resulting in no rate enhancement and perhaps a marginal rate depression at 10 mol %.

To provide a thorough discussion of this system, examination of the reactions conducted in IL and reactions in neutral solvents should be compared. To enable this, hydrolysis experiments were conducted within nitromethane. These suggested that in a neutral solvent, ion-pairing between the chloride ion and $[Ar_3CPic]$ cation had a more significant effect on the rate than even the concentration of water. This is most likely due to the chloride acting as a water carrier as chloride is a strong hydrogen bond acceptor, meaning that an ion-paired substrate is more likely to contain a cybotactic water molecule than a free cation. Further to this, in more weakly hydrogen-bonding solvents, such as chloroform or benzene, $[Ar_3CPic][Cl]$ was not formed, and only the neutral FDMC was observed in solution. A direct comparison between the results observed in IL and in neutral solvent, therefore, cannot be made as the underlying mechanisms in all cases are quite different. However, for completeness, the rate data obtained in nitromethane and the speciation data in benzene and chloroform are available in the Supporting Information, along with a more thorough discussion of those results.

It is also interesting to consider the results of this investigation in light of other results obtained for unimolecular solvolysis reactions within ILs. The primary such example is the methanolysis of a tertiary alkyl chloride, extensively studied by Harper et al.[51−53] In their system, the IL stabilized the transition state electrostatically as the charge developed upon dissociation of the carbon chlorine bond. This stabilization was offset by the entropy cost of solvent reorganization upon ionization of the substrate.[51−53] It should be noted that for the alkyl chloride methanolysis, it is the solvation of the carbocation and the chloride nucleofuge that is of primary significance, as has been well-established for S_N1 reactions in neutral solvents.[54] In the hydrolysis of $[Ar_3CPic][Cl]$, however, we have found that the rate-determining factor is the solvation of the nucleophile, not the nucleofuge, by the IL, thereby indicating a clear difference between these two processes. Hence, the varying extent of charge development, as has previously been discussed, is responsible for the different behaviors observed.

Given that the apparent polarity of the medium toward water appears to be responsible for the rate enhancement, the linearity observed upon varying the proportion of $[BMMIM][NTf_2]$ in $[BMIM][NTf_2]$ is extremely interesting in light of the preferential solvation of Reichardt's dye. Recent reports have suggested that water diffuses several times faster than either the cation or anion in imidazolium based ILs.[55−57] Conversely, larger molecules have been found to diffuse more slowly, limited by the formation of suitably sized cavities.[2,58] These factors may result in the water molecules encountering a more representative solvation environment than Reichardt's dye does, with the latter molecule diffusing slower than the general rate of solvent reorganization. This hypothesis is currently being further investigated within our laboratory.

CONCLUSIONS

The presence of a TSA in $[BMIM][NTf_2]$ did lead to a rate enhancement for the hydrolysis of $[Ar_3CPic][Cl]$. This enhancement, however, could also be achieved via the use of other cations, including $[PBu_4][NTf_2]$ and $[BMMIM][NTf_2]$. The mechanism of the rate enhancement was therefore attributed to the dilution of the more strongly hydrogen-bonding [BMIM] cation by a weaker hydrogen bond donor. This illustrates that dissolved salts within ILs can modulate the polarity of the medium in a similar fashion to conventional binary solvent systems. These findings also indicate that reaction engineering through the rational use of binary ILs consisting of a salt with desirable solvation properties, such as strong hydrogen bond donating or accepting groups, and another IL with relevant physical properties, such as low viscosity or melting point, is feasible and may enable new classes of chemical transformations to proceed more selectively and/or under milder conditions.

ASSOCIATED CONTENT

Supporting Information

Experimental details for the synthesis and characterization of all compounds, calculation details for dimerization experiments, Reichardt's dye polarity measurements and two-step preferential solvation model, comparison of $[PBu_4][NTf_2]$ and the TSA at various loadings, and rate and speciation data for neutral solvent experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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