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Kemp Elimination: A Probe Reaction To Study Ionic Liquids Properties

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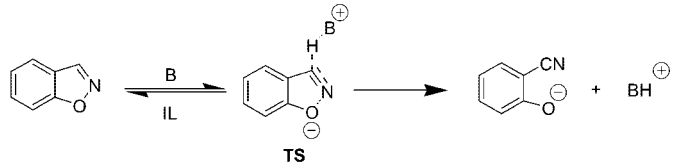

IL = [bmim][BF_4]; [bmim][PF_6]; [bmim][NTf_2]; [bm_2im][NTf_2]; [bmpyrr][NTf_2]

B = Amine

The amino induced elimination of benzisoxazole into the relevant *o*-cyanophenolate ion (Kemp elimination) has been studied in [bmim][BF_4] solution at 298 K. To have information about the interactions between reactants and ionic liquid, the reaction has been carried out at different temperatures (293–313 K). Several primary, secondary, and tertiary amines have been used to study the effect of amine structure on the reaction rate. The collected data show that the amine structure seems to have a crucial role in determining the reaction rate. Furthermore, as different cation or anion structures of an ionic liquid can significantly affect its properties, the title reaction has been performed in four different ionic liquids ([bmim][PF_6], [bmim][NTf_2], [bm_2im][NTf_2], and [bmpyrr][NTf_2]), using pyrrolidine and piperidine as model amines. An H-donor negative solvent (MeOH and [bmim][NTf_2]) effect on reaction rate was detected. Finally, a narrow range of activation parameters was calculated both for the reaction induced by different amines and for pyrrolidine and piperidine, in the presence of different ILs. This fact suggests the occurrence of an "early" transition state.

Introduction

Organic chemists are very interested in the development of environmental friendly catalysts and solvents. Among solvents much interest is focused on room temperature ionic liquids (RTILs).[1] This is due to their low vapor pressure and negligible flammability, which make ionic liquids (ILs) attractive candidates as replacements for volatile organic solvents.[2]

The nature of solvent is frequently one of the most important factors in determining the outcome of a given reaction and the study of solvent properties becomes, under this light, an area of considerable importance. Studying ILs, this subject can assume a particular perspective. Indeed, being formed only by ions, ILs can produce different electrostatic environments, which can significantly affect a given reaction.[3] On the other hand, ILs formed by aromatic cations, such as imidazolium ions, have been recently described as polymeric hydrogen bonded supramolecules whose order degree can be differently affected by guest reactants molecules.[4] Furthermore, as has been pointed out recently, ILs are able to give $\pi-\pi$ and $\pi-$cation interactions that in some cases may significantly affect the reactivity in these solvent media.[5]

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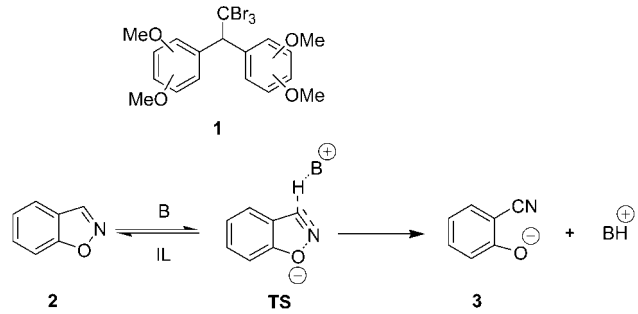
Among the methods used to achieve a better understanding of the properties of a given solvent, the kinetic study of a probe reaction, having a well-known mechanism, may represent a useful tool. Therefore, we believed it would be interesting to investigate kinetically the effect that ILs have on a classical organic reaction such as an elimination reaction. We have previously studied the effect of ILs on the amine-induced elimination of 1,1,1-tribromo-2,2-bis(phenyl-substituted)ethane (**1**).[5b] The reaction studied in this work is the base-induced elimination of benzisoxazole (**2**) into the relevant *o*-cyanophenolate (**3**), the so-called Kemp elimination, for which a concerted E2 elimination mechanism has been accepted. This reaction has been previously studied in water, using hydroxide or trimethylamine as bases,[6] as well as in the presence of cationic vesicles,[7] biocatalysts (enzymes and antibodies),[8] and cyclodextrins.[9] The Kemp elimination proceeds through a charge separated and ordered transition state, in which both C−H and N−O bonds are extensively cleaved.[6] For all the above reasons, according to our previous findings,[5b–d] it should be a suitable probe to study ionic liquids properties (Chart 1).

The reaction rates were measured spectrophotometrically at 298 K, following the appearance of **3** at 346 nm. We chose as bases some primary, secondary, and tertiary amines with different structures (cyclic or acyclic), basicities, and steric requirements that are widely soluble in the used ionic liquids (Chart 2).

CHART 1. Schematic Representation of Substrates and Reaction Studied



The reaction was carried out in 1-butyl-3-methylimidazolium tetrafluoroborate solution ([bmim][BF_4]) at various amines concentrations (0.00870–0.022 M) over the temperature range 293–313 K.

It is well-known that differences in both the cation and the anion may have significant effects on RTILs structure and properties. Under this light, we chose pyrrolidine and piperidine as model amines and we studied the title reaction in different ILs, such as [bmim][PF_6], [bmim][NTf_2], [bm_2im][NTf_2], and [bmpyrr][NTf_2] [where bm_2im = 1-butyl-2,3-dimethylimidazolium, bmpyrr = *N*-butyl-*N*-methylpyrrolidinium, NTf_2 = bis(trifluoromethylsulfonylimide)] (Chart 3).

Among these, bm_2im^+ and $bmpyrr^+$ have a lesser hydrogen bond donor ability than $bmim^+$; furthermore, the $bmpyrr^+$ is not able to give $\pi-\pi$ interactions that in some cases determine a strong effect on reactivity. At last, the substitution of the anion part of [bmim][X] going from [BF_4^-] and [PF_6^-] to [NTf_2^-] should cause a different packing and possibly a different catalytic effect.

To have a comparison with reactivity in conventional organic solvents, the reaction was also studied in MeOH and DMF solutions.

Results and Discussion

First, we checked for the possible occurrence of the spontaneous reaction in IL solution. We verified that the substrate remains unchanged, in IL solution, for at least 48 h. This suggests that uncatalyzed reaction did not proceed at an appreciable rate ($k \ll 1.2 \times 10^{-5}$ s^{-1}). As substrate and amines were added to IL as concentrated solution in 1,4-dioxane[10] (see the Experimental Section), we checked for the reaction in this solvent. However, also in this case, in the presence of the highest pyrrolidine (the most efficient base catalyst) concentration used in this work, the reaction did not proceed.

In IL solution, we did not have any evidence about the formation of intermediates and we confidently supposed that the mechanism of the base-catalyzed elimination of the benzisoxazole proceeded, as well as in water solution, through a concerted E2 elimination.[6]

It is noteworthy that a significant blue-shift in the UV–vis spectrum of *o*-cyanophenolate (**3**) was detected in [bmim][BF_4] solution with respect to MeOH (λ_{MAX} = 327 and 346 nm in MeOH and [bmim][BF_4], respectively).

Kinetic Data in [bmim][BF_4]. Among amines used, the most basic pyrrolidine was the most effective, whereas diisoprop-

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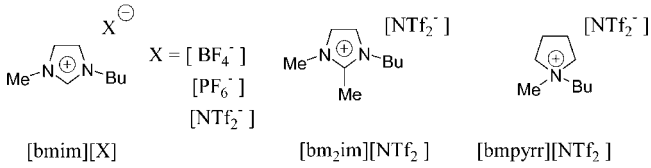
(10) The kinetic solutions contain 13% (v:v) of 1,4-dioxane. According to our previous report,[5d] however, the obtained results can be well referred to neat ionic liquid, i.e., to a partially organized solvent medium.

CHART 2. List of Amines Used

Primary amines	Secondary amines	Tertiary amines
Butylamine (bua)	Diisopropylamine (d^{i}pra)	Triethylamine (tea)
Cyclohexylamine (cha)	Dibutylamine (dbua)	N-Methylpyrrolidine (mpyrr)
	N-Butyl-N-methylamine (bma)	N-Methylpiperidine (mpip)
	Pyrrolidine (pyrr)	N-Methylmorpholine (mmor)
	Piperidine (pip)	
	Hexamethyleneimine (h6mi)	
	2,2,6,6-Tetramethylpiperidine (tmpip)	
	Heptamethyleneimine (h7mi)	
	Morpholine (mor)	

CHART 3. Structures of Ionic Liquids



[bmim][X] [bm$_2$im][NTf$_2$] [bmpyrr][NTf$_2$]

TABLE 1. Calculated Second-Order Rate Constants at 298 K for the Elimination Reaction of 2, in [bmim][BF$_4$] Solution, in the Presence of Amines

amine	$10^2 k_{II}$ (M^{-1} s^{-1})	R	pK_{BH}^{+a}
butylamine	0.569 ± 0.049	0.982	10.68
cyclohexylamine	0.408 ± 0.027	0.989	10.66
diisopropylamine	0.157 ± 0.031	0.999	
dibutylamine	2.30 ± 0.08	0.997	11.20
N-butyl-*N*-methylamine	2.62 ± 0.14	0.992	
pyrrolidine	10.9 ± 0.4	0.996	11.27
piperidine	3.76 ± 0.10	0.993	11.12
hexamethyleneimine	5.99 ± 0.11	0.999	10.89
heptamethyleneimine	3.99 ± 0.24	0.991	10.78
morpholine	n.r.		8.33
2,2,6,6-tetramethylpiperidine	2.40 ± 0.18	0.992	11.07
triethylamine	3.34 ± 0.10	0.998	10.75
N-methylpyrrolidine	6.36 ± 0.34	0.993	10.46
N-methylpiperidine	1.86 ± 0.03	0.999	10.08
N-methylmorpholine	n.r.		7.41

[a] See ref 11.

ylamine was least effective. Moreover, morpholine and *N*-methylmorpholine were not able to induce the elimination reaction. This behavior is different from that previously observed for the E2 elimination on 1,1,1-tribromo-2,2-bis(phenyl-substituted)ethane (**1**).[5b] Indeed, for this compound only secondary cyclic amines were capable of inducing the reaction.

For all reactive amines, the observed rate constant k_{obs} shows a linear correlation as a function of base concentration, according to eq 1

$$k_{obs} = i + k_{II}[Am] \quad (1)$$

Second-order rate constant values (k_{II}) as a function of amine, together with pK_{BH}^{+} values collected in aqueous solution,[11] are reported in Table 1 (Data collected at different amine concentrations are reported in Table 5 of the Supporting Information).

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For a quick overall evaluation purpose, the reactivity ranges (Δk) as a function of amines nature are reported in Figure 1. Data reported in Figure 1 show that the reactivity range increases along the series as follows: primary amines < tertiary amines < secondary amines. We recently found the same order, studying the ion pair stability of 4-nitrophenol/amine in IL solution.[12] Furthermore, as far as secondary amines are concerned, Δk values increase on going from acyclic to cyclic amines. A comparison among reactivity and basicity ranges indicates that this latter factor is not the only one involved in affecting the reaction rate.

Indeed, ΔpK_{BH}^{+} is larger for tertiary amines than for secondary ones ($\Delta pK_{BH}^{+} = 0.49$ and 0.67 for secondary and tertiary amines, respectively), but Δk results are larger for the latter ones ($\Delta k = 0.107$ and 0.045 M^{-1} s^{-1} for secondary and tertiary amines, respectively).

A similar result can be obtained considering amines of the same class. As a matter of fact, in the presence of primary amines, cyclohexylamine and butylamine have comparable pK_{BH}^{+} values, but the reaction in the presence of butylamine is faster ($k_{bua}/k_{cha} = 1.4$). Again, in the presence of secondary amines, significant differences in reactivity are not due to large differences in basicity. For example, dibutylamine and pyrrolidine have similar pK_{BH}^{+} values (11.20 and 11.27, respectively), but $k_{pyrr}/k_{dbua} = 4.8$. Furthermore, piperidine is a stronger base than hexamethyleneimine (p$K_{BH}^{+} = 11.12$ and 10.89, respectively), but $k_{pip}/k_{h6mi} = 0.63$. Finally, among tertiary amines,

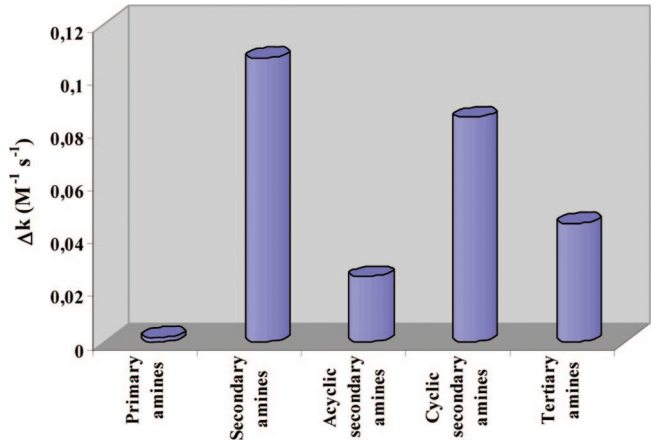

FIGURE 1. Plot of reactivity ranges as a function of the nature of the amine relative to the base-catalyzed elimination of **2** in [bmim][BF$_4$] solution.

triethylamine is a stronger base than *N*-methylpiperidine (pK_{BH}^+ = 10.75 and 10.46 for triethylamine and *N*-methylpiperidine, respectively), but the reaction proceeds faster in the presence of the last amine (k_{mpip}/k_{tea} = 1.9). However, irrespective of structure, tertiary amines in [bmim][BF_4] are more efficient than in water solution [$k_{II,303K}$ = (8.0 ± 0.7) × 10^{-3} M^{-1} s^{-1}].[6]

As we previously said, reactivity of secondary amines increases on going from acyclic to cyclic ones. In particular, for the three acyclic amines used, k_{II} values increase on going from diisopropylamine to dibutylamine and *N*-butyl-*N*-methylamine. Amines having linear alkyl groups (dbua and bma) react faster than amines having branched alkyl groups such as diisopropylamine. In the presence of cyclic amines, reactivity decreases on going from pyrrolidine to piperidine or to other larger amines. It is noteworthy that a similar result was previously obtained for amino-induced elimination of **1**.[5b] However, in this case the effect due to the amine ring size is more important. In fact, k_{pyrr}/k_{h7mi} = 22.7 and 2.73 for **1** and **2**, respectively.

The different amine effect on elimination reaction of **2** and **1** could be due to different substrate geometries. The former substrate has suitable geometry for elimination, whereas **1** should be constrained in order to assume a planar conformation, which possibly allows the electronic effects exerted by the aromatic rings on the reaction route to be maximized. This results in a larger sensitivity to structural requirements of the amine. Moreover, the significant role played by cyclic amine structure emerges comparing the reactivity of *N*-butyl-*N*-methylamine, pyrrolidine, and *N*-methylpyrrolidine. Indeed, going from bma to pyrr an increase in reactivity (∼4) is observed. A similar result is obtained going from the secondary amine (bma), generally more reactive, to the tertiary amine (mpyrr) (∼2.4).

In the presence of cyclic tertiary amines, reactivity decreases on going from pyrrolidine to piperidine derivatives. It is noteworthy that the comparison among pyrrolidine, piperidine, and corresponding *N*-methylderivatives shows that the methylation of amine nitrogen has a comparable effect on the reactivity. Indeed, quite similar reactivity ratios can be calculated between secondary and corresponding tertiary amines (k_{pyrr}/k_{mpyrr} = 1.7 and k_{pip}/k_{mpip} = 2.0), in spite of more significant differences in basicity (ΔpK_{BH}^+ = 0.81 and 1.04 respectively).

On the whole, collected data show that the amino-catalyzed elimination of **2** is very sensitive to amine structure (i.e., flexibility, steric hindrance, and geometry). In contrast, the base strength plays a minor role. Similar results were previously reported by Yadav et al.[13] studying the nucleophilic substitution reaction in the presence of secondary amines. Considering secondary acyclic amines, the reactivity seems to be a function of alkyl group structure and of steric hindrance on the amino nitrogen. The considerable influence of the amine structure on the reaction rate could be further evidence for the occurrence of a concerted E2 mechanism, where a crowded transition state suffers from the effect of base structure.

Kinetic Data in Different ILs. We chose pyrrolidine and piperidine to study the target reaction in different ILs, because the former amine was the best catalyst, whereas piperidine, according to previous reports,[5b] did not induce significant variations in organized RTIL structure. In all the cases considered, the absorbance as a function of time showed a typical trend for a simple kinetic process, with the only exception being the pyrrolidine-induced elimination in [bmpyrr][NTf_2]. In the latter case at least two kinetically prominent steps were responsible for the observed trend (Figure 2).

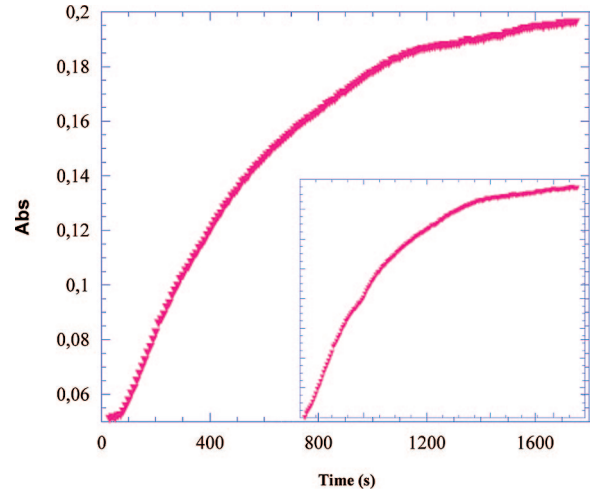

FIGURE 2. Plot of absorbance as a function of time relative to the pyrrolidine-catalyzed elimination of **2** in [bmpyrr][NTf_2] at 298 K ([pyrr] = 0.0217 M).

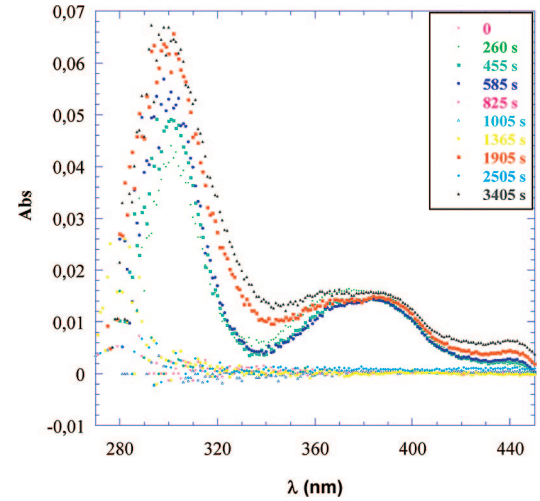

FIGURE 3. UV–vis spectra of [bmpyrr][NTf_2] in the presence of [pyrr] = 0.0217 M collected in 1 h.

In fact, first or higher order kinetic equations do not fit the experimental trace. From a careful analysis of the system we found that the absorbance of the IL−pyrrolidine mixture changed as function of time. Furthermore, a variation in the UV–vis spectrum of [bmpyrr][NTf_2] induced by pyrrolidine was observed. For example, in Figure 3 the spectra of IL in the presence of pyrrolidine collected over a time range are reported. Spectral analysis shows that the absorbance at 300 nm and at ∼360 nm first increases as a function of the time and then decreases to a constant value.

The IL−pyrrolidine mixtures were analyzed also by ^{1}H NMR spectroscopy. ^{1}H NMR spectra, recorded at different times, are reported in Figure 4 (spectra recorded at t = 1.5 and 24 h are available in Figure 5 of the Supporting Information). In all cases the analyzed solutions were perfectly clear.

As can be seen, after adding 75 μL of 1,4-dioxane all signals related to the [bmpyrr] cation were enlarged and lose their multiplicity. The same trend was observed in the presence of a

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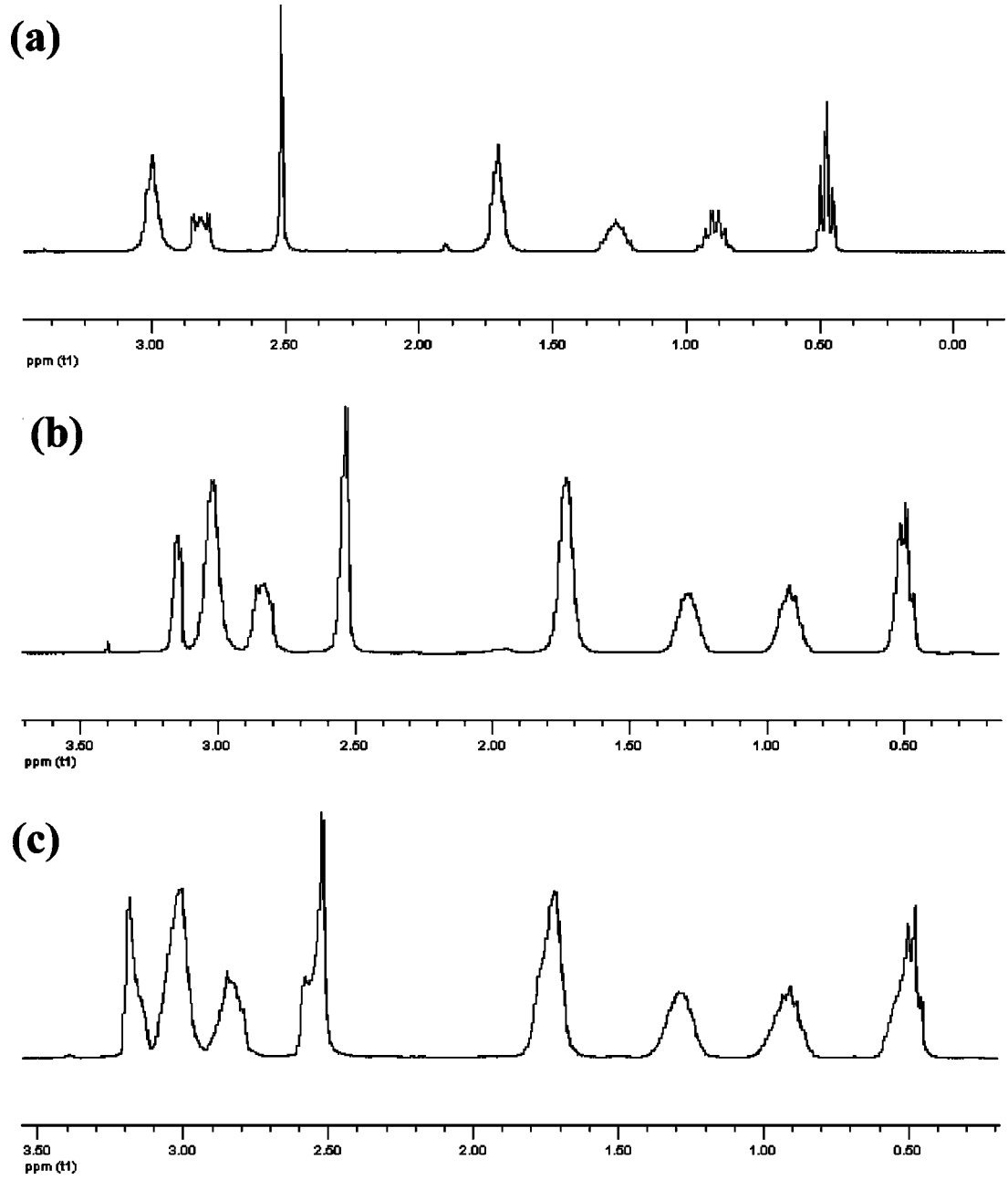

FIGURE 4. ^{1}H NMR spectra of (a) neat [bmpyrr][NTf_2], (b) [bmpyrr][NTf_2] in the presence of 75 mL of 1,4-dioxane, and (c) [bmpyrr][NTf_2] in the presence of a dioxane solution of [pyrr] = 0.0217 M at t = 0 min.

pyrrolidine solution in 1,4-dioxane. However, according to variations detected in the UV–vis spectra, after 1.5 h, all signals showed the typical multiplicity that became more defined in 24 h.

The variation in UV–vis and ^{1}H NMR spectra cannot be accounted for by the occurrence of an IL degradation reaction. Indeed, the IL−pyrrolidine mixture, was extracted with diethyl ether after some days and the analysis of extract did not show any presence of either methylamine or other reaction products. Therefore, according to data previously reported,[5b] we ascribed the variations in UV–vis spectra to a reorganization process of IL molecules induced by amine. It has been recently claimed that several experimental methods indicate broadly distributed dynamics of the ions, which is not typical for molecular solvents of similar viscosity. So unusual features of ILs can be attributed to a microheterogeneous environment of the moving particles.[14]

To avoid invalidating the kinetic data by variations in the UV–vis spectrum of the [bmpyrr][NTf_2]−pyrrolidine mixture, the kinetic runs were registered by using as a blank a sample of IL containing the same amine concentration as the kinetic run. In this manner, excellent pseudo-first-order curves were obtained (see the inset of Figure 1).

In Table 2 second-order rate constant values (k_{II}) as a function of ILs and amines are reported. Furthermore, for a useful comparison rate constant values related to pyrrolidine- and piperidine-catalyzed elimination of **2** in MeOH and DMF are

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TABLE 2. Calculated Second-Order Rate Constants at 298 K for the Pyrrolidine- and Piperidine-Catalyzed Elimination Reaction of 2, in Different Solvent Media

solvent	$k_{II,\ pyrri}$ (M^{-1} s^{-1})	R	$k_{II,\ pip}$ (M^{-1} s^{-1})	R
MeOH	0.0195 ± 0.001	0.990	0.0124 ± 0.0007	0.993
DMF	0.097 ± 0.007	0.986	0.0210 ± 0.002	0.980
[bmim][BF_4]	0.109 ± 0.004	0.996	0.0376 ± 0.001	0.993
[bmim][PF_6]	0.101 ± 0.007	0.986	0.0267 ± 0.002	0.990
[bmim][NTf_2]	0.0686 ± 0.0033	0.994	0.0234 ± 0.0007	0.997
[bm_2im][NTf_2]	0.0756 ± 0.004	0.992	0.0303 ± 0.0005	0.999
[bmpyrr][NTf_2]	0.101 ± 0.004	0.996	0.0389 ± 0.001	0.998

also reported (data collected at different amines concentrations are reported in Table 6 of the Supporting Information).

The collected data show that the elimination process occurs easier in ILs than in MeOH. Furthermore, the reaction proceeds faster in DMF than in MeOH, so an H-donor negative solvent effect could be operating, as well as data for [NTf_2^-] ILs (see after) seem to indicate.

Taking into account $bmim^+$ ILs, the reaction rate decreases along the series as follows: [bmim][BF_4] > [bmim][PF_6] > [bmim][NTf_2]. However, the detected order is completely different from that determined on the basis of solvent parameter β values (β = 0.376, 0.207, and 0.243 for [bmim][BF_4], [bmim][PF_6], and [bmim][NTf_2], respectively).[15] On the other hand, considering [NTf_2^-] ILs, the reaction rate decreases along the series as follows: [bmpyrr][NTf_2] > [bm_2im][NTf_2] > [bmim][NTf_2], i.e., the two ILs with less acidic protons favor the elimination. Also in this case the observed reactivity trend cannot be explained only on the basis of α values (α = 0.427, 0.381, and 0.617 for [bmpyrr][NTf_2], [bm_2im][NTf_2], and [bmim][NTf_2], respectively).[15] Likewise, the reactivity trend is different from that obtained considering classical polarity parameters such as E_T^N and π^* (E_T^N = 0.544, 0.576, 0.644 for [bmpyrr][NTf_2], [bm_2im][NTf_2], and [bmim][NTf_2], respectively; π^* = 0.954, 1.083, and 0.984 for [bmpyrr][NTf_2], [bm_2im][NTf_2], and [bmim][NTf_2], respectively).[15]

However, for the same anion ([NTf_2^-]), the reaction seems to be favored in the presence of an aliphatic cation such as $bmpyrr^+$. Fixing the cation, the reaction seems to be favored by anions having a higher symmetry and coordination ability, such as [BF_4^-] and [PF_6^-].[16]

As far as comparison among reactivity data in conventional solvents and in different ILs is concerned, the higher reactivity of **2** in ionic liquid media cannot be ascribed to higher polarity effects. An increase in this parameter should favor the reaction; some of the ILs used in this work have E_{NR} values comparable to those for MeOH and lower than those for DMF (E_{NR} = 217.2, 218.5, 218.0, 217.7, and 221.0 for [bmim][BF_4], [bmim][PF_6], [bmim][NTf_2], MeOH, and DMF, respectively).[17] Probably the higher reactivity could be a consequence of electrostatic interactions. Bearing in mind the transition state structure, ions constituting ILs could induce different effects. According to data previously reported by Welton et al.,[18] and confirmed by us,[5c] an ammonium-charged transition state could be stabilized by interaction between the IL anion and the hydrogen atom on the ammonium nitrogen. On the other hand, the IL cation could coordinate by means of its acidic hydrogen atom (H2 on $bmim^+$, CH_3 on bm_2im^+)[18] the oxygen atom on the isoxazole unit, favoring the O−N bond breaking. Furthermore, as the transition state of the title reaction has a lower aromatic character than the substrate, also $\pi-\pi$[19] and $\pi-$cation[20] interactions should act by stabilizing the ground state to a higher degree than the transition state. Data collected here show that the anion coordination ability and the cation ability to give $\pi-\pi$ interactions are the most important effects. Indeed, reactivity decreases on going from [BF_4^-] and [PF_6^-] ILs up to [NTf_2^-] IL, according to the lower coordination ability of the last anion. On the other hand, reactivity increases on going from $bmim^+$ and bm_2im^+ ILs up to $bmpyrr^+$ IL, according to the different ability to give $\pi-\pi$ interactions and/or to act as H-donor species.

TABLE 3. Activation Parameter Values for the Elimination Reaction of 2, in [bmim][BF_4] Solution, in the Presence of Amines

amine	$\Delta H^{\neq}$ (kJ/mol)	$\Delta S^{\neq}$ (J/(K mol))
butylamine	58 ± 7	−134 ± 21
cyclohexylamine	51 ± 4	−156 ± 13
diisopropylamine	54 ± 1	−139 ± 5
dibutylamine	53 ± 1	−139 ± 3
N-butyl-*N*-methylamine	51 ± 2	−146 ± 7
pyrrolidine	46 ± 1	−149 ± 4
piperidine	54 ± 1	−131 ± 4
hexamethyleneimine	49 ± 2	−146 ± 6
heptamethyleneimine	49 ± 3	−148 ± 10
2,2,6,6-tetramethylpiperidine	51 ± 3	−147 ± 9
triethylamine	52 ± 2	−140 ± 7
N-methylpyrrolidine	52 ± 3	−135 ± 10
N-methylpiperidine	57 ± 1	−130 ± 5

Activation Parameters. It has been reported that, for kinetics carried out in RTILs, a sharp curvature in Arrhenius or Eyring plots could be observed as a consequence of some significant structural changes in the RTIL.[21] So for a careful analysis of the temperature effect, the reaction was carried out at five temperatures going from 293 to 313 K.

In all the cases considered, an excellent linear correlation of $\log(k_{A,R}/T)$ versus 1/T was obtained, indicating that the above upsetting effect is not operating in the analyzed range and that the calculated activation parameters depend only on the nature of the elimination process. In Table 3 activation parameter

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TABLE 4. Activation Parameter Values for the Pyrrolidine- and Piperidine-Elimination Reaction of 2, in Different Solvent Media

solvent	$\Delta H^{\neq}_{pyrr}$ (kJ/mol)	$\Delta S^{\neq}_{pyrr}$ (J/(K mol))	$\Delta H^{\neq}_{pip}$ (kJ/mol)	$\Delta S^{\neq}_{pip}$ (J/(K mol))
MeOH	48 ± 2	−154 ± 5	41 ± 2	−183 ± 8
DMF	45 ± 3	−152 ± 11	55 ± 2	−124 ± 7
[bmim][BF_4]	46 ± 1	−149 ± 4	54 ± 1	−131 ± 4
[bmim][PF_6]	49 ± 3	−144 ± 10	48 ± 2	−156 ± 8
[bmim][NTf_2]	49 ± 2	−144 ± 8	51 ± 1	−145 ± 5
[bm_2im][NTf_2]	45 ± 3	−154 ± 8	49 ± 2	−149 ± 7
[bmpyrr][NTf_2]	46 ± 2	−152 ± 7	45 ± 2	−163 ± 5

values, collected in [bmim][BF_4] solution, as a function of amine, are reported (data collected at different temperatures are available in Table 7 of the Supporting Information).

In Table 4 activation parameter values collected for the pyrrolidine and piperidine elimination of **2** in different solvent media are reported (data collected at different temperature are available in Table 8 of the Supporting Information).

The activation parameters calculated span a narrow range. In particular mean values of $\Delta H^{\ddagger} = (52 \pm 2)$ kJ/mol and of $\Delta S^{\ddagger}$ (-142 ± 8) J/(K mol) were calculated for elimination induced by different amines in [bmim][BF_4]. Similar results were also obtained for pyrrolidine-induced elimination in conventional solvent and ILs [mean values: $\Delta H^{\ddagger} = (47 \pm 2)$ kJ/mol and of $\Delta S^{\ddagger} = (-150 \pm 8)$ J/(K mol)]. A little wider spread of values was calculated for piperidine [mean values: $\Delta H^{\ddagger} = (49 \pm 2)$ kJ/mol and of $\Delta S^{\ddagger} = (-150 \pm 6)$ J/(K mol)].

The above data about the reaction in ILs are not surprising. Indeed, they confirm that weak interactions are operative. The scarce relevance of amine structure on activation parameters could be a consequence of an "early" transition state, having a low C−H bond-breaking degree. This would not allow significant differences to be detected by varying the amine structure. For the same reason only small differences were observed on changing the reaction media.

Conclusions

On the whole, collected data show that the target reaction is sensitive to amine structure rather than to amine basicity. It is interesting to note that once more, for an E2 reaction, cyclic secondary amines are more effective than acyclic ones. This should be a consequence of a partially ordered structure of the solvent medium. Moreover, for the studied reaction classical solvent parameters do not unequivocally allow the effect of ILs to be rationalized. This is consistent with data reported by Kobrak about the differences in solvation phenomena in ionic liquids and molecular solvents.[23] Actually, a relationship between polarity and the microscopic (molecular) electrostatic behavior of the IL may exist, but it is quite different than that observed in conventional solvents. Activation parameters seem to indicate a low degree of C−H bond breaking in the transition state. Consequently, a scarce relevance of variation in amines and ILs structure on activation parameters was detected.

Finally, it is interesting to note that the IL effect is a function of the probe reaction used. In particular, relative to the utilized ILs in the present work, we have verified that an aliphatic cation and an anion having higher coordination ability are more efficient in catalyzing the reaction.

Experimental Section

Materials. Commercial 1,4-dioxane, [bmim][BF_4], and [bmim][PF_6] were used without any other purification. [bmim][NTf_2], [bm_2im][NTf_2], and [bmpyrr][NTf_2] were prepared according to a procedure previously reported.[24] All ionic liquids, before use, were dried on a vacuum line at 60 °C for at least 2 h, then stored in a dryer under argon and over calcium chloride. Amines were freshly distilled before use. Commercial 1,4-benzisoxazole was freshly distilled before use.

Kinetics Measurements and Calculations. UV–vis spectra and kinetic measurements were carried out by using a spectrophotometer equipped with a Peltier temperature controller, able to keep the temperature constant within 0.1 K. Kinetic runs were carried out over the temperature range 293–313 K. The sample for a typical kinetic run was prepared by mixing into a quarz cuvette (optical path 0.2 cm) 500 μL of IL, 50 μL of a solution of substrate in 1,4-dioxane, and then 25 μL of a concentrated solution of amine in 1,4-dioxane, previously thermostated. The obtained solution was thermostated and the opportune volume of amine solution was added. The concentration of substrate was constant and equal to 2.0×10^{-4} M; the amine concentration ranged from 8.7×10^{-3} to 22×10^{-3} M. The reactions were studied over at least three half-lives. In every case, the correlation coefficients were higher than 0.9998. The apparent first-order rate constants obtained were reproducible within ±3%. All kinetic data were analyzed by means of the KALEIDAGRAPH 3.0.1 software.

^{1}H NMR Measurements. NMR spectra were collected on a 300 MHz spectrometer. In NMR measurements the opportune volumes of RTIL and cosolvent were mixed in a 5 mm NMR tube. A steam coaxial capillary tube loaded with DMSO-d_6 was used for the external lock of the NMR magnetic field/frequency and its signal was used as the ^{1}H NMR external reference at 2.56 ppm.

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Supporting Information Available: Rate constants collected at different amines concentrations and at different temperature values and ^{1}H NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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