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## Influence of the ionic liquid on the rate and the mechanism of reaction of *p*-nitrophenyl acetate with secondary alicyclic amines†

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The reaction of *p*-nitrophenyl acetate (**1**) with piperidine was studied in nine organic solvents and in nine ionic liquids. The aminolysis of **1** by four different secondary amines was also studied in [Bmim]BF<sub>4</sub> and their basicities were determined in this solvent using two different methods. Medium effects were analysed and interpreted by comparing the rate constants of aminolysis for the two sets of solvents.

### 1. Introduction

Nucleophilic substitutions have been used to investigate the effects of solvents on chemical reactions: they are thought to be the best kind of reactions to study these effects.<sup>1</sup>

The aminolysis reactions of aryl esters in aqueous solution have been recently studied and they have shown interesting mechanistic changes by varying the solvent medium, the kinetics and mechanisms of these processes being well known.<sup>2</sup> In these reactions, as well as in other related ones, several factors have been described, through experimental and theoretical studies,<sup>3</sup> as affecting the kinetics and mechanisms. Among these are nucleophilic nature,<sup>4</sup> leaving-group ability (nucleofugality),<sup>5</sup> nonleaving-group effects<sup>6</sup> and solvent effects.<sup>7</sup> Aryl esters can react by two possible mechanisms: (i) a concerted pathway, where the nucleophile attack at the electrophilic carbon in the carbonyl group occurs simultaneously with the leaving group departure within a single step and (ii) a stepwise mechanism where the interaction of the nucleophile with the electrophilic carbon may lead to the formation of a tetrahedral intermediate, T<sup>±</sup>, from which the leaving group detaches.

The booming interest in the use of ionic liquids (ILs) as reaction media has produced a large quantity of studies in both experimental and theoretical fields in the last few decades.<sup>8</sup> Due to their remarkable physicochemical properties, such as non-flammable, non-corrosive, non-volatile at normal pressure and the fact that they can dissolve a significant number of

organic species, they are being used as potential substitutes for volatile organic compounds (VOCs).<sup>9</sup> Certainly the most important attribute of these substances is the large number of cations and anions that can potentially be combined to form new ILs with specific properties. This latter property has opened the possibility of obtaining a wide range of solvents with very different characteristics, converting them into designer solvents whose properties can be adjusted to suite the requirements of a particular reaction.<sup>10</sup>

In this work, we report the kinetics and the mechanism of the reaction of *p*-nitrophenyl acetate (**1**) with a series of secondary alicyclic (SA) amines in ionic liquids and conventional solvents. These ionic liquids (Scheme 1) were chosen to investigate the anion and the cation effect. Thus the anions were selected taking into account their size and coordinating ability while the cations to evaluate the hydrogen bond donor ability of the imidazolium cation.

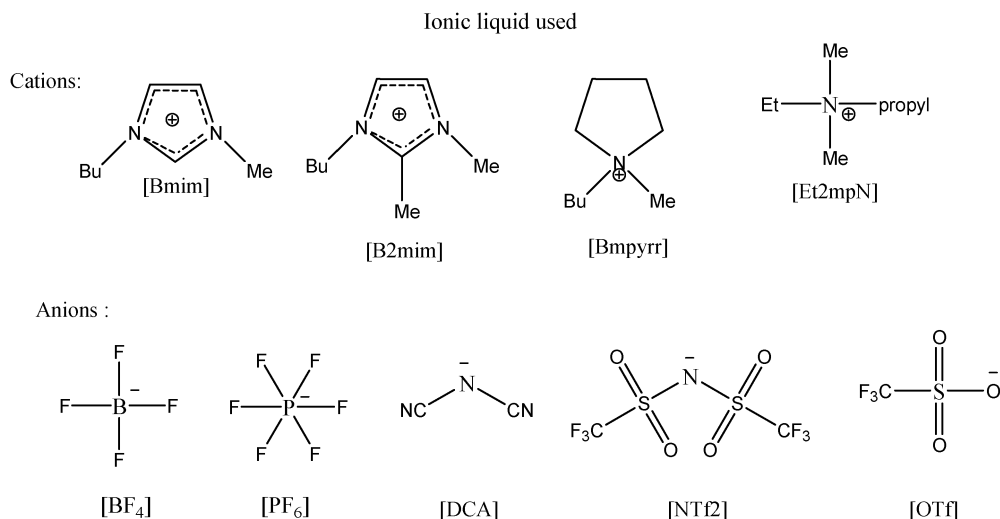
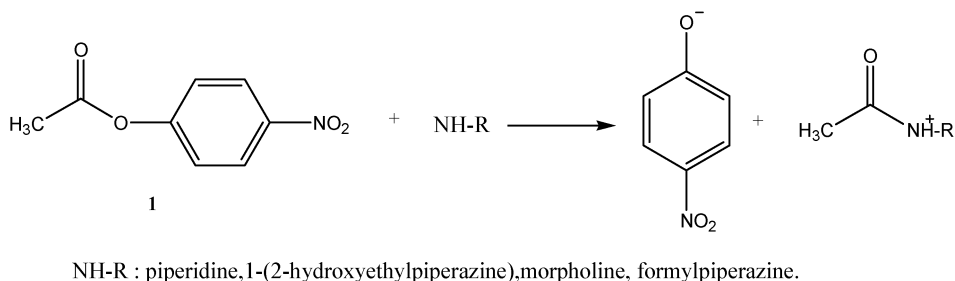
One of the most challenging aspects of this work consists of determining the mechanism of this reaction in ILs. To achieve this, it is necessary to know the p*K*<sub>a</sub> of the studied amines in the reaction media in order to obtain the Brønsted-type plots (log *k* vs. p*K*<sub>a</sub> of amine), which is a usual procedure to shed light on these mechanisms. This is a difficult task because works on basicity of amines in ILs are scarce.<sup>11,12</sup> In fact p*K*<sub>a</sub> data of secondary alicyclic amines in ILs have not been published in the literature so far.

To determine the basicity or acidity of solutes in non-aqueous medium different analytical techniques have been used, the spectroscopic method being the most utilized in conventional solvents. In IL medium this approach has already been applied for strong Brønsted acidity<sup>11</sup> and weak carboxylic acids.<sup>12</sup> The first approach to investigate the basicity of some amines in ILs has also been by spectroscopic methods *via* their

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**Scheme 1**  $S_N2$  reaction studied and ionic liquids used.

reaction with 4-nitrophenol<sup>13</sup> and trifluoroacetic acid.<sup>14</sup> Although the results obtained in these works allow comparison of the basicity strength of the investigated amines in ILs, they do not really give  $pK_a$  values. Recently, two articles about absolute  $pK_a$  in ILs have been published. In one of them Cheng *et al.*<sup>15</sup> describe a general approach to measure absolute  $pK_a$  values of C–H type acid indicators in ILs, whilst in the other article Doherty *et al.*<sup>16</sup> report the first absolute  $pK_b$  of N-aromatic bases in ILs by electrochemical approaches.

In order to shed more light on the mechanism of the proposed reaction we have determined the  $pK_a$  of SA amines in [Bmim]BF<sub>4</sub> through cyclic voltammetry (CV) at a P–Pt electrode. From these measurements we obtained the Brønsted-type plots, which will give us useful information about the reaction mechanism in ILs.

## 2. Results and discussion

### 2.1 Influence of the ionic liquid on the reaction mechanism

We next chose [Bmim]BF<sub>4</sub>, as a model IL, for the study of the aminolysis of **1** in this solvent with four different secondary amines: piperidine, morpholine, 1-(2-hydroxyethyl)piperazine, and 1-formylpiperazine.

The second-order rate coefficients for aminolysis ( $k_N$ ) were obtained as the slopes of plots of eqn (1), where  $k_0$  and  $k_N$  are

the rate constant for solvolysis and aminolysis of the substrate, respectively. These values are reported in Table 1.

$$k_{\text{obs}} = k_0 + k_N[\text{amine}] \quad (1)$$

Brønsted plots of  $\log k_N$  vs. amine  $pK_b$ 's may be used as an indication of the type of mechanism of these reactions.<sup>17</sup> The slope of these plots may be used as evidence for a concerted or for a stepwise process.<sup>18</sup>

We are aware of the fact that a comparison between rate constants measured in ionic liquid and  $pK_a$  of amines determined in water is not entirely accurate. For this reason, the next step to get correct Brønsted correlations is to determine the basicity of these amines in [Bmim]BF<sub>4</sub>.

In order to obtain these values in [Bmim]BF<sub>4</sub> for the studied amines we employed two methods, the first of them by means

**Table 1** Second-order rate constant values  $k_N$ , experimental  $K_{\text{rel}}$  values for alicyclic secondary amines in [Bmim]BF<sub>4</sub>

Amine	$K_{\text{rel}}^a$ (M <sup>-1</sup> )	$k_N^b$ (s <sup>-1</sup> M <sup>-1</sup> )
Piperidine	1076	5.78
1-(2-Hydroxyethyl)piperazine	81	0.84
Morpholine	12	0.39
Formylpiperazine	6	0.072

<sup>a</sup> Standard deviation no higher than  $\pm 10\%$ . <sup>b</sup> Data were reproducible within  $\pm 5\%$ .

of spectroscopic measurements, and the other by an electrochemical technique.

The first approach was introduced by D'anna *et al.*<sup>13</sup> which determined the basic strength of aliphatic amines in ionic liquids by means of the formation of amine-*p*-nitrophenol ion pairs through UV-Vis measurements employing 4-nitrophenol as reference. Following this procedure, the basicities of the four employed amines were evaluated in [Bmim]BF<sub>4</sub> through their  $K_{\text{rel}}$  value, where  $K_{\text{rel}} = [\text{ammonium cation}][\text{nitrophenoxide}]/[\text{amine}][\text{nitrophenol}]$ . These values are listed in Table 1.

As expected, the  $K_{\text{rel}}$  values decrease from piperidine to formylpiperazine in good agreement with second-order rate constant determined for the same amines in this ionic liquid.

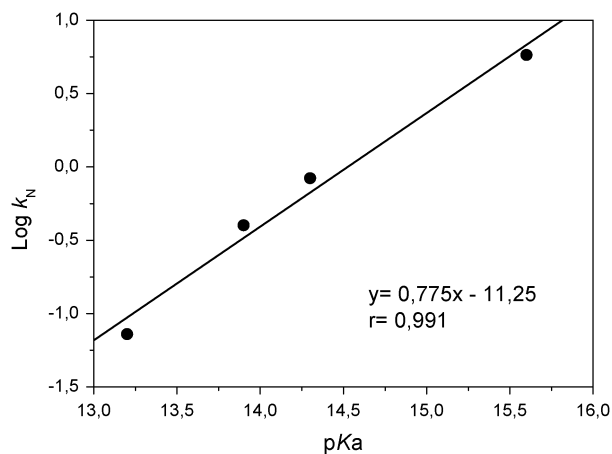
A Brønsted-type plot drawn with these  $K_{\text{rel}}$  values is shown in Fig. S-1 (ESI<sup>†</sup>). The slope of this plot ( $\beta = 0.75$ ) suggests that the reaction mechanism in [Bmim]BF<sub>4</sub> occurs through a stepwise mechanism.

The second approach follows the procedure described by Doherty *et al.*<sup>16</sup> (see Experimental section). Cyclic voltammograms of the amines and a strong acid (HOTf) in [Bmim]BF<sub>4</sub> were recorded (Fig. S-2 and S-3, ESI<sup>†</sup>) and their relative redox potentials for the present species were determined, then the approach described in eqn (10) (Experimental section) was used. Thus, the  $\text{p}K_{\text{a}}$  values in [Bmim]BF<sub>4</sub> calculated for the series of amines are reported in Table 2.

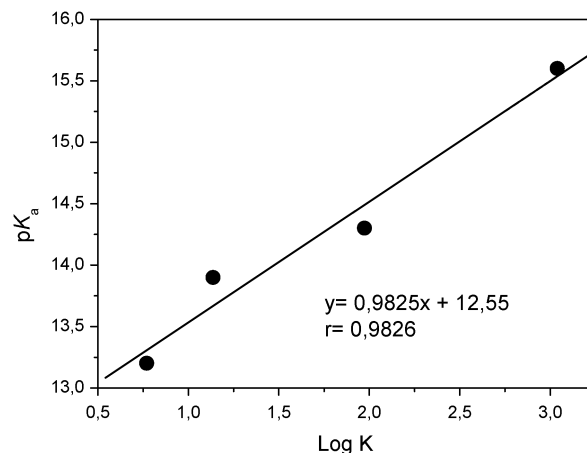
A comparison of the  $\text{p}K_{\text{a}}$  values in water and in [Bmim]BF<sub>4</sub> listed in Table 2 shows that, in general,  $\text{p}K_{\text{a}}$  values measured in [Bmim]BF<sub>4</sub> are *ca.* 5 units higher than those reported in aqueous solution. The trends in basicity of the four amines are maintained in both media, decreasing in the order piperidine > 1-(2-hydroxyethyl)piperazine > morpholine > formylpiperazine.

**Table 2**  $\text{p}K_{\text{a}}$  of alicyclic secondary amines used in this study in [Bmim]BF<sub>4</sub> determined by cyclic voltammetry

	Piperidine	1-(2-Hydroxyethyl)piperazine	Morpholine	Formylpiperazine
$\text{p}K_{\text{a}}$	15.6	14.3	13.9	13.2



**Fig. 1** Brønsted type plot for the reaction of **1** with SA amines in [Bmim]BF<sub>4</sub>.



**Fig. 2** Correlation plot between  $\log K_{\text{R}}$  and  $\text{p}K_{\text{a}}$  of amines in [Bmim]BF<sub>4</sub>.

A Brønsted plot of  $\log k_{\text{N}}$  vs.  $\text{p}K_{\text{a}}$  values in [Bmim]BF<sub>4</sub> is shown in Fig. 1, which yields a slope of  $\beta = 0.77$ , rather similar to that obtained in Fig. S-1 (ESI<sup>†</sup>). This result is reasonable, because of the good correlation ( $r = 0.98$ ) found between  $\log K_{\text{rel}}$  and  $\text{p}K_{\text{a}}$  values in [Bmim]BF<sub>4</sub> (Fig. 2).

Such a good correlation between the basicities of the four amines, calculated using the two methods, validates our analysis and conclusions.

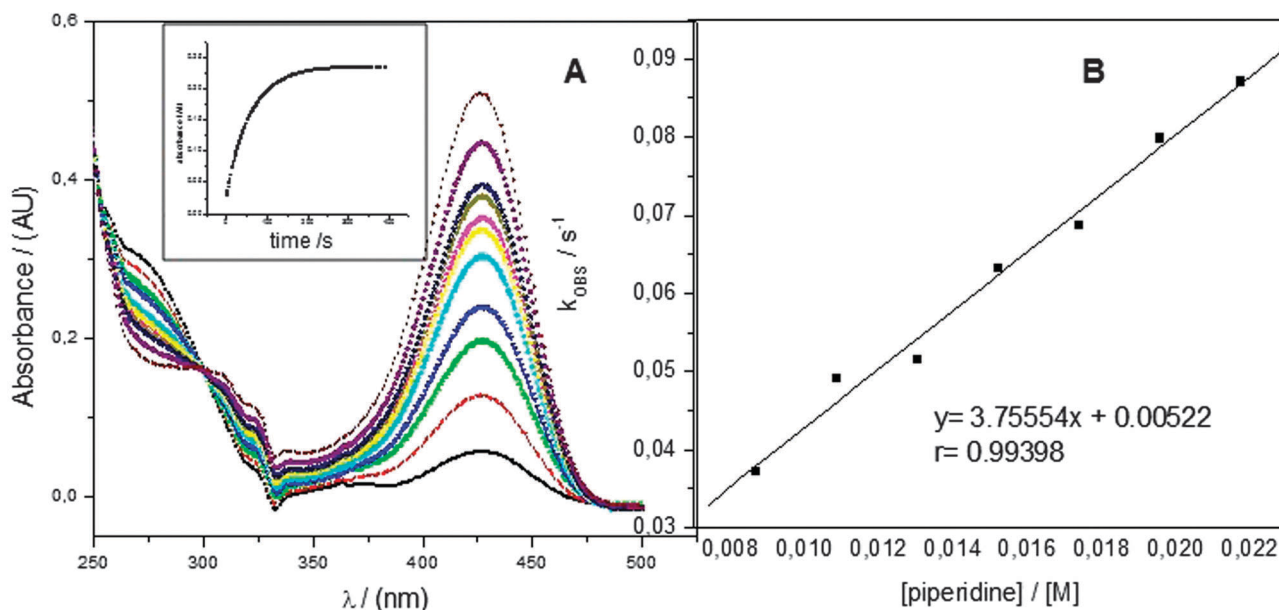
The  $\beta$  (0.77) value found is closely similar to that described by Jencks for the same reaction in water ( $\beta = 0.86$ ),<sup>19</sup> which proceeds through a stepwise mechanism where  $\text{T}^{\pm}$  breakdown to products is rate-limiting. Nevertheless, this value also is in accordance with the  $\beta$  value found for reactions where the C–N bond formation and the C–O breaking are simultaneous through a single transition state.<sup>20</sup>

In order to shed more light on the mechanism we have followed the reaction of **1** with piperidine at the 20–35 °C range with the aim of obtaining the activation parameters in [Bmim]BF<sub>4</sub>.

The values of  $\Delta H^{\ddagger}$  and  $\Delta S^{\ddagger}$  obtained (4.8 kcal mol<sup>−1</sup> and −38.9 cal mol<sup>−1</sup> K<sup>−1</sup>) are closely similar to those reported by Jencks for the same reaction in water solution (7.4 kcal mol<sup>−1</sup> and −26 cal mol<sup>−1</sup> K<sup>−1</sup>).<sup>2</sup> The more negative entropy value in ionic liquid has been explained by Welton<sup>21</sup> as a disruption in the ionic liquid structure induced by a charge-separated activated complex with respect to neutral starting materials. Taking into account the value of the slope of the Brønsted type plot and the values of activation parameters we are prone to accept the stepwise mechanism for the title reaction in [Bmim]BF<sub>4</sub>.

## 2.2 Kinetic measurements

Piperidine was chosen as a model amine to study the effect of the solvent on the aminolysis of *p*-nitrophenyl acetate. As an example Fig. 3A shows the time-dependent UV-vis spectra of piperidine (0.04 M) with **1** in [Bmim]PF<sub>6</sub>. The inset of Fig. 3A shows the time-dependent response of **1** to piperidine under pseudo-first-order conditions (large excess of the amine). Similar results were obtained for the UV-Vis spectra of **1** with piperidine in conventional solvents and ionic liquids (not shown).



**Fig. 3** (A) UV-vis spectra of piperidine (0.04 M) with **1** in [Bmim]PF<sub>6</sub>. The inset shows the experimental plot of absorbance (at 420 nm) vs. time for the reaction of piperidine (0.04 M) with **1** in ([Bmim]PF<sub>6</sub>) at 25 °C. (B) Linear dependence of  $k_{\text{obs}}$  on piperidine concentration in [Bmim]PF<sub>6</sub>.

The kinetics of the reaction of **1** with SA amines in conventional solvents and ionic liquids show an excellent linear dependence of  $k_{\text{obs}}$  on amine concentration, according to eqn (1) (Fig 3B).

Values of  $k_{\text{obs}}$  obtained for the kinetic study are summarized in ESI† (Tables S-1–S-3).

When the solvent was an ionic liquid these plots were always with a slightly negative intercept, this behavior had been reported before<sup>22</sup> and it was attributed to an acid–base interaction between the acidic imidazolium ion and the amine.

The values of  $k_{\text{N}}$  for the reaction of **1** with piperidine in various solvents are shown in Table 3.

**Table 3** Second-order rate constants ( $k_{\text{N}}$ ) for the reaction of **1** with piperidine in conventional solvents and ionic liquids, at 25 °C

Solvent	$k_{\text{N}}^a$ (s <sup>-1</sup> M <sup>-1</sup> )	No of runs <sup>b</sup>	$R^c$
THF	1.52	6	0.992
Acetone	2.77	6	0.999
ACN	2.27	6	0.999
EtOH	0.41	6	0.998
MeOH	0.88	6	0.998
DMSO	42.21	6	0.972
Heptane	0.049	6	0.999
Dichloromethane	0.137	6	0.996
Diethyl ether	0.082	6	0.999
[Bmim]PF <sub>6</sub>	0.34	7	0.992
[Bmim]BF <sub>4</sub>	5.80	7	0.995
[Bmim]DCA	3.76	7	0.997
[Bmim]NTf <sub>2</sub>	2.65	7	0.994
[Bm <sub>2</sub> im]NTf <sub>2</sub>	3.23	7	0.989
[Bm <sub>2</sub> im]BF <sub>4</sub>	1.20	7	0.994
[Bmpyrr]OTf	1.46	7	0.997
[Bmpyrr]NTf <sub>2</sub>	1.06	7	0.991
[Etm <sub>2</sub> pN]NTf <sub>2</sub>	3.05	7	0.993

<sup>a</sup> Second-order rate constants were reproducible within a  $\pm 5\%$ . <sup>b</sup> Number of data points for different amine concentrations. <sup>c</sup> Correlation coefficient for the linear plots of eqn (1).

Confirmation of the formation of the reaction products was achieved by comparison of the UV-vis spectra after completion of the reaction with that of an authentic sample of the *p*-nitrophenoxide ion under the same experimental conditions. Further confirmation of the nature of the products was obtained by extraction of the reaction media with diethyl ether and analysis of the extracted products by GC/MS. Once confirmed the formation of *p*-nitrophenoxide as the sole leaving group of these reactions in conventional solvents, we checked for the possible occurrence of an aromatic nucleophilic substitution (S<sub>N</sub>Ar) at the C-1 of the aromatic ring of **1**, since it has been described that in ionic liquids S<sub>N</sub>Ar processes are favoured for nitro-substituted aromatics.<sup>23</sup> Therefore, a solution of **1** and piperidine in [Bmim]BF<sub>4</sub> was kept at 25 °C for 4 h and then extracted with diethyl ether. The analysis by GC-MS of the extract did not show any presence of the S<sub>N</sub>Ar reaction product, such as 1-piperidino-4-nitrobenzene; instead, *N*-acetyl piperidine was identified as expected. This result confirms that the only pathway for the reaction was a nucleophilic attack at the carbonylic center.

### 2.3 Influence of the solvent on the rate constant

Analysis of data reported in Table 3 shows that the highest  $k_{\text{N}}$  value was found in DMSO ( $k_{\text{N}} = 42.2 \text{ s}^{-1} \text{ M}^{-1}$ ) while the lowest was found in heptane ( $k_{\text{N}} = 0.049 \text{ s}^{-1} \text{ M}^{-1}$ ). On the other hand, for the rate constants in ionic liquids the ratio between fastest and lowest was *ca.* 16 (5.8 and 0.36 for [Bmim]BF<sub>4</sub> and [Bmim]PF<sub>6</sub>).

Attempts to correlate the obtained  $k_{\text{N}}$  values with some empirical measure of solvent polarity, such as the  $E_{\text{T}}(30)$  value, failed for both the conventional solvents and the ILs. As an example the decrease in the reaction rate from DMSO to ILs cannot be rationalized on the grounds of a decrease of polarity, because all ILs used show  $E_{\text{T}}(30)$  values higher (ranging from 48.1 to 52.2 kcal mol<sup>-1</sup>)<sup>24</sup> than DMSO ( $E_{\text{T}}(30) = 45.1 \text{ kcal mol}^{-1}$ ).<sup>25</sup>

**Table 4** Statistical data from the multiple regression procedure including  $\alpha$ ,  $\beta$  and  $\pi^*$  Kamlet–Taft's parameters

Equation	$F^a$	$R^b$	$\pi^{*c}$	$\beta^c$	$\alpha^c$
2	18.4	0.96	0.83(0.49)	2.70(0.62)	−1.86(0.38)
3	2.9	0.73	1.68(1.06)	0.92(1.18)	
4	5.6	0.69	2.09(0.9)		
5	4.1	0.79	2.07(0.83)		−0.89(0.66)
6	1.1	0.39			−0.09(0.9)
7	19	0.94		3.31(0.6)	−2.09(0.42)
8	2.6	0.55		1.86(1.14)	

<sup>a</sup> Statistical  $F$ . <sup>b</sup> Correlation coefficient. <sup>c</sup> Standard deviations are given in parentheses.

A treatment based on a multiparametric regression with Kamlet–Taft's solvent parameters<sup>26</sup> also failed, when the data from conventional solvents were analysed together with those from ionic liquids. We therefore decided to analyse the effect of conventional solvents and of ionic liquids separately, since, as concluded by other authors<sup>27</sup> particular care should be taken with the concept of liquid polarity in ionic liquid solutions.

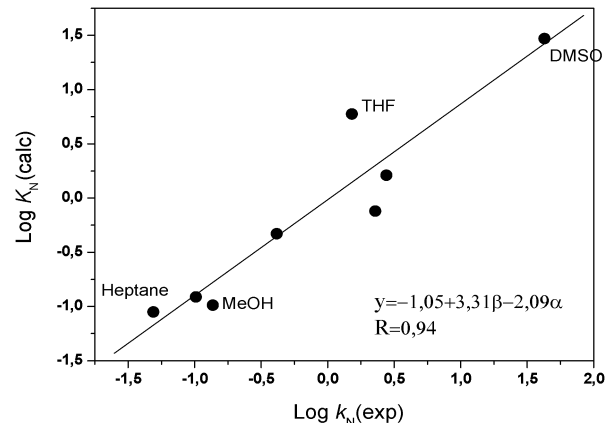
For that reason and in order to have a better understanding of our kinetic results we resolved to discuss them as a function of the solvent nature.

**2.3.1 Conventional solvent effect.** In conventional solvents, second-order rate constants ( $k_N$  in Table 1) decrease in the order DMSO > acetone > ACN > THF > MeOH > CH<sub>2</sub>Cl<sub>2</sub> > EtOH > diethyl ether > heptane. The change in solvent from DMSO to heptane decreases the reaction rate by *ca.* 1000-fold. This decrease could be explained by using  $\alpha$ ,  $\beta$ ,  $\gamma$   $\pi^*$  Kamlet–Taft's solvent parameters. In fact, it seems promising to discuss the solvent effect of this reaction in terms of  $\pi^*$  because, with exception of dichloromethane and methanol, as the  $\pi^*$  value increases the rate constant also increases, in good agreement with previous data reported by us<sup>28</sup> on the aminolysis of dithiocarbonates. Thus, we tried to correlate  $\log k_N$  with each solvent parameter and these results are shown in Table 4.

As can be seen correlations with “one” solvent parameter gave poor correlation coefficients. For that reason a multiparametric regression analysis was performed. This analysis allowed us to estimate the separate contributions of the acidity, basicity and polarizability of the media to the rate constant for this reaction by employing  $\alpha$ ,  $\beta$ ,  $\gamma$   $\pi^*$  Kamlet–Taft's parameters.

$$\log k_{N\text{calc}} = -1.58 + 3.31\beta - 2.09\alpha \quad N = 8, R = 0.94, F = 19 \quad (7)$$

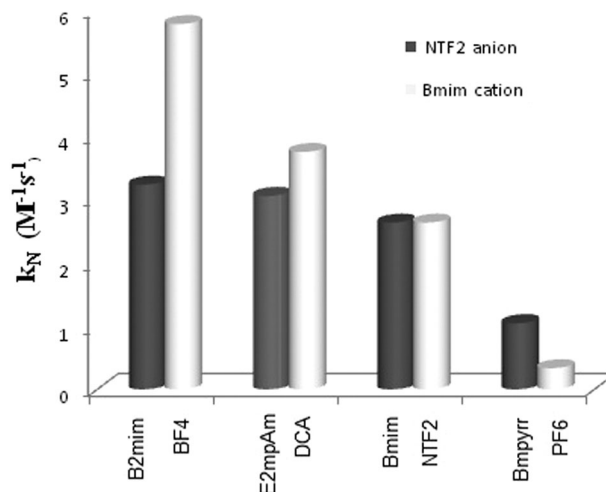
These results can be explained in terms of the ability of the non-hydrogen-bond donor (non-HBD) of solvents to assist proton abstraction in the transition state, which would be accepting a proton from the amine in the TS favouring the formation of the C–N bond. On the other hand, solvents with ability to donate hydrogen bonds (HBD solvent) would act on the nucleophile–electrophile pair solvating the nucleophile by hydrogen bonds. This solvation would increase the free energy of activation of the concerted mechanism, therefore, decreasing the rate constant, which is in accordance with the negative value (−2.09) for the  $\alpha$  parameter in eqn (7).

**Fig. 4** Double logarithmic plot of  $k_N(\text{exp.})$  against  $k_N(\text{calc.})$ , obtained from eqn (7).

The predicted  $k_N$  value for this reaction in water, calculated from eqn (7), shows a much slower rate constant than that reported in water by Jencks.<sup>2</sup> This result demonstrates that this reaction proceeds by a different mechanism in conventional solvents, otherwise the calculated  $k_N$  value for the reaction in water should be in the same trend shown in Fig. 4.

**2.3.2 Effect of ionic liquids.** The above analysis could not be applied to the piperidinolysis of **1** in ionic liquids. Inspection of collected data in Table 3 shows that the rate constant decreases along [Bmim]BF<sub>4</sub> > [Bmim]DCA > [B<sub>2</sub>mim]NTf<sub>2</sub> > [Em<sub>2</sub>pAm]NTf<sub>2</sub> > [Bmim]NTf<sub>2</sub> > [Bmpyr]OTf > [B<sub>2</sub>mim]BF<sub>4</sub> > [Bmpyr]NTf<sub>2</sub> > [Bmim]PF<sub>6</sub>. The effect of the nature of the anion and the cation of ionic liquid on the second-order rate constant can be seen in Fig. 5.

The importance of the anion in these ion pairs is evident from a comparison of reaction rates in ILs that share a common cation: [Bmim]BF<sub>4</sub> (5.80) > [Bmim]DCA (3.76) > [Bmim]NTf<sub>2</sub> (2.65) > [Bmim]PF<sub>6</sub> (0.34). Following the observation made above, of rate acceleration by basic solvents, capable of assisting a proton abstraction from the amine in the transition state, we

**Fig. 5** Variation of the second-order rate constant values ( $k_N$ ) for the aminolysis of **1** with the nature of the ionic liquid.



may speculate that the anion in these ILs might play a similar role. By binding to the N–H hydrogen in the transition state, these anions should facilitate the nucleophilic attack on the carbonyl group of **1**. This is in line with their HBA ability, and with their size. If similar charged atoms are compared, the dicyanamide group  $[(\text{CN})_2\text{N}^-]$ , DCA] has a less hindered nitrogen anion than the bistrifluoromethylsulfonyl group  $[(\text{CF}_3\text{SO}_2)_2\text{N}^-]$ , NTf<sub>2</sub>], so that its HBA interaction with the N–H hydrogen is greater. Comparison of the polyfluorides BF<sub>4</sub><sup>−</sup> and PF<sub>6</sub><sup>−</sup> leads to the same conclusion: charge is more concentrated on the four F atoms of the tetrafluoroborate anion than on the six atoms of the hexafluorophosphate anion. This factor, and the smaller size of the BF<sub>4</sub><sup>−</sup> anion, make it a better HBA agent than PF<sub>6</sub><sup>−</sup>, in line with the almost 20-fold-greater rate constant observed in [Bmim]BF<sub>4</sub>, when compared with [Bmim]PF<sub>6</sub>.

Trends are less clear when anions from different families are compared, as for example, when a fluoride is compared with an amide anion. Thus, for the [Bmim]BF<sub>4</sub>–[Bmim]NTf<sub>2</sub> pair, the rate is greater for the tetrafluoroborate anion, whereas, for the [B<sub>2</sub>mim]BF<sub>4</sub>–[B<sub>2</sub>mim]NTf<sub>2</sub>, the opposite is true.

The importance of the cation in the ionic liquids may be gathered from a comparison of ILs that share a common anion. This is the case of the [Bmim]–[Bm<sub>2</sub>im] pair, which shares a common BF<sub>4</sub><sup>−</sup> and also a common NTf<sub>2</sub><sup>−</sup> group. Reports on the acidity of the hydrogen atom at position 2 of the benzimidazolium ring<sup>29</sup> would suggest the [Bmim] cation to be a stronger hydrogen-bond-donor than Bm<sub>2</sub>im, where position 2 is blocked by a methyl group. This expectation is born out by a comparison of the rates of aminolysis in [Bm<sub>2</sub>im] NTf<sub>2</sub> (3.23) and [Bmim]NTf<sub>2</sub> (2.65). However, this is not the case for the rates in [Bm<sub>2</sub>im] BF<sub>4</sub> (1.20) and [Bmim]BF<sub>4</sub> (5.80). It is clear that our analysis, by ignoring ion-pair interactions in these organic salts, and treating anions and cations as separate entities in these solvents, is not capable of uncovering all the subtle factors involved in such complex systems. The contribution of the medium to the stability of a large and polarized transition state, with considerable charge dispersion, reflected in the positive  $\pi^*$  coefficient of eqn (7) above, may be one of these factors. This contribution, when different ILs are compared, should depend not only on the nature of their isolated anions and/or cations, but also on their interaction as associated pairs with the transition state of the studied reaction.

A comparison of the  $k_N$  values of the reaction with piperidine in various solvents in Table 3 shows that, with the exception of the process in DMSO (42.21), the aminolysis in [Bmim]BF<sub>4</sub> proceeds with the highest rate (5.80). Our preceding analysis of Section 2.2, based on Kamlet–Taft's protocol, may be used to interpret these observations. The major difference between the two solvents is the much higher hydrogen-bond-accepting (HBA) strength of DMSO, when compared with that of the BF<sub>4</sub><sup>−</sup> anion, which assists more effectively the N–H proton abstraction in the transition state. The deterring effect of the hydrogen-bond-donation by the solvent (a negative  $\alpha$  coefficient in eqn (7)) is perhaps larger in the [Bmim] cation than in DMSO, but it is not as important as in other strong HBD solvents, like ethanol, or methanol, where  $k_N$  values are much

smaller (0.4–0.9 M<sup>−1</sup> s<sup>−1</sup>) than in [Bmim]BF<sub>4</sub>. Finally, [Bmim]BF<sub>4</sub>, because of its ionic nature, is capable of stabilizing a polarized transition state with significant charge dispersion more effectively than most organic solvents of low (heptane or dichloromethane) or intermediate (acetone or acetonitrile) polarities.

### 3. Conclusions

Data reported here demonstrate that the mechanism of this reaction in [Bmim]BF<sub>4</sub> is stepwise, different from the concerted mechanism found in conventional solvents. In addition, in [Bmim]BF<sub>4</sub> a linear Brønsted plot shows a high  $\beta$  value (0.77). This result is similar to that reported in water for the same reaction. Nevertheless, it is noteworthy that although this reaction proceeds by the same path in both water and ionic liquid, a moderate effect of the ionic environment was found in the reaction mechanism.

On the other hand, Kamlet–Taft treatment of kinetic data collected in IL solution indicate that different structural features should be taken into account in order to rationalize reactivity results in these solvent media. In particular, among different factors, the three-dimensional structure of solvents seems to play a significant role.

The acidity of alicyclic secondary amines can be rationalized in terms of  $K_{\text{rel}}$  and acidity constants determined by UV-Vis and cyclic voltammetry, respectively, and both can be used to build Brønsted type plots.

### 4. Experimental section

#### 4.1 Materials

All ionic liquids, SA amines and conventional solvents were purchased from Aldrich. All ionic liquids were dried before use in a vacuum oven at 70 °C for at least 2 h, stored in a dryer under nitrogen and over calcium chloride. Water contents determined by Karl–Fisher titration were <200 ppm. *p*-Nitrophenyl acetate (**1**) was prepared as described.<sup>30</sup>

#### 4.2 Kinetic measurements

Kinetic measurements were performed by UV-vis spectrophotometry, following the disappearance of *p*-nitrophenoxide (400 nm) after at least four half-lives. The kinetic experiments were carried out in ionic liquid solutions at 25 °C under pseudo-first order conditions. Each sample was made in triplicate. In a typical spectrophotometric measurement a quartz cuvette (light-path 0.2 cm) containing 500  $\mu\text{L}$  of ionic liquid was thermostated at 25 °C for 10 minutes. Then a solution of **1** (50  $\mu\text{L}$ ,  $2 \times 10^{-4}$  M in ACN) and the concentrated amine (25  $\mu\text{L}$ ) were added. The spectra were recorded at different reaction times and pseudo-first-order rate coefficients ( $k_{\text{obs}}$ ) were found for all reactions.

#### 4.3 Product studies

The product, *p*-nitrophenoxide, was identified by comparison of the UV-vis spectra after completion of the reaction with that of an authentic sample of the *p*-nitrophenoxide ion under the same experimental conditions. To confirm the presence of the

products, extractions with diethyl ether were made from the reaction media and this extract was analyzed by GC/MS.

#### 4.4 Electrochemical measurements

All electrochemical measurements were carried out using a CH Instrument 760c potentiostat, in a three-electrode cell. The working electrode was a platinized Platinum disk from CH instrument ( $r = 1.5$  mm), Pt wire ( $14\text{ cm}^2$ ) was a counter electrode and Ag/AgCl was the reference electrode. For measurements in Ionic Liquid media the reference electrode was separated from solution by a Luggin capillary with a Pt bridge avoiding moisture contamination to the working solution. All measurements were performed at 298 K under a nitrogen atmosphere. CVs were recorded in IL solutions containing both strong (subject to precedent considerations in the theoretical part) and weak acids.

**4.4.1 Electrode preparation.** The Pt disk electrode was covered with a fresh electrochemical coating of platinized platinum, which allows obtaining an electrochemically quasi-reversible  $\text{H}^+/\text{H}_2$  redox couple. The electrodeposition of platinum on the electrode surface was obtained under electrolysis at controlled potential (2 V) by 30 seconds, in a solution of chloroplatinic acid (3 g) and lead acetate (0.02 g) dissolved in 100 mL of distilled water. A Pt wire was the anode during electrodeposition.

**4.4.2 Determination of  $\text{p}K_{\text{a}}$ .** The  $\text{p}K_{\text{a}}$  values for the conjugate acids of the SA amines in [Bmim] $\text{BF}_4$  were determined through cyclic voltammetry (CV) using the reported method.<sup>16</sup> This method is based on eqn (9),

$$\Delta E^0 = E_2^0 - E_1^0 = -0.059\text{p}K_{\text{a}} \quad (9)$$

where  $E_1^0$  and  $E_2^0$  are the respective standard reduction potentials, in the medium being examined, of the amine and strong acid, respectively.

In this case, the cathodic peak potentials were employed to determine  $\Delta E^0$ , since both anodic ( $\Delta E_{\text{ap}}$ ) and cathodic peaks ( $\Delta E_{\text{cp}}$ ) and half-wave potential ( $\Delta E_{1/2}$ ) are equal to the difference between their respective standard potential  $\Delta E^0$  (eqn (10)).

$$\Delta E^0 = \Delta E_{\text{cp}} = \Delta E_{\text{ap}} = \Delta E_{1/2} \quad (10)$$

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