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Anion nucleophilicity in ionic liquids: a comparison with traditional molecular solvents of different polarity

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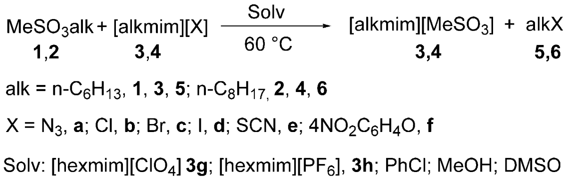
Abstract—The nucleophilic reactivity of a homogeneous series of anions (halides, pseudohalides and organic anions) in the ionic liquids [hexmim] [ClO_4] and [hexmim] [PF_6] has been measured in their reaction with *n*-alkyl methanesulfonates, and compared with that found in traditional molecular solvents of different polarity, that is, chlorobenzene, DMSO, and MeOH.

Room temperature ionic liquids (RTILs) are attracting increasing attention as a powerful alternative to conventional molecular organic solvents. Negligible vapor pressure combined with excellent stability and ease of recycle makes them possible environmentally friendly media for a number of chemical processes, both stoichiometric and catalytic. RTILs have found application in synthesis, catalysis, polymerization, industrial cleaning, liquid/liquid extraction, and separation as documented by recent reviews and books.[1] Despite great improvements in yields and reaction rates and the growing current interest in anion-promoted reactions in ILs, only few studies have considered the effect that this new class of solvents could have on the anion activation.[2,3] The reaction medium is well known to play a crucial role in determining the rate and outcome of a chemical process, particularly when anionic species are involved. In addition, when the organic medium is not rigorously anhydrous, the reactivity of the anion (nucleophilicity, basicity) is reduced, even remarkably, by the specific interaction, via hydrogen bonding, with the molecules of water.[4,5] To the best of our knowledge, till now little attention has been paid by the current literature[1i,2,3b] to the effect that the presence of water in ILs could have on the anion nucleophilicity.

Here, we report a systematic study of nucleophilic reactivity of a representative series of anions (halides, pseudohalides and organic anions) in the nucleophilic substitution reaction of the methanesulfonic group in *n*-hexyl (**1**) and *n*-octyl methanesulfonate (**2**) in the non-nucleophilic ILs 1-hexyl-3-methylimidazolium perchlorate, [hexmim][ClO_4] (**3g**), and hexafluorophosphate, [hexmim][PF_6] (**3h**) (Scheme 1). The results have been compared with those obtained in typical molecular solvents of different polarity (chlorobenzene, DMSO, and MeOH) under the same conditions (Scheme 1).

Kinetics were carried out at 60 °C by reacting comparable amounts of substrate **1** or **2** and nucleophile [alkmim] [X] **3a**–**f**, **4a**–**f** in the appropriate medium.[6] They were found to obey a regular second-order kinetic equation, up to almost 75% conversion (Table 1). The results of Table 1 show that the reactivity of all the anions X^- increases (1.4–2 times) changing from [hexmim][PF_6] **3h** to [hexmim][ClO_4] **3g**. The nucleophilicity sequences obtained in both ionic liquids ($N_3^- \gg I^- = Br^- \approx Cl^- \approx 4\text{-}NO_2PhO^- > SCN^-$ in [hexmim][PF_6] **3h** and $N_3^- \gg I^- > Cl^- > 4\text{-}NO_2PhO^- \approx Br^- > SCN^-$ in



$$\underset{\mathbf{1,2}}{MeSO_3alk} + \underset{\mathbf{3,4}}{[alkmim][X]} \xrightarrow[60\ °C]{Solv} \underset{\mathbf{3,4}}{[alkmim][MeSO_3]} + \underset{\mathbf{5,6}}{alkX}$$

alk = n-C_6H_{13}, **1**, **3**, **5**; n-C_8H_{17}, **2**, **4**, **6**

X = N_3, **a**; Cl, **b**; Br, **c**; I, **d**; SCN, **e**; $4NO_2C_6H_4O$, **f**

Solv: [hexmim][ClO_4] **3g**; [hexmim][PF_6], **3h**; PhCl; MeOH; DMSO

Scheme 1.

Keywords: Nucleophilic substitutions; Anion reactivity; Ionic liquids; Hydrogen bonding effect; Water effect.

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Table 1. Second-order rate constants k ($M^{-1}\ s^{-1}$) for the S_N2 substitution reaction of the methanesulfonic group in **1** and **2** by anions X^- in ionic liquids[a] and molecular solvents (PhCl[b], MeOH[c], DMSO[c]) at 60 °C

X	$10^4\ k$ ($M^{-1}\ s^{-1}$)				
	[hexmim][PF_6][d]	[hexmim][ClO_4][d]	PhCl[b,e]	MeOH[c]	DMSO[c]
N_3	31.7	56.3	358 (1560)	6.0	135
Cl	3.3	7.1[f,g]	75 (370)	0.9	36
Br	3.7	5.3	71 (200)	2.2	23
I	3.7	8.2	32 (68)	5.8	5.3
SCN	0.8	1.3	7.2 (7.5)	1.7	2.7
$4NO_2PhO$	3.2	5.4	41.5 (60)	—	—

[a] A solution of **1** (0.03–0.05 M), internal standard, phenetole (0.02 M) and **3a–f** (0.06–0.08 M) (reactions monitored by GLC analysis).

[b] A chlorobenzene solution of **2** (0.01–0.03 M) and **4a–f** (0.02–0.05 M) (reactions titrimetrically monitored).

[c] Data from Ref. 8.

[d] 2000 ± 100 ppm water (average value of water retained by IL after a normal work-up).

[e] Data in parentheses from Ref. 7 (same conditions of b with $Octyl_4N^+X^-$).

[f] $10^4\ k$ ($M^{-1}\ s^{-1}$) = 1.7, 2.6, 3.7, 4.3, 7.4, 7.7, and 30.4 for 18,800, 9680, 5550, 4500, 1750, 1275, and 124 water ppm, respectively.

[g] $10^4 k_{extrap}$ = 71 and 487 for water ppm 30 and anhydrous medium, respectively.

[hexmim][ClO_4] **3g**) are anomalous if compared with the well-known scales of these anions in molecular solvents.[5] Moreover, the reactivity spans a narrow range (Table 1). Our results are in agreement with those reported by Welton and co-workers[2] in previous studies concerning the halide nucleophilicity in ILs.

When the reaction (1) was carried out with the [octmim][X] imidazolium salts (**4a–f**) in anhydrous PhCl (⩽30 ppm water), the rate constants k ($M^{-1}\ s^{-1}$) were found to increase (6–23 times) (Table 1). This enhancement was expected because the anion, scarcely stabilized by the non-polar medium and non-hydrated, is known to be very reactive.[5,7,8] However, the sequence in PhCl was not so different from those obtained in ILs and the nucleophilicity range was also narrow. Since the water content in this medium is negligible, the reactivity of the anion is mainly determined by its interaction with the cation $[octmim]^+$ **4** to give most likely ion pairs or more complex aggregates. Convincing evidences for both the formation of tight ion pairs[9] and hydrogen bonding[10] between the imidazolium cation and the naked anion in anhydrous ILs were suggested by NMR spectroscopy, in line with the Kamlet-Taft α values (0.6–0.7).[11] In addition, we experimentally found that, by changing the imidazolium with the bulky tetraoctylammonium cation, less prone to hydrogen-bond formation,[12] the nucleophilicity of all the anions X^- further increases (up to about 5 times) and the reactivity sequence becomes that typical for these anions in dipolar non-hydrogen bond donor (non-HBD) media and in the gas phase ($N_3^- > Cl^- > Br^- > I^- > SCN^- >$ 4-NO_2PhO^-).[5,7,8] It is worth noting that the enhancement, on going from the imidazolium to tetraalkylammonium salt, follows the order: 4-NO_2PhO^- (1.4) < I^- (2.2) < Br^- (2.8) < Cl^- (4.9). It clearly reflects, as in the series of halides, the increasing interaction (hydrogen bonding) of the anion with the ion-paired imidazolium cation[9,10] on increasing the charge density (charge vs ionic radius) of X^-.

Ionic liquids are known to be hygroscopic materials, which in a normal work-up retain significant amounts of water, unless very accurate drying protocols are employed just before their use.[1i,2,3b] The presence of water molecules that preferentially solvate (H-bonding) the anion[13] could remarkably affect the reaction rates in ILs. A study performed in parallel for [hexmim][Cl] **3b** in the ionic liquid [hexmim][ClO_4] **3g** has shown an excellent linear correlation between the rate constant k ($M^{-1}\ s^{-1}$) and the water content (ppm) of the IL ($y = -0.5682x + 3.6873$, $r = 0.998$; Log k + 5 *vs.* Log ppm H_2O). We have found (see Table 1, footnote f) that the nucleophilic reactivity of **3b** increases by progressively reducing the amount of water of IL. In this case, the gain of nucleophilicity is extrapolated to be 286 times from 18,800 ppm water to the hypothetical anhydrous medium (Table 1, footnote g). Such a behavior parallels that previously found when the reaction (1) was performed with tetraalkylonium salts in PhCl. In that non-HBD solvent, the dehydration of the anion produced dramatic reactivity enhancements, especially for highly hydrophilic anions (F^- and OH^-).[7]

As reported in Table 1, the anion nucleophilicity in the ionic liquid (though not completely anhydrous) is comparable with or even higher than that in anhydrous (<50 ppm water) methanol, particularly for anions with localized and/or less polarizable charge such as Br^-, N_3^-, and Cl^-. These results highlight the high reactivity of [hexmim][X] **3a–f** in the IL **3g** if compared with that of the free ion X^-[7], specifically solvated by hydrogen bonding in anhydrous MeOH. As expected, in DMSO (where mostly free ions are present)[5,7,8] the nucleophilicity of the anion X^- noticeably increases, overcoming that of the ion pair in the IL (Table 1).[7,8] Finally, it is worth noting that, when the water content of [hexmim][ClO_4] **3g** is the same as that of anhydrous PhCl (about 30 ppm water), the nucleophilic reactivity of [alkmim][Cl] **3b**, **4b** is also the same in both media ($k = 0.0071$ and 0.0075 in [hexmim][ClO_4] **3g** and PhCl, respectively). The value is even higher than that found for the chloride anion in DMSO ($k = 0.0036$) (Table 1).

In conclusion, our results provide a quantitative measure of the effects that both the interaction with the imidazolium cation and the specific solvation by water produce on the nucleophilicity of a representative series of anions in typical ILs.[14] Comparison with molecular solvents shows that the reactivity of the [alkmim][X] ion pair in IL is in between that of the free ions X^- in MeOH and in DMSO (Table 1). It even approaches that in non-HBD (DMSO) and scarcely polar (PhCl) media when the IL is largely dehydrated. Due to the noticeable gain in reactivity, it should be desirable that the largest quantity of water be removed from the IL, particularly for reactions that involve highly hydrophilic anions. Under these conditions, the reactivity of the anion is mainly determined by its interaction with the hydrogen-bonded cation.

Acknowledgments

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