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Reactivity of anionic nucleophiles in ionic liquids and molecular solvents

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Abstract

The nucleophilic reactivity of a representative series of anions has been measured in [hmim][ClO_4] **3i**, [hm_2im][ClO_4] **3′i**, and [hmim][PF_6] **3l** ILs in the reaction with *n*-alkyl methanesulfonates and compared with that found in common molecular solvents (MeOH, DMSO, PhCl). The reactivity is found to depend on both the imidazolium cation−anion interaction and the specific solvation by water present in the IL, the water playing the main effect, in particular with hydrophilic anions. Removal of the largest quantity of water remarkably increases the ion pair reactivity in the IL up to rate constant value *k* comparable with those obtained in DMSO and in low polarity media (PhCl).

1. Introduction

Ionic liquids (ILs) are a class of novel solvents, which are attracting increasing interest as a potential ‘green’ alternative to conventional volatile organic solvents (VOCs), generally used in large amounts. They are low-melting (<100 °C) salts composed of bulky organic cations and a variety of anions whose characteristics can be tailored by a suitable choice of the cation/anion combination.

The most attractive property of ILs is their negligible vapor pressure that combined with excellent thermal stability, high ionic conductivity, and ease of recycling makes them possible ecosustainable media for both stoichiometric and catalytic processes. Ionic liquids solubilize a number of organic and inorganic materials and hence they have found wide application in synthesis, catalysis, polymerization, industrial cleaning, liquid/liquid extraction, and separation as documented by the dramatic increase of reviews and books published in the last few years.[1−6]

However, the most efficient utilization of these green solvents still needs a deeper knowledge of their physico-chemical properties and the correlation between these and the molecular structure. In addition, it is of primary importance to understand how the physico-chemical characteristics of ILs are able to affect organic reactivity in order to predict and precisely tailor the best IL for every chemical reaction.[5] The medium is well known to play a leading role in determining the rate and outcome of a chemical process, particularly when anionic species are involved.[7] To date only a few studies have quantitatively evaluated the effect of this novel class of solvents on the anion reactivity and made a comparison with traditional molecular media. A kinetic study of the Menschutkin reaction of 1,2-dimethyl imidazole with benzyl bromide has shown that the rate constants in the ILs are comparable with those in polar aprotic molecular solvents, but much higher than those in weakly polar organic solvents and in alcohols. They depend on the IL anion whereas the variations with the solvent cations are minimal.[8] In other studies, the nature of the IL, both cation and anion, was found to affect the relative nucleophilicities of anionic nucleophiles in the S_N2 reaction with methyl *p*-nitrobenzenesulfonate.[9]

Recently, we have studied the nucleophilic reactivity of anions associated with imidazolium cations in ionic liquids and in traditional molecular solvents of different polarity. Preliminary results have indicated that the nucleophilicity of the

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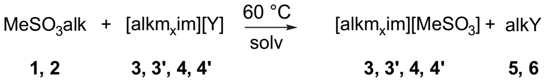
anion is mainly determined by both its interaction with the IL cation and the specific solvation by water molecules present in the medium.[10](1).



$$\underset{\mathbf{1,\,2}}{MeSO_3alk} + \underset{\mathbf{3,\,3',\,4,\,4'}}{[alkm_xim][Y]} \xrightarrow[\text{solv}]{60\ °C} \underset{\mathbf{3,\,3',\,4,\,4'}}{[alkm_xim][MeSO_3]} + \underset{\mathbf{5,\,6}}{alkY}$$

alk = n-C_6H_{13} **1, 3, 5**; n-C_8H_{17} **2, 4, 6** (1)
x = 1 (**3, 4**); 2 (**3', 4'**)
Y = N_3, **a**; Cl, **b**; Br, **c**; I, **d**; SCN, **e**; 4-$NO_2C_6H_4O$, **f**; C_6H_5COO, **g**; $C_6H_5CH_2COO$, **h**;ClO_4, **i**; $MeSO_3$, **j**; PF_6, **l**
solv = [hmim][ClO_4], **3i**; [hm$_2$im][ClO_4], **3'i**; [hmim][PF_6], **3l**; PhCl; DMSO; MeOH

Here, we report a systematic study on nucleophilicity of a representative series of anions (halides, pseudohalides, organic anions) by imidazolium salts (**3a–h**, **4a–f**, **4′b–d**,**f**) in the S_N2 reaction of the methanesulfonic group in *n*-hexyl (**1**) and *n*-octyl methanesulfonate (**2**) in the non-nucleophilic ILs 1-hexyl-3-methylimidazolium perchlorate [hmim][ClO_4] (**3i**), 1-hexyl-2,3-dimethylimidazolium perchlorate [hm$_2$im][ClO_4] (**3′i**), and 1-hexyl-3-methylimidazolium hexafluorophosphate [hmim][PF_6] (**3l**) (Eq. 1). The reactivity found in these ILs has been compared with that obtained in molecular solvents of different polarity (chlorobenzene, MeOH, DMSO) (Eq. 1).

2. Results and discussion

Kinetics were performed by reacting comparable amounts of substrate **1** or **2** (0.03–0.05 M) and nucleophile (**3a–h**, **4a–f**, **4′b–d**,**f**) (0.06–0.08 M) in the appropriate solvent, at 60 °C (Eq. 1). Rates have been measured by gas chromatographic determination of the reaction products alkY **5** and **6**, evaluated with respect to an internal standard (phenetole) or by potentiometric titration of the nucleophile Y^-. Under these conditions, the reactions follow regular second-order kinetics (Eq. 2) up to at least three half-life times ($R^2=0.999$) (Fig. 1). Results are reported in Tables 1–4.

$$\text{Rate} = k[\text{substrate}][Y^-] \tag{2}$$

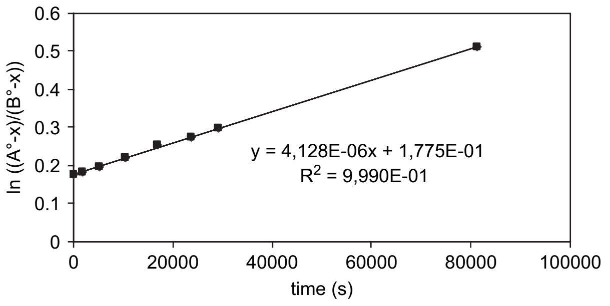


Figure 1. Second-order plot of the substitution reaction of the methanesulfonic group in **1** by [hmim][Cl] **3b** in [hmim][ClO_4] **3i**, at 60 °C.

Table 1
Second-order rate constants k ($M^{-1}\,s^{-1}$) for the substitution reaction of the methanesulfonic group by [hmim][Y] in ionic liquids[a] and chlorobenzene,[b] at 60 °C

Y	$k\times10^4$ ($M^{-1}\,s^{-1}$)		
	[hmim][PF_6][c]	[hmim][ClO_4][c]	PhCl[d]
N_3	31.7	56.3	358
Cl	3.3	7.1 (71)[e]	75
Br	3.7	5.3	71
I	3.7	4.2	32
SCN	0.8	1.3	7.2
4-NO_2–PhO	3.2	5.4	41.5
PhCOO	—	5.3	32
$PhCH_2COO$	—	5.6	7.4

[a] A solution of **1** (0.03–0.05 M), internal standard phenetole (0.02 M), and **3a–h** (0.06–0.08 M) (reactions monitored by GLC analysis).
[b] A chlorobenzene solution of **2** (0.01–0.03 M) and **4a–f** or **3g**,**h** (0.02–0.05 M) (reactions titrimetrically monitored).
[c] 2000±100 ppm H_2O (average value of water retained by IL after a standard work-up) (see Section 4).
[d] 30 ppm H_2O.
[e] $10^4\times k_{extrap}=71$ for water ppm 30 (see Table 2).

The results in Table 1 show that the reactivity of all the anions Y^- increases, up to two times, on going from [hmim][PF_6] **3l** to [hmim][ClO_4] **3i**. The nucleophilicity sequences are also different ($N_3^->I^-=Br^-\sim Cl^-\sim 4NO_2PhO^->SCN^-$ in [hmim][PF_6] **3l** and $N_3^->Cl^->Br^-\sim 4NO_2PhO^-\sim PhCOO^-\sim PhCH_2COO^->I^->SCN^-$ in [hmim][ClO_4] **3i**). It is worth noting that the reactivity scale found in [hmim][ClO_4] **3i** is in line with the well known orders of nucleophilicity obtained for these anions in polar aprotic molecular solvents and in gas phase even if in the ILs the values span a relatively narrow range.[7,10–13]

When the lipophilic salts **4a–f** and **3g**,**h** (soluble also in the non-polar medium) were reacted with substrate **1** in anhydrous chlorobenzene (≤30 ppm H_2O) the rate constants k ($M^{-1}\,s^{-1}$) of all the anions increased, up to 23 times. The enhancements obtained are expected because the anion is non-hydrated and scarcely stabilized by the non-polar medium, hence very reactive.[7,10–13] However, as shown in Table 1, the sequence obtained in PhCl ($N_3^->Cl^->Br^->4NO_2PhO^->I^-=PhCOO^->SCN^-=PhCH_2COO^-$) was not so different from that in [hmim][ClO_4] **3i** and the reactivity range was still narrow. Since no water is present the nucleophilicity values must be largely determined

Table 2
Effect of the water on the second-order rate constant k ($M^{-1}\,s^{-1}$) for the substitution reaction of the methanesulfonic group in **1** by [hmim][Cl] **3b** in [hmim][ClO_4] **3i**, at 60 °C[a]

ppm H_2O[b] (µg/g)	log(ppm H_2O)	$k\times10^4$ ($M^{-1}\,s^{-1}$)
18,621	4.27	1.70
9772	3.99	2.57
5495	3.74	3.72
4467	3.65	4.27
2089	3.32	7.08
1738	3.24	7.41
1259	3.1	7.94
123	2.09	30.2
—	0	486 (extrapolated)[c]

[a] A solution of **1** (0.03–0.05 M), internal standard phenetole (0.02 M), and **3b** (0.06–0.08 M) (reaction monitored by GC analysis).
[b] 2000±100 ppm H_2O was the average value retained by IL after a standard work-up. Higher water contents were obtained by adding the appropriate amounts of H_2O. Lower values were obtained by further dehydration under high vacuum and heating (see Section 4).
[c] Extrapolated value obtained by plotting log k versus log(ppm H_2O).

Table 3
Effect of the water on the second-order rate constant k ($M^{-1}\,s^{-1}$) for the substitution reaction of the methanesulfonic group in **1** by [hmim][PhCOO] **3g** in [hmim][ClO_4] **3i**, at 60 °C[a]

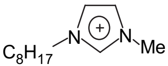
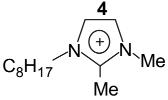
ppm H_2O[b] (μg/g)	log(ppm H_2O)	$k\times10^4$ ($M^{-1}\,s^{-1}$)
18,800	4.27	3.09
10,235	4.01	3.37
1881	3.27	5.33
493	2.69	6.66
58	1.76	10.23
—	0	24.56 (extrapolated)[c]

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

[b] 2000±100 ppm H_2O was the value retained by IL after a standard work-up. Higher water contents were obtained by adding the appropriate amounts of H_2O. Lower values were obtained by further dehydration under high vacuum and heating (see Section 4).

[c] Extrapolated value obtained by plotting log k versus log(ppm H_2O).

Table 4
Second-order rate constants k ($M^{-1}\,s^{-1}$) for the substitution reaction of the methanesulfonic group in **2** by Q^+Y^- in chlorobenzene, at 60 °C[a]

Q^+	$k\times10^3$ ($M^{-1}\,s^{-1}$)			
	Y^-=Cl^-, **b**	Br^-, **c**	I^-, **d**	$4NO_2PhO^-$, **f**
 **4**	13.3	8.3	4.6	5.2
 **4'**	28	19.6	5.9	7.3
$(C_8H_{17})_4N^+$	37	20	6.8	7.1

[a] See conditions of footnote b in Table 1.

in this case by interaction of the anion with the hydrogen atoms (in particular H_2) of the imidazolium cation.[10]

2.1. Effect of the cation–anion interaction

The possibility of association of the imidazolium cation with the anion has been explored both in solution and in solid phase. In particular, the formation of tight ion pairs through hydrogen bonding between the IL cation ([bmim]) and the naked anion ([BF_4] and [PF_6]) was revealed by NMR spectroscopy of the neat IL[14] and in different deuterated solvents,[15] according to the Kamlet–Taft α values (0.6–0.7). In addition, the X-ray crystal structures of a series of 1-ethyl-3-methylimidazolium salts confirmed the presence of hydrogen bonding C–H···Y, with the hydrogen atom at position 2 exhibiting the strongest interactions (shortest bond).[16]

In order to quantitatively evaluate the effect of the cation–anion interaction on the nucleophilic reactivity of the imidazolium salts we prepared a series of 1-octyl-2,3-dimethyl derivatives [om_2im][Y], Y=Cl, Br, I, $4NO_2PhO$, **4′b–d**,**f**, in which the hydrogen in the C2 position is substituted by a methyl group. When the reaction (**1**) was carried out with these salts in anhydrous chlorobenzene, the nucleophilicity of all the anions was found to increase from 1.3 up to 2.4 times (Table 4).

Interestingly, these values are very similar, or identical, to those obtained for the same reaction with the corresponding bulky tetraoctylammonium salts that, due to their topology, are known to be less prone to hydrogen-bond formation (Table 4).[17] The nucleophilicity sequence becomes that found for these anions in dipolar non-HBD solvents and in gas phase (N_3^->Cl^->Br^->I^->SCN^->4-NO_2PhO^-).[7,11,12] The enhancement found changing from the imidazolium to tetraalkylammonium salt, follows the order: $4NO_2PhO^-$ (1.4)<I^- (1.5)<Br^- (2.4)<Cl^- (2.8). This probably reflects the increasing interaction (hydrogen bonding) of Y^- with the ion-paired IL cation on increasing the charge density (charge vs ionic radius) of the anion, in particular for halides (I^-<Br^-<Cl^-).

In addition, UV–vis studies performed in parallel on the 4-nitrophenoxide derivatives [omim][$4NO_2PhO$] **4f** and [om_2im][$4NO_2PhO$] **4′f** in chlorobenzene have shown that λ_{max} increases, from 417 to 423 nm, on going from **4f** to **4′f**.[18] Since bathochromic shifts correspond to less interaction between cation and anion within the ion-pair, the higher λ_{max} value of **4′f** is a clear independent proof of the increased interionic distance (better cation–anion separation), and hence higher reactivity, of the 1-octyl-2,3-dimethyl derivative.[19]

2.2. Effect of the water

Ionic liquids are in general hygroscopic materials, which retain a significant quantity of water after a standard work-up. This residual water can lead to unwanted byproducts and change the product distribution unless very accurate drying protocols are employed just before use. Most importantly, the presence of water in solution could affect even remarkably the reaction rates, especially when hydrophilic anions are involved. In previous kinetic works we found that the nucleophilic reactivity of bulky quaternary onium salts in chlorobenzene dramatically increases, by up to several powers of 10, by removing the hydration sphere of the ion-paired anion, in particular for F^-, OH^-, Cl^-.[11–13] Comparison with anhydrous more polar MeOH and DMSO, where quaternary salts are largely dissociated, showed that the second-order rate constant k decreases, up to more than two orders of magnitude, on changing from PhCl to DMSO and to MeOH (Table 5).

Table 5
Second-order rate constant k ($M^{-1}\,s^{-1}$) for the S_N2 substitution reaction of the methanesulfonic group in **1** and **2** by anions Y^- **a–h** in [hmim][ClO_4] **3i**[a] and molecular solvents (PhC,[b] MeOH,[c] DMSO[c]), at 60 °C

Y	$k\times10^4$ ($M^{-1}\,s^{-1}$)			
	MeOH[c] (E_T^N=0.762)	[hmim][ClO_4][a] ($E_T^N\approx$0.68)	DMSO[c] (E_T^N=0.44)	PhCl[b] (E_T^N=0.188)
N_3	6.0	56.3	135	358
Cl	0.9	7.1	36	75
Br	2.2	5.3	23	71
I	5.8	4.2	5.3	32
SCN	1.7	1.3	2.7	7.2
$4NO_2PhO$	—	5.4	—	41.5
PhCOO	—	5.3	—	32
$PhCH_2COO$	—	5.6	—	7.4

[a] See footnote a in Table 1.

[b] See footnote b in Table 1.

[c] Data from Ref. 11.

Interestingly, our data indicated that the nucleophilicity of the free ion, specifically solvated by the polar medium, is lower than that of the ion-paired anion in chlorobenzene. In the latter, the scarce stabilization by the poor solvating medium and the low interaction with the bulky cation make the anion (naked) particularly reactive.[11–13]

Contrary to molecular solvents, pure ILs may not be regarded as homogeneous media but have to be considered as well-organized hydrogen-bonded polymeric supramolecules.[20] X-ray studies recently reported that they form, in the solid state, an extended network of cations and anions connected together by hydrogen bonds. This structural feature is likely to be maintained in the liquid phase and to some extent even in the gas phase. However, the introduction of other molecules, such as water, can produce a disruption of the H-bonded network and in some cases generate nano-structures with polar and non-polar regions. Mele and co-workers recently proposed for [bmim][BF_4] that water progressively replaces the cation–anion interactions [C(sp^2)–H···F] (tight ion pairs) with H-bonds involving H_2O as an acceptor toward the cation and as donor toward the $[BF_4]^-$ ion.[14] By contrast, ATR-IR determinations of water absorbed from the air into several ILs indicated that 'free' molecules of water interact via H-bonds mainly with the anions in a symmetric 2:1 complex (both protons of H_2O bound to two discrete anions A^-): $A^-\cdots HOH\cdots A^-$.[21] Very recently, Ludwig and co-workers by FTIR spectroscopy provided strong evidence that water molecules are mainly H-bonded to the IL anion with both or only one OH group and the other one 'quasi free'.[22]

The effect of water on the anion reactivity in ILs was explored by us in a wide hydration range (about 60–19,000 ppm H_2O) for [hmim][Cl] **3b** and [hmim][PhCOO] **3g** in the IL [hmim][ClO_4] **3i**, and [om_2im][Cl] **4′b** in the IL [hm_2im][ClO_4] **3′i**. The data reported in Tables 2 and 3 show that the progressive reduction of the amount of water in the IL results in a remarkable increase of the second-order rate constant k (M^{-1} s^{-1}). In addition, an excellent linear correlation was obtained by plotting log k versus log(ppm H_2O) so allowing to obtain the k value under hypothetical anhydrous conditions (Fig. 2). It is worth noting that changing from about 18,800 to 0 ppm H_2O the gain of nucleophilicity is extrapolated to be 8 and 287 times for $PhCOO^-$ and Cl^-, respectively (Tables 2 and 3). The reactivity enhancement is found to be even higher (about 359 times) when the reaction was carried out with the dimethyl derivative [om_2im][Cl] **4′b**. Figure 2 shows that, under the same hydration conditions, the dimethyl derivative **4′b** is always more reactive than **3b** confirming the data previously obtained for these salts in chlorobenzene (Table 4).

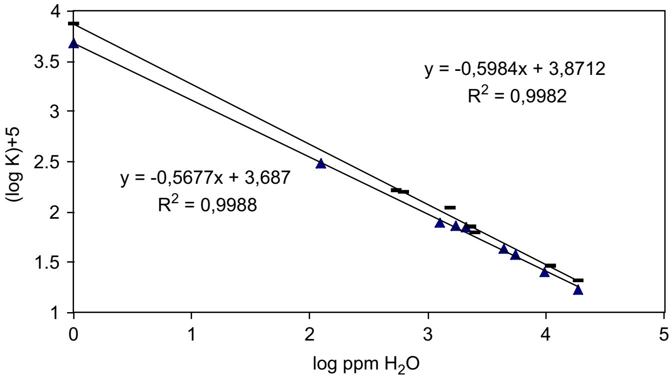


Figure 2. Effect of the water (0–18,700 ppm H_2O) on the nucleophilic reactivity of [hmim][Cl] **3b** in [hmim][ClO_4] **3i** (▲) and of [om_2im][Cl] **4′b** in [hm_2im][ClO_4] **3′i** (–).

In addition, the rate constant values extrapolated at 0 ppm H_2O (k=486×10^{-4} for **3b** and 744×10^{-4} M^{-1} s^{-1} for **4′b**) provide a first quantitative evaluation of the effect of the H-bonding in the C2 position of the imidazole ring on the Cl^- nucleophilicity of [hmim][Cl] **3b** in the IL. Finally, it is worth noting that the dimethyl derivative **4′b** seems to be slightly more sensitive to the water content of the IL (slightly higher slope of the straight line in Fig. 2). A tentative explanation lies in the different structure of **3b** and **4′b**. In [hmim][Cl] **3b** the chloride anion is stabilized by interaction (H-bonding) with the H in the C2 position, whereas in the case of [om_2im][Cl] **4′b** it is bound to the imidazolium cation in a looser ion pair, as also proved by the higher reactivity observed (see Table 4). It is likely that in the latter case the water molecules are specifically bound to the anion so determining a more pronounced variation of reactivity, especially at low hydration levels.

2.3. Comparison with molecular solvents

Though the polarity values reported for the most common ILs are similar to those of short chain alcohols (E_T^N=0.5–0.7 for IL and 0.762 for MeOH) our data in Table 5 show that the reactivities of [hmim][Y] in the IL wet (about 2000 ppm H_2O) are higher than those of the corresponding free ions Y^-, specifically solvated by H-bonding, in dry methanol. This is particularly evident for anions with localized and/or less polarizable charge such as N_3^-, Br^-, Cl^- with enhancements up to 10 times. In addition, the nucleophilicity order in [hmim][ClO_4] **3i** ($N_3^->Cl^->Br^->I^->SCN^-$) parallels the well known sequences obtained in dipolar non-HBD (non-hydrogen bonding donors) solvents and in gas phase, but it is opposite to that found for these anions in methanol.[7]

It is worth noting, however, that, when the water content of [hmim][ClO_4] **3i** is progressively reduced, the anion reactivity noticeably increases (Tables 2 and 3). As reported in Table 1, in the case of Cl^-, the k value in [hmim][ClO_4] **3i** approaches that in PhCl when the hydration is the same in both media (about 30 ppm H_2O) (k=0.0071 in the IL and k=0.0075 in PhCl, respectively). Remarkably, the k value is even higher than that found for Cl^- in DMSO (k=0.0036) (Table 5).

3. Conclusion

In summary our results have emphasized that the nucleophilicity of a representative series of anions in imidazolium ionic liquids (**3i**, **3′i**, and **3l**) depends on the interaction with the cation as well as the specific solvation by water present in the medium. Interestingly our data have quantitatively proved that for hydrophilic anions (Cl^-, $PhCOO^-$) water plays the main role in determining the anion reactivity whereas the interaction with the imidazolium cation has in this case a lower effect. Comparison with molecular solvents has shown that when the IL is largely dehydrated the [hmim][Y] reactivity approaches that of the free ion Y^- in DMSO and of the 'loose' ion pair in low polarity media (PhCl).

4. Experimental

4.1. General

^1H NMR spectra were recorded on a Bruker AC 300 or AC 200 spectrometers, operating at 300.13 and 200.13 MHz, respectively. Coupling constants *J* are in Hertz. Chemical shifts were reported by using $CHCl_3$ as external standard (7.24 ppm). ESI mass spectra were performed on a LCQ advantage Finningan mass spectrometer (I spray voltage: 3.44 kV; capillary voltage: 10.83 V) at different temperatures (T=280–175 °C). The sample was dissolved in 80/20/0.2 vol% of $MeOH/H_2O/CH_3COOH$ at a concentration of 1 mg mL^{-1}, and was introduced continuously at a flow rate of 20 L min^{-1}. Mass spectra (FAB) were accomplished on a Perkin–Elmer TurboMass spectrometer. The water content of each IL was measured using a coulometric Karl–Fischer titrator (Metrohm 684KF Coulometer). Samples were prepared by dissolving 0.250–0.350 g of IL in anhydrous acetonitrile in a 2 mL calibrated flask and duplicate determinations were performed on each sample with results agreeing to within 5%. GLC data were obtained with a Hewlett–Packard 6890 by using a HP-5.5% phenylmethylsiloxane column (30 m×320 mm×0.25 mm). Potentiometric titrations were carried out with a Metrohm 751 GPD Titrino using a combined silver electrode isolated with a potassium nitrate bridge or a combined glass electrode isolated with a potassium chloride bridge. Melting points were determined on a Büchi 535 and are corrected.

4.2. Materials and solvents

Alkyl methanesulfonates **1** and **2** were prepared according to the literature.[23] Hexyl methanesulfonate **1**, bp 99–100 °C at 2 mmHg, n_D^{20} 1.4335 (lit.[23] bp 78 °C at 1 mmHg, n_D^{20} 1.4336); octyl methanesulfonate **2**, bp 92–94 °C at 0.3 mmHg, n_D^{20} 1.4392 (lit.[23] bp 98 °C at 1.5 mmHg, n_D^{20} 1.4390). ILs **3b–d**,[24] **3g**,[25] **3i**,[26] **3j**,[27] and **4b–d**[24] are known compounds, prepared according to the literature.[24–28] ILs **3a**,**e**,**f**,**h** and **4a**,**e**,**f** were obtained from **3b** and **4b**, respectively, by anion metathesis, following a previously reported procedure.[24,28] Yield, and physical and spectroscopic data of ILs **3a**,**e**,**f**,**h** and **4a**,**e–h** are as follows.

4.2.1. 1-Hexyl-3-methylimidazolium azide [hmim][N_3] (3a)

A very hygroscopic waxy oil; 70%; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 9.75 (s, 1H), 7.46 (A part of an AB system, d, 1H, J=3.4 Hz), 7.35 (B part of an AB system, d, 1H, J=3.4 Hz), 4.25 (t, 2H, J=7.4 Hz), 4.08 (s, 3H), 1.94–1.85 (m, 2H), 1.35–1.25 (m, 6H), 0.85 (t, 3H, J=6.9 Hz); MS (ES^+): *m/z* 167.1 ($[hmim]^+$, 100), 376.1 ($[(hmim)_2N_3]^+$, 48); Elemental analysis calcd (%) for $C_{10}H_{19}N_5$: C 57.39, H 9.15, N 33.46; found: C 57.1, H 9.2, N 33.5.

4.2.2. 1-Hexyl-3-methylimidazolium thiocyanate [hmim]-[SCN] (3e)

Waxy oil; 95%; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 9.53 (s, 1H), 7.45 (A part of an AB system, d, 1H, J=3.4 Hz), 7.37 (B part of an AB system, d, 1H, J=3.4 Hz), 4.28 (t, 2H, J=7.4 Hz), 4.09 (s, 3H), 1.96–1.86 (m, 2H), 1.39–1.23 (m, 6H), 0.86 (t, 3H, J=7.0 Hz); MS (ES^+): *m/z* 167.0 ($[hmim]^+$, 100), 392.0 ($[(hmim)_2(SCN)]^+$, 21); Elemental analysis calcd (%) for $C_{11}H_{19}N_3S$: C 58.63, H 8.50, N 18.65; found: C 58.2, H 8.6, N 18.6.

4.2.3. 1-Hexyl-3-methylimidazolium 4-nitrophenoxide [hmim][$4NO_2PhO$] (3f)

Yellow solid; mp=83–84 °C; 90%; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 9.71 (s, 1H), 7.95 (d, 2H, J=9.2 Hz), 7.29–7.25 (m, 2H), 6.40 (d, 2H, J=9.2 Hz), 4.13 (t, 2H, J=7.5 Hz), 3.94 (s, 3H), 1.86–1.78 (m, 2H), 1.30–1.24 (m, 6H), 0.84 (t, 3H, J=6.4 Hz); MS (FAB^+): *m/z* 167 ($[hmim]^+$, 100), 472 ($[(hmim)_2(4NO_2PhO)]^+$, 21); Elemental analysis calcd (%) for $C_{16}H_{23}N_3O_3$: C 62.93, H 7.59, N 13.76; found: C 63.2, H 7.4, N 13.8.

4.2.4. 1-Hexyl-3-methylimidazolium α-phenyl acetate [hmim][$PhCH_2CO_2$] (3h)

Waxy oil; 96%; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 10.09 (s, 1H), 7.30–7.04 (m, 7H), 4.07 (t, 2H, J=7.4 Hz), 3.82 (s, 3H), 3.53 (s, 2H), 1.79–1.73 (m, 2H), 1.27–1.22 (m, 6H), 0.87 (t, 3H, J=6.6 Hz); MS (ES^+): *m/z* 167.1 ($[hmim]^+$, 100), 468.9 ($[(hmim)_2(PhCH_2CO_2)]^+$, 95); elemental analysis calcd (%) for $C_{18}H_{26}N_2O_2$: C 71.49, H 8.67, N 9.26; found: C 71.8, H 8.5, N 9.3.

4.2.5. 1-Octyl-3-methylimidazolium azide [omim][N_3] (4a)

Waxy oil; 88%; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 9.85 (s, 1H), 7.36 (A part of an AB system, d, 1H, J=2.5 Hz), 7.27 (B part of an AB system, d, 1H, J=2.5 Hz), 4.27 (t, 2H, J=7.5 Hz), 4.10 (s, 3H), 2.00–1.84 (m, 2H), 1.33–1.25 (m, 10H), 0.86 (t, 3H, J=6.6 Hz); MS (ES^+): *m/z* 195.1 ($[omim]^+$, 100), 431.8 ($[(omim)_2N_3]^+$, 47); Elemental analysis calcd (%) for $C_{12}H_{23}N_5$: C 60.73, H 9.77, N 29.51; found: C 61.0, H 9.6, N 29.4.

4.2.6. 1-Octyl-3-methylimidazolium thiocyanate [omim]-[SCN] (4e)

Waxy oil; 98%; ^1H NMR (200 MHz, $CDCl_3$) δ (ppm) 9.46 (s, 1H), 7.39 (A part of an AB system, d, 1H, J=3.4 Hz), 7.32 (B part of an AB system, d, 1H, J=3.4 Hz), 4.30 (t, 2H, J=7.4 Hz), 4.10 (s, 3H), 2.05–1.72 (m, 2H), 1.35–1.23 (m, 10H), 0.86 (t, 3H, J=6.8 Hz); MS (FAB^+): *m/z* ($[omim]^+$, 100), 448 ($[(omim)_2(SCN)]^+$, 25); Elemental analysis calcd (%) for $C_{13}H_{23}N_3S$: C 61.62, H 9.15, N 16.58; found: C 61.4, H 9.0, N 16.5.

4.2.7. 1-Octyl-3-methylimidazolium 4-nitrophenoxide [omim][4NO$_2$PhO] (*4f*)

Waxy oil; 94%; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm) 9.94 (s, 1H), 7.91 (d, 2H, J=9.4 Hz), 7.25–7.22 (m, 2H), 6.28 (d, 2H, J=9.4 Hz), 4.10 (t, 2H, J=7.5 Hz), 3.91 (s, 3H), 1.82–1.75 (m, 2H), 1.24–1.20 (m, 10H), 0.84 (t, 3H, J=6.8 Hz); MS (FAB$^+$): *m/z* 195 ([omim]$^+$, 100), 528 ([(omim)$_2$(4NO$_2$PhO)]$^+$, 18); Elemental analysis calcd (%) for $C_{18}H_{27}N_3O_3$: C 64.84, H 8.16, N 12.60; found: C 64.5, H 8.2, N 12.5.

IL **3l** was commercially available material, used after dehydration under vacuum (60–70 °C at <0.01 mmHg for 6 h).

4.2.8. 1-Hexyl-2,3-dimethylimidazolium methanesulfonate [hm$_2$im][MeSO$_3$] (*3′j*)

n-Hexyl methanesulfonate[23] (18.03 g, 0.1 mol) and 1,2-dimethyl imidazole (9.90 g, 0.103 mol) were placed in a 100 mL round-bottomed flask, fitted with a reflux condenser, and a CaCl$_2$ drying tube. The mixture was then heated at 90 °C under stirring for 3 h until the methanesulfonate disappeared (the progress of the reaction was monitored by NMR), dissolved in CH$_2$Cl$_2$ (80 mL), washed with a solution of saturated Na$_2$SO$_4$ containing 5% methanesulfonic acid (2×5 mL), and then with saturated Na$_2$SO$_4$ (3×5 mL) until neutrality. The organic phase was dried over anhydrous Na$_2$SO$_4$, concentrated by using a rotary evaporator, and dried under vacuum (60–70 °C at <0.01 mmHg) for 6 h, obtaining 26.26 g (95% yield) of a very hygroscopic solid; mp=127–128 °C; ^{1}H NMR (200 MHz, CDCl$_3$) δ (ppm) 7.50 (A part of an AB system, d, 1H, J=2.1 Hz), 7.27 (B part of an AB system, d, 1H, J=2.1 Hz), 4.13 (t, 2H, J=7.5 Hz), 3.94 (s, 3H), 2.73 (s, 3H), 2.72 (s, 3H), 1.85–1.73 (m, 2H), 1.38–1.27 (m, 6H), 0.88 (t, 3H, J=6.8 Hz); MS (ES$^+$): *m/z* 181.3 ([hm$_2$im]$^+$, 100), 457.4 ([(hm$_2$im)$_2$(MeSO$_3$)]$^+$, 38); MS (ES$^-$): *m/z* 95.0 ([MeSO$_3$]$^-$, 100), 650.0 ([((hm$_2$im)(MeSO$_3$))$_2$(MeSO$_3$)]$^-$, 60); Elemental analysis calcd (%) for $C_{12}H_{24}N_2O_3S$: C 52.15, H 8.75, N 10.14; found: C 52.4, H 8.6, N 10.2.

4.2.9. 1-Hexyl-2,3-dimethylimidazolium perchlorate [hm$_2$im][ClO$_4$] (*3′i*)

Obtained from **3′j** by anion metathesis, according to a previously described procedure;[24,28] 99.7% yield; oil; n_D^{20} 1.4732; ρ^{25}=1.172 g mL^{-1}; ρ^{60}=1.141; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm) 7.30 (A part of an AB system, d, 1H, J=2.2 Hz), 7.23 (B part of an AB system, d, 1H, J=2.1 Hz), 4.04 (t, 2H, J=7.5 Hz), 3.81 (s, 3H), 2.62 (s, 3H), 1.82–1.72 (m, 2H), 1.36–1.27 (m, 6H), 0.85 (t, 3H, J=6.8 Hz); MS (ES$^+$): *m/z* 181.3 ([hm$_2$im]$^+$, 100), 461.8 ([(hm$_2$im)$_2$(ClO$_4$)]$^+$, 68); Elemental analysis calcd (%) for $C_{11}H_{21}ClN_2O_4$: C 47.06, H 7.54, Cl 12.63, N 9.98; found: C 46.8, H 7.7, N 10.0.

4.3. General procedure for the synthesis of 1-octyl-2,3-dimethylimidazolinium halides [om$_2$im][Hal] (*4′b–d*)

1,2-Dimethyl imidazole (1.0 mol) and an excess of an *n*-octyl halide (**6b–d**) (1.1 mol) were placed in a 100 mL round-bottomed flask, fitted with a reflux condenser and a CaCl$_2$ drying tube. The mixture was then heated at 90 °C under stirring until the 1,2-dimethyl imidazole disappeared (the progress of the reaction was monitored by GC and/or NMR). The crude was rinsed several times with *n*-hexane to remove the unreacted octyl halide. Residual solvent was removed from the imidazolium salts **4′b–d** under vacuum (90 °C at ≤0.01 mmHg) for 6 h. Reaction time, yield, and physical, spectroscopic and analytical data of ILs **4′b–d** are as follows.

4.3.1. 1-Octyl-2,3-dimethylimidazolium chloride [om$_2$im]-[Cl] (*4′b*)

A very hygroscopic wax; 84 h; 98%; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm) 7.78 (A part of an AB system, d, 1H, J=2.08 Hz), 7.40 (B part of an AB system, d, 1H, J=2.08 Hz), 4.17 (t, 2H, J=7.5 Hz), 4.05 (s, 3H), 2.81 (s, 3H), 1.84–1.76 (m, 2H), 1.32–1.25 (m, 10H), 0.86 (t, 3H, J=6.7 Hz); MS (ES$^+$): *m/z* 209.2 ([om$_2$im]$^+$, 100), 453.1 ([(om$_2$im)$_2$Cl]$^+$, 52); Elemental analysis calcd (%) for $C_{13}H_{25}ClN_2$: C 63.78, H 10.29, N 11.44; found: C 63.5, H 10.5, N 11.5.

4.3.2. 1-Octyl-2,3-dimethylimidazolium bromide [om$_2$im]-[Br] (*4′c*)

Wax; 48 h; 88%; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm) 7.72 (A part of an AB system, d, 1H, J=2.0 Hz), 7.43 (B part of an AB system, d, 1H, J=2.0 Hz), 4.16 (t, 2H, J=7.5 Hz), 4.01 (s, 3H), 2.78 (s, 3H), 1.82–1.75 (m, 2H), 1.29–1.22 (m, 10H), 0.84 (t, 3H, J=6.6 Hz); MS (ES$^+$): *m/z* 209.2 ([om$_2$im]$^+$, 100), 497.0 ([(om$_2$im)$_2^{79}$Br]$^+$, 10), 499.0 ([(om$_2$im)$_2^{81}$Br]$^+$, 10); Elemental analysis calcd (%) for $C_{13}H_{25}BrN_2$: C 53.98, H 8.71, N 9.68; found: C 53.6, H 8.9, N 9.7.

4.3.3. 1-Octyl-2,3-dimethylimidazolium iodide [om$_2$im]-[I] (*4′d*)

Pale yellow solid; mp=86–87 °C; 24 h; 89%; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm) 7.56 (A part of an AB system, d, 1H, J=2.0 Hz), 7.36 (B part of an AB system, d, 1H, J=2.0 Hz), 4.15 (t, 2H, J=7.5 Hz), 3.98 (s, 3H), 2.81 (s, 3H), 1.88–1.78 (m, 2H), 1.33–1.24 (m, 10H), 0.86 (t, 3H, J=6.6 Hz); MS (ES$^+$): *m/z* 209.2 ([om$_2$im]$^+$, 100), 544.9 ([(om$_2$im)$_2$I]$^+$, 34); Elemental analysis calcd (%) for $C_{13}H_{25}IN_2$: C 46.43, H 7.49, N 8.33; found: C 46.6, H 7.6, N 8.4.

4.3.4. 1-Octyl-2,3-dimethylimidazolium 4-nitrophenoxide [om$_2$im][4NO$_2$PhO] (*4′f*)

Obtained from **4′b** by anion metathesis, according to a previously described procedure;[24,28] 93% yield; hygroscopic solid; mp=85–86 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm) 7.81 (d, 2H, J=9.3 Hz), 7.18 (A part of an AB system, d, 1H, J=2.1 Hz), 7.10 (B part of an AB system, d, 1H, J=2.1 Hz), 6.20 (d, 2H, J=9.3 Hz), 3.95 (t, 2H, J=7.5 Hz), 3.75 (s, 3H), 2.53 (s, 3H), 1.78–1.72 (m, 2H), 1.29–1.24 (m, 10H), 0.86 (t, 3H, J=6.7 Hz); MS (ES$^+$): *m/z* 209.2 ([om$_2$im]$^+$, 100), 555.7 ([(om$_2$im)$_2$(4NO$_2$PhO)]$^+$, 12); Elemental analysis calcd (%) for $C_{19}H_{29}N_3O_3$: C 65.68, H 8.41, N 12.09; found: C 65.9, H 8.3, N 12.0.

Tetrahexylammonium halides were Analar grade commercial compounds, used without further purification. The synthesis of the tetrahexylammonium 4-nitrophenoxide was previously reported by us.[29]

4.4. Hydration state of ILs

Karl–Fischer titrations showed that the water content of ILs after a standard work-up was 2000±100 ppm H_2O (e.g., salt **3′j**). To further reduce the water amount (60–500 ppm H_2O), a CH_2Cl_2 solution of IL was left over molecular sieves (4 Å) overnight. After the solvent removal the residue was dried under high vacuum (10^{-4} mmHg) at 70–80 °C for 6–12 h.

4.5. Kinetic procedure

Typical kinetic experiment in IL: in a flask, fitted with a magnetic stirrer and thermostatted at 60±0.10 °C, a vial containing the appropriate amount of **1** or **2** (0.03–0.05 M) was added to a standardized solution of phenetole (0.02 M), as internal standard, and **3a–h** or **4′b** (0.06–0.08 M) in **3i**, **3l**, or **3′i**. At zero time, the vial was broken and stirring and timing were started. Samples, withdrawn periodically, were quenched by adding aqueous silver nitrate in the case of **3a–e** and **4′b**, and hydrochloric acid in the case of **3f–h** and **4′f**. The IL phase was extracted with ethyl acetate or di-*iso*-propyl ether and analyzed by GLC. In all cases examined, the mass balance was ≥95%. The kinetic measurements in chlorobenzene were performed as previously reported.[11] Dry (Fluka) chlorobenzene ($H_2O \leq 30$ ppm) was used.

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