DOI: 10.1002/ejoc.200700784

Transition-Metal-Free Synthesis of Perdeuterated Imidazolium Ionic Liquids by Alkylation and H/D Exchange

Ralf Giernoth*[a] and Dennis Bankmann[a]

Keywords: Ionic liquids / Imidazole / Deuterium exchange

Economic, transition-metal-free syntheses of partially or completely deuterated imidazolium ionic liquids (ILs) were developed. Double alkylation starting from imidazole afforded side-chain deuterated imidazolium ionic liquids, which subsequently were fully deuterated by H/D-exchange on the cation ring. Isotopic exchange was studied for a range of ionic liquids, solvents and bases. Here, the presence of small amounts of basic impurities was found to significantly affect the exchange behaviour.

Introduction

The imidazolium cation is a prominent building block for many room-temperature ionic liquids (ILs). Alongside properties such as low resultant melting point, high thermal stability and easy preparation, considerable evidence has accumulated regarding the "non-innocent" or non-inert nature of imidazolium cations in ionic liquids.

The ease of deprotonation of the N**CH**N position of the ring is of course a long-known fact and is commonly used in the formation of imidazol-2-ylidene complexes and free carbenes.[1] The IL stability can therefore be assumed to be limited by the reactivity of the 2-position of the imidazolium moiety.

Furthermore, all the protons on the imidazolium ring are prone to H/D-exchange, as was demonstrated repeatedly: exchange in the 2-position was observed in several protic solvents for a variety of ILs.[2] Upon addition of bases,[3–5] Lewis acids[6] or metal clusters,[7] exchange in all positions was found. Even small amounts of a weak base like potassium carbonate facilitated a complete H/D-exchange, interestingly, with different rates for the three ring positions. The relative exchange rates have already been studied for a range of substances,[2,5,8] and the 4- and 5-position rates were increasingly disparate in our work as side chain length increased.

There are, however, some contradictory reports on the exchange behaviour. Dymek et al. prepared $[D_1][C_2mim]Cl$ (i.e. 1-ethyl-3-methylimidazolium chloride; in our nomenclature, C_x denotes the length of the alkyl chain) by dissolving $[C_2mim]Cl$ in D_2O and evaporating the solvent.[4] For the synthesis of $[D_3][C_2mim]Cl$, they added K_2CO_3 and were able to deuterate all three ring positions. Also for $[C_2mim]Cl$, Seddon, Welton et al. reported exchange in all positions in D_2O without addition of base.[3] Lin et al. found exchange only in the 2-position of the homologous series $[C_2mim]...[C_8mim]Br$ in D_2O and CD_3OD, with the rate decreasing with increasing side chain length.[2] BF_4^- and PF_6^- salts were reported not to undergo exchange. Handy et al. found no exchange for $[C_4mim]BF_4$ in D_2O without base, whereas $[C_4mim]N(CN)_2$ was found to exchange in the 2-position.[5] This was attributed to the fact that the dicyanamide IL formed slightly basic solutions.

So far, very few syntheses of deuterated ionic liquids have appeared in the literature. The groups of Dymek and of Hardacre have reported experimental details for the synthesis of perdeuterated ILs.[4,9,10] Dymek prepared $[D_1]$-$[C_2mim]$ and$[D_3][C_2mim]$, using K_2CO_3 for the second compound, whereas Hardacre employed a Pd/C suspension in D_2O in the preparation of perdeuterated methylimidazole from $[D_3]$methylimidazole, which was obtained by ruthenium catalysed alkylation of imidazole. Subsequent alkylation with $[D_3]$methyl chloride or $[D_5]$ethyl iodide afforded the perdeuterated salts. The authors pointed out that a selective 4,5-deuteration should be possible by reprotiation of the 2-position, and that either side chain or the whole of the ring may be left protonated.

In addition, Arduengo et al. have published a transition-metal-free route to $[D_{12}]$-1,3,4,5-tetramethylimidazolium chloride,[11] which is not an ionic liquid. Furthermore, this case is different, for exchange cannot be studied here due to the absence of protons in the 4- and 5-positions.

The group of Dupont has used our previously published procedure[8] to synthesize imidazolium ILs in which only the imidazolium ring protons are exchanged by deuterium.[12]

Perdeuterated ILs may be used as solvents for NMR studies. Furthermore, they may be used as isotopically lab-

[a] Institute of Organic Chemistry, University of Cologne, Greinstrasse 4, Köln, Germany
Fax: +49-221-470-5102;
E-mail: Ralf.Giernoth@uni-koeln.de

elled compounds to shed light on reaction mechanisms in ionic liquids where heterocyclic carbene formation or proton equilibria are suspected. Finally, neutron diffraction measurements in ILs are aided by the availability of these proton-free compounds, as demonstrated by Arduengo et al.[11]

In this work, we present the facile and generic synthesis of perdeuterated and partially deuterated ionic liquids by application of isotopic exchange on imidazolium cations. The syntheses were performed either in transition-metal-free or completely metal-free ways.

Results and Discussion

After investigations on H/D-exchange and the synthesis of $[D_3][C_4mim]BF_4$ and -Tf_2N salts,[8] we now present C-2 and C-4/C-5-selective deuteration of the imidazolium ring (Figure 1 and Table 1). The method utilizes the fact that

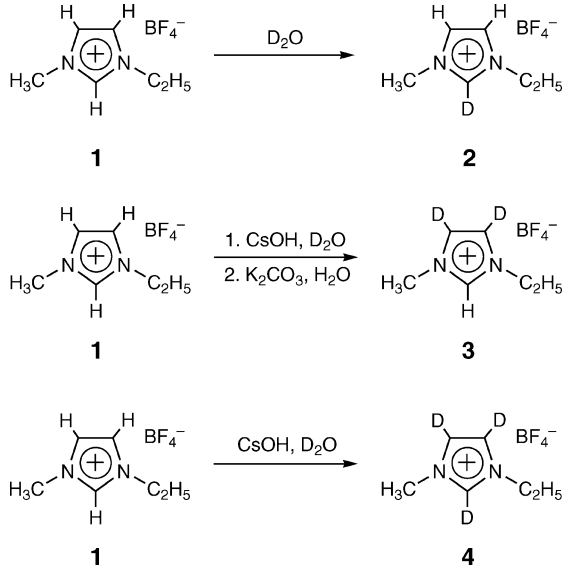

Figure 1. Synthesis of partially deuterated imidazolium salts.

Table 1. Results of selective deuteration experiments in deuterium oxide.

Product	Base	Yield (%)	% Deuterium[a] C-2	C-4	C-5
$[D_1][C_4mim]BF_4$ **2**	–	80	96	0	0
$[D_2][C_4mim]BF_4$ **3**	CsOH, K_2CO_3	41	0	95	95
$[D_3][C_4mim]BF_4$ **4**	CsOH	90	94	94	94

[a] Determined from ^1H NMR integrals vs. NCH_2 integral; error margin around 5%.

only the 2-position exchanges measurably in slightly basic solution. Monodeuterated species are obtained by stirring in D_2O or, depending on the hydrophobicity of the IL, in CH_3OD. After 16 h at 60 °C (40 °C for methanol), the H/D-exchange equilibrium is reached for all ionic liquids studied.

Complete ring deuteration is achieved as described earlier[8] by addition of 10 mol-% of a hydroxide base to the D_2O solution of the IL and stirring.

The D_2O solutions are neutralized with the acid corresponding to the IL anion and extracted with dichloromethane or ethyl acetate to recover the IL. Highly water soluble ILs like $[C_2mim]TfO$ can be prepared this way since efficient extraction of $[C_2mim]TfO$ from water fails. As a consequence, when sodium carbonate is used as base, removal of metal salts is not possible, leading to precipitation of mixed imidazolium/sodium triflates (Figure 2). Bases on solid support were considered to circumvent the introduction of metal salts into the ionic liquid and allow for base removal. Here, Amberlite IRA-400(OH) (styrene-divinylbenzene matrix with ion quaternary ammonium groups) exchange resin loaded with hydroxide anions is effective.

Bis-deuterated compounds can be prepared by complete deuteration of the imidazolium ring under basic conditions followed by a second exchange step to reprotiate the 2-position.

Ring deuteration can be employed as one step in the synthesis of perdeuterated ionic liquids when these are built from adequately deuterated alkylating agents and imid-

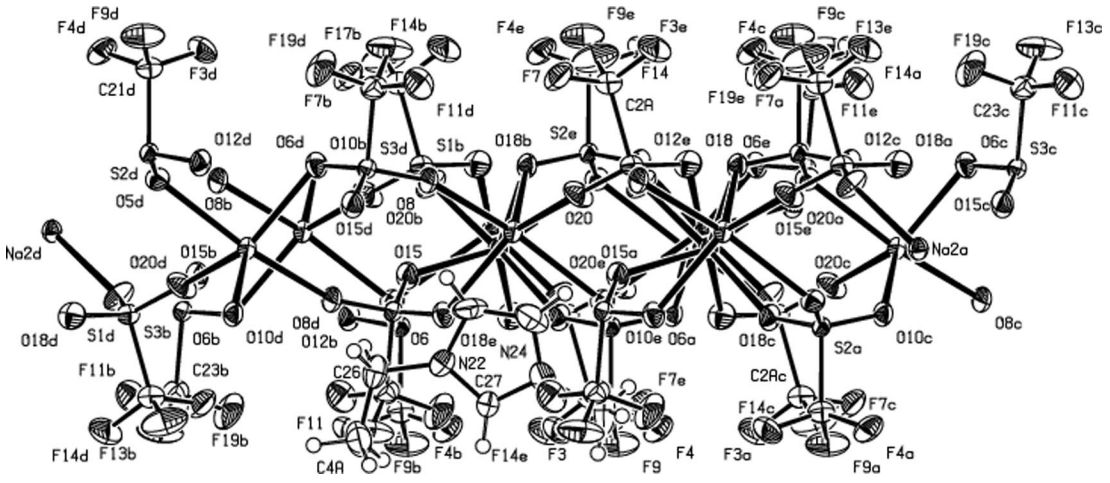

Figure 2. Crystal structure of a mixed sodium imidazolium triflate.

azole. (Perdeuterated imidazole as the starting material would be extremely costly and could result in significant loss of deuterium in the synthetic procedure – especially during anion exchange, which is typically done in protic solvents like water or octanol.) For economic reasons, the side chain length here is limited to methyl and ethyl. We synthesized both [D_3]-1-methylimidazole and [D_5]-1-ethylimidazole, since the choice of the initial counterion determines (or rather limits) the availability of the corresponding methylating and ethylating agents.

These alkylated imidazoles can then be quaternized either by [D_3]methyl iodide or [D_5]ethyl bromide and subsequently be subjected to anion exchange or alkylated with other agents like e.g. [D_3]methyl triflate.

With these imidazolium salts that are deuterated in the side-chains, an exchange of the ring protons can be carried out, yielding the perdeuterated compounds in the fashion described above. We have synthesized two example substances, [D_{11}][C_2mim]Tf_2N (Figure 3) and [D_{11}][C_2mim]TfO (Figure 4).

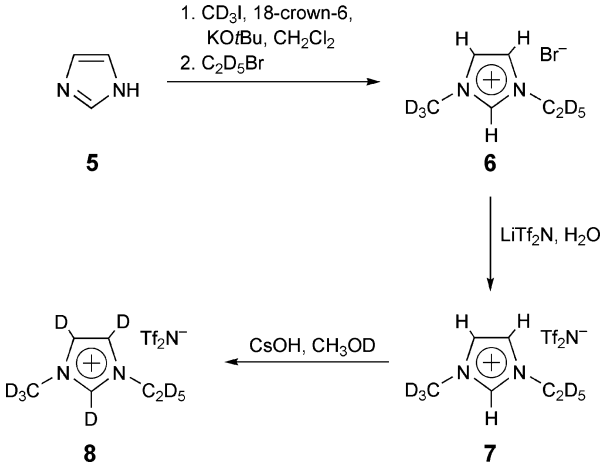

Figure 3. Synthesis of perdeuterated [D_{11}][C_2mim]Tf_2N.

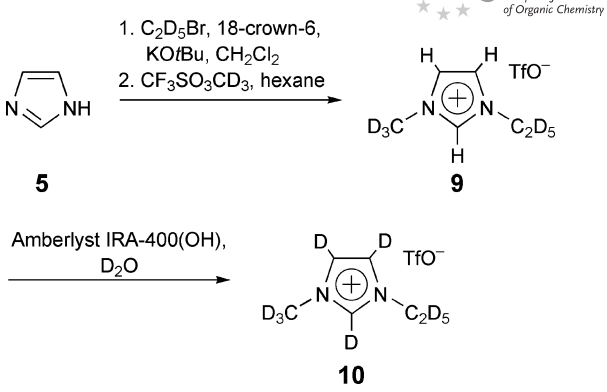

Figure 4. Synthesis of perdeuterated [D_{11}][C_2mim]TfO.

Imidazole can also be alkylated using [D_3]methyl iodide and [D_5]ethyl bromide under deprotonation/phase transfer conditions in CH_2Cl_2.[13] With potassium *tert*-butoxide, imidazole is deprotonated and subsequently alkylated by means of the alkyl halide. Our yields are, however, somewhat below those reported in the literature, and the products were always contaminated with *tert*-butyl alcohol after kugelrohr distillation.

A screening experiment was set up to evaluate the applicability to various commercial and synthesized IL samples (Table 2) and to assess which ILs are prone to exchange on the imidazolium cation. The ionic liquids were treated with D_2O or CH_3OD and shaken for 16 h at 60 °C or 40 °C, respectively. 20 mol-% $CsOH·H_2O$ or 20 vol.-% of a CH_3OD solution saturated with K_2CO_3 were used as bases and an additional screening was run without base.

It sould be noted that, although it is known that BF_4^--ILs are prone to produce HF in the presence of water, our final samples were all free of fluoride – probably a result of our workup procedure (see Exp. Sect.).

Very low water solubility in the longer side chain ionic liquids led to low exchange in initial experiments in D_2O. Therefore, [D_1]methanol was chosen as a solvent for the

Table 2. Screening of the substrate scope.

IL	Solvent	*t* / h	*T* / °C	No base % Deuterium[a]		0.2 Equiv. of $CsOH·H_2O$ % Deuterium[a]		K_2CO_3 solution % Deuterium[a]	
				C-2	C-4/5	C-2	C-4/5	C-2	C-4/5
[C_2mim]Br	CH_3OD	16	40	89	0		precipitation	(exp. not done)	
[C_2mim]$EtSO_4$	CH_3OD	16	40	86	0	77	83	79	85
[C_2mim]Tf_2N	CH_3OD	16	40	16	0	62	82	84	51
[C_2mim]$MeSO_3$	CH_3OD	16	40	42	24	82	85	72	86
[C_4mim]Br	CH_3OD	16	40	12	0		precipitation	75	64
[C_4mim]Tf_2N	CH_3OD	16	40	87	10	88	86	82	60
[C_{10}mim]Tf_2N	CH_3OD	16	40	76	10	90	86	(exp. not done)	
[C_4mim]BF_4	CH_3OD	16	40	92	3	80	79	82	45
[C_5mim]BF_4	CH_3OD	16	40	2	0	70	78	88	3
[C_7mim]BF_4	CH_3OD	16	40	6	5	74	76	86	4
[C_8mim]BF_4	CH_3OD	16	40	8	0	73	78	79	6
[C_9mim]BF_4	CH_3OD	16	40	11	5	74	79	78	6
[C_{10}mim]BF_4	CH_3OD	16	40	3	0	65	75	83	85
[C_{11}mim]BF_4	CH_3OD	16	40	10	0	71	77	79	0

[a] Determined from ^1H NMR integrals vs. NCH_2 integral; error margin around 5%.

screening. Apart from economic reasons, [D_1]methanol can be used as a universal method, since water-soluble ILs can also be deuterated in [D_1]methanol with comparable results.

Upon addition of cesium hydroxide, all ILs were found to exchange in all three ring positions in CH_3OD, proving the generic scope of the method described here. Interestingly, some of the ionic liquids showed significant exchange in the 2-position without any added base whereas others did not. This kind of discrepancy was discussed in the introduction and can be attributed to basic impurities (see below).

It should be noted that the addition of K_2CO_3 only afforded exchange in the 2-position of the ILs that did not exchange significantly without added base. The ILs that do exchange under these conditions show significant exchange at C-4 and C-5 when K_2CO_3 is added. Therefore, selective C-2 deuteration should only be attempted with ILs that are known to be free of basic impurities.

Differences in exchange behaviour noted above appear between samples of similar ionic liquids, especially regarding the 2-position. Assuming that basic impurities are the source of the more ready exchange in some IL samples, we considered methylimidazole to be the most likely basic contaminant in imidazolium ILs. NMR experiments on undiluted samples accordingly revealed the presence of up to 1% of methylimidazole.

To assess whether such a concentration would be able to influence the exchange, a series of experiments was performed using a clean (not exchanging) IL and mixtures of that IL with increasing amounts of methylimidazole (Table 3). The results demonstrate very significant exchange in the 2-position even with 1 mol-% of base. Interestingly, it was reported that the addition of water to imidazolium-ILs decreases the acidity of certain ILs and H_2O effectively behaves as a base.[14] However, D_2O (and CH_3OD) are not basic enough for measurable effects under the conditions presented here.

Table 3. Influence of 1-methylimidazole (mim) on H/D exchange.

Product	Solvent	Equiv. of mim	% Deuterium[a]	
			C-2	C-4/5
[C_5mim]BF_4	CD_3OD	0	2	0
[C_5mim]BF_4	CD_3OD	0.01	74	0
[C_5mim]BF_4	CD_3OD	0.025	86	0
[C_5mim]BF_4	CD_3OD	0.05	88	7
[C_5mim]BF_4	CD_3OD	0.1	85	8
[C_5mim]BF_4	CD_3OD	0.2	84	3

[a] Determined from ^{1}H NMR integrals vs. NCH_2 integral; error margin around 5%.

Conclusions

The protocols presented here are reasonably economic routes to perdeuterated ILs that may be combined in a desired manner to afford partially or fully deuterated ionic liquids or, more generally, imidazolium salts. The substrate scope was probed by screening experiments and the procedures were found to be very generic. From the low exchange observed in [C_2mim]Tf_2N, [C_4mim]Br, [C_5mim]BF_4 and additional results for other substrates, it can be concluded that ionic liquids with these anions do not exchange significantly unless contaminated by basic impurities.

Experimental Section

General Methods: The ionic liquids were either obtained from Solvent Innovation GmbH or synthesized according to established literature procedures. Deuterium oxide (99.9%D) and [D_1]methanol (99.0%D) were obtained from Deutero GmbH and used without further purification. [D_3]Methyl iodide, [D_3]methyl triflate and [D_5]ethyl bromide were obtained from Aldrich (manufactured at Cambridge Isotope Labs) and used from fresh ampoules without further purification. Steps including methyl triflate were performed under an argon atmosphere. ^{1}H, ^{2}D and ^{13}C NMR spectra were measured at 298 K on Bruker AC-300, DPX-300 and DRX-500 instruments. [D_2]Dichloromethane and [D_6]DMSO were taken from fresh bottles and dried with 3-Å molecular sieves in septum-capped bottles. ESI-HRMS data were obtained with a Finnigan MAT 900S spectrometer.

1-Butyl-3-methyl-[D_1]imidazolium Tetrafluoroborate (2): 1-Butyl-3-methylimidazolium tetrafluoroborate (1.00 g, 4.42 mmol) and deuterium oxide (2.73 mL, 3.00 g, 150 mmol) were mixed and stirred for 16 h at 60 °C. The mixture was extracted twice with dichloromethane (3 mL each), and the solvent of the combined organic layers was removed in vacuo. The residue was dried for 2 h at 60 °C under high vacuum to obtain the product as a colourless oil (0.8 g, 80%, 96% D at C-2). ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 9.06 (s, 0.04 H), 7.74 (m, 1 H), 7.67 (m, 1 H), 4.14 (t, J = 7.2 Hz, 2 H), 3.83 (s, 3 H), 1.75 (quint, J = 7.6 Hz, 2 H), 1.25 (sext, J = 7.5 Hz, 2 H), 0.89 (t, J = 7.5 Hz, 3 H) ppm. ^{2}H NMR (46 MHz, [D_6]-DMSO): δ = 9.06 (s) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 136.5 (m, J = 34.2 Hz), 123.6, 122.2, 48.5, 35.7, 31.3, 18.8, 13.2 ppm.

1-Butyl-3-methyl-[D_2]imidazolium Tetrafluoroborate (3): 1-Butyl-3-methylimidazolium tetrafluoroborate (1.00 g, 4.42 mmol) was dissolved in deuterium oxide (2.73 mL, 3.00 g, 150 mmol) and treated with cesium hydroxide monohydrate (0.12 g, 0.71 mmol). The solution was stirred for 28 h at 60 °C, and after cooling, extracted twice with dichloromethane (5 mL). The solvent of the combined organic layers was removed in vacuo, yielding a clear, colourless oil (0.72 g), which was dissolved in water (5 mL) and treated with potassium carbonate (12.2 mg, 0.09 mmol). The solution was stirred for 24 h at 60 °C, extracted four times with dichloromethane (5 mL each) and washed with a small portion of water. The solvent of the combined organic layers was removed in vacuo to obtain the product as a colourless oil (0.41 g, 41%, 95% D at C-4 and C-5). ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 9.03 (s, 1 H), 7.71 (s, 0.05 H), 7.65 (s, 0.05 H), 4.14 (t, J = 7.2 Hz, 2 H), 3.83 (s, 3 H), 1.76 (quint, J = 7.6 Hz, 2 H), 1.25 (sext, J = 7.5 Hz, 2 H), 0.89 (t, J = 7.5 Hz, 3 H) ppm. ^{2}H NMR (77 MHz, [D_6]DMSO): δ = 7.75 (s), 7.70 (s) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 136.4, 123.3 (m, J = 31.5 Hz), 122.0 (m, J = 31.0 Hz), 48.5, 35.7, 31.4, 18.8, 13.3 ppm.

1-Butyl-3-methyl-[D_3]imidazolium Tetrafluoroborate (4): 1-Butyl-3-methylimidazolium tetrafluoroborate (1.00 g, 4.42 mmol), deuterium oxide (3.00 mL, 3.30 g, 165 mmol) and cesium hydroxide monohydrate (0.12 g, 0.71 mmol) were mixed and stirred for 12 h at 60 °C. After cooling, the mixture was neutralized with 48% aqueous tetrafluoroboric acid and extracted twice with dichloromethane (5 mL each). The solvent of the combined organic layers

was removed in vacuo, and the residue was dried for 2 h at 60 °C under high vacuum to obtain the product as a very slightly yellow oil (0.92 g, 90%, 94%D at C-2, C-4 and C-5). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.04 (s, 0.04 H), 7.73 (m, 0.04 H), 7.65 (m, 0.04 H), 4.15 (t, J = 7.2 Hz, 2 H), 3.83 (s, 3 H), 1.75 (quint, J = 7.6 Hz, 2 H), 1.25 (sext, J = 7.5 Hz, 2 H), 0.89 (t, J = 7.5 Hz, 3 H) ppm. ^{2}H NMR (46 MHz, [D$_6$]DMSO): δ = 9.06 (s), 7.74 (s) ppm. ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 136.2 (m, J = 33.9 Hz), 123.2 (m, J = 30.5 Hz), 121.9 (m, J = 30.5 Hz), 48.5, 35.7, 31.4, 18.8, 13.3 ppm.

1-[D$_3$]Methylimidazole: Imidazole (4.42 g, 65.0 mmol) was dissolved in dry dichloromethane (150 mL) and treated with 18-crown-6 (1.64 g, 6.20 mmol) and potassium *tert*-butoxide (7.85 g, 70.0 mmol). The resulting slurry was stirred for 20 min at room temp., during which time a brownish colour evolved. Methyl iodide (10.0 g, 69.0 mmol) in dry dichloromethane (40 mL) was added dropwise and the mixture then stirred for another 3 h at room temp. The solution was filtered and the solvent of the filtrate was removed in vacuo. The residual brown oil was distilled at 60–100 °C (0.2 mbar) to obtain the product containing residual *tert*-butyl alcohol as a colourless oil (2.91 g, 53%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 7.55 (s, 1 H), 7.08 (s, 1 H), 6.87 (s, 1 H) ppm. ^{2}H NMR (46 MHz, [D$_6$]DMSO): δ = 3.59 (s) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 137.8, 128.4, 120.4, 32.0 (m, J = 20.75 Hz) ppm.

[D$_8$]-1-Ethyl-3-methylimidazolium Bromide (6): [D$_3$]Methylimidazole (2.91 g, 34.2 mmol) was added dropwise to [D$_5$]ethyl bromide (2.82 mL, 4.29 g, 37.6 mmol). The mixture was stirred for 15 min at 50 °C and for 2 h at 70 °C, until the initial turbidity disappeared. Upon cooling, the mixture solidified to a yellowish mass, which was minced and treated with ethyl acetate and stirred at –10 °C for 1 h. A colourless solid precipitated, which was filtered off in the cold. The solid was dried in vacuo, and the product was obtained as a colourless solid (5.02 g, 74%). ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 9.23 (s, 1 H), 7.81 (m, 1 H), 7.72 (m, 1 H) ppm. ^{2}H NMR (46 MHz, [D$_6$]DMSO): δ = 4.14 (s), 3.80 (s), 1.35 (s) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 136.2, 123.5, 121.9 ppm. HRMS (ESI): calcd. [M]$^+$ 119.1416; found 119.142.

[D$_8$]-1-Ethyl-3-methylimidazolium Bis(trifluoromethylsulfonyl)amide (7): [D$_8$]-1-Ethyl-3-methylimidazolium bromide (5.02 g, 25.2 mmol) and lithium bis(trifluoromethylsulfonyl)amide (7.96 g, 27.7 mmol) were stirred for 24 h at room temp. in water (10 mL). The biphasic mixture was treated with ethyl acetate (20 mL), the layers were separated and the aqueous phase was extracted with ethyl acetate (10 mL). The solvent of the combined organic layers was removed in vacuo, and the crude product was partitioned between ethyl acetate (30 mL) and water (10 mL) to remove residual halides. The solvent of the organic layer was removed in vacuo, and the residue was dried for 2 h at 60 °C under high vacuum to obtain the product as a yellowish oil (7.9 g, 78%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.07 (s, 1 H), 7.73 (m, 1 H), 7.65 (m, 1 H) ppm. ^{2}H NMR (77 MHz, [D$_6$]DMSO): δ = 4.13 (s), 3.79 (s), 1.35 (s) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 136.3, 123.5, 121.9, 119.6 (q, J = 321 Hz), 43.5 (m, J = 22 Hz), 35.0 (m), 14.0 (m) ppm. HRMS (ESI): calcd. [M]$^+$ 119.1416; found 119.142.

[D$_{11}$]-1-Ethyl-3-methylimidazolium Bis(trifluoromethylsulfonyl)-amide (8): [D$_8$]-1-Ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)amide (0.97 g, 2.43 mmol) was dissolved in [D$_1$]methanol (6.00 mL, 4.86 g, 147.1 mmol), treated with cesium hydroxide monohydrate (0.12 g, 0.71 mmol) and stirred for 24 h at 50 °C. The mixture was neutralized with bis(trifluoromethylsulfonyl)amide, and the solvent was removed in vacuo. The residue was partitioned between dichloromethane (5 mL) and deuterium oxide (3 mL), the layers were separated, and the water layer was extracted with dichloromethane (5 mL). The combined organic layers were washed with deuterium oxide (3 mL), and the solvent was removed in vacuo. The resulting oil was dried for 2 h at 60 °C under high vacuum to obtain the product as a colourless oil (0.76 g, 85%). ^{2}H NMR (46 MHz, [D$_6$]DMSO): δ = 9.07 (s), 7.74 (s) 7.68 (s), 4.12 (s), 3.79 (s), 1.35 (s) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 136.1 (m), 123.3 (m), 121.7 (m), 119.5 (q, J = 322 Hz), 43.4 (m), 35.0 (m), 13.9 (m) ppm. HRMS (ESI): calcd. [M]$^+$ 121.1539; found 121.154.

[D$_5$]-1-Ethylimidazole: Imidazole (5.97 g, 87.7 mmol) was dissolved in dry dichloromethane (50 mL) and treated with 18-crown-6 (2.32 g, 8.77 mmol) and potassium *tert*-butoxide (9.84 g, 87.7 mmol). The resulting slurry was stirred for 40 min at room temp. during which a brownish colour evolved. [D$_5$]Ethyl bromide (6.58 mL, 10.0 g, 87.7 mmol) was added dropwise and the mixture then stirred overnight at room temp. The solution was filtered and the solvent of the filtrate was removed in vacuo. The residual brown oil was distilled at 85–115 °C (0.2 mbar) and subsequently dried at 150 mbar to obtain the product containing residual *tert*-butyl alcohol as a colourless oil (4.59 g, 52%). ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 7.61 (s, 1 H), 7.15 (m, 1 H), 6.88 (m, 1 H) ppm. ^{2}H NMR (77 MHz, [D$_6$]DMSO): δ = 3.91 (s), 1.25 (s) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 136.7, 128.3, 118.8, 28.8 (m), 15.1 (m) ppm. HRMS (ESI): calcd. [M]$^+$ 102.1074; found 102.108.

[D$_8$]-1-Ethyl-3-methylimidazolium Trifluoromethanesulfonate (9): [D$_5$]-1-Ethylimidazole (4.50 g, 44.5 mmol) was dissolved in dry hexane (40 mL) and cooled to 0 °C. The solution was treated dropwise with trifluoromethanesulfonic acid [D$_3$]methyl ester (5.08 mL, 7.51 g, 44.9 mmol), instantaneosly leading to turbidity in the solution. After the addition was complete, the mixture was allowed to reach room temperature over 30 min. The resulting biphasic mixture was refluxed for 2 h and stirred for 18 h. The layers were separated, and the lower layer dried in a rotary evaporator. The brown, oily residue was partitioned between water (10 mL) and dichloromethane (10 mL), the layers were separated and the aqueous layer was washed with dichloromethane (10 mL). The solvent of the aqueous layer was removed in vacuo, and the residue was dried for 3 h at 60 °C under high vacuum to obtain the product as a colourless oil (10.15 g, 85%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.06 (s, 1 H), 7.75 (s, 1 H), 7.66 (s, 1 H) ppm. ^{2}H NMR (46 MHz, [D$_6$]DMSO): δ = 4.14 (s), 3.80 (s), 1.35 (s) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 136.2, 123.6, 121.9, 120.7 (q, J = 322 Hz), 43.4 (m), 35.0 (m), 14.0 (m) ppm. HRMS (ESI): calcd. [M]$^+$ 119.1416; found 119.142.

[D$_{11}$]-1-Ethyl-3-methylimidazolium Trifluoromethanesulfonate (10): [D$_8$]-1-Ethyl-3-methylimidazolium trifluoromethanesulfonate (4.00 g, 14.9 mmol) was dissolved in deuterium oxide (25 mL) and treated with Amberlite IRA-400(OH) (2 g). The mixture was stirred for 48 h at 45 °C and for 18 h at room temp. The polymer beads were removed by filtration, and the filtrate was neutralized with trifluoromethanesulfonic acid. The solvent was removed in vacuo, and the resulting slightly yellow oil was dried for 2 h at 60 °C under high vacuum. The residue was treated with deuterium oxide (10 mL) and stirred for 3 d at 60 °C. The solvent was removed in vacuo, and the residue was dried for 2 h at 60 °C under high vacuum to obtain the product as a yellowish oil (2.88 g, 71%). ^{2}H NMR (77 MHz, [D$_6$]DMSO): δ = 9.11 (s), 7.78 (s), 7.69 (s), 4.13 (s), 3.79 (s), 1.32 (s) ppm. ^{13}C NMR (75 MHz, [D$_4$]methanol): δ = 137.8 (m), 124.9 (m), 123.3 (m), 121.8 (q, J = 319 Hz), 45.4 (m), 35.9 (m), 14.4 (m) ppm. HRMS (ESI): calcd. [M]$^+$ 122.16009; found 122.161.

Exchange Screening: Exchange in deuterium oxide was performed by mixing the IL (1 mmol) with D_2O (1 g) and shaking for 16 h at 60 °C. CH_2Cl_2 (0.5 mL) was added to the solution (0.5 mL), and the phases were separated. The organic phase (100–300 μL) was filled up to 500 μL with CD_2Cl_2 and ^1H NMR spectra were measured.

For exchange in [D_1]methanol, the IL (1 mmol) was mixed with CH_3OD (1 g), and the mixture was shaken for 16 h at 40 °C. The solutions were transferred to a desiccator, and the organic solvent was removed in vacuo. Samples (ca. 50 μL) were dissolved in CD_2Cl_2 (200 μL) and CH_2Cl_2 (300 μL) and ^1H NMR spectra were obtained.

Exchange experiments with base were performed by mixing of stock solutions of the base in [D_1]methanol and solutions of IL in [D_1]methanol to obtain a total of 1 g of solvent, 1 mmol IL and the amounts of base reported in the text. After cooling to room temperature, neutralization was done with the acids corresponding to the IL anions (HBF_4 was used also for $MeSO_3^-$ and $EtSO_4^-$) and then treated as for the mixtures without added base.

Integrals were reported relative to NCH_2 (however, this was equivalent to using NCH_3, as no exchange was observed on any of the side chain positions).

Acknowledgments

We would like to thank Deutsche Forschungsgemeinschaft (DFG) for financial support through the Emmy Noether programme and Solvent Innovation GmbH for the donation of several ionic liquid samples. We also thank Merck KGaA, especially Dr. Urs Wels-Biermann, without whom we probably never would have carried out this project so much in detail.

[1] R. Singh, S. P. Nolan, *Annu. Rep. Prog. Chem., Sect. B: Org. Chem.* **2006**, *102*, 168–196.
[2] S.-T. Lin, M.-F. Ding, C.-W. Chang, S.-S. Lue, *Tetrahedron* **2004**, *60*, 9441–9446.
[3] A. G. Avent, P. A. Chaloner, M. P. Day, K. R. Seddon, T. Welton, *J. Chem. Soc., Dalton Trans.* **1994**, 3405–3413.
[4] K. M. Dieter, C. J. Dymek, N. E. Heimer, J. W. Rovang, J. S. Wilkes, *J. Am. Chem. Soc.* **1988**, *110*, 2722–2726.
[5] S. T. Handy, M. Okello, *J. Org. Chem.* **2005**, *70*, 1915–1918.
[6] P. C. Trulove, R. A. Osteryoung, *Inorg. Chem.* **1992**, *31*, 3980–3985.
[7] L. S. Ott, M. L. Cline, M. Deetlefs, K. R. Seddon, R. G. Finke, *J. Am. Chem. Soc.* **2005**, *127*, 5758–5759.
[8] R. Giernoth, D. Bankmann, *Tetrahedron Lett.* **2006**, *47*, 4293–4296.
[9] C. Hardacre, J. D. Holbrey, S. E. J. McMath, *Chem. Commun.* **2001**, 367–368.
[10] C. Hardacre, S. McMath, M. Nieuwenhuyzen, D. Bowron, A. Soper, *J. Phys.: Condens. Matter* **2003**, *15*, S159–S166.
[11] A. J. Arduengo, H. V. R. Dias, D. A. Dixon, R. L. Harlow, W. T. Klooster, T. F. Koetzle, *J. Am. Chem. Soc.* **1994**, *116*, 6812–6822.
[12] J. D. Scholten, G. Ebeling, J. Dupont, *Dalton Trans.* **2007**, 5554–5560.
[13] W. C. Guida, D. J. Mathre, *J. Org. Chem.* **1980**, *45*, 3172–3176.
[14] C. Thomazeau, H. Olivier-Bourbigou, L. Magna, S. Luts, B. Gilbert, *J. Am. Chem. Soc.* **2003**, *125*, 5264–5265.

Received: August 24, 2007
Published Online: April 25, 2008

