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Transition-metal free ring deuteration of imidazolium ionic liquid cations

Ralf Giernoth* and Dennis Bankmann

Institute of Organic Chemistry, University of Cologne, Greinstrasse 4, D-50939 Köln, Germany

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Abstract—A simple, low-cost and transition-metal free ring deuteration procedure applicable to ionic liquids (ILs) with imidazolium cations has been developed. Reaction profiles for the exchange have been measured.

1. Introduction

The recent surge in ionic liquid (ILs)[1] research and their application in both academia and industry have left chemists with questions regarding structure and reactivity of reaction systems contained in these new solvents. Repeatedly it has been found that several ionic liquids—especially those based on imidazolium ions—are not really inert solvents.[2]

The most discussed reactivity pattern of ILs has been the formation of *N*-heterocyclic carbenes or carbene-complexes from imidazolium cations,[3–6] which may influence reactivity—be it advantageously or adversely. The ease of abstraction of the proton in the 2-position of the imidazolium ring is expected to largely determine the electrochemical and chemical stability of ILs.[7]

To further the possibility for investigations on reaction systems in which cation acidity may play a role, we developed a deuteration procedure for common ionic liquids with imidazolium cations. The ILs obtained are useful labelled compounds in conjunction with NMR spectroscopy and mass spectrometry. The aforementioned analytical techniques possess the potential to answer questions regarding the participation of the solvent by simply tracing the incorporation of the labels into products. Furthermore, as recently demonstrated by our group,[8] high-resolution NMR spectroscopy is possible in ionic liquids in spite of strong solvent signals and allows for in situ reaction and monitoring and tracking of the deuterium labels. Deuterium NMR in ionic liquids was previously described.[9] The procedure presented here may also find application as one step in the preparation of perdeuterated ionic liquids for use with NMR spectroscopy in cases where solvent signals cannot be tolerated at all as opposed to NMR-based solvent filtering techniques.[10]

In contrast to prior efforts described in the literature,[11,12] we focussed on labelling room temperature common ionic liquids themselves, not their precursors like alkylimidazoles or imidazolium halide salts. To the best of our knowledge, we report here for the first time the full ring deuteration of ionic liquids with anions apart from halides. For halides, this has been done by Dymek Jr. et al.[11] with potassium carbonate base. The 2-position of dicyanamide and chloride 1-butyl-3-methylimidazolium salts has been deuterated by Handy et al.[3] who also determined the respective rate constants. However, the authors do not observe exchange in 4- and 5-position or give deuterium contents for their products presumably because their experiments were not designed with preparation of deuterated ILs in mind. In one paper, exchange of the 2-position was observed in CD_3OD and D_2O with imidazolium bromides but not with other anions.[13]

2. Deuteration procedures

Water-miscible and water-stable ionic liquids with the BF_4 anion may be readily deuterated by stirring the IL with a threefold volume excess of D_2O and 15 mol %

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* Corresponding author. Fax: +49 221 470 5102; e-mail: Ralf.Giernoth@uni-koeln.de

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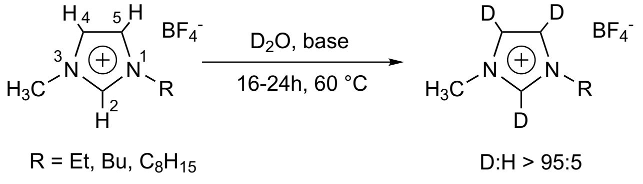
alkali metal hydroxide at 60 °C overnight (Scheme 1). The solution is then neutralized with the corresponding aqueous acid HBF_4. Since the exchange reaction is quenched on acidification, the use of HBF_4/H_2O does not significantly compromise the deuterium content of the product. Recovery of the ionic liquid is achieved by extraction with dichloromethane and removal of the organic solvent under vacuum and elevated temperature. The deuterated product is obtained in yields of 90% and deuterium content of 95–98% in each position.

Bistriflic amide salts as examples of water-immiscible ILs may be deuterated by stirring in CH_3OD with 30 mol % alkali metal hydroxide overnight at 60 °C (Scheme 2). After neutralization with solid $(CF_3SO_2)_2NH$ and removal of the organic solvent, the IL is partitioned between water and ethyl acetate or dichloromethane. Separation and removal of the organic solvent affords the product in nearly quantitative yield and with a deuterium content of about 90%.

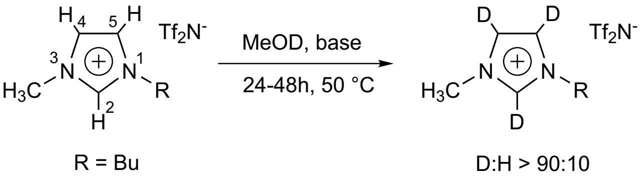
Except for cations with two very short side chains and thus high water-miscibility like in $[bmim]BF_4$, this procedure is found to be generic, though sterically very hindered ILs can be expected to require more fierce reaction conditions. The aforementioned small cations do undergo exchange, yet the recovery from the aqueous phase is an unsolved issue.

Alkali metal hydroxides seem to be optimal bases due to their low solubility in organic solvents, the negligible catalytic activity of alkali metal cations and the fact that neutralization of hydroxides yields only water and easily separable salts.

Good results have been obtained in all cases with caesium hydroxide as the base. However, sodium and potassium hydroxides lead to comparable results. Potassium carbonate affords a partially deuterated product unless reaction times are increased significantly (Table 1). Again, no anion contamination of the ionic liquid should take place, since on acidification and subsequent heating CO_2 is expelled.



Scheme 1. Deuteration procedure for tetrafluoroborate ionic liquids.



Scheme 2. Deuteration procedure for bistriflic amide ionic liquids.

Table 1. Yields and deuterium content of labelled ionic liquids

Ionic liquid	Base	Solvent	*t* (h)	*T* (°C)	Yield[a] (%)	Deuterium content[b]
$[bmim]BF_4$	CsOH	D_2O	12	60	90	0.95, 0.95, 0.95
$[omim]BF_4$	CsOH	D_2O	18	60	82	0.98, 0.98, 0.97
$[bmim]BF_4$	KOH	D_2O	18	60	67	0.95, 0.95, 0.95
$[bmim]BF_4$	NaOH	D_2O	18	60	77	0.95, 0.95, 0.95
$[bmim]BF_4$	K_2CO_3	D_2O	12	60	86	0.98, 0.47, 0.57
$[bmim]BF_4$	K_2CO_3	D_2O	48	60	71	0.96, 0.65, 0.74
$[bmim]Tf_2N$	CsOH	CH_3OD	24	rt	87	0.91, 0.84, 0.86
$[bmim]Tf_2N$	CsOH	CH_3OD	48	60	98	0.89, 0.90, 0.90

[a] Subject to further optimization.

[b] Deuterium content determined from ^1H NMR integration, ordered from low to high field. For assignment, see Supplementary data.

3. Characterization of the products

^1H NMR spectra of the products (Fig. 1) show no decomposition by the bases. If the exchange is allowed to run for a sufficient amount of time, integration of the residual ring proton signals indicates equal deuterium content in all three positions, confirming that the exchange reactions have reached equilibrium and

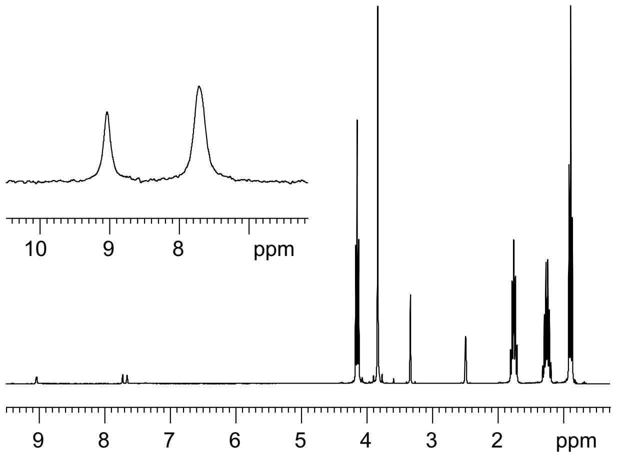


Figure 1. Proton and deuterium (inset) spectra of $[bmim]-d_3BF_4$ (300 MHz, DMSO-d_6).

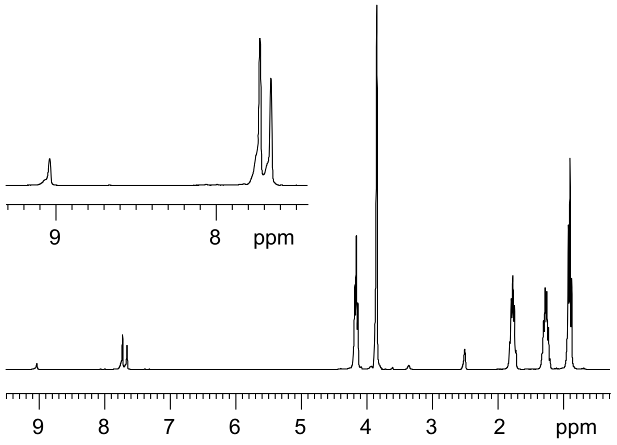


Figure 2. Proton NMR spectrum of $[bmim]-d_3BF_4$ showing incomplete exchange (300 MHz, DMSO-d_6).

that deuterium is statistically distributed between all exchanging positions (cf. discussion below).

The uniform incorporation of deuterium into all three positions is confirmed by ^{2}D NMR spectroscopy (Fig. 1, inset). Since the 4- and 5-position are not individually resolved, the two integrals exhibit a 1:2 ratio.

4. Reaction profiles

If the exchange reaction is not allowed to run until equilibrium is reached, unequal deuterium content can be observed in the proton NMR spectra. A sample treated for 12 h with the weak base K_2CO_3 at 60 °C was 98% deuterated at the 2-position, while the 4- and 5-position were unevenly deuterated at 47% and 57% D, respectively (Fig. 2), implying that the reaction had not reached equilibrium. From the integration, a first semi-quantitative statement on the relative exchange rates could be made (assuming constant rates over the reaction time) in that the ratio between the rates of the 2-, 4- and 5-position is approximately 6.3:1:1.3.

The exchange of [bmim]BF_4 in D_2O (Fig. 3) and [bmim]Tf_2N in CD_3OD (Fig. 4) has been followed in situ by means of ^{1}H NMR spectroscopy at 45 °C and with stoichiometries according to the preparative

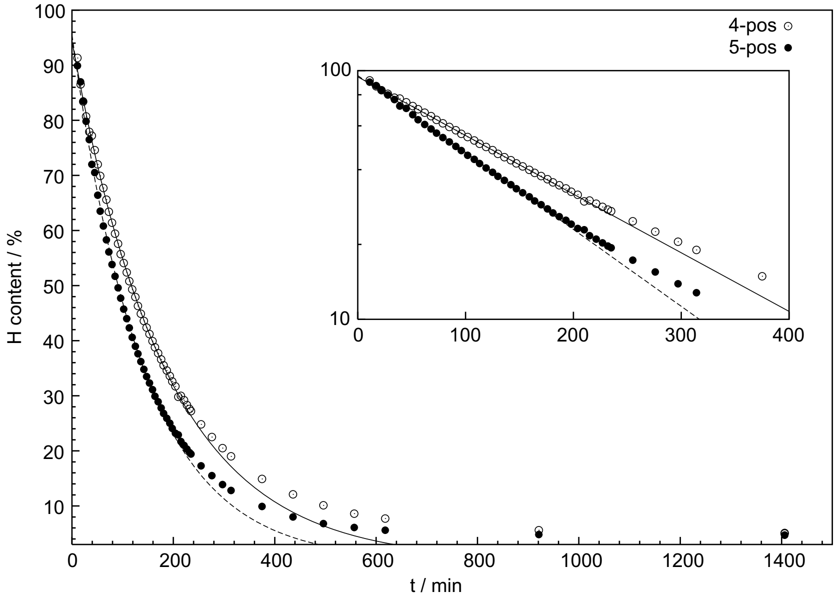


Figure 3. Reaction profile of the deuteration of 0.2 g [bmim]BF_4 in 0.6 mL D_2O with 24 mg caesium hydroxide at 45 °C. Curves show exponential functions fitted to the first-order regime of the reactions. Inset shows data in logarithmic scale.

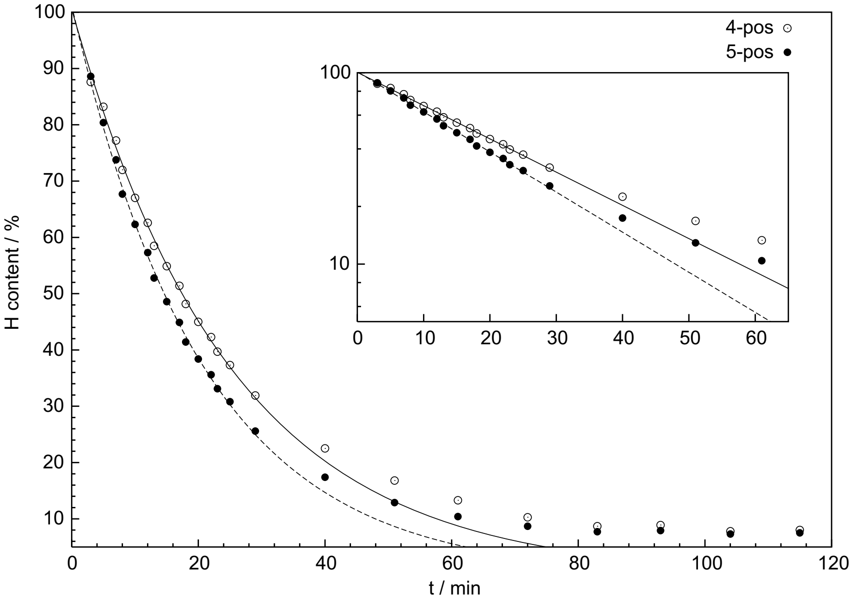


Figure 4. Reaction profile of the deuteration of 0.2 g [bmim]Tf_2N in 0.6 mL CD_3OD with 24 mg caesium hydroxide at 45 °C. Curves show exponential functions fitted to the first-order regime of the reactions. Inset shows data in logarithmic scale.

procedures. Though the latter reaction is considerably faster, both exhibit common trends. In both cases, the 2-position was fully deuterated from the start of the NMR measurements, indicating a very fast exchange. In contrast, without the addition of base, exchange in this position took 2 h to complete for the BF_4 salt and exchange of only 30% was observed after 4 h for the Tf_2N salt.

The reactions exhibit three domains. In the first, [bmim]-d_1 is abundant and a clean pseudo-first-order reaction is found. The exchange rates of the 4- and 5-proton differ by a factor of 1.3 (BF_4 salt) and 1.2 (Tf_2N salt), respectively. This is in good agreement with the notion that the exchange in the 4- and 5-position is mainly determined by the nature of the 1- and 3-substituent, which are identical between both cases presented here. Variation of the side chains will, in future kinetics investigations, provide insight into whether the rate constants are determinated mainly by sterical or electronic effects.

With advancement of the exchange reaction, kinetics deviate from exponential behaviour, suggesting increasing exchange between species other than [bmim]-d_1 and D_2O. As a multitude of deuterium bearing moieties exist in the mixture at this point (thus rendering the kinetics quite intricate), no analytical treatment of this region was performed. The final region shows a steady decrease in deuterium content difference between the 4- and 5-position, marking the path towards statistical (equilibrium) concentrations of deuterium in all exchanging species. Further increase of deuterium content in the product can then only be achieved by isolation and repeated exchange with fresh deuterium source.

5. Conclusions

The fact that deuteration of all positions in the imidazolium ring occurs even in the presence of a weak base (and thus at low pH) clearly demonstrates the highly noninert nature of ionic liquids containing this cation. As significant exchange in the 2-position can be observed even in the absence of added base, imidazolium ionic liquids should in fact be considered to be protic solvents. Catalytic amounts of base were shown to be sufficient for complete proton exchange in all ring positions. This stresses on the fact that purity considerations for ionic liquids should include the absence of contamination with bases (such as the starting material *N*-methylimidazole), which can be inferred to largely influence reactivity on the imidazolium ring.

In conclusion, we could demonstrate an extremely simple and at the same time versatile deuteration procedure for ionic liquids with imidazolium cations. The results shown here are expected to be generic with respect to imidazolium cation sidechain constitution and anion type. Apart from simplicity, this procedure has further conceptional advantages over known methods. If deuterated ILs are to be used for the study of reaction mechanisms, exceptional purity is crucial. Since no transition metal is used, no metal contamination of the product ionic liquid can occur. No decomposition of the ionic liquid as a result of basic treatment could be detected. Furthermore, direct deuteration of the IL to be used in contrast to deuterating its precursors minimizes loss of expensive labels in further preparative steps and allows for deuteration on demand, with no need to resynthesize ILs already available from prior syntheses or commercial suppliers.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.04.032.

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