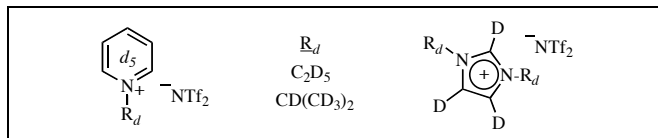


Sergei V. Dzyuba, Shengfu Li and Richard A. Bartsch*

Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79409
Received February 28, 2006

Facile, gram-scale, one-pot or two-step syntheses for two different types of perdeuterated room-temperature ionic liquids from commercially available starting materials are described.

J. Heterocyclic Chem., **44**, 223 (2007).

INTRODUCTION

Room-temperature ionic liquids (RTILs) have become versatile and attractive media for performing numerous synthetic transformations ranging from organic to material chemistry [1]. Numerous other applications for these thermally stable, low volatility media in analytical chemistry have been realized, as well [2]. Deuterated RTILs have potential applications in nmr spectroscopy, mass spectrometry and small angle neutron scattering studies [3]. Although some syntheses of partially deuterated RTILs have been published [3a,4], the currently available preparations of fully deuterated analogues require sophisticated methodologies [5].

Among the most commonly used cation components of RTILs are *N*-alkylpyridinium and 1-alkyl-3-alkyl-imidazolium ions [2a,b]. We now report the facile preparation of two different types of perdeuterated RTIL of these general types from commercially available deuterated starting materials.

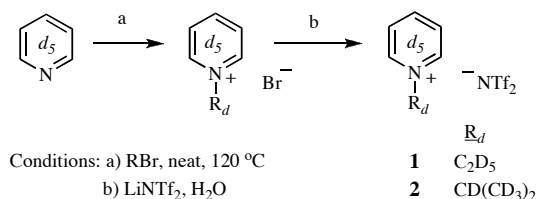
Perdeuterated ethyl and isopropyl groups were selected for incorporation as a compromise between the highest possible lipophilicity of the RTIL and expense of the labelled alkyl bromide reactants. Of the frequently encountered anion components for RTILs [2a,b], bis(trifluoromethanesulfonyl)imide was chosen for its tendency to produce water-immiscible liquids with low viscosities [6].

RESULTS AND DISCUSSION

In terms of simplicity, the preparation of perdeuterated *N*-alkylpyridinium RTILs is very attractive, since they can be obtained in a one-pot synthesis from commercially available deuterated starting materials (Scheme 1). To maximize the efficiency of the alkylation step, the reaction was performed in a 15-mL, glass pressure vessel. Neat reaction of equimolar amounts of pentadeuterio-pyridine and perdeuterated ethyl or isopropyl bromide at 120 °C for 4 hours gave the corresponding perdeuterated *N*-alkylpyridinium bromides. These white solids were not isolated due to their low utility as RTILs [1a,b], but were

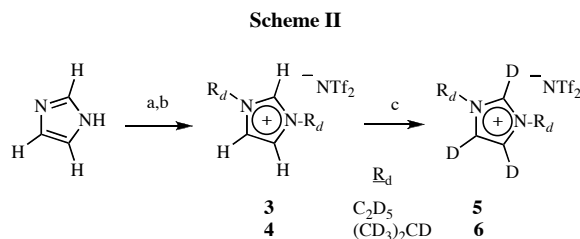
directly converted into the corresponding bis(trifluoromethanesulfonyl)imide salts **1** and **2** in 85 and 76% overall yields, respectively. Either water or deuterium oxide can be used for the anion metathesis reaction, since control experiments (by nmr) showed no H/D exchange over a 2-day period. Both **1** and **2** are low-viscosity, colorless liquids, which are identical in appearance to their undeuterated analogues.

Scheme I



One of the most widely utilized RTIL types is 1-alkyl-3-alkyl-imidazolium salts [1a,b,2a,b]. However, reported preparations of this type of perdeuterated RTIL requires the use of high-pressure apparatus, microwave irradiation and transition metal catalysts [5]. Recently, we described the facile preparation of C_{2v}-symmetric 1,3-dialkylimidazolium hexafluorophosphates from imidazole, alkyl bromides and sodium hydride [7]. This procedure suggests an appealing entry to perdeuterated C_{2v}-symmetric RTILs. However, under the reported conditions, reaction of imidazole with 2 equivalents of perdeuterated ethyl bromide gave 1-(perdeuterioethyl)imidazole as the major product with only 10% of the desired 1,3-di(perdeuterioethyl)imidazolium bromide. Changing to a glass pressure vessel for the alkylation reaction gave an effective dialkylation step for the production of perdeuterated 1,3-diethyl- and 1,3-di-(isopropyl)imidazolium bis(trifluoromethanesulfonyl)imides, **5** and **6** (Scheme 2) [8].

A glass pressure vessel containing sodium hydride under nitrogen was closed with a septum and cooled in an ice bath. With magnetic stirring, a solution of imidazole



Conditions: a) NaH, THF, 0 °C to r.t., then 2.5 R_dBr, 130 °C
 b) LiNTf₂, H₂O
 c) K₂CO₃, D₂O, 130 °C

in tetrahydrofuran was added over 30 minutes and the contents of the vessel were stirred at room temperature for 2 hours. After adding 2.5 equivalents of perdeuterated ethyl or isopropyl bromide, the pressure vessel was sealed with a screw cap and heated at 130 °C for 5 hours to give the 1,3-di(perdeuterioalkyl)imidazolium bromides, which were subjected directly to anion metathesis with lithium bis(trifluoromethanesulfonyl)imide in water to give the 1,3-di(perdeuterioalkyl)imidazolium bis(trifluoromethanesulfonyl)imides **3** and **4** in 77 and 68% yields, respectively.

A hydrogen at the 2-position in an imidazolium salt is quite labile and may be readily exchanged with deuterium [4b]. H/D exchange can be induced at the 4- and 5-positions under more vigorous reaction conditions [9]. We found that H/D exchange of all hydrogens on the imidazolium nucleus can be accomplished by heating **3** and **4** with potassium carbonate in deuterium oxide in a glass pressure vessel at 130 °C for 24 hours to give the perdeuterated 1,3-dialkylimidazolium bis(trifluoromethanesulfonyl)imides **5** and **6** in overall 72 and 61% yields, respectively, based on starting imidazole. Both **5** and **6** are free-flowing, colorless liquids, which are identical in appearance to their undeuterated analogues.

Thus viable synthetic routes have been established for synthesis of perdeuterated *N*-ethyl and *N*-isopropylpyridinium bis(trifluoromethanesulfonyl)imides (**1** and **2**, respectively) and 1,3-diethyl- and 1,3-diisopropylimidazolium bis(trifluoromethanesulfonyl)imides (**5** and **6**, respectively).

EXPERIMENTAL

Deuterium nmr and cmr spectra were measured with a Varian Unity INOVA NMR spectrometer at 77 and 126 megahertz, respectively. The deuterium nmr was run unlocked with the deuterium lock system disabled to avoid interference with the sample spectrum acquisition. Chemical shifts are referenced to deuterioacetone (2.05 ppm), which was used as the solvent for recording nmr spectra of the RTILs [10]. The carbon nmr spectra were run locked on deuterium in the solvent. The 15- and 75-mL, heavy-wall glass pressure vessels were from Chemglass (#CG-1880) with CG-309 perfluoroelastomer O-rings. The deuterated reactants (≥ 98% D) were purchased from

Cambridge Isotope Laboratories, Inc. Molecular organic solvents were dried before use. Combustion analysis was performed by Desert Analytics Laboratory of Tucson, Arizona.

General procedure for preparation of perdeuterated *N*-alkylpyridinium bis(trifluoromethanesulfonyl)imides. A 15-ml, glass pressure vessel was charged with perdeuterated pyridine (0.83 ml, 10.3 mmole), the perdeuterated alkyl bromide (10.3 mmole) and a magnetic stirring bar. The pressure vessel was sealed with a screw cap and the lower portion was immersed in a silicone oil bath. The contents were stirred at 120 °C for 4 hours, after which they were allowed to cool to room temperature. The resulting white solid was dissolved in 10 ml of water-dichloromethane (1:1) and lithium bis(trifluoromethanesulfonyl)imide (2.96 g, 10.3 mmole) was added. The mixture was stirred vigorously at room temperature for 30 minutes. The aqueous layer was replaced with 20 ml of water and the mixture was stirred for 30 minutes. The dichloromethane layer was removed and evaporated *in vacuo* to afford a colorless liquid, which was dried with benzene in a Dean-Stark apparatus. After evaporation of the benzene *in vacuo*, the residue was dried at 0.5 Torr at room temperature for 5 hours to provide the RTIL.

Perdeuterated *N*-ethylpyridinium bis(trifluoromethanesulfonyl)imide (1**):** 85% yield. dmr (77 MHz, deuterioacetone): δ 1.63 (3D), 4.87 (2D), 8.31 (2D), 8.78 (1D), 9.21 (2D). cmr (126 MHz, deuterioacetone): δ 15.6, 57.3, 122.0, 128.7, 144.6, 146.0. Anal. [11] Calcd for C₉D₁₀F₆N₂O₄S₂: C, 27.14; D, 2.53; N, 7.03. Found: C, 27.18; D, 2.79; N, 6.93.

Perdeuterated *N*-isopropylpyridinium bis(trifluoromethanesulfonyl)imide (2**):** 76% yield. dmr (77 MHz, deuterioacetone) δ 1.78 (6D), 5.23 (1D), 8.33 (2D), 8.78 (1D), 9.28 (2D). cmr (126 MHz, *d*₆-acetone): δ 21.9, 65.4, 122.3, 128.9, 143.4, 146.3. Anal. [11] Calcd for C₁₀D₁₂F₆N₂O₄S₂: C, 28.99; D, 5.81; N, 6.76. Found: C, 28.87; D, 5.96; N, 6.79.

General procedure for preparation of perdeuterated 1,3-dialkylimidazolium bis(trifluoromethanesulfonyl)imides. Into a 75-ml pressure vessel containing a stirring bar was weighed 0.40 g (14.7 mmole) of 95% sodium hydride powder. The pressure vessel was capped with a rubber septum, evacuated and back-filled with nitrogen. After addition of tetrahydrofuran (10 ml) by syringe, the pressure vessel was cooled to 0 °C in an ice-salt bath. To the stirred mixture, a solution of imidazole (1.00 g, 14.7 mmole) in tetrahydrofuran (10 ml) was added by syringe over a 0.5-hour period. The pressure vessel was allowed to warm to room temperature and stirring was continued for 2 hours. Following addition of the perdeuterated alkyl bromide (36.8 mmole) in tetrahydrofuran (10 ml) by syringe, the rubber septum was replaced with the screw cap. The lower portion of the pressure vessel was immersed in a 130 °C silicone oil bath and the reaction mixture was stirred for 5 hours. After cooling to room temperature, the mixture was filtered and the solid was washed with dichloromethane. The combined filtrate and washings were evaporated *in vacuo*. The residue was dissolved in water (30 ml) and lithium bis(trifluoromethanesulfonyl)imide (4.22 g, 14.7 mmole) was added. After stirring the mixture for 30 minutes, the aqueous layer was decanted and fresh water (20 ml) was added. After stirring for another 30 minutes, the layers were separated and the RTIL was dried with benzene in a Dean-Stark apparatus and then by heating overnight at 100 °C and 0.5 Torr.

Decadeuterio-1,3-diethylimidazolium bis(trifluoromethanesulfonyl)imide (3**):** 77% yield. dmr (77 MHz, deuterioacetone) δ 1.52 (6D), 4.36 (4D). cmr (126 MHz, deuterioacetone) δ 14.9, 45.5, 121.4, 123.5, 136.3. Anal. [11]

Calcd for $C_9D_{10}H_3F_6N_3O_4S_2 \cdot 0.2C_6H_6$: C, 27.09; D, 3.26; N, 10.30. Found: C, 27.30; D, 3.21; N, 9.88.

Tetradecyldeuterio-1,3-di-(isopropyl)imidazolium bis-(trifluoromethanesulfonyl)imide (4): 68% yield [12]. dmr (77 MHz, deuterioacetone) δ 1.59 (12D), 4.77 (2D). cmr (126 MHz, deuterioacetone) δ 14.6, 45.2, 121.0, 122.8, 136.1. *Anal.* [11] Calcd for $C_{11}D_{14}H_3F_6N_3O_4S_2$: C, 29.53; D, 3.83; N, 9.39. Found: C, 29.39; D, 4.01; N, 9.12.

Into a 15-ml, glass pressure vessel was placed 2.67 mmole of this liquid together with a stirring bar, potassium carbonate (1.95 g, 14.1 mmole) and deuterium oxide (6.0 ml). The pressure vessel was sealed with the screw cap and the lower portion was immersed in a silicone oil bath at 130 °C. After heating with stirring for 24 hours, the reaction mixture was allowed to cool to room temperature and extracted with dichloromethane. The organic layer was evaporated *in vacuo* and the residue was heated at 100 °C and 0.5 Torr overnight to produce **5** and **6**.

Perdeuterated 1,3-diethylimidazolium bis(trifluoromethanesulfonyl)imide (5): 94% yield. dmr (77 MHz, deuterioacetone): δ 1.53 (6D), 4.38 (4D), 7.82 (2D), 9.11 (1D). cmr (126 MHz, deuterioacetone): δ 21.7, 53.4, 120.9, 121.6, 124.1. *Anal.* [11] Calcd for $C_9D_{13}F_6N_3O_4S_2 \cdot 0.2C_6H_6$: C, 27.09; D, 3.26; N, 10.30. Found: C, 27.10; D, 3.21; N, 9.99.

Perdeuterated 1,3-di-(isopropyl)imidazolium bis(trifluoromethanesulfonyl)imide (6): 89% yield. dmr (77 MHz, deuterioacetone): δ 1.58 (12D), 4.76 (2D), 7.88 (2D), 9.13 (1D). cmr (126 MHz, deuterioacetone): δ 21.8, 53.4, 121.0, 121.1, 133.8. *Anal.* [11] Calcd for $C_{11}D_{17}F_6N_3O_4S_2$: C, 29.33; D, 3.80; N, 9.32. Found: C, 29.33; D, 3.69; N, 9.20.

Acknowledgment. This research was supported by the Texas Higher Education Coordinating Board Advanced Research Program. We would like to thank David Purkiss for assistance in acquiring the deuterium nmr and the cmr spectra. We would like to express our appreciation to the National Science Foundation for Grant CHE-9808436, which was used to

purchase the Varian Unity INOVA 500 MHz NMR spectrometer.

REFERENCES AND NOTES

- [1a] T. Welton, *Chem. Rev.*, **99**, 2071 (1999); [b] P. Wasserscheid and T. Welton, *Ionic Liquids in Synthesis*, Wiley-VCH, Weinheim, Germany, 2003; [c] K. R. Seddon, *Nature Materials*, **2**, 363 (2003); [d] N. Jain, A. Kumar, S. Chauhan and S. M. S. Chauhan, *Tetrahedron*, **61**, 1015 (2005); [e] J. Ding and D. W. Armstrong, *Chirality*, **17**, 281 (2005).
- [2] J.-f. Liu, J. Å Jönsson, *Trends Anal. Chem.*, **24**, 20 (2005); [b] G. A. Baker, S. N. Baker, S. Pandey and F. V. Bright, *Analyst*, **130**, 800 (2005); [c] M. Koel, *Crit. Rev. Anal. Chem.*, **35**, 177 (2005).
- [3a] R. Giernoth and D. Bankmann, *Tetrahedron Lett.*, **47**, 4293 (2006); [b] A. Triolo, O. Russina, U. Keiderling and J. Kohlbrecher, *J. Phys. Chem. B Lett.*, **110**, 1513 (2006).
- [4a] R. N. Garman, G. S. Getvoldsen, J. R. Jones, K. W. M. Lawrie, S. Y. Lu, P. Marsden, J. C. Russell and K. R. Seddon, In *Synthesis and Applications of Isotopically Labelled Compounds*, U. Pleiss and R. Voges, Eds., Wiley, Chichester, UK, 2001, pp 97-100; [b] S. T. Handy and M. Okello, *J. Org. Chem.*, **70**, 1915 (2005).
- [5] C. H. Hardacre, J. D. Holbrey and S. E. J. McMath, *Chem. Commun.*, 367 (2001).
- [6] Modification of the procedures to incorporate other anions, such as hexafluorophosphate or tetrafluoroborate, would be straightforward.
- [7] S. V. Dzyuba and R. A. Bartsch, *Chem. Commun.*, 1466 (2001).
- [8] A synthetic route beginning with tetradecyldeuterioimidazole was excluded due to the high cost of this commercially available compound.
- [9] K. M. Dieter, Jr., C. J. Dymerk, N. E. Heimer, J. W. Rovang and J. S. Wilkes, *J. Am. Chem. Soc.*, **110**, 2722 (1988).
- [10] The deuterium spectra exhibited broad absorptions similar to those shown in Reference 3a.
- [11] Deuterium was analyzed as hydrogen.
- [12] The yield for this alkylation reaction increased to 79% when a sealed tube was utilized.