Convenient and General Synthesis of Symmetrical *N,N'*-Disubstituted Imidazolium Halides

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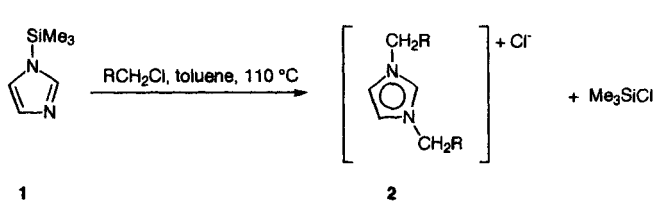
N,N'-Dialkyl- and *N,N*-dibenzylimidazolium chlorides or bromides were synthesized in high yield from the appropriate primary alkyl or benzyl halide and *N*-trimethylsilylimidazole.

N,N'-Dialkylimidazolium salts have recently attracted considerable interest due to their use in the preparation of ambient temperature ionic liquids, by combination with aluminium halides,[1] and of surprisingly stable carbenes, by deprotonation.[2] A number of classical routes to these ionic heterocycles are available[3-6] although each of these routes has its own particular synthetic problems when applied to a range of derivatives. Reaction of an *N*-substituted imidazole with the halide of the desired substituent is typically the method of choice for simple alkyl derivatives.[3] This reaction is limited by the narrow range of *N*-substituted imidazoles which are commercially available and those that are, are often expensive. Alternatively, 1,3-disubstituted imidazolium salts have been prepared by the condensation of 2 equivalents of a bisimine with an acid catalyst[4] or by desulfurisation of imidazole-2-thiones.[5] This second route, however, requires several steps to synthesise the starting imidazole-2-thione. Recently, a one-step synthesis of 1,3-disubstituted imidazolium salts, with the capacity for the inclusion of simple substituents in the 2-, 3-, and 5-positions, was reported.[6] In our hands, this synthetic approach provided salts which proved extremely difficult to isolate in the purity required for ionic liquid studies, often being contaminated with small amounts of highly coloured impurities. This led us to develop an expedient one-step route (Scheme) to such compounds using commercially available *N*-trimethylsilylimidazole in combination with two equivalents of a range of alkyl and benzyl halides.



1 **2**

Scheme

The reactions presumably proceed via *N*-trimethylsilyl-*N'*-alkylimidazolium salts which are then prone to halodesilylation to provide *N*-alkylimidazoles in situ. The reaction is typically carried out in refluxing toluene for up to 24 hours with an excess of RCH_2Cl. For expensive alkyl halides, acceptable yields are obtained with three equivalents. As the reactions proceed the mixture becomes biphasic due to the convenient insolubility of the imidazolium salts in toluene. Furthermore, the reaction may also be extended to the synthesis of bromide derivatives, e.g., **2b** derived from *N*-trimethylsilylimidazole and propyl bromide. The Table illustrates the range of salts prepared so far, however some failures of this approach are notable. Aryl chlorides fail to react, as do neophyl and neopentyl chloride, whilst secondary halides (e.g., 2-chloropropane) lead to excessive contamination with unsubstituted imidazolium chloride. The spectroscopic characterization was in general unremarkable, however one notable feature which emerges from the FAB mass spectra is the prevalence of clusters of composition $[M(MX)_n]^+$ in addition to peaks due to the isolated imidazolium cations. This behaviour has been observed previously with the technique and may arise from hydrogen bonding between the anions and cations.[7]

Table. Yields of *N,N*-Disubstituted Imidazolium Halides $[R_2N_2C_3H_3]X$

2	R	X	Yield (%)[a]
a	Me	Cl	40
b	Pr	Br	34
c	Bu	Cl	75
d	Bn	Cl	42
e	$CH_2C_6H_4Me$-4	Cl	98

[a] Yields based on Me_3SiIm.

In conclusion, the advantages offered by this approach, in addition to economy and convenience, include: (i) The preparations may be carried out under completely anhydrous conditions, a requisite feature for the subsequent application of these salts as precursors for both ionic liquids or free imidazolidenes. (ii) The reactions generally proceed in high yield with all side products being either volatile or toluene soluble.

All reagents were obtained from commercial sources. The alkyl halides were distilled from P_2O_5 prior to use. *N*-Trimethylsilylimidazole was stored over 3 Å molecular sieves. All reactions were routinely carried out under anaerobic and anhydrous conditions in dry and freshly distilled solvents unless otherwise indicated. IR spectra were obtained from Nujol mulls using a Perkin Elmer 1720-X FTIR spectrometer. ^1H and ^{13}C-$\{^1H\}$-NMR spectra were determined on a JEOL 270 MHz instrument. Fab mass spectra were obtained from nitrobenzyl alcohol matrices using an Autospec-Q instrument. 'M' refers to the imidazolium cation.

1,3-Dimethylimidazolium Chloride (2a):
N-Trimethylsilylimidazole (18.2 mL, 0.124 mol) was frozen (liquid N_2) in a glass pressure Schlenk tube and MeCl (15 mL, 0.272 mol) was then condensed into the tube using a cold finger held at − 78 °C. The vessel was then sealed and allowed to warm up to r.t. overnight. This led to the formation of a large crystalline mass of product. Excess gas was allowed to escape via a $CaCl_2$ drying tube and the crude product crystallised from a mixture of MeCN and EtOAc giving white crystals of product; yield (based on *N*-trimethylsilylimidazole): 6.55 g (40 %). The compound was characterised by comparison of spectroscopic data with those previously reported.[3] Mp 71–73 °C.

IR (Nujol): $\nu = 1575$s, 1344s, 1291m, 1175vs, 1092m, 1017w, 883–873m, 799s, 717m cm^{-1}.

^1H NMR ($CDCl_3$, 270 MHz): $\delta = 3.61$ (s, 6H, NCH_3), 7.30 [s, 2H, $H^{4,5}$ (Im)], 9.88 [s, 1H, H^2 (Im)].

FAB MS: m/z (%) = 97 (100) $[M]^+$, 221 (24) $[M_2Cl]^+$, 493 (42) $[M_3Cl_2]^+$.

Anal $C_5H_9ClN_2$ (132.6) requires C 45.4; H 6.9; N 21.2. Found C 45.4; H 7.4; N 20.7.

1,3-Dipropylimidazolium Bromide (2b):
N-Trimethylsilylimidazole (5 mL, 0.034 mol) was stirred with PrBr in toluene (20 mL) at r.t. for 4 h. At this point the product began to precipitate from solution. Addition of further toluene (20 mL) precipitated the remainder of the white crystals of product from solution which were isolated by filtration under dry N_2. The product was dried in vacuo for 4 h; yield: 2.69 g (34%); mp 134–136°C.

^1H NMR ($CDCl_3$/270 MHz): $\delta = 0.72$ (t, 6H, CH_3), $J_{(HH)} = 7.3$ Hz), 1.75 (m, 4H, NCH_2CH_2), 4.13 (m, 4H, NCH_2), 7.55 [s, 2H, $H^{4,5}$ (Im)], 10.17 [s, 1H, H^2 (Im)].

^{13}C-{^1H} NMR ($CDCl_3$, 25°C): $\delta = 10.5$ (CH_3), 23.6 (NCH_2CH_2), 51.1 (NCH_2), 122.4 ($C^{4,5}$), 136.5 (C^2).

FAB MS: m/z (%) = 153 (100) $[M]^+$, 385 (62) $[M_2Br]^+$, 619 (59) $[M_3Br_2]^+$, 851 $MM_4Br_3]^+$.

1,3-Dibutylimidazolium Chloride (2c):
N-Trimethylsilylimidazole (20 mL, 0.14 mol) was heated under reflux with BuCl (42.6 mL, 0.41 mol) in toluene (50 mL) overnight. This produced a layered mixture which was homogenised by the addition of the minimum amount of dry MeCN. The resulting solution was placed in the freezer until white crystals of product had formed. These were isolated by filtration under dry N_2 and dried in vacuo for 4 h; yield: 22.10 g (75%); mp 58–61°C.

IR (Nujol): $\nu = 1563$vs, 1261m, 1168vs, 1021s, 879m, 801s, 753m cm^{-1}.

^1H NMR ($CDCl_3$, 270 MHz): $\delta = 0.40$ (t, 6H, CH_3, $J_{(HH)} = 6.6$ Hz), 0.83 (m, 4H, CH_2CH_3), 1.38 (m, 4H, NCH_2CH_2), 3.84 (t, 4H, NCH_2CH_2), 3.84 (t, 4H, NCH_2, $J_{(HH)} = 6.6$ Hz), 7.26 [s, 2H, $H^{4,5}$ (Im)], 10.11 [s, 1H, H^2 (Im)].

^{13}C-{^1H}NMR ($CDCl_3$, 270 MHz): $\delta = 13.0$ (CH_3), 18.9 (CH_2CH_3), 31.7 (NCH_2CH_2), 49.1 (NCH_2), 122.1 [$C^{4,5}$ (Im)], 136.6 [C^2 (Im)].

FAB MS: m/z (%) = 181 (100) $[M]^+$, 397 (15) $[M_2Cl]^+$.

Anal. $C_{11}H_{21}ClN_2$ (216.75) requires C 61.0; H 9.8; N 12.9. Found C 60.7; H 10.0; N 12.9.

1,3-Dibenzylimidazolium Chloride (2d):
N-Trimethylsilylimidazole (25 mL, 0.17 mol) was heated under reflux with BnCl (60 mL, 0.51 mol) in toluene (25 mL) overnight. Once layering was observed the solution was cooled and the product recrystallised from dry MeCN and toluene. White crystals of product were isolated from the solvent by filtration under dry N_2 and dried in vacuo for 4 h; yield: 20.23 g (42%); mp 119–122°C.

IR (Nujol): $\nu = 1564$s, 1551s, 1334s, 1309s, 1208s, 1141vs, 1074s, 1032s, 1018s, 885m, 846w, 819w, 788w, 767m, 720vs, 694vs, 641vs, 614vs cm^{-1}.

^1H NMR ($CDCl_3$, 25°C): $\delta = 5.42$ (s, 4H, NCH_2), 7.20, 7.37 (m × 2, 10H, Ph), 7.34 [s, 2H, $H^{4,5}$ (Im)], 10.79 [s, 1H, H^2 (Im)].

^{13}C-{^1H} NMR ($CDCl_3$, 25°C): $\delta = 53.3$ (NCH_2), 122.1 [$C^{4,5}$ (Im)], 128.9 [$C^{2,6}$ (Ph)], 129.4 [C^{3-5} (Ph)], 133.1 (C^1 (Ph)], 137.3 [C^2 (Im)].

FAB MS: m/z (%) = 249 (100) $[M]^+$, 533 (5) $[M_2Cl]^+$.

Anal $C_{17}H_{17}ClN_2$ (284.78) requires C 71.7; H 6.0; N 10.0. Found C 71.2; H 5.8; N 10.0.

1,3-Bis(4-tolylmethyl)imidazolium Chloride (2e):
N-Trimethylsilylimidazole (20 mL, 0.14 mol) was heated under reflux with 4-tolyl CH_2Cl (54 mL, 0.41 mol) in toluene (50 mL) overnight. Once layering of the solution had occurred the products were cooled and white crystals of the product isolated and recrystallised from dry MeCN and toluene followed by filtration under dry N_2. The product was dried in vacuo for 4 h; yield: 41.73 g (98%); mp 157–158°C.

IR (Nujol): $\nu = 1558$vs, 1517s, 1315m, 1188vs, 1151vs, 1106m, 1016m, 818s, 760vs, 745vs, 723s, 695w, 635vs, 616vs cm^{-1}.

^1H NMR ($CDCl_3$, 270 MHz): $\delta = 1.83$ (s, 6H, CH_3), 5.09 (s, 4H, NCH_2), 6.82 [$(AB)_2$, 8H, C_6H_4; $J_{(HH)} = 7.6$ Hz], 7.24 [s, 2H, $H^{4,5}$ (Im)], 10.49 [s, 1H, H^2 (Im)].

^{13}C-{^1H}NMR ($CDCl_3$, 25°C): $\delta = 20.9$ (CH_3), 52.4 (NCH_2), 122.0 [$C^{4,5}$ (Im)], 128.6 [$C^{2,6}$ (C_6H_4)], 129.5 [$C^{3,5}$ (C_6H_4)], 130.2 [$C^4(C_6H_4)$], 136.2 [C^2 (Im)], 138.8 [C^1 (C_6H_4)].

FAB MS: m/z (%) = 105 (27) $[CH_2C_6H_4CH_3]^+$, 277 (100) $[M]^+$, 589 (5) $[M_2Cl]^+$.

Anal $C_{19}H_{21}ClN_2$ (312.83) requires C 73.0; H 6.8; N 9.0. Found C 72.2; H 6.6; N 9.2.

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(1) Hussey, C.L. *Adv. Molten Salt Chem.* **1983**, *5*, 185.
(2) Arduengo, A.J. III; Dias, H.V.R.; Harlow, R.L.; Kline, M. *J. Am. Chem. Soc.* **1992**, *114*, 5530.
(3) Chan, B.K.M.; Chang, N-H.; Grimmel, M.R. *Aust. J. Chem.* **1977**, *30*, 2005.
(4) Zettlitzer, M.; Dieck, H.T.; Haupt, E.T.K.; Stamp, L. *Chem. Ber.* **1986**, *119*, 1868.
(5) Wanzlick, H.; Schönherr, H. *Angew. Chem.* **1968**, *80*, 153; *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 141.
(6) Arduengo, A.J., III U.S. Patent 5077414, 1991.
(7) (a) Abdul-Sada, A.K.; Greenway, A.M.; Seddon, K.R.; Welton, T. *Org. Mass Spectrom.* **1993**, *28*, 759.
(b) Abdul-Sada, A.K.; Elawi, A.; Seddon K.R.; Welton, T. unpublished results.