N'-Activation of N-Arylimidazoles: Facile Syntheses of N-Alkyl-N'-arylimidazolium Iodides from Less Expensive Chloro Substrates

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Abstract: A series of N,N'-asymmetrically substituted imidazolium iodide salts have been synthesized, starting from N-arylimidazoles and the less expensive, but less reactive, 1-chlorobutane or (3-chloropropyl)trimethoxysilane. The addition of potassium iodide to the reaction medium is also presented herein.

Key words: arylimidazoles, imidazolium salts, trimethoxysilyl, chloroalkyls, N-heterocyclic carbenes

N,N'-Disubstituted imidazolium salts are important intermediates in the synthesis of transition metal complexes that contain N-heterocyclic carbene (NHC) ligands. Complexes with NHC ligands have become increasingly important in homogeneous and, more recently, in heterogeneous catalysis. N,N'-Disubstituted imidazolium salts have also found applications in their own right as ionic liquids and ‘green’ solvents.

We have developed an interest in the synthesis and catalytic properties of the nickel NHC complexes [Ni(η^2-C_2R_2)(NHC)X] [R = H (Cp) or Me (Cp^*); X = Cl, I]. These complexes may be prepared in a straightforward manner by reaction of NiCp or Cp^* species with imidazolium salts. We are investigating the homogeneous catalytic properties of such species and are also looking into grafting them with trimethoxysilyl-substituted NHC ligands onto solid supports for heterogeneous catalytic applications.

The repertoire of commercially available imidazolium salts is limited. In the present method, we describe the easy syntheses of N,N'-asymmetrically substituted imidazolium salts, which are either new (1b, 2a, 3a, 3b, 4b) or for which no convenient route has been described (1a, 2b, 3a, 4a^-[2]). All the prepared imidazolium salts contain either an N-bound butyl group or else, an N-bound 3-(trimethoxysilyl)propyl [CH_3CH_2CH_2Si(OCH_3)_3] group (Equation 1, Table 1). Most contain N-arylimidazolium moieties and have iodide as the anion.

Known synthetic procedures for N-alkyl-N'-arylimidazolium salts often require the use of alkyl iodides or bromides when starting from the less reactive arylimidazoles. The chlorides are often inert or require forcing conditions. We present here a simple new synthetic method to prepare not easily accessible N-alkyl-N'-arylimidazolium cations from the less reactive alkyl chlorides, under moderate conditions.

All the N-alkyl-N'-arylimidazolium salts were synthesized by direct reaction of 1-chlorobutane or (3-chloropropyl)trimethoxysilane with the readily available corresponding N-arylimidazoles using (i) 1,2-dimethoxyethane as a solvent, and simultaneously (ii) an equimolar (or larger) quantity of potassium iodide (Equation 1).

The addition of potassium iodide leads to the formation by precipitation of the sparingly soluble potassium chloride from the reaction medium. The large N,N'-disubstituted imidazolium cations are presumably better stabilized in the solid state with a big (I^-) counteranion.

Preparations of the N-alkyl-N'-isopropylimidazolium derivatives (4a, 4b) from the more reactive 1-isopropyl-1H-imidazole do not require the addition of potassium iodide. Moreover, 4a does not even require any solvent addition, as simply refluxing neat 1-isopropyl-1H-imidazole with an equimolar quantity of 1-chlorobutane affords 4a in good yield. The synthesis of 4b is similar, but 1,2-dimethoxyethane was added to slightly raise the reflux temperature.

The chloride salt of 2b could be synthesized by heating 1,2-dimethoxyethane and (3-chloropropyl)trimethoxysilane in a microwave oven; the addition of potassium iodide was not needed to form the cation, and the chloride salt of 2b was obtained this way in 82% yield, after 20 minutes of reaction time at 180 °C. Higher temperatures led to decomposition, while addition of potassium iodide or shorter reaction times produced less of the desired cation.

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Table 1 Preparation of N,N'-Imidazolium Salts 1-4

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>R1</th>
<th>X</th>
<th>Yield (%)</th>
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<td>1</td>
<td>1a</td>
<td>Ph</td>
<td>I</td>
<td>50</td>
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<tr>
<td>2</td>
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<tr>
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<tr>
<td>5</td>
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<td>82b</td>
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<tr>
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<td>8</td>
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<tr>
<td>9</td>
<td>4b</td>
<td>i-Pr</td>
<td>Cl</td>
<td>35d</td>
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a Conditions: R1Cl, KI, DME, heat; unless otherwise stated.
b Microwave irradiation.
c R1Cl, heat.
d R1Cl, DME, heat.

All the butylimidazolium iodides described here are hydroscopic solids that can liberate traces of free iodine, in the presence of light, which makes the salts appear cream colored, or even pale yellow unless very pure and/ or freshly prepared. The [3-(trimethoxysilyl)propyl]imidazolium iodide salts are nonvolatile oils that also often appear as white or colorless, or even pale yellow unless very pure and/ or freshly prepared. The [3-(trimethoxysilyl)propyl]imidazolium iodide salts are nonvolatile oils that also often appear as white or colorless solids that appear to liberate traces of free iodine.

All reactions were carried out using standard Schlenk techniques under an atmosphere of dry argon. Solvents were distilled from appropriate drying agents under argon prior to use. Solution NMR spectra were recorded on a FT-Bruker Ultra Shield 300 spectrometer operating at 300.13 MHz for 1H NMR, and at 75.47 MHz for 13C NMR. HRMS and HRMS spectra were recorded on a MALDI-TOF Biflex Bruker mass spectrometer. Coupling constants (Hz) are given in parentheses. Spectra were recorded on appropriate drying agents under argon prior to use. Solution NMR and HRMS) were obtained for all the described salts.

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a Conditions: R1Cl, KI, DME, heat; unless otherwise stated.
b Microwave irradiation.
c R1Cl, heat.
d R1Cl, DME, heat.

1-Phenyl-3-[3-(trimethoxysilyl)propyl]imidazolium Iodide (1b)
A suspension of 1-phenyl-1H-imidazole (1.58 g, 11.00 mmol), 3-chloropropyltrimethoxysilane (2.18 g, 2.00 mL, 10.97 mmol), and KI (3.10 g, 18.67 mmol) in DME (40 mL) was vigorously stirred at 85 °C for 63 h. The mixture was cooled to r.t. and the solvent was removed under vacuum. The residue was extracted with MeCN (20 mL), filtered over Celite, and rinsed with MeCN (2 × 10 mL). The MeCN was evaporated and the residue was washed with toluene (4 × 5 mL) and dried in vacuo. The product was obtained as a brown oil (3.63 g, 76%), that was contaminated with small quantities of [3-(chloropropyl)trimethoxysilane].

1H NMR: δ = 10.57 (1 H, NCHN), 7.80–7.54 (m, 7 H, Ph, 2 NCH), 4.60 (t, J = 7.3 Hz, 2 H), 3.57 (9 H, Me), 2.10 (m, J = 8.1, 7.3 Hz, 2 H, NCH2CH3), 0.74–0.69 (m, 2 H, SiCH2).

1C NMR: δ = 135.3 (NCN), 134.5 (ipso-C), Ph), 130.8 and 122.2 (o-C, m-C, Ph), 130.6 (p-C, Ph), 123.5 and 121.0 (NCH), 52.4 (NCH2), 51.0 (Me), 24.3 (NCH2CH3), 6.1 (SiCH2).


1-Butyl-3-[2,4,6-trimethylphenylimidazolium Iodide (2a)
A suspension of 1-mesityl-1H-imidazole (1.856 g, 9.97 mmol), 1-chlorobutane (0.470 g, 0.530 mL, 5.07 mmol), and KI (0.830 g, 5.00 mmol) in DME (10 mL) was vigorously stirred at 75 °C for 18 h. The mixture was cooled to r.t. and the solvent was removed under vacuum. The residue was extracted with MeCN (10 mL), filtered over a Celite pad, and rinsed with MeCN (2 × 10 mL). The MeCN was evaporated, the residue was washed with toluene (3 × 2 mL) and Et2O (3 × 2 mL) and dried in vacuo. The product was obtained as a light brown solid (0.825 g, 50%).

1H NMR: δ = 7.3 (1 H, NCHN), 7.82 (dd, J = 1.7 Hz, 1 H, NCH), 7.21 (dd, J = 1.7 Hz, 1 H, NCH), 6.99 (s, 2 H, m-H2), 4.71 (t, J = 7.3 Hz, 2 H, NCH2), 2.33 (s, 3 H, Me), 2.07 (s, 6 H, o-Me), 1.97 (tt, J = 7.3, 7.8 Hz, 2 H, NCH2CH3), 1.42 (qt, J = 7.8, 7.3 Hz, 2 H, CH2CH3), 0.97 (t, J = 7.3 Hz, 3 H, CH3).

1C NMR: δ = 141.6 (p-C), 137.5 (NCHN), 134.4 (o-C), 130.7 (ipso-C), 130.9 (m-C), 123.4 and 123.3 (NCH), 50.6 (NCH2), 32.7 (NCH2CH3), 21.3 (p-Me), 19.5 (CH2CH3), 18.0 (o-Me), 13.8 (CH3).


1-[3-(Trimethoxysilyl)propyl]-3-[2,4,6-trimethylphenylimidazolium Iodide (2b) by Thermal Synthesis
A suspension of 1-mesityl-1H-imidazole (0.923 g, 4.96 mmol), 3-chloropropyltrimethoxysilane (1.003 g, 0.92 mL, 5.05 mmol), and KI (0.996 g, 6.00 mmol) in DME (20 mL) was vigorously stirred at 85 °C for 60 h. The mixture was cooled to r.t. and the solvent was removed under vacuum. The residue was extracted with MeCN (12 mL), filtered over Celite, and rinsed with MeCN (3 × 4 mL). MeCN

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was evaporated and the residue was washed with hot toluene (3 x 5 mL) and dried in vacuo. The product was obtained as a pale yellow solid (2.212 g, 94%).

1H NMR: δ = 9.99 (br s, 1 H, NCHN), 7.76 (dd, J = 1.7 Hz, 1 H, NCH), 7.21 (dd, J = 1.7 Hz, 1 H, NCH), 6.99 (s, 2 H, m-H), 4.70 (t, J = 7.2 Hz, 2 H, NCH), 3.56 (s, 9 H, OMe), 2.33 (s, 3 H, p-Me), 2.10 (tt, J = 7.2, 7.9 Hz, 2 H, NCH₂CH₃), 2.08 (s, 6 H, o-Me), 0.68 (m, J = 7.9 Hz, 2 H, CH₃).

13C NMR: δ = 141.6 (p-C₆), 137.5 (NCHN), 134.4 (o-C₆), 130.7 (ipso-C₆), 130.1 (m-C₆), 123.4 (2 NCH), 52.4 (NCH₂), 51.0 (OMe), 24.6 (NCH₂CH₃), 21.3 (p-Me), 18.0 (o-Me), 5.8 (CH₃).

HRMS (MALDI TOF): m/z [M]+ calcd for C₁₉H₂₉N₂O₃Si: 391.2423; found: 391.2411.

1-[(Trimethoxysilyl)propyl]-2-(4,6-trimethylphenyl)imidazolium Chloride (2b) by Microwave Synthesis

1-Mesityl-1H-imidazole (186 mg, 1.00 mmol) and (3-chloropropyl)trimethoxysilane (204 mg, 0.19 mL, 1.03 mmol) were mixed in a 10-mL sealed vessel and placed in a Discover CEM S-class microwave oven at 2450 MHz. The mixture was heated rapidly and kept at 180 °C for 20 min while stirred magnetically. The resinous product was purified following procedures described in the thermal synthesis for 2b and was formed in 82% yield (by NMR).

1-Butyl-3-(2,6-diisopropylphenyl)imidazolium Iodide (3a)

A suspension of 1-(2,6-diisopropylphenyl)-1H-imidazole (2.288 g, 10.02 mmol), (3-chloropropyl)trimethoxysilane (1.962 g, 1.80 mL, 10.15 mmol), and KI (1.999 g, 12.04 mmol) in DME (40 mL) was vigorously stirred at 75 °C for 47 h. The mixture was cooled to r.t. and the solvent removed under vacuum. The resultant oil was further dried in vacuo (30 °C, 2 h). The product was obtained as a colorless oil (1.071 g, 35%).

1H NMR: δ = 10.80 (br s, 1 H, NCHN), 7.58 (dd, J = 1.8 Hz, 1 H, NCH), 7.48 (dd, J = 1.8 Hz, 1 H, NCH), 4.85 (hept, J = 6.7 Hz, 1 H, CHMe₂), 4.30 (t, J = 7.5 Hz, 2 H, NCH₂), 1.83 (t, J = 7.5, 7.6 Hz, 2 H, NCH₂CH₃), 1.54 (d, J = 6.7 Hz, 6 H, CH₃), 1.30 (qt, J = 7.6, 7.4 Hz, 2 H, CH₂CH₂), 0.87 (t, J = 7.4 Hz, 3 H, CH₃).

13C NMR: δ = 136.7 (NCHN), 122.2 and 120.1 (NCH), 53.2 (CHMe₂), 49.7 (NCH₂), 32.3 (NCH₂CH₃), 23.3 (CHMe), 19.6 (CH₂CH₃), 13.5 (CH₃).


1-Isopropyl-3-[3-(trimethoxysilyl)propyl]imidazolium Chloride (4b)

A solution of 1-isopropyl-1H-imidazole (1.093 g, 9.92 mmol) and (3-chloropropyl)trimethoxysilane (2.017 g, 1.85 mL, 10.15 mmol) in DME (10 mL) was stirred at 85 °C for 96 h. The mixture was cooled to r.t. and the solvent removed under vacuum. The resulting oil was washed with toluene (5 x 3 mL) and dried in vacuo. The product was obtained as a colorless oil (1.071 g, 35%).

1H NMR: δ = 10.96 (br s, 1 H, NCHN), 7.49 (dd, J = 1.7 Hz, 1 H, NCH), 7.33 (dd, J = 1.7 Hz, 1 H, NCH), 4.90 (hept, J = 6.7 Hz, 1 H, CHMe₂), 4.34 (t, J = 7.4 Hz, 2 H, NCH₂), 3.52 (s, 9 H, OMe), 1.98 (tt, J = 7.4, 8.1 Hz, 2 H, NCH₂CH₃), 1.58 (d, J = 6.7 Hz, 6 H, CH₃), 0.61 (m, J = 8.1 Hz, 2 H, CH₂Si).

13C NMR: δ = 136.6 (NCHN), 122.1 and 120.4 (NCH), 53.2 (CHMe₂), 51.7 (NCH₂), 50.7 (OMe), 24.2 (NCH₂CH₃), 23.2 (CHMe), 6.1 (CH₃).


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References


(9) The triethoxysilyl derivative of 2b was prepared by refluxing of a mixture of 1-mesityl-1H-imidazole and (3-chloropropyl)triethoxysilane for five days: Koehler, K.; Weigl, K. WO 2005016940, 2005.


(14) Another example where I– (in this case as NaI) was used in imidazolium salt synthesis: Wang, X.; Liu, S.; Jin, G.-X. Organometallics 2004, 23, 6002.

(15) Stanikova, O. V.; Dolgushin, G. V.; Larina, L. I.; Komarova, T. N.; Lopyrev, V. A. ARKIVOC 2003, (xii), 119.
