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Facile and scalable synthesis of imidazolium halides using dimethylmethyleneammonium salts as ring closing reagents

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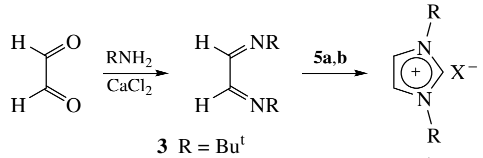
An efficient procedure is proposed for the synthesis of 1,3-dialkylimidazolium salts starting from 1,4-diaza-1,3-dienes and methyleneammonium salts.

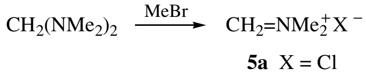
1,3-Dialkylimidazolium salts (DAISs) are of great interest as intermediates and reagents due to their unique properties. Deprotonation of DAIS produces stable N-heterocyclic carbenes used for the preparation of transition metal complexes, which are very good catalysts for important reactions.[1] DAISs possess a remarkable ability to solubilise Cu, Ni, Co and Pd chlorides in methylene chloride due to powerfull solvatation of these inorganic salts.

In the course of our investigations with sterically hindered DAISs **1** and **2**, we encountered the problem of improving and scaling-up the existing synthetic procedures. The published one-pot procedures for **1** and **2** need long reaction times (15 h stirring) and, sometimes, a tedious isolation.[2,3] The other general method of DAIS synthesis makes the use of N,N′-disubstituted



3 R = Bu^t
4 R = cyclohexyl

1a R = Bu^t, X = Cl
1b R = Bu^t, X = Br
2a R = cyclohexyl, X = Cl



5a X = Cl
5b X = Br

1,4-diazadiene condensation with chloromethyl ether or ester.[4,5] However, we found the condensation of diazadienes **3** and **4** with $ClCH_2OEt$ or $BrCH_2OMe$ to produce the corresponding DAIS in unsatisfactory yields of 20–25% at best.

Therefore, we turned our attention to electrophilic dimethylmethyleneammonium salts **5a**,**b**. To our satisfaction, these salts proved to be the reagents of choice for imidazolium ring formation starting with diazadienes **3** and **4**. The reaction is fast (10–15 min), mildly exothermic and easily controllable thus lending itself for scaling up. The isolation of formed products **1a**,**b**, **2a** consists in the evaporation of the reaction mixture and crystallization of the product.[†]

Although the proposed method consists of two steps (iminium salts are generated *in situ*), both of these steps are experimentally simple and short-timed and could be easily performed during a working day on a several-gram level. Therefore, the method is deemed to be a viable alternative to the existing one-pot method for the preparative synthesis of DAISs.

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[†] *1,4-Diazadienes* **3** *and* **4**. Glyoxal (25 ml of 40% aqueous solution, 0.22 mol) was gradually mixed (5 min) with a solution of Bu^tNH_2 (46 ml, 0.44 mol) in CH_2Cl_2 (60 ml). Anhydrous $CaCl_2$ (20 g, 0.18 mol) was added to this solution with stirring and cooling (ice bath). After 30 min, the mixture was warmed close to boiling and an organic layer was separated by decantation. The layer was rotary evaporated in a vacuum and the crystallization of an oily residue was induced by moistening with diethyl ether with the subsequent vacuum drying. The yield of crystalline diazadiene **3** was 34.1 g (92%), mp 55 °C.[6] The same procedure in $(CH_2Cl)_2$ was applied to synthesise diazadiene **4**, yield 80%, mp 146–147 °C.[6] Both diazadienes are used in the next step without additional purification.

*1,3-Di-*tert*-butylimidazolium chloride* **1a**. Acetyl chloride (3.14 ml, 44 mmol) was added with stirring and cooling below 15 °C to a solution of $CH_2(NMe)_2$ (6 ml, 44 mmol) in $(CH_2Cl)_2$ (20 ml). A white suspension of salt **5a** was formed. The solution of diazadiene **3** (6.7 g, 40 mmol) in $(CH_2Cl)_2$ (10 ml) was added in one portion to this suspension. Cooling was removed and after a spontaneous exothermal stage (*ca.* 15 min) the solution was rotary evaporated at 75 °C in a vacuum leaving the oily mixture of the product with $AcNMe_2$ (formed during salt **5a** generation). This mixture after dilution with $(CH_2Cl)_2$ (5 ml) and EtOAc (10 ml) and cooling separated the crystals of DAIS **1a**. Filtration, washing with EtOAc and drying afforded 6.7 g (79%) of **1a**. ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 1.62 (s, 18H, 2Bu^t), 8.17 (s, 2H, NCHCHN), 9.42 (s, 1H, NCHN).[2] When crystallization is performed from CH_2Cl_2–EtOAc, **1a** forms a solvate with one molecule of CH_2Cl_2.

*1,3-Di-*tert*-butylimidazolium bromide* **1b**. Mixed salt **5b** and NMe_4Br was prepared by a reaction of $CH_2(NMe_2)_2$ with MeBr in MeCN. Diazadiene **3** (7.8 g, 0.046 mol) in CH_2Cl_2 (30 ml) was added to this salt mixture (14.6 g, 0.05 mol of **5b**) producing almost immediate exothermal reaction. After 30 min, the reaction mixture was filtered, the filtrate was concentrated in a vacuum, and the residue was crystallised from MeCN–$(CH_2Cl)_2$, giving 4.23 g (49%) of DAIS **1b**. ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 1.62 (s, 18H, 2Bu^t), 8.10 (s, 2H, NCHCHN), 9.10 (s, 1H, NCHN).

1,3-Dicyclohexylimidazolium chloride **2a** was prepared analogously to **1a** starting from diazadiene **4** (13.4 g), yield 16.2 g (81.5%). ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 1.2–2.2 (m, 20H, 10CH_2), 4.40 (t, 2H, 2CH), 8.00 (s, 2H, NCHCHN), 9.80 (s, 1H, NCHN).