Synthesis of anovel sterically hindered imidazolinium chloride: an N-heterocyclic carbene precursor

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A hindered imidazolinium chloride which is a bulky, strongly donating N-heterocyclic carbene precursor has been synthesised from pinacolone in six steps. The chlorides can be easily converted to its corresponding hexafluorophosphate salt in near quantitative yield. The two new compounds were characterised by ^{1}H and ^{13}C NMR, IR, and elemental analyses.

Keywords: N-heterocyclic carbine, steric hindrance, imidazolinium chloride, imidazolinium hexafluorophosphate

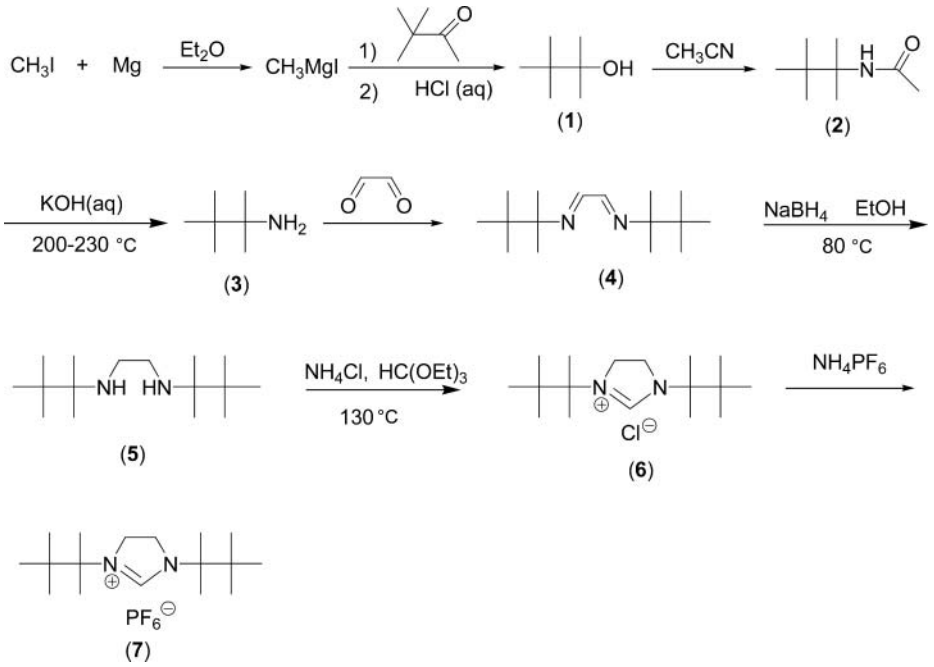
The chemistry of N-heterocyclic carbenes (NHCs) and their complexes has been thoroughly investigated in recent years and a large number of publications relating to NHC complexes have been published.[1–5] Palladium complexes with NHC ligands have become important in Pd-catalysed cross-coupling reactions,[6,7] which are extremely useful tools in several areas of chemistry. It is known that sterically hindered and strongly electron-donating ligands can form more active catalysts.[8] Hence there is a need to develop bulky, strongly donating ligands.[9–10] In order to explore new efficient NHC ligands for Pd catalysis, we have prepared two sterically hindered, strongly donating N-heterocyclic carbene precursors (imidazolinium salts **6** and **7**).

The imidazolinium chloride (**6**) was prepared from pinacolone in an overall 30% yield by six steps (Scheme 1). Firstly, 2,3,3-trimethylbutan-2-ol (**1**) was prepared by Grignard reaction of pinacolone with methylmagnesium iodide which was generated *in situ* from methyl iodide with magnesium in anhydrous diethyl ether. The alcohol was colourless liquid; however, when heated in presence of water it was converted to a white solid hydrate ($\mathbf{1}\cdot 0.5H_2O$). The Ritter reaction of **1** with acetonitrile in a strongly acidic medium gave the acetamide **2**. The total yield for these two steps was 72%. The hydrolysis of amide **2** in aqueous KOH solution gave amine **3** in 69% yield. The Schiff reaction of amine **3** with a 30% glyoxal aqueous solution generated diimine **4** in high yield. The reduction of **4** with $NaBH_4$ gave diamine **5** in 82% yield. The cycloadditon reaction of **5** with NH_4Cl in triethyl orthoformate gave the imidazolinium chloride **6.** The imidazolinium chloride **6** was converted quantitatively to imidazolinium hexafluorophosphate **7** with NH_4PF_6 in water. Compounds **1**-**3** are known compounds. However, they are not fully characterised in the literature[11]. Therefore, their data along with that for compounds **4**–**7** which are new compounds is given in the experimental.

In conclusion, we have demonstrated a method for preparing two sterically hindered, strongly donating N-heterocyclic carbene precursors (**6** and **7**) starting from pinacoline in several steps in a total 30% yield. Compounds **6** and **7** are new and are fully characterised by NMR spectroscopy, IR and elemental analyses.

Experimental

All reagents were commercially available and were used without further purification. ^{1}H NMR spectra were recorded on a Bruker DPX



Scheme 1

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400 MHz spectrometer at room temperature and referenced to the residual ^{1}H signals of the solvent. IR spectra were recorded on KBr pellets on a FTIR-Tensor 27 spectrometer. Melting points were detected by microscope melting point apparatus. Elemental analyses were performed on a EuroVektor Euro EA-300 elemental analyser.

2,3,3-Trimethylbutan-2-ol (**1**): Mg (41.1 mmol, 1.0 g) and anhydrous diethyl ether (20 mL) were added to a three-necked flash equipped with a condenser and dropping funnel under argon. Methyl iodide (2.6 mL, 41.1 mmol) was added dropwise to the reaction mixture. The reaction was stirred at room temperature for 1 h, after which time, pinacolone (34.3 mmol, 4.3 mL) was added dropwise. The reaction was stirred at room temperature for another 5 h and quenched with 1 N HCl. The organic phase was separated and the water phase was extracted with ether three times (3 × 15 mL). The combined organic phase was dried over $MgSO_4$. The volatile solvent was removed with a rotatory evaporator to give the product. The product was used in the next step directly without further purification. Its hydrate compound $\mathbf{1}\cdot 0.5H_2O$ could be sublimed to give the pure compound as a white solid (3.73 g, 87%). Data for $\mathbf{1}\cdot 0.5H_2O$: m.p. 53–54 °C. IR (KBr): 3444, 2982, 1637, 1558, 1474, 1367, 1131, 1022, 947, 885 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 1.82 (s, 1H), 1.30 (s, 1H), 1.18 (s, 6H), 0.94 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 75.0, 37.4, 25.3, 25.2. Anal. Calcd for $C_7H_{17}O_{1.5}$ (125.21 g mol^{-1}): C, 67.15; H, 13.69; N, 19.17. Found: C, 66.86; H, 13.45; N, 19.42%.

N-(2,3,3-Trimethylbutan-2-yl)acetamide (**2**): Acetic acid (3 mL) and concentrated sulfuric acid (1 mL) were added to an acetonitrile (25 mL) solution of **1** (3.48 g , 30 mmol) in a 50 mL round bottom flask. The reaction was stirred at room temperature for 12 h, after which time, 10% aqueous KOH was added to the reaction mixture until the pH reached 7–8. The organic phase was separated and the water layer was extracted with ether (3 × 15 mL). The combined organic phase was dried over $MgSO_4$ and the volatile solvent was removed. The crude white solid which was obtained, was washed with petroleum ether to give the product in 83% yield (3.92 g). m.p. 115–116 °C [lit.[11] 115–116 °C]. IR (KBr): 3446, 2201, 3106, 3017, 2976, 1655, 1572, 1474, 1400, 1371, 1305, 1238, 1180, 1158, 1032, 998, 968, 758, 607 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 5.31 (s, 1H), 1.90 (s, 3H), 1.34 (s, 6H), 0.92 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 59.1, 37.5, 25.3, 25.1, 21.9. Anal. Calcd for $C_9H_{19}NO$ (157.25 g mol^{-1}): C, 68.74; H, 12.18; N, 8.91. Found: C, 67.47; H, 11.97; N, 9.20%.

2,3,3-Trimethylbutan-2-amine (**3**): Compound **2** (1.0 g, 6.4 mmol) in a 23% aqueous KOH solution (20 mL) was heated in an autoclave at 200 ºC for 24 h. After the reaction the mixture was cooled to room temperature and extracted with ether (3 × 15 mL). The product was obtained as a light yellow oil by evaporation of the solvent in 67% yield (0.49 g). IR (KBr): 3799, 3742, 3732, 3686, 3668, 3646, 3626, 3363, 2972, 1645, 1602, 1557, 1471, 1372, 1232, 1158, 1093, 1051, 982, 876, 828, 792, 651 cm $^{-1}$. ^{1}H NMR (400 MHz, $CDCl_3$): 1.56 (s, 2H), 1.03 (s, 6H), 0.89 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.8, 36.7, 26.2, 25.4. Anal. Calcd for $C_7H_{17}N$ (115.22 g mol^{-1}): C, 72.97; H, 14.87; N, 12.16. Found: C, 73.31; H, 14.63; N, 12.28%.

N,N'-(Ethane-1,2-diylidene)bis(2,3,3-trimethylbutan-2-amine) (**4**): Compound **3** (1.0 g, 8.7 mmol) was added to a 30% of aqueous solution (0.84 g, 4.35 mmol) in anhydrous ethanol (20 mL) in a 50 mL beaker. The reaction mixture was stirred at room temperature for 10 min, when a copious white solid appeared. Filtration gave the product as a white solid in 90% yield (0.98 g). m.p. 112–113ºC. IR (KBr): 3449, 2972, 1636, 1559, 1258, 1418, 1362, 1154 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.89 (s, 2H), 1.17 (s, 12H), 0.93 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): 158.0, 65.1, 36.9, 25.7, 22.6. Anal. Calcd for $C_{16}H_{32}N_2$ (252.44 g mol^{-1}): C, 76.13; H, 12.78; N, 11.10. Found: C, 75.86; H, 12.55; N, 11.29%.

Bis(2,3,3-trimethylbutan-2-yl)ethane-1,2-diamine (**5**): Sodium barahydride (3.0 g, 79 mmol) was added to a solution of compound **4** (2.0 g, 7.9 mmol) in anhydrous ethanol (25 mL) in a 50 mL round bottom flask. The reaction mixture was heated at 80 °C for 2–3 h, after which time, water (100 mL) was added to quench the reaction. The organic layer was separated and the water layer was extracted with DCM (3×15 mL). The combined organic phase was dried over $MgSO_4$, and the solvent was removed to give the product as a white solid in 82% yield (1.65 g). m.p. 68–69 ºC. IR (KBr): 3763, 3447, 2973, 1637, 1559, 1485, 1394, 1362, 1176, 738, 672 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.62 (s, 4H), 0.98 (s, 12H), 0.91 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.4, 43.0, 37.4, 25.5, 21.2. Anal. Calcd for $C_{16}H_{36}N_2$ (256.47 g mol^{-1}): C, 74.93; H, 14.15; N, 10.92. Found: C, 75.25; H, 14.02; N, 10.79%.

1,3-Bis(2,3,3-trimethylbutan-2-yl)-4,5-dihydro-1H-imidazol-3-ium chloride (**6**): Compound **5** (2.0 g, 7.8 mmol) and ammonium chloride (0.42 g, 7.8 mmol) were added to a 50 mL round-bottomed flask with triethyl orthoformate (25 mL). The reaction mixture was heated at 130ºC for 12 h, whilst a large amount of white solid appeared. The solid was filtered and washed with ether to give the of product (2.0 g) 85% yield. IR (KBr): 3736, 3677, 3630, 2970, 1635, 1457, 1385, 1365, 1304, 1232, 1163, 1023, 670 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) 8.31 (s, 1H), 4.16 (s, 4H), 1.51 (s, 12H), 0.97 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) 156.7, 65.2, 49.2, 38.6, 26.2, 23.6. Anal. Calcd for $C_{17}H_{35}ClN_2$ (302.93 g mol^{-1}): C, 67.40; H, 11.65; N, 9.25. Found: C, 67.03; H, 11.46; N, 9.51%.

1,3-Bis(2,3,3-trimethylbutan-2-yl)-4,5-dihydro-1H-imidazol-3-ium hexafluorophosphate (**7**): Compound **6** (1.03 g, 2.0 mmol) dissolved into water (6 mL) was added drop-wise into a saturated NH_4PF_6 (30 mL) aqueous solution in a 50 mL beaker. A large amount of a white solid appeared. The solid was filtered and washed with water to give the product as a white solid in 99% yield (1.46 g). IR (KBr): 3763, 3691, 3677, 3650, 3630, 3112, 2975, 1619, 1542, 1508, 1475, 1390, 1284, 1205, 1154, 859, 833, 670 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) 7.49 (s, 1H), 3.94 (s, 4H), 1.16 (s, 12H), 1.01 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 65.0, 48.9, 38.7, 26.1, 22.5; Anal. Calcd for $C_{17}H_{35}F_6N_2P$ (412.44 g mol^{-1}): C, 49.51; H, 8.55; N, 6.79. Found: C, 49.21; H, 8.38; N, 6.90%.

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