A New Reagent for Nucleophilic Aminomethylation: Doubly Lithiated Bis(dimethylamino)methane and Its Use for the Synthesis of Si,N-Heterocycles

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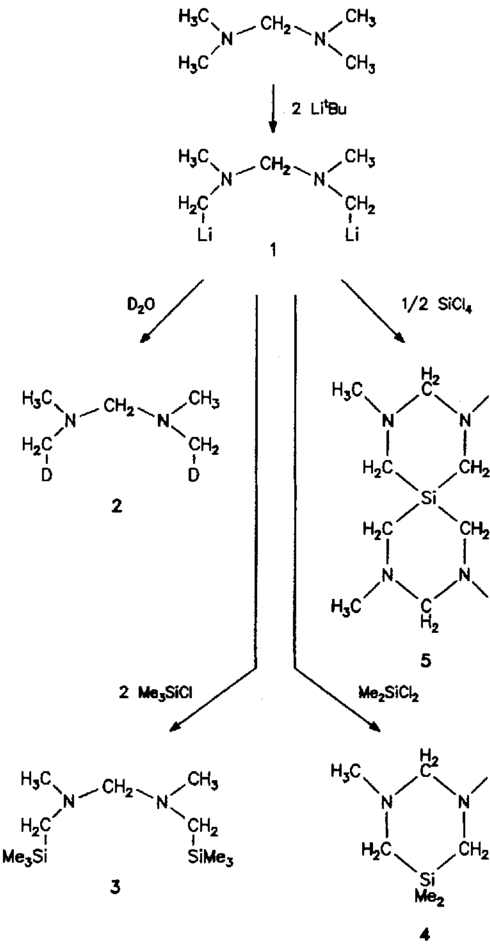
The aminal $Me_2NCH_2NMe_2$ is doubly metalated by Li*t*Bu to give $LiCH_2N(Me)CH_2N(Me)CH_2Li$, which reacts with chlorosilanes to afford the respective silylated species, including the six-membered heterocycle $Me_2\overline{SiCH_2N(Me)CH_2N(Me)\text{-}CH_2}$ and the spiroheterocycle $\overline{Si[CH_2N(Me)CH_2N(Me)CH_2}]_2$.

Aminomethylation reactions rank among organic synthetic procedures as one of the most useful methods for the synthesis of nitrogen containing compounds. Normally these reactions are restricted to electrophilic aminomethylations, however. Metalation of tertiary amines needs activated species in most cases[1]. Only a few examples for the direct metalation of tertiary methyl amines are known, the yields being satisfactory only in a few special cases and the metalated products were characterized only by "in situ" aminomethylation reactions[2]. Therefore, lithiation was often successfully performed via the stannyl intermediate[3], but the overall yield was modest, the prodcedure time-consuming and the separation from the by-products LiCl and $SnBu_4$, which were wasted, sometimes was difficult. Two attempts at the direct metalation of bis-tertiary amines were reported: $Me_2NCH_2CH_2NMe_2$ (TMEDA) was monometalated by organolithium reagents in low to medium yields, and methyl and methylene lithiation with subsequent N−C cleavage were observed to proceed unselectively[4]; $Me_2NCH_2NMe_2$ (TMMDA) was reported to react with organolithium compounds to give an insoluble precipitate, which was not investigated further[5].

The treatment of TMMDA with Li*t*Bu in hexane yielded a white, highly pyrophoric precipitate, which was identified as the doubly lithiated species **1** (Scheme 1) by elemental analysis and by further reactions. Compound **1**, which is only slightly soluble in toluene or THF was formed also as the only product, if less than the necessary two equivalents of Li*t*Bu were used: a monolithiated species was not found. The overall yield of **1** amounts to 90% and even increased after prolonged reaction times (10 d), but some impurities probably due to N−C cleavage were also formed in this case. In order to obtain pure products in subsequent reactions and thus to avoid tedious and yield-reducing purification steps in certain cases, it is advisable to stop the reaction after 3 d (ca. 60% yield).

As a first test for the synthetic utility of **1**, deuteration and the nucleophilic aminomethylation of chlorosilanes were performed. Compounds **2**−**5** were obtained as colorless, distillable liquids and identified by spectroscopic methods. These reactions demonstrate, that nucleophilic aminomethylation with the doubly lithiated aminal TMMDA is feasible at heteroatomic centers and that novel heterocycles can thus be obtained. An extension to the synthesis of germanium, tin, and phosphorus heterocycles is also possible[6], but side reactions and/or lower yields were often obtained. Nevertheless, the facile doubly metalation of TMMDA is a unique case for tertiary amines (note that the phosphorus homologue $Me_2PCH_2PMe_2$ is only metalated at the methylene carbon atom[7]). Its synthetic utility for olefin polymerizations and for organic as well as for organoelement synthesis is currently under investigation.

Scheme 1



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Experimental

All operations were performed under a dry nitrogen atmosphere and with thoroughly dried solvents and glassware. Standard high-vacuum-line techniques were used. – $Me_2NCH_2NMe_2$ and chlorosilanes were purchased by Merck, Li*t*Bu by Chemetal. $Me_2NCH_2NMe_2$ was distilled and stored over molecular sieve, chlorosilanes were dried over K_2CO_3 and distilled immediately prior to use. Yields of the liquid products are not rigorously optimized and relate to the purified products (by distillation).

Synthesis of **1**: 79.25 ml (146.6 mmol) of an 1.85 M solution of Li*t*Bu in hexane is added to a solution of 7.49 g (73.3 mmol) of $Me_2NCH_2NMe_2$ in 40 ml of pentane at −78 °C. The mixture is allowed to warm up to room temp. The white precipitate formed during 3 d is isolated by decanting the mother liquor and washing the solid three times with 40 ml of pentane, drying in vacuo gives 5.60 g (67%). The solid is highly pyrophoric. Due to its low solubility, it is characterized by elemental analysis and the derivatizations described below. Addition of TMEDA, DME, or THF do not decisively improve the solubility nor are crystals obtained. From the mother liquor, on storage at room temp. for 14 d, an additional amount [2.34 g (28%)] of a slightly yellowish precipitate is obtained, which likewise can be used for derivatization reactions, but more unidentified impurities are observed in the reactions. – $C_5H_{12}Li_2N_2$ (114.0): calcd. C 52.65, H 10.61, Li 12.17, N 24.56; found C 51.95, H 10.54, Li 13.01, N 23.17.

Synthesis of **2**: Two drops of D_2O are added to a sample of **1** (approximately 100 mg), suspended in C_6D_6 in an NMR tube (10 mm). After 2 d, the ^1H-NMR spectrum is recorded; it exhibits three product signals: δ = 2.55 (2H, s, NCH_2N), 2.17 (6H, s, NCH_3), 2.14 (4H, 1:1:1 triplet, $^2J_{HD}$ = 1.7 Hz, NCH_2D).

Synthesis of **3**: 2 ml of Me_3SiCl (15.76 mmol) are added to a suspension of 0.9 g of **1** (7.89 mmol) in 40 ml of Et_2O at −78 °C with stirring. The solution is slowly warmed to room temp. (3 h) and stirred for another 10 h. Subsequently, the solvent is replaced by 40 ml of pentane and the resulting suspension filtered through a sinter disk. The solvent is removed from the pentane solution and an oily residue is obtained, which is subjected to fractional distillation: colorless liquid, b.p. 54–56 °C/1.33 · 10^{-2} mbar, yield 0.8 g (43%). – ^1H NMR (C_6D_6, 25 °C): δ = 2.64 (2H, s, NCH_2N), 2.24 (6H, s, NCH_3), 1.95 (4H, s, NCH_2Si), 0.09 (18H, s, $SiCH_3$). – $^{13}C\{^1H\}$ NMR (C_6D_6, 25 °C): δ = 88.11 (s, NCH_2N), 46.93 (s, NCH_2Si), 43.97 (s, NCH_3), −1.10 (s, $SiCH_3$); the assignment of signals is confirmed by ^{13}C NMR. – EI MS (70 eV); *m/z* (%): 247 (4) [M^+ + H], 232 (10) [M^+ − CH_3], 146 (100) [M^+ − $(CH_2)_2SiMe_3$]. – $C_{11}H_{30}N_2Si_2$ (246.5): calcd. C 53.59, H 12.26, N 11.36; found C 52.87, H 12.10, N 10.58.

Synthesis of **4**: 0.70 ml (5.8 mmol) of Me_2SiCl_2 is added to a suspension of 0.66 g of **1** (5.8 mmol) in 30 ml of THF at −78 °C with stirring. After warming up to room temp. and continued stirring for 3 h, the solvent is removed in vacuo and the residue extracted twice with 30-ml portions of pentane. From the combined extracts the pentane is evaporated to afford 0.57 g (63%) of a colorless liquid. – ^1H NMR (C_6D_6, 25 °C): δ = 2.78 (2H, s, NCH_2N), 2.19 (6H, s, NCH_3), 1.75 (4H, s, NCH_2Si), 0.06 (6H, s, $SiCH_3$). – $^{13}C\{^1H\}$ NMR (C_6D_6, 25 °C): δ = 82.66 (s, NCH_2N), 48.47 (s, NCH_3), 46.30 (s, NCH_2, ^{29}Si satellites: $^1J_{SiC}$ = 53.7 Hz), −3.83 (s, $SiCH_3$). – $^{29}Si\{^1H\}$ NMR (C_6D_6, 25 °C): δ = −11.71(s). – EI MS (70 eV); *m/z* (%): 158 (13) [M^+], 143 (65) [M^+ − CH_3], 100 (37) [M^+ − $Si(CH_3)_2$], 73 (100) [$SiMe_3$]. – $C_7H_{18}N_2Si$ (158.3): calcd. C 53.11, H 11.46, N 17.69; found C 52.88, H 11.17, N 17.25.

Synthesis of **5**: A procedure analogous to the preparation of **3** is used, the solvent is THF. 5.75 g (50.5 mmol) of **1** and 2.9 ml of $SiCl_4$ (25.3 mmol) are used. A colorless liquid (2.12 g, 37%), b.p. 116 °C/1.33 · 10^{-2} mbar is obtained after fractional distillation. – ^1H NMR (C_6D_6, 25 °C): δ = 2.84 (4H, s, NCH_2N), 2.20 (12H, s, NCH_3), 1.97 (8H, s, NCH_2Si). – $^{13}C\{^1H\}$ NMR (C_6D_6, 25 °C): δ = 82.44 (s, NCH_2N), 48.00 (s, NCH_3), 43.66 (s, NCH_2Si, ^{29}Si satellites: $^1J_{SiC}$ = 55.8 Hz). – EI MS (70 eV); *m/z* (%): 228 (16) [M^+], 213 (24) [M^+ − CH_3], 184 (16) [M^+ − 2 CH_3, CH_2], 58 (100) [$SiMe_2$]. – $C_{10}H_{24}N_4Si$ (228.4): calcd. C 52.58, H 10.59, N 24.53; found C 52.08, H 10.22, N 23.77.

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