Heteroatom-Facilitated Lithiations of *N*-Methyl-*N*-(trimethylsilyl)methylbenzylamine and Benzyl (Trimethylsilyl)methyl Ether with Butyllithium

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Lithiation of the Si-methyl groups of *N*-methyl-*N*-[(trimethylsilyl)methyl]benzylamine (1) occurred in preference to *ortho*-lithiation of the benzyl group with butyllithium in ether. In a similar reaction with benzyl (trimethylsilyl)methyl ether (7), lithiation of the benzylic position competed with that of the Si-methyl groups.

Keywords lithiation; chelation; organosilicon compound; heteroatom-facilitated lithiation; silylmethylamine; silylmethyl ether

The Si-methyl groups of organosilicon compounds do not usually undergo ready lithiation with organolithium compounds.[1] We previously reported that the lithiation of the Si-methyl groups of (dialkylaminomethyl)trimethylsilanes with butyllithium was accelerated by the chelation between the lithium and the amino groups.[2] Heteroatom-facilitated lithiations have been observed on ether compounds as well as amines,[3] and *ortho*-lithiation of benzylamines is a well known example.[4] We examined the lithiation of *N*-methyl-*N*-[(trimethylsilyl)methyl]benzylamine (**1**) and benzyl (trimethylsilyl)methyl ether (**7**) with butyllithium.

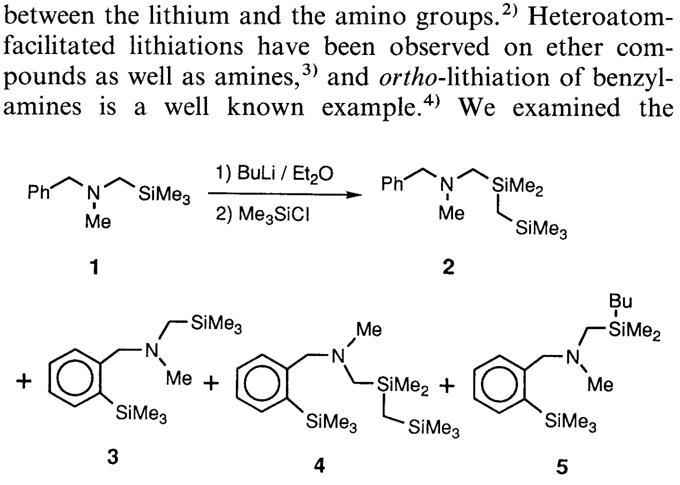

Chart 1

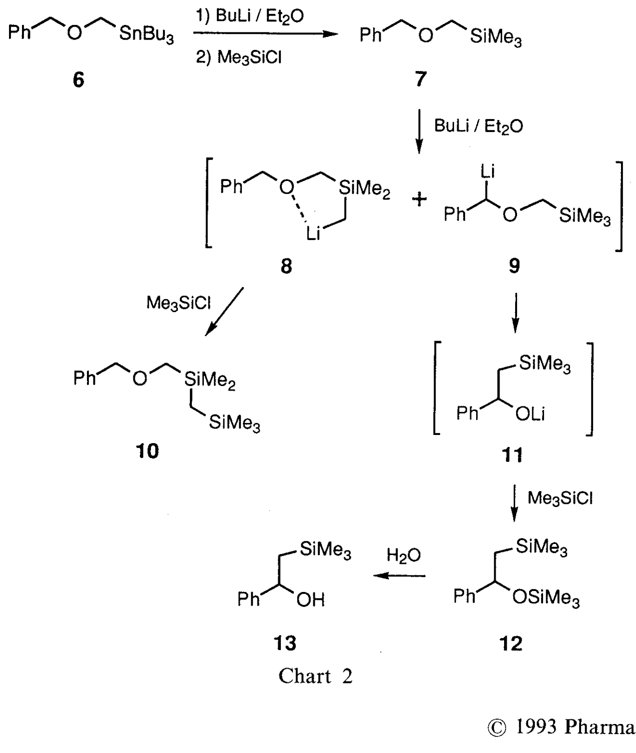

Chart 2

For synthesis of **7**, Chakraborty and Reddy[5] tried the reaction of (iodomethyl)trimethylsilane with sodium alcoholate, but the trimethylsilyl ether was formed instead of the expected (trimethylsilyl)methyl ether. Application of the Williamson ether synthesis to **7** is difficult because (trimethylsilyl)methyl alcoholate easily isomerizes to methoxytrimethylsilane (Brook rearrangement).[6] We therefore prepared **7** from benzyl (tributylstannyl)methyl ether[9] (**6**) by *trans*-metallation (Chart 2).

When **1** was treated with butyllithium at room temperature and quenched with chlorotrimethylsilane, the products were *N*-methyl-*N*-(2,2,4,4-tetramethyl-2,4-disilapentyl)benzylamine (**2**, 42%), *N*-methyl-*N*-(trimethylsilyl)methyl-2-(trimethylsilyl)benzylamine (**3**, 15%), *N*-methyl-*N*-(2,2,4,4-tetramethyl-2,4-disilapentyl)-2-(trimethylsilyl)benzylamine (**4**, 3%), and *N*-(butyldimethylsilyl)methyl-*N*-methyl-2-(trimethylsilyl)benzylamine (**5**, 3%) (Chart 1). Lithiation of the Si-methyl group occurred in preference to *ortho*-lithiation of the benzyl group.

A similar treatment of **7** with butyllithium at room temperature followed by reaction with chlorotrimethylsilane afforded a mixture of 1-phenyl-2-(trimethylsilyl)ethanol (**13**, 29%) and benzyl 2,2,4,4-tetramethyl-2,4-disilapentyl ether (**10**, 17%) (Chart 2). When the reaction was carried out at 0 °C, the ratio of **13** to **10** changed to 95 : 5 (total yield, 20%). The alcohol **13** may be formed during aqueous work-up from 1-phenyl-2-(trimethylsilyl)-1-(trimethylsiloxy)ethane (**12**), which was formed by Witting rearrangement of **9**. Thus, lithiation of the Si-methyl group of **7** competed with that of the benzylic position at room temperature.

Experimental

All reactions were carried out under a nitrogen atmosphere. Diethyl ether and tetrahydrofuran (THF) were distilled under nitrogen from sodium–benzophenone. Boiling points are given as the oven temperature of a Büchi Kugelrohr distillation apparatus.

***N*-Methyl-*N*-[(trimethylsilyl)methyl]benzylamine (1)** A solution of *N*-methylbenzylamine (16.97 g, 140 mmol) and (chloromethyl)trimethylsilane (8.59 g, 70 mmol) in MeCN (40 ml) was heated at reflux for 9 h and then water was added. The ethereal extract of the reaction mixture was dried ($MgSO_4$) and concentrated. Acetic anhydride (16 ml) was added to the residue at room temperature in order to remove unreacted secondary amine, and the mixture was stirred for 10 h and then poured into water. The mixture was made acidic with 10% HCl and washed with diethyl ether. The aqueous layer was made alkaline with 10% NaOH and extracted with diethyl ether. The extract was washed with water, dried ($MgSO_4$), and concentrated. Distillation of the residue yielded **1** (10.18 g, 71%), bp 98—99 °C (5 Torr). ^{1}H-NMR ($CDCl_3$) δ: 0.08 (9H, s), 1.90 (2H, s), 2.15 (3H, s), 3.40 (2H, s), 7.30 (5H, s). *Anal.* Calcd for $C_{12}H_{21}NSi$: C, 69.52; H, 10.22; N, 6.76. Found: C, 69.48; H, 10.11; N, 6.80.

Reaction of 1 with BuLi Followed by Quenching with Chlorotrimethylsilane BuLi (1.5 M hexane solution, 10 ml, 15 mmol) was slowly added to a solution of **1** (621 mg, 3 mmol) in diethyl ether (10 ml) and the mixture was stirred for 20 h at room temperature. A solution of chlorotrimethylsilane (1.79 g, 16.5 mmol) in diethyl ether (5 ml) was added to the mixture under ice cooling. The reaction was quenched with aqueous NH_4Cl and the mixture was extracted with diethyl ether. The extract was washed with water, dried ($MgSO_4$), and concentrated. Distillation of the residue at bp 65—120 °C (1 Torr) gave a mixture of *N*-methyl-*N*-(2,2,4,4-tetramethyl-2,4-disilapentyl)benzylamine (**2**, 42%), *N*-methyl-*N*-(trimethylsilyl)methyl-2-(trimethylsilyl)benzylamine (**3**, 15%), *N*-methyl-*N*-(2,2,4,4-tetramethyl-2,4-disilapentyl)-2-(trimethylsilyl)benzylamine (**4**, 3%), *N*-(butyldimethylsilyl)methyl-*N*-methyl-2-(trimethylsilyl)benzylamine (**5**, 3%), and unconsumed **1** (16%). The structure of each product was confirmed by comparison of the GC-mass spectrum (2-m, 2% silicone SE-30 column, EI 70 eV) with that of the corresponding the authentic sample prepared as described below. Yields were determined on the basis of the integrated GLC values relative to an internal standard (*N*,*N*-dimethylbenzylamine).

***N*-Methyl-*N*-(2,2,4,4-tetramethyl-2,4-disilapentyl)benzylamine (2)** A mixture of *N*-methylbenzylamine (1.21 g, 10 mmol), 2,2,4,4-tetramethyl-2,4-disilapentyl chloride[7] (942 mg, 4.8 mmol) and KI (835 mg, 5 mmol) in MeCN (10 ml) was heated at reflux for 20 h. Aqueous NH_4Cl was added, and the mixture was extracted with diethyl ether. The extract was washed with water, dried ($MgSO_4$), and concentrated. Distillation of the residue gave **2** (1.049 g, 78%), bp 70—80 °C (0.9 Torr). ^{1}H-NMR ($CDCl_3$) δ: -0.22 (2H, s), 0.01 (9H, s), 0.09 (6H, s), 1.89 (2H, s), 2.17 (3H, s), 3.43 (2H, s), 7.22—7.31 (5H, m). MS (rel. intensity) *m*/*z*: 279 (52, M^+), 264 (10), 188 (53), 134 (100), 91 (92). *Anal.* Calcd for $C_{15}H_{29}NSi_2$: C, 64.44; H, 10.45; N, 5.01. Found: C, 64.66; H, 10.63; N, 4.78.

***N*-Methyl-*N*-(trimethylsilyl)methyl-2-(trimethylsilyl)benzylamine (3)** A mixture of *N*-methylbenzylamine (1.45 g, 12 mmol), BuLi (1 M hexane solution, 15.5 ml, 24 mmol) and diethyl ether (20 ml) was stirred for 48 h at room temperature. Chlorotrimethylsilane (2.82 g, 26 mmol) was added to the mixture under ice-cooling and stirring was continued for 1 h at room temperature. Aqueous NH_4Cl was added, and the mixture was extracted with diethyl ether. The extract was washed with water, dried ($MgSO_4$), and concentrated. Distillation of the residue gave *N*-methyl-2-(trimethylsilyl)benzylamine (1.73 g, 75%), bp 90—100 °C (16 Torr). ^{1}H-NMR ($CDCl_3$) δ: 0.33 (9H, s), 1.32 (1H, s), 2.46 (3H, s), 3.80 (2H, s), 7.06—7.57 (4H, m). *Anal.* Calcd for $C_{11}H_{19}NSi$: C, 68.33; H, 9.90; N, 7.24. Found: C, 68.51; H, 9.85; N, 7.04.

A solution of *N*-methyl-2-(trimethylsilyl)benzylamine (1.51 g, 8 mmol) and (chloromethyl)trimethylsilane (0.50 g, 4 mmol) in MeCN (10 ml) was heated at reflux for 20 h and then mixed with water. The ethereal extract of the mixture was washed with water, dried ($MgSO_4$), and concentrated. Chromatography of the residue on alumina with hexane as the eluent yielded **3** (424 mg, 38%), bp 80—85°C (0.8 Torr). ^{1}H-NMR ($CDCl_3$) δ: 0.07 (9H, s), 0.32 (9H, s), 1.94 (2H, s), 2.17 (3H, s), 3.54 (2H, s), 7.19—7.57 (4H, m). MS (rel. intensity) *m*/*z*: 279 (12, M^+), 264 (12), 206 (78), 163 (100), 116 (33). *Anal.* Calcd for $C_{15}H_{29}NSi_2$: C, 64.44; H, 10.45; N, 5.01. Found: C, 64.34; H, 10.73; N, 4.73.

***N*-Methyl-*N*-(2,2,4,4-tetramethyl-2,4-disilapentyl)-2-(trimethylsilyl)benzylamine (4)** A mixture of *N*-methyl-2-(trimethylsilyl)benzylamine (1.216 g, 6 mmol), 2,2,4,4-tetramethyl-2,4-disilapentyl chloride (496 mg, 3 mmol), and KI (501 mg, 3 mmol) in MeCN (10 ml) was treated in a manner similar to that described for **3** to give **4** (491 mg, 47%), bp 100—110 °C (0.8 Torr). ^{1}H-NMR ($CDCl_3$) δ: -0.21 (2H, s), 0.01 (9H, s), 0.10 (6H, s), 0.33 (9H, s), 1.92 (2H, s), 2.18 (3H, s), 3.53 (2H, s), 7.19—7.60 (4H, m). MS (rel. intensity) *m*/*z*: 351 (12, M^+), 336 (17), 206 (100), 163 (98). *Anal.* Calcd for $C_{18}H_{37}NSi_3$: C, 61.46; H, 10.60; N, 3.98. Found: C, 61.12; H, 10.63; N, 3.83.

***N*-(Butyldimethylsilyl)methyl-*N*-methyl-2-(trimethylsilyl)benzylamine (5)** A solution *N*-methyl-2-(trimethylsilyl)benzylamine (1.216 g, 6 mmol) and butyl(chloromethyl)dimethylsilane[8] (496 mg, 3 mmol) in MeCN (10 ml) was heated at reflux for 20 h and worked up in a manner similar to that described for **3** to give **5** (500 mg, 70%), bp 100—110 °C (0.8 Torr). ^{1}H-NMR ($CDCl_3$) δ: 0.05 (6H, s), 0.34 (9H, s), 0.54—0.59 (2H, m), 0.89 (3H, t, $J=7$ Hz), 1.24—1.35 (4H, m), 1.96 (2H, s), 2.17 (3H, s), 3.55 (2H, s), 7.20—7.59 (4H, m). MS (rel. intensity) *m*/*z*: 321 (5, M^+), 306 (13), 206 (100), 163 (95). *Anal.* Calcd for $C_{18}H_{35}NSi_2$: C, 67.21; H, 10.97; N, 4.35. Found: C, 67.26; H, 11.02; N, 4.13.

Benzyl (Trimethylsilyl)methyl Ether (7) A solution of benzyl (tributylstannyl)methyl ether[9] (42.17 g, 103 mmol) in THF (350 ml) was treated with BuLi (1.6 M hexane solution, 82 ml, 130 mmol) at -78 °C and stirring was continued for 45 min. A solution of chlorotrimethylsilane (14.13 g, 130 mmol) in THF (100 ml) was added. After 1.2 h of stirring, aqueous NH_4Cl (300 ml) was added and the mixture was extracted with EtOAc (4 × 200 ml). The extract was washed with water and aqueous NaCl, dried ($MgSO_4$), and concentrated. The residue was distilled at bp 90—130 °C (23 Torr). Chromatography of the distillate on silica gel with hexane–ethyl acetate (100 : 1) as the eluent yielded **7** (8.92 g, 45%). IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 1250, 1090, 1075, 860, 735, 700. ^{1}H-NMR ($CDCl_3$) δ: 0.06 (9H, s), 3.11 (2H, s), 4.48 (2H, s), 7.29—7.34 (5H, m). *Anal.* Calcd for $C_{11}H_{18}OSi$: C, 67.98; H, 9.34. Found: C, 68.04; H, 9.46.

Reaction of 7 with BuLi Followed by Quenching with Chlorotrimethylsilane A solution of **7** (291 mg, 1.50 mmol) in ether (10 ml) was treated with BuLi (1.6 M in hexane, 4.7 ml, 7.5 mmol) under ice cooling. The mixture was stirred at room temperature for 20 h. Then a solution of chlorotrimethylsilane (820 mg, 7.5 mmol) in ether (5 ml) was added under ice cooling with additional stirring for 3 h. Aqueous NH_4Cl (5 ml) was added and the mixture was extracted with ether. The extract was washed with water and aqueous NaCl, dried ($MgSO_4$), and concentrated. ^{1}H-NMR spectroscopy and GLC spectra revealed the presence of 1-phenyl-2-(trimethylsilyl)ethanol[9] (**13**, 29%), benzyl 2,2,4,4-tetramethyl-2,4-disilapentyl ether (**10**, 17%), and unconsumed **7** (4%). Samples were isolated on a silica gel column with hexane–ethyl acetate (40 : 1). The yields were determined from integrated values of ^{1}H-NMR signals based on an internal standard (diphenylmethane).

Ether **10**: ^{1}H-NMR ($CDCl_3$) δ: -0.22 (2H, s), 0.01 (9H, s), 0.07 (6H, s), 3.08 (2H, s), 4.48 (2H, s), 7.27—7.34 (5H, m). MS (rel. intensity) *m*/*z*: 175 (8), 145 (100), 91 (60), 73 (25). *Anal.* Calcd for $C_{14}H_{26}OSi_2$: C, 63:09; H, 9.83. Found: C, 63.15; H, 9.68.

References and Notes

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