Intramolecular Reductive Cleavage of *tert*-Butyldimethylsilyl Ethers. Selective Mono-Deprotection of Bis-Silyl-Protected Diols

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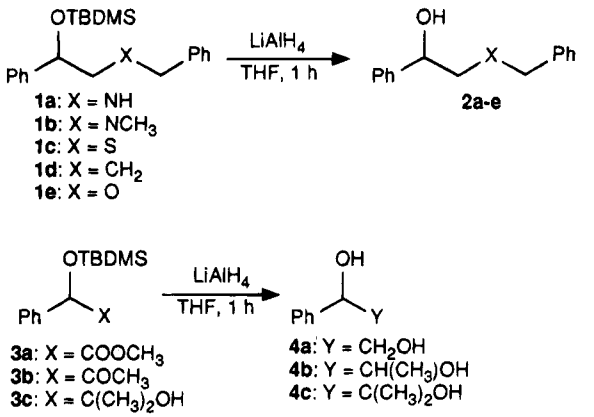
The *tert*-butyldimethylsilyl (TBDMS) group is an attractive protecting group for alcohols, since TBDMS ethers can easily be prepared in high yield under mild conditions and are stable under a wide range of reaction conditions.[1] The TBDMS protecting group is usually removed with fluoride ions or with aqueous acid.[1,2] Although TBDMS ethers are supposedly stable in reducing media,[1] incidental examples of reductive removal of the TBDMS protecting group by exposure to NaH,[3] DIBALH,[4] or DDQ[5] have been reported.

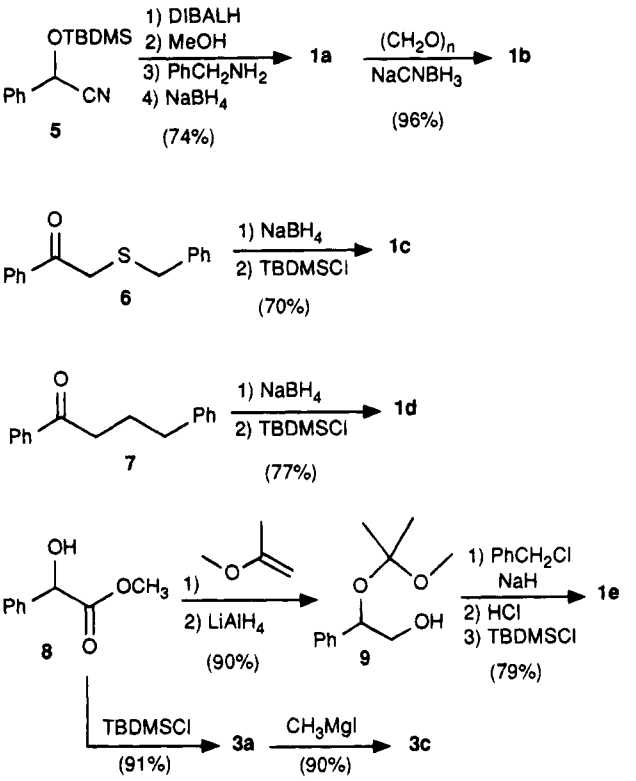
Loss of the silyl group during $LiAlH_4$ reduction has been reported for TBDMS-protected cyanohydrins,[6] α-hydroxy lactones[7] and β-nitro alcohols[8] and has recently been applied in our laboratories for the deprotection of O-TBDMS ethanolamines[6] and diethanolamines.[9] It was suggested[6] that the presence of a polar group close to the silyl ether might be a prerequisite for this reaction to occur. We now report a study on the reductive cleavage of TBDMS ethers **1a–e** and **3a–c** by $LiAlH_4$ (Scheme 1). In compounds **1a–e**, the group X attached to the carbon atom neighboring the one carrying the protected alcohol function is systematically varied. **3a–c** are examples of a TBDMS-protected α-hydroxy ester, a TBDMS-protected α-hydroxy ketone, and a mono-TBDMS-protected diol, respectively. With these compounds, the conditions necessary for the reductive cleavage of TBDMS ethers were determined, and a better insight into the mechanistic aspects of the reaction was obtained. This information was subsequently used to achieve selective removal of one protective group in bis-silylated diols **14** and **17a,b**.

Synthesis of TBDMS Ethers 1a–e and 3a–c. TBDMS ether **1a** was prepared by a one-pot reduction–transimination–reduction procedure[10] from cyanohydrin **5**[11] in 74% yield (Scheme 2). Upon methylation,[12] tertiary amine **1b** was obtained in almost quantitative yield.

Scheme 1. Reductive Silyl Ether Cleavage of Compounds 1a–e and 3a–c by $LiAlH_4$



Scheme 2. Synthesis of TBDMS Ethers 1a–e and 3a–c



Sulfide **1c** was prepared from ketone **6**[13] in two steps in 70% overall yield. TBDMS ether **1d** was prepared from 1,4-diphenyl-1-butanone (**7**) in 77% yield by reduction of the carbonyl group followed by silylation. For the synthesis of TBDMS ether **1e**, methyl mandelate (**8**) was protected as a methoxy isopropyl (MIP) ether and subsequently reduced by $LiAlH_4$ to give mono-protected diol **9**.[14] After benzylation of the free hydroxyl group in **9**, removal of the MIP protecting group, and silylation of the secondary alcohol function, TBDMS ether **1e** was obtained in 79% yield. Finally, TBDMS-protected methyl

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(14) Attempts to synthesize the TBDMS protected analogue of **10** *via* reduction of **3a** led to extensive 1,2-silyl shift to the primary hydroxyl group (Jones, S. S.; Reese, C. B. *J. Chem. Soc., Perkin Trans. I.* **1979**, 2762).

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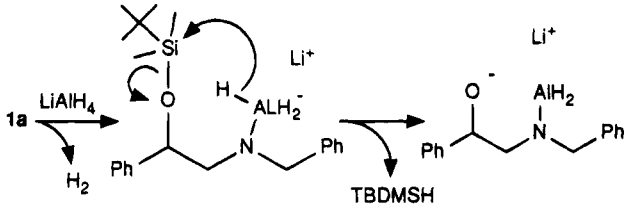
Table 1. Reductive Desilylation of TBDMS-Protected Alcohols 1a–e and 3a–c with $LiAlH_4$ (1 h reflux in THF)

compd	X	conv (%)[a]	yield (%)[b]
1a	NH	>99	93
1b	NCH_3	13	n.d.[c]
1c	S	1	n.d.
1d	CH_2	<0.1	n.d.
1e	O	2	n.d.
3a	$COOCH_3$	>99	98[d]
3b	$COCH_3$	>99	90[d]
3c	$C(CH_3)_2OH$	>99	100

[a] Determined by GC analysis. [b] Isolated yield of deprotected product. [c] Not determined. [d] Isolated yield of deprotected and reduced product.

Scheme 3. Mechanistic Representation of the Cleavage of TBDMS Ethers by $LiAlH_4$

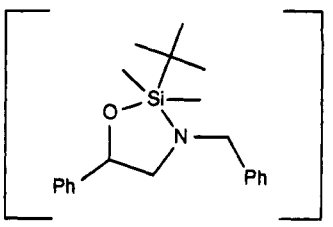


mandelate (**3a**) was treated with an excess of methylmagnesium iodide to afford α-hydroxysilyl ether **3c** in 90% yield. Ketone **3b** was prepared from O-TBDMS-protected mandelonitrile (**5**) as described before.[15]

Reductive Removal of the TBDMS Group. TBDMS protected alcohols **1a–e** and **3a–c** were treated with 2 equiv of $LiAlH_4$ in THF. After 1 h of reflux, the reaction was quenched, the product was isolated without purification, and the conversion was determined by GC analysis.

As shown in Table 1, TBDMS ether **1d** was not affected at all by $LiAlH_4$ under these conditions. The starting material was recovered unchanged. With silyl ethers **1b,c,e**, only a small amount of starting material was converted. This implies, contrary to what was suggested before,[6] that the presence of a polar group neighboring the TBDMS ether by itself is not sufficient for the deprotection reaction to occur at an expedient rate. The reductive cleavage of TBDMS-protected alcohols **1a** and **3a–c**, on the other hand, was complete within 1 h. Apparently, the presence of a $LiAlH_4$-reducible group, such as an ester or ketone, or of an atom bearing a relatively acidic proton adjacent to the silyl ether is a prerequisite for the deprotection reaction to proceed rapidly.

These results can be explained by the mechanism depicted in Scheme 3. If a relatively acidic proton is present in the molecule, this will be readily abstracted by hydride and AlH_3 will remain bound to the anion formed. If this aluminum hydride moiety is present in close proximity to the TBDMS-protected alcohol, hydride transfer from aluminum to silicon can take place intramolecularly, resulting in formation of *tert*-butyldimethylsilane and an aluminum complex of the alcohol anion. The presence of an ester or ketone group near the TBDMS-protected alcohol as in **3a** and **3b** likewise promotes deprotection. Upon reduction of the ester or ketone to the corresponding alcoholate, an aluminum complex is formed, in which hydride transfer again can occur intramolecularly, causing cleavage of the Si–O bond. The reductive removal of the TBDMS protecting group in O-protected cyanohydrins,[6] α-hydroxy lactones[7] and β-nitro alcohols[8] can also be explained by this mechanism. Intramolecular hydride transfer mechanisms have been proposed earlier to explain the reduction of propargylic alcohols[16] and the stereoselectivity in the reduction of 1,3-diketones[17] by $LiAlH_4$.



10

Figure 1. Cyclic pentavalent silicon intermediate **10**.

An alternative explanation for the rapid cleavage of TBDMS ethers in which an anion can be formed close to the protected alcohol, either by deprotonation or by reduction of a functional group, would be the formation of a cyclic pentavalent silicon intermediate, such as **10** (Figure 1). Compared to tetravalent silicon compounds, a pentavalent silicon intermediate would show enhanced reactivity toward nucleophiles.[18] However, since no silyl ether cleavage is observed during the synthesis of **3c** from **3a** *via* a Grignard reaction with excess methylmagnesium iodide, the intermediacy of such a pentavalent silicon intermediate seems to be less likely.

Selective Deprotection of Bis-Silyl Ethers. Next, compounds **14**, **17a**, and **17b** were prepared (Scheme 4), all carrying two silyl-protected hydroxyl groups, of which only one has a neighboring acidic proton. It was hoped that this structural feature would allow selective cleavage of one of the two silyl ethers present in the molecule. Although selective cleavage of primary TBDMS ethers in the presence of secondary ones has been reported,[19] these would present, to the best of our knowledge, the first examples of selective deprotection of one secondary TBDMS ether over another secondary one and of one primary silyl ether in the presence of another primary one.

The synthesis of amine **14** from 4-acetylbenzonitrile (**11**) is shown in Scheme 4. Nitrile **12** was obtained in 91% overall yield and converted to protected diol **14** *via* a one-pot reduction–transimination–reduction procedure[10] in 84% yield, using **13** in the transimination[20] step.

When bis-TBDMS ether **14** was allowed to react with an excess of $LiAlH_4$ in refluxing THF for 1 h, mono-TBDMS-protected diol **15** was obtained in almost quantitative yield. The selectivity, as determined by GC analysis, was >99%. Thus, the TBDMS ether neighboring the secondary amino group, which is the sterically more hindered one, has been selectively cleaved by $LiAlH_4$.

To determine the selectivity of the deprotection of bis-TBDMS-protected primary diols in a more flexible mol-

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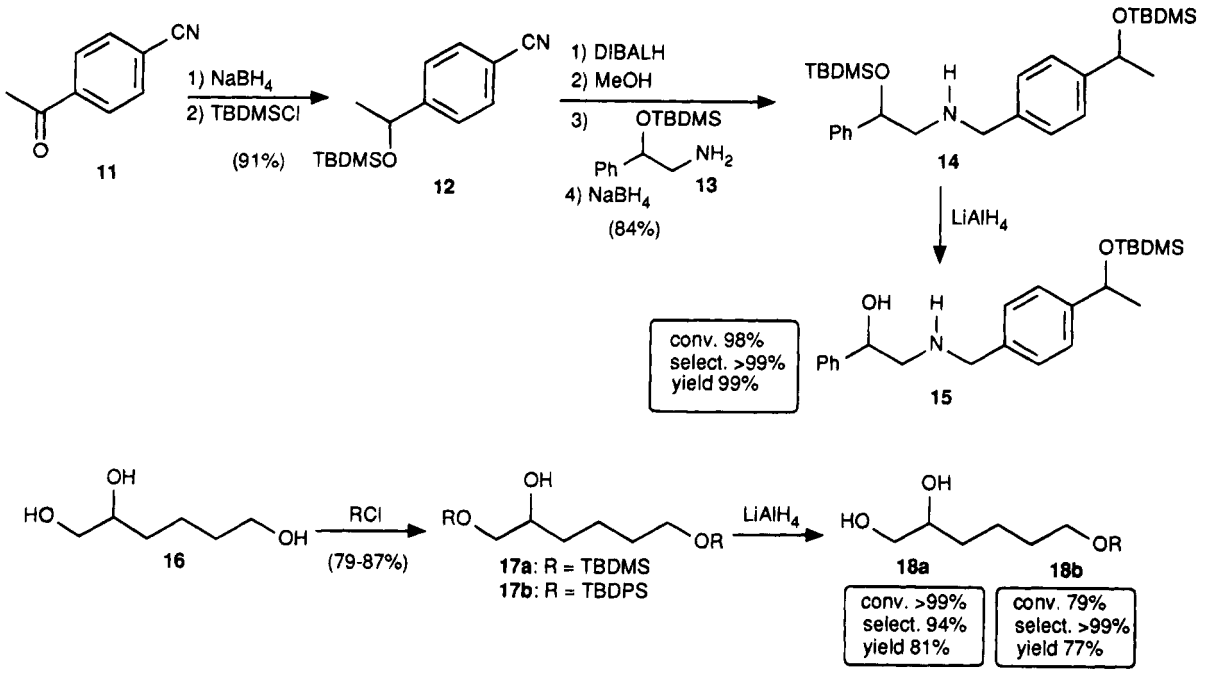
Scheme 4. Synthesis and Selective Deprotection of Bis-Silyl Protected Diols



ecule, compound **17a**, prepared from 1,2,6-hexanetriol (**16**) by selective silylation of the primary alcohol functions[21] in 79% yield (Scheme 4), was treated with an excess of $LiAlH_4$ in refluxing THF. After 1 h a mixture of mono-protected triol **18a** and 1,2,6-hexanetriol (**16**) in a ratio of 94 to 6 had been formed (GC analysis). Although the selectivity of the reductive deprotection of **17a** is still high, it is lower than that observed for **14**. The reason may be that the more flexible **17a** can adopt a conformation in which intramolecular hydride transfer from aluminum to silicon is also possible to the remote silyl ether.

Although *tert*-butyldiphenylsilyl (TBDPS) ethers are known to be more stable toward attack by nucleophiles than TBDMS ethers,[1] we were able to show that TBDPS ethers can also be cleaved by $LiAlH_4$. When bis-TBDPS-protected hexanetriol **17b**, prepared similar to **17a** from **16** by selective silylation, was allowed to react with an excess of $LiAlH_4$ in refluxing THF for 1 h, a mixture of **17b**, **18b**, and *tert*-butyldiphenylsilane was obtained. GC analysis showed the conversion to be 79%. Removal of the TBDPS group had exclusively taken place at the silyl ether flanked by the free hydroxyl group (selectivity >99%). Product **18b** was obtained pure after flash column chromatography in 77% yield. The lower conversion and the higher selectivity of the reaction of **17b** with $LiAlH_4$, compared to **17a**, clearly reflect the higher stability of TBDPS ethers over TBDMS ethers.

In conclusion, it can be said that the presence of an atom bearing a proton that reacts with $LiAlH_4$, or a functional group which is reduced by $LiAlH_4$, at the carbon atom neighboring the one carrying the TBDMS ether allows the intramolecular reductive deprotection of TBDMS-protected alcohols with $LiAlH_4$. This allows the selective cleavage of one TBDMS ether over one that lacks such a structural feature. Compared to TBDMS ethers, TBDPS ethers show a similar but attenuated reactivity toward $LiAlH_4$.

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Experimental Section

^1H NMR and ^{13}C NMR spectra were measured in $CDCl_3$, with TMS as an internal standard for ^1H NMR and $CDCl_3$ as an internal standard for ^{13}C NMR. Mass spectrometry experiments were performed on a Finnigan MAT TSQ-70 equipped with an electrospray interface. Experiments were done in positive ionization mode. Samples were dissolved in CH_2Cl_2 and diluted in methanol/water (80/20) with 1% acetic acid and were introduced by means of constant infusion at a flowrate of 1 μL/min. The conversion and selectivity of the reductive silyl ether cleavage were determined by GC analysis, using a WCOT fused silica column with a CP-Sil-5 CB liquid phase, a column length of 10 m, and an inside diameter of 0.22 mm. The reaction products obtained from **1a–e** were analyzed at 130 °C, those from **3a–c** at 80 °C, and those from **14** at 190 °C. For the analysis of the product obtained from **17a** and **17b**, the column temperature was kept at 80 °C for 5 min, after which it was raised to 120 °C with 5 °C/min (**17a**) or to 290 °C with 10 °C/min (**17b**).

Chemicals. Commercially available chemicals were used, with the exception of **3b**,[15] **5**,[11] **6**,[13] and **13**,[9] which were synthesized by methods described earlier. THF was freshly distilled from $LiAlH_4$ prior to use. Diethyl ether was dried on sodium wire. Methanol and DMF were dried on molecular sieves (3 Å). All reactions were carried out in a nitrogen atmosphere.

2-(Benzylamino)-1-[(*tert*-butyldimethylsilyl)oxy]-1-phenylethane (1a). To a solution of 2.50 g (10 mmol) of **5** in 80 mL of anhyd ether was added 20 mL of a 1 M DIBALH solution in hexane at −80 °C. After the mixture was stirred at this temperature for 3 h, 20 mL of dry methanol and a solution of 4.30 g (40 mmol) of benzylamine in 20 mL of methanol were added successively to the reaction mixture at −90 °C. The reaction mixture was allowed to warm to rt and stirred for 90 min. At 0 °C, 0.76 g (20 mmol) of $NaBH_4$ was added in small portions, after which the mixture was stirred overnight at rt. The reaction mixture was poured into 100 mL of water and extracted with ether (3 × 50 mL). The combined organic layers were washed with 75 mL of a 1 N HCl solution, 50 mL of water, and 50 mL of a 1 N NaOH solution, dried on $MgSO_4$, and concd *in vacuo*. The crude product was dissolved in 50 mL of anhyd alcohol and acidified to pH 2 with a 0.48 N HCl solution in alcohol (4 mL of 12 N HCl in 96 mL of anhyd alcohol). The solvent was evaporated, and the residue was recrystallized from 2-propanol. The ammonium salt was dissolved in a mixture of 50 mL of ether and 50 mL of 1 N NaOH. The layers were separated, and the water layer was extracted again with 50 mL of ether. The combined organic layers were dried on $MgSO_4$ and

concd *in vacuo*, yielding 2.57 g (74%) of **1a** as a colorless oil. ^{1}H NMR: δ (ppm) 7.34 (m, 10H), 4.85 (dd, 1H, J = 4.3 Hz, J = 7.9 Hz), 3.85 (d, 1H, J = 13.9 Hz), 3.77 (d, 1H, J = 13.9 Hz), 2.84 (dd, 1H, J = 7.9 Hz, J = 12.0 Hz), 2.71 (dd, 1H, J = 4.3 Hz, J = 12.0 Hz), 1.66 (bs, 1H), 0.88 (s, 9H), 0.04 (s, 3H), −0.15 (s, 3H). ^{13}C NMR: δ (ppm) 143.4, 140.3, 128.2, 128.0, 127.8, 127.2, 126.7, 126.0, 74.5, 58.0, 53.5, 25.8, 18.1, −4.6, −5.0. Anal. Calcd for $C_{21}H_{31}NOSi$: C, 73.84; H, 9.15; N, 4.10. Found: C, 73.34; H, 9.09; N, 3.90.

2-(Benzylmethylamino)-1-[(*tert*-butyldimethylsilyl)oxy]-1-phenylethane (1b). To a solution of 1.00 g (2.9 mmol) of **1a** in 10 mL of methanol was added 176 mg (5.9 mmol) of paraformaldehyde. After 1 h of stirring at rt, 370 mg (5.9 mmol) of $NaBH_3CN$ was added. Acetic acid was added to the reaction mixture until pH 6. The mixture was stirred at rt for 18 h, after which 50 mL of water was added. The mixture was extracted three times with 25 mL of ether. After the combined organic layers were washed with 25 mL of saturated brine, dried with $MgSO_4$, and concd *in vacuo*, 1.00 g (96%) **1b** was obtained as a colorless oil. ^{1}H NMR: δ (ppm) 7.26 (m, 10H), 4.82 (dd, 1H, J = 5.1 Hz, J = 7.2 Hz), 3.67 (d, 1H, J = 13.1 Hz), 3.56 (d, 1H, J = 13.1 Hz), 2.73 (dd, 1H, J = 7.2 Hz, J = 13.0 Hz), 2.57 (dd, 1H, J = 5.1 Hz, J = 13.0 Hz), 2.30 (s, 3H), 0.88 (s, 9H), 0.07 (s, 3H), −0.15 (s, 3H). ^{13}C NMR: δ (ppm) 144.0, 138.3, 129.0, 128.1, 127.9, 127.1, 127.0, 126.3, 73.6, 65.9, 62.6, 42.9, 25.8, 18.1, −4.6, −4.8. Anal. Calcd for $C_{22}H_{33}NOSi$: C, 74.31; H, 9.35; N, 3.94. Found: C, 73.45; H, 9.29; N, 3.90.

2-(Benzylthio)-1-[(*tert*-butyldimethylsilyl)oxy]-1-phenylethane (1c). At 0 °C, 170 mg (4.5 mmol) of $NaBH_4$ was added to a solution of 1.10 g (4.5 mmol) of **6** in 20 mL of methanol. After being stirred at rt for 18 h, the reaction mixture was poured into 50 mL of water and extracted with ether (3 × 25 mL). The combined ethereal layers were washed with 25 mL of saturated brine, dried on $MgSO_4$, and concd, yielding 1.10 g (99%) of the crude alcohol. The crude product was dissolved in 10 mL of DMF. To this solution were added 0.34 g (5.0 mmol) of imidazole and 0.76 g (5.0 mmol) of TBDMSCl successively. After being stirred at rt for 6 h, the reaction mixture was poured into 50 mL of water and extracted with ether (3 × 25 mL). The combined organic layers were washed with 25 mL of saturated brine, dried on $MgSO_4$, and concd *in vacuo*. Purification by flash column chromatography (FCC), (eluent: ether/petroleum ether 40−60 = 5/95) afforded 1.15 g (71%) of **1c** (colorless oil). ^{1}H NMR: δ (ppm) 7.26 (m, 10H), 4.67 (dd, 1H, J = 5.1 Hz, J = 7.7 Hz), 3.63 (d, 1H, J = 13.1 Hz), 3.55 (d, 1H, J = 13.1 Hz), 2.76 (dd, 1H, J = 7.7 Hz, J = 13.3 Hz), 2.59 (dd, 1H, J = 5.1 Hz, J = 13.3 Hz), 0.87 (s, 9H), 0.05 (s, 3H), −0.14 (s, 3H). ^{13}C NMR: δ (ppm) 144.0, 138.5, 128.9, 128.3, 128.0, 127.3, 126.8, 126.0, 75.3, 41.3, 37.0, 25.8, 18.1, −4.7, −4.9. Anal. Calcd for $C_{21}H_{30}OSSi$: C, 70.33; H, 8.43. Found: C, 70.04; H, 8.56.

1-[(*tert*-Butyldimethylsilyl)oxy]-1,4-diphenylbutane (1d) was prepared as described for **1c**, using **7** as the starting material. Yield: 77%. ^{1}H NMR: δ (ppm) 7.21 (m, 10H), 4.26 (m, 1H), 2.59 (t, 2H, J = 7.2 Hz), 1.65 (m, 4H), 0.87 (s, 9H), 0.01 (s, 3H), −0.16 (s, 3H). ^{13}C NMR: δ (ppm) 145.6, 142.5, 128.4, 128.2, 128.0, 126.8, 125.8, 125.6, 74.9, 40.5, 35.8, 27.2, 25.9, 18.2, −4.6, −4.9. Anal. Calcd for $C_{22}H_{32}OSi$: C, 77.59; H, 9.47. Found: C, 77.50; H, 9.46.

2-[(2-Methoxy-2-propyl)oxy]-2-phenylethanol (9). At 0 °C, one drop of $POCl_3$ was added to a suspension of 5.20 g (31 mmol) of **8** in 20 mL of 2-methoxypropene. After the solution was stirred at rt for 1 h, three drops of triethylamine were added. The reaction mixture was dissolved in 40 mL of ether and washed with 15 mL of water and 15 mL of a saturated $NaHCO_3$ solution. The organic layer was dried on $MgSO_4$. Evaporation of the solvent afforded 7.39 g (97%) of 2-methoxy-2-propyl-protected **8**. A solution of the crude product in 60 mL of dry THF was added to a suspension of 1.18 g (31 mmol) of $LiAlH_4$ in 60 mL of THF. The reaction mixture was stirred at rt for 1 h, after which 1.2 mL of water in 2 mL of THF, 1.2 mL of 4 N NaOH, and 3.6 mL of water were added successively at 0 °C. After being stirred at rt for 18 h, the reaction mixture was dried on $MgSO_4$ and filtered. The residue was thoroughly washed with ether, and the combined filtrates were concd *in vacuo*. Purification by FCC (eluent: triethylamine/ether/petroleum ether 40−60 = 5/25/70) afforded 5.85 g (90%) **9** as a colorless oil. ^{1}H NMR: δ (ppm) 7.30 (m, 5H), 4.83 (t, 1H, J = 6.0 Hz), 2.64 (bd, 2H, J = 9.0 Hz), 3.18 (s, 3H), 2.22 (bs, 1H), 1.44 (s, 3H), 1.20 (s, 3H). ^{13}C NMR: δ (ppm) 141.3, 128.2, 127.4, 126.6, 101.3, 74.3, 67.7, 49.2, 25.7, 25.1.

2-(Benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-1-phenylethane (1e). To a suspension of 0.36 g (60% suspension in mineral oil, 9.6 mmol) of NaH in 5 mL of THF was added a solution of 1.00 g (4.8 mmol) **9** in 10 mL of THF at 0 °C. The reaction mixture was stirred at rt for 1$^1/_2$ h, after which a solution of 1.66 mL (14 mmol) of benzyl chloride in 10 mL of THF and 80 mg (0.5 mmol) of NaI were added. After being stirred at rt for 18 h, the mixture was poured into 50 mL of ice−water and extracted with ether (3 × 25 mL). The combined organic layers were washed with 25 mL of 1 N HCl, dried on $MgSO_4$, and concd *in vacuo*. After the crude product was dissolved in 10 mL of DMF, 0.34 g (5.0 mmol) imidazole and 0.76 g (5.0 mmol) of TBDMSCl were added successively. The reaction mixture was stirred at rt for 6 h, after which it was poured into 50 mL of water and extracted with ether (3 × 25 mL). The combined organic layers were washed with 25 mL of saturated brine, dried on $MgSO_4$, and concd *in vacuo*. Purification by FCC (eluent: ether/petroleum ether 40−60 = 5/95) afforded 1.30 g (79%) **1e** (colorless oil). ^{1}H NMR: δ (ppm) 7.34 (m, 10H), 4.89 (dd, 1H, J = 4.9 Hz, J = 6.9 Hz), 4.58 (d, 1H, J = 12.3 Hz), 4.50 (d, 1H, J = 12.3 Hz), 3.56 (dd, 1H, J = 6.9 Hz, J = 10.0 Hz), 3.50 (dd, 1H, J = 4.9 Hz, J = 10.0 Hz), 0.89 (s, 9H), 0.07 (s, 3H), −0.04 (s, 3H). ^{13}C NMR: δ (ppm) 142.3, 138.4, 128.1, 128.0, 127.3, 127.2, 126.1, 76.9, 74.4, 73.2, 25.8, 18.3, −4.8, −4.8. Anal. Calcd for $C_{21}H_{30}O_2Si$: C, 73.63; H, 8.83. Found: C, 73.74; H, 8.81.

Methyl 1-[(*tert*-Butyldimethylsilyl)oxy]-1-phenylacetate (3a). To a solution of 5.00 g (30 mmol) of **8** in 50 mL of DMF were added 2.20 g (33 mmol) of imidazole and 5.30 g (35 mmol) of TBDMSCl successively. After being stirred at rt for 3 h, the reaction mixture was poured into 150 mL of water and extracted with ether (3 × 25 mL). The combined ethereal layers were washed with 50 mL of saturated brine, dried on $MgSO_4$, and concd *in vacuo*. After purification by FCC (eluent: ether/petroleum ether 40−60 = 5/95), 7.70 g (91%) of **3a** was obtained as a colorless oil. Analytical data were identical to those reported in the literature.[22]

1-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-1-phenyl-2-propanol (3b). At 0 °C, 3.6 mL (11 mmol) of a 3.0 M CH_3MgI solution in ether was added to a solution of 1.00 g (3.6 mmol) of **3a** in 15 mL of anhyd ether. After being stirred at 0 °C for 30 min, the reaction mixture was poured into 50 mL of ice−water and extracted with ether (3 × 25 mL). The combined organic layers were washed with 25 mL of saturated brine, dried on $MgSO_4$, and concd *in vacuo*. Yield: 0.90 g (90%). ^{1}H NMR: δ (ppm) 7.28 (m, 5H), 4.43 (s, 1H), 2.31 (s, 1H), 1.16 (s, 3H), 1.06 (s, 3H), 0.91 (s, 9H), 0.04 (s, 3H), −0.25 (s, 3H). ^{13}C NMR: δ (ppm) 141.0, 127.7, 127.5, 127.4, 81.9, 73.1, 25.9, 25.8, 24.4, 18.1, −4.6, −5.3. Anal. Calcd for $C_{16}H_{28}O_2Si$: C, 68.52; H, 10.06. Found: C, 68.45; H, 9.94.

4-{1-[(*tert*-Butyldimethylsilyl)oxy]ethyl}benzonitrile (12) was prepared as described for **1c**, using **11** as the starting material. Yield: 91%. ^{1}H NMR: δ (ppm) 7.61 (d, 2H, J = 8.5 Hz), 7.43 (d, 2H, J = 8.5 Hz), 4.90 (q, 1H, J = 6.3 Hz), 1.40 (d, 3H, J = 6.2 Hz), 0.90 (s, 9H), 0.07 (s, 3H), −0.02 (s, 3H). ^{13}C NMR: δ (ppm) 152.1, 131.9, 125.7, 118.8, 110.4, 70.0, 26.8, 25.6, 18.0, −5.0, −5.1.

1-[(*tert*-Butyldimethylsilyl)oxy]-2-{4-[1-((*tert*-butyldimethylsilyl)oxy)ethyl]benzylamino}-1-phenylethane (14) was prepared as described for **1a**, using **12** for the DIBALH reduction and **13** in the transimination reaction. **Work up Procedure.** The reaction mixture was poured into water and extracted three times with ether. The combined ethereal layers were washed with saturated brine, dried on $MgSO_4$, and concd. After FCC (eluent: triethylamine/ether/petroleum ether 40−60 = 3/5/92), **14** was obtained as a colorless oil in 82% yield. ^{1}H NMR: δ (ppm) 7.26 (m, 9H), 4.83 (m, 2H), 3.82 (d, 1H, J = 13.0 Hz), 3.75 (d, 1H, J = 13.0 Hz), 2.83 (dd, 1H, J = 8.2 Hz, J = 11.8 Hz), 2.70 (dd, 1H, J = 4.1 Hz, J = 11.8 Hz), 1.39 (d, 3H, J = 6.2 Hz), 0.89 (s, 9H), 0.88 (s, 3H), 0.04 (s, 3H), −0.04 (s, 3H), −0.15 (s, 3H). ^{13}C NMR: δ (ppm) 145.4, 143.5, 138.7, 128.1, 127.6, 127.3, 126.1, 125.2, 74.5, 70.7, 58.1, 53.3, 27.2, 25.8, 18.2,

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18.2, −4.5, −4.8, −4.9. Anal. Calcd for $C_{29}H_{49}NO_2Si_2$: C, 69.68; H, 9.88; N, 2.80. Found: C, 68.92; H, 9.78; N, 2.42.

1,6-Bis[(*tert*-butyldimethylsilyl)oxy]-2-hexanol (17a). At 0 °C, 3.10 g (45 mmol) of imidazole and 4.50 g (30 mmol) of TBDMSCl were added successively to a solution of 2.00 g (15 mmol) of **16** in 15 mL of DMF. After being stirred at 5 °C for 18 h, the mixture was poured into 150 mL of water and extracted with ether (3 × 50 mL). The combined organic layers were washed with 50 mL of saturated brine, dried on $MgSO_4$, and concd. Purification by FCC (eluent: ether/petroleum ether 40–60 = 1/9) afforded 4.28 g (79%) of **17a** (colorless oil). ^1H NMR: δ (ppm) 3.62 (m, 4H), 3.39 (dd, 1H, J = 8.4 Hz, J = 10.5 Hz), 2.44 (d, 1H, J = 3.3 Hz), 1.5 (m, 6H), 0.90 (s, 9H), 0.89 (s, 9H), 0.07 (s, 6H), 0.05 (s, 6H). ^{13}C NMR: δ (ppm) 71.7, 67.2, 63.0, 32.8, 32.5, 25.9, 25.8, 21.8, 18.2, −5.3. Anal. Calcd for $C_{18}H_{42}O_3Si_2$: C, 59.61; H, 11.67. Found: C, 60.17; H, 11.64.

1,6-Bis[(*tert*-butyldiphenylsilyl)oxy]-2-hexanol (17b) was prepared as described for **17a**, using *tert*-butyldiphenylsilyl chloride as the silylating agent. Yield: 87%. ^1H NMR: δ (ppm) 7.65 (m, 4H), 7.37 (m, 6H), 3.62 (m, 4H), 3.45 (dd, 1H, J = 7.2 Hz, J = 9.8 Hz), 2.46 (d, 1H, J = 3.6 Hz), 1.55–1.36 (m, 6H), 1.06 (s, 9H), 1.02 (s, 9H). ^{13}C NMR: δ (ppm) 135.5, 134.0, 133.1, 129.8, 129.4, 127.7, 127.5, 71.8, 68.0, 63.6, 32.5, 26.8, 21.8, 19.2. Anal. Calcd for $C_{38}H_{50}O_3Si_2$: C, 74.70; H, 8.25. Found: C, 74.58; H, 8.22.

Reductive Cleavage of Silyl Ethers. General Procedure. To a suspension of 114 mg (3.0 mmol) of $LiAlH_4$ in 5 mL of anhyd THF was added dropwise a solution of 1.5 mmol of TBDMS ether in 5 mL of THF. The reaction mixture was refluxed for 1 h, after which 0.10 mL of water in 3 mL of THF, 0.20 mL of 4 N NaOH, and 0.30 mL of water were added successively at 0 °C. After being stirred at rt for 1 h, the reaction mixture was dried on $MgSO_4$ and filtered. The residue was washed twice with 10 mL of ether. The combined filtrates were concd and analyzed by GC.

2-(Benzylamino)-1-phenylethanol (2a). Conversion >99%; yield 93%. Mp: 114 °C (lit.[23] mp 100–102 °C). Analytical data were in agreement with those reported in the literature.[23]

1-Phenyl-1,2-ethanediol (4a). Conversion >99%; yield 98%. Analytical data were identical to those of an authentic sample.

1-Phenyl-1,2-propanediol (4b). Compound **4b** was obtained as a mixture of the *threo* and *erythro* isomers in a ratio of 1 to 4 (GC and NMR). Conversion >99%; yield 90%. Analytical data were in agreement with those reported in the literature.[24]

2-Methyl-1-phenyl-1,2-propanediol (4c). Conversion >99%; yield 100%. Mp: 58–59 °C. Analytical data were identical to those reported in the literature.[25]

2-{4-[1-((*tert*-Butyldimethylsilyl)oxy)ethyl]benzylamino}-1-phenylethanol (15). Conversion 98%; selectivity >99%; yield 99%. ^1H NMR: δ (ppm) 7.28 (m, 9H), 4.86 (q, 1H, J = 6.2 Hz), 4.72 (dd, 1H, J = 3.9 Hz, J = 9.0 Hz), 3.84 (d, 1H, J = 12.9 Hz), 3.77 (d, 1H, J = 12.9 Hz), 2.90 (dd, 1H, J = 3.9 Hz, J = 12.1 Hz), 2.74 (dd, 1H, J = 9.0 Hz, J = 12.1 Hz), 1.40 (d, 3H, J = 6.2 Hz), 0.90 (s, 9H), 0.05 (s, 3H), −0.03 (s, 3H). ^{13}C NMR: δ (ppm) 145.8, 142.6, 138.2, 128.3, 127.8, 127.4, 125.8, 125.3, 71.8, 70.5, 56.6, 53.3, 27.2, 25.8, 18.2, −4.8. MS: m/z 386 ($M + H^+$), 771 ($2M + H^+$).

6-[(*tert*-Butyldimethylsilyl)oxy]-1,2-hexanediol (18a). Conversion >99%; selectivity 94%; yield 79%. ^1H NMR: δ (ppm) 3.65 (m, 4H), 3.44 (m, 1H), 2.12 (bs, 1H), 1.90 (bs, 1H), 1.5 (m, 6H), 0.89 (s, 9H), 0.05. ^{13}C NMR: δ (ppm) 72.1, 66.6, 63.0, 32.7, 32.6, 25.9, 21.8, 18.3, −5.3. MS: m/z 249 ($M + H^+$).

6-[(*tert*-Butyldiphenylsilyl)oxy]-1,2-hexanediol (18b). Conversion 79%; selectivity >99%. The crude product was purified by FCC (eluent: methanol/CH_2Cl_2 = 5/95). Yield: 77%. ^1H NMR: δ (ppm) 7.65 (m, 4H), 7.39 (m, 6H), 3.65 (m, 4H), 3.41 (m, 1H), 2.04 (s, 1H), 1.80 (bs, 1H), 1.60–1.40 (m, 6H), 1.05 (s, 9H). ^{13}C NMR: δ (ppm) 135.4, 133.9, 129.4, 127.5, 72.1, 66.6, 63.6, 32.6, 32.4, 26.8, 21.8, 19.1. MS: m/z 373 ($M + H^+$).

Supplementary Material Available: Copies of the ^1H NMR and ^{13}C NMR spectra for compounds **9**, **12**, **15**, and **18a,b** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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