GEMINAL DISILYLMETHYLATION OF DIOXOLANES WITH SILYLMETHYL GRIGNARD REAGENTS†

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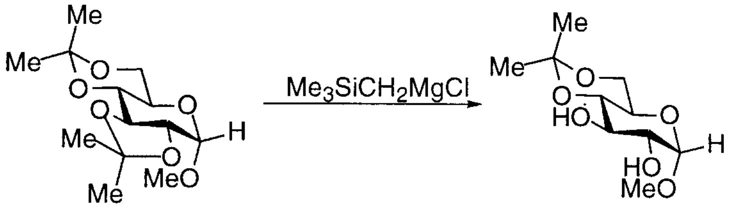
Abstract-Reactions of dioxolanes with excess Me_3SiCH_2MgCl in refluxing benzene yield the corresponding geminal disilylmethylation products in moderate to good yields. Intermediate alkoxy alcohol (**11**) was isolated. Similar reactions with ketals give the corresponding olefins and/or allylsilanes depending on the nature of the starting materials.

Direct conversion of a carbonyl equivalent into a geminal dialkyl product is useful in organic synthesis, but not many methods are known in the literature.[1,2] Tebbe-like reagents are effective for converting a carbonyl group into a gem-dimethyl substituent.[1] However, the reaction is limited to dimethylation and their applications to α,β-unsaturated carbonyl substrates in general result in poor regioselectivity. The use of allylic dithioacetals in the nickel-catalyzed cross coupling reactions with methyl Grignard reagents has paved a complimentary pathway for geminal dimethylation of an α,β-unsaturated carbonyl equivalent.[2,3] Nevertheless, simple aliphatic dithioacetals do not react under these conditions, nor can the reaction be extended to reagents other than methyl nucleophile.[4] Acetals are known to react with Grignard reagents to yield the corresponding alkoxy alcohols.[5-7] Recent studies indicated that a neighboring alkoxy or amino group will assist the regioselective ring opening of cyclic acetals upon treatment with Grignard reagents.[5-7] We recently found that acetals can be deprotected to liberate diols regioselectively upon treatment with Me_3SiCH_2MgCl (eq 1).[8] It is highly desirable to know the fate of the carbonyl equivalent of this reaction because it would be helpful to understand actual mode of this reaction and, in the mean time, it may provide a practical transformation involving acetals.



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In the beginning of this investigation, treatment of **1** with 2 equiv of Me_3SiCH_2MgCl in refluxing benzene solution for 24 h afforded after workup a mixture of **2** and **3** in 21% and 72% yields, respectively

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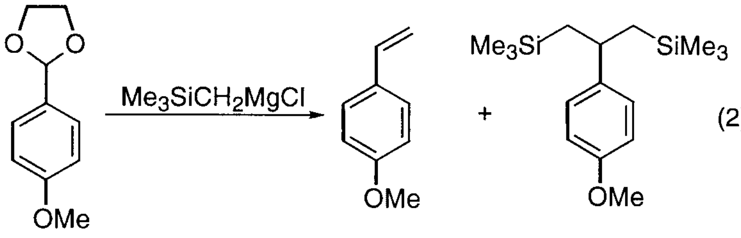
†Dedicated to Professor Teruaki Mukaiyama on the occasion of his 73rd birthday.

(eq 2). This preliminary experiment turned out to be the first example of one pot conversion of both carbon-oxygen bonds of an acetal into two carbon-carbon bonds. As a carbon-silicon bond can readily be converted into the corresponding carbon-heteroatom bond, the formation of **3** from **1** could be particular useful in synthesis. The intermediate (**4**) might be involved to proceed either a Peterson-like elimination process to give **2** or further coupling with another equiv of Me_3SiCH_2MgCl leading to **3**.



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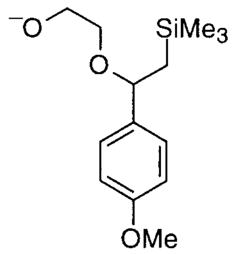
1 **2** **3**



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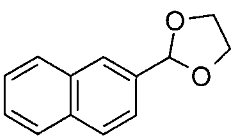

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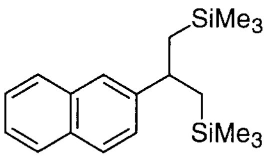

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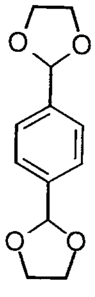
Since the conversion of **4** into **2** and **3** is competitive, we felt that an excess amount of the silylmethyl Grignard reagent may furnish an exclusive formation of **3**. Indeed, when excess amount of Me_3SiCH_2MgCl was employed, **3a** and **3b** were obtained in 78 and 69% yield, respectively, from the corresponding dioxolanes (**1a**) and (**1b**). It is noteworthy that the olefination product (**2**) was not detected. Naphthaldehyde acetal (**5**) behaved similarly to give **6** in 61% yield. Interestingly, the reaction of bisacetal (**7**) with 5 equiv of Me_3SiCH_2MgCl afforded a mixture of **8** and **9** in 39% and 26% yields, respectively. When large excess of Me_3SiCH_2MgCl (e.g. 20 equiv) was employed, the yield of **8** improved to 56%, but **9** was still isolated in 16% yield.



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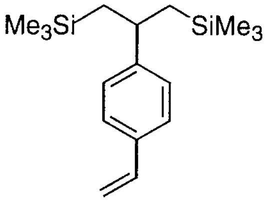

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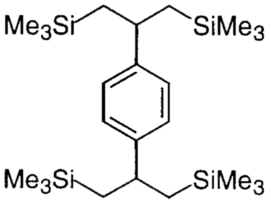

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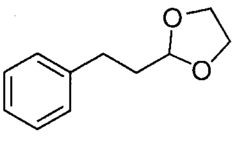
When aliphatic acetal (**10**) was treated with 1 equiv of Me_3SiCH_2MgCl in refluxing benzene for 18 h, intermediate alkoxy alcohol (**11**) was obtained in 65% yield. The isolation of **11** clearly indicated that the two carbon-oxygen bonds are replaced sequentially. Further reaction of **11** with excess of Me_3SiCH_2MgCl in refluxing toluene gave **12** in 68% yield. It is noteworthy that other nucleophiles such as NaH, BuLi or TBAF under the same conditions did not react with **11**, over 90% of the starting **11** being recovered. Direct treatment of **10** with 5 equiv of Me_3SiCH_2MgCl afforded **12** in 68% yield together with a small amount of alkene (**13**) (7%) which was readily separated from **12**.



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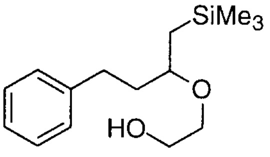

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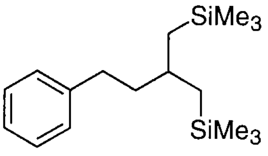

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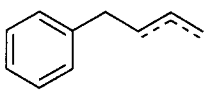

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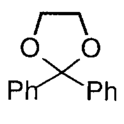
Whereas Peterson-type olefination product (**15**) was obtained in 70% yield from the reaction of benzophenone derivative (**14**) with 5 eq of Me_3SiCH_2MgCl in refluxing benzene, similar treatment of ketal (**16**) afforded allylsilane (**17**) exclusively. Acyclic benzylic ketal (**18**), however, yielded a mixture of (**19**) (19%) and allylsilane (**20**) (48%) in addition to a small amount of the geminal disilylmethylation product (**21**) (12%). Presumably, steric hindrance in ketals may prohibit the sequential carbon-carbon bond formation as observed in acetals. It is interesting to note that the reaction of fluorenone derivative (**22**) under similar conditions with Me_3SiCH_2MgCl afforded the corresponding geminal disilylmethylation product (**23**) in 52% yield.



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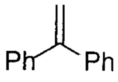

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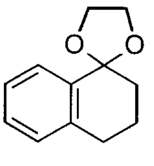

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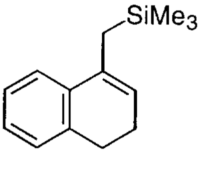

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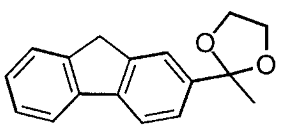

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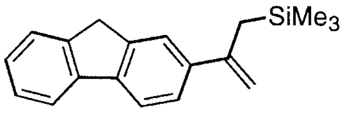

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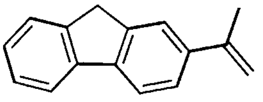

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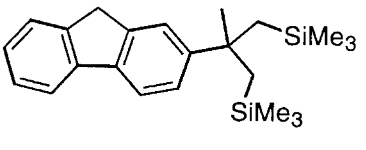

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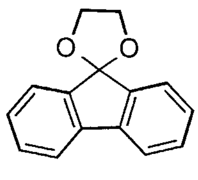

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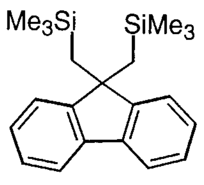

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In summary, we have depicted the first example of the conversion of both carbon-oxygen bonds in acetals into carbon-carbon bonds by means of geminal disilylmethylation reactions. Silylmethyl

Grignard reagent has illustrated a unique role in this transformation. The isolation of the intermediate alcohol (**11**) indicates that the reaction proceeds stepwisely.

EXPERIMENTAL SECTION

General Procedure. Under a nitrogen atmosphere, an ethereal solution of Me_3SiCH_2MgCl (25 mL, 1.0 M) was evacuated to remove the solvent to give a sticky residue to which a benzene solution (50 mL) of acetal (5 mmol) was added. The mixture was refluxed for 6 h and the reaction was monitored by TLC. After the reaction was complete, the solution was cooled to rt and quenched with 5% $NaHCO_3$ (15 mL). The organic layer was separated and the aqueous layer was extracted with ether (50 mL x 3). The combined organic solution was washed with brine, dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was chromatographed on silica gel (hexane) to give the geminal disilylmethylation product.

1,3-Bis(trimethylsilyl)-2-(4-methoxyphenyl)propane (3a). According to the general procedure, a benzene solution (50 mL) of **1a** (0.90 g, 5.0 mmol) was allowed to react with Me_3SiCH_2MgCl (75 mL of a 1.0 M solution in ether, 75 mmol) to yield **3a** as an oil (1.15 g, 78%): ^1H NMR (300 MHz, $CDCl_3$) δ -0.22 (s, 18 H), 0.91 (dd, J = 5.9, 14.6 Hz, 2 H), 0.98 (dd, J = 8.9, 14.6 Hz, 2 H), 2.79 (tt, J = 5.9, 8.9 Hz, 1 H), 3.76 (s, 3 H), 6.76 (d, J = 6.7 Hz, 2 H), 7.06 (d, J = 6.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -1.1, 30.4, 37.5, 55.2, 113.5, 127.9, 141.5, 157.7; HRMS calcd for $C_{16}H_{30}OSi_2$ 294.1835; found 294.1830; Anal. Calcd for $C_{16}H_{30}OSi_2$: C, 65.24; H, 10.26. Found C, 64.71; H, 10.33.

1,3-Bis(trimethylsilyl)-2-(4-methylphenyl)propane (3b). According to the general procedure, a benzene solution (50 mL) of **1b** (0.82 g, 5.0 mmol) was allowed to react with Me_3SiCH_2MgCl (20 mL of a 1.0 M solution in ether, 20 mmol) to yield **3b** (0.96 g, 69%): mp 33-35 °C; ^1H NMR (300 MHz, $CDCl_3$) δ -0.21 (s, 18 H), 0.94 (dd, J = 6.2, 14.6 Hz, 2 H), 1.00 (dd, J = 8.9, 14.6 Hz, 2 H), 2.29 (s, 3 H), 2.81 (tt, J = 6.2, 8.9 Hz, 1 H), 6.95-7.10 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -1.0, 21.0, 30.2, 38.0, 127.0, 128.8, 135.1, 146.4; HRMS calcd for $C_{16}H_{30}Si_2$ 278.1886; found 278.1884; Anal. Calcd for $C_{16}H_{30}Si_2$: C, 68.98; H, 10.85. Found C, 69.33; H, 10.77.

1,3-Bis(trimethylsilyl)-2-(2-naphthyl)propane (6). According to the general procedure, a benzene solution (50 mL) of **5** (1.00 g, 5.0 mmol) was allowed to react with Me_3SiCH_2MgCl (25 mL of a 1.0 M solution in ether, 25 mmol) to yield **6** (0.96 g, 61%): mp 37-38 °C; ^1H NMR (300 MHz, $CDCl_3$) δ -0.19 (s, 18 H), 1.05 (dd, J = 5.9, 14.7 Hz, 2 H), 1.14 (dd, J = 9.0, 14.7 Hz, 2 H), 3.06 (tt, J = 5.9, 9.0 Hz, 1 H), 7.35-7.48 (m, 3 H), 7.59 (s, 1 H), 7.73-7.82 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -1.0, 29.9, 38.6, 124.9, 125.3, 125.7, 125.8, 127.5, 127.6, 127.9, 132.2, 133.6, 146.9; HRMS calcd for $C_{19}H_{30}Si_2$ 314.1886; found 314.1885; Anal. Calcd for $C_{19}H_{30}Si_2$: C, 72.54; H, 9.61. Found C, 72.22; H, 9.77.

1,3-Bis(trimethylsilyl)-2-(4-vinylphenyl)propane (8) and 1,4-Di-[1,3-bis(trimethylsilyl)-2-propyl]-benzene (9). In a manner similar to that described in the general procedure, the reaction of **7** with Me_3SiCH_2MgCl (25 mL of a 1.0 M solution in ether, 25 mmol) in benzene (50 mL) afforded **8** as an oil (0.38 g, 26%) and **9** (0.88 g, 39%): **8:** ^1H NMR (300 MHz, $CDCl_3$) δ -0.20 (s, 18 H), 0.94 (dd, J = 5.9, 14.7 Hz, 2 H), 1.14 (dd, J = 9.0, 14.7 Hz, 2 H), 2.83 (tt, J = 5.9, 9.0 Hz, 1 H), 5.15 (d, J = 11.1 Hz, 1 H), 5.68 (d, J = 17.6 Hz, 1 H), 6.67 (dd, J = 11.1, 17.6 Hz, 1 H), 7.12 (d, J = 8.1 Hz, 2 H), 7.28 (d, J = 8.1 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -0.7, 30.4, 38.5, 112.8, 126.4, 127.6, 135.5, 137.2, 149.6; HRMS calcd for $C_{17}H_{30}Si_2$ 290.1886; found 290.1900; Anal. Calcd for $C_{17}H_{30}Si_2$: C, 70.26; H, 10.41. Found C, 70.65; H, 10.48. **9:** mp 61-62 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ -0.17 (s, 36 H), 0.91 (dd, J = 5.9, 14.7 Hz, 4 H), 0.99 (dd, J = 9.0, 14.7 Hz, 4 H), 2.81 (tt, J = 5.9, 9.0 Hz, 2 H), 7.04 (s, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -0.5, 30.4, 38.2, 127.2, 147.5; HRMS calcd for $C_{24}H_{50}Si_4$ 450.2989; found 450.2984; Anal. Calcd for $C_{24}H_{50}Si_4$: C, 63.92; H, 11.17. Found C, 63.68; H, 10.92.

2-Trimethylsilylmethyl-4-phenyl-1-trimethylsilylbutane (12). In a manner similar to that described in the general procedure, the reaction of **10** (0.89 g, 5.0 mmol) with Me_3SiCH_2MgCl (25 mL of a 1.0 M solution in ether, 25 mmol) in benzene (30 mL) yielded **12** as an oil (0.99 g, 68%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.02 (s, 18 H), 0.61 (dd, J = 6.0, 14.7 Hz, 2 H), 0.74 (dd, J = 6.8, 14.7 Hz, 2 H), 1.50-1.64 (m, 2 H), 1.69-1.81 (m, 1 H), 2.60 (t, J = 8.0 Hz, 2 H), 7.14-7.33 (m, 5 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ -0.3, 25.5, 30.7, 33.1, 41.7, 125.5, 128.3, 128.4, 143.1; HRMS calcd for $C_{17}H_{32}Si_2$ 292.2042; found 292.2044.

6-Phenyl-4-trimethylsilylmethyl-3-oxa-1-hexanol (11). According to the general procedure, a mixture of **10** (0.89 g, 5.0 mmol) and Me_3SiCH_2MgCl (5 mL of a 1.0 M solution in ether, 5 mmol) in benzene (50 mL) was refluxed for 24 h and worked up as usual to give **11** as an oil (0.87 g, 65%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.00 (s, 9 H), 0.83 (dd, J = 7.6, 14.5 Hz, 1 H), 1.01 (dd, J = 6.3, 14.5 Hz, 1 H), 1.55-1.75 (br s, 1 H), 1.73-1.86 (m, 2 H), 2.55-2.73 (m, 2 H), 3.43-3.52 (m, 3 H), 3.70 (t, J = 4.7 Hz, 2 H), 7.10-7.32 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -0.7, 22.5, 31.5, 38.0, 62.2, 68.8, 77.2, 125.7, 128.3, 142.2; IR (neat) ν 3443; HRMS calcd for $C_{15}H_{26}O_2Si$: 266.1702; found 266.1718.

9,9-Bis(trimethylsilylmethyl)fluorene (23). According to the general procedure, a mixture of **22** (1.12 g, 5.0 mmol) and Me_3SiCH_2MgCl (25 mL of a 1.0 M solution in ether, 25 mmol) in benzene (50 mL) was refluxed for 24 h and worked up as usual to give **23** (0.88 g, 52%): mp 89-90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ -0.75 (s, 18 H), 1.59 (s, 4 H), 7.18-7.38 (m, 6 H), 7.68 (d, J = 7.1 Hz, 2 H); ^{13}C NMR (75 MHz, CDC13) δ -1.0, 35.1, 50.8, 119.7, 124.1, 126.8, 126.9, 139.9, 152.4; HRMS calcd for $C_{21}H_{30}Si_2$ 338.1886; found 338.1891; Anal. Calcd for $C_{21}H_{30}Si_2$: C, 74.48; H, 8.93. Found C, 74.87; H, 8.60.

1,1-Diphenylethene (15). In a manner similar to that described in the general procedure, the reaction of **14** (1.13 g, 5.0 mmol) with Me_3SiCH_2MgCl (25 mL of a 1.0 M solution in ether, 25 mmol) in benzene (30 mL) yielded **15** as an oil (0.63 g, 70%) which exhibited identical physical properties as those of the authentic sample.[9]

4-Trimethylsilylmethyl-1,2-dihydronaphthalene (17). In a manner similar to that described in the general procedure, the reaction of **16** (0.95 g, 5.0 mmol) with Me_3SiCH_2MgCl (25 mL of a 1.0 M solution in ether, 25 mmol) in benzene (50 mL) afforded **17** as an oil (0.80 g, 74%) which showed identical spectroscopic properties as those of the authentic sample.[10]

2-(2-Fluorenyl)propene (19), 2-(2-Fluorenyl)-3-trimethylsilylpropene (20) and 2-(2-Fluorenyl)-2-methyl-1,3-bis(trimethylsilyl)propane (21). In a manner similar to that described in the general procedure, the reaction of **18** (1.26 g, 5.0 mmol) with Me_3SiCH_2MgCl (25 mL of a 1.0 M solution in ether, 25 mmol) in benzene (50 mL) afforded **19** (0.31 g, 22%),[9] **20** (0.67 g, 48%), and **21** (12%) as an oil: **20**: mp 78-79 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ -0.11 (s, 9 H), 2.06 (s, 2 H), 3.88 (s, 2 H), 4.87 (s, 1 H), 5.16 (s, 1 H), 7.26-7.43 (m, 2 H), 7.50-7.56 (m, 2 H), 7.67-7.73 (m, 3 H); HRMS calcd for $C_{19}H_{22}Si$ 278.1491; found 278.1482; Anal. Calcd for $C_{19}H_{22}Si$: C, 81.95; H, 7.96. Found C, 81.56; H, 8.21. **21**: ^{1}H NMR (200 MHz, $CDCl_3$) δ -0.23 (s, 18 H), 1.17 (d, *J* = 14.6 Hz, 2 H), 1.37 (d, *J* = 14.6 Hz, 2 H), 1.53 (s, 3 H), 3.88 (s, 2 H), 7.22-7.70 (m, 7 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 0.5, 29.3, 37.0, 38.9, 40.2, 119.1, 119.6, 122.6, 124.5, 125.0, 126.1, 126.6, 138.8, 142.0, 142.9, 143.4, 150.0; HRMS calcd for $C_{23}H_{34}Si_2$ 366.2199; found 366.2197; Anal. Calcd for $C_{23}H_{34}Si_2$: C, 75.34; H, 9.35. Found C, 75.05; H, 9.18.

ACKNOWLEDGMENT

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4. Only benzylic dithioacetals (derived from an aldehyde) can afford the corresponding geminal diethylation products under the $NiCl_2$(dppe)-catalyzed conditions. Dithioketals, in general, do not give the corresponding dialkylation products. Geminal allylation reaction is observed when fluorenone or benzophenone dithioketal is treated with allyl Grignard reagent under the nickel-catalyzed conditions (ref. 2b).
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