Synthesis of Bis(trimethylsilyl) Ketone and Reactions with Organometallic Compounds

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Bis(trimethylsilyl) ketone (1) was reported in 1968 as a hydrolysis product of 1,1-bis(trimethylsilyl)-1,3-dithiane. The compound could, however, not be purified because of its lability. Hydrolysis of bis(trimethylsilyl)bis(methylthio)methane met with the same problems. The pure ketone has been isolated from the ozonolysis of bis(trimethylsilyl)methylene(triphenylphosphorane and by oxidation of tris(trimethylsilyl) methylthiomeethane with m-chloroperbenzoic acid followed by a sila-Pummerer rearrangement.

We have recently reported that bis(trimethylsilyl) ketone (1) can be readily prepared in good yield (75%) from the α-bromo ether 3a by hydrolysis on a silica gel column. It turns out that the corresponding α-chloro ether 3b can be used equally well (Scheme 1).

\[
\begin{align*}
\text{PhS} & \quad \text{SiMe}_3 \\
\text{OMe} & \quad \text{SiMe}_3 \\
\text{SO}_2\text{Cl}_2 \text{ or Br}_2 & \quad \text{CH}_2\text{Cl}_2 \\
\text{TMS} & \quad \text{TMS} \\
\text{SiMe}_3 & \quad \text{SiMe}_3 \\
\text{OMe} & \quad \text{SiMe}_3 \\
\text{Et}_2\text{O} & \quad \text{pentane} \\
\text{X} & = \text{Cl}, \quad \text{X} = \text{Br} \\
\end{align*}
\]

Scheme 1.

The α-chloro ether 3a was prepared by cleavage of the O,S-acetal 2° by sulfuryl chloride. The benzenesulfenyl chloride generated was trapped with cyclohexene. This adduct has a much higher boiling point than the α-chloro ether 3a, which could then be separated from the adduct by distillation. Addition of the α-chloro ether 3a to a silica gel column and elution under N₂ with a mixture of pentane and diethyl ether gave the ketone 1 in 78% yield.

It has been shown that bis(trimethylsilyl) ketone (1) can be regarded as a CO₂⁻ equivalent. Thus treatment of ketone 1 with fluoride ion in the presence of 2-cyclohexenone afforded, after hydrolysis, 3-formylcyclohexenone. In this paper we show that bis(trimethylsilyl) ketone (1) also reacts like a ‘normal’ ketone by addition of different organometallic compounds giving 1,1-bis(trimethylsilyl) substituted alcohols. Such compounds have previously been prepared by reductive silylation of carboxylic esters. The reactivity of 1 towards organometallic compounds has, as far as we know, not been reported.

The reaction of bis(trimethylsilyl) ketone (1) with excess methyl organometallic reagents gave 1,1-bis(trimethylsilyl) ethanol in 44–59% yield (Scheme 2, entries 1–3). Lower yields were obtained when the organometallic compound was not used in excess.

As expected methylmagnesium bromide and methyl lithium react more rapidly with 1 than does trimethylaluminum; ca. 30 min for completion for the magnesium and lithium reagents and 24 h for the aluminum reagent. (Trimethylsilylmethyl)magnesium chloride reacted to give the adduct 4b in good yield (79%, entry 4). From the reaction of butylmagnesium bromide only the reduction product bis(trimethylsilyl)methanol (5) (entry 5) was isolated. In the crude product there was <10% of compound 4c according to ¹H NMR spectroscopy. The corresponding lithium compound, however, gave a 2:1 mixture of 4c and 5 according to ¹H NMR spectroscopy (entry 6). Compound 5 was the only product in the reaction with triisobutylaluminum and disobutylaluminum hydride (DIBAH) (entries 7 and 8). Vinylmagnesium bromide and phenylmagnesium bromide gave the addition products 4d and 4e, respectively, in low yield (entries 9 and 10). Compound 4e could be identified only by ¹H NMR, due to rapid decomposition.

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1141
Entry | RM | Product | Yield 4 (%)a | Yield 5 (%)a
--- | --- | --- | --- | ---
1 | MeMgBr | 4a | 59 | —
2 | MeLi | 4a | 58 | —
3 | Me₂Al | 4a | 44 | —
4 | Me₂SiCl₂MgCl | 4b | 79 | —
5 | n-BuMgBr | 4c | 35 | 46
6 | n-BuLi | 4c | —b | —c
7 | (i-Bu₂)₂Al | — | —d | 54
8 | (i-Bu₂)₂AlH | — | —d | 58
9 | VinylMgBr | 4d | 32 | —
10 | PhMgBr | 4e | 25 | —
11 | PhC≡CCLI | — | — | —

*aIsolated. <10% of the crude product (1H NMR). 'A 2:1 mixture of 4c and 5 in the crude product (1H NMR). 'Not observed in the crude product (1H NMR).

Scheme 2.

The reaction of lithium phenylacetylide no addition product was observed (entry 11).

It seems that the stability of the 1,1-bis(trimethylsilyl) alcohols 4 may be dependant on the electronic properties of the R-group. The group R is the more easily the compounds decompose. From the literature only 1,1-bis(trimethylsilyl)-alkan-1-ols having electron-donating substituents on the alcohol carbon are known.6

The reactivity of 1,1-bis(trimethylsilyl)alkan-1-ols has been very little investigated. We can report that treatment of compound 4b with sodium hydride in boiling THF for 2 h gave the Peterson elimination product 6 in good yield (Scheme 3). We are currently investigating the synthesis and reactivity of other bis(silyl) ketones.

Scheme 3.

Experimental

The 1H NMR spectra were recorded at 200 MHz with a Varian Gemini 200 or a Bruker DPX 200 instrument. The 13C NMR spectra were recorded at 50 MHz with a Gemini 200 or a Bruker DPX 200. The NMR spectra were recorded in CDCl₃. The mass spectra, under electron impact conditions, were recorded at 70 eV ionizing energy. Isobutane was used for chemical ionization (Cl); the spectra are presented as m/z (% rel. int.).

Bis(trimethylsilyl) ketone (1).³⁻⁵ Bis(trimethylsilyl)-chloro(methoxy)methane (0.674 g, 3.0 mmol) in pentane (3.0 ml) was added to silica gel in degassed pentane. The elution was conducted essentially as described for the purification of ketone 1 in the literature.³ᵇ Elution was first done with degassed pentane and then with a degassed mixture of pentane and diethyl ether (20:1). All the colourless fractions were discarded. Yield 0.410 g (78%). The analytical data were in accordance with the previously published values.³⁻⁵

Bis(trimethylsilyl) chloro(methoxy) methane (3a). Sulfuryl chloride (0.81 ml, 10 mmol) in dry dichloromethane (7 ml) was added dropwise with stirring to a solution of bis(trimethylsilyl) methoxy(phenylthio)methane⁶ (2.98 g, 10 mmol) in dry dichloromethane (14 ml) under N₂ at 0°C. Cyclohexene (1.22 ml, 12 mmol) in dry dichloromethane (7 ml) was then added dropwise and stirred for 30 min. The solvent was evaporated off and the residue was purified by Kugelrohr distillation (1.0 mmHg, temp. 45–55°C). Yield 1.47 g (65%). 1H NMR (CDCl₃): δ 0.18 (s, 2 x SiMe₃), 3.47 (s, OMe). 13C NMR (CDCl₃): δ −1.1 (SiMe₃), 56.4 (OMe), 109.5 (CCI).

1,1-Bis(trimethylsilyl) ethanol (4a). To a solution of bis(trimethylsilyl) ketone (0.205 g, 1.18 mmol) in THF (6 ml) at −78°C under N₂ was added allylmagnesium bromide (2.0 ml, 1.4 M in toluene–THF 3:1, 2.8 mmol). After the pink colour of the solution had disappeared (30 min), the mixture was allowed to warm to 0°C, before 10% NH₄Cl (10 ml) and diethyl ether (20 ml) were added. The mixture was stirred for another 30 min before the organic layer was separated and washed with saturated aqueous NaHCO₃ (2 x 10 ml) and saturated aqueous NaCl (2 x 10 ml), successively. The dried (MgSO₄) solution was evaporated and the crude product purified by flash chromatography on silica gel using hexane–ethyl acetate (8:1) for elution. Yield: 0.132 g (59%). Oil. 1H NMR (CDCl₃): δ 0.026 (s, 2 x SiMe₃), 1.14 (s, Me). 13C NMR (CDCl₃): δ −2.7 (SiMe₃), 21.9 (Me). 58.6 (C–OH). MS (Cl): 190 (M⁺, 24), 189 (34), 175 (31), 164 (123), 159 (7), 148 (14), 117 (8), 102 (22), 90 (100), 73 (20).

1,1,2-Tris(trimethylsilyl)ethanol (4b). Procedure as for 4a. Compound 4b was prepared from bis(trimethylsilyl) ketone (0.07 g, 0.44 mmol) and (trimethylsilyl)methylmagnesium bromide (1 M in THF, 1.5 ml, 1.5 mmol). The crude product was purified by flash chromatography on silica gel using hexane–ethyl acetate (20:1) for elution. Yield 0.082 g (79%). 1H NMR (CDCl₃): δ 0.024 (s, 2 x SiMe₃), 0.19 (s, SiMe₃), 1.24 (s, CH₃). 13C NMR (CDCl₃): δ −1.92 (C–SiH₃), 2.19 (CH₂SiH₃), 23.69 (CH₃), 60.94 (COH). MS (Cl): 259 (0.3), 247 (1), 231 (27), 172 (28), 159 (28), 158 (16), 157 (77), 147 (26), 143 (35), 79 (16), 75 (20), 73 (100).

1,1-Bis(trimethylsilyl) pentan-1-ol (4e). Procedure as for 4a. Compound 4e was prepared from bis(trimethylsilyl) ketone (0.125 g, 0.72 mmol) and n-butyllithium (1.6 M in hexane, 1.0 ml, 1.6 mmol). The crude product was a
mixture of 4c and 5 (2:1, 1H NMR), which was separated by flash chromatography on silica gel using hexane–ethyl acetate (10:1) for elution. Yield 0.056 g (35%). 1H NMR (C₆D₆): δ 0.095 (s, 2 × SiMe₃), 0.88 (t, Me, J 7 Hz), 1.17–1.38 (m, 4 H), 1.60–1.72 (m, 2 H). 13C NMR (C₆D₆): δ 1.4 (SiCH₃), 14.3 (CH₃), 24.2 (CH₂), 28.2 (CH₂), 37.7 (C–CH₃), 62.7 (COH). MS (Cl): 232 (M⁺, 1), 217 (5), 201 (15), 185 (4), 173 (8), 159 (11), 149 (10), 148 (28), 147 (100), 127 (77), 99 (22), 73 (94).

1,1-Bis(trimethylsilyl)prop-2-en-1-ol (4d). Procedure as for 4a. Compound 4d was prepared from bis(trimethylsilyl) ketone (0.44 g, 2.5 mmol) and vinyl magnesium bromide (1 M in THF, 5.0 ml, 5.0 mmol). The crude product was purified by flash chromatography on silica gel using hexane–ethyl acetate (6:1) for elution. Yield 0.164 g (32%). 1H NMR (C₆D₆): δ 0.042 (s, 2 × SiMe₃), 4.76 (d, 1 H, J 16.9 Hz), 4.87 (d, 1 H, J 11.0 Hz), 5.96 (dd, 1 H, J 11.0, 16.9 Hz). 13C NMR (C₆D₆): δ −1.3 (SiMe₃), 70.7 (COH), 104.8 (=CH₂), 141.3 (=CH). MS (EI): 202 (M⁺, 5), 171 (7), 148 (9), 147 (53), 133 (9), 97 (12), 75 (29), 74 (9), 73 (100), 45 (16).

Bis(trimethylsilyl)phenylmethanol (4e). Procedure as for 4a. Compound 4e was prepared from bis(trimethylsilyl) ketone (0.087 g, 0.5 mmol) and phenylmagnesium bromide (1 M in THF, 1.5 ml, 1.5 mmol). The crude product was purified by flash chromatography on silica gel using hexane–ethyl acetate (10:1) for elution. Yield 0.032 g (25%). 1H NMR (C₆D₆): δ 0.023 (s, 2 × SiMe₃), 6.95–7.03 (m, 2 H), 7.14–7.19 (m, 3 H).

Bis(trimethylsilyl)methanol (5). Diisobutylaluminium hydride solution (≈20% in hexane, 2 ml, 2 mmol) was added dropwise to a solution of bis(trimethylsilyl) ketone (0.157 g, 0.9 mmol) in THF (5 ml) under N₂ at −78 °C. The mixture was stirred for 30 min, quenched with water (10 ml), extracted with diethyl ether (20 ml), dried (MgSO₄) and evaporated. The crude product was purified by flash chromatography on silica gel using hexane–ethyl acetate (8:1) for elution. Yield 0.092 g (58%). 1H NMR (C₆D₆): δ 0.045 (s, 2 × SiMe₃), 2.77 (s, 1 H). 13C NMR (C₆D₆): δ 0.0 (SiCH₃), 59.8 (COH). IR (neat, cm⁻¹): 3450 (br), 2950, 1725, 1250, 1045. MS (Cl): 176 (M⁺, 11), 175 (12), 161 (31), 160 (24), 143 (6), 130 (6), 102 (17), 90 (100), 73 (30).

1,1-Bis(trimethylsilyl)ethene (6). Sodium hydride (0.06 g, 2.5 mmol) was added to a solution of 1,1,2-tris(trimethylsilyl)ethanol (0.113 g, 0.43 mmol) in THF (10 ml). The mixture was stirred under reflux for 3 h before the reaction was quenched with saturated NH₄Cl, washed with water, dried (MgSO₄) and evaporated. The crude product was purified by Kugelrohr distillation (oven temp. 50–60°C, 95 mmHg). Yield 0.063 g (85%). 1H NMR (C₆D₆): δ −0.13 (s, 2 × SiMe₃), 6.31 (s, 2 H).

References

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