Reaction of Silylketenes with Carbanions: Simple Preparation of \(\alpha\)-Silylketones Using Organocerium Reagents

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Preparation of \(\alpha\)-silylketones 1 by the reaction of three kinds of silylketenes 3a—c with various organometallic reagents 4 was studied. Although the use of \(n\)-BuLi, MeMgBr, Me₂CuLi, Et₃Al, and Et₂Zn resulted in complicated reactions, organocerium reagents 4 (\(M = \text{CeCl}_3\)) added selectively to the carbonyl carbon of 3 to generate enolate anions A, which were treated with aqueous \(\text{NH}_2\text{Cl}\) or alkyl halides 5 to give 1. Seventeen \(\alpha\)-silylketones 1a—q were prepared in 31—99% yields from three components, 3, alkyl- or arylcyclo reagents 4, and proton or alkyl halides 5. This method was applied to a regiocontrolled preparation of two isomeric \(\alpha\)-silylketones 1r,s.

Key words silylketene; \(\alpha\)-silylketone; organocerium reagent; silyl enol ether

\(\alpha\)-Silylketones 1 rearrange stereoselectively to either (E)- or (Z)-silyl enol ethers 2 depending on the choice of the reaction conditions. In addition to the wide range of useful reactions of 2, \(2^1\) compounds 1 react with carbon and heteroatom electrophiles with the assistance of Lewis acid \(2^3\) or fluoride ion. \(2^0\) Other attractive synthetic utilities of 1 exist in stereospecific alkene formation \(2^5\) and silicon-directed diastereoselective reactions. \(2^6\) Therefore, effective preparation of 1 is of increasing interest. Although a variety of synthetic methods for 1 have been reported, most of them need several steps via individual intermediates.

In the course of our studies to establish a convenient preparation of silylated reactive compounds using silylketenes 3, \(2^1\) we planned a one-pot preparation of the \(\alpha\)-silylketones 1 from 3. \(2^3, 2^4\) Thus, addition of carbanions 4 to the carbonyl carbon of 3 would generate silylated enolate anions A (route a), and then quenching with proton or alkyl halides 5 would afford \(\alpha\)-silylketones 1. However, the reaction of 3 with \(n\)-BuLi had been reported by Rathke et al. to cause proton abstraction (route b) exclusively generating the enolate anion B (Chart 1). \(2^5\) Other than this report, no studies on the reaction of 3 with carbanions 4 have ever been presented. \(2^6, 2^7\) Therefore, we focused on how to achieve the route a reaction. Very recently, we briefly communicated the use of organocerium reagents 4 (\(M = \text{CeCl}_3\)) cleanly solved this issue, leading to a one-pot synthesis of 1. \(2^8, 2^9\) Here we present full details of these studies.

**Results and Discussion**

As mentioned above, Rathke et al. reported that the reaction of (trimethylsilyl)ketene 3a with \(n\)-BuLi resulted in a complicated reaction without formation of any carbonyl compounds, due to preferential abstraction of the proton by \(n\)-BuLi. This was deduced because the same reaction run at \(-100^\circ\text{C}\) followed by quenching with trimethylsilyl chloride gave the bis(trimethylsilyl)ketene 6 (\(R^1 = \text{Me}\)) in 85% yield. \(2^{10}\) Though the use of bulkier (tert-butyldimethylsilyl)ketene 3c instead of 3a was expected to suppress the proton abstraction and to cause addition to the carbonyl group, our examination of the reaction of 3c and \(n\)-BuLi at \(-100^\circ\text{C}\) and quenching with trimethylsilyl chloride gave only the bis(trimethylsilyl)ketene 6 (\(R^1 = \text{tert-BuMe}_2\)) in 96% yield. \(2^{11}\) Attempts to use MeMgBr, Me₂CuLi, Et₃Al, or Et₂Zn for the reaction with 3c produced complex mixtures with little or none of the desired \(\alpha\)-silylketones 1. On the other hand, the organocerium reagent 4 (\(M = \text{CeCl}_3\)) \(2^{12}\) selectively added to the carbonyl group of 3c to afford 1 in high yield. For example, a tetrahydrofuran (THF) solution of 3c was slowly added over 10 min to a THF solution of \(n\)-BuCeCl₂, prepared from anhydrous CeCl₃ and \(n\)-BuLi by the usual method. The mixture was stirred for 1.5 h at \(-78^\circ\text{C}\), then the

![Chart 1](image-url)

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Table 1. Preparation of α-Silylketones

| Entry | Silylketene | Cerium reagent | Quenching method*  
(R'=X for method B) | α-Silylketone 1 |
<table>
<thead>
<tr>
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<tr>
<td></td>
<td>3</td>
<td>R=</td>
<td></td>
<td>R1=</td>
</tr>
<tr>
<td>1</td>
<td>3a</td>
<td>Ph</td>
<td>A</td>
<td>1a</td>
</tr>
<tr>
<td>2</td>
<td>3b</td>
<td>Me</td>
<td>A</td>
<td>1b</td>
</tr>
<tr>
<td>3</td>
<td>3b</td>
<td>n-Bu</td>
<td>A</td>
<td>1c</td>
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<tr>
<td>4</td>
<td>3b</td>
<td>Ph</td>
<td>A</td>
<td>1d</td>
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<tr>
<td>5</td>
<td>3c</td>
<td>Me</td>
<td>A</td>
<td>1e</td>
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<td>6</td>
<td>3c</td>
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<tr>
<td>7</td>
<td>3c</td>
<td>n-Pr</td>
<td>A</td>
<td>1g</td>
</tr>
<tr>
<td>8</td>
<td>3c</td>
<td>n-Bu</td>
<td>A</td>
<td>1h</td>
</tr>
<tr>
<td>9</td>
<td>3c</td>
<td>sec-Bu</td>
<td>A</td>
<td>1i</td>
</tr>
<tr>
<td>10</td>
<td>3c</td>
<td>n-Bu</td>
<td>B (MeI)</td>
<td>1j</td>
</tr>
<tr>
<td>11</td>
<td>3c</td>
<td>n-Bu</td>
<td>B (EtI)</td>
<td>1k</td>
</tr>
<tr>
<td>12</td>
<td>3c</td>
<td>n-Bu</td>
<td>B (EtBr)</td>
<td>1k</td>
</tr>
<tr>
<td>13</td>
<td>3c</td>
<td>n-Bu</td>
<td>(n-PrI)</td>
<td>1l</td>
</tr>
<tr>
<td>14</td>
<td>3c</td>
<td>n-Bu</td>
<td>B (CH&lt;sub&gt;2&lt;/sub&gt;=CHCH&lt;sub&gt;2&lt;/sub&gt;)</td>
<td>1m</td>
</tr>
<tr>
<td>15</td>
<td>3c</td>
<td>n-Bu</td>
<td>B (CH&lt;sub&gt;2&lt;/sub&gt;=CHCH&lt;sub&gt;2&lt;/sub&gt;)</td>
<td>1m</td>
</tr>
<tr>
<td>16</td>
<td>3c</td>
<td>n-Bu</td>
<td>B (PhCH&lt;sub&gt;2&lt;/sub&gt;Br)</td>
<td>1n</td>
</tr>
<tr>
<td>17</td>
<td>3c</td>
<td>n-Bu</td>
<td>B (EtO&lt;sub&gt;2&lt;/sub&gt;CCH&lt;sub&gt;2&lt;/sub&gt;Br)</td>
<td>1o</td>
</tr>
<tr>
<td>18</td>
<td>3c</td>
<td>Ph</td>
<td>A</td>
<td>1p</td>
</tr>
<tr>
<td>19</td>
<td>3c</td>
<td>Ph</td>
<td>B (MeI)</td>
<td>1p</td>
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* Quenching with saturated aqueous NH<sub>4</sub>Cl (method A) or R'=X for method B.

The advantage of the present method is as follows. Although silyl enol ethers are usually prepared from the corresponding ketones through base-induced enolization and subsequent O-silylation, regioselective enolization of asymmetric ketones having two similar alkyl groups, such as hexan-3-one 7 or its homologous congeners, is difficult. In fact, treatment of 7 by the usual method (lithium disopropylamide (LDA) in THF at -78°C and tert-butylmethylsilyl chloride with HMPTA at -78°C to room temperature) gave a mixture (64:36) of the two regioisomers 2r and 2s (Chart 2). On the other hand, the present method readily achieved a regiocontrolled synthesis of the two isomeric α-silylketones 1r and 1s. Thus, the reaction of 3c with n-PrCeCl<sub>2</sub> and subsequent quenching with MeI gave a 67% yield of 1r, and that with EtCeCl<sub>3</sub> and EtI gave the regioisomer 1s in 54% yield. Because selective conversion of α-silylketones to (E)- and (Z)-O-silyl enol ethers 2 has been developed, our method would provide an alternative and promising preparation of O-silyl enol ethers 2.

Thus, we have developed a convenient synthetic method for various types of α-silylketones featuring the operational convenience of silylketenes, the use of readily available organocerium reagents and alkyl halides, and a simple procedure.

**Experimental**

All boiling points are uncorrected. IR absorption spectra were recorded on JASCO HPR-102 and Shimadzu FTIR-8100 spectrometers. 1H-
NMR spectra were recorded on JEOL JNM-FX90 and Hitachi R-25HT spectrometers with CHCl₃ as an internal standard. Mass spectra (MS) and high-resolution mass spectra (HR-MS) were recorded at 70 or 20 eV with a direct inlet system on a JEOL JMS-HX100 spectrometer. E. Merck Silica gel 60 (230–400 mesh ASTM) was used for flash column chromatography. Anhydrous THF was obtained by distillation from sodium benzophenone ketyl. Silylketenes \(3a, 14a, 3b, 14b, 3c, 14c\) were prepared according to the reported methods. Anhydrous CeCl₃ was prepared from commercially available CeCl₃·7H₂O by means of the reported procedure.¹

**General Procedure for the Preparation of \(\alpha\)-Silylketones (1a–i, 1p)**

**(Method A)** Under a nitrogen atmosphere, dry THF (6 ml) was added to anhydrous CeCl₃ (490 mg, 2 mmol) and the resulting suspension was stirred overnight at room temperature, then cooled to –78 °C. n-BuLi (1.6 m hexane solution, 1.25 ml, 2 mmol) was added and the mixture was stirred for 1.5 h. A solution of \(3 (1.33 \text{ mmol})\) in dry THF (1 ml) was added gradually over 10 min, and the reaction mixture was stirred at –78 °C for 1.5 h. The reaction was quenched with saturated aqueous NH₄Cl, and the mixture was vigorously stirred for 10 min and then filtered through Celite. The filtrate was extracted with Et₂O three times, and the combined organic layer was washed with brine, dried with MgSO₄, and concentrated in vacuo to give \(I\). The yields of the products are shown in Table 1. The purity (≥95%) of \(Ia, e, h, n, p\) and thus obtained was determined by 250 MHz \(^1\)H-NMR analysis. Yields of relatively volatile products (1b, 1e) were determined by 250 MHz \(^1\)H-NMR analysis of crude products, which were contaminated only by THF. Distillation of these products gave analytically pure samples in 58% for (1b) and 60% for (1e) yields. Other products (1f, 1g) were purified by flash column chromatography (pentane-EtO).

1-(Trimethylsilyl)-1-phenylethylene-1-one (1a): A colorless oil; bp 65–70 °C (0.18 mmHg) (bath temp.): \[\text{lit.}^{10} 89–90°C (10 \text{mmHg})\]; IR (CHCl₃): 1655, 1595 cm⁻¹; \(^1\)H-NMR (CDCl₃) δ: 0.08 (9H, s, SiMe₃), 2.76 (2H, s, SiCH₂CO), 7.34–7.62 (2H, m, arom. H), 7.88–7.99 (2H, m, arom. H). MS m/z: 192 (M⁺), 177 (M⁺ – Me).

1-(Triethylsilyl)propan-2-one (1b): A colorless oil; bp 85–90 °C (10 mmHg) (bath temp.): \[\text{lit.}^{1, 10} 89–90°C (10 \text{mmHg})\]; IR (CHCl₃): 1680 cm⁻¹; \(^1\)H-NMR (CDCl₃) δ: 0.56–0.66 (6H, m, SiCH₂Et), 0.87–1.00 (9H, m, CH₃ x 3), 2.10 (3H, s, COCH₃), 2.23 (2H, s, SiCH₂CO), 172 (M⁺), 143 (M⁺ – Et).

1-(Tert-Butyldimethylsilyl)-1-phenylethylene-1-one (1i): A colorless oil; bp 125–130 °C (25 mmHg) (bath temp.); IR (CHCl₃): 1680 cm⁻¹; \(^1\)H-NMR (CDCl₃) δ: 0.55–0.71 (6H, m, SiCH₂Et), 0.85–1.02 (12H, m, CH₃ x 4), 1.31 (2H, sextet, J = 7.5 Hz, CH₂), 1.53 (2H, quartet, J = 7.5 Hz, CH₂), 2.19 (2H, s, SiCH₂CO), 2.35 (2H, t, J = 7.5 Hz, COCH₃). MS m/z: 183 (M⁺ – Et).

**General Procedure for the Preparation of \(\alpha\)-Silylketones (1j–o, 1q–s)**

**(Method B)** By the same procedure as described in method A, 3c (1.0 mmol) was treated with the organocatalyst, prepared from anhydrous CeCl₃ (370 mg, 1.5 mmol) and the organolithium reagent (1.5 mmol) in dry THF (4.5 ml). The reaction mixture was stirred at –78 °C for 1.5 h, and to it were added dry HMPA (1.5 ml) and alkyl halide 5 (5 mmol). The whole mixture was gradually warmed to room temperature and stirred overnight and then at 40 °C for 2h–1d. Work-up as described in method A gave a crude product, which was purified by flash column chromatography (pentane-EtO) to give pure \(\alpha\) in the yields shown in Table 1 or Chart 2.

1-(Tert-Butyldimethylsilyl)propan-3-one (1j): A colorless oil; bp 80–85 °C (20 mmHg) (bath temp.); IR (CHCl₃): 1670 cm⁻¹; \(^1\)H-NMR (CDCl₃) δ: –0.01 (3H, s, SiMe), 0.04 (3H, s, SiMe), 0.90 (3H, t, J = 7.5 Hz, CH₃), 0.86 (9H, s, tert-Bu), 2.10 (3H, d, J = 7.0 Hz, CH₃), 1.39 (2H, m, CH₃), 1.41–1.62 (2H, m, CH₂), 2.22–2.39 (2H, m, COCH₂), 2.52 (1H, q, J = 7.0 Hz, SiCH₂CO). MS m/z: 171 (M⁺ – tert-Bu).
Anal. Caled for C_{12}H_{22}O_5Si: C, 68.35; H, 12.35. Found: C, 68.43; H, 12.51.

3-(1-b-Butylmethylsilyl)octan-4-one (1k): A colorless oil; bp 105—110°C (8 mmHg) (bath temp); IR (CHCl_3): 1680 cm⁻¹; 1H-NMR (CDCl_3) δ: 0.98 (3H, s, SiMe), 1.11—1.15 (6H, 4 H, CH_2 x 2), 0.91—1.01 (7H, 2H, CH), 1.24—1.66 (5H, m, CH_2 x 2), 1.88—2.07 (1H, m, CH), 2.18—2.43 (3H, m, COCH_3, SiCHCO_2H). MS m/z: 227 (M⁺ → Me), 185 (M⁺ → tert-But), Anal. Caled for C_{15}H_{26}O_4Si: C, 69.35; H, 12.47. Found: C, 69.09; H, 12.48.

4-(1,1-Butylmethylsilyl)octan-5-one (1l): A colorless oil; bp 105—110°C (8 mmHg) (bath temp); IR (CHCl_3): 1680 cm⁻¹; 1H-NMR (CDCl_3) δ: 0.04 (3H, s, SiMe), 0.03 (3H, s, SiMe), 0.068 (3H, s, CH_3), 0.73 (7H, t, J = 7.0 Hz, CH), 1.21—1.69 (8H, m, CH_2 x 2), 2.32—2.61 (3H, m, COCH_3, SiCHCO_2H), 3.19—3.29 (2H, m, SiCHCO_2H), 7.50—7.57 (2H, m, arom. H). MS m/z: 254 (M⁺ → tert-But), Anal. Caled for C_{17}H_{30}O_5Si: C, 70.80; H, 11.80. Found: C, 70.45; H, 11.80.

4-(1,1-Butylmethylsilyl)pentan-1-one (1m): A colorless oil; bp 77—80°C (10 mmHg); IR (CHCl_3); 1685, 1640 cm⁻¹; 1H-NMR (CDCl_3) δ: 0.90 (3H, s, SiMe), 0.04 (3H, s, SiMe), 0.087 (3H, s, CH_3), 0.92 (9H, s, tert-But), 1.21—1.75 (4H, 4H, CH_2 x 2), 0.82—2.42 (2H, m, COCH_3, SiCHCO_2H), 2.53 (1H, dd, J = 12.0, 2.0 Hz, CHCO_2H), 2.63—2.76 (1H, m, CH_2CO_2H), 4.95 (ht, J = 17.0 Hz, 1H, br, CH), 6.57 (1H, ddd, J = 17.0, 10.6, 6.5 Hz, vinyl H); MS m/z: 254 (M⁺ → tert-But), Anal. Caled for C_{14}H_{22}O_3Si: C, 70.80; H, 11.80. Found: C, 70.45; H, 11.80.

Ethyl 3-(1,1-Butylmethylsilyl)-4-octoxoacetoacetate (1o): A colorless oil; bp 115—120°C (4 mmHg); IR (CHCl_3); 1725, 1690 cm⁻¹; 1H-NMR (CDCl_3) δ: 0.00 (3H, s, SiMe), 0.13 (3H, s, SiMe), 0.73 (7H, t, J = 7.8 Hz, CH), 1.63—2.33 (6H, m, CH_2 x 2), 2.60—3.39 (2H, m, CH_2CO_2H), 2.81—3.20 (2H, m, CH_2CO_2H), 4.80—5.54 (2H, 2H, CH_2SiMe_3), 6.66—6.77 (2H, m, arom. H); HR-MS Caled for C_{24}H_{37}O_5Si: M⁺+ 364.2220. Found: 364.2220.

8. The reported methods are based on the reaction of carboxylic acid derivatives with N-silyl carbamions,\(^{8,10,11}\) C-silylation of azanoles\(^{12}\) or ester enolates\(^{12}\) and successive conversion to ketones, migration from carbon-containing compounds prepared by other methods,\(^{10}\) oxidation of β-silyl alcohols,\(^{3,4,10,11}\) and Si-H insertion of diazo ketones.\(^{12}\)

References and Notes


The silylketenes are easy-to-handle, distillable liquid monomers, and can be stored for a long time without polymerization, in marked contrast to the parent ketene and alkylketenes.\(^{14}\)


16) Reaction of silyketenes with carbon nucleophiles, trimethylsilyl cyanide\(^{17a}\) and O-trimethylsilyl ketene acetals\(^{17a}\) has been reported. Other heteroatom nucleophiles\(^{14b,15a-c}\) have also been reported to react with silyketenes.

