Thiocarbonyl Ylides. VI.1) New Generation of Thiocarbonyl Ylides from Organosilicon Compounds Containing Sulfur and Their 1,3-Cycloadditions

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Thermolysis of bromo(trimethylsilyl)methyl trimethylsilylmethyl sulfide was found to give a thiocarbonyl ylide, the 1,3-cycloaddition of which proved a new method for the synthesis of tetrahydrothiophenes. The effect of the silyl group of the ylide on the regio- and stereoselectivity in these 1,3-dipolar cycloadditions is discussed.

Keywords—thiocarbonyl ylide; 1,3-cycloaddition; organosilicon compound; thermolysis; tetrahydrothiophene; regioselectivity

Thiocarbonyl ylides are useful intermediates not only in heterocyclic synthesis but also in carbon–carbon bond formation reactions. Although several methods for the generation of thiocarbonyl ylides have been reported,2) they are generally not convenient due to the difficulties of synthesizing the starting materials or limited applicability.

As mentioned in the preliminary communication,3) we have found a convenient method for generating thiocarbonyl ylides and for carrying out their 1,3-dipolar cycloaddition leading to tetrahydrothiophene derivatives by using organosilicon compounds. In this paper we present the details of this work.

Our strategy for the generation of thiocarbonyl ylides involved silicon–carbon bond cleavage,4) which would be accelerated by stabilization of the carbanion arising from the formation of a thiocarbonyl ylide. We designed an organosilicon compound containing sulfur, bromo(trimethylsilyl)methyl trimethylsilylmethyl sulfide (2a), which was easily prepared by bromination of bis(trimethylsilylmethyl) sulfide (1a) with N-bromosuccinimide (NBS). After several preliminary experiments, thermolysis of 2a in N,N-dimethylformamide (DMF) has been found to afford trimethylsilylthioaldehyde S-methylide (3). The results of initial experiments on the 1,3-cycloaddition of 3 to several symmetrical dipolarophiles are shown in Table I.
These reactions were carried out by heating 2a at 110 °C with dipolarophiles in DMF to give the corresponding 2-trimethylsilyltetrahydrothiophenes (4–9) in excellent yields. It is noteworthy that the reaction with cyclic dipolarophiles produced a single stereoisomer (entries 1–3). However, dimethyl fumarate or fumaronitrile gave a mixture of two possible stereoisomers, the major one of which was assumed to be the 2,3-trans isomer (entries 4 and 6), and dimethyl maleate gave a mixture of four possible isomers which may be formed by epimerization of the 3,4-cis isomers initially formed (entry 5). The possibility of cyclopropane ring formation by 1,1-cycloaddition via a carbene-like intermediate was definitely excluded on the basis of the proton and carbon-13 nuclear magnetic resonance (1H- and 13C-NMR) spectra of the products (Table IV); no signal was observed at the higher magnetic field characteristic of cyclopropane rings. This conclusion was supported by the finding that treatment of 4 with cesium fluoride in hexamethylphosphoramide (HMPA) containing a little water gave the corresponding desilylated tetrahydrothiophenes (10) in 73% yield.

From the mechanistic point of view, the stabilization of the β-cation by silicon5) promotes the formation of the sulfonium salt in the initial step, and the stabilization of the carbanion due to the formation of thiocarbonyl ylide aids the carbon–silicon bond cleavage by nucleophilic attack of the bromide anion on the silicon atom in the second step (Chart 1). Since we failed to obtain any cycloadduct by the reaction of α-bromo-α-trimethylsilylbenzyl

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**Table I. 1,3-Cycloaddition via Trimethylsilylthioaldehyde S-Methylide (3)**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Dipolarophile</th>
<th>Producta)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td><img src="entry1.png" alt="Image" /></td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td><img src="entry2.png" alt="Image" /></td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td><img src="entry3.png" alt="Image" /></td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>MeO₂C:C=CH₂C=CH₂</td>
<td><img src="entry4.png" alt="Image" /></td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>MeO₂C:C=CH₂C=CH₂</td>
<td><img src="entry5.png" alt="Image" /></td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td>MeO₂C:C=CH₂C=CH₂</td>
<td><img src="entry6.png" alt="Image" /></td>
<td>98</td>
</tr>
</tbody>
</table>

a) The ratio of the isomers is given in parentheses. b) A mixture of 3,4-cis and 3,4-trans isomers.
phenyl sulfide with a dipolarophile under similar conditions, the silyl group at the carbon without bromine seems to play a role as a leaving group.

One of the novel features in this reaction is that the generated thiocarbonyl ylide has a silyl group at the terminus. Therefore, in order to reveal the effects of the silyl group on the regio-

**Table II. Effect of the Silyl Group on Regio- and Stereoselectivity in 1,3-Dipolar Cycloaddition**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reagent</th>
<th>Dipolarophile</th>
<th>Product (Ratio of isomers)</th>
<th>Total yield (°)</th>
</tr>
</thead>
</table>
| 7     | Me₅SiCHSCH₂SiMe₃ Br \( \text{2a} \) | H₂C=CHCO₂Me | \( \begin{array}{ll}
11a & \text{SiMe₃} \\
11b & \text{SiMe₃}
\end{array} \) (3 : 1) | 52 |
| 8     | \textbf{2a} | H₂C=CHCN | \( \begin{array}{ll}
12a & \text{SiMe₃} \\
12b & \text{SiMe₃}
\end{array} \) (3 : 2) | 56 |
| 9     | Me₅Si-C-SCH₂SiMe₃ Br \( \text{2b} \) | H₂C=CHCO₂Me | \( \begin{array}{ll}
13a & \text{SiMe₃} \\
13b & \text{SiMe₃}
\end{array} \) (7 : 6) | 46 |
| 10    | Me₅Si-C-SCH₂SiMe₃ Br \( \text{2c} \) | H₂C=CHCO₂Me | \( \begin{array}{ll}
14a & \text{SiMe₃} \\
14b & \text{SiMe₃}
\end{array} \) (5 : 2) | 72 |
| 11    | \textbf{2c} | H₂C=CHCN | \( \begin{array}{ll}
15a & \text{SiMe₃} \\
15b & \text{SiMe₃}
\end{array} \) (3 : 1) | 87 |
| 12    | \textbf{2c} | MeO₂C=CHCO₂Me | \( \begin{array}{ll}
16a & \text{SiMe₃} \\
16b & \text{SiMe₃}
\end{array} \) (4 : 3) | 95 |

\( a \) A mixture of two possible stereoisomers.

\[ \text{H}_2\text{C} = \text{CHCO}_2\text{Me} \xrightarrow{\text{Raney Ni}} \begin{array}{c}
\text{CO}_2\text{Me} \\
\text{SiMe}_3
\end{array} + \begin{array}{c}
\text{MeO}_2\text{C} \\
\text{SiMe}_3
\end{array} \]

\[ \text{3 : 1} \]

Chart 3

One of the novel features in this reaction is that the generated thiocarbonyl ylide has a silyl group at the terminus. Therefore, in order to reveal the effects of the silyl group on the regio-
and stereoselectivity in 1,3-dipolar cycloadditions, we examined the 1,3-cycloadditions of 2a–c to several unsymmetrical dipolarophiles, and the results are summarized in Table II. Entry 7 (Table II) shows a clear regioselective effect due to the trimethylsilyl group. For the structure elucidation, 11a and 11b were desulfurized quantitatively with Raney Ni to 2-(methoxycarbonyl)butyltrimethylsilane (17a) and its 3-isomer (17b), respectively. The 1H-NMR spectrum of 17a shows a triplet at 0.87 ppm (J = 6.8 Hz) due to the terminal methyl. On the other hand, that of 17b shows a doublet at 1.15 ppm (J = 7.1 Hz) due to the corresponding terminal methyl. The ratio of 11a to 11b was determined by gas chromatography (GC) of the mixture of 17a and 17b obtained from the crude cycloadduct. The structures and ratio of the isomers in entries 8 and 9 were determined similarly. The regioselectivity observed in entry 9 is not negligible in view of the fact that the 2,2,3-trisubstituted cycloadduct was produced in a slight excess in spite of the large sterical hindrance of the two trimethylsilyl groups. Compound 2c reacted with methyl acrylate to give the corresponding tetrahydrothiophenes (14a and 14b); the product was isolated as a single regio isomer but a mixture of two stereoisomers. The 1H-NMR spectra show two characteristic signals: 14a, 3.63 ppm (1H, dd, J = 4.4, 5.6 Hz, -CH), 3.75 ppm (3H, s, OCH3); 14b, 3.52 ppm (1H, t, J = 6.4 Hz, -CH), 3.49 ppm (3H, s, OCH3). Shift of the signal due to the ester methyl of 14b to higher magnetic field indicates that the methoxycarbonyl group at the 3-position is cis to the phenyl group at the 2-position. The structures of 15a and 15b were established by comparison of their 1H-NMR spectra with those of 14a and 14b, respectively.

We reported previously that the phenyl group at the dipole terminus affected the stereoselectivity as well as the regioselectivity in the 1,3-dipolar cycloaddition of azomethine ylides. Therefore, the high regioselectivity in entries 10 and 11 seems to be mostly owing to the effect of the phenyl group. Entries 10—12 suggest that the stereoselectivity may be attributed to the steric effect of the silyl group on the conformation of the neighboring phenyl group.

An examination of these effects in terms of molecular orbital theory will be reported in the near future.

Experimental

All melting points and boiling points are uncorrected. 1H-NMR and 13C-NMR spectra were taken at 90 MHz with a JEOL FX-90Q spectrometer. Chemical shifts are expressed in δ (ppm) values. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. Mass spectra (MS) were obtained on a Hitachi RMS-4 mass spectrometer.

Bis(trimethylsilylmethyl) Sulfide (1a)—Chloromethyltrimethylsilane (12.3 g, 0.1 mol) and tetrabutylammonium bromide (200 mg) were added to an aqueous solution of sodium sulfide pentahydrate (12 g, 0.05 mol) in 20 ml of water. The mixture was stirred at refluxing temperature for 5 h, then allowed to cool. The organic layer was separated and the aqueous layer was extracted with hexane. The combined hexane solution was dried over MgSO4 and concentrated under reduced pressure. The residue was subjected to distillation to give a colorless oil, bp 83—84 °C (15 mmHg), 8.8 g (86%). 1H-NMR (CDCl3): δ: 0.07 (18H, s, Si(CH3)3), 1.80 (4H, s, -CH2-). Anal. Calcd for C8H22SSi2: C, 46.53; H, 10.74. Found: C, 46.69; H, 10.83.

Bis(trimethylsilylmethyl) Trimethylsilylmethyl Sulfide (1b)—A hexane solution of sec-butyllithium (23 ml of 1.3 M solution) was added to a solution of bis(trimethylsilylmethyl) sulfide (1a) (4.1 g, 20 mmol) and tetramethylethylenediamine (TMEDA) (2.3 g, 20 mmol) in tetrahydrofuran (THF) (50 ml) with stirring at 0 °C. After the whole had been stirred for 30 min, a solution of chlorotrimethylsilane (2.2 g, 20 mmol) in THF (10 ml) was added dropwise. The solution was stirred for 1 h at 0 °C and for an additional 1 h at room temperature, and then poured into cold water. The organic product was extracted with hexane. The extract was dried over MgSO4 and evaporated under reduced pressure. The residual liquid was subjected to column chromatography on silica gel with hexane to give a colorless oil, bp 83—84 °C (15 mmHg), 8.8 g (86%). 1H-NMR (CDCl3): δ: 0.07 (18H, s, Si(CH3)3), 1.80 (2H, s, -CH2-). Anal. Calcd for C11H30SSi3: C, 47.41; H, 10.85. Found: C, 47.54; H, 10.92.

α-(Trimethylsilyl)benzyl Trimethylsilylmethyl Sulfide (1c)—A solution of chloromethyltrimethylsilane (3.1 g, 25 mmol) in THF (5 ml) was added dropwise to a mixture of sodium α-(trimethylsilyl)benzylthiolate [prepared from α-(trimethylsilyl)benzylthiolate (4.9 g, 25 mmol), sodium hydride (35 mmol eq), and THF (30 ml)] with stirring in an iced-bath. After being stirred overnight at room temperature, the reaction mixture was poured into cold water and
extracted with benzene. The benzene solution was dried over MgSO₄ and concentrated under reduced pressure. The residual oil was subjected to column chromatography on silica gel with hexane to give a colorless oil, 4.6 g (65%). ¹H-NMR (CDCl₃) 6: 0.07 (18H, s, 2Si(CH₃)₃), 1.64 (2H, s, -CH₂-), 3.26 (1H, s, -CH), 7.26 (5H, br s, C₆H₅). Anal. Calcd for C₁₄H₂₆SSi₂: C, 59.50; H, 9.27. Found: C, 59.72; H, 9.06.

General Procedure for Bromination of la-c: N-Bromosuccinimide (3.6 g, 20 mmol) was added in portions to a solution of la-c (20 mmol) in carbon tetrachloride (40 ml) with stirring at room temperature. After the mixture had been stirred overnight, the precipitate was removed by filtration. The filtrate was concentrated under reduced pressure (followed by extraction with petroleum ether, if necessary) to give quantitatively enough pure product to be used in the subsequent reaction without further purification. 2a: ¹H-NMR (CDCl₃) δ: 0.07 (18H, s, Si(CH₃)₃), 1.64 (2H, s, -CH₂-), 3.26 (1H, s, -CH), 7.26 (5H, br s, C₆H₅). Anal. Calcd for C₁₄H₂₆SSi₂: C, 59.50; H, 9.27. Found: C, 59.72; H, 9.06.

### TABLE III. Analytical Data for 2-Trimethylsilyltetrahydrothiophenes (4—7, 9)

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>mp °C (Recryst. solv.⁹) or bp °C (mmHg)</th>
<th>MS m/z (M⁺)</th>
<th>Formula</th>
<th>Analysis (%) Calcd (Found)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>108—109 (IPE)</td>
<td>305</td>
<td>C₁₄H₁₉NO₂SSi</td>
<td>58.98 6.27 4.59</td>
</tr>
<tr>
<td>5</td>
<td>98—99 (1)</td>
<td>243</td>
<td>C₁₀H₁₇NO₂SSi</td>
<td>49.33 7.04 5.76</td>
</tr>
<tr>
<td>6</td>
<td>129—130 (IPE)</td>
<td>230</td>
<td>C₉H₁₄O₂SSi</td>
<td>46.93 6.13 5.40</td>
</tr>
<tr>
<td>7a</td>
<td>123—124 (8)</td>
<td>276</td>
<td>C₁₁H₂₉O₄SSi</td>
<td>47.80 7.29 (47.68 7.21)</td>
</tr>
<tr>
<td>7b</td>
<td>Oil⁹</td>
<td>276</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9a</td>
<td>80—82 (IPE)</td>
<td>210</td>
<td>C₈H₁₄N₂SSi</td>
<td>51.39 6.71 13.32</td>
</tr>
<tr>
<td>9b</td>
<td>82—83 (IPE)</td>
<td>210</td>
<td>C₁₄H₁₆N₂SSi</td>
<td>51.39 6.71 13.32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>¹H-NMR (CDCl₃) δ (J = Hz)</th>
<th>¹³C-NMR (CDCl₃) δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>-1.2 (q), 38.4 (t), 41.4 (d), 50.2 (d), 51.0 (d)</td>
<td>-2.3 (q), 58.3 (t), 71.8 (d), 120.9 (d), 123.4 (d), 51.0 (d), 51.0 (d)</td>
</tr>
<tr>
<td>5</td>
<td>126.6 (d), 128.8 (d), 129.2 (d), 132.3 (s)</td>
<td>176.6 (s), 177.4 (s)</td>
</tr>
<tr>
<td>7a</td>
<td>-2.3 (q), 1.6 (q), 58.3 (t), 71.8 (d), 120.9 (d), 123.4 (d), 51.0 (d), 51.0 (d)</td>
<td>-3.3 (q), 58.3 (t), 71.8 (d), 120.9 (d), 123.4 (d), 51.0 (d), 51.0 (d)</td>
</tr>
<tr>
<td>7b</td>
<td>173.5 (s), 174.3 (s)</td>
<td>-2.8 (q), 33.1 (t), 36.4 (d), 52.0 (d), 52.2 (d), 52.2 (d)</td>
</tr>
<tr>
<td>9a</td>
<td>51.3 (q), 54.5 (q), 172.2 (d), 173.0 (s)</td>
<td>51.3 (q), 54.5 (q), 172.2 (d), 173.0 (s)</td>
</tr>
<tr>
<td>9b</td>
<td>117.0 (2 × s)</td>
<td>-2.2 (q), 34.0 (t), 35.0 (d), 39.2 (d), 40.9 (d)</td>
</tr>
</tbody>
</table>

### TABLE IV. NMR Spectral Data for 2-Trimethylsilyltetrahydrothiophenes (4—7, 9)

a) IPE = isopropyl ether. b) The amount of this product was too small for distillation.
2 x Si(CH₃)₃, 2.01 (2H, s, -CH₂-). 2c: ¹H-NMR (CDCl₃) δ: 0.09 (9H, s, Si(CH₃)₃), 0.17 (9H, s, Si(CH₃)₃), 1.85 (2H, brs, -CH₂-), 7.11—7.74 (5H, m, C₆H₅).

**General Procedure for 1,3-Cycloaddition of 2a to Symmetrical Dipolarophiles (Table I)**—A solution of 2a (4.5 mmol) and a dipolarophile (3 mmol) in DMF (2 ml) was stirred for 2 h at 110 °C. The reaction solution was diluted with benzene (50 ml), washed with saturated aqueous sodium chloride, and then dried over MgSO₄. After removal of the benzene, the residue was subjected to column chromatography on silica gel with hexane-isopropyl ether (IPE) to give the corresponding cycloadduct. Yields and analytical and spectral data for the products are listed in Tables I, III, and IV.

In entry 5 (Table I), the ¹C-NMR spectrum of the product (8) revealed that it was a mixture of four isomers, two of which were identified as 7a and 7b. The GC-MS of each peak of 8 showed the same M⁺ peak at 276 (m/z) and similar fragment patterns.

**Desilylation of 4**—A mixture of 4 (300 mg, 1 mmol) and cesium fluoride (150 mg, 1 mmol) in hexamethylphosphoramide (4 ml) containing a drop of water was stirred at 80 °C for 150 min. The reaction mixture was diluted with benzene and washed with water and then saturated aqueous sodium chloride. The benzene solution was dried over MgSO₄ and concentrated under reduced pressure to give a solid, 180 mg (77%). 10: mp 152-153 °C (EtOH). ¹H-NMR (CDCl₃) δ: 0.19 (9H, s, Si(CH₃)₃), 2.12-2.39 (2H, m, -CH₂-), 2.69-3.20 (2H, com. ddt, dt, SCH₂-), 3.49 (1H, s, OCH₃), 3.52 (1H, t, J=5.6 Hz, -CH), 7.04-7.56 (6H, m, C₆F₁₅). ¹³C-NMR (CDCl₃) δ: -1.7 (q), 29.7 (t), 33.5 (t), 51.3 (q), 54.0 (s), 55.2 (d), 125.1 (d), 127.5 (2 x d), 128.2 (2 x d), 142.1 (s), 172.8 (s). 15a: mp 70-72 °C. ¹H-NMR (CDCl₃) δ: 0.02 (9H, s, Si(CH₃)₃), 1.75—2.1 (1H, ddt, J=5.6, 7.3, 13.0 Hz, -CH₂-), 2.07—2.42 (1H, dddt, 5.6, 7.3, 13.0 Hz, -CH₂-), 2.61-2.86 (1H, ddt, J=5.6, 7.3, 10.7 Hz, S-CH₂-), 2.86-2.98 (1H, dt, J=7.3, 10.7 Hz, S-CH₂-), 3.56 (1H, t, J=5.6 Hz, S-CH₂-), 7.04-7.56 (5H, m, C₆H₅). ¹³C-NMR (CDCl₃) δ: -1.6 (q), 29.9 (t), 35.2 (t), 43.1 (d), 53.5 (s), 120.9 (s), 126.1 (s), 128.2 (2 x s), 143.5 (s). Anal. Caled for C₁₄H₁₉NSSi: C, 64.31; H, 7.21; N, 5.42. 15b: mp 105—106 °C. ¹H-NMR (CDCl₃) δ: 0.11 (9H, s, Si(CH₃)₃), 1.96—2.63 (2H, m, -CH₂-), 2.71—3.25 (2H, m, S-CH₂-), 3.41—3.56 (1H, dd, J=5.6, 7.3 Hz, S-CH₂-), 6.99—7.69 (5H, m, C₆H₅). ¹³C-NMR (CDCl₃) δ: -2.1 (q), 28.9 (t), 33.3 (t), 40.7 (d), 52.9 (s), 119.7 (s), 126.4 (d), 127.9 (2 x d), 128.2 (2 x d), 140.4 (s). Anal. Caled for C₁₄H₁₉NSSi: C, 64.31; H, 7.27; N, 5.28.

In entry 12, the structures of 16a and 16b were determined on the basis of the NMR spectra and the ratio of 16a to 16b was determined by gas chromatographic analysis. 16a: oil. ¹H-NMR (CDCl₃) δ: 0.19 (9H, s, Si(CH₃)₃), 2.70—3.36 (4H, m, -CH₂-CH₂-), 3.65 (3H, s, OCH₃), 3.67 (3H, s, OCH₃), 7.07—7.74 (5H, m, C₆H₅). ¹³C-NMR (CDCl₃) δ: -1.5 (q), 32.3 (t), 51.6 (d), 51.9 (q), 52.2 (q), 53.6 (s), 60.6 (d), 125.8
(d), 127.6 (2 × d), 128.0 (2 × d), 144.4 (s), 171.7 (s), 173.1 (s).

Acknowledgement The authors are grateful to Dr. T. Katori, Central Research Laboratories of S S Pharmaceutical Co., Ltd., for high-resolution MS measurements.

References and Notes

7) The $^1$H-NMR signals of an ester methyl oriented cis to a phenyl on a 5-membered ring are usually shifted to higher magnetic field due to the shielding effect of the phenyl group: M. Joucla, D. Grée, and J. Hamelin, Tetrahedron, 29, 2531 (1973).