

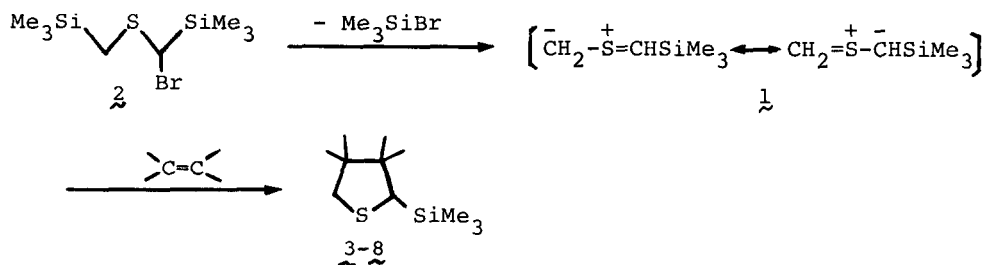
NEW GENERATION OF THIOCARBONYL YLIDE AND ITS 1,3-CYCLOADDITION  
 LEADING TO TETRAHYDROTHIOPHENE DERIVATIVES<sup>1)</sup>

Yoshiyasu Terao, Masaki Tanaka, Nobuyuki Imai, and Kazuo Achiwa\*  
 Shizuoka College of Pharmacy, 2-2-1 Oshika, Shizuoka 422, Japan

Abstract: Thiocarbonyl ylide was found to be generated by thermolysis of bromo(trimethylsilylmethylthio)methyltrimethylsilane and its 1,3-cycloaddition provided a new method for synthesis of tetrahydrothiophenes.

Thiocarbonyl ylides are synthetically important species<sup>2)</sup> which can be generated by the thermal extrusion of nitrogen from thiadiazolidines<sup>3)</sup> and of carbon dioxide from some phenyl-substituted 1,3-oxathiolan-5-ones<sup>4)</sup> or by Pummerer rearrangement of certain sulfoxides<sup>5)</sup> yielding thiirans or cycloadducts. Huisgen and Xingya<sup>6)</sup> have recently reported a new thiocarbonyl ylide produced from thiobenzophenone and diazoalkanes. Unfortunately, these methods seem not to be convenient due to the difficulty of the starting material synthesis or lack of the generality of these reactions.

We wish to describe here a new and simple generation of the thiocarbonyl ylide (1) by the thermal extrusion of trimethylsilyl bromide<sup>7)</sup> from bromo(trimethylsilylmethylthio)methyltrimethylsilane (2) and its 1,3-cycloaddition to conjugated olefins leading to tetrahydrothiophene derivatives in excellent yields as shown below.



The starting material (2) was easily prepared by bromination<sup>8)</sup> of bis(trimethylsilylmethyl)sulfide with N-bromosuccinimide. After preliminary experiments 1,3-cycloaddition of 2 was found to proceed smoothly under such conditions as described in a following typical procedure.

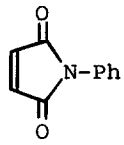
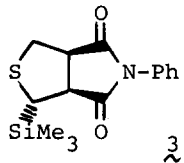
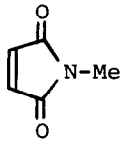
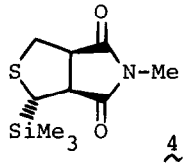
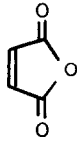
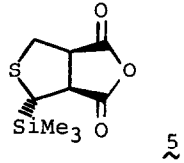
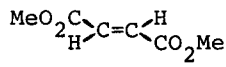
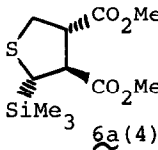
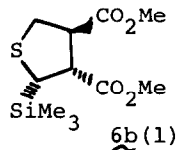
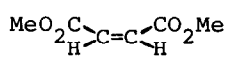
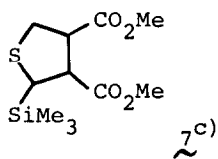
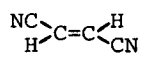
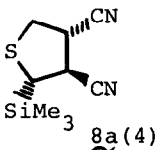
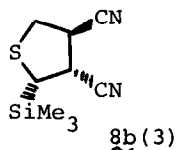
A solution of 2 (4.5 mmol) and N-phenylmaleimide (3 mmol) in dried dimethylformamide (DMF) (2 ml) was stirred for 2 hours with heating at 110 °C. The reaction solution was diluted with benzene (50 ml) and washed with saturated aqueous NaCl, and dried over MgSO<sub>4</sub>. After removal of the benzene, the residue was subjected to column chromatography (silica gel, hexane/iso-Pr<sub>2</sub>O = 1/4 as an eluent) to give the pure product (3) in 95% yield. 3: mp 108-109 °C, IR(KBr) cm<sup>-1</sup>; 1786, 1717, MS m/z; 305 (M<sup>+</sup>), <sup>1</sup>H-NMR δ (CDCl<sub>3</sub>); 2.56(1H, dd, J= 1.2, 6.8 Hz, Me<sub>3</sub>SiCH<sub>2</sub>), 2.88-3.16, 3.43-3.65(4H, m, the other ring protons), 7.16-7.53(5H, m, C<sub>6</sub>H<sub>5</sub>), <sup>13</sup>C-NMR δ (CDCl<sub>3</sub>); -1.24(q), 38.4(t), 41.4(d), 50.2(d), 51.0(d), 126.6(d), 128.8(d), 129.2(d), 132.3(s), 176.6(s), 177.4(s).

The possibility of cyclopropane ring formation by 1,1-cycloaddition via a carbene-like intermediate was definitely excluded on the basis of the <sup>1</sup>H- and <sup>13</sup>C-NMR spectra of the product, in which no signal was observed at the higher magnetic field characteristic of cyclopropane rings. This conclusion was also proved by a following experiment. Treatment of 3 with cesium fluoride in hexamethylphosphoramide containing a little water gave the corresponding desilylated tetrahydrothiophene derivative<sup>9)</sup> in a good yield.

Table 1 presents the representative data obtained by 1,3-cycloaddition to several dipolarophiles. In general, these reactions proceeded under the mild conditions and yields of the cycloadducts are extremely high. Furthermore, it is noticeable that the reaction with cyclic dipolarophile produced the single product, tetrahydrothiophenes with 2-exo-trimethylsilyl group<sup>10)</sup> (entries 1, 2, and 3). However, dimethyl fumarate or fumaronitrile gave a mixture of two possible stereoisomers, where the major one 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 resulted by an epimerization of the 3,4-cis isomers initially formed (entry 5).

It should be noted that this experimentally simple method is a first example of using an organosilicon compound as a synthon of thiocarbonyl ylide. Further investigations on stereo- and regioselectivity of the present reaction and the mechanistic roles of non-eliminated trimethylsilyl group of 2 in generation of thiocarbonyl ylide are under way.

Table 1. 1,3-Cycloaddition<sup>a)</sup> via the Thicarbonyl Ylide

| Entry | Dipolarophile   | Product <sup>b)</sup>   | Yield (%)   |    |
|-------|---|---|---|----|
| 1     |    |              | 95  |    |
| 2     |    |              | 96  |    |
| 3     |    |              | 91  |    |
| 4     |   | <br>6a (4)  | <br>6b (1)  | 90 |
| 5     |  | <br>7c)    | 94  |    |
| 6     |  | <br>8a (4) | <br>8b (3) | 98 |

a) Reaction conditions: molar ratio;  $\frac{2}{\text{dipolarophile}} = 1.5$ , solvent; DMF, temp.; 110 °C, time; 2 hours.

b) Ratio of the isomers is described in parentheses. All new compounds gave IR, NMR, and mass spectral data which are consistent with the structures proposed.

c) This product was isolated as a mixture of 3,4-cis and 3,4-trans isomers.

## REFERENCES AND NOTES

- 1) Thiocarbonyl Ylides. I.
- 2) D. R. Hogg, Ed., "Organic Compounds of Sulphur, Selenium, and Tellurium", The Royal Society of Chemistry, London, Vol. 2, pp 222-223 (1972), Vol. 3, pp 246-248 (1975), Vol. 4, pp 89-90 (1977), Vol. 6, pp 87-89 (1981).
- 3) R. M. Kellogg and S. Wassenaar, *Tetrahedron Lett.*, 1970, 1987; R. M. Kellogg, S. Wassenaar, and J. Buter, *ibid.*, 1970, 4689; J. Buter, S. Wassenaar, and R. M. Kellogg, *J. Org. Chem.*, 37, 4045 (1972); R. M. Kellogg and W. P. Prins, *ibid.*, 39, 2366 (1974).
- 4) T. B. Cameron and H. W. Pinnick, *J. Am. Chem. Soc.*, 102, 744 (1980).
- 5) M. Ikeda, Y. Miki, S. Kaita, Y. Nishikawa, and Y. Tamura, *J. Chem. Soc. Perkin I*, 1977, 44; M. Ikeda, Y. Tamura, M. Yamagishi, K. Goto, T. Niiya, and K. Sumoto, *Heterocycles*, 22, 981 (1984).
- 6) R. Huisgen and Li Xingya, *Heterocycles*, 20, 2363 (1983).
- 7) The similar desilylation process has been employed recently for generation of azomethine ylide: E. Vedjes and G. R. Martinez, *J. Am. Chem. Soc.*, 101, 6452 (1979); K. Achiwa and M. Sekiya, *Chem. Lett.*, 1981, 1213; *Tetrahedron Lett.*, 23, 2589 (1982); K. Achiwa, N. Imai, T. Inaoka, and M. Sekiya, *Chem. Pharm. Bull.*, 32, 2878 (1984); A. Hosomi, Y. Sakata, and H. Sakurai, *Chem. Lett.*, 1984, 1117; K. Achiwa, N. Imai, T. Motoyama, and M. Sekiya, *ibid.*, 1984, 2041; A. Padwa, G. Haffmanns, and M. Tomas, *J. Org. Chem.*, 48, 3314 (1984); Y. Terao, H. Kotaki, N. Imai, and K. Achiwa, *Chem. Pharm. Bull.*, 33, 896 (1985), and references cited therein.
- 8) N-Bromosuccinimide (0.05 mol) was added in portions to a solution of bis(trimethylsilylmethyl)sulfide (0.05 mol) in 50 ml of carbon tetrachloride with stirring. The reaction mixture was stirred overnight at room temperature. After usual workup, 2 was obtained as an almost pure oil without purification in 98% yield.  $^1\text{H-NMR } \delta$  ( $\text{CDCl}_3$ ); 0.11(9H, s,  $\text{Si}(\text{CH}_3)_3$ ), 0.23(9H, s,  $\text{Si}(\text{CH}_3)_3$ ), 1.83(1H, d,  $J=12.7$  Hz,  $\text{SCH}_A\text{Si}$ ), 2.31(1H, d,  $J=12.7$  Hz,  $\text{SCH}_B\text{Si}$ ), 4.68(1H, s,  $\text{SCHBr}$ ),  $^{13}\text{H-NMR } \delta$  ( $\text{CDCl}_3$ ); -2.27(q), -1.62(q), 21.8(t), 58.3(d).
- 9) Tetrahydrothiophene-3,4-N-phenyldicarboxyimide: mp 152-153 °C (from EtOH), IR(KBr)  $\text{cm}^{-1}$ ; 1780, 1715,  $^1\text{H-NMR } \delta$  ( $\text{CDCl}_3$ ); 2.88-3.64(6H, m, ring protons), 7.15-7.56(5H, m,  $\text{C}_6\text{H}_5$ ),  $^1\text{H-NMR } \delta$  ( $\text{CDCl}_3$ ); 36.5(2xt), 48.5(2xd), 126.5(2xd), 128.7(d), 129.1(2xd), 132.5(s), 177.1(2xs). This result also suggests that various 2-substituted tetrahydrothiophenes (e.g., biotin) can be derived from these 2-trimethylsilylated products by the electrophilic substitution in the presence of fluoride anion.
- 10) In the  $^1\text{H-NMR}$  spectrum of 3, the coupling constant (6.8 Hz) of the proton on C-2 indicated coupling to the cis proton on adjacent carbon based on comparison with that of analogous compound, 2-phenylpyrrolidine-3,4-N-methyldicarboxyimide (cis;  $J_{2,3} = 7.6$  Hz, trans;  $J_{2,3} < 4$  Hz): K. Achiwa, K. Sugiyama, and M. Sekiya, *Chem. Pharm. Bull.*, in press.

(Received in Japan 7 March 1985)