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# EFFECT OF A SILYL GROUP ON THE REGIO- AND STEREOSELECTIVITY IN 1,3-DIPOLAR CYCLOADDITION[1]

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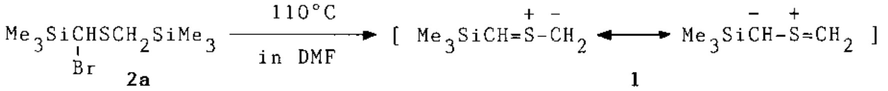
Abstract ——— Certain effect of a silyl group on the regio- and stereoselectivity in 1,3-dipolar cycloaddition has been demonstrated by cycloaddition of the thiocarbonyl ylide with a silyl group at the termini to unsymmetrical dipolarophiles.

Application of organosilicon compounds in pericyclic reactions[2] has grown during the last ten years. Especially, a silyl group has been utilized in 1,3-dipolar cycloadditions[3] as an excellent leaving group to generate the dipole species. However, the effect of a silyl group on the regio- and stereoselectivity, which is great importance for further synthetic application, has been unexplored. We now wish to report the first demonstration of the effect of a silyl group on the selectivity in 1,3-dipolar cycloadditions.

In preceding communication[4], we discribed the convenient generation of a new thiocarbonyl ylide (**1**) from bromo(trimethylsilyl)methyltrimethylsilylmethylsilane (**2a**). The dipole species 1 with a trimethylsilyl group at the termini is well suited for the investigation on the effect of a silyl group.[5]



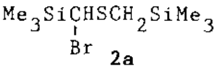
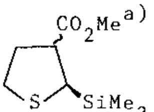
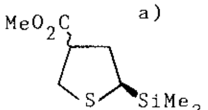
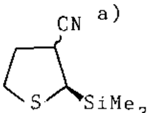
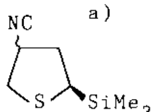
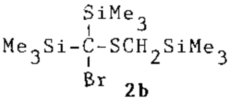
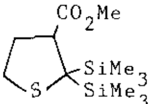
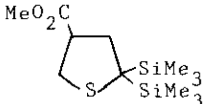
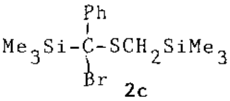
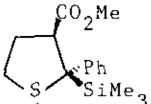
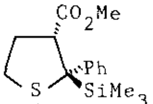
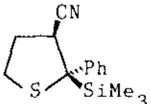
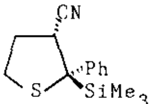
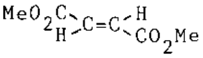
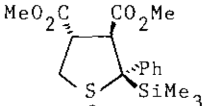
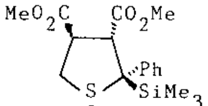
$$\mathrm{Me_3Si\underset{Br}{C}HSCH_2SiMe_3} \xrightarrow[\text{in DMF}]{110°\mathrm{C}} [\ \mathrm{Me_3SiCH{=}\overset{+}{S}{-}\overset{-}{C}H_2} \longleftrightarrow \mathrm{Me_3Si\overset{-}{C}H{-}\overset{+}{S}{=}CH_2}\ ]$$

**2a** **1**

Our results of the cycloadditions of **1** to several unsymmetrical dipolarophiles are summerized in Table 1.

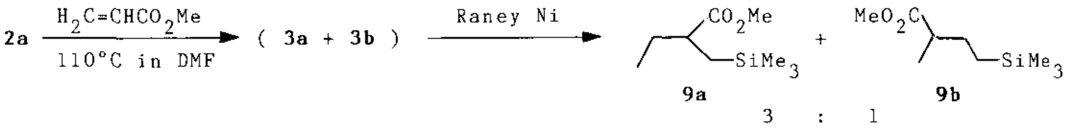
The reaction was generally carried out as follows: A solution of **2a** (3 mmol) and a dipolarophile (2 mmol) in N,N-dimethylformamide (DMF)(10 ml) was heated at 110°C for 2 h with stirring. After the usual workup, the product was isolated by column chromatography (silica gel, diisopropyl ether/hexane = 1/20 as an eluent). Entry 1 (Table 1) shows the obvious regioselection due to the substitution of a

Table 1. Regio- and Stereoselectivity in 1,3-Dipolar Cycloaddition via Thiocarbonyl Ylide

| Entry No. | Reagent | Dipolarophile | Product (Ratio of isomers) | Total yield (%) |
|---|---|---|---|---|
| 1 |  $\mathrm{Me_3Si\underset{Br}{C}HSCH_2SiMe_3}$ **2a** | $\mathrm{H_2C{=}CHCO_2Me}$ |  **3a** ( 3 : 1 )  **3b** | 52 |
| 2 | **2a** | $\mathrm{H_2C{=}CHCN}$ |  **4a** ( 3 : 2 )  **4b** | 56 |
| 3 |  $\mathrm{Me_3Si{-}\underset{Br}{\overset{SiMe_3}{C}}{-}SCH_2SiMe_3}$ **2b** | $\mathrm{H_2C{=}CHCO_2Me}$ |  **5a** ( 7 : 6 )  **5b** | 46 |
| 4 |  $\mathrm{Me_3Si{-}\underset{Br}{\overset{Ph}{C}}{-}SCH_2SiMe_3}$ **2c** | $\mathrm{H_2C{=}CHCO_2Me}$ |  **6a** ( 5 : 2 )  **6b** | 72 |
| 5 | **2c** | $\mathrm{H_2C{=}CHCN}$ |  **7a** ( 3 : 1 )  **7b** | 87 |
| 6 | **2c** |  $\mathrm{MeO_2CHC{=}CHCO_2Me}$ |  **8a** ( 4 : 3 )  **8b** | 95 |

a) Mixture of two possible stereoisomers.

trimethylsilyl group. For the structure elucidation, **3a** and **3b** were desulfurized quantitatively with Raney Ni to 2-(methoxycarbonyl)butyltrimethylsilane (**9a**) and its 3-isomer (**9b**), respectively. Their $^1$H-NMR spectra[6] clearly established their structures.



*The ratio of* **3a** *to* **3b** *was determined on the basis of the gas chromatogram* (20% SE-30 on Chrom. W, 80-100 mesh) of the mixture of **9a** and **9b** obtained from the crude cycloadduct. The structures and the ratios of isomers in entries 2 and 3 were determined by a method similar to that described above. The regioselectivity observed in entry 3 is never negligible in view of the fact that 2,2,3-trisubstituted cycloadduct was produced in a slight excess in spite of the large steric hindrance of two trimethylsilyl groups.

In order to clarify the stereoselectivity we designed a new dipole generating agent (**2c**)[7]. Compound **2c** reacted with methyl acrylate to give the corresponding tetrahydrothiophenes (**6a** and **6b**), where the product was isolated as a single regioisomer but a mixture of two stereoisomers. The $^1$H-NMR (in CDCl$_3$) spectra[8] show two characteristic signals: **6a**, 3.63 ppm (1H, dd, J= 4.4, 5.6 Hz, $\geqslant$CH), 3.75 ppm (3H, s, OCH$_3$); **6b**, 3.52 ppm (1H, t, J= 6.4 Hz, $\geqslant$CH), 3.49 ppm (3H, s, OCH$_3$). Shift of the signal due to ester methyl of **6b** to higher field indicates[9] that the methoxycarbonyl group at the 3-position is *cis* to the phenyl group at the 2-position.

We reported[10] previously that the phenyl group at dipole termini affected the stereoselectivity as well as the regioselectivity in the 1,3-dipolar cycloaddition of azomethine ylide. Therefore, high regioselectivity in entries 4 and 5 seems to be mostly owing to the effect of phenyl group. The stereoselectivity in entries 4-6, however, suggests that it may be attributed to the effect of silyl group. Clarification of this unexpected effect will be an interesting theme in future. Recently, the regioselectivity in pericyclic reactions including 1,3-dipolar cycloadditions has been well elucidated by molecular orbital theory[11]. Adoption of MO theory in this area is under investigation.

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3) Y. Terao, H. Kotaki, N. Imai, and K. Achiwa, *Chem. Pharm. Bull.*, 1985, **33**, 2762 and references cited therein; A. Padwa, Y.-Y. Chen, U. Chiacchio, and W. Dent, *Tetrahedron*, 1985, **41**, 3529; for a review, N. Imai, Y. Terao, and K. Achiwa, *J. Synth. Org. Chem. Japan*, 1985, **43**, 862.

4) Y. Terao, M. Tanaka, N. Imai, and K. Achiwa, *Tetrahedron Lett.*, 1985, **26**, 3011; the related work, Y. Matsuyama, A. Hosomi, and H. Sakurai, the 52th Annual Meeting of Chemical Society of Japan, Kyoto, April, 1986, Abstracts II, 1W30.

5) The effect of trimethylsilyl group was discussed on the regioselectivity in Diels-Alder reaction: I. Fleming and A. Percival, *J. Chem. Soc., Chem. Commun.*, 1976, 681; M. J. Carter, I. Fleming, and A. Percival, *J. Chem. Soc., Perkin I*, 1981, 2415.

6) $^1$H-NMR $\delta$ ($CDCl_3$): **9a**, 0.05(9H, s, $Si(CH_3)_3$), 0.75(1H, dd, J=6.0, 14.8 Hz, $SiCHH_A$-), 0.87(3H, t, J=6.8 Hz, $CH_3$), 0.88(1H, dd, J=8.8, 14.8 Hz, $SiCHH_B$-), 1.40-1.82(2H, m, $CH_2$), 2.20-2.53(1H, m, $\geq$CH), 3.66(3H, s, $OCH_3$). **9b**, 0.05(9H, s, $Si(CH_3)_3$), 0.88(1H, t, J=6.9 Hz, -$CH_2Si$), 1.15(3H, d, J=7.1 Hz, $CH_3$), 1.39-1.89(2H, m, $CH_2$), 2.37(1H, ca. sex, J=7.1 Hz, $\geq$CH), 3.68(3H, s, $OCH_3$).

7) **2b** and **2c** were prepared by bromination of the corresponding sulfides with N-bromosuccinimide in $CCl_4$ (see ref. 4).

8) **6a**, oil, $^1$H-NMR $\delta$ ($CDCl_3$): 0.01(9H, s, $Si(CH_3)_3$), 1.68-1.89(1H, complicated ddt, -$CHH_A$-), 2.16-2.49(1H, comp. ddt, -$CHH_B$-), 2.71-3.26(2H, comp. dt & ddt, -$CH_2S$), 3.63(1H, dd, J=4.4, 5.6 Hz, $\geq$CH), 3.75(3H, s, $OCH_3$), 7.11-7.26(5H, m, $C_6H_5$); **6b**, oil, $^1$H-NMR $\delta$ ($CDCl_3$): 0.09(9H, s, $Si(CH_3)_3$), 2.12-2.39(2H, m, -$CH_2$-), 2.69-3.20(2H, comp. ddd & dt, -$CH_2S$), 3.49(1H, s, $OCH_3$), 3.52(1H, t, J=6.4 Hz, $\geq$CH), 7.09-7.61(5H, m, $C_6H_5$).

9) $^1$H-NMR signals of ester methyl oriented *cis* to phenyl group on the 5-membered ring usually shift to near 0.3 ppm due to the shielding effect of phenyl group. M. Joucla, D. Grée, and J. Hamelin, *Tetrahedron*, 1973, **29**, 2531.

10) K. Achiwa and M. Sekiya, *Tetrahedron Lett.*, 1982, **23**, 2589; K. Achiwa, N. Imai, T. Motoyama, and M. Sekiya, *Chem. Lett.*, 1984, 3241.

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