

EFFECT OF A SILYL GROUP ON THE REGIO- AND STEREOSELECTIVITY
IN 1,3-DIPOLAR CYCLOADDITION¹

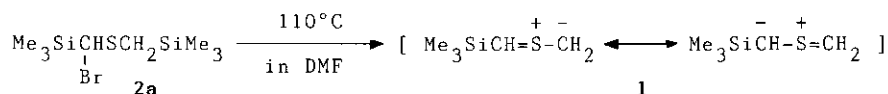
Yoshiyasu Terao, Masahiro Aono, and Kazuo Achiwa*

Shizuoka College of Pharmacy, Shizuoka 422, Japan

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 reactions² has grown during the last ten years. Especially, a silyl group has been utilized in 1,3-dipolar cycloadditions³ 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.

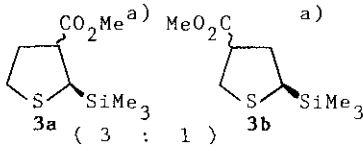
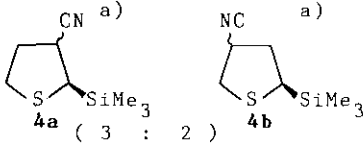
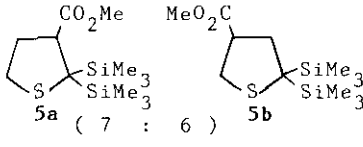
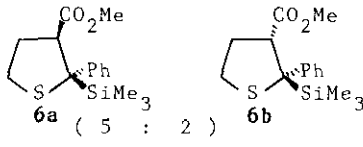
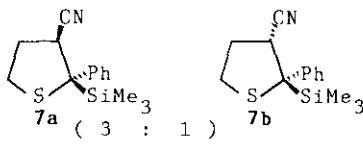
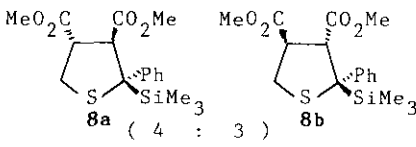
In preceding communication⁴, we described the convenient generation of a new thiocarbonyl ylide (**1**) from bromo(trimethylsilyl)methyltrimethylsilylmethylsilane (**2a**). The dipole species **1** with a trimethylsilyl group at the termini is well suited for the investigation on the effect of a silyl group.⁵



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

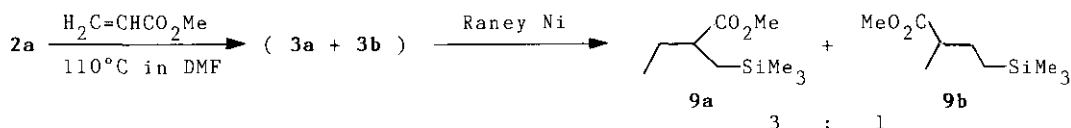
The reaction was generally carried out as follows: A solution of **2a** (3 mmol) and a dipolarophile (2 mmol) in *N,N*-dimethylformamide (DMF) (10 ml) was heated at 110°C for 2 h with stirring. After the usual workup, the product was isolated by column chromatography (silica gel, diisopropyl ether/hexane = 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	$\text{Me}_3\text{SiCHSCH}_2\text{SiMe}_3$ Br 2a	$\text{H}_2\text{C}=\text{CHCO}_2\text{Me}$	 3a (3 : 1) 3b	52
2	2a	$\text{H}_2\text{C}=\text{CHCN}$	 4a (3 : 2) 4b	56
3	$\text{Me}_3\text{Si}-\overset{\text{SiMe}_3}{\underset{\text{Br}}{\text{C}}}-\text{SCH}_2\text{SiMe}_3$ 2b	$\text{H}_2\text{C}=\text{CHCO}_2\text{Me}$	 5a (7 : 6) 5b	46
4	$\text{Me}_3\text{Si}-\overset{\text{Ph}}{\underset{\text{Br}}{\text{C}}}-\text{SCH}_2\text{SiMe}_3$ 2c	$\text{H}_2\text{C}=\text{CHCO}_2\text{Me}$	 6a (5 : 2) 6b	72
5	2c	$\text{H}_2\text{C}=\text{CHCN}$	 7a (3 : 1) 7b	87
6	2c	$\text{MeO}_2\text{C}-\text{CH}=\text{CH}-\text{CO}_2\text{Me}$	 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 ^1H -NMR spectra⁶ 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 ¹H-NMR (in CDCl₃) spectra⁸ show two characteristic signals: **6a**, 3.63 ppm (1H, dd, J= 4.4, 5.6 Hz, \geq CH), 3.75 ppm (3H, s, OCH₃); **6b**, 3.52 ppm (1H, t, J= 6.4 Hz, \geq CH), 3.49 ppm (3H, s, OCH₃). Shift of the signal due to ester methyl of **6b** to higher field indicates⁹ that the methoxycarbonyl group at the 3-position is *cis* to the phenyl group at the 2-position.

We reported¹⁰ 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 theory¹¹. Adoption of MO theory in this area is under investigation.

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- 6) $^1\text{H-NMR}$ δ (CDCl_3): **9a**, 0.05(9H, s, $\text{Si}(\text{CH}_3)_3$), 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, CH), 3.66(3H, s, OCH_3). **9b**, 0.05(9H, s, $\text{Si}(\text{CH}_3)_3$), 0.88(1H, t, $J=6.9$ Hz, $-\text{CH}_2\text{Si}$), 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, 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, $^1\text{H-NMR}$ δ (CDCl_3): 0.01(9H, s, $\text{Si}(\text{CH}_3)_3$), 1.68-1.89(1H, complicated ddt, $-\text{CHH}_A^-$), 2.16-2.49(1H, comp. ddt, $-\text{CHH}_B^-$), 2.71-3.26(2H, comp. dt & ddt, $-\text{CH}_2\text{S}$), 3.63(1H, dd, $J=4.4$, 5.6 Hz, CH), 3.75(3H, s, OCH_3), 7.11-7.26(5H, m, C_6H_5); **6b**, oil, $^1\text{H-NMR}$ δ (CDCl_3): 0.09(9H, s, $\text{Si}(\text{CH}_3)_3$), 2.12-2.39(2H, m, $-\text{CH}_2-$), 2.69-3.20(2H, comp. ddd & dt, $-\text{CH}_2\text{S}$), 3.49(1H, s, OCH_3), 3.52(1H, t, $J=6.4$ Hz, CH), 7.09-7.61(5H, m, C_6H_5).
- 9) $^1\text{H-NMR}$ 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.
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