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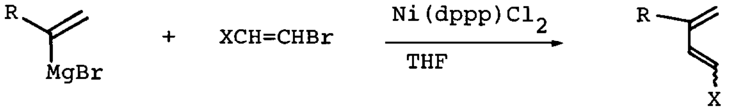
# REGIOSPECIFIC CYCLOADDITION REACTIONS USING FUNCTIONALIZED ISOPRENYLSILANE AND RELATED COMPOUNDS[1]

Akira Hosomi,* Yasuyuki Sakata, and Hideki Sakurai*
Department of Chemistry, Tohoku University, Sendai 980, Japan

*Summary: 1-Alkoxy-3-trimethylsilylmethyl- and 1-alkoxy-3-trimethylsilyl-1,3-butadienes (**1**) were newly prepared. The cycloaddition reactions of **1** with various dienophiles including heterodienophiles were found to proceed very smoothly in a perfectly regiospecific mode.*

Previously, we have reported 2-trimethylsilylmethyl-1,3-butadiene (**1a**) as a convenient reagent for the nucleophilic isoprenylation and also as an excellent diene for the regio- and stereo-selective Diels-Alder reaction with unsymmetrical dienophiles.[2] Introduction of a functionality into **1a** is an interesting extention of the work, and thus we now report 1-methoxy- and 1-ethoxy-3-trimethylsilylmethyl-1,3-butadienes (**1b** and **1c**, respectively) and 1-methoxy-3-trimethylsilyl-1,3-butadiene (**1d**), which undergo perfectly regiospecific cycloaddition reactions with dienophiles involving heterodienophiles.

Isoprenylsilanes (**1a**-**1c**) and related compounds (**1d**) are prepared by the cross-coupling reaction of Grignard reagents[3] as shown below.[4-8]



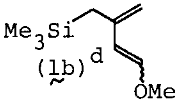
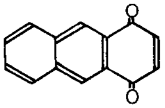
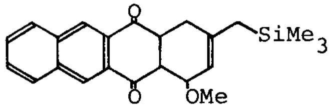
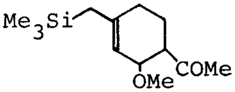
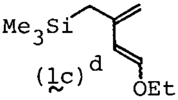
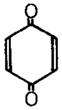
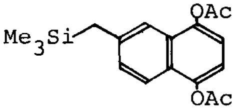
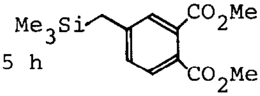
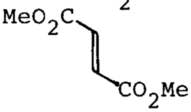
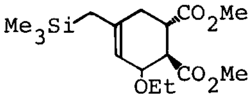
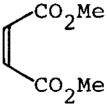
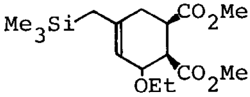
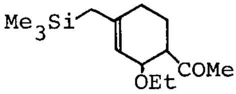
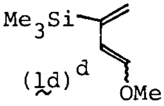
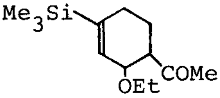
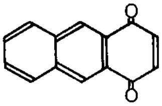
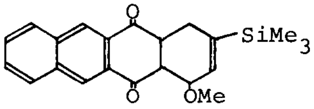
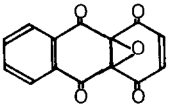
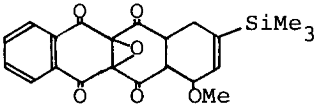
(1)

**2a**,[4] R = $CH_2SiMe_3$  **3a**, X = H
b, R = $SiMe_3$  b, X = OMe
c, X = OEt
dppp: $Ph_2P(CH_2)_3PPh_2$

**1a**, R = $CH_2SiMe_3$; X = H
b, R = $CH_2SiMe_3$; X = OMe
c, R = $CH_2SiMe_3$; X = OEt
d, R = $SiMe_3$; X = OMe

Di-functionalized 1,3-dienes (**1b**-**1d**), thus obtained, display high reactivity and regio- and stereo-specificity toward various dienophiles, the representative results of which are listed in Table 1. (eq. 2) In all cases, the thermal reaction of **1b**-**1d** proceeds very smoothly without any catalyst to afford the corresponding cycloadducts (**6**) in good yield, although the elimination of

Table 1. Thermal reactions of 1,3-dienes (1b-1d) with dienophiles (5)

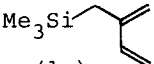
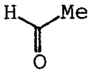
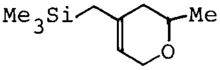
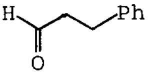
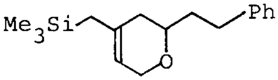
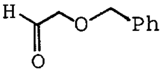
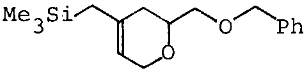
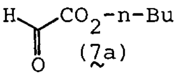
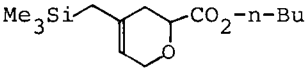
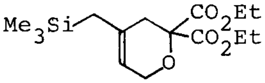
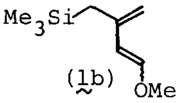
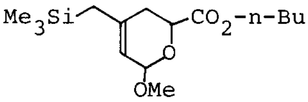
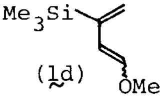
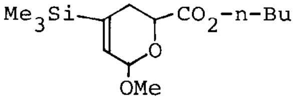
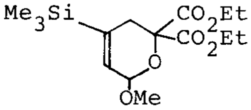
| Entry | 1,3-Diene(1) | Dienophile(5) | Conditions | Cycloadduct(6) | %Yield[b]<br>(cis/trans)[c] |
|---|---|---|---|---|---|
| 1 |  (1b)[d] |  | rt, 40 min |  | 82 |
| 2 | 1b |  (5a) | reflux, 3 h |  | 70<br>(69/31) |
| 3 |  (1c)[d] |  | 1) rt, 40 min<br>2) $Ac_2O$, Py<br>rt, 36 h<br>80 °C, 1 h |  | 80 |
| 4 | 1c |  | 1) 50 °C, 3 h<br>2) $CCl_4$, rt, 15 h |  | 85 |
| 5 | 1c |  | reflux, 5 h |  | 90<br>(55/45) |
| 6 | 1c |  | reflux, 25 h |  | 87<br>(75/25) |
| 7 | 1c | 5a | reflux, 2 h |  | 62<br>(75/25) |
| 8 |  (1d)[d] | 5a | reflux, 8 h |  | 60<br>(86/14) |
| 9 | 1d |  | 60 °C, 12 h |  | 90[e] |
| 10 | 1d |  | 60 °C, 1 h |  | 75[e] |

[a] All the reactions were conducted in PhH, using 1.5-2:1 ratio of 1:5. [b] Yield after isolation by HPLC and/or NMR. [c] Determined by NMR. [d] A mixture of stereoisomers (E:Z) in the ratio of 4:1, 2:1, and 1.2:1 for 1b-1d, respectively, was used. In all cases the E-isomer reacted more rapidly than the Z-isomer. [e] After recrystallization from $Et_2O$-Hex.

1 5 6 (2)

an alcohol from the cycloadduct with acetylenic dienophiles takes place readily, resulting in the formation of aromatic derivatives.

Table 2. Reactions of 1,3-dienes (1) with heterodienophiles (7)

| Entry | 1,3-Diene (1) | Heterodienophile (7) | Conditions | Cycloadduct (8) | %Yield[a] |
|---|---|---|---|---|---|
| 1 |  (1a) |  | $BF_3 \cdot OEt_2$, $Et_2O$<br>-78 °C, 1.5 h |  | $46^b$ |
| 2 | 1a |  | $BF_3 \cdot OEt_2$, $Et_2O$<br>-78 °C, 6 h |  | $40^b$<br>$(28)^{b,c}$ |
| 3 | 1a |  | $BF_3 \cdot OEt_2$, $Et_2O$<br>-78 °C, 6 h |  | $61^b$<br>$(45)^{b,d}$ |
| 4 | 1a |  (7a) | PhH<br>rt, 24 h |  | 74 |
| 5 | 1a | $O{=}C(CO_2Et)_2$<br>(7b) | PhH<br>reflux, 10 h |  | 71 |
| 6 |  (1b) | 7a | PhH<br>rt, 1 h |  | $93^e$ |
| 7 |  (1d) | 7a | PhH<br>reflux, 3 h |  | $73^e$ |
| 8 | 1d | 7b | PhH<br>50 °C, 10 h |  | 100 |

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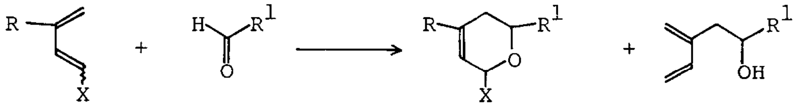
[a] Yield after isolation by TLC. [b] The corresponding isoprenylated alcohols (9) were obtained in 30, 41 (39), and 16 (32)% yield in entries 1∿3, respectively. [c] Conditions: $AlCl_3$, $CH_2Cl_2$, -78 °C, 2 min. [d] Conditions: $ZnCl_2$, PhH, rt, 3 h. [e] Products were obtained as a mixture of stereoisomers, the ratio depending upon procedures employed due to ready epimerization.

It is interesting to examine the reaction of 1 with aldehydes which can enter the reaction as electrophiles as well as heterodienophiles.[10] In the presence of a Lewis acid catalyst, 1a reacts with a variety of aldehydes to give dihydropyran derivatives (8) along with isoprenylated alcohols (9),[2a] the relative yields being dependent on the structure of aldehydes and a Lewis acid as a catalyst. (eq. 3) The results are summarized in Table 2.



1 7 8 9 (from 1a) (3)

Interestingly the perfect regiospecificity of the thermal reaction can be achieved with unsymmetrical dienophiles, only one regioisomer being obtained.[9]

It is worth to note that carbonyl compounds such as glyoxylate (7a) and oxomalonate (7b) reveal high reactivity toward 1, giving the corresponding cycloadduct (8) exclusively under the thermal conditions. The reaction proceeds in a perfectly regiospecific mode even without a Lewis acid catalyst.

The cycloadducts (6 and 8), containing an allylsilane and vinylsilane structure, may be further transformed to a variety of functionalized compounds by an easy process. For example, the simple availability of pyran and tetracene derivatives provides particular interest with respect to glycoside, anthracycline antibiotics, and antitumor agents.

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References and Notes

1. Chemistry of organosilicon compounds 206.
2. a) A. Hosomi, M. Saito, and H. Sakurai, Tetrahedron Lett., 1979, 429; b) Idem, idid., 21, 355 (1980); c) A. Hosomi, H. Iguchi, J. Sasaki, and H. Sakurai, ibid., 23, 551 (1982); d) H. Sakurai, A. Hosomi, M. Saito, K. Sasaki, H. Iguchi, J. Sasaki, and Y. Araki, Tetrahedron, 39, 883 (1983).
3. K. Tamao, K. Sumitani, and Y. Kiso, M. Zembayashi, A. Fujioka, S. Komada, I. Nakajima, A. Minato, and M. Kumada, Bull. Chem. Soc. Japan, 49, 1958 (1976).
4. a) H. Nishiyama, H. Yokoyama, S. Narimatsu, and K. Itoh, Tetrahderon Lett., 23, 1267 (1982); b) B. M. Trost and B. P. Coppola, J. Am. Chem. Soc., 104, 6879 (1982).
5. Although 1a was prepared by the most economical route reported earlier,[2] the cross-coupling between 2a and 3a or, reversely, between vinylmagnesium bromide and 4a also gave 1a readily in laboratory scale.
6. 1b (E/Z = 4/1) was obtained from 3b (E/Z = 1/1) in 41 % yield. bp 76-78 °C (25 torr). E-1b: $^1$H NMR ($C_6D_6$) δ 0.20 (9H, s), 1.77 (2H, d, J = 1.2Hz), 3.30 (3H, s), 4.73 (1H, m), 4.98 (1H, m), 5.74 (1H, d, J = 12.8Hz), 6.70 (1H, d, J = 12.8Hz); $^{13}$C NMR ($CDCl_3$) δ -1.3 (q), 22.9 (t), 56.1 (q), 108.5 (d), 108.7 (t), 141.1 (s), 148.9 (d). Z-1b: $^1$H NMR ($C_6D_6$) δ 0.33 (9H, s), 2.19 (2H, d, J = 1.2Hz), 3.23 (3H, s), 4.95 (1H, d, J = 6.8Hz), 5.00 (1H, m), 5.38 (1H, m), 5.60 (1H, d, J = 6.8Hz); $^{13}$C NMR ($CDCl_3$) δ -1.7 (q), 26.8 (t), 59.9 (q), 108.5 (d), 110.4 (t), 141.6 (s), 146.5 (d). All new compounds obtained in this work gave satisfactory spectral data and elemental analysis.
7. 1c (E/Z = 2/1) was obtained from 3b (E/Z = 1/4) in 51 % yield. bp 86-87 °C (16 torr).
8. 1d (E/Z = 1.2/1) was obtained from 3b (E/Z = 1/2) in 40 % yield. bp 55-62 °C (22 torr).
9. Cycloaddition of 2-triethylsilyl-1,3-butadiene (1e) could not be always achieved in a highly regioselective mode under any condition. See D. B. Batt and B. Ganem, Tetrahedron Lett., 1978, 3323.
10. a) M. Bednarski and S. Danishefsky, J. Am. Chem. Soc., 105, 3716 (1983); b) S. Danishefsky, J. F. Kerwin, Jr., and S. Kobayashi, ibid., 104, 358 (1982) and references cited therein; c) For a review, see S. W. Weinreb and R. P. Starb, Tetrahderon, 38, 3087 (1982).

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