

α -Oxoketene Dithioacetals in Organic Synthesis. A New Access to 1-Siloxy-1,3-butadienes and Their Selective Reactions with Electrophiles¹⁾

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Reactions of α -oxoketene dithioacetals with trimethylsilylmethylmagnesium chloride in the presence of cuprous iodide gave the corresponding 1-trimethylsiloxy-3-methylthio-1,3-butadienes selectively in excellent yields. 1-Siloxydienes react with various carbon electrophiles such as carbonyl compounds to furnish the desired dienones and 4-dihydropyrones selectively.

Silyl enol ethers are versatile and important reagents for the various types of selective carbon-carbon bond formations in organic synthesis.²⁾ Among them, silyl dienol ethers are particularly useful and interesting dienes for the stereo- and regioselective cycloaddition reactions and expedient nucleophiles which react with a variety of electrophiles under a mild condition.²⁻⁷⁾ However, in sharp contrast with versatilely utilized 2-siloxydienes,²⁻⁵⁾ 1-trimethylsiloxy-1,3-butadienes, are not used so extensively in organic synthesis, in spite of useful and convenient reagents for the regioselective introduction of carbon electrophiles at the γ -position.^{6,7)} On the other hand, α -oxoketene dithioacetals are also synthetically useful reagents, numerous preparative methods and synthetic reactions of which have been reported.⁸⁻¹⁰⁾ In an extension of the study on ketene dithioacetals in organic synthesis, we now report that a convenient and efficient synthesis of various 1-trimethylsiloxy-3-methylthio-1,3-butadienes (**4**) can be readily achieved by the reaction of α -oxoketene dithioacetals (**1**) with trimethylsilylmethylmagnesium chloride (**2**)¹¹⁾ in the presence of cuprous iodide followed by a 1,5-C \rightarrow O Si shift¹²⁾ of the conjugate addition-elimination products (**3**) (Eq. 1), and that dienones and 4-dihydropyrones are selectively obtained by their reactions with electrophiles such as carbonyl compounds.

In order to establish optimum conditions for the synthesis of 1-siloxydienes (**4**), the effects of solvents and molar ratios of the reagent (**2**) and cuprous iodide as a catalyst were examined for the reaction of benzoylketene dithioacetal (**1a**) and trimethylsilylmethylmagnesium chloride (**2**) (Table 1). As a result, the reaction of **1** with **2** in the presence of cuprous iodide at -78 °C for 4 h with

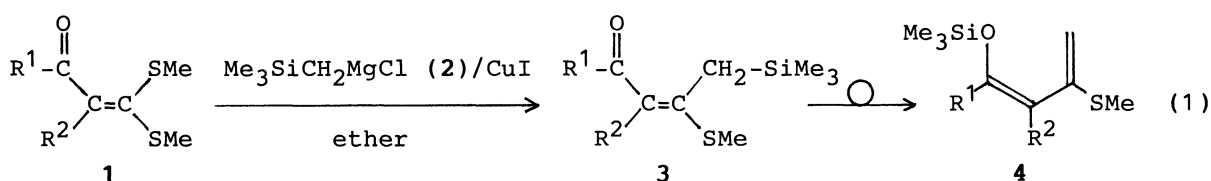


Table 1. The Effect of the Catalyst^{a)}

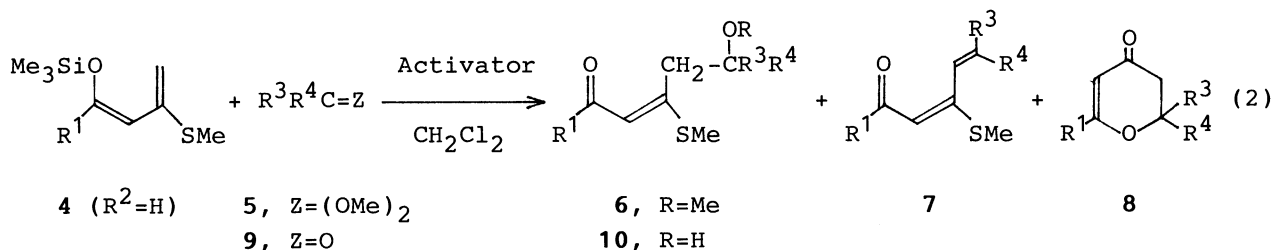
Entry	CuI/2 ^{b)}	Yield/%	Entry	CuI/2 ^{b)}	Yield/%
1	none	42	4	0.50	54
2	0.17	99	5	1.00	49
3	0.37	94			

a) At -78 °C for 4 h and then rt for 12 h in Et₂O. b) Molar ratio.

Table 2. Synthesis of 1-Siloxydienes (4)^{a)}

Product (4)	R ¹	R ²	Yield/% ^{b)}
4a	C ₆ H ₅	H	99
4b	p-ClC ₆ H ₄	H	85
4c	p-MeOC ₆ H ₄	H	68
4d	t-Butyl	H	91
4e	-(CH ₂) ₄ -	H	96
4f	2-Furyl	H	84
4g	2-Thienyl	H	87

a) All reactions were carried out by using 1 (0.5 mmol), 2 (1.5 mmol), and CuI (0.25 mmol) at -78 °C→rt for 4 h in ether. b) Yield after isolation by silica gel column chromatography.



stirring followed by at room temperature for 15 h in ether gave smoothly the corresponding 1-substituted 1-trimethylsiloxy-3-methylthio-1,3-butadiene (4a).¹³⁾ The yield was found to depend on the reaction conditions (temperature, time, %yield): -78 °C, 1 h, 24; -78 °C→0 °C, 4 h, 46; -78 °C→rt, 4 h, 99; 0 °C, 12 h, 60; -20 °C→rt, 12 h, 10; rt, 12 h, 0. Apparently, without isolation of the intermediate (3) which was obtained by the conjugate addition of 2 to 1 followed by the elimination of the methylthio group, conversion of 3 to 4 by a 1,5-C→O Si shift took place sufficiently at room temperature. Thus the best condition was found to be when the reaction was carried out at -78 °C and then allowed to stand at room temperature for total 4 h in the presence of ca. 20 mol% of cuprous iodide to 2 in ether. Cerium chloride¹⁴⁾ had no strong influence on both the yield and the addition mode of the present reaction. Nickel and palladium complexes, used for the cross-coupling reaction in vinyl sulfides,¹⁵⁾ were not effective as a catalyst for the present reaction. Thus a variety of desired 1-siloxydienes (4b-g) were similarly prepared by the reaction of the corresponding α-oxoketene dithioacetals (1b-g) with 2 catalyzed by ca. 20 mol% of cuprous iodide in good yields (Table 2).

It has been found that the reaction of 1-siloxydienes (4, R²=H), thus obtained, with acetals [R³CH(OMe)₂, 5] smoothly occurs in the presence of titanium chloride (TiCl₄) in dichloromethane to give the corresponding δ-alkoxy ketones (6), derived by the selective γ-attack, in almost cases (Table 3, Eq. 2).⁷⁾ In

Table 3. Reaction of Siloxydienes (**4a,b**) with Acetals [$R^3CH(OMe)_2$, **5**]^{a)}

Entry	R ¹	R ³	6 (%) (E/Z) ^{b)}	7 (%)	8 (%)
1	C ₆ H ₅	Me ₂ CHCH ₂	39 (54/46)	--	--
2	C ₆ H ₅	CH ₃ (CH ₂) ₃	60 (67/33)	--	--
3	p-ClC ₆ H ₄	Me ₂ CHCH ₂	63 (25/75)	--	--
4	p-ClC ₆ H ₄	CH ₃ (CH ₂) ₃	59 (66/34)	--	--
5	p-ClC ₆ H ₄	CH ₃	51 (57/43)	--	--
6	C ₆ H ₅	p-ClC ₆ H ₄	--	19 ^{c)}	30
7	p-ClC ₆ H ₄	p-ClC ₆ H ₄	--	28 ^{c)}	49

a) All reactions promoted by TiCl₄ were carried out in CH₂Cl₂ at -78 °C. b) Yield after isolation by TLC. The assignment of the geometry was done by NMR.¹⁶⁾ c) Before isolation by TLC, only (E, E)-isomer was found in the reaction mixture by NMR.

contrast with the loss of γ -regioselectivity in several cases of 3-substituted 1-siloxydienes,⁶⁾ the present reaction displayed fortunately high regioselectivity, presumably due to the effect of the 3-methylthio group of **4**. However, the selectivity with respect to the formation of (Z)- and (E)-isomers could not be attained in the present reaction, different from the reaction of **4** with aldehydes shown later. An aromatic acetal (**5**) was allowed to react with **4a** and **4b** in the presence of TiCl₄ to give the corresponding dienones (**7**) formed by the elimination of methanol from **6** and 4-dihydropyrones (**8**) formed by the cyclization of **6** in a considerable amount (Entries 6 and 7).

Reactions of 1-siloxydienes with carbonyl compounds are not sufficiently examined. We found that the reaction of **4a** with benzaldehyde (**9a**) in the presence of TiCl₄ gave a dienone (**7a**) along with a 4-dihydropyrone (**8a**). In this case, TiCl₄ did not give satisfactory results. After screening other activators and reaction conditions, we found that **10** was selectively obtained in a moderate yield when BF₃·OEt₂ was used at -78 °C for 1 h. However for prolonged reaction times and at higher temperature, dienones (**7**) instead of **10** are obtained selectively along with a small amount of 4-dihydropyrones (**8**) which are formed by the cyclization of **10**. It is noteworthy to state that dienones (**7**) are only (E, E)-isomers, though its mechanism remains obscure. The results are summarized in Table 4.

Finally, 1-siloxydienes (**4a,b**) were also found for the first time to react

Table 4. Reaction of 1-Siloxydienes (**4a-c,g**) with Aldehydes [R^3CHO , **9**]

Entry	R ¹	R ³	Activator	Conditions	10 (%) ^{a,b)}	7 (%) ^{a)}	8 (%) ^{a)}
1	C ₆ H ₅	C ₆ H ₅	BF ₃ ·OEt ₂	-78→-40 °C, 4 h	--	66	6
2	C ₆ H ₅	C ₆ H ₅	TiCl ₄	-78→-40 °C, 4 h	--	14	18
3	C ₆ H ₅	p-ClC ₆ H ₄	BF ₃ ·OEt ₂	-78 °C, 1 h	45	15	--
4	C ₆ H ₅	p-ClC ₆ H ₄	BF ₃ ·OEt ₂	-78 °C→rt, 12 h	--	35	--
5	C ₆ H ₅	p-O ₂ NC ₆ H ₄	BF ₃ ·OEt ₂	-78 °C→rt, 12 h	--	38	--
6	C ₆ H ₅	iso-Pr	BF ₃ ·OEt ₂	-78 °C→rt, 12 h	--	--	6
7	p-ClC ₆ H ₄	C ₆ H ₅	BF ₃ ·OEt ₂	-78 °C, 1 h	34	--	--
8	p-ClC ₆ H ₄	C ₆ H ₅	BF ₃ ·OEt ₂	-78 °C→rt, 12 h	--	56	5
9	p-ClC ₆ H ₄	p-ClC ₆ H ₄	BF ₃ ·OEt ₂	-78→-40 °C, 4 h	--	41	9
10	p-MeOC ₆ H ₄	C ₆ H ₅	BF ₃ ·OEt ₂	-78 °C→rt, 12 h	--	29	--
11	2-Thienyl	C ₆ H ₅	BF ₃ ·OEt ₂	-78 °C→rt, 12 h	--	21	15

a) Yield after isolation by TLC. b) The (E)/(Z) ratio was not determined.

Table 5. Reaction of Siloxydienes (**4a,b**) with Ketones (**9**)^{a)}

Entry	R ¹	R ³	R ⁴	8(%) ^{b,c)}
1	C ₆ H ₅	C ₆ H ₅	CH ₃	40
2	C ₆ H ₅	p-ClC ₆ H ₄	CH ₃	22
3	C ₆ H ₅	-(CH ₂) ₅ -		36
4	p-ClC ₆ H ₄	C ₆ H ₅	CH ₃	32
5	p-ClC ₆ H ₄	p-ClC ₆ H ₄	CH ₃	13

a) All reactions were carried out in the presence of BF₃·OEt₂ in CH₂Cl₂ at -78 °C for 12 h. b) Yield after isolation by TLC. c) All products showed satisfactory spectral data.

with ketones (**9**) under a similar condition to furnish only **8**, though the yields were rather low at present (Table 5).

In summary, a new and ready route to a variety of 1-siloxydienes (**4**) and their use for the selective carbon-carbon bond formation shown in this work reveals that **4** is a useful and promising reagent in organic synthesis.

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References

- 1) Studies on Organosilicon Chemistry, No. 105.
- 2) W. P. Weber, "Silicon Reagents for Organic Synthesis," Springer-Verlag, Berlin (1983); J. K. Rasmussen, *Synthesis*, **1977**, 91.
- 3) R. C. Gupta, P. A. Harland, and R. T. Stoodley, *Tetrahedron*, **40**, 4657 (1984).
- 4) M. Bednarski and S. J. Danishefsky, *J. Am. Chem. Soc.*, **105**, 3716 (1983); S. J. Danishefsky, E. Larson, D. Askin, and N. Kato, *ibid.*, **107**, 1246 (1985), and references cited therein.
- 5) V. Guay and P. Brassard, *Tetrahedron*, **43**, 5039 (1984); L. Boisvert and P. Brassard, *J. Org. Chem.*, **53**, 4052 (1988) and references cited therein.
- 6) I. Fleming, J. Goldhill, and I. Paterson, *Tetrahedron Lett.*, **1979**, 3209.
- 7) T. Mukaiyama and A. Ishida, *Chem. Lett.*, **1975**, 319; *ibid.*, **1975**, 1201; T. Mukaiyama and A. Ishida, *Bull. Chem. Soc. Jpn.*, **51**, 2077 (1978).
- 8) A. K. Gupta, H. Iia, and H. Junjappa, *Tetrahedron Lett.*, **29**, 6633 (1988); M. P. Balu, H. Iia, and H. Junjappa, *ibid.*, **28**, 3023 (1987) and references cited therein.
- 9) R. K. Dieter, Y. J. Lin, and J. W. Dieter, *J. Org. Chem.*, **49**, 3183 (1984); R. K. Dieter and J. R. Fishpaugh, *ibid.*, **53**, 2031 (1988). For a review, see, R. K. Dieter, *Tetrahedron*, **42**, 3029 (1986) and references cited therein.
- 10) A. Ushirogouchi, Y. Tominaga, Y. Matsuda, and G. Kobayashi, *Heterocycles*, **14**, 7 (1980).
- 11) E. E. Royals and K. C. Brannock, *J. Am. Chem. Soc.*, **75**, 2050 (1953).
- 12) C. P. Casey, C. R. Jones, and H. Tukada, *J. Org. Chem.*, **46**, 2089 (1981). For the 1,3-shift, see A. Hosomi, H. Hayashida, and Y. Tominaga, *ibid.*, in press.
- 13) Compound (**4a**) is hydrolyzed with 10% hydrochloric acid to give a mixture of (Z)- and (E)-isomers (35:65) of 3-methylthio-1-phenyl-2-buten-1-one. These isomers, easily assigned by NMR spectra,¹⁶⁾ could be readily separated by TLC by using benzene as an eluent. Namely, an α -proton of the (Z)-isomer (6.93 ppm) is lower field than that of the (E)-isomer (6.40 ppm).
- 14) T. Imamoto, N. Takiyama, K. Nakamura, T. Hatajima, and Y. Kamiya, *J. Am. Chem. Soc.*, **111**, 4392 (1989) and references cited therein.
- 15) H. Okamura, M. Miura, and H. Takei, *Tetrahedron Lett.*, **1979**, 43; K. Tamao and M. Kumada, "Use of Organonickel Compounds in Organic Synthesis," in "The Chemistry of the Metal-Carbon Bond," ed by F. R. Hartley, John-Wiley & Sons, New York (1987), Vol. 4, Chap. 9, pp.820-887.
- 16) T. Nishio and Y. Omote, *J. Chem. Soc., Perkin Trans. 1*, **1981**, 934.

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