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KETENE DITHIOACETALS IN ORGANIC SYNTHESIS: SYNTHESIS OF SILYL KETENE DITHIOACETAL AND SOME REACTIONS WITH SUBSTITUTED BENZALDEHYDES[1)]

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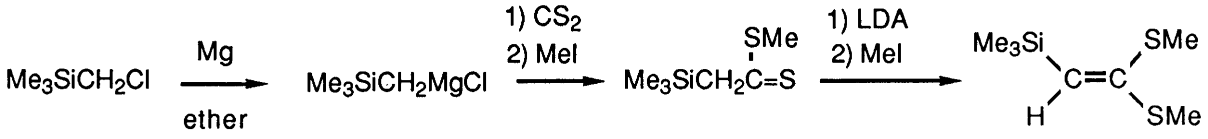
A new silyl ketene dithioacetal, 1,1-bis(methylthio)-2-trimethylsilylethene, was synthesized by the reaction of the enolate of methyl trimethylsilylmethyldithiocarboxylate, which was prepared by treating trimethylsilylmethylmagnesium chloride with carbon disulfide followed by successive treatment with methyl iodide and then lithium diisopropylamide in ether combined with methyl iodide. The silyl ketene dithioacetal, which can be viewed as a vinylsilane, reacted with substituted benzaldehydes in the presence of a Lewis acid to give the corresponding allylic alcohols.

KEYWORDS silyl ketene dithioacetal; vinylsilane; allylic alcohol; trimethylsilylmethylmagnesium chloride; 1,1-bis(methylthio)-2-trimethylsilylethene

In organic synthesis, much attention has been directed to organosilicon compounds, particularly vinylsilanes[2)] and allylsilanes,[3)] as highly nucleophilic reagents. Although the allylsilanes can react with a variety of electrophiles, vinylsilanes do not react with weak carbon electrophiles such as carbonyl compounds and acetals, even when promoted by a Lewis acid, except for acid halides and dichloromethyl ethers. This is apparently because of low nucleophilicity and for steric reasons. Moreover, ketene dithioacetals, bearing electron-withdrawing and electron-donating groups on the carbon atoms of a double bond are useful for synthesizing intermediates.[4)] A number of preparative methods have been reported.[5)] So silyl ketene dithioacetal, consisting of these two skeletons, should be highly nucleophilic and reactive due to the methylthio group and the trimethylsilyl group. In an extension of the work on the ketene dithioacetals in organic synthesis, we now report that a silyl ketene dithioacetal can be readily prepared starting from trimethylsilylmethylmagnesium chloride and carbon disulfide in two steps and reacts with carbonyl compounds to give allylic alcohols. This is the first example of the reaction of vinylsilanes with ordinary unactivated carbonyl compounds.

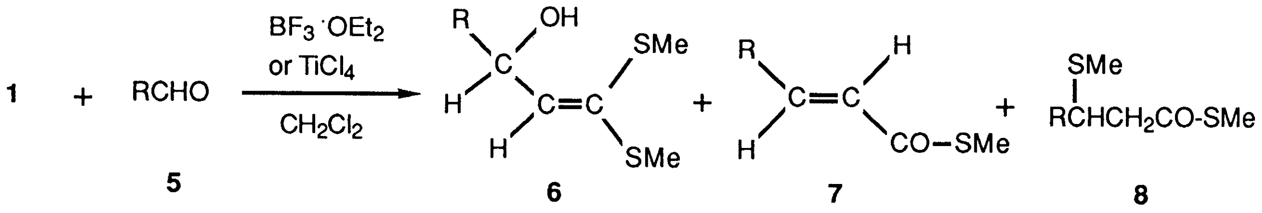
The reaction of trimethylsilylmethylmagnesium chloride (**3**) with carbon disulfide at room temperature in ether followed by the methylation with methyl iodide gave the corresponding methyl dithiocarboxylate (**4**)[6)] in 89% yield. An ester enolate is readily formed by adding an equivalent of lithium diisopropylamide (LDA) to the methyl dithiocarboxylate (**4**) at in ether -78°C. Quenching the enolate with methyl iodide smoothly gave a new silyl ketene dithioacetal, 1,1-bis(methylthio)-2-trimethylsilylethene (**1**),[7)] almost in quantitative yield.



2 **3** **4** **1**

For the first time, it was found that the reaction of **1**, thus newly obtained, proceeds smoothly with carbon electrophiles such as carbonyl compounds in the presence of a Lewis acid. Thus, at the outset of this work, the $BF_3\cdot OEt_2$-promoted reaction of **1** with benzaldehyde (**5a**) was examined. This reaction gave the corresponding allylic alcohol (**6a**) in 46% yield together with two thioesters (**7a** and **8a**). The results are listed in Table I. Titanium tetrachloride is also an effective activator for this reaction. Note that the chemoselectivity toward *p*-cyano- and *p*-nitrobenzaldehydes can be attained. Although $TiCl_4$-promoted the reaction of **1** with benzaldehyde (**5a**) and *p*-methylbenzaldehyde (**5b**) gave a mixture of **6**, **7** and **8**, the allylic alcohol (**6**) was obtained selectively from **5** bearing an electron-withdrawing group. Thus in the case of the reaction of **1** with *p*-nitrobenzaldehyde (**5e**), only the alcohol (**6e**) was obtained, in 63% yield. The allyl alcohol (**6c**), obtained from *p*-chlorobenzaldehyde (**5c**), was smoothly converted to methyl cinnamate (**9**) and methyl 2-methylthiophenethylate (**10**) in 15 and 80% yields, respectively, after treatment with hydrochloric acid in methanol.[8,9] So the primary product (**6**) can be viewed as an intermediate of the secondary products (**7** and **8**).

A typical experimental procedure is as follows. A mixture of **1** (96 mg, 0.5 mmol), an aldehyde (0.5 mmol), and $TiCl_4$ (0.055 ml, 0.5 mmol) was stirred at -78°C for 3 h, then for 10 h at room temperature. Hydrolysis of the reaction mixture with 10% hydrochloric acid followed by the preparative TLC on silica gel (benzene) gave the allylic alcohol (**6**).



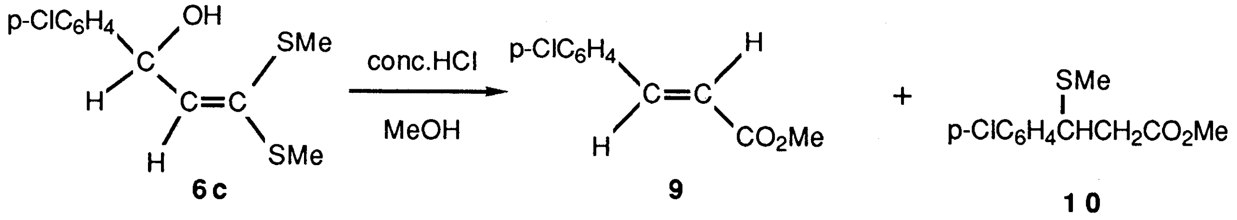


Table 1. Reaction of Silyl Ketene Dithioacetal (**1**) with Aldehydes (**5**)

Entry	Aldehyde (**5**)	Lewis acid	% Yield[b] **6**	**7**	**8**
1	PhCHO (**5a**)	$BF_3\cdot OEt_2$	46	19	3
2	**5a**	$TiCl_4$	32	24	10
3	*p*-MeC_6H_4CHO (**5b**)	$TiCl_4$	40	19	---
4	*p*-ClC_6H_4CHO (**5c**)	$TiCl_4$	44	---	---
5	*p*-NCC_6H_4CHO (**5d**)	$BF_3\cdot OEt_2$	21	18	---
6	**5d**	$TiCl_4$	56	---	---
7	*p*-$O_2NC_6H_4CHO$ (**5e**)	$TiCl_4$	63	---	---

[a] All reactions were carried out in CH_2Cl_2 at -78°C~rt for 3-10 h.
[b] Yield after isolation by TLC.

A new silyl ketene dithioacetal, 1,1-bis(methylthio)-2-trimethylsilylethylene, reacts with carbonyl compounds such as substituted benzaldehydes as the carbon electrophile to give the corresponding alcohols in moderate yields accompanyed by the carbon-carbon bond formation. This is the first example of the reaction of vinylic silanes with carbonyl compounds. Only fluoride ion-promoted reactions using activated vinylsilane such as α-phenylthiovinylsilane had been known.[10)]

From the viewpoint of the chemoselectivity and simple operation, the present new C-C bond formation using the silyl ketene dithioacetal is valuable for the synthesis of the corresponding allylic alcohol and cinnamate derivatives. Also, the synthesis utility of the present reaction is mostly displayed by the ready accessibility of starting materials and mild conditions. This vinylsilane with its dithioacetal skeleton will become a useful nucleophilic reagent. Further studies of the synthesis and reactions of new types of vinylsilanes are in progress.[11)]

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4) Recently, Mukaiyama et al. have found that the cyclic ketene dithioacetals react with alkyl methyl ethers or α, β-unsaturated orthoesters in the presence of a catalytic amount of trityl chloride or chlorotrimethylsilane and tin(II) chloride to afford in good yields the corresponding displacement products at the β-carbon. See, T. Mukaiyama, H. Sugumi, H. Uchiro, and S. Kobayashi, Chem. Lett., **1988**, 1291.

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6) **4**: 63-65°C/15mmHg: ^{1}H-NMR(60MHz, δ ppm in $CDCl_3$); 0.00(9H, s, $SiMe_3$), 2.37(3H, s, SMe).

7) **1**: 63-65°C/18mmHg: ^{1}H-NMR(60MHz, δ ppm in $CDCl_3$): 0.00(9H, s, $SiMe_3$), 2.05(3H, s, SMe), 5.47(1H, s, H-C=); ms(m/z); 192(M^+: 82), 177(52), 145(51), 105(73), 73(100); IR(neat) ν max cm^{-1}: 3585, 2915, 1692, 1664, 1421, 1252, 846. This compound is smoothly hydrolyzed by the treatment of 10% hydrochloric acid to give bis(methylthio)ethylene, the simplest ketene dithioacetal, in a quantitative yield. See, R. Kaya and N. R. Beller, J. Org. Chem., **46**, 196 (1981).

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10) H. Oda, M. Sato, Y. Morizawa, K. Oshima, and H. Nozaki, Tetrahderon Lett., **24**, 2877 (1983).

11) The reaction of **1** with 3-phenylpropanal dimethyladetal promoted by $TiCl_4$ proceeds smoothly to give mainly a diene [$PhCH_2CH=CHCH=C(SMe)_2$], an elimination product of methanol, along with a methyl ether of allyl alcohol for a prolonged reaction time. Details will be published in a forthcoming papaer.

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