

The Trityl Cation Mediated Michael Reaction of
Ethylthioacetene Dithioacetals with Silyl Enol Ethers

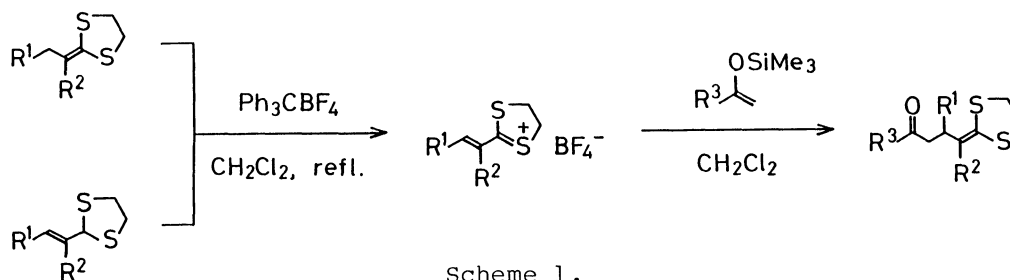
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In the presence of trityl tetrafluoroborate, 2-(2-ethylthio-alkylidene)-1,3-dithiolanes smoothly react with silyl enol ethers at low temperature to afford the corresponding oxoketene dithioacetal adducts in good yields. This reaction is formally equivalent to the Michael reaction between ketone enolates and α,β -unsaturated esters.

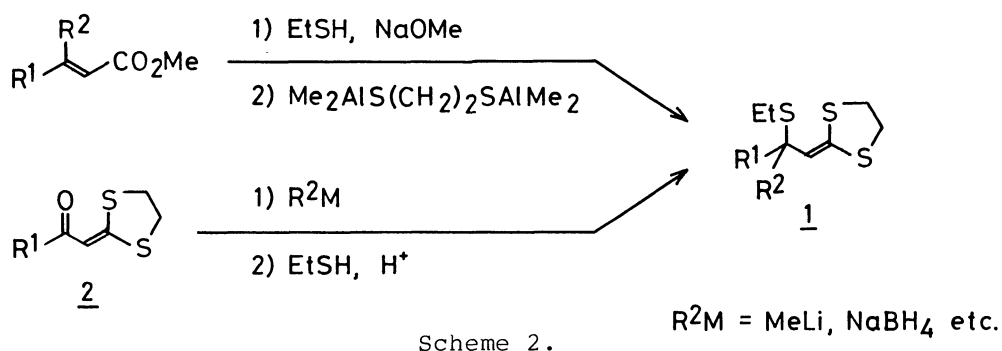
The Michael reaction is one of the most fundamental carbon-carbon bond forming reactions and much interest is currently focused on this reaction.¹⁾ However, the reaction between α,β -unsaturated esters and ketone enolates is generally hard to give desired adducts and only few reports on this subject have been reported. For example, Enders and coworkers have demonstrated that lithium salts of hydrazones as ketone enolate equivalents smoothly add to α,β -unsaturated esters,²⁾ and recently, the trityl perchlorate catalyzed Michael reaction of α,β -unsaturated orthoesters with silyl enol ethers has been reported from our laboratory.³⁾ In this communication, we wish to report the Michael type reaction using ethylthioacetene dithioacetals which are new and useful synthetic equivalents to α,β -unsaturated esters.

In the previous paper,⁴⁾ we have already reported the oxidative Michael reaction between silylated carbon nucleophiles and ketene dithioacetals or ethylenedithioacetals of α,β -unsaturated aldehydes through the intermediate salts formed by the hydride abstraction (Scheme 1). In the generation step of cationic species, somewhat high temperature is required and under this condition trityl



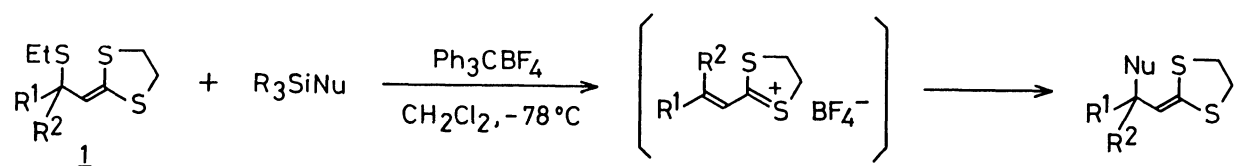
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cation cannot coexist with silyl enol ether in the reaction media,⁵⁾ so the reaction must be performed in a stepwise procedure. Therefore when a starting material was a highly reactive ketene dithioacetal, troublesome side reactions such as oligomerization occurred and the desired product was isolated only in a low yield; the reaction between 2-propylidene-1,3-dithiolane and silyl enol ether derived from pinacolone under the above mentioned hydride abstraction conditions gave only 39% yield of the corresponding adduct, 2-(2,5,5-trimethyl-4-oxo-hexylidene)-1,3-dithiolane. To overcome this difficulty, the employment of a starting material bearing a more labile leaving group than hydride was studied so that the generation of intermediate cation would be achieved in the presence of a nucleophile at low temperature. After the investigation of several Michael acceptors, ethylthioketene dithioacetals 1 were found to be suitable for this purpose. These compounds can be easily prepared according to Corey's procedure⁶⁾ or from oxoketene dithioacetals 2 (Scheme 2) and are stable enough to be stored in a refrigerator.



A typical procedure is described for the preparation of 2-(2-ethylthio-2-methylpropylidene)-1,3-dithiolane (1a): To a THF solution (60 ml) of 2-(2-oxopropylidene)-1,3-dithiolane⁷⁾ (1.96 g, 12.2 mmol) was added ethereal methyl-lithium solution (19 mmol) and the mixture was stirred at $-60\text{ }^{\circ}\text{C}$ to $-10\text{ }^{\circ}\text{C}$ for 2 h.⁸⁾ After the subsequent addition of ethanethiol (2 ml, 27 mmol) and dichloro-methane (20 ml) solution of trifluoroacetic acid (30 mmol), the mixture was stirred at $0\text{ }^{\circ}\text{C}$ for 3 h, and quenched with triethylamine. After the organic layer was washed with brine, dried and evaporated, the residue was purified by column chromatography to afford 1a in 59% yield (1.59 g, 7.2 mmol).

Next, we examine the generation of cationic species from ethylthioketene dithioacetals 1 and the reaction with silyl enol ethers. The elimination of ethylthio group was conducted by the use of several activators. It is well known that alkylthio group can be activated by heavy metal salts,⁹⁾ Lewis acids,¹⁰⁾ or alkylating reagents.¹¹⁾ After a number of activators including the above mentioned ones were screened, it was found that trityl tetrafluoroborate¹²⁾ gave the highest yield. Then, the reaction with various combination of ethylthioketene dithioacetals 1 and silyl enol ethers was tried by using trityl tetrafluoroborate and the results are summarized in Table 1. In almost all cases, except for allylsilane (entry 7), the reaction smoothly proceeded at $-78\text{ }^{\circ}\text{C}$.

Table 1. Reaction of 1 with Silylated Carbon Nucleophiles^{a)}

Entry	R ¹	R ²	Nucleophile	Yield/% (anti:syn) ^{b)}	Product
1	Me	H		59	c)
2	Me	H		85 (96:4)	
3	Me	H		54 (71:29)	
4	Me	H		73	d)
5	Me	H		75	
6	Me	H		70	
7	Me	H		trace	
8	n-Pr	H		87 (93:7)	
9	Ph	H		89 (97:3)	
10	Me	Me		83	
11	Me	Me		91	d)
12	Me	Me		98	

a) All new compounds gave satisfactory spectroscopic data.

b) Determined by HPLC or NMR analysis.

c) Trityl tetrafluoroborate was added over a period of 1 h.

d) Reaction temperature: $-78^\circ\text{C} \longrightarrow 0^\circ\text{C}$.

The following experimental procedure is representative: To a stirred suspension of trityl tetrafluoroborate (98 mg, 0.30 mmol) in 1 ml of dichloromethane was added a dichloromethane (2 ml) solution of 2-(2-ethylthio-2-methylpropylidene)-1,3-dithiolane (1a, 59 mg, 0.27 mmol) and 1-methoxy-2-methyl-1-trimethylsiloxypropene (91 mg, 0.52 mmol) at -78°C . The mixture was stirred at the same temperature for 8 h. The reaction was worked up by adding aqueous sodium hydrogencarbonate and organic materials were extracted with dichloromethane. After the organic layer was dried and evaporated, the residue was purified by thin layer chromatography to give 2-(3-methoxycarbonyl-2,2,3-trimethylbutylidene)-1,3-dithiolane in 98% yield (68 mg, 0.26 mmol).

Among several ethylthio ketene dithioacetals 1 shown in Table 1, the sterically hindered compound 1a ($\text{R}^1=\text{R}^2=\text{Me}$) is a synthetically valuable Michael acceptor. Namely, silyl enol ethers could smoothly react with 1a and the corresponding adducts were obtained in high yields (entries 10-12), while β,β -disubstituted α,β -unsaturated ester, which is equivalent to 1a, is known as an inert Michael acceptor.³⁾ These results demonstrate that the present procedure provides a new and efficient Michael type carbon-carbon bond forming method.

References

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