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OXIDATIVE COUPLING OF KETENE DITHIOACETALS WITH SILYLATED CARBON NUCLEOPHILES BY THE USE OF TRITYL TETRAFLUOROBORATE

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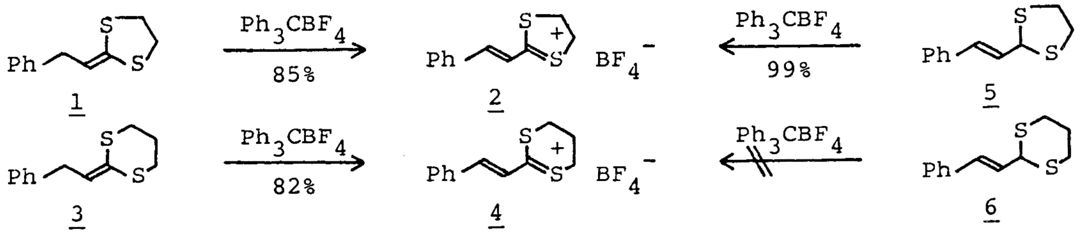
2-Alkenyl-1,3-dithiolan or dithian-2-ylium cations are yielded by hydride abstraction of cyclic ketene dithioacetals with trityl tetrafluoroborate. These cations react with silyl enol ethers or an allylsilane completely regioselectively to give the corresponding functionalized ketene dithioacetals.

For the effective carbon-carbon bond formation at the β-position of a carbonyl compound, the Michael addition of a nucleophile to the corresponding α,β-unsaturated carbonyl compound is generally employed. Therefore, starting from a saturated carbonyl compound, it is fundamentally necessary to introduce α,β-unsaturation for the preparation of the starting material. Now, we wish to report here a new and convenient method for the carbon-carbon bond forming reaction at the β-position of saturated esters via the corresponding ketene dithioacetals using a trityl salt as an oxidant.1)

We have recently studied the chemistry of the trityl2) and related3) cations and found that they behave as efficient Lewis acids. On the other hand, it is well known that trityl cation can abstract hydride from appropriate substrates such as silyl ethers,4) silyl enol ethers,5) and cycloheptatrienes.6) 1,3-Dithian-2-ylium tetrafluoroborate is also obtained by the reaction of 1,3-dithiane with trityl tetrafluoroborate7) and several synthetic reactions using this salt have been already reported.7,8) However, it has recently been found that 2-substituted-1,3-dithianes resist the hydride abstraction with the trityl cation,9) therefore the above mentioned reactions are not generally applicable to these 2-substituted compounds.10)

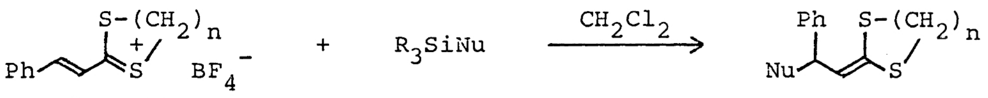
We have found here that hydride abstraction from cyclic ketene dithioacetals is smoothly achieved with the trityl cation, giving the corresponding carbenium ion stabilized by two sulfur atoms and a carbon-carbon double bond. For example, 2-(2-phenylethylidene)-1,3-dithiolane (1), prepared from methyl 3-phenylpropionate,11) gave 2-styryl-1,3-dithiolan-2-ylium tetrafluoroborate (2) as orange crystals on treatment with trityl tetrafluoroborate12) in dichloromethane at reflux temperature for 1 h (85%). In the same manner, 2-(2-phenylethylidene)-1,3-dithiane (3) gave the corresponding salt 4 as yellow crystals in 82% yield. It is noted that hydride ion is readily abstracted from 2-styryl-1,3-dithiolane (5) to afford the same salt 2, while almost no hydride abstraction is observed from 2-



Scheme 1.

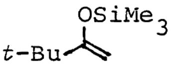
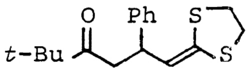
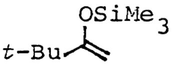
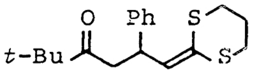
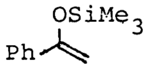
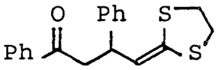
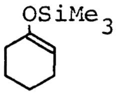
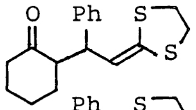
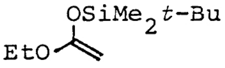
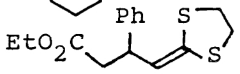
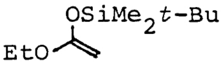
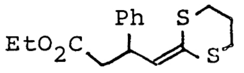
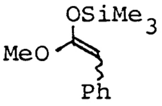
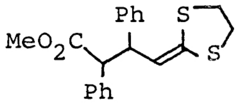
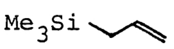
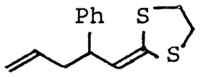
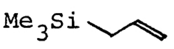
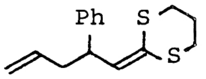
styryl-1,3-dithiane (6) similar to the above mentioned results[9] (Scheme 1).

Next, the salts thus obtained were employed in the carbon-carbon bond forming reactions with various nucleophiles such as organometallics, silylated nucleophiles, and electron rich aromatics. Among the nucleophiles examined, silyl enol ethers and an allylsilane in dichloromethane gave good results and the desired functionalized ketene dithioacetals were obtained in high yields as summarized in Table 1.[13]



2 (n=2)
4 (n=3)

Table 1. Reaction of 2 or 4 with Silylated Carbon Nucleophiles[a]

Entry	Cation	R_3SiNu	Yield/%	Product	
1	2 (n=2)		96		
2	4 (n=3)		77		
3	2 (n=2)		88		
4	2 (n=2)		84		b)
5	2 (n=2)		88		
6	4 (n=3)		79		
7	2 (n=2)		88		c)
8	2 (n=2)		86		
9	4 (n=3)		72		d)

a) All the reactions were carried out at 0 °C to rt except for entries 3, 4, 7 (-78 °C). b) Diastereomer ratio 65:35. c) Diastereomer ratio 65:35. d) The reaction was carried out in the presence of potassium fluoride.

Generally, better results were obtained in the case of the dithiolane type salt 2 compared with the dithiane type salt 4 (entries 1 vs. 2, 5 vs. 6, 8 vs. 9), and it is noted that complete regioselectivity is achieved in this reaction. No regioisomer, obtained from nucleophilic attack at the 2-position of the dithiolane or dithiane ring, is detected even in the case of a sterically hindered nucleophile (entry 7). It is also noted that functionalized ketene dithioacetals thus obtianed by the reaction with silyl enol ethers are hard to synthesize according to the conventional methods for the synthesis of ketene dithioacetals.14)

In the next place, this oxidative coupling reactin was carried out in a one-pot procedure using various ketene dithioacetals11) or ethylene dithioacetals of α, β-unsaturated aldehydes with silyl enol ethers and the results are summarized in Table 2.13)

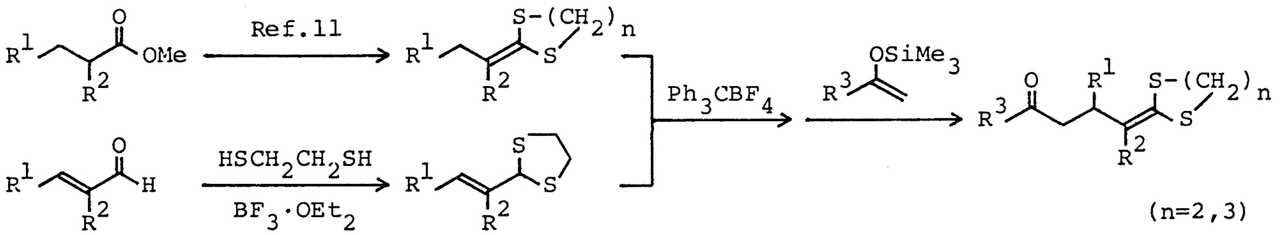
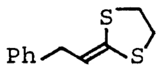
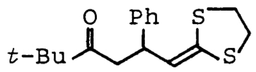
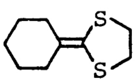
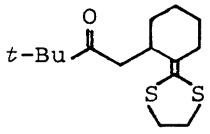
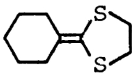
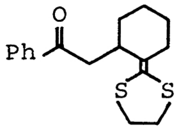
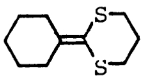
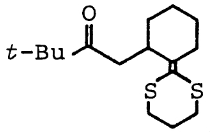
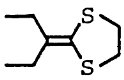
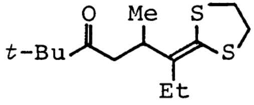
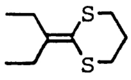
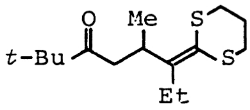
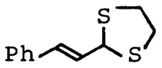
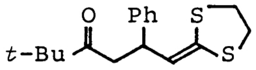
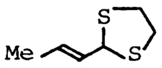
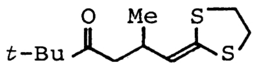


Table 2. Oxidative Carbon-Carbon Bond Forming Reaction

Starting Material	R^3	Yield/%	Product	
	*t*-Bu	86		
	*t*-Bu	85		
	Ph	86		a)
	*t*-Bu	86		
	*t*-Bu	81		
	*t*-Bu	74		
	*t*-Bu	81		
	*t*-Bu	54		

a) The coupling reaction was carried out at -78 °C.

The following is a typical procedure for the synthesis of 2-(5,5-dimethyl-4-oxo-2-phenylhexylidene)-1,3-dithiolane from 2-(2-phenylethylidene)-1,3-dithiolane (1): Trityl tetrafluoroborate (68 mg, 0.21 mmol) is dried for 1 h in vacuo and a dichloromethane (3 ml) solution of 2-(2-phenylethylidene)-1,3-dithiolane (1, 41 mg, 0.20 mmol) is added. The mixture is refluxed for 1 h, then cooled to 0 ℃. At this temperature, a dichloromethane (2 ml) solution of 3,3-dimethyl-2-trimethylsiloxy-1-butene (78 mg, 0.45 mmol) is added dropwise and the mixture is stirred for 2 h at 0 °C and overnight at room temperature. The reaction is worked up by adding aqueous sodium hydrogencarbonate and organic materials are extracted with dichloromethane. After the organic layer is dried and evaporated, the residue is purified by thin layer chromatography to give 2-(5,5-dimethyl-4-oxo-2-phenylhexylidene)-1,3-dithiolane (52 mg, 86%) as white crystals.

It is noted that the present procedure is useful for the functionalization of the β-position of saturated esters, because ketene dithioacetals, starting materials, can be easily prepared from the esters.[11] In addition, it also provides a new method for the synthesis of functionalized ketene dithioacetals from α,β-unsaturated aldehydes or saturated esters. The functionalized ketene dithioacetals thus obtained are considered to be interesting synthetic intermediates and further transformations from these products are now in progress.

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