GaCl$_3$-Promoted Ethenylation of Thioester Silyl Enolate and Dienolate with Silylethyne

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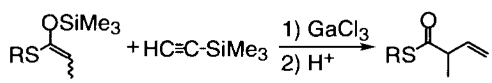
In the presence of GaCl$_3$, silyl enol ethers derived from either *S*-alkyl or *S*-aryl thioesters are ethenylated at the α-carbon atom with trimethylsilylethyne in high yields. The reactions of dienolates give α,α-diethenyl thioesters.

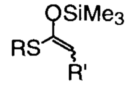
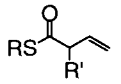
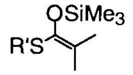
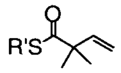
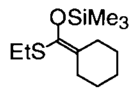
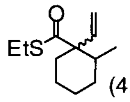
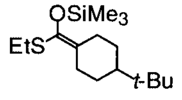
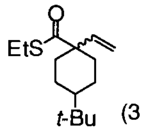
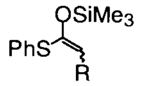
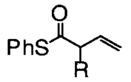
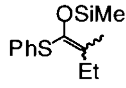
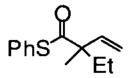
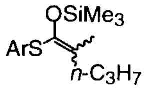
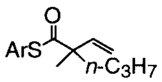
Previously, we developed a one step ethenylation reaction of silyl enol ethers derived from ketones with trimethylsilylethyne in the presence of GaCl$_3$.[1] The reaction involving carbogallation between gallium enolate and ethynylgallium was found to exhibit equatorial preferences in the ethenylation of cyclohexanone derivatives.[2] The reaction can also be applied to the silyl enol ethers derived from β-dicarbonyl compounds giving 2-ethenylated acetoacetates and malonates.[3] Notably, 2-ethenylmalonate was obtained by this method. In order to reveal scope of this methodology, the reactions of carboxylic acid derivatives were examined, and described here is the ethenylation of thioester silyl enol ethers. It is also shown that the reactions of thioester dienolates give α,α-diethenyl derivatives.

Trimethylsilylethyne (1.0 mmol) and an *S*-alkyl thioester silyl enol ether (0.5 mmol) reacted with GaCl$_3$ (2.0 mmol) in methylcyclohexane at room temperature for 5 min. Then, the reaction was quenched with THF and 6 M sulfuric acid, and an α-ethenylthioester was obtained in a high yield. A broad scope of this method is shown by the reactions of α-mono- and α,α-disubstituted thioesters (Table 1).[4] No isomerizaton to α,β-unsaturated thioesters is observed. Acidic workup with 6 M sulfuric acid is critical for the effective protonation of C–Ga bond. The stereochemistry of thioester silyl enol ether is unimportant, and the reactions of silyl enol ethers being ca. 1:1 mixtures of (*E*)- and (*Z*)-isomers give the ethenylated product in high yields. When an *S*-aryl thioester silyl enol ethers is used, acidic workup with 10 M hydrochloric acid for 3 h at room temperature gives better results than 6 M sulfuric acid, saturated aqueous ammonium chloride, or saturated aqueous triethylamine hydrochloride. In some cases small amounts of silylethenyl thioesters are formed. As for the synthesis of α-ethenylated carboxylic acid derivatives, α-alkylation reactions of 3-propenoate were reported.[5] The present method is an alternative, which directly introduces the ethenyl group.

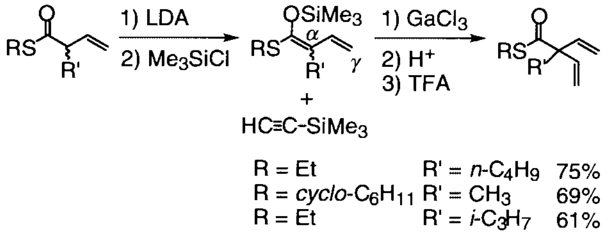
The reactions of dienolates have attracted much interest, since the nucleophiles possess two possible reaction sites. In general, alkylation reactions of alkali metal dienolates take place at the α-carbon atom. In order to compare the selectivity, the ethenylation reactions of dienolates were conducted. A dienolate was prepared from *S*-ethyl 2-ethenyl-1-hexanethioate with LDA in THF at –78 °C followed by trimethylsilyl chloride in 78% yield (Scheme 1). Then, trimethylsilylethyne (4.0 mmol) and the dienolate (0.5 mmol) were treated with GaCl$_3$ (2.0 mmol) in methylcyclohexane at room temperature for 5

Table 1. Ethenylation of silylated thioester with silylethyne



Substrate[a]	Product	Yield/%
		
R = Et	R' = CH$_2$Ph	85
R = Et	R' = n-C$_4$H$_9$	83
R = Et	R' = n-C$_6$H$_{13}$	83
R = Et	R' = i-C$_3$H$_7$	76
R = Et	R' = t-C$_4$H$_9$	72
R = Ph(CH$_2$)$_2$	R' = i-C$_3$H$_7$	70
R = *cyclo*-C$_6$H$_{11}$	R' = Me	81
R = *cyclo*-C$_6$H$_{11}$	R' = i-C$_3$H$_7$	92
		
R = *cyclo*-C$_6$H$_{11}$		86
R = (CH$_2$)$_2$Ph		61
R = Ph		91[b]
	 (4.5 : 1)[c]	82
	 (3 : 1)[c]	78
		
R = n-C$_3$H$_7$		63 + 7[b,d]
R = n-C$_4$H$_9$		54 + 7[b,d]
R = i-C$_3$H$_7$		74 + 11[b,d]
 [a]		94[b]
		
Ar = C$_6$H$_5$		91[b]
Ar = p-MeC$_6$H$_4$		83[b]

[a] Silyl enol ether with different α-substituents is a mixture of isomers (ca. $E : Z = 1 : 1$). [b] The acidic workup was conducted with 10 M HCl. [c] In parentheses are shown the diastereomer ratio. [d] Yields of ethenyl product and 2-trimethylsilylethenyl product are shown.



Scheme 1.

min. This reaction was quenched with THF and 10 M hydrochloric acid for 30 min, giving a 1:1 mixture of α,α-diethenylated thioester and α-ethenyl-α-silylethenylated thioester. The crude product was treated with trifluoroacetic acid at room temperature for 1 h for desilylation, and *S*-ethyl 2-ethenyl-2-butyl-3-butenethioate[6] was obtained in 75% yield.

It has now become clear that, as was the dienolate alkylation, the ethenylation takes place at the α-carbon atom and not at the γ-carbon atom. It should also be noted that such α,α-diethenylcarboxylic acid derivatives are not easy to prepare. For example, 5-methylbicyclo[2.1.0]pentanecarboxylates were converted at temperatures above 300 °C to α,α-diethenylpropanoates.[7] α,α-Bis(β-hydroxyethyl)phenylacetonitrile was transformed to the α,α-diethenylphenylacetic acid by a stepwise method.[8] In contrast, the present synthesis provides the α,α-diethenylated acid derivatives by simply repeating the enolization and the ethenylation processes.

Dedicated to Prof. Hideki Sakurai on the occasion of his 70th birthday.

References and Notes

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4 Typical procedures are as follows. Under an argon atmosphere, a solution of $GaCl_3$ (1.0 M, 2.0 mmol) in methylcyclohexane (2.0 mL) was added to a mixture of *S*-ethyl 3-phenylpropanethioate silyl enol ether (0.5 mmol, 133 mg) and trimethylsilylethyne (0.14 mL, 1.0 mmol) in methylcyclohexane (2.0 mL) at room temperature. After being stirred at room temperature for 5 min, THF (5.0 mL) was added to dissolve the insoluble materials. Sulfuric acid (6 M, 5.0 mL) was added, and stirring was continued for another 5 min. Then, the organic materials were extracted twice with ether. The combined organic layers were washed with water and brine, dried over magnesium sulfate, and concentrated. The residue was purified by flash column chromatography to give *S*-ethyl 2-ethenyl-3-phenylpropanethioate (93.5 mg, 85%).

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6 ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 7.6 Hz), 1.23 (3H, t, J = 7.6 Hz), 1.21–1.34 (4H, m), 1.82–1.86 (2H, m), 2.84 (2H, q, J = 7.6 Hz), 5.21 (2H, d, J = 17.6 Hz), 5.32 (2H, d, J = 10.8 Hz), 6.05 (2H, dd, J = 17.6, 12.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.6, 23.3, 23.7, 26.5, 36.6, 62.3, 117.1, 138.0, 201.9. IR (neat) 1681, 1634 cm^{-1}. MS (EI) *m/z* 212 (M^+, 2%), 67 ($M^+ - 145$, 100%). HRMS Calcd for $C_{12}H_{20}OS$, 212.1235; Found, 212.1239.

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