

Ethenylation of Silyl Enol Ether with Silylethyne

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Alkylation of enolate is one of the most fundamental carbon–carbon bond formations in organic synthesis, and it is used to attach an sp^3 -carbon atom to the carbonyl α -carbon atom. Such enolate reaction at an sp^2 -carbon atom, however, has been problematic, due to the inertness of vinyl halides or acetylenes toward metal enolates. Enolate usually does not undergo S_N1 and S_N2 reactions with vinylic halides, and does not add to acetylenes. Another serious problem is that product possessing the β -enone structure can readily isomerize to conjugate α -enone. Of the enolate olefinations,^{1,2} ethenylation, i.e. C_2 -olefination, is the most underdeveloped. Very few examples are known,² and unfortunately they are applicable only to the synthesis of unenolizable ethenylated products which do not possess an acidic proton at the carbonyl α -position. Stepwise methods, therefore, have been employed for enolate ethenylation. Reagents such as vinyl sulfone, ethynyl sulfone, trichloroethylene, α -phenylselenylacetaldehyde, α -trimethylsilylaldehyde, or vinyl ether–iron complex were reacted with enolates, and the adducts were subjected to subsequent transformations to generate the ethenyl group.³ Described here is the direct ethenylation of silyl enol ether with trimethylsilylethyne in the presence of $GaCl_3$. The reaction can be applied to the synthesis of not only unenolizable α -ethenylated ketones but also enolizable products.

Trimethylsilylethyne and silyl enol ether were reacted with $GaCl_3$ in methylcyclohexane at room temperature, and after treatment with THF and 6 M sulfuric acid, α -ethenyl ketone was obtained in a high yield (Table 1). Carbon–carbon bond formation was very rapid at room temperature, and was completed within 5 min. Use of hydrocarbon solvents such as methylcyclohexane or toluene gave better results than use of dichloromethane, THF, or acetonitrile. The organogallium compound (*vide infra*) generated in this reaction was insoluble in the nonpolar solvent, and THF was added to form a homogeneous solution. The acidic workup with 6 M sulfuric acid was also critical for the effective protonation of the C–Ga bond, and use of 1 M sulfuric acid or saturated ammonium chloride considerably lowered the yield of the product. Employment of $GaCl_3$ was essential, and no reaction took place with $AlCl_3$ and $InCl_3$, other Lewis acids of the group 13 elements. The present reaction allowed the synthesis of ethenylated ketones with an enolizable structure without isomerization to conjugated enones. The reaction can be applied to both

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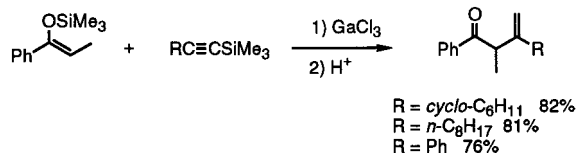
Table 1. α -Ethenylation of Silyl Enol Ethers

substrate	product	yield/%
		75 72 70
Ar = C ₆ H ₅ Ar = <i>p</i> -FC ₆ H ₄ Ar = <i>p</i> -MeOC ₆ H ₄		
		76
		74
		74
		77
		68
		63
		65
		53 + 10 ^{c)}
		11 + 46 ^{c)}

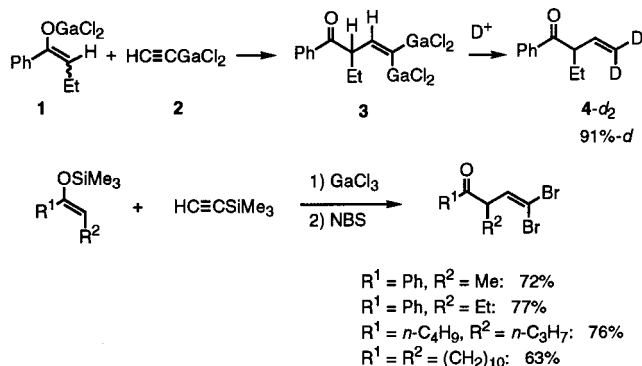
^a Z-isomer was used. ^b A mixture of isomers (*E*:*Z* = ca. 1:1) was used. ^c Yields of β -enone and α -enone are shown.

acyclic and cyclic ketones. The stereochemistry of silyl enol ether is unimportant in the ethenylation. Exceptionally cyclic ketones of relatively small ring number such as cyclohexanone and cycloheptanone gave varying amounts of conjugated α -enones. The ratio of the β -enone to the α -enone could be increased by carefully quenching the reaction at 0 °C. The α -enone, however, was still the major product in the case of cyclohexanone. Alkenylation of silyl enol ethers also took place with trimethyl-

Scheme 1



Scheme 2



silylated aliphatic and aromatic 1-alkynes (Scheme 1). C–C bond formation occurred at the internal carbon atom of 1-alkynes.

The mechanism of the reaction involved carbogallation^{4,5} at the carbon–carbon triple bond (Scheme 2). The transmetalation of silyl enol ether with GaCl₃ gave gallium enolate **1**, which was confirmed spectroscopically: ¹H NMR (CDCl₃) δ 5.79 (1H, t, *J* = 7.2 Hz). Alkynylgallium **2** was also formed by the transmetalation of silylethyne.⁴ The carbogallation then gave γ,γ-digalloyl-β-enone **3**, which precipitated from the solution. The organogallium compound **3** could be characterized by NMR when the supernatant was removed and the residue was dissolved in CDCl₃: ¹H NMR (CDCl₃) δ 4.87 (1 H, q, *J* = 6.4 Hz), 7.47 (1

H, d, *J* = 6.0 Hz). In this reaction, a black polymeric substance of unknown structure was formed, which may be the product of the self-carbogallation reaction of **2**.⁴ Finally, deuteriodegallation of **3** by the acidic workup with 6 M D₂SO₄ in D₂O gave the ethenylated ketone **4-d₂**. The organogallium intermediate could also be trapped by bromination of the C–Ga bond. Treatment of the reaction mixtures with dimethoxyethane followed by *N*-bromosuccinimide (NBS) gave γ,γ-dibromoethenylated ketones in high yields (Scheme 2). The combination of dimethoxyethane and NBS gave better results than THF and bromine in this bromination. Isomerization to the conjugated enone again was not observed for the substrates shown here.

To summarize, silyl enol ether reacted rapidly with silylethyne in the presence of GaCl₃ to give α-ethenylated ketone. The use of convenient promoter and vinylating reagent and the simple procedures make the present methodology useful.

Under an argon atmosphere, a solution of GaCl₃ (1.0 M, 20.0 mmol) in methylcyclohexane (20 mL) was added dropwise to a mixture of (*Z*)-1-phenyl-1-trimethylsilyloxy-1-butene (1.10 g, 5.0 mmol) and trimethylsilylethyne (1.40 mL, 10.0 mmol) in methylcyclohexane (20 mL) at room temperature. The mixture was stirred at room temperature for 5 min, when THF (20 mL) was added to dissolve insoluble materials. Sulfuric acid (6 M, 30 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 2-ethyl-1-phenyl-3-buten-1-one (645 mg, 74%).

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Supporting Information Available: Experimental procedures and ¹H NMR and ¹³C NMR spectral data of ethenylated ketones and γ,γ-dibromoethenylated ketones (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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