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One-Step Ethynylation of Silyl Enol Ether with Chlorosilylethyne

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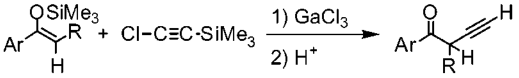
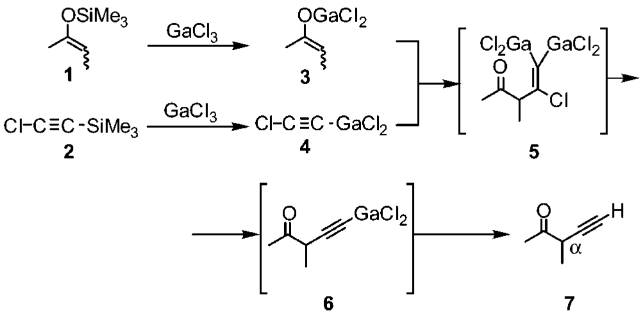
ABSTRACT



In the presence of $GaCl_3$, silyl enol ethers are ethynylated at the α-carbon atom with chlorotrimethylsilylethyne. This reaction can provide α-ethynylated aryl ketones possessing acidic α-protons without isomerization to conjugated allenyl ketones.

Ethynylation of enolate has been problematic due to the low reactivity of alkynyl halides and related compounds toward S_N1 and S_N2, and only a few methods have been reported. Dichloroethylene was reacted with ketone lithium enolates, and the adducts were subjected to reduction to generate an ethynyl group.[1] In the same paper, the reaction of lithium enolate derived from methyl cyclohexanecarbonylate with chlorotrimethylsilylethyne was reported to give α-silylethynylated ketone in 38% yield, although the scope of this one-step method remains unclear. Alkynyllead triacetates and 1-alkynyl(phenyl)iodonium tetrafluorobrate were reacted with alkali metal enolates derived from β-dicarbonyl compounds or nitroalkanes to give the ethynylated products.[2,3] All of these methods, however, have limited applicability and were not used for the synthesis of ethynylated ketones possessing an acidic proton at the carbonyl α-position. Such α-ethynyl ketones have been obtained only by the oxidation of the corresponding acetylene alcohols[4] or the acylation of allenylmetal reagents.[5] We recently reported a one-step ethynylation reaction of phenol catalyzed by $GaCl_3$.[6] We also developed a one-step ethenylation reaction of silyl enol ether in the presence of $GaCl_3$, which involved carbometalation between gallium enolate and ethynylgallium.[7] Described here is the reaction of silyl enol ether **1** with trimethylsilylated chloroethyne **2**[8] in the presence of $GaCl_3$, which gives α-ethynyl ketones **7** in one-step. The reaction proceeds via several organogallium intermediates, gallium enolate **3**, galliochloroethyne **4**, digallated β-enone **5,** and gallated ethynyl ketone **6** (Scheme 1). It is also notable that the reaction provides **7** not only with α-quaternary centers but also those possessing α-tertiary centers.

Scheme 1



2-Methyl-1-phenyl-1-trimethylsilyloxy-1-propene and **2** were reacted with $GaCl_3$ at −40 °C for 5 min, and the reaction was quenched by addition of MeOH and 6 M sulfuric acid to give 2,2-dimethyl-1-phenyl-3-butyn-1-one in

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(1) (a) Kende, A. S.; Fludzinski, P.; Hill, J. H.; Swenson, W.; Clardy, J. *J. Am. Chem. Soc.* **1984**, *106*, 3551. (b) Kende, A. S.; Fludzinski, P. *Tetrahedron Lett.* **1982**, *23*, 2373. (c) Kende, A. S.; Fludzinski, P. *Synthesis* **1982**, 455.

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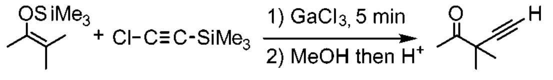
Table 1. α-Ethynylation of α,α-Disubstituted Silyl Enol Ethers[a]



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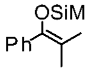
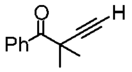
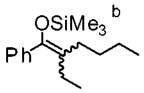
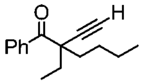
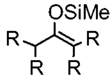
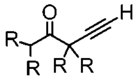
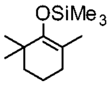
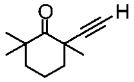
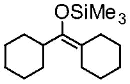
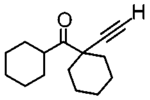
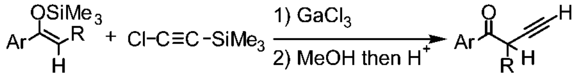
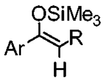
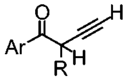
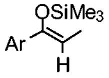
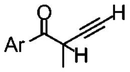
1			73
2			69
3	 R = Me		59
4	R = n-C$_4$H$_9$		93
5			58
6			95

[a] See the Supporting Information for the experimental procedures. [b] E/Z = ca. 1:1.

73% yield (Table 1, entry 1). Organogallium compound either **5** or **6** precipitated from the reaction mixture, which was dissolved by addition of MeOH. The acid workup with 6 M sulfuric acid was critical for the effective protonation of the organogallium intermediate, and use of acetic acid or saturated ammonium chloride considerably lowered the yield of the product. The reaction was applied to several silyl enol ethers giving the α-ethynylated ketones with α-quaternary centers in high yields (Table 1).

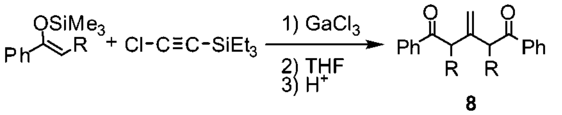
Table 2. α-Ethynylation of α-Monosubstituted Silyl Enol Ethers[a]



entry	substrate	product	yield/%
			
1	Ar = Ph, R = n-C$_5$H$_{11}$		64[b,c]
2			85
3	Ar = Ph, R = n-C$_8$H$_{17}$		93
4	Ar = p-MeC$_6$H$_4$, R = n-C$_6$H$_{13}$		78
			
5	Ar = C$_6$H$_5$		40[b]
6			75[d]
7	Ar = p-MeOC$_6$H$_4$		74[d]
8	Ar = p-FC$_6$H$_4$		75[d]

[a] See reference 9 for the experimental procedures. [b] 0.5 mmol of the substrate was reacted in 4 mL of methylcyclohexane for 5 min. [c] Accompanied by a byproduct **8** (8%). [d] 0.5 mmol of the substrate was reacted in a mixed solvent of methylcyclohexane and ClC$_6$H$_5$ (12 and 10 mL).

Scheme 2



8

R = n-C$_5$H$_{11}$

63% (meso : dl = 3 : 4)

When (Z)-1-phenyl-1-trimethylsilyloxy-1-heptene was reacted under the same conditions, 2-pentyl-1-phenyl-3-butyn-1-one was obtained in 64% yield (Table 2, entry 1).[9] The extract was rapidly passed through a short silica gel column to remove traces of gallium salts, and the product was purified by flash column chromatography (neutral silica gel) at −78 °C. Isomerization of the product to conjugate α-allenyl ketones could be avoided by these isolation procedures. α-Ethynyl ketones are more susceptible to isomerization compared to α-ethenyl ketones.[7] The product was accompanied by a small amount of 3-methylene-2,4-dipentyl-1,5-diphenyl-1,5-pentanedione **8** (8%), which may be formed by the carbogallation of **3** and **6**. The yield of **8** increased to 63%, when the reaction was conducted at 0 °C using triethylsilylated chloroethyne (Scheme 2). In contrast, formation of **8** was inhibited by reacting at −40 °C under diluted conditions in methylcyclohexane−chlorobenzene (10:1) for 30 s, and the ethynylated product was obtained in 85% yield (Table 2, entry 2). In the case of (Z)-1-trimethylsilyloxy-1-phenyl-1-propane, a 6:5 mixed solvent of methylcyclohexane and chlorobenzene gave better results (Table 2, entries 5 and 6). The different optimum solvent ratio may reflect the solubility of the organogallium intermediates: While solubilization of gallium enolate **3** promotes the

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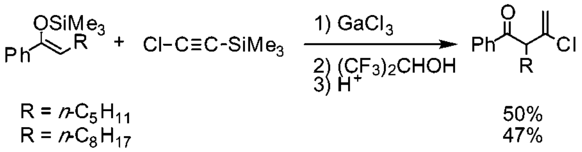
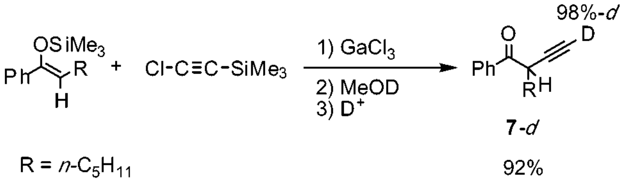
(9) **Typical Procedures for the α-Ethynylation of α-Monosubstituted Silyl Enol Ethers.** Under an argon atmosphere, a solution of 1.0 M GaCl$_3$ (2 mmol) in methylcyclohexane (2 mL) was added to a mixture of (Z)-1-phenyl-1-trimethylsilyloxy-1-heptene (131 mg, 0.5 mmol) and chlorotrimethylsilylethyne (132 mg, 1.0 mmol) in a mixed solvent of methylcyclohexane (18 mL) and chlorobenzene (2 mL) at −40 °C. The mixture was stirred for 30 s, when MeOH (2 mL) was added. After the mixture was stirred for 5 min at −40 °C, 6 M sulfuric acid (7 mL) was added, and the solution was warmed to room temperature. Stirring was continued for 1 h, and the organic materials were extracted twice with diethyl ether. The combined organic layers were washed with brine and dried over MgSO$_4$. The extracts were passed through short silica gel column (hexane/diethyl ether = 10) and were concentrated. The residue was purified by flash column chromatography (Kanto Chemical, silica gel 60 N (spherical, neutral), 40−100 μm, hexane/ethyl acetate = 400) at −78 °C to give 2-pentyl-1-phenyl-3-butyn-1-one (91 mg, 85%).

reaction, the higher amount of **5** or **6** in solution results in the side reactions such as the formation of **8**. Notably, when 1,1,1,3,3,3-hexafluoro-2-propanol was added in place of MeOH, *β*-chloro-*β*-enones were obtained (Scheme 3). The result suggests that the *β*-elimination of *γ*,*γ*-digallio-*β*-enone **5** takes place on addition of MeOH to give **6** and then **7**. Formation of metalated **6** in the reaction mixture was indicated by deuteration experiment (Scheme 4). Unfortunately, this ethynylation reaction proceeded effectively only for the aromatic ketone enolates. An aliphatic enolate, 6-trimethylsilyloxy-5-undecene, gave the α-ethynylated ketone in only 16% yield with the recovered ketone in 40% yield.

Scheme 3



Scheme 4



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Supporting Information Available: Spectroscopic data for all new products. This material is available free of charge via the Internet at http://pubs.acs.org.

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