

Sequential Carbometallation/Elimination Reaction Takes Place between Gallium Enolate and Chloroethyne

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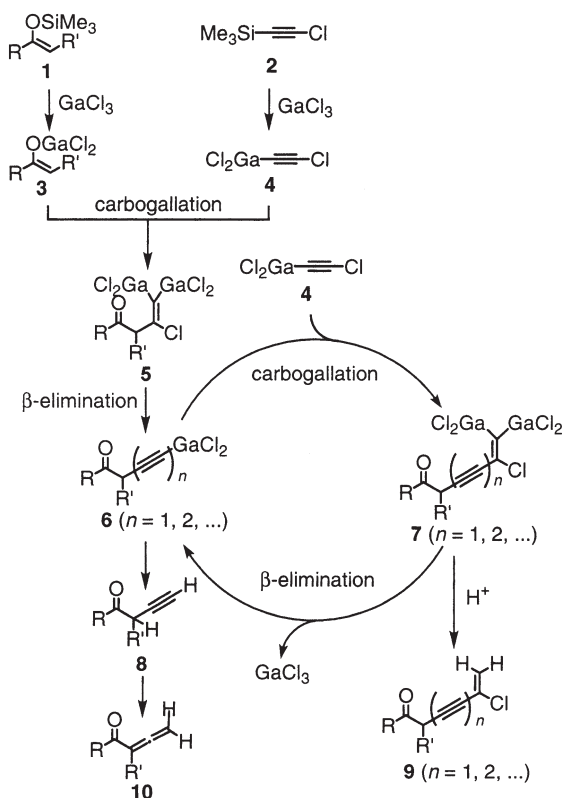
(Received December 20, 2002; CL-021080)

In the presence of GaCl_3 , silyl enol ethers are sequentially ethynylated at the α -carbon atom with chlorotrimethylsilyl-ethyne giving α -enynylated, α -endiynylated and α -entriynylated ketones.

Recently, we reported that GaCl_3 promotes α -ethynylation reaction of silyl enol ether **1** with chlorotrimethylsilyl-ethyne (**2**) in methylcyclohexane or in the hydrocarbon solvent containing a small amount of chlorobenzene.¹ Carbometallation (carbogallation) reaction between gallium enolate **3** and ethynylgallium **4** generated from **1** and **2** gives digallio ketone **5**, which on treatment with methanol is converted to ethynylgallium **6** ($n = 1$) (Scheme 1). The product either α -ethynyl ketone **8** or α -allenyl ketone **10** is obtained by protodegallation of **6** ($n = 1$). Since alkynylgalliums can dimerize via carbogallation giving 1,1-dimetallo-1-buten-3-yne derivatives,² it was considered that **6** ($n = 1$) would undergo further carbogallation to give the digallated enyne **7** ($n = 1$), which could be isolated as an enyne **9** ($n = 1$) after protodegallation. Further elimination reaction of **7**

($n = 1$) would also give **6** ($n = 2, \dots$) and then **7** ($n = 2, \dots$). This one-pot reaction can be an interest method for the preparation of conjugated polyene compounds **9** ($n = 1, 2, \dots$). It was found that, when the reaction of **1** and **2** was conducted in dichloromethane–methylcyclohexane (1:1) instead of the hydrocarbon solvent, α -enynylated ketones **9** ($n = 1$), α -endiynylated ketones **9** ($n = 2$), and α -entriynylated ketones **9** ($n = 3$) were obtained. Although a stepwise synthesis of polyene compounds from alkynylmetal and 1,1-dichloro-2,2-difluoroethene via addition/elimination is known,³ such one-pot synthesis as described here was not reported.^{4,5}

A silyl enol ether **11** derived from 1-phenyl-1-heptanone was treated with **2** (2 eq.) and GaCl_3 (4 eq.) in dichloromethane–methylcyclohexane (1:1) at -40°C for 0.5 min, which was followed by the treatment with methanol and 6 M sulfuric acid. Silica gel chromatography gave 5-chloro-2-pentyl-1-phenyl-5-hexen-3-yn-1-one (**12**) ($n = 1$) in 55% yield (Table 1, Entry 1): ^{13}C -NMR (CDCl_3) δ 68.5, 69.3. IR 2207 cm^{-1} . Allene **13** was also obtained in 30% yield, which was formed from the α -ethynylated ketone **14** during the chromatography. The α -enynylated ketone **12** ($n = 1$) turned out to be more stable to silica gel compared to **14**. When the enynylation reaction was quenched after 5 min at -40°C , **12** ($n = 1$) was obtained in 74% yield, and the amount of **13** decreased (Entry 2). After 15 min, diynyl ketone **12** ($n = 2$) was obtained along with **12** ($n = 1$) in 10% yield (Entry 4): ^{13}C -NMR (CDCl_3) δ 55.2, 62.0, 73.3, 74.7. IR $2220, 2146\text{ cm}^{-1}$. A small amount of **12** ($n = 3$) (2%) was also isolated: ^{13}C -NMR (CDCl_3) δ 56.0, 58.9, 59.5, 67.0, 74.8, 75.3.



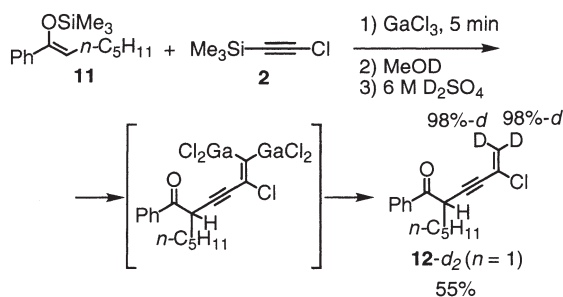
Scheme 1.

Table 1. Enynylation of **11**

$\text{Ph}-\text{CH}=\text{CH}-\text{OSiMe}_3 + \text{Me}_3\text{Si}-\text{C}\equiv\text{CH} \xrightarrow[\text{2) MeOH, 3) 6 M H}_2\text{SO}_4]{\text{1) GaCl}_3, \text{Time, } -40^\circ\text{C}}$					
Entry	Time/min	Yield/%			
		12 ($n = 1$)	12 ($n = 2$)	12 ($n = 3$)	13
1	0.5	55	trace	N.D. ^a	30
2	5	74	N.D.	N.D.	4
3 ^b		9	N.D.	N.D.	63
4	15	61	10	2	11
5 ^c		54	20	4	N.D.
6	30	62	10	1	8

^a N.D.: Not detected. ^b The reaction was conducted in methylcyclohexane.
^c 6 equiv. of **2** was used.

IR 2198, 2105 cm^{-1} . Since yields of **12** ($n = 1, 2, 3$) did not change after 30 min, the sequential ethynylation stopped at the stage probably due to the consumption of **2** and/or GaCl_3 . When **11** was treated with 6 equiv. of **2** in the presence of GaCl_3 (4 equiv.), yields of **12** ($n = 2$) and **12** ($n = 3$) increased (Entry 5). It is therefore apparent that **11** reacts in stepwise way with **2** to give **14**, **12** ($n = 1$), **12** ($n = 2$), and **12** ($n = 3$) in this order. Formation of 1,1-digallated intermediate before aqueous workup was indicated by a deuteration experiment. When the reaction of **11** and **2** was quenched after 5 min with MeOD and 6 M D_2SO_4 , deuterium was incorporated at both *exo*-olefin protons of **12** ($n = 1$) (Scheme 2).



Scheme 2.

It is also notable that a simple change of the solvent gives either **12** ($n = 1$) or **13** under otherwise identical conditions (Table 1, Entries 2 and 3): Use of methylcyclohexane gave **13** in 63% yield; use of dichloromethane–methylcyclohexane (1:1) mixture gave **12** ($n = 1$) in 74% yield. The solvent effect is probably reflecting the facility of the β -elimination from **5** giving **6** ($n = 1$) during the reaction (Scheme 1). As previously observed, addition of a Lewis basic solvent such as methanol promoted the β -elimination of **5** giving **6** ($n = 1$) in the ethynylation reaction.¹ In the present reaction, *in situ* β -elimination of **5** may be facilitated by dichloromethane giving **6** ($n = 1, 2, \dots$), which undergo carbogallation leading to **7** ($n = 1, 2, \dots$).

The enynylation reaction was applied to several silyl enol ethers by treating with **2** in dichloromethane–methylcyclohexane (1:1) mixture at -40°C for 5 min (Table 2). The length of the alkyl chain of phenyl alkyl ketone enolates has some effect on the yield: The substrates with shorter alkyl groups give higher yields of α -endiynylated products **9** ($n = 2$) (Entries 1–5). Aromatic silyl enol ethers with electron-withdrawing *p*-substitutes gave **9** ($n = 1$) in higher yields (Entries 6 and 7) compared to those possessing electron-donating groups (Entries 8 and 10). In the latter cases, allenyl ketones **10** were obtained as the major products at -40°C . Since the yields of **9** ($n = 1, 2$) increased when the reactions were carried out at higher temperatures (Entry 9, 11), the β -elimination from **5** to **6** ($n = 1$) is slower for the aromatic ketones with the electron-donating groups. Aliphatic enolates also give enynes **9** ($n = 1, 2, 3$) (Entries 13 and 14).

Although efficiency is still not very high, this methodology can be an interesting approach for the preparation of conjugated polyyne compounds.

The authors express thanks to JSPS for Grants (No. 13557193 and No. 13771323). M. A. expresses her thanks to the Hayashi Memorial Foundation for Female Natural Scientists, and the Sankio Chemical Award in Synthetic Organic Chemistry, Japan.

Table 2. Enynylation of silyl enol ether with **2**

Entry	Substrate	Product	Yield/%	
			9 ($n = 1$)	9 ($n = 2$)
1			45	14
2	$\text{CH}_2\text{CH}(\text{CH}_3)_2$		49	9
3	$n\text{-C}_3\text{H}_7$		66	4
4	$n\text{-C}_5\text{H}_{11}$		74	0
5	$n\text{-C}_8\text{H}_{17}$		73	0
6			71	0
7	$p\text{-CF}_3\text{C}_6\text{H}_4$		50	0
8	$p\text{-MeOC}_6\text{H}_4$		5	6 ^{a)}
9 ^{b)}			37	15 ^{c)}
10	$p\text{-MeC}_6\text{H}_4$		13	9
11 ^{d)}			37	21
12	1-Naphthyl		58	7
13			42	15
14 ^{e)}	$\text{R} = \text{R}' = n\text{-C}_4\text{H}_9$		29	18

^a Allenyl ketone was obtained in 54% yield. ^b Reaction temperature: -20°C . ^c Allenyl ketone was obtained in 65% yield. ^d Reaction temperature: -10°C . ^e Entriynylated ketone **9** ($n = 3$) was obtained in 3% yield.

References and Notes

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- An α -enynylation reaction of 2,6-dimethyl-2-cyclohexene-1-one enolate with hexachloro-1,3-butadiene was reported: A. S. Kende, P. Fludzinski, J. H. Hill, W. Swenson, and J. Clardy, *J. Am. Chem. Soc.*, **106**, 3551 (1984).
- Under an argon atmosphere, a solution of GaCl_3 (1.0 M, 4.0 mmol) in methylcyclohexane (2 mL) was added to a mixture of **11** (131 mg, 0.5 mmol) and **2** (132 mg, 1.0 mmol) in dichloromethane (2 mL) at -40°C . The mixture was stirred for 5 min at -40°C , and then methanol (2 mL) and 6 M sulfuric acid (7 mL) were added. The mixture was warmed to room temperature, and stirred for 1 h. The organic materials were extracted twice with ether. The combined organic layers were washed with brine, and dried over MgSO_4 . The solution was passed through short silica gel column to remove traces of gallium salts, and was concentrated. The residue was purified by flash column chromatography (hexane) to give **12** ($n = 1$) (102 mg, 74%) and **13** (4 mg, 4%).