

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

Ryo Amemiya, Akiko Fujii, Mieko Arisawa, and Masahiko Yamaguchi*

Department of Organic Chemistry, Graduate School of Pharmaceutical Sciences,
Tohoku University, Aoba, Sendai 980-8578

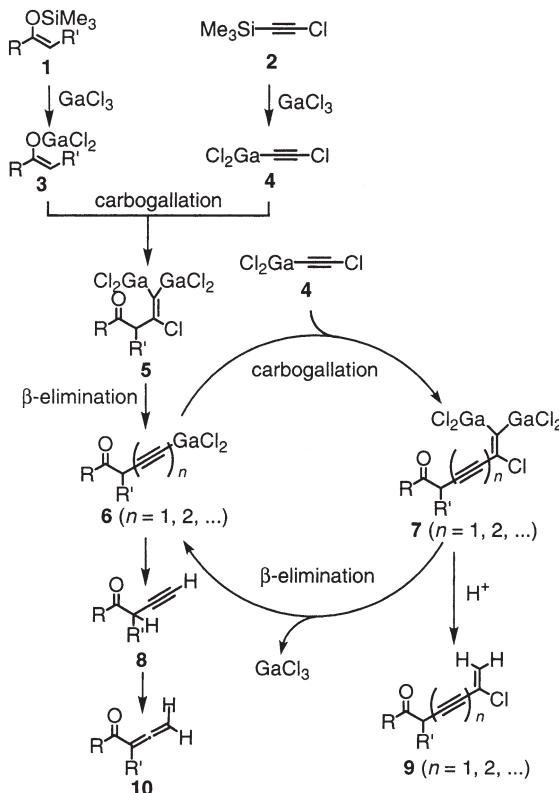
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In the presence of GaCl_3 , silyl enol ethers are sequentially ethynylated at the α -carbon atom with chlorotrimethylsilyl-ethyne giving α -enynylated, α -endiynylated and α -trienylated ketones.

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 Carbometalation (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-dimetalloc-1-buten-3-yne derivatives,² it was considered that **6** ($n = 1$) would undergo further carbogallation to give the digalliated enyne **7** ($n = 1$), which could be isolated as an enyne **9** ($n = 1$) after protodegallation. Further elimination reaction of **7**

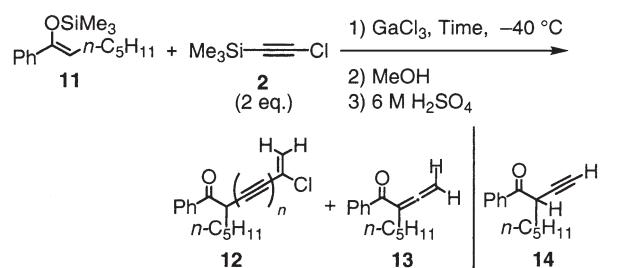
($n = 1$) would also give **6** ($n = 2, \dots$) and then **7** ($n = 2, \dots$). This one-pot reaction can be an interest method for the preparation of conjugated polyyne compounds **9** ($n = 1, 2, \dots$). It was found that, when the reaction of **1** and **2** was conducted in dichloromethane–methylcyclohexane (1:1) instead of the hydrocarbon solvent, α -enynylated ketones **9** ($n = 1$), α -endiynylated ketones **9** ($n = 2$), and α -trienylated ketones **9** ($n = 3$) were obtained. Although a stepwise synthesis of polyyne 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 -enynylated 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 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**

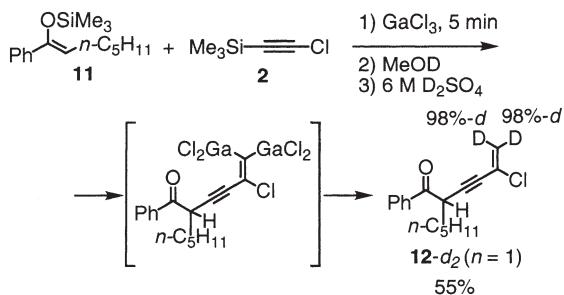


Entry	Time/min	Yield/%			
		12 ($n = 1$)	12 ($n = 2$)	12 ($n = 3$)	13
1	0.5	55	trace	N.D. ^{a)}	30
2	5	74	N.D.	N.D.	4
3 ^{b)}		9	N.D.	N.D.	63
4	15	61	10	2	11
5 ^{c)}		54	20	4	N.D.
6	30	62	10	1	8

^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-digalliated 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.

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

Entry	Substrate	Product	Yield/%	
			9 ($n = 1$)	9 ($n = 2$)
1			45	14
2			49	9
3			66	4
4			74	0
5			73	0
6			71	0
7			50	0
8			5	6 ^{a)}
9 ^{b)}			37	15 ^{c)}
10			13	9 ^{c)}
11 ^{d)}			37	21
12			58	7
13			42	15
14 ^{e)}			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 Entrynated ketone **9** ($n = 3$) was obtained in 3% yield.

References and Notes

- 1 M. Arisawa, R. Amemiya, and M. Yamaguchi, *Org. Lett.*, **4**, 2209 (2002); Also see catalytic ethynylation reaction of phenols using GaCl_3 : K. Kobayashi, M. Arisawa, and M. Yamaguchi, *J. Am. Chem. Soc.*, **124**, 8528 (2002).
- 2 M. Yamaguchi, A. Hayashi, and M. Hirama, *Chem. Lett.*, **1995**, 1093.
- 3 K. Okuhara, *J. Org. Chem.*, **41**, 1487 (1976).
- 4 Sequential carbometalation reaction of organocupper reagent with acetylene is known: M. Fuber and R. J. K. Taylor, *J. Chem. Soc., Perkin Trans. 1*, **1986**, 1809.
- 5 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).
- 6 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%).