

Tertiary Amine-Accelerated Allylgallation of Terminal Alkynes

Kazuhiko Takai,* Yoshito Ikawa, Keiji Ishii, and Makoto Kumanda

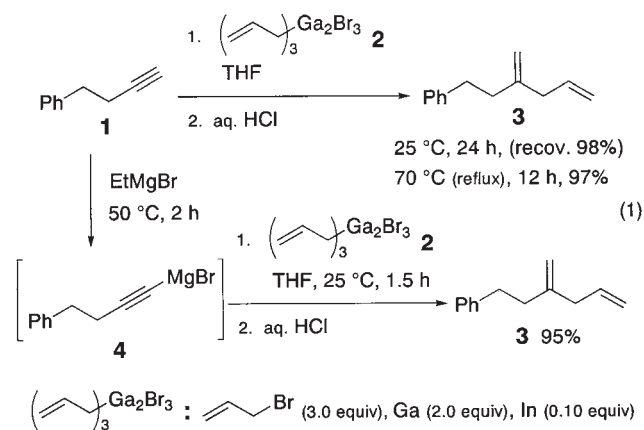
Department of Applied Chemistry, Faculty of Engineering, Okayama University, Tsushima, Okayama 700-8530

(Received November 19, 2001; CL-011165)

Allylic gallium sesquibromides prepared by reduction of allylic bromides with gallium metal in the presence of a catalytic amount of indium, add to terminal alkynes with the aid of a tertiary amine to give 1,4-dienes.

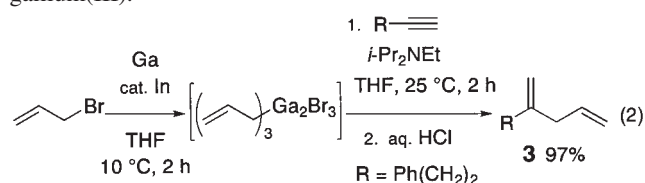
Addition of allylic metal compounds to carbon-carbon triple bonds is an important method for constructing carbon skeletons, and employs such metals as Al, Zn, B, and In.¹⁻³ In 1997, Yamaguchi reported the addition of allylic gallium compounds to alkynes, and the reaction was conducted in cyclohexane, a non-polar solvent.⁴ We have recently found that allylic gallium compounds are prepared from allylic halides and gallium metal in THF using indium as a mediator.⁵ Thus, we examined the addition of the allylic gallium compounds to alkynes in the THF solvent, and found that trialkylamines have an accelerating effect on the addition.

In contrast to the reaction in cyclohexane,⁴ the addition of the allylgallium compound **2**⁶ to alkyne **1** in THF did not proceed at 25 °C, and the starting alkyne **1** was recovered in 98% yield after 24 h stirring (eq 1). Upon heating at reflux, the reaction completed in 12 h and the 1,4-diene **3** was obtained in 97% yield after acidic workup. Such allylations of alkynes are sometimes accelerated using alkynylmagnesium compounds. Thus, the alkyne **1** was treated with ethylmagnesium bromide (1.0 equiv) at 50 °C for 2 h before addition of **2**, and the addition proceeded at 25 °C in 1.5 h to give **3** in 95% yield (eq 1).

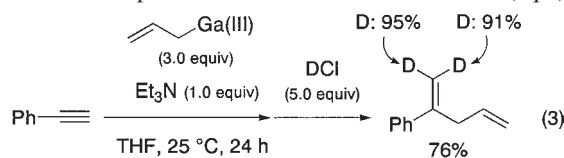


Because the formation of the alkynyl Grignard reagent **4** requires heating at 50 °C, we examined several additives to promote the reaction under milder conditions. Addition of an equimolar amount of a tertiary amine was found to accelerate the reaction at 25 °C. For example, when the alkyne **1** (1.0 equiv) was treated with a solution of allylgallium (**2**, 3.0 equiv)⁶ in THF at 25 °C for 20 h in the presence of Et₃N (1.0 equiv),⁷ the 1,4-diene **3** was obtained in 99% yield after workup with aqueous hydrochloric acid (1 M). Addition of *i*-Pr₂NEt (1.0 equiv) was

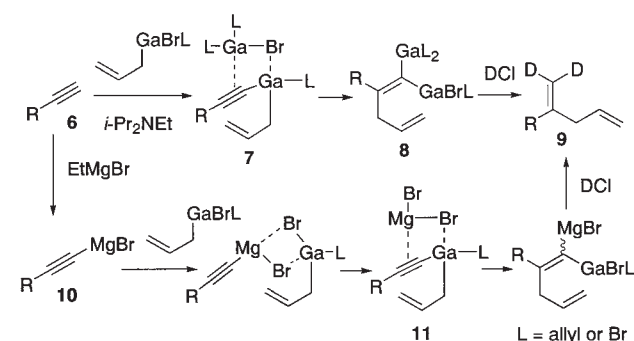
more effective for the allylation, and the reaction completed in 2 h and **3** was obtained in 97% yield (eq 2). In contrast, pyridine and DABCO did not accelerate the reaction and 88% and 95% of **1** were recovered, respectively, after 24 h stirring. In addition to basicity, steric hindrance is an important factor for the acceleration, as it influences the coordination of the amine to gallium(III).



Under the conditions in eq. 2, an internal alkyne, 5-phenyl-2-pentyne (**5**), did not react with the allylgallium compound, and 99% of the alkyne **5** was recovered. This suggests that the addition proceeded via deprotonation of the terminal alkyne. In order to examine this postulate, the reaction was quenched with deuterated hydrochloric acid, and deuterium was introduced at both the olefinic positions with a content of over 90% (eq 3).



We assume the following mechanism for the reaction (Scheme 1). An allylalkynylgallium species **7** is produced by deprotonation of the terminal alkyne **6** with an amine and metalation (upper pathway). Gallium(III)-assisted allylgallation generates the 1,1-digallium compound **8**.^{2b,2c,3b,8,9} Hydrolysis of **8** with DCl gives the dideuterated 1,4-diene **9**. When the alkyne **6** is treated with EtMgBr, the magnesium acetylide **10** is formed (lower pathway). Transmetalation to **11** followed by rearrangement and hydrolysis affords **9**.



Scheme 1.

The results of the addition of allylic gallium compounds to terminal alkynes are shown in Table 1. 2-Substituted 1,4-dienes

Table 1. Addition of allylic gallium compounds to terminal alkynes^a

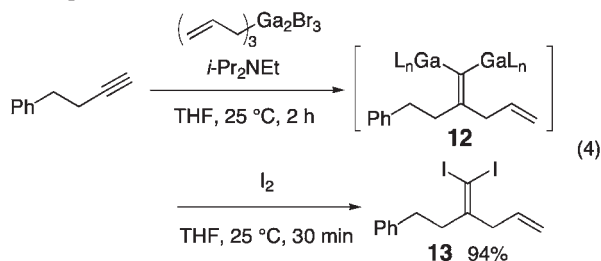
R	allylic bromide	time h	Yield ^b %	product
<i>n</i> -C ₁₀ H ₂₁		4	96	
Ph(CH ₂) ₂		20	85 ^c	
Ph		7	77	
		5	92	
MeO ₂ C(CH ₂) ₈		5	82 ^e	

^aThe reaction was conducted on a 1.0 mmol scale. Allylic bromide (3.0 mol), Ga (2.0 mol), In (0.10 mol), and *i*-Pr₂NEt₂ (1.0 mol) were used per mole of alkyne. ^bIsolated yields. ^cA mixture of isomeric bromides was used. ^d4-Phenyl-1-butyne was recovered in 17% yield. ^e4-Allyl-13-methylene-1,15-hexadecadien-4-ol derived by the desired allylation to the carbon-carbon triple bond and bis-allylation of the ester group, was obtained in 5% yield.

are obtained selectively in all cases. In the case of crotyl bromide, the reaction proceeded slowly, and the carbon-carbon bond was produced at the more substituted carbon of the crotylmethyl species, which is the same tendency as for the indium case.^{3b,c} Such functional groups as ether and ester groups were not affected during the allylation of alkynes.

Allylaluminum sesquibromide derived from allyl bromide and aluminum metal under indium catalysis did not react with the alkyne **1** at 25 °C.

The geminal digallium alkene **12** could be trapped with iodine at 25 °C to give the 1,1-diiodo-1,4-alkadiene **13** in 94% yield (eq 4).



Typical procedure for **3** (eq 2): To a solution of allylgallium sesquibromide in THF prepared from allyl bromide (0.36 g, 3.0 mmol), gallium powder (0.14 g, 2.0 mmol), and indium metal (12 mg, 0.10 mmol),⁶ were added *i*-Pr₂NEt (0.17 mL, 1.0 mmol)

at 25 °C, and a solution of **1** (0.13 g, 1.0 mmol) in THF (2 mL), successively. After stirring at 25 °C for 2 h, the mixture was poured into aq. hydrochloric acid (6 M, 10 mL), and extracted with hexane (3 × 10 mL). The organic extracts were washed with brine, and concentrated by an evaporator. Purification by column chromatography (hexane) gave **3** in 97% yield (0.17 g).

Dedicated to Professor Teruaki Mukaiyama on the occasion of his 75th birthday.

References and Notes

- For reviews, see: a) J. F. Normant and A. Alexakis, *Synthesis*, **1981**, 841. b) P. Knochel, "Carbometallation of Alkenes and Alkynes," in "Comprehensive Organic Synthesis," ed. by B. M. Trost, Pergamon, Oxford (1991), Vol. 4, Chap. 4.4, p 865. c) I. Marek and J. F. Normant, "Carbometallation Reactions," in "Metal-catalyzed Cross-coupling Reactions," ed. by F. Diederich and P. J. Stang, Wiley-VCH, Weinheim (1998), p 271.
- For allylmethylation of alkynes, see: a) Al: J. A. Miller and E. Negishi, *Tetrahedron Lett.*, **25**, 5863 (1984). b) Zn: Y. Frangin and M. Gaudemar, *Bull. Soc. Chim. Fr.*, **1976**, 1173. c) E. Negishi and J. A. Miller, *J. Am. Chem. Soc.*, **105**, 6761 (1983). d) G. A. Molander, *J. Org. Chem.*, **48**, 5409 (1983). e) I. Creton, I. Marek, and J. F. Normant, *Tetrahedron Lett.*, **36**, 7451 (1995). f) B: N. Bubnov, M. S. Grigorian, A. V. Tsyban, and B. M. Mikhailov, *Synthesis*, **1980**, 902; Y. N. Bubnov, A. V. Tsyban, and B. M. Mikhailov, *Synthesis*, **1980**, 904. g) Mg: K. Okada, K. Oshima, and K. Utimoto, *J. Am. Chem. Soc.*, **118**, 6076 (1996). h) Ti: J. J. Eisch and M. P. Boleslawski, *J. Organomet. Chem.*, **334**, C1 (1987). i) Zr: S. Yamanoi, T. Imai, T. Matsumoto, and K. Suzuki, *Tetrahedron Lett.*, **38**, 3031 (1997).
- In: a) S. Araki, A. Imai, K. Shimizu, M. Yamada, A. Mori, and Y. Butsugan, *J. Org. Chem.*, **60**, 1841 (1995). b) N. Fujiwara and Y. Yamamoto, *J. Org. Chem.*, **62**, 2318 (1997); N. Fujiwara and Y. Yamamoto, *J. Org. Chem.*, **64**, 4095 (1999). c) B. Ranu and A. Majee, *Chem. Commun.*, **1997**, 1225.
- M. Yamaguchi, T. Sotokawa, and M. Hiram, *Chem. Commun.*, **1997**, 743.
- K. Takai and Y. Ikawa, submitted for publication.
- A solution of allylgallium in THF (ca. 1.35 M solution) was prepared as follows. A catalytic amount of indium powder (1.0 mmol) was added to a mixture of allyl bromide (30 mmol) and gallium metal (shot, 20 mmol) in THF (20 mL), and the mixture was stirred at 10 °C for 24 h. When gallium powder was used, all the gallium dissolved at 10 °C within 2 h. The solution of allylgallium in THF could be stored at 5 °C (in a refrigerator) for 1 month without decreasing the reactivity, but the reactivity decreased gradually at 25 °C.
- Y. Han and Y.-Z. Huang, *Tetrahedron Lett.*, **36**, 7277 (1995).
- M. Yamaguchi, A. Hayashi, and M. Hiram, *Chem. Lett.*, **1995**, 1093.
- For addition of allylmetal species to alkenylmetals, see: K. Suzuki, T. Imai, S. Yamanoi, M. Chino, and T. Matsumoto, *Angew. Chem., Int. Ed. Engl.*, **36**, 2469 (1997); A. Hirai, M. Nakamura, and E. Nakamura, *J. Am. Chem. Soc.*, **121**, 8665 (1999); I. Marek, P. R. Schreiner, and J. F. Normant, *Org. Lett.*, **1**, 929 (1999).