2318 *J. Org. Chem.* **1997,** *62,* 2318−2319

Allylation of Unactivated and/or Functionalized Alkynes with Allylindiums

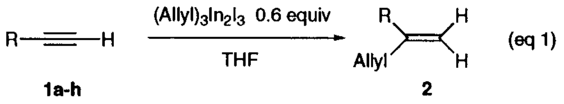
Naoya Fujiwara and Yoshinori Yamamoto*

Department of Chemistry, Graduate School of Science, Tohoku University, Sendai 980−77, Japan

Received January 22, 1997

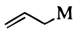
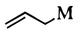
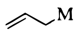
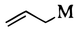
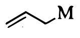
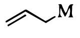
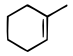
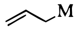
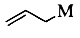
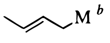
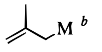
Since the first carbometalation discovered by Ziegler and Bähr in 1927,[1] a number of additions of organometallics to carbon−carbon multiple bonds have been reported.[2] Although the allylmetalation of activated alkynes, such as alkynyl ketones (Michael acceptor) and alkynols (functional group substituted alkynes), and/or the intramolecular allylmetalation proceed smoothly with various other allylmetals,[2] allylmetalation of simple unactivated alkynes **1** is not so easy and only a limited number of allylmetals are available for this purpose.[3] More recently, Araki and his co-workers reported that the reaction of allylindium[4] with terminal alkynols[5a] and allenols[5b] *in DMF* at 100−140 °C gave the corresponding allylation products in good to high yields. However, the presence of a hydroxy group was essential for facilitating the addition, and the allylation of simple unactivated alkynes was sluggish even at higher temperatures (150−180 °C), giving the allylation products in low yields (12−28%).[5a]

We wish to report that allylindium reagents react with both unactivated alkynes and functionalized alkynes very readily *in THF*[6] to give the corresponding allylation products in good to high yields (eq 1). Perhaps, the allylindium addition to alkynes is the most widely applicable procedure among a variety of allylmetalation methods.[3]



2a: R = Ph, Allyl = $CH_2CH{=}CH_2$
2b: R = p-$CH_3C_6H_4$, Allyl = $CH_2CH{=}CH_2$
2c: R = p-$CH_3OC_6H_4$, Allyl = $CH_2CH{=}CH_2$
2d: R = $PhCH_2$, Allyl = $CH_2CH{=}CH_2$
2e: R = n-Hex, Allyl = $CH_2CH{=}CH_2$
2f: R = n-Dec, Allyl = $CH_2CH{=}CH_2$
2g: R = 1-Cyclohexenyl, Allyl = $CH_2CH{=}CH_2$
2h: R = Et_2NCH_2, Allyl = $CH_2CH{=}CH_2$

Table 1. Allylation of Alkynes with Allylindiums

entry	alkynes **1**	alkynes R	allyl-M	product	yield[a] (%)
1	**1a**	Ph		**2a**	94
2	**1b**	p-$CH_3C_6H_4$		**2b**	81
3	**1c**	p-$CH_3OC_6H_4$		**2c**	66
4	**1d**	$PhCH_2$		**2d**	72
5	**1e**	n-Hex		**2e**	60
6	**1f**	n-Dec		**2f**	70
7	**1g**			**2g**	93
8	**1h**	Et_2NCH_2		**2h**	75
9	**1a**	Ph		**3**	88
10	**1a**	Ph		**4**	90

[a] Isolated yield. [b] Bromides were used as starting materials instead of iodide.[5]

The results are summarized in Table 1. The reaction of phenylacetylene (**1a**) with 0.6 equiv of allylindium,[7] generated in situ by mixing In powder (1.2 equiv) with allyl iodide (1.8 equiv) *in THF*, gave the allylation product **2a** regioselectively in 94% yield (Table 1, entry 1). The reactions of *para*-substituted arylalkynes **1b** and **1c** and of benzylacetylene **1d** proceeded smoothly to give **2b**−**d**, respectively, in high to good yields (Table 1, entries 2−4). The reactions shown in entries 1−4 (Table 1) were complete with 2 h at 70 °C. The reactions of 1-octyne **1e** and 1-dodecyne **1f** gave **2e** and **2f**, respectively, in good yields (Table 1, entries 5 and 6). The allylation of the enyne **1g** also proceeded smoothly to give the corresponding allylation product **2g** in excellent yield (Table 1, entry 7). The allylations in entries 5−7 were complete within 1 h at 70 °C. The amino-substituted alkyne **1h**, which was inert to the Lewis acid-catalyzed allylsilylation[3j] due to the coordination of Lewis acid to the nitrogen atom,[8] reacted with allylindium at 70 °C for 2 h, giving the corresponding allylation product **2h** in 75% yield (Table 1, entry 8). It should be noted that the regioselectivity of the allylation of **1h** is opposite to that of propargyl alcohol and related hydroxy-substituted alkynes;[5a] chelation-promoted allylation[5] is not involved in the allylation of **1h**.

---

(1) Ziegler, K.; Bähr, K. *Chem. Ber.* **1928**, *61*, 253.

(2) For reviews, see: (a) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841 (organo-Li, -Mg, -Zn, -B, -Al, and -Cu compounds). (b) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 38 (stoichiometric organo-Li, -Mg, and -Zn and catalytic Ni, Pd, and Pt compounds). (c) Negishi, E. *Pure Appl. Chem.* **1981**, *53*, 2333 (organo-Al/Ti and -Al/Zr system). (d) Knochel, P. *Comprehensive Organometallic Chemistry II*; Able, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: Oxford, 1995; Vol. 11, p 159 (organo-Li, -Mg, -Zn, -B, -Al, -Cu, -Hg/Pd, -Ni, -Mn compounds). (e) Knochel, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, p 865. (f) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207 (organo-Li, -Mg, -Zn, -B, -Al compounds).

(3) (a) Takai, K.; Yamada, M.; Odaka, H.; Utimoto, K.; Fujii, T.; Furukawa, I. *Chem. Lett.* **1995**, 315 (allyl-Ta). (b) Takahashi, T.; Kotora, M.; Kasai, K.; Suzuki, N. *Tetrahedron Lett.* **1994**, *35*, 5685 (allyl-Zr). (c) Chatani, N.; Amishiro, N.; Morii, T.; Yamashita, T.; Murai, S. *J. Org. Chem.* **1995**, *60*, 1834 (allyl-Zn). (d) Molander, G. A. *J. Org. Chem.* **1983**, *48*, 5409 (allyl-Zn). (e) Miller, J. A.; Negishi, E. *Tetrahedron Lett.* **1984**, *25*, 5863 (allyl-Al). (f) Negishi, E.; Miller, J. A. *J. Am. Chem. Soc.* **1983**, *105*, 6761 (allyl-Zn). (g) Eishi, J. J.; Boleslawski, M. P. *J. Organomet. Chem.* **1987**, *334*, C1 (allyl-Ti). (h) Yeon, S. H.; Han, J. S.; Hong, E.; Do, Y.; Jung, I. N. *J. Organomet. Chem.* **1995**, *499*, 159 (Lewis acid-catalyzed allyl-Si). (i) Asao, N.; Matsukawa, Y.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1996**, 1513 (Lewis acid-catalyzed allyl-Sn). (j) Asao, N.; Yoshikawa, E.; Yamamoto, Y. *J. Org. Chem.* **1996**, 4874 (Lewis acid-catalyzed allyl-Si).

(4) Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1831.

(5) (a) Araki, S.; Imai, A.; Shimizu, K.; Yamada, M.; Mori, A.; Butsugan, Y. *J. Org. Chem.* **1995**, *60*, 1841. (b) Araki, S.; Usui, H.; Kato, M.; Butsugan, Y. *J. Am. Chem. Soc.* **1996**, *118*, 4699.

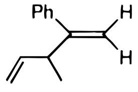
(6) The reactions of α- and/or β-oxy aldehydes with allylindiums in H_2O and aqueous/dry THF have been studied: (a) Paquette, L. A.; Mitzel, T. M. *Tetrahedron Lett.* **1995**, *36*, 6863. (b) Paquette, L. A.; Mitzel, T. M. *J. Am. Chem. Soc.* **1996**, *118*, 1931. (c) Paquette, L. A.; Mitzel, T. M. *J. Org. Chem.* **1996**, *61*, 8799.

(7) Two allyl groups among $(allyl)_3In_2I_3$ are used for the allylation reaction, and the third allyl group acts as a ligand of the In complex (ref 4). Accordingly, 0.6 equiv of allylindium corresponds to 1.2 equiv of allylating agent in the ordinary sense.

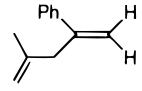
(8) Yamamoto, Y.; Yoshikawa, E. Unpublished results.

S0022-3263(97)00104-7 CCC: $14.00

In addition, the reaction of **1a** with crotylindium, prepared from In powder and crotyl bromide in THF, gave the γ-adduct **3** in 88% yield (Table 1, entry 9); the straight chain α-adduct was not detected. The reaction of **1a** with methallylindium gave **4** in 90% yield (Table 1, entry 10).

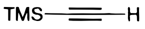


3

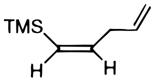


4

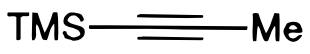
Interestingly, the use of silyl-substituted alkynes brought a regioselectivity different from the cases shown above. The allylation of (trimethylsilyl)acetylene (**1i**) occurred on the terminal carbon,[9] giving the (*Z*)-allylation product **5a** stereoselectivity in 75% yield. The reaction of silyl-substituted internal alkyne, 1-(trimethylsilyl)-1-propyne (**1j**), gave a mixture of *trans*- and *cis*-allylation products **5b** in 50% yield. In the case of the silyl-substituted acetylenes, an exceptionally longer reaction time (~36 h) was necessary to complete the allylation reaction.



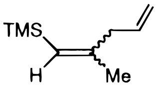
1i



5a

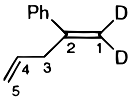


1j

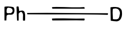


5b

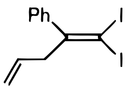
Preparation of **2a** from **1a** is representative. Allylindium was prepared by mixing In powder (0.069 g, 0.6 mmol) with allyl iodide (0.82 mL, 0.9 mmol) in THF (1.0 mL) at room temperature for 1 h.[10] To a THF solution of allylindium was added phenylacetylene (**1a**) (0.55 mL, 0.5 mmol) at room temperature. The reaction mixture was heated to 70 °C and stirred for 2 h. The reaction was quenched with dilute hydrochloric acid (15 v/v %, 2.0 mL) at room temperature. The reaction product was extracted with ether, washed with brine, dried with anhyd Mg_2SO_4, concentrated under reduced pressure, and purified by silica gel column chromatography using hexane as an eluent, giving **2a** (0.068 g) in 94% yield.



2a-*d*$_2$

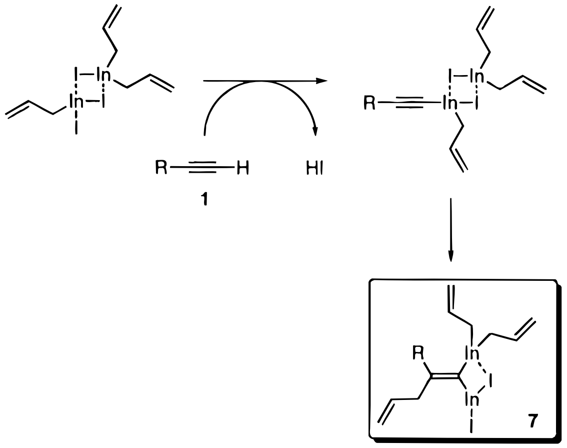


1a-*d*

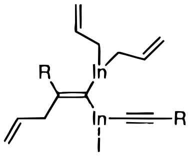


6

Scheme 1



To help clarify the mechanism of the allylindation, the reaction of **1a** with allylindium was quenched with DCl (20 wt % solution in D_2O), giving the d_2-allylation product **2a**-d_2 (95% *d*-content) in which two deuteriums were incorporated at the C-1 position. The allylation reaction of phenylacetylene-*d* **1a**−*d* followed by the usual workup using HCl−H_2O afforded **2a**, in which no deuterium was incorporated, in 91% yield. Furthermore, the allylation of **1a** followed by treatment with I_2 (5.0 equiv) at room temperature gave the diiodinated product **6** in 74% yield. These results suggest that the allylation of terminal alkynes **1** would proceed through the double-indation intermediate **7** (Scheme 1),[11] which still has a reactive allyl group. Another allyl group of **7** would react further with **1**: a possible intermediate is shown in **8**, although it is highly speculative.



8

Although further study is needed to settle the mechanism of allyation, we are now in a position to carry out the allylindation of unactivated and functionalized alkynes in good to high yields and to synthesize various 2-substituted 1,4-pentadiene derivatives in a regio- and stereocontrolled manner.

Supporting Information Available: Characterization data for reaction products (16 pages).

JO9701041

---

[9] The allylation of TMS-substituted alkynes with allylzinc bromide gives the same regioselectivity as the present allylindation: Molander, G. A. *J. Org. Chem.* **1983**, *48*, 5409.

(10) The allylindium reagent was prepared originally in DMF (ref 4). Since then, the allylindation reactions of acetylenes have been carried out in this solvent. Now, it is clear that the reagent can be prepared in THF, and this finding expands the scope of this reagent to the carboindation.

(11) A double-zincation intermediate was proposed in the allylzincation of terminal alkynes: Frangin, Y.; Gaudemar, M. *J. Organomet. Chem.* **1977**, *142*, 9. See also: Knochel, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, p 883.