Nickel-catalyzed Carbometalation Reactions of [2-(1-Propynyl)phenyl]methanol with 1-Alkenylmagnesium Reagents

Kei Murakami, Hirohisa Ohmiya, Hideki Yorimitsu,* and Koichiro Oshima*
Department of Material Chemistry, Graduate School of Engineering, Kyoto University,
Kyoto-daigaku Katsura, Nishikyo-ku, Kyoto 615-8510

(Received May 24, 2007; CL-070558; E-mail: yori@orgrxn.mbox.media.kyoto-u.ac.jp, oshima@orgrxn.mbox.media.kyoto-u.ac.jp)

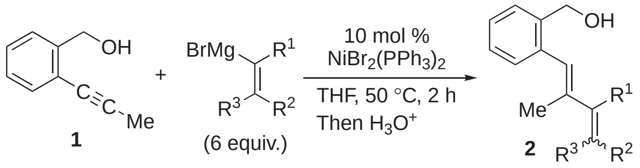
Treatment of [2-(1-propynyl)phenyl]methanol with 1-alkenyl Grignard reagents under nickel catalysis results in carbomagnesiation across the alkynyl part. The 1-alkenylation reaction proceeds in a syn fashion to yield the corresponding 1,3-butadienyl-substituted benzyl alcohol.

Transition-metal-catalyzed carbometalation of alkynes is a powerful tool for the synthesis of multisubstituted alkenes.[1] However, 1-alkenylation reaction of alkyne with 1-alkenylmetal reagents is difficult to achieve, while there are many examples of addition reactions of aryl-,[2] allyl-,[3] alkynyl-,[4] and alkylmetal[5] reagents to alkynes. Here, we report an example of 1-alkenylation reaction of an alkyne, [2-(1-propynyl)phenyl]methanol (**1**), with 1-alkenylmagnesium bromide.

Treatment of **1** with an excess of vinylmagnesium bromide in the presence of $NiBr_2(PPh_3)_2$ in THF at 20 °C for 5 h provided the vinylated product **2a** in good yield (Table 1, Entry 1).[6] The vinylation reaction proceeded to completion within 1 h at 50 °C (Entry 2). The alkenylation reactions with Grignard reagents bearing a substituent R^1, R^2, or R^3 did not proceed at 20 °C. The reaction of **1** with isopropenylmagnesium bromide provided the adduct **2b** in good yield (Entry 3). However, a trimethylsilyl or a phenyl group as R^1 considerably retarded the reaction (Entries 4 and 5). The reaction is sensitive to the steric factor at the 1 positions of the 1-alkenyl Grignard reagents. The reaction with 1-propenylmagnesium bromide (E/Z = 2:8)[7] afforded the product **2e** in good yield in a 1E, 3E/1E, 3Z ratio of 25:75 (Entry 6). The stereochemistry of the product reflects that of the Grignard reagent. Interestingly, the reaction with 2-trimethylsilylethenylmagnesium bromide yielded the 1E, 3E isomer exclusively (Entry 7). The exclusive formation indicates that (*E*)-2-trimethylsilylethenylmagnesium bromide would be more reactive than its Z form because of the steric hindrance. The use of a 1:1 mixture of (*E*)- and (*Z*)-styrylmagnesium reagent provided the E adduct predominantly (Entry 8). A 1-alkenyl Grignard reagent, 2-methyl-1-propenylmagnesium bromide, reacted smoothly with **1** under the nickel catalysis (Entry 9).

The reactions of other alkynes were unsatisfactory. The methyl ether **3** was much less reactive (eq 1). Replacement of the methyl group of **1** with a butyl group resulted in significant decrease in reaction efficiency (eq 2). The reaction of 1-phenylpropyne (**7**) having no heteroatom for 12 h provided 1,3-diene **8** in a similar yield (eq 3). A diphenylacetylene derivative **9** underwent the vinylation slowly, providing a mixture of regioisomers **10** and **11** (eq 4). The reactions of other alkynes shown in Figure 1 resulted in failure.

Table 1. 1-Alkenylation of [2-(1-propynyl)phenyl]methanol (**1**) with 1-alkenyl Grignard reagents under nickel catalysis



Entry	R^1	R^2	R^3	**2**	Yield
1[a]	H	H	H	**2a**	72%
2[b]	H	H	H	**2a**	70%
3	Me	H	H	**2b**	63%
4	Me_3Si	H	H	**2c**	<20%
5	Ph	H	H	**2d**	<5%
6	H	Me (H) (2:8)[c]	H (Me)	**2e**	75% (25:75)[d]
7	H	Me_3Si (H) (8:2)[c]	H (Me_3Si)	**2f**	74% (>99:1)[d]
8[e]	H	Ph (H) (5:5)[c]	H (Ph)	**2g**	74% (83:17)[d]
9	H	Me	Me	**2h**	74%

[a] Performed at 20 °C for 5 h. [b] Performed for 1 h. [c] E/Z ratio of the Grignard reagent. [d] 1E, 3E/1E, 3Z ratio of **2**.

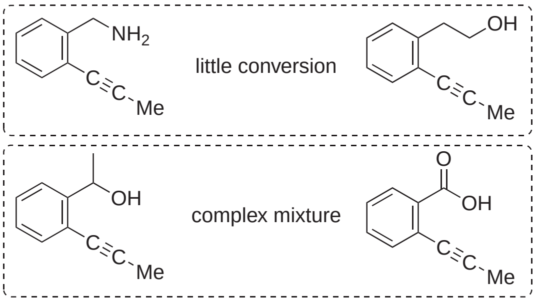
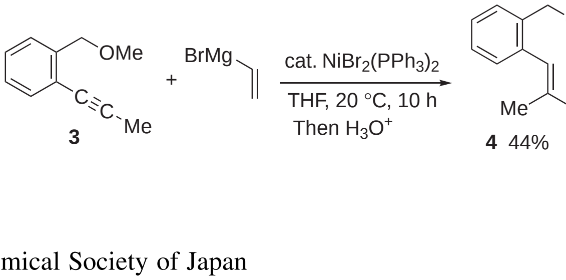


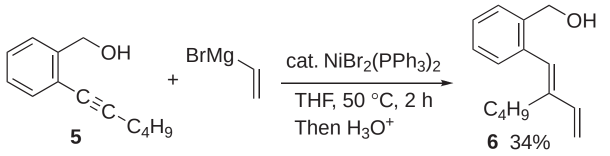
Figure 1.

The syn mode of the carbometalation was confirmed by NOE analysis of **2b**. Irradiation of the methyl group at the 3 position enhanced the signal of the proton at the 1 position, geminal to the aromatic ring. We also performed spectroscopic comparison of **8** with an authentic sample prepared by the Wittig methylenation reaction of (*E*)-α-methylcinnamaldehyde.

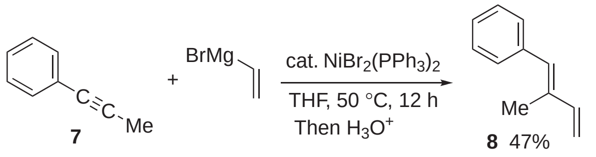


(1)

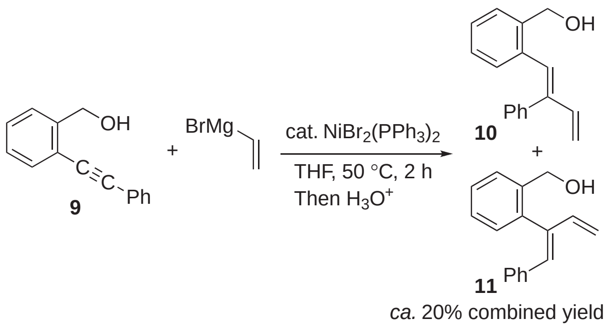
Copyright © 2007 The Chemical Society of Japan



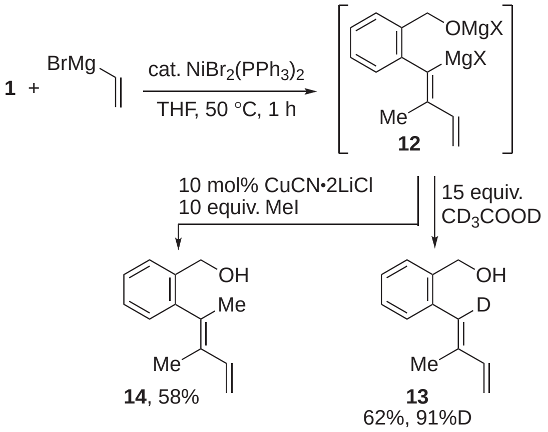
(2)



(3)



(4)



Scheme 1.

The vinylmagnesiated adduct **12** was trapped with CD_3COOD or iodomethane in the presence of CuCN•2LiCl (Scheme 1). Unfortunately, many attempts to trap the intermediate **12** with I_2, allyl bromide, benzoyl chloride, benzaldehyde, and iodobenzene resulted in failure. The intermediate is not reactive probably because of the proximal alkoxide moiety and steric hindrance.

In summary, we have found examples of carbometalation with 1-alkenylmetal reagents. The reaction proceeds in a syn fashion, yielding 1,3-butadiene skeleton.

Dedicated to the memory of the late Prof. Yoshihiko Ito.

References and Notes

1 J. F. Normant, A. Alexakis, *Synthesis* **1981**, 841; L. H. Lipshutz, S. Sengupta, *Org. React.* **1992**, *41*, 135; E. Negishi, *Dalton Trans.* **2005**, 827; I. Marek, *J. Chem. Soc., Perkin Trans. 1* **1999**, 535; N. Asao, Y. Yamamoto, *Bull. Chem. Soc. Jpn.* **2000**, *73*, 1071; H. Shinokubo, K. Oshima, *Eur. J. Org. Chem.* **2004**, 2081; A. G. Fallis, P. Forgione, *Tetrahedron* **2001**, *57*, 5899.

2 T. Yamagami, R. Shintani, E. Shirakawa, T. Hayashi, *Org. Lett.* **2007**, *9*, 1045; E. Shirakawa, T. Yamagami, T. Kimura, S. Yamaguchi, T. Hayashi, *J. Am. Chem. Soc.* **2005**, *127*, 17164; H. Yorimitsu, J. Tang, K. Okada, H. Shinokubo, K. Oshima, *Chem. Lett.* **1998**, 11; K. Murakami, H. Ohmiya, H. Yorimitsu, K. Oshima, *Org. Lett.* **2007**, *9*, 1569; K. Itami, T. Kamei, J. Yoshida, *J. Am. Chem. Soc.* **2003**, *125*, 14670; H. Oda, M. Morishita, K. Fugami, H. Sano, M. Kosugi, *Chem. Lett.* **1996**, 811.

3 K. Okada, K. Oshima, K. Utimoto, *J. Am. Chem. Soc.* **1996**, *118*, 6076; T. Nishikawa, H. Shinokubo, K. Oshima, *Org. Lett.* **2002**, *4*, 2795; H. Yasui, T. Nishikawa, H. Yorimitsu, K. Oshima, *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1271.

4 E. Shirakawa, H. Yoshida, T. Kurahashi, Y. Nakao, T. Hiyama, *J. Am. Chem. Soc.* **1998**, *120*, 2975; M. Suginome, M. Shirakura, A. Yamamoto, *J. Am. Chem. Soc.* **2006**, *128*, 14438.

5 S. Nishimae, R. Inoue, H. Shinokubo, K. Oshima, *Chem. Lett.* **1998**, 785; M. Hojo, Y. Murakami, H. Aihara, R. Sakuragi, Y. Baba, A. Hosomi, *Angew. Chem., Int. Ed.* **2001**, *40*, 621; D. Zhang, J. M. Ready, *J. Am. Chem. Soc.* **2006**, *128*, 15050.

6 Typical experimental procedure: $NiBr_2(PPh_3)_2$ (19 mg, 0.025 mmol) was placed in a 20-mL reaction flask under argon. [2-(1-Propynyl)phenyl]methanol (**1**, 47 mg, 0.25 mmol) in THF (1.0 mL) was added to the flask. A solution of vinylmagnesium bromide (1.5 mL, 1.0 M THF solution, 1.5 mmol) was then added at 20 °C. The mixture was stirred at 20 °C for 5 h. A saturated solution of NH_4Cl (2 mL) was added. The organic compounds were extracted with ethyl acetate three times. The combined organic part was dried over Na_2SO_4 and concentrated in vacuo. Chromatographic purification on silica gel by using hexane/ethyl acetate = 5:1 as an eluent afforded **2a** (31 mg, 0.18 mmol) in 72% yield. (*E*)-[2-(2-Methyl-1,3-butadienyl)phenyl]methanol (**2a**): IR(neat): 752, 1015, 1448, 1604, 2918, 3319 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.61 (t, $J = 6.0$ Hz, 1H), 1.85 (d, $J = 1.2$ Hz, 3H), 4.66 (d, $J = 6.0$ Hz, 2H), 5.16 (d, $J = 10.8$ Hz, 1H), 5.31 (d, $J = 17.4$ Hz, 1H), 6.59 (dd, $J = 10.8$, 17.4 Hz, 1H), 6.63 (s, 1H), 7.19–7.30 (m, 3H), 7.42–7.45 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.45, 63.66, 113.67, 127.47, 127.51, 127.76, 129.06, 129.98, 136.24, 137.61, 139.09, 141.35. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72: H, 8.10%. Found: C, 82.59: H, 8.12%.

7 The E/Z ratios of the Grignard reagents were determined as follows: The reaction of benzaldehyde with an equimolar amount of alkenylmagnesium bromide afforded the corresponding allyl alcohol in excellent yield. The E/Z ratio of the allyl alcohol would be roughly equal to the E/Z ratio of the Grignard reagent used.

Published on the web (Advance View) July 21, 2007; doi:10.1246/cl.2007.1066