ORGANIC
LETTERS

2008
Vol. 10, No. 22
5183−5186

Regiocontrolled Addition of Arylboronic Acids to Allenes Using Palladium and Platinum Catalysts

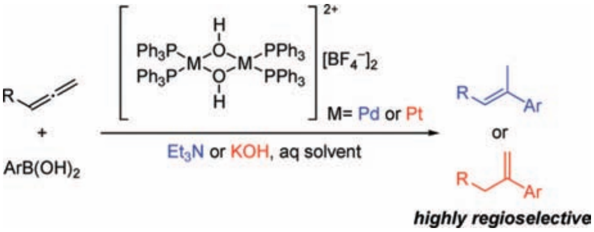
Masahiro Yoshida,*,[†] Kennosuke Matsuda,[†] Yasunobu Shoji,[†] Takahiro Gotou,[‡] Masataka Ihara,[§] and Kozo Shishido[†]

Graduate School of Pharmaceutical Sciences, The University of Tokushima, 1-78-1 Sho-machi, Tokushima 770-8505, Japan, Graduate School of Pharmaceutical Sciences, Tohoku University, Aobayama, Sendai 980-8578, Japan, and Institute of Medicinal Chemistry, Hoshi University, 2-4-41 Ebara, Shinagawa, 142-8501 Japan

yoshida@ph.tokushima-u.ac.jp

Received September 16, 2008

ABSTRACT



Studies about the regiocontrolled addition of arylboronic acids to allenes using a palladium or a platinum catalyst have been described. The selectivity of the reaction can be altered by the choice of the metal reagent and base. Contrary to the formation of *endo*-olefinic products in the reactions using hydroxopalladium complex, predominant production of *exo*-olefinic products was observed by the reaction with hydroxoplatinum complex.

The unique reactivity of allenes which derives from the existence of two orthogonal π-bonds makes them important compounds in organic and synthetic organic chemistry. As a result, the reactions of allenes have been the object of extensive examination.[1] Moreover, during the last two decades, the reactivity of allenes, particularly in the presence of transition-metal catalysts, has attracted increasing interest.[1,2] Oh and Ma reported the palladium-catalyzed addition of organoboronic acids to allenes under acidic conditions, in which tri- and tetrasubstituted alkenes were stereoselectively produced.[3,4] During the course of our studies on transition-metal-catalyzed reactions of allenes,[5] we found that similar reactions occurred using a hydroxo-

---

[†] The University of Tokushima.
[‡] Tohoku University.
[§] Hoshi University.

(1) (a) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; John Wiley & Sons: New York, 1988. (b) Krause, N.; Hashmi, A. S. K. *Modern Allene Chemistry*; VCH Verlagsgesellschaft Mbh: Weinheim, 2004. (c) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590. (d) Brummond, K. M.; DeForrest, J. E. *Synthesis* **2007**, 795.

(2) Zimmer, R.; Dinesh, C. U.; Nadanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067.

(3) (a) Oh, C. H.; Ahn, T. W.; Reddy, V. R. *Chem. Commun.* **2003**, 2622. (b) Ma, S.; Jiao, N.; Ye, L. *Chem.—Eur. J.* **2003**, *9*, 6049. (c) Ma, S.; Guo, H.; Yu, F. *J. Org. Chem.* **2006**, *71*, 6634. (d) Guo, H.; Ma, S. *Synthesis* **2007**, 2731.

(4) Other examples of transition-metal-catalyzed reactions of allenes with organoboron compounds include the following: (a) Yamamoto, Y.; Fujikawa, R.; Yamada, A.; Miyaura, N. *Chem. Lett.* **1999**, 1069. (b) Onozawa, S.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1999**, 1863. (c) Suginome, M.; Ohmori, Y.; Ito, Y. *J. Organomet. Chem.* **2000**, *611*, 403. (d) Hopkins, C. D.; Guan, L.; Malinakova, H. C. *J. Org. Chem.* **2005**, *70*, 6848. (e) Takahashi, G.; Shirakawa, E.; Tsuchimoto, T.; Kawakami, Y. *Adv. Synth. Catal.* **2006**, *348*, 837. (f) Nishimura, T.; Hirabayashi, S.; Yasuhara, Y.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 2556. (g) Tsukamoto, H.; Matsumoto, T.; Kondo, Y. *Org. Lett.* **2008**, *10*, 1047.

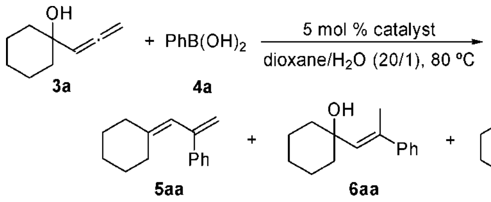
(5) (a) Nemoto, H.; Yoshida, M.; Fukumoto, K. *J. Org. Chem.* **1997**, *62*, 6450. (b) Yoshida, M.; Sugimoto, K.; Ihara, M. *Tetrahedron Lett.* **2000**, *41*, 5089. (c) Yoshida, M.; Sugimoto, K.; Ihara, M. *Tetrahedron Lett.* **2001**, *42*, 3877. (d) Yoshida, M.; Sugimoto, K.; Ihara, M. *Tetrahedron* **2002**, *58*, 7839. (e) Yoshida, M.; Gotou, T.; Ihara, M. *Tetrahedron Lett.* **2003**, *44*, 7151. (f) Yoshida, M.; Gotou, T.; Ihara, M. *Chem. Commun.* **2004**, 1124.

10.1021/ol8021484 CCC: $40.75

palladium complex $[Pd_2(OH)_2(PPh_3)_4][BF_4]_2$ (**1**)[6] under aqueous basic conditions. Furthermore, it was revealed that using the hydroxoplatinum complex $[Pt_2(OH)_2(PPh_3)_4][BF_4]_2$ (**2**) was key to producing one regioisomer selectively. Herein, we describe our results.

In our previous study involving the palladium-catalyzed direct coupling reaction of allenic alcohol **3a** with phenylboronic acid (**4a**),[5f] it was shown that adduct **6aa** having an *endo* olefin was obtained predominately in 73% yield along with 8% of diene **5aa** when the reaction was conducted under aqueous conditions (dioxane/H_2O =20/1) (entry 1 in Table 1). Although the reaction in the presence of only **1** was unsuccessful (entry 2), the reactivity was dramatically improved by the addition of Et_3N to afford **6aa** in 81% yield (entry 3). When the hydroxoplatinum complex **2** was used as the catalyst, a small amount of the *exo*-olefinic adduct **7aa**, the regioisomer of **6aa**, was generated in 7% yield with the production of **5aa** and **6aa** being major (entry 4). However, the yield of **7aa** increased to 66% when the reaction was conducted in the presence of KOH (entry 5).

Table 1. Palladium- and Platinum-Catalyzed Addition of Arylboronic Acid **4a** to Allenic Alcohol **3a**

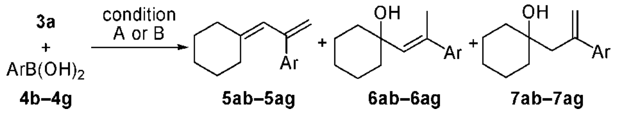


entry	reagents	yields, % 5aa	6aa	7aa
1	$Pd_2(dba)_3$·$CHCl_3$, 40 mol % PPh_3	8	73	
2	$[Pd_2(OH)_2(PPh_3)_4][BF_4]_2$ (**1**)	37	6	
3	$[Pd_2(OH)_2(PPh_3)_4][BF_4]_2$ (**1**), Et_3N	3	81	
4	$[Pt_2(OH)_2(PPh_3)_4][BF_4]_2$ (**2**), Et_3N	47	16	7
5[a]	$[Pt_2(OH)_2(PPh_3)_4][BF_4]_2$ (**2**), KOH	20	2	66

[a] The reaction was carried out at 100 °C.

Results of the reactions of **3a** with various arylboronic acids **4b**−**g** in the presence of palladium or platinum complexes **1** or **2** are summarized in Table 2. The *endo*-olefinic products **6ab**−**ag** were regio- and stereoselectively obtained in high yields from the reactions of **4b**−**g** in the presence of **1** and Et_3N (conditions A, entries 1, 3, 5, 7, 9, and 11). On the other hand, predominant production of the *exo*-olefinic products **7ab**−**ag** was observed in moderate to good yields along with dienes **5ab**−**5ag** when the reactions were carried out with KOH in the presence of **2** (conditions B, entries 2, 4, 6, 8, 10, and 12).

Table 2. Reactions of **3a** with Various Arylboronic Acids **4b**−**g**[a]



entry	Ar	conditions	products (yield, %) 5	6	7
1	2-methylphenyl (**4b**)	A		**6ab** (91)	trace
2	2-methylphenyl (**4b**)	B	**5ab** (18)		**7ab** (70)
3	4-methylphenyl (**4c**)	A		**6ac** (80)	trace
4	4-methylphenyl (**4c**)	B	**5ac** (19)	**6ac** (6)	**7ac** (59)
5	2-methoxyphenyl (**4d**)	A		**6ad** (88)	trace
6	2-methoxyphenyl (**4d**)	B	**5ad** (18)	**6ad** (10)	**7ad** (59)
7	4-methoxyphenyl (**4e**)	A		**6ae** (83)	trace
8	4-methoxyphenyl (**4e**)	B	**5ae** (23)	trace	**7ae** (61)
9	1-naphthalene (**4f**)	A		**6af** (96)	trace
10	1-naphthalene (**4f**)	B	**5af** (38)	trace	**7af** (58)
11	4-acetylphenyl (**4g**)	A		**6ag** (68)	trace
12	4-acetylphenyl (**4g**)	B	**5ag** (18)	trace	**7ag** (39)

[a] Conditions A: Reactions were carried out in the presence of 5 mol % of **1** and 5 equiv of Et_3N in dioxane/H_2O (20/1) at 80 °C. Conditions B: Reactions were carried out in the presence of 5 mol % of **2** and 5 equiv of KOH in dioxane/H_2O (20/1) at 100 °C.

Table 3 shows results of the reactions of various substituted allenes **3b**−**3h** with 2-methoxyphenylboronic acid (**4d**). When the siloxyethyl-substituted allene **3b** was subjected to reactions under palladium- and platinum-catalyzed conditions, adducts **6bd** and **7bd**, respectively, were selectively obtained (entries 1 and 2). It is noteworthy that the yield of the *exo*-olefinic product **7bd** increased (entry 2). The substrates **3c**−**f** having other alkyl side chains also reacted regioselectively with **4d** to afford the corresponding products **6cd**−**fd** or **7cd**−**fd**, depending on the reaction conditions (entries 3−10). Similarly, while the reactions of the aryl-substituted allenes **3g** and **3h** using the palladium catalyst **1** provided **6gd** and **6hd** as the sole products, the regioisomers **7gd** and **7hd** were selectively produced in the presence of the platinum catalyst **2** (entries 11−14).

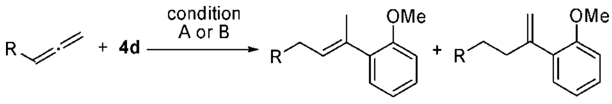
A plausible mechanism for the reaction is shown in Scheme 1. It is presumed that the (dihydroxo)metal complex **1′** or **2′** exists as an active species in this reaction and that a catalytic cycle would involve the transmetalation with the arylboronic acid to give the arylmetal complex **8** as the initial step. Although it is not clear why the observed regioselectivities depend on the metal species,[7] it is presumed that the insertion of the allene to **8** is the crucial step. In the reaction using **1** with Et_3N, palladium undergoes coordination with the amine to increase the electron density of the corresponding complex Pd−**8**. As a result, regio- and stereoselective insertion occurs at the relatively electron-poor terminal double bond of the allene **9**, leading to the allylpalladium **10**. The complex **10** is then subjected to hydrolysis with water to afford the *endo*-olefinic product **6**. In the reaction of **2** and KOH, the resulting arylplatinum species Pt−**8** is preferentially coordinated to the electron-rich internal double bond **11**

---

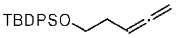
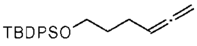
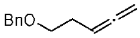
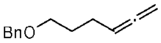
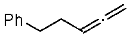
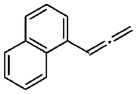
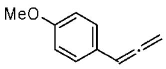
(6) Bushnell, G. W.; Dixon, K. R.; Hunter, R. G.; McFarland, J. J. *Can. J. Chem.* **1972**, *50*, 3694.

(7) Control of regiochemistry depending on the metal catalyst has been observed in the hydro- and silaboration of allenes; see refs 4a and 4b.

Table 3. Reactions of Various Allenes **3b−h** with **4d**[a]



3b–3h **6bd–6hd** **7bd–7hd**

entry	allene **3**	condition	total yields (%) ratio[b]
1	 **3b**	A	77 **6bd**:**7bd** = 14:1
2	**3b**	B	97 **6bd**:**7bd** = 1:12
3	 **3c**	A	77 **6cd**:**7cd** = >20:1
4	**3c**	B	97 **6cd**:**7cd** = 1:>20
5	 **3d**	A	64 **6dd**:**7dd** = >20:1
6	**3d**	B	85 **6cd**:**7cd** = 1:>20
7	 **3e**	A	69 **6ed**:**7ed** = >20:1
8	**3e**	B	83 **6ed**:**7ed** = 1:>20
9	 **3f**	A	76 **6fd**:**7fd** = 6:1
10	**3f**	B	86 **6fd**:**7fd** = 1:>20
11	 **3g**	A	91 **6gd**:**7gd** = >20:1
12	**3g**	B	80 **6gd**:**7gd** = 1:14[c]
13	 **3h**	A	54 **6hd**:**7hd** = >20:1
14	**3h**	B	84 **6hd**:**7hd** = 1:12

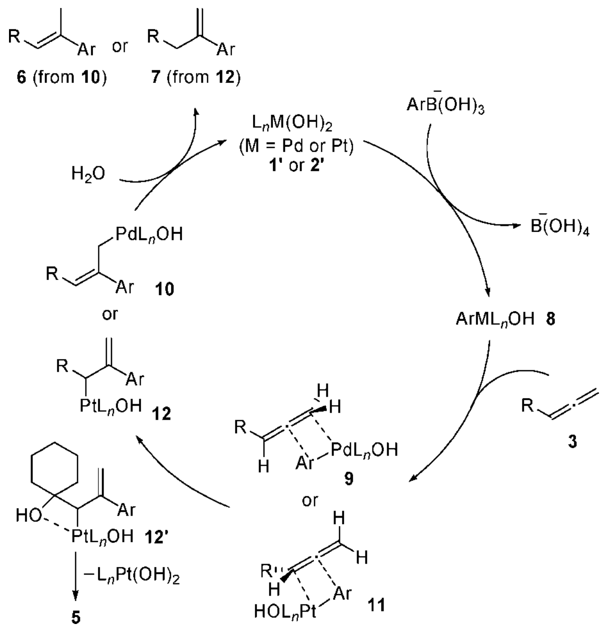
[a] Conditions A: Reactions were carried out in the presence of 5 mol % of **1** and 5 equiv of Et_3N in dioxane/H_2O (20/1) at 80 °C. Conditions B: Reactions were carried out in the presence of 5 mol % of **2** and 5 equiv of KOH in dioxane/H_2O (20/1) at 100 °C. [b] The ratios were determined by ^1H NMR integration of the olefinic proton signals. [c] The ratio was determined by the isolation of each product.

due to the comparatively low electron density of Pt−**8** and furnishes predominantly the *exo*-olefinic product **7** via the allylplatinum intermediate **12**. The diene **5**, which is a byproduct in the platinum-catalyzed reaction of the allenic alcohol, results from the β-OH elimination of the corresponding allylplatinum intermediate **12′**.

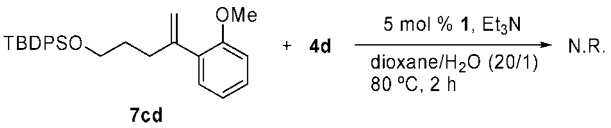
Another pathway, in which the initially formed *exo*-olefinic product **7** isomerizes to the thermodynamically more stable **6**, is possible. We subjected the isolated **7cd** to the palladium-catalyzed reaction with **4d** for the detection of isomerization (Scheme 2). However, no reaction occurred, which implies that the *endo*-olefinic product is produced directly via the allylpalladium.

Additional information on the reaction mechanism was gained when the reaction of the allenyl alcohol **3a** with 2-methylphenylboronic acid (**4b**) was conducted in D_2O (Scheme 3). In the palladium-catalyzed reaction, 70% of the deuterium was incorporated at the allylic position to give **6ab-D**. Similarly, the corresponding deuterated product **7ab-D** was obtained when the platinum-catalyzed reaction was carried out (62% deuterated). These results support the hypothesis that the reactions proceeds via the formation of the allylmetal intermediates **10** and **12**, respectively.

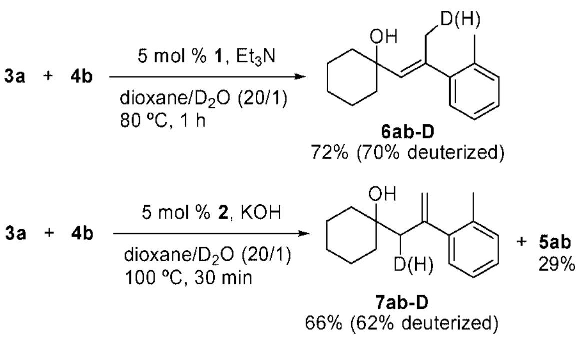
Scheme 1



Scheme 2



Scheme 3



In summary, the studies described above have resulted in the regiocontrolled addition of arylboronic acids to allenes using a palladium or a platinum catalyst. It is noteworthy that the selectivity of the reaction can be altered by the choice of the metal reagent and base. Continuing studies probing the scope and synthetic applications of this reaction are now in progress.

Acknowledgment. This study was supported in part by a Grant-in-Aid for the Encouragement of Young Scientists (B) from the Japan Society for the Promotion of Science (JSPS) and the Research Foundation for Pharmaceutical Sciences.

Supporting Information Available: Experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL8021484