

Mizoroki–Heck Type Reaction of Organoboron Reagents with Alkenes and Alkynes. A Pd(II)-Catalyzed Pathway with $\text{Cu}(\text{OAc})_2$ as an Oxidant

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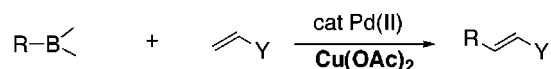
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Received August 3, 2001

ABSTRACT

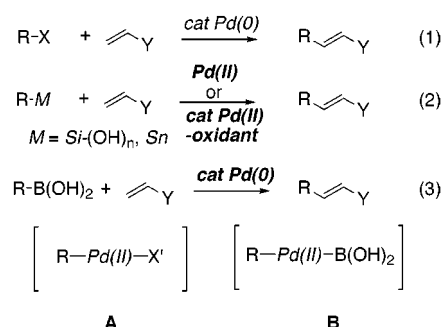


In contrast to the Pd(0)-catalyzed mechanism by Uemura, Mizoroki–Heck type reaction of boronic acids is found to proceed under a Pd(II)-mediated pathway using a catalytic amount of Pd(OAc)₂ in the presence of Cu(OAc)₂ as an oxidant. Treatment of a variety of alkenes with boronic acids, boronates, and sodium tetraphenylborate furnishes β -arylated and alkenylated products in good to excellent yields. The reactions with norbornene, norbornadiene, and diphenylacetylene are also performed to give 1:2 or 2:1 coupling products.

In addition to the conventional Mizoroki–Heck (MH) reaction of unsaturated compounds with organic halides as an *electrophile*,^{1,2} the related reactions with several *nucleophilic* organometallic reagents such as silanols³ and organostannanes⁴ have also attracted much attention recently. In contrast to MH reaction catalyzed by Pd(0) as shown in eq 1 of Scheme 1, organometallic reagent-mediated MH-type reactions usually require stoichiometric Pd(II) or a catalytic

amount of Pd(II) in the presence of an appropriate oxidant. This is the case with the reaction of silanol and trialkyltin (eq 2). This is because the reaction involves *transmetalation* between the reagents and Pd(II) species to form the organopalladium complex like **A** as a key step. On the other hand, the MH-type reaction of boronic acid was shown by Uemura

Scheme 1



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(1) (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Heck, R. F.; Nolley, J. P., Jr. *J. Org. Chem.* **1972**, *37*, 2320.

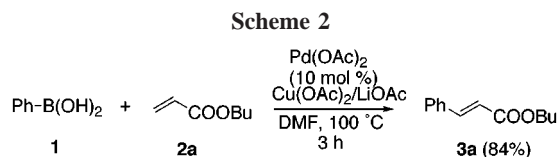
(2) For reviews, see: (a) Heck, R. F. *Org. React.* **1982**, *27*, 345. (b) Tsuji, J. *Palladium Reagents and Catalysts; Innovations in Organic Synthesis*; Wiley: Chichester, 1996.

(3) (a) Hirabayashi, K.; Nishihara, Y.; Mori, A.; Hiyama, T. *Tetrahedron Lett.* **1998**, *39*, 7893. (b) Hirabayashi, K.; Kondo, T.; Toriyama, F.; Nishihara, Y.; Mori, A. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 749. (c) Hirabayashi, K.; Ando, J.; Kawashima, J.; Nishihara, Y.; Mori, A.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 1409.

(4) (a) Oda, H.; Morishita, M.; Fugami, K.; Sano, H.; Kosugi, M. *Chem. Lett.* **1996**, 811. (b) Fugami, K.; Hagiwara, S.; Oda, H.; Kosugi, M. *Synlett* **1998**, 477. (c) Hirabayashi, K.; Ando, J.; Nishihara, Y.; Mori, A.; Hiyama, T. *Synlett* **1999**, 99. See also: (d) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5518. (e) Heck, R. F. *J. Am. Chem. Soc.* **1969**, *91*, 6707.

to proceed under Pd(0)-catalyzed conditions (eq 3).⁵ In this reaction, *oxidative addition* of the carbon–boron bond to Pd(0) to give **B** is shown to be the initial step of the catalytic cycle. We have been interested in studying the difference of such organometalloids. Here we report our recent findings on organoboron-mediated catalytic MH-type reaction, which can be performed also via a Pd(II)-catalyzed pathway in an aprotic polar solvent such as DMF using copper(II) acetate as an inexpensive oxidant.

The reaction of phenylboronic acid (**1**, 1 mmol) with butyl acrylate (**2a**, 1 mmol) was carried out as shown in Scheme 2 under the similar conditions as for silanol or tin using 10



mol % of Pd(OAc)₂, 2.0 equiv of Cu(OAc)₂, and 3.0 equiv of LiOAc in DMF (7.5 mL) at 100 °C.^{3c} In contrast to the reactions of silanols and tin reagents, which required a reaction period of 24 h to result in a reasonable yield, the product, butyl 3-phenyl-2-propenoate (**3a**), was obtained in

Table 1. MH-Type Reaction of PhB(OH)₂ with Various Alkenes^a

alkene	product	%yield
		84
		63
		82
		58
	3d (<i>E:Z</i> =3:1)	
		79
		82
		62
		58

^a The reaction was carried out using 5 mol % of Pd(OAc)₂, alkene **2** (0.2 mmol), and **1** (0.24 mmol) in the presence of Cu(OAc)₂ (0.4 mmol) and LiOAc (0.6 mmol) in DMF (1.5 mL) at 100 °C for 4 h.

65% yield after stirring for only 3 h. Use of a slightly excess amount (1.2 equiv) of phenylboronic acid improved the yield to 84%.

As summarized in Table 1, we examined the MH-type reaction of phenylboronic acid (**1**) with various alkenes. The reactions proceeded smoothly to afford the corresponding phenylated products in reasonable yields. In addition to alkenes bearing an electron-withdrawing substituent (**2a–d**), allyl phenyl ether (**2e**) and styrene (**2f**) also affected the reaction. All the alkenes examined except acrylonitrile (**2d**) afforded the products with *E*-configuration, exclusively. The reaction with 1,2-disubstituted alkenes such as ethyl crotonate (**2g**) and ethyl fumarate (**2h**) also proceeded stereoselectively. Although these reactions required a higher reaction temperature than those of Pd(0)-catalyzed reactions (rt, 1 d),^{5a} boronic acid was much more reactive than silanols and aryltin reagents.

Table 2 shows the reaction of various boron reagents with butyl acrylate. Use of boronic acids **4–8** that possess an electron-withdrawing or -donating substituent on the aromatic ring was found to be equally effective irrespective of the electronic effect. Sodium tetraphenylborate (**9**) also underwent the arylation in a good yield.⁶ Moreover, the reaction of alkenylpinacolboranes **10** instead of the corresponding boronic acids was also effective to give the corresponding dienates in notably good yields.^{5a} Thus, the boronic esters

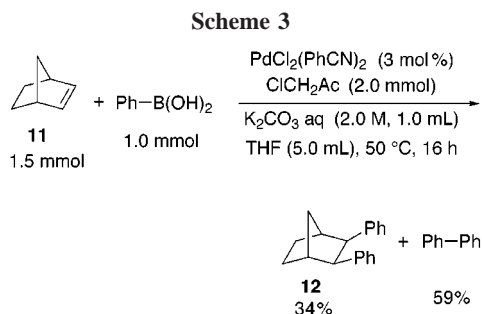
Table 2. MH-Type Reaction of Organoboron Reagents **4–10** with Butyl Acrylate (**2a**)^a

boron reagent		%yield
	4	76
	5	66
	6	75
	7	78
	8	58
NaBPh ₄	9	95 ^b
	10a	67 ^c
	10b	59 ^d

^a The reaction was performed under the same conditions as those in Table 1 unless otherwise noted. ^b The ratio of **2a**/**9** was 2.2, and the reaction was carried out in the absence of LiOAc. The yield was estimated on the basis of the mol amount of **9**. ^c The reaction of **10a** (0.5 mmol) was carried out with **2a** (0.6 mmol) in DMF (2 mL) at 75 °C for 4.3 h in the absence of LiOAc. ^d The reaction was carried out using 3 mol % of PdCl₂(PhCN)₂ and 2.0 equiv of Cu(OAc)₂ in DMF (2 mL) at 82 °C for 5.3 h in the absence of LiOAc.

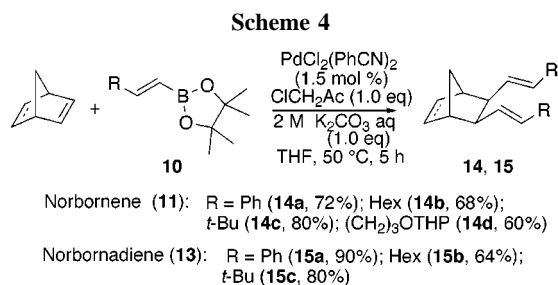
were found to be available for the alkenylmetal-based MH-type reaction without hydrolysis of the boronate moiety.

Employment of substrates that generate an intermediate not amenable to β -hydride elimination results in remarkable 1:2 condensation reactions. Indeed, the reaction with norbornene (**11**) induced double arylation as shown in Scheme 3.^{4b,7} In this reaction, chloroacetone was found to be an



effective oxidant, whereas none of the copper(II) salts examined gave good results. The doubly arylated product **12** was obtained in 34% yield accompanied by 59% of biphenyl, while the corresponding organotin-mediated reaction gave much better yields of diarylated norbornane derivatives.^{4b}

The reaction of alkenylboronic esters **10** with norbornene (**11**) and norbornadiene (**13**) gave much better results (Scheme 4). When the reactions of *B*-(2-phenylethenyl)-



pinacolborane (**10a**) were carried out with 1.5 mol % of PdCl₂(PhCN)₂ in the presence of 1.0 equiv of chloroacetone and 1.0 equiv of potassium carbonate in THF (6.0 mL), 2,3-bis[*E*]-2-phenylethenyl]norbornane (**14a**) and 5,6-bis[*E*]-2-phenylethenyl]norbornene (**15a**) were obtained as single isomers in 72% and 90% yields, respectively.^{4a,b} Some other alkenylboronates **10b–d** with a different R group also

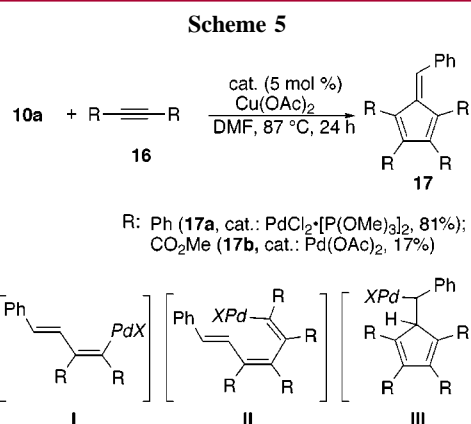
(5) (a) Cho, C. S.; Uemura, S. *J. Organomet. Chem.* **1994**, 465, 85. (b) Rhodium-catalyzed MH-type reaction of boronic acid: Lautens, M.; Roy, Amélie, Fukuoka, K.; Fagnou, K.; Martín-Matute, B. *J. Am. Chem. Soc.* **2001**, 123, 5358. See also: (c) Dieck, H. A.; Heck, R. F. *J. Org. Chem.* **1975**, 40, 1083. (d) Karabelas, K.; Hallberg, A. *J. Org. Chem.* **1988**, 53, 4909.

(6) The reaction using NaBPh₄ with AgOAc in acetic acid was also shown by Uemura: Cho, C. S.; Itotani, K.; Uemura, S. *J. Organomet. Chem.* **1993**, 443, 253.

(7) Rossi, B.; Carpita, A.; Bigelli, C. *Tetrahedron Lett.* **1985**, 26, 523.

smoothly underwent the double alkenylation. These results are generally better than their tin counterparts.^{4b} Moreover, alkenylboron-based protocol is advantageous because the reagents are much more readily accessible in stereoselective fashion in comparison to the corresponding tributyltin reagents. We assume that the reaction pathway is rationalized as follows: alkenylpalladation to norbornene would form an intermediary palladium adduct through *syn*-addition as proposed in the usual MH-type reaction. However, the rigid bicyclo[2.2.1] structure would circumvent conformational rotation leading to the *syn*-periplanar orientation of Pd–C–C–H unit that facilitates the β -hydride elimination. Thus, subsequent transmetalation with the second alkenylboronate **10** to the palladated intermediate followed by reductive elimination would afford the double alkenylated product.

On the other hand, *B*-(2-phenylethenyl)pinacolborane (**10a**) reacted with diphenylacetylene (**16a**) and dimethyl acetylenedicarboxylate (**16b**) to give 5-(benzylidene)-1,2,3,4-tetraphenyl-1,3-cyclopentadiene (**17a**) and 5-(benzylidene)-1,2,3,4-tetrakis(methoxycarbonyl)-1,3-cyclopentadiene (**17b**), the 1:2 condensation products of the boron reagent and alkynes (Scheme 5). These products are potentially interest-



ing precursors of densely substituted cyclopentadienyl ligands.^{8,9} The reaction is assumed to proceed via alkenylpalladation giving an intermediate **I**. Insertion of the second alkyne molecule gives **II**.¹⁰ Then, intramolecular carbopalladation becomes feasible, leading to **III**, and subsequent dehydropalladation produces **17**. Neither double alkenylated products nor any noncyclized alkyne oligomers were obtained at all.

In summary, we have shown that the Mizoroki–Heck type reaction of several organoboron reagents occurs in aprotic

(8) (a) Wu, G.; Rheingold, A. L.; Geib, S. J.; Heck, R. F. *Organometallics* **1987**, 6, 1941. (b) Silverberg, L. J.; Wu, G.; Rheingold, A. L.; Heck, R. F. *J. Organomet. Chem.* **1991**, 409, 411 and references therein. (c) Yagyu, T.; Osakada, K.; Brookhart, M. *Organometallics* **2000**, 19, 2125 and references therein. (d) Takahashi, T.; Seki, S.; Kotoru, M. Jpn. Kokai Tokkyo Koho JP 08301792 A2 19 Nov 1996 Heisei; *Chem. Abstr.* **1997**, 126, 89089.

(9) Bailey, P. M.; Mann, B. E.; Brown, I. D.; Maitlis, P. M. *J. Chem. Soc., Chem. Commun.* **1976**, 238.

(10) (a) A related reaction catalyzed by Pd(0) is reported to proceed via a formation of palladacyclopentadiene intermediate: Shirakawa, E.; Yoshida, H.; Nakao, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1999**, 121, 4290. (b) A fulvene formation via nickelacyclopentadiene: Iyoda, M.; Mizusuna, A.; Oda, M. *Chem. Lett.* **1988**, 149.

polar solvents with various alkenes and alkynes in good to excellent yields. MH-type reaction of organoboron reagents were revealed to proceed via both Pd(0)-^{5a} and Pd(II)-catalyzed pathways. Such divergent characteristics have not been observed in the MH-type reactions with related silicon or tin.

Acknowledgment. This work was partially supported by a Grant-in-Aid for Scientific Research (no. 13650915) from Japan Society for the Promotion of Science.

OL016529Y