

Rhodium-Catalyzed Hydroarylation of Alkynes with Arylboronic Acids: 1,4-Shift of Rhodium from 2-Aryl-1-alkenylrhodium to 2-Alkenylarylrhodium Intermediate

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Since Miyaura reported the addition of aryl- and alkenylboronic acids to α,β -unsaturated ketones in an aqueous solvent under catalysis by a rhodium–phosphine complex in 1997,¹ this rhodium-catalyzed reaction has been successfully extended to catalytic asymmetric 1,4-addition by use of binap as a chiral ligand.^{2–5} Recently, it has been also reported that the reaction of arylboronic acids takes place with norbornene giving a multiple alkylation product⁶ and with terminal olefins such as styrenes and vinylpyridines.⁷ Here we report, as another example of the rhodium-catalyzed reaction of organoboronic acids, the hydroarylation of alkynes which proceeds with high *syn*-selectivity and whose catalytic cycle involves an interesting 1,4-shift of rhodium from an alkenyl carbon to an aryl carbon.

The reaction of 4-octyne (**1a**) with phenylboronic acid (**2m**) was examined under several reaction conditions (Scheme 1). It was found that hydrophenylation of the alkyne takes place smoothly in an aqueous solvent in the presence of a bisphosphine–rhodium catalyst. Thus, a mixture of **1a**, **2m** (1.2 equiv to **1a**), and 3 mol % of a rhodium catalyst generated from Rh(acac)(C₂H₄)₂ and dppb⁸ in dioxane/water (10/1) was heated at 100 °C for 3 h. Evaporation of the solvent followed by silica gel chromatography (hexane) gave 87% yield of (*E*)-4-phenyl-4-octene (**4am**), whose isomeric purity determined by NMR analyses is over 97% (entry 1 in Table 1). The formation of the *E* isomer indicates that hydrogen and phenyl add to the triple bond in a *syn* fashion. The use of an excess of boronic acid **2m** slightly increased the yield of **4am**, the yield being 93 and 95% with 2.0 and 5.0 equiv of **2m**, respectively (entries 2 and 3). Some other chelating bisphosphine ligands, dppf,⁸ dppe,⁸ and binap,⁸ gave essentially the same high chemical yield as dppb, while the

Scheme 1

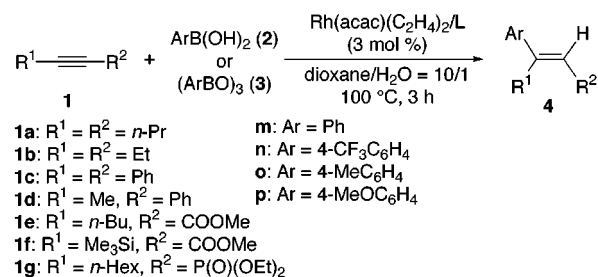


Table 1. Rhodium-Catalyzed Hydroarylation of Alkynes **1** with Arylboronic Acid **2**^a

entry	alkyne 1	ArB(OH) ₂ 2 or (ArBO) ₃ 3	ligand	product 4	yield (%) ^b
1 ^c	1a	2m	dppb	4am	87
2 ^d	1a	2m	dppb	4am	93
3	1a	2m	dppb	4am	95
4	1a	2m	dppf	4am	91
5	1a	2m	dppe	4am	94
6	1a	2m	binap	4am	95
7	1a	2m	PPh ₃	4am	48
8	1a	3m	dppb	4am	90
9	1a	2n	dppb	4an	93
10	1a	2o	dppb	4ao	92
11	1a	3p	dppb	4ap	31
12 ^e	1a	3p	dppb	4ap	97
13	1b	2m	dppb	4bm	89
14	1c	2n	dppb	4cn	96
15	1d	2m	dppb	4dm	96 ^f
16	1e	2m	dppf	4em	81
17	1f	2m	dppf	4fm	70
18	1g	2m	dppf	4gm	87

^a The reaction was carried out with **1** (0.40 mmol) and boronic acid **2** (2.0 mmol) or arylboroxine **3** (0.67 mmol) in 1.0 mL of dioxane and 0.1 mL of water in the presence of 3 mol % of the catalyst generated from Rh(acac)(C₂H₄)₂ and a phosphine ligand (Rh/P = 1/2.2) at 100 °C for 3 h, unless otherwise noted. ^b Isolated yield by silica gel chromatography. ^c The amount of phenylboronic acid was 0.48 mmol. ^d The amount of phenylboronic acid was 0.80 mmol. ^e Reaction at 60 °C for 3 h. ^f A mixture of (*E*)-1,2-diphenylpropene (**4dm**) and its regioisomer, 1,1-diphenylpropene, in a ratio of 3 to 1.

yield was much lower with triphenylphosphine (entries 4–7). Triphenylcyclotriboroxane (**3m**, phenylboroxine)^{3c} which is a cyclic anhydride of phenylboronic acid (**2m**) can be used as well as the boronic acid (entry 8). Arylboronic acids, **2n** and **2o**, which have trifluoromethyl and methyl, respectively, at the 4-position of the phenyl gave the corresponding hydroarylation products (*E*)-**4an** and **4ao** in over 90% yield (entries 9 and 10). In the reaction with 4-methoxyphenylboronic acid (**2p**) or its boroxine **3p**, the yield of **4ap** was low at 100 °C, because the hydrolysis giving anisole is fast at this temperature. Lowering the reaction temperature to 60 °C greatly improved the yield of **4ap** (97%) (entry 12). The hydroarylation of diphenylethyne (**1c**) also proceeded with *syn*-selectivity, giving (*E*)-1,2-diphenyl-1-(4-trifluoromethylphenyl)ethene (**4cn**) (>99% *E*) in the reaction with 4-trifluoromethylphenylboronic acid (**2n**) (entry 14). In the reaction of acetylenes substituted with an ester or phosphonate group, the regio- and *syn*-selectivity was so high that no regio- or geometrical isomers were detected by NMR analysis (entries 16–18). The aryl group was introduced selectively at the β position to the electron-withdrawing group.

It is assumed that the catalytic cycle involves addition of an arylrhodium intermediate to an alkyne in a *syn* fashion and hydrolysis of the resulting alkenylrhodium bond giving the

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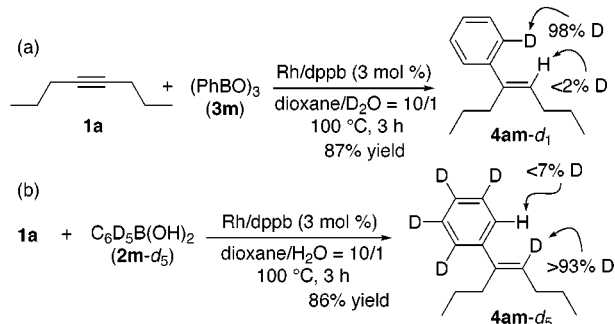
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(7) Lautens, M.; Roy, A.; Fukuoka, K.; Fagnou, K.; Martín-Matute, B. *J. Am. Chem. Soc.* **2001**, *123*, 5358.

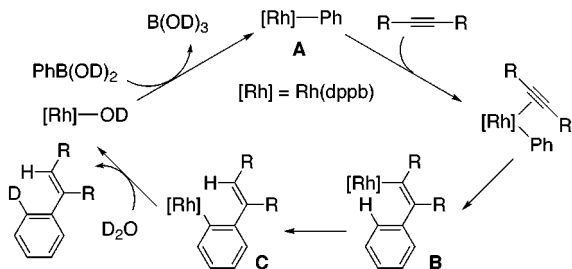
(8) Abbreviations: dppb = 1,4-bis(diphenylphosphino)butane, dppf = 1,1'-bis(diphenylphosphino)ferrocene, dppe = 1,2-bis(diphenylphosphino)ethane, binap = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl.

(9) Gao, Y.; Harada, K.; Hata, T.; Urabe, H.; Sato, F. *J. Org. Chem.* **1995**, *60*, 290. The *E* geometry of **4am** was confirmed by NOE experiments (Supporting Information).

Scheme 2



Scheme 3

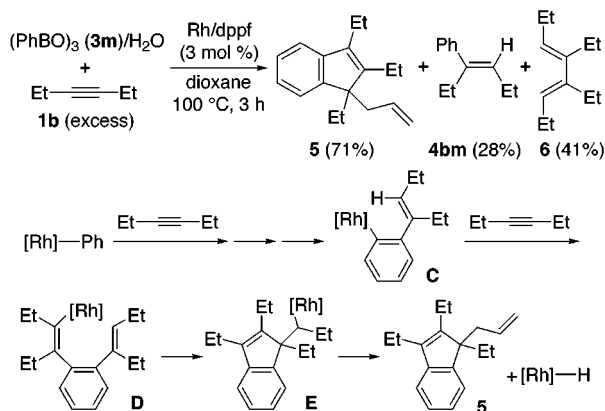


hydroarylation product. In this catalytic cycle, the hydrogen on the vinylic carbon should come from water. To confirm this catalytic cycle, the reaction of 4-octyne (**1a**) with phenylboroxine (**3m**) was carried out in D₂O ((a) in Scheme 2). Rather surprisingly, the hydrophenylation product **4am-d₁**, which was formed in 87% yield, did not incorporate the deuterium (<2%) on the vinylic carbon, and the deuterium was observed at the ortho position (98%) of the phenyl group instead. It follows that rhodium moved from the vinylic position of the alkenylrhodium intermediate (**B** in Scheme 3) to the ortho position of the phenyl, probably by way of a rhodium(III) intermediate formed by oxidative addition of a C-H bond on the phenyl to rhodium(I), and the 2-(alkenyl)phenylrhodium intermediate **C** undergoes the hydrolysis with water giving the hydrophenylation product (Scheme 3). The reaction of **1a** with C₆D₅B(OH)₂ (**2m-d₅**) in H₂O gave the hydrophenylation product **4am-d₅** where one of the deuterium atoms on the ortho position of the pentadeuteriophenyl moved to the vinylic position ((b) in Scheme 2). This 1,4-shift of the deuterium also supports the rearrangement of the alkenylrhodium intermediate **B** into the 2-(alkenyl)phenylrhodium intermediate **C**. A similar 1,4-shift of rhodium has been reported by Miura⁶ in the reaction of norbornene with arylboronic acids, where rhodium moves from alkyl *sp*³ carbon to aryl *sp*² carbon and the arylrhodium species further reacts with another molecule of norbornene. In our hydroarylation of alkynes, rhodium moves from alkenyl *sp*² carbon to phenyl *sp*² carbon¹⁰ before hydrolysis. For the catalytic cycle to be completed to give a high yield of the hydrophenylation product, the addition of the phenylrhodium intermediate **A** must occur before its hydrolysis with water, and the 2-(alkenyl)phenylrhodium intermediate **C**, generated by the phenylrhodium of alkyne followed by the 1,4-rearrangement, must undergo the hydrolysis rather than insertion of alkyne. The high selectivity in giving the one-to-one hydroarylation products observed here may be ascribed to the 1,4-rearrangement of rhodium forming the 2-(alkenyl)phenylrhodium intermediate **C** which is less reactive toward the alkyne insertion than phenylrhodium **A** or alkenylrhodium intermediate **B** because of its steric bulkiness.

Although the 2-(alkenyl)phenylrhodium intermediate **C** does not add to another molecule of alkyne under the reaction

(10) A similar migration of vinylic palladium(II) to arylpalladium(II) has been proposed in the palladium-catalyzed synthesis of 9-alkylidene-9H-fluorenes: Tian, Q.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3329.

Scheme 4



conditions where an excess of arylboronic acid is used in the presence of a large excess of water as a solvent, the addition does take place in the reaction of an arylboroxine with excess alkyne in the presence of a minimum amount of water. Thus, the reaction of phenylboroxine (**3m**) with 8 equiv of 3-hexyne (**1b**) in the presence of one equiv (to boron) of water¹¹ and rhodium-dppf catalyst (3 mol %) in dioxane at 100 °C for 3 h gave 71% yield of indene **5** together with the hydrophenylation product **4bm** (28%) and diene **6** (41%) (Scheme 4). The formation of indene **5** can be rationalized by the catalytic cycle involving addition of 2-(alkenyl)phenylrhodium species **C** to 3-hexyne and intramolecular carboration in the new alkenylrhodium intermediate **D**. β-Hydrogen elimination on the alkenylrhodium **E** followed by isomerization of the double bond gives indene **5** containing the allyl group and a hydridorhodium species. The formation of diene **6** may suggest that the hydridorhodium comes back to the catalytic cycle after it effects the reductive dimerization of alkyne **1b** forming **6**.

The addition of an aryl group and hydrogen to alkynes has been attained, for example, by nickel-catalyzed addition of arylmagnesium or -zinc reagent^{12,13} followed by hydrolysis, or palladium-catalyzed cross-coupling of aryl halides with alkenylmetal reagents generated by hydroboration¹⁴ or titanium-catalyzed hydrozincation of alkynes.^{9,15} From a synthetic point of view, the present hydroarylation of alkynes has advantages over other methods in that it is carried out in an aqueous solvent, functional groups such as ester are intact during the reaction, and the *syn*-selectivity at the addition is very high.

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Supporting Information Available: Experimental procedures, spectroscopic and analytical data for the products (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(11) Since arylboroxine and water is in an equilibrium with arylboronic acid under the reaction conditions, the reaction starting from arylboroxine and that starting from arylboronic acid and water (1 equiv to boron) should result in the same outcome. Nevertheless, the combination of the boroxine and water was used in this experiment, because the ratio of boron to water can be kept more precisely. Chemically pure arylboroxines can be readily obtained by dehydration of arylboronic acids by azeotropic removal of water from their benzene solution, while arylboronic acids obtained by recrystallization from water are usually contaminated with arylboroxines to some extent. For a review: Lappert, M. F. *Chem. Rev.* **1956**, *56*, 959.

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(13) For a review on the organozinc reagents: Knochel, P.; Almendra Perea, J. J.; Jones, P. *Tetrahedron* **1998**, *54*, 8275.

(14) For a review on the cross-coupling of organoboron reagents: Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(15) For a review on the organotitanium reagents: Sato, F.; Urabe, H.; Okamoto, S. *Chem. Rev.* **2000**, *100*, 2835.