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Rhodium-Catalyzed Arylation Using Arylboron Compounds: Efficient Coupling with Aryl Halides and Unexpected Multiple Arylation of Benzonitrile

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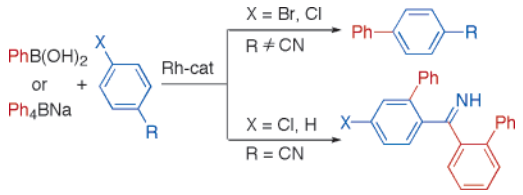
ABSTRACT



The Suzuki–Miyaura-type cross-coupling of arylboron compounds with aryl halides proceeds efficiently in the presence of a rhodium-based catalyst system to produce the corresponding biaryls. Furthermore, it has unexpectedly been observed that the treatment with benzonitrile under similar conditions brings about its multiple arylation, in which nucleophilic arylation on the cyano group and subsequent ortho arylation via C–H bond cleavage are involved.

The palladium-catalyzed arylation of alkenes, terminal alkynes, and organometallic reagents with aryl halides is now recognized to be a powerful tool for constructing various aromatic fine chemicals.[1] They involve the formation of a common arylpalladium(II) intermediate and subsequent insertion, substitution, and transmetalation, respectively. The arylpalladium species is also known to be so electron-deficient as to react with carbon nucleophiles, including electron-rich aromatic and heteroaromatic compounds.[2]

On the other hand, an arylrhodium(I) species, which can be readily generated via transmetalation with the corresponding arylmetal reagents, is relatively electron-rich and capable of inducing the nucleophilic arylation of aldehydes, aldimines, and α,β-unsaturated carbonyl compounds.[3] It may be conceived that such an electron-rich arylrhodium intermediate undergoes oxidative addition of electrophilic aromatic substrates. While the catalytic cross-coupling of arylboron reagents with acid anhydrides via transmetalation and oxidative addition to produce aryl ketones or biaryls has been reported by us[4] and other groups,[5] the reaction with more general substrates, aryl halides, has been less explored; only one example of the cross-coupling of arylzinc reagents with aryl iodides has been reported.[6] In the context of our study

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of rhodium-catalyzed arylation reactions,[4,7] we have found that arylboron compounds can be coupled efficiently with various aryl bromides and electron-deficient aryl chlorides in the presence of an appropriate rhodium-based catalyst system such as $[RhCl(cod)]_2$-dppp.[8] While the stoichiometric activation of aryl chlorides on a phenylrhodium complex was recently realized,[9] an effective catalytic example has, at least to our knowledge, never been disclosed. Moreover, during the examination of the applicable scope of aryl halides, it was observed unexpectedly that the treatment with benzonitrile under similar conditions brings about its multiple arylation, in which nucleophilic arylation on the cyano group and subsequent ortho arylation via C−H bond cleavage are involved. The unprecedented reaction is also described briefly.

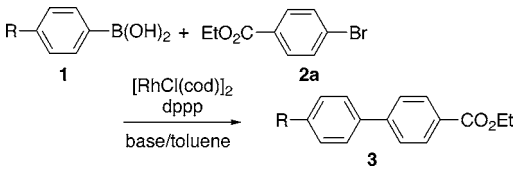
In an initial attempt, phenylboronic acid (**1a**) (1 mmol) was treated with ethyl 4-bromobenzoate (**2a**) (1 mmol) in the presence of Cs_2CO_3 (1 mmol) as a base and $[RhCl(cod)]_2$ (0.005 mmol)-dppp (0.01 mmol) as a catalyst in *o*-xylene at 120 °C for 2 h under nitrogen, ethyl 4-biphenylcarboxylate (**3a**) being formed in 56% yield (Table 1, entry 1). It was found that dppp is the ligand of choice for the reaction. The product yield decreased to 32, 27, and 33% in the cases using dppe, dppb, and dppf, respectively,[8] in place of dppp. Increasing the amount of **1a** to 2 mmol enhanced the product yield slightly (entry 2). CsF was more effective than Cs_2CO_3 (entry 3). Finally, the best yield of **3a** (92%) was obtained by conducting the reaction in refluxing toluene (entry 4). Under the optimized conditions, the reaction of other arylboronic acids **1b**−**e** with **2a** proceeded smoothly to afford the corresponding biaryls **3b**−**e** in good yields (entries 5−8).

The use of sodium tetraphenylborate (**4**) in place of **1a** allowed elimination of the addition of base. Thus, the reaction of **4** (1 mmol) with **2a** (1 mmol) in the absence of CsF proceeded to give **3a** in 72% yield after 20 h (Table 2, entry 1). In contrast to the reaction using **1a**, a substrate ratio of **4**:**2a** = 1:2 afforded a better result, and **3a** was obtained in 87% yield within 5 h (entry 2). Bromobenzenes substituted by chloro (**2b**) and methoxy (**2c**) groups at the 4-position also reacted with **4** to give **3f** and **3g**, respectively (entries 3 and 4).

A number of aryl chlorides also underwent the cross-coupling with **4**. The treatment of **4** with ethyl 4-chlorobenzoate (**2d**) using the $[RhCl(cod)]_2$-dppp catalyst system afforded **3a** in 73% yield (entry 5). Other electron-deficient aryl chlorides **2e**−**g** could also be reacted to produce biaryls **3h**−**j** (entries 6−8).

To our surprise, the treatment of **4** with one of the activated chlorides, 4-chlorobenzonitrile, under the same conditions gave, not a normal biaryl, but a complex mixture of mono-, di-, and triphenylated products, in which the chloro moiety remained in each of them. When **4** (0.5 mmol) was treated with unsubstituted benzonitrile (**5**) (2 mmol) in the presence of $[RhCl(cod)]_2$ (0.005 mmol)-dppp (0.01 mmol) in *o*-xylene at 120 °C for 44 h, the product mixture was relatively simple and was found to involve benzophenone imine (**6**)[10] and di- and triphenylated products (**7** and **8**, respectively) (Scheme

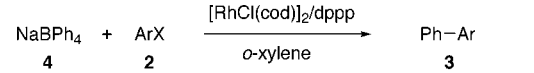
Table 1. Reaction of Arylboronic Acids **1** with Ethyl 4-Bromobenzoate (**2a**)[a]



entry	R	**1**	base	**3**, % yield[b]
1[c,d]	H	**1a**	Cs_2CO_3	**3a**, 56
2[c]	H	**1a**	Cs_2CO_3	**3a**, 65
3[c]	H	**1a**	CsF	**3a**, 83
4	H	**1a**	CsF	**3a**, 92 (82)
5	Cl	**1b**	CsF	**3b**, 95 (85)
6[e]	F	**1c**	CsF	**3c**, 88 (74)
7	Me	**1d**	CsF	**3d**, 96 (87)
8	OMe	**1e**	CsF	**3e**, 98 (70)

[a] Reaction conditions: **1** (2 mmol), **2a** (1 mmol), $[RhCl(cod)]_2$ (0.005 mmol), dppp (0.01 mmol), base (2 mmol) in toluene (5 mL) at 120 °C for 2 h under N_2. [b] GC yield based on the amount of **2a** used. Value in parentheses indicates isolated yield. [c] In *o*-xylene (5 mL). [d] With **1** (1 mmol) and base (1 mmol). [e] For 4 h.

Table 2. Reaction of Sodium Tetraphenylborate (**4**) with Aryl Halides **2**[a]



entry	Ar	**2**, X	time (h)	**3**, % yield[b]
1[c]	EtO_2C−	**2a**, Br	20	**3a**, 72
2	EtO_2C−	**2a**, Br	5	**3a**, 87
3	Cl−	**2b**, Br	20	**3f**, 74 (55)
4	MeO−	**2c**, Br	20	**3g**, 82 (58)
5	EtO_2C−	**2d**, Cl	20	**3a**, 73
6	N	**2e**, Cl	20	**3h**, 71 (67)
7	N	**2f**, Cl	20	**3i**, 82 (56)
8	F_3C−	**2g**, Cl	44	**3j**, 51 (28)

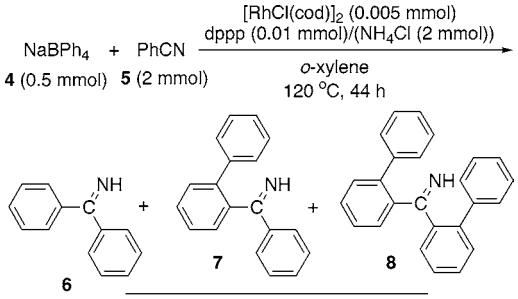
[a] Reaction conditions: **4** (0.5 mmol), **2** (1 mmol), $[RhCl(cod)]_2$ (0.005 mmol), dppp (0.01 mmol) in *o*-xylene (5 mL) at 120 °C under N_2. [b] GC yield based on the amount of **4** used. Value in parentheses indicates isolated yield. [c] With **4** (1 mmol).

(7) Oguma, K.; Miura, M.; Satoh, T.; Nomura, M. *J. Am. Chem. Soc.* **2000**, *122*, 10464.

(8) Abbreviations: cod = 1,5-cyclooctadiene; dppp = 1,3-bis(diphenylphosphino)propane; dppe = 1,2-bis(diphenylphosphino)ethane; dppb = 1,4-bis(diphenylphosphino)butane; dppf = 1,1′-bis(diphenylphosphino)-ferrocene.

(9) Grushin, V. V.; Marshall, W. J. *J. Am. Chem. Soc.* **2004**, *126*, 3068.

Scheme 1



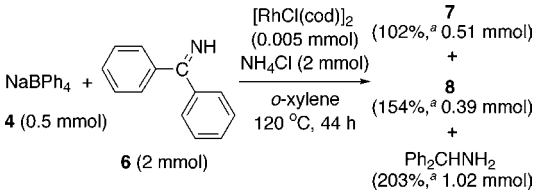
NH_4Cl	products, % yield[a]
–	**6**, 21% (0.11 mmol) **7**, 36% (0.09 mmol) **8**, 11% (0.02 mmol)
+	**7**, 71% (0.18 mmol) **8**, 63% (0.11 mmol)

[a] GC yield based on the amount of **4** used.

1). The reaction efficiency was improved by the addition of NH_4Cl (2 mmol) to afford **7** and **8** in 71 and 63% yields, respectively, **6** being consumed completely.[11] The fact that the total yield exceeded 100% means that more than one phenyl group in **4** can be utilized in this case.[12]

The imine **6** is considered to be generated by a nucleophilic mechanism.[3] Products **7** and **8** may be formed via the coordination-assisted ortho phenylation of **6** as proposed below.[13] Expectedly, the treatment of **4** (0.5 mmol) with **6** (2 mmol) in the presence of $[RhCl(cod)]_2$ (0.005 mmol) and NH_4Cl (2 mmol) gave **7** and **8** in 102 and 154% yields, respectively (Scheme 2).[12] In this case, dppp was no longer needed. The fact that a significant amount of aminodiphenylmethane was also formed as a byproduct suggests that part

Scheme 2

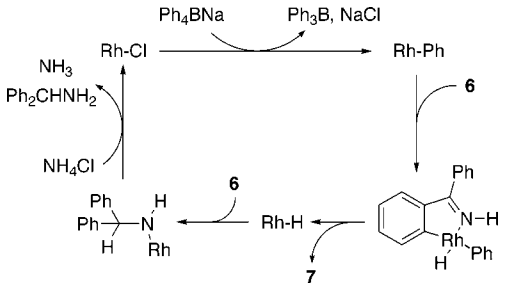


[a] GC yield based on the amount of **4** used.

of **6** acted as the acceptor of hydrogen eliminated by the C−H phenylation.[13n]

A plausible mechanism for the formation of **7** as well as the amine is illustrated in Scheme 3. Coordination of the

Scheme 3



nitrogen atom of **6** to a phenylrhodium species generated in the medium followed by ortho rhodation gives a rhodacycle intermediate. The subsequent reductive elimination affords monophenylated product **7** and a rhodium hydride. Then, insertion of another molecule of **6** into the Rh−H bond and protonolysis of the resulting amidorhodium species by NH_4Cl may occur to give the amine, regenerating a rhodium chloride. The second ortho phenylation may proceed by the same mechanism to produce **8**.

In summary, we have shown that the Suzuki−Miyaura-type cross-coupling of arylboron compounds with aryl halides, including a number of chlorides, can be performed efficiently in the presence of a rhodium catalyst using a common bidentate ligand such as dppp. Also included is an unprecedented sequential multiple phenylation of benzonitrile on the cyano group followed by the ortho positions. These observations appear to demonstrate the versatility of arylrhodium species further and provide useful information for designing new catalytic cycles.

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

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(11) Formation of aminodiphenylmethane was also detected by GC-MS.

(12) Yields of **7** and **8** were defined as follows: yield (%) = [product (mmol)/**4** (mmol)] x (the number of phenyl groups introduced to the product) x 100.

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