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Rhodium(I)-Catalyzed Borylation of Nitriles through the Cleavage of Carbon−Cyano Bonds

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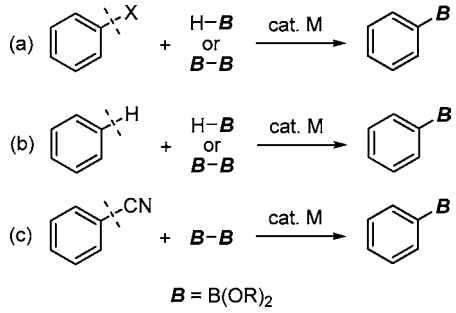
Supporting Information

ABSTRACT: The reaction of aryl cyanides with diboron in the presence of a rhodium/Xantphos catalyst and DABCO affords arylboronic esters via carbon−cyano bond cleavage. This unprecedented mode of reactivity for a borylrhodium species allows the regioselective introduction of a boryl group in a late stage of synthesis.

Arylboronic acids and their derivatives are versatile reagents in modern organic synthesis.[1] Traditional methods for their preparation involve the reaction of either organolithium or -magnesium reagents with boron-centered electrophiles. Recent efforts have been focused on the development of more functional-group-tolerant catalytic methods. In this context, two types of catalytic borylation reactions have been established. The catalytic borylation of aryl halides can be achieved using diboron or hydroboron reagents (Scheme 1a).[2]

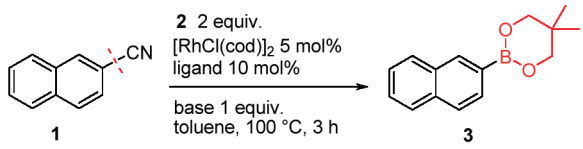
Scheme 1. Catalytic Borylation Reactions



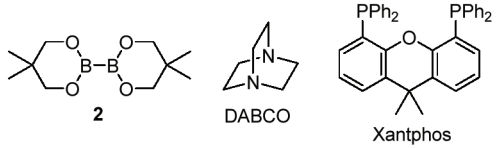
Aromatic C−H bonds can also be borylated directly in the presence of a rhodium or iridium catalyst (Scheme 1b).[3] Herein we report a new class of catalytic borylation whereby aryl cyanides can be borylated through cleavage of the carbon−cyano (C−CN) bond (Scheme 1c).

We have recently developed a series of catalytic methods to convert C−CN bonds into C−Si,[4] C−H,[5] and C−C[4b,6] bonds in the presence of a rhodium catalyst and organosilicon reagents. In these reactions, a silylrhodium complex, which is generated in situ through the reaction of a Rh(I) precatalyst with an organosilicon reagent, is postulated to be the catalytically active species. This active species mediates the cleavage of the C−CN bond via silylrhodation of the cyano group and the extrusion of silyl isocyanide.[7] The unique reactivity of this silylrhodium species toward C−CN bonds prompted us to investigate the potential of other main-group reagents in regard to the cleavage of C−CN bonds.[8] After some experimentation, we were intrigued to find that the rhodium-catalyzed reaction of nitrile **1** in the presence of diboron **2** afforded trace levels of borylated product **3** (4% yield by GC; Table 1, entry 1). Further investigation revealed that the addition of a base and phosphine ligands improved the yield of **3**.[9] The use of 1,4-diazabicyclo[2.2.2]octane (DABCO) as the base and Xantphos as the ligand proved to be the optimal combination for a successful rhodium-catalyzed nitrile borylation (entry 10).[10] To date, the activation of C−CN bonds in catalytic reactions has required the use of either Ni(0) or silylmetal complexes.[11] The present reaction represents the first example of C−CN bond cleavage in the presence of a borylmetal species without the need for a silylmetal complex or Ni(0).

Table 1. Optimization Studies[a]



entry	base	ligand	GC yield of **3**
1	none	none	4
2	K_3PO_4	none	7
3	Et_3N	none	3
4	DABCO	none	10
5	DABCO	PPh_3	55 (57)[b]
6	DABCO	PCy_3	20
7	DABCO	dppe	13
8	DABCO	dppb	51
9	DABCO	BINAP	43
10	DABCO	Xantphos	57 (**86**)[b]



[a]Reaction conditions: **1** (0.50 mmol), **2** (1.0 mmol), $[RhCl(cod)]_2$ (0.025 mmol), and ligand (0.050 mmol) in toluene (0.5 mL) at 100 °C for 3 h. [b]Run for 15 h using 0.10 mol of the indicated ligand.

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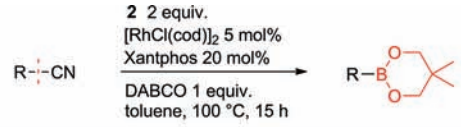
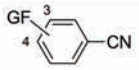
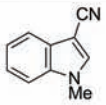
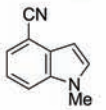
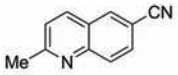
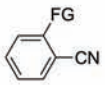
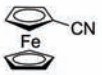
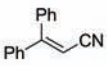
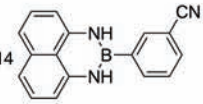
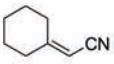
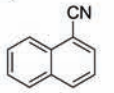
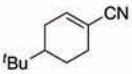
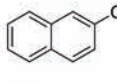
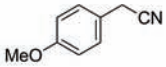
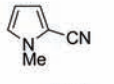
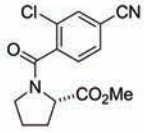
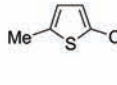
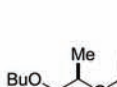
The optimized conditions for **1** proved to be general for the rhodium-catalyzed borylation of a range of aryl cyanides (Table 2). Common functional groups, including fluorides (entries 2, 4, and 28), esters (entry 3, 27, and 28), ethers (entries 6, 9, and 28), and amines (7 and 10), were all compatible with this catalytic borylation reaction. Of particular note, aryl chlorides survived under these conditions (entries 5 and 27),[12] which would allow orthogonal functionalization via conventional cross-coupling technologies. The application of sterically demanding cyanides proceeded more efficiently using the less bulky PPh_3 ligand, to afford ortho-substituted arylboronic esters in good yields (entries 11–13). A boryl group protected with 1,8-diaminonaphthalene was also tolerated, furnishing a diborylated arene, which may be applied to sequential cross-coupling cascades (entry 14).[13] The methodology can also be successfully applied to fused (entries 15 and 16) and ferrocene-containing (entry 22) substrates. Moreover, a range of heteroaromatic substrates, including pyrroles (entry 17), thiophenes (entry 18), indoles (entries 19 and 20), and quinolines (entry 21), underwent this decyanative borylation in an efficient manner. Alkenyl cyanides were also examined as potential substrates. Monosubstituted acrylonitrile derivatives such as cinnnamonitrile did not deliver the desired products under the optimized conditions.[14] In contrast, α,β- and β,β-disubstituted acrylonitriles proved to be suitable substrates, producing their corresponding alkenylboronic esters (entries 23–25). Although alkyl cyanides were generally inapplicable, benzylic substrates were exceptionally reactive, affording the corresponding benzylboronic esters (entry 26). This protocol can also be applied to nitriles in biorelated compounds such as amino acid derivatives (entry 27) and pesticides (entry 28)[15] to afford the corresponding borylated products, which can act as versatile platforms for further derivatization.

A proposed mechanism for this rhodium-catalyzed nitrile borylation is outlined in Scheme 2. The reaction of the rhodium precatalyst **A** with diboron **2** initially generates borylrhodium **B**. The formation of B(nep)–Cl (nep = neopentylglycolate) was confirmed by ^{11}B NMR analysis of the stoichiometric reaction of $[RhCl(cod)]_2$, Xantphos, and **2**.[16] The addition of **B** to the nitrile then forms the iminylrhodium species **C**,[17,18b] which is followed by *E*/*Z* isomerization. β-Aryl elimination[18] generates arylrhodium **E** and boryl cyanide **F**.[19] Finally, the reaction of **E** with **2** affords the borylated product and regenerates **B**.

The ortho-directing ability of the cyano group[20] allows a reactivity pattern that cannot be achieved using other borylation methodologies (Scheme 3). The C–H bond at the ortho position of benzonitrile (**4**) can be directly arylated using palladium catalysis[20g] to form the 2-cyanobiphenyl derivative **6**, which can then be borylated using a rhodium catalyst and **2**. Thus, benzonitriles can serve as simple precursors for 2-substituted phenylboronic acids. The inherent stability of the cyano group under typical transition-metal-catalyzed conditions allows the combined use of catalytic borylation methods. This leads to the regioselective introduction of a boryl group at a

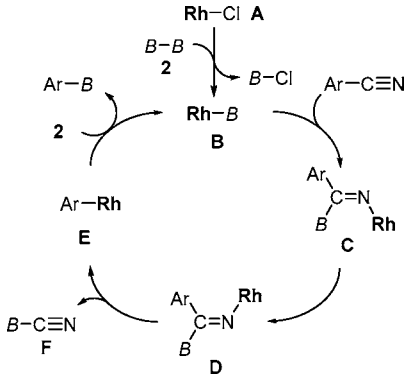
Table 2. Rh-Catalyzed Borylation of Nitriles with 2[a]



entry	nitrile	yield (%)[b]	entry	nitrile	yield (%)[b]
			19[e]		87
1	FG = H	73			
2	4-CF_3	91			
3	4-CO_2Et	80			
4	4-F	83	20		81
5	4-Cl	86			
6	4-OMe	75			
7	4-NMe_2	72			
8	4-B(nep)[c]	70	21		82
9	3-OMe	87			
10	3-NMe_2	82			
			22[d]		73
11[d]	FG = Me	69			
12[d]	Ph	82			
13[d]	OPh	85	23		65
			24		40
14		74			
			25		47[f]
15[d]		62			
			26		64[f]
16		86			
			27[g]		53
17[e]		73			
					
18		64			
					
28[h]		69			
					

[a]Reaction conditions: nitrile (0.50 mmol), **2** (1.0 mmol), $[RhCl(cod)]_2$ (0.025 mmol), Xantphos (0.10 mmol), and DABCO (0.5 mmol) in toluene (0.5 mL) at 100 °C for 15 h. [b]Isolated yields based on nitrile. [c]Nep = neopentylglycolate. [d]PPh_3 (0.15 mmol) was used as the ligand. [e]Run for 48 h. [f]Yield was determined by ^1H NMR analysis because of the instability of the boronic ester during purification. [g]$[Rh(cod)_2]BF_4$ (0.10 mmol) was used as a catalyst at 80 °C. [h]Rh catalyst (0.050 mmol) and Xantphos (0.20 mmol) were used.

Scheme 2. A Possible Mechanistic Pathway



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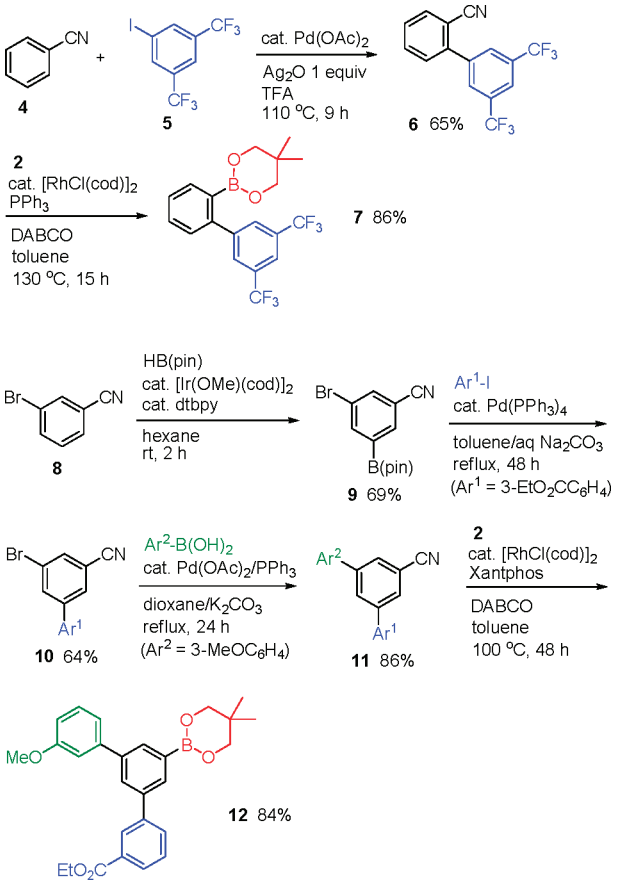
Scheme 3. Synthetic Applications



later stage of a synthesis. For instance, the C−H bond borylation of **8**[21] followed by two sequential Suzuki−Miyaura couplings at the iodide and bromide sites furnishes nitrile **11**, which can finally be converted into boronic ester **12** using our rhodium methodology.

In summary, we have developed a rhodium-catalyzed nitrile borylation using diboron **2**. The reaction involves an unprecedented C−CN bond activation that is promoted by a borylrhodium complex. In addition, the reaction offers a new strategy for the synthesis of complex boronic acid derivatives wherein a cyano group can now be utilized as a boron equivalent. Further mechanistic and synthetic studies are in progress.

■ ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures and characterization of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) It has been reported that Fe−CH_3, Fe−$GeMe_3$, and Fe−$SnMe_3$ complexes failed to promote the cleavage of a CH_3−CN bond (see ref 7c).

(9) (a) Bis(pinacolato)diboron, $B_2(pin)_2$, could also be used in place of **2**, although the yield was slightly decreased. For example, the reaction of **1** with $B_2(pin)_2$ under conditions identical to those shown in Table 2 except for a reaction time of 60 h afforded a borylated product in 60% yield. (b) See the Supporting Information (SI) for a complete table of results of the optimization studies.

(10) Although PPh_3 and Xantphos afforded **3** in almost identical yields after 3 h, **1** was completely consumed when PPh_3 was used, while ca. 30% of **1** was recovered when Xantphos was employed.

(11) Reviews of C−CN bond activation: (a) Tobisu, M.; Chatani, N. *Chem. Soc. Rev.* **2008**, *37*, 300. (b) Nakao, Y.; Hiyama, T. *Pure Appl. Chem.* **2008**, *80*, 1097. Recent reports on Ni(0)-catalyzed C−CN bond cleavage reactions: (c) Nakao, Y.; Yada, A.; Hiyama, T. *J. Am. Chem. Soc.* **2010**, *132*, 10024. (d) Sun, M.; Zhang, H.-Y.; Han, Q.; Yang, K.; Yang, S.-D. *Chem.—Eur. J.* **2011**, *17*, 9566. (e) Nakai, K.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2011**, *133*, 11066.

(12) Aryl bromides were borylated under the presented conditions. Competition studies revealed relative reactivities of ArBr and ArCN towards Rh-catalyzed borylation to be ca. 1:2.4.

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(14) Unsuccessful applications to *β*-monosubstituted acrylonitriles were due in part to the involvement of an undesired dehydrogenative borylation pathway in which the borylrhodium species adds across the alkene moiety rather than to a cyano group. See: Kondoh, A.; Jamison, T. F. *Chem. Commun.* **2010**, *46*, 907.

(15) Commercially available from Kanto Chemical Co., Inc. as Cyhalohop butyl.

(16) See the SI for details.

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(19) For a sole example of the synthesis of $(RO)_2B-CN$-type compounds, see: Jiang, B.; Kan, Y.; Zhang, A. *Tetrahedron* **2001**, *57*, 1581.

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