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Ruthenium-Catalyzed Ortho C−H Arylation of Aromatic Nitriles with Arylboronates and Observation of Partial Para Arylation

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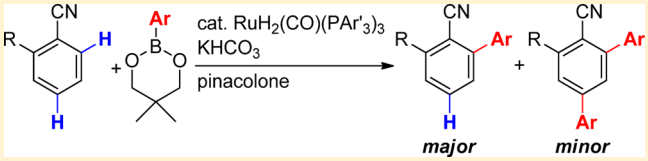
Supporting Information

ABSTRACT: Ruthenium-catalyzed C−H arylation of aromatic nitriles with arylboronates is described. The use of $RuH_2(CO)\{P(4\text{-}MeC_6H_4)_3\}_3$ as a catalyst provided higher yields of the ortho arylation products than the conventional $RuH_2(CO)(PPh_3)_3$ catalyst. The arylation takes place mostly at the ortho positions, but unprecedented para arylation was also partially observed to give ortho,para diarylation products. In addition to C−H bond cleavage, the cyano group was also found to function as a directing group for cleavage of C−O bonds in aryl ethers.



INTRODUCTION

Catalytic C−C bond formation via C−H bond cleavage by transition-metal catalysts has been studied extensively in the past decade and become a useful method in organic synthesis.[1] Control of the regioselectivity of the C−H functionalization is one of the most important issues in development of useful transformations. There are two major strategies to achieve high regioselectivity in C−H functionalizations; one is to employ heteroarenes as substrates to differentiate and potentially activate the C−H bonds,[2] and the other is the use of arenes bearing directing groups.[3] Direct functionalization of the latter substrates is usually controlled at the ortho positions because pre-coordination of the directing group to a metal center occurs and C−H bond cleavage is assisted by chelate formation. A variety of directing groups have been used for regioselective C−H functionalization, but most of the examples have employed directing groups containing sp^2- and sp^3-hybridized nitrogen, oxygen, phosphorus, and sulfur atoms as coordinating atoms to facilitate the chelate formation.

In contrast, the use of π-electrons in multiple bonds such as those in alkynes[4] and nitriles[5−8] to direct the C−H functionalization sites has been less explored. Benzonitriles usually coordinate to metals using the lone pair on the nitrogen atom, but it is difficult to consider that the coordination mode facilitates the chelation-assisted C−H bond cleavage. Instead, the π-coordination of the cyano group may bring the metal closer to the ortho C−H bond to facilitate the bond cleavage. In 1999, Murai, Kakiuchi, and co-workers reported the $RuH_2(CO)(PPh_3)_3$-catalyzed alkylation of aryl nitriles with alkenes via oxidative addition of C−H bonds to a low-valent ruthenium complex.[5] In 2011, Sun and co-workers found the palladium(II)-catalyzed cyano group directed arylation of aromatic nitriles with aryl iodides where the C−H bond cleavage was proposed to take place via electrophilic palladation.[6a] Subsequently, they have expanded this cyano group directed C−H functionalization to catalytic regioselective introduction of oxygen[6b] and halogen atoms[6c] on aromatic rings. Recently, the Jeganmohan group also reported a ruthenium(II)-catalyzed ortho C−H alkenylation of aromatic nitriles with alkenes.[6d]

Here, we report ruthenium-catalyzed C−H arylation of aromatic nitriles with arylboronates. The optimized catalyst for this arylation was $RuH_2(CO)\{P(4\text{-}MeC_6H_4)_3\}_3$, which was recently developed in our group and is clearly more efficient for this reaction than the conventional $RuH_2(CO)(PPh_3)_3$ catalyst. The arylation mostly took place at the ortho positions, but unprecedented *para* C−H arylation was also observed.

RESULTS AND DISCUSSION

Our group has developed ortho C−H arylation of aromatic ketones and esters with arylboronates using $RuH_2(CO)(PPh_3)_3$ (**1a**) as catalyst, pinacolone as solvent and $H-B(OR)_2$ acceptor.[9] Considering the previous observation that complex **1a** can cleave the ortho C−H bonds of benzonitriles, we decided to examine the ruthenium-catalyzed arylation of benzonitriles with arylboronates. When a reaction of 2-(trifluoromethyl)benzonitrile (**2a**)[10] with 2 equiv of phenylboronic acid neopentylglycol ester (**3a**) was carried out using **1a** as a catalyst under pinacolone refluxing conditions for 24 h, ortho phenylation product **4aa** was obtained in 10% GC yield (Table 1, entry 1). Other ruthenium complexes, such as $RuH_2(PPh_3)_4$, $Ru(CO)_2(PPh_3)_3$, and $Ru_3(CO)_{12}$, showed lower or no catalytic activity for this reaction (entries 2−4). Recently, we established a synthetic method to access $RuH_2(CO)(PAr_3)_3$-type complexes using various triarylphosphines[11,12] and the use of these complexes for arylation of sterically congested C−H bonds of aromatic ketones.[11] Therefore, several ruthenium complexes

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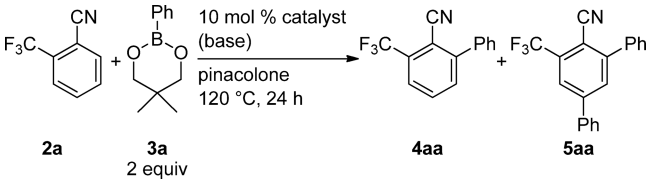
Table 1. Ruthenium-Catalyzed C−H Arylation of 2a with 3a[a]



entry	catalyst	base	GC yield of **4aa** (**5aa**) (%)
1	$RuH_2(CO)(PPh_3)_3$ (**1a**)	none	10
2	$RuH_2(PPh_3)_4$	none	6
3	$Ru(CO)_2(PPh_3)_3$	none	nd[c]
4	$Ru_3(CO)_{12}$	none	nd[c]
5	$RuH_2(CO)(P(4\text{-}FC_6H_4)_3)_3$ (**1b**)	none	25 (trace)
6	$RuH_2(CO)(P(4\text{-}MeOC_6H_4)_3)_3$ (**1c**)	none	32 (trace)
7	$RuH_2(CO)(P(3\text{-}MeC_6H_4)_3)_3$ (**1d**)	none	47 (1)
8	$RuH_2(CO)(P(4\text{-}MeC_6H_4)_3)_3$ (**1e**)	none	47 (1)
9	**1d**	$KHCO_3$	78 (1)
10	**1e**	$KHCO_3$	81 (1)
11	**1e**	$NaHCO_3$	66 (2)
12	**1e**	$CsHCO_3$	53 (trace)
13	**1e**	KF	30 (trace)
14	**1e**	NaF	33 (trace)
15	**1e**	CsF	21 (trace)
16	**1e**	K_2CO_3	80 (2)
17	**1e**	Na_2CO_3	65 (1)
18	**1e**	Cs_2CO_3	24 (1)
19	**1e**	KO^{t}Bu	48 (2)
20	**1e**	NaO^{t}Bu	14 (trace)
21[b]	**1e**	$KHCO_3$	82 (2)

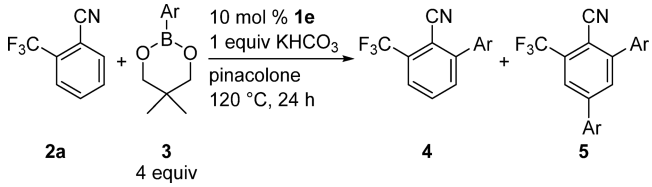
[a]Reaction conditions: **2a** (0.2 mmol), **3a** (2 equiv), catalyst (10 mol %), base (1 equiv, if any), pinacolone (0.2 mL), 120 °C, 24 h. [b]4 equiv of **3a** was used. [c]Not detected.

1b−e containing triarylphosphines other than PPh_3 were investigated for this reaction (entries 5−8). The product yields were generally improved using these para- or meta-substituted triarylphosphines, and in particular, $RuH_2(CO)\{P(3\text{-}MeC_6H_4)_3\}_3$ (**1d**) and $RuH_2(CO)\{P(4\text{-}MeC_6H_4)_3\}_3$ (**1e**) provided ortho phenylation product **4aa** in 47% yields (entries 7 and 8). The ortho,para diphenylation product, 4,6-diphenyl-2-(trifluoromethyl)benzonitrile (**5aa**), was also obtained, albeit in very low yield. Although catalytic C−H functionalization at a position para to the directing group is not unprecedented,[13] this is the first observation of para C−H functionalization of benzonitriles. This process should be regarded as non-chelation-assisted arylation and may be facilitated by the strongly electron-withdrawing cyano group at the para position of the electron-deficient aromatic ring possessing a trifluoromethyl group.[13b]

Addition of the base was then examined using complexes **1d** and **1e** as catalysts. The use of $KHCO_3$ dramatically improved the catalytic activity of **1d** and **1e**, and ortho arylation product **4aa** was obtained in 78 and 81% yields, respectively (entries 9 and 10). Other alkali metal bicarbonates (entries 11 and 12), fluorides (entries 13−15), carbonates (entries 16−18), and alkoxides (entries 19 and 20) were less effective compared to $KHCO_3$. Increasing the amount of **3a** to 4 equiv slightly improved the yield (entry 21). From these results, the conditions used for entry 21 were considered optimal and used for further investigations.[14]

Various arylboronates can be used for the C−H arylation of benzonitrile **2a** (Table 2). The reactions with

Table 2. Ruthenium-Catalyzed C−H Arylation of 2a with Various Arylboronates 3[a]



			yield (%)	
entry	**3**	Ar	**4**	**5**
1	**3b**	$4\text{-}F_3CC_6H_4$	**4ab**: 87	**5ab**: nd[b]
2	**3c**	$4\text{-}FC_6H_4$	**4ac**: 77	**5ac**: –[c]
3	**3d**	$4\text{-}MeC_6H_4$	**4ad**: 88	**5ad**: 5
4	**3e**	$4\text{-}^nHexC_6H_4$	**4ae**: 82	**5ae**: nd[b]
5	**3f**	$4\text{-}MeOC_6H_4$	**4af**: 89	**5af**: nd[b]
6	**3g**	$4\text{-}Me_2NC_6H_4$	**4ag**: 80	**5ag**: nd[b]
7	**3h**	$3\text{-}MeC_6H_4$	**4ah**: 84	**5ah**: 2
8	**3i**	$3,5\text{-}Me_2C_6H_3$	**4ai**: 74	**5ai**: –[c]
9	**3j**	$2\text{-}MeC_6H_4$	**4aj**: 24	**5aj**: nd[b]
10	**3k**	1-naphthyl	**4ak**: 49	**5ak**: nd[b]
11	**3l**	2-naphthyl	**4al**: 87	**5al**: nd[b]

[a]Reaction conditions: **2a** (0.2 mmol), **3** (4 equiv), **1e** (10 mol %), $KHCO_3$ (1 equiv), pinacolone (0.2 mL), 120 °C, 24 h. [b]Not detected. [c]Formation of a small amount of **5** was suggested by GCMS and ^{1}H NMR analyses, but the corresponding fractions could not be completely purified.

4-(trifluoromethyl)phenylboronate **3b** and 4-(fluorophenyl)-boronate **3c** afforded coupling products **4ab** and **4ac** in 87 and 77% yields, respectively (entries 1 and 2). The arylation with arylboronates bearing electron-donating para substituents such as methyl, *n*-hexyl, methoxy, and dimethylamino groups (**3d−g**) gave **4ad−ag** in 80−89% yields (entries 3−6). These results suggest that the electronic nature of the substituents has no significant effect on the reactivity. The arylations with meta-substituted arylboronates **3h** and **3i** also provided the corresponding monoarylation products **4ah** and **4ai** in high yields (entries 7 and 8). The reactions with bulky 2-tolyl- and 1-naphthylboronates **3j,k** resulted in lower yields (entries 9 and 10). In contrast, less sterically congested 2-naphthylboronate **3l** smoothly reacted to give **4al** in 87% yield (entry 11). The reaction was also examined with the corresponding 2-methyl-1-propenylboronate but did not provide the desired alkenylation product.

Our group has developed several carbonyl-directed C−H arylations,[9] but no para C−H arylation product has been observed. Therefore, improvement of the yields of the para C−H arylation products was examined by conducting the reaction using higher catalyst loading (Table 3). When the reaction was carried out with 20 mol % of catalyst **1e** for 24 h, **4aa** and **5aa** were obtained in 85 and 5% yields, respectively (entry 1). The reaction using 20 mol % of **1a** instead of **1e** as a catalyst led to significant improvement of the yield of **5aa** to 17% (entry 2). The arylation with arylboronates **3b−j** also gave the corresponding ortho,para diarylation products **5ab−aj**, albeit in lower yields than **5aa** (entries 3−6). The reaction with

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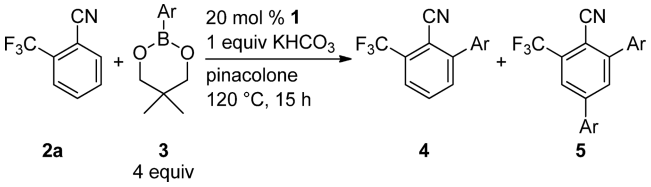
Table 3. Formation of Ortho,Para Diarylation Products 5 Using High Catalyst Loading[a]

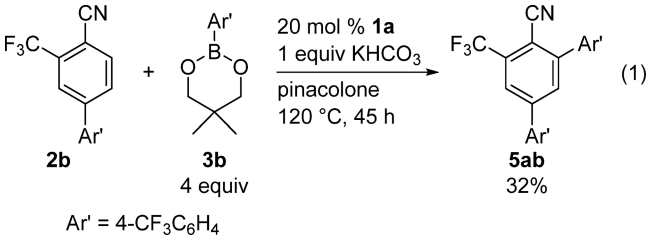


entry	3	Ar	catalyst 1	yield (%) 4	yield (%) 5
1[b]	3a	Ph	1e	4aa: 85	5aa: 5
2	3a	Ph	1a	4aa: 66	5aa: 17
3	3b	4-$F_3CC_6H_4$	1a	4ab: 66	5ab: 5
4	3d	4-MeC_6H_4	1a	4ad: 67	5ad: 8
5	3f	4-$MeOC_6H_4$	1a	4af: 43	5af: 2
6	3h	3-MeC_6H_4	1a	4ah: 75	5ah: 6
7[c]	3j	2-MeC_6H_4	1a	4aj: 60	5aj: nd[d]

[a]Reaction conditions: **2a** (0.5 mmol), **3** (4 equiv), **1a** (20 mol %), $KHCO_3$ (1 equiv), pinacolone (0.5 mL), 120 °C, 15 h. [b]Reaction conditions: **2a** (0.2 mmol), **3a** (4 equiv), **1e** (20 mol %), $KHCO_3$ (1 equiv), pinacolone (0.2 mL), 120 °C, 24 h. [c]2 equiv of **3j** was used. [d]Not detected.

2-methylphenylboronate **3j** did not give the diarylation product even in the presence of 20 mol % of **1a** (entry 7).

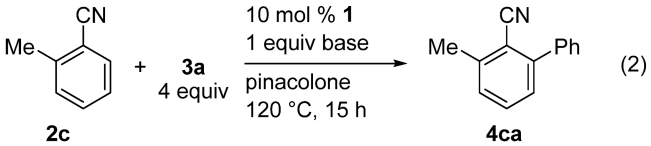
The structures of the diarylation products were determined by NMR analyses, but synthesis of the same diarylation product via a different route was also investigated (eq 1). Diarylation



(1)

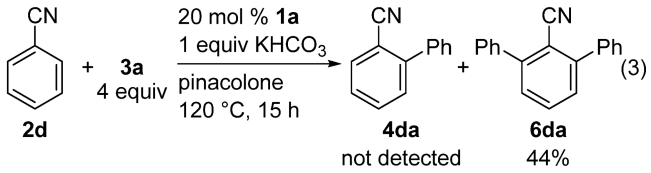
product **5ab** was chosen as a target here because it seems to be a crystalline material that may be used to form a single crystal for X-ray analysis. The C−H arylation of *p*-(trifluoromethyl)-phenyl benzonitrile **2b** with **3b** gave 32% yield of *o*,*p*-diaryl-benzonitrile **5ab**, which shows the NMR spectra identical to those of **5ab** prepared in entry 3 of Table 3. As expected, the structure of **5ab** was further confirmed by X-ray diffraction analysis of a single crystal prepared by recrystallization of the material synthesized here.

Other benzonitriles were also examined for the C−H arylation. The reaction of 2-methylbenzonirile **2c** with **3a** using catalyst **1e** provided ortho arylation product **4ca** in 29% yield (eq 2). Elongation of the reaction time to 45 h only slightly increased the yield to 31%. Screening of the reaction conditions for this substrate showed that the use of catalyst **1a** with NaO^{t}Bu as a base also gave a similar yield within 24 h, but extension of the reaction time to 45 h improved the yield in this case to 44% without any significant decomposition of cyano groups. In the case of benzonitrile **2d**, complex **1a** was found to be the most effective catalyst, and the reaction with 4 equiv of **3a** provided ortho,ortho′ diarylation product **6da** in 44% yield with no formation of monoarylation product **4da** detected (eq 3). Interestingly, Sun and co-workers reported that the Pd-catalyzed coupling of benzonitrile with aryl iodides yielded



(2)

catalyst **1e**, $KHCO_3$: 29% GC yield (24 h)
31% GC yield (45 h)
catalyst **1a**, NaO^{t}Bu: 26% GC yield (24 h)
44% GC yield (45 h)



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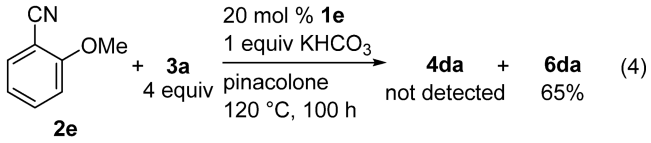
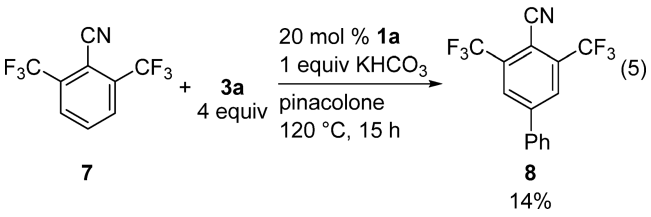


(4)



(5)

monoarylation product exclusively,[6a] and our C−H arylation can be regarded complementary to Sun's cyano-directed C−H arylation. The phenylation of 2-methoxybenzonitrile **2e** with **3a** provided **6da** in 65% yield predominantly (eq 4). This result suggests that the cyano group can be used as a directing group not only for C−H bond cleavage but also for cleavage of C−O bonds in aryl ethers, similarly to acyl groups.[15] The C−H phenylation was also investigated using 2,6-bis(trifluoromethyl)-benzonitrile **7**, which has no C−H bond at the ortho positions of the cyano group, and para phenylation product **8** was obtained in 14% yield (eq 5). The formation of **8** from **7** shows that the para C−H arylation does not require preceding ortho C−H arylation. Other nitriles such as acrylonitrile, cinnamonitrile, and phenyl-acetonitrile were also tested as substrates for the reaction with **3a** but failed to give more than a trace amount of the desired phenylation product. The reaction of an electron-deficient arene, 1,3-bis(trifluoromethyl)benzene, did not proceed either, indicating that the presence of a cyano group on the benzene ring is necessary for this reaction.

In order to gain insight into the mechanism, the reaction of a 1:1 mixture of benzonitrile (**2d**) and benzonitrile-d_5 (**2d-d_5**) was performed using only 1 equiv of phenylboronate **3a** (eq 6). As a result, the corresponding diphenylation product was isolated in 11% yield as a ca. 2:1 mixture of **6da** and **6da-d_3**. This result suggests that the reaction of **2d-d_5**, which proceed via C−D bond cleavage, is much slower than that of **2d**, and the C−H(or D) bond cleavage is the turnover-limiting step in the catalytic cycle. The detailed mechanism for the ruthenium-catalyzed C−H arylation of aromatic nitriles is unclear, but the C−H bond cleavage step may proceed via oxidative addition as was considered for the C−H/olefin coupling of aromatic nitriles catalyzed by complex **1a**. The catalytic cycle of this reaction may be similar to that of ortho C−H arylation of aromatic ketones with arylboronates catalyzed by **1a**. The C−H

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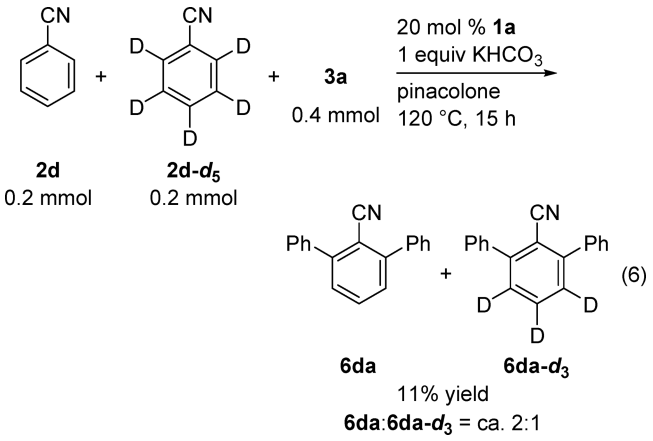

bond cleavage step became slow and turnover-limiting because it could not be effectively assisted by chelate formation.[16]

CONCLUSION

We developed the ruthenium-catalyzed C−H arylation of aromatic nitriles with arylboronates. The use of $RuH_2(CO)(PAr_3)_3$ catalysts containing triarylphosphines other than PPh_3 was important in obtaining high yields of the ortho arylation products. The reaction was mostly ortho selective, but unprecedented para arylation was also partially observed to give *o,p*-diarylation products. A cyano group was found to function as a directing group not only for C−H bond cleavage but also for cleavage of C−O bonds in aryl ethers.

EXPERIMENTAL SECTION

General Information. Aromatic nitriles **2** except for **2b** were purchased from commercial suppliers, dried from CaH_2, and distilled under nitrogen prior to use. Pinacolone was dried from $CaSO_4$ and distilled under nitrogen. Bases were purchased from commercial suppliers and used as received. $RuH_2(CO)(PPh_3)_3$- (**1a**),[17a] $RuH_2(PPh_3)_3$-,[17b] $Ru(CO)_2(PPh_3)_3$-,[17c] and $RuH_2(CO)(PAr_3)_3$-type complexes using various triarylphosphines (**1b−e**)[11] were prepared according to the literature procedure. $Ru_2(CO)_{12}$ were recrystallized from dry hexane under nitrogen prior to use.

General Procedures for Syntheses of Arylboronates 3. A round-bottom flask was charged with arylboronic acid, neopentylglycol, and solvent (Et_2O or THF). The mixture was stirred for 0.5−2 h at room temperature under air. After the reaction, an excess amount (ca. 5−10 equiv) of $CaCl_2$ was added to the mixture, which was then stirred for at least 0.5 h, filtered through Celite, and concentrated. Purification of the crude material by silica gel column chromatography (hexane/EtOAc) afforded the arylboronate.

*Phenylboronic Acid Neopentylglycol Ester (**3a**).* The general procedure was followed with phenylboronic acid (2.19 g, 18 mmol), neopentylglycol (2.08 g, 20 mmol), and Et_2O as solvent. Purification by silica gel column chromatography (30:1 hexane/EtOAc) afforded **3a** as a white solid (3.34 g, 98% yield). The spectroscopic data of **3a** are in good agreement with those reported in the literature.[18a]

*4-(Trifluoromethyl)phenylboronic Acid Neopentylglycol Ester (**3b**).* The general procedure was followed with 4-(trifluoromethyl)-phenylboronic acid (5.13 g, 27 mmol), neopentylglycol (3.02 g, 29 mmol), and Et_2O as solvent. Purification by silica gel column chromatography (2:1 hexane/EtOAc) afforded **3b** as a white solid (6.59 g, 95% yield). The spectroscopic data of **3b** are in good agreement with those reported in the literature.[18b]

*4-Fluorophenylboronic Acid Neopentylglycol Ester (**3c**).* The general procedure was followed with 4-(fluorophenyl)boronic acid (699.6 mg, 5 mmol), neopentylglycol (572.8 mg, 5.5 mmol), and Et_2O as solvent. Purification by silica gel column chromatography (5:1 hexane/EtOAc) afforded **3c** as a white solid (994.7 mg, 98% yield). The spectroscopic data of **3c** are in good agreement with those reported in the literature.[18c]

*4-Methylphenylboronic Acid Neopentylglycol Ester (**3d**).* The general procedure was followed with 4-(methylphenyl)boronic acid (5.44 g, 40 mmol), neopentylglycol (4.17 g, 40 mmol), and Et_2O as solvent. Purification by silica gel column chromatography (19:1 hexane/EtOAc) afforded **3d** as a white solid (7.98 g, 98% yield). The spectroscopic data of **3d** are in good agreement with those reported in the literature.[18d]

*4-n-Hexylphenylboronic Acid Neopentylglycol Ester (**3e**).* The general procedure was followed with 4-*n*-hexylphenylboronic acid (5.15 g, 25 mmol), neopentylglycol (3.12 g, 30 mmol), and Et_2O as solvent. Purification by silica gel column chromatography (20:1 hexane/EtOAc) afforded **3e** as a white solid (6.12 g, 89% yield): mp 49−50 °C; ^{1}H NMR (399.7 MHz, $CDCl_3$) δ 0.87 (br t, 3H), 1.02 (s, 6H), 1.22−1.37 (br m, 6H), 1.59−1.61 (m, 2H), 2.61 (t, J = 7.8 Hz, 2H), 3.76 (s, 4H), 7.17 (d, J = 7.6 Hz, 2H), 7.71 (d, J = 7.6 Hz, 2H); ^{13}C{^{1}H} NMR (98.5 MHz, $CDCl_3$) δ 14.1, 21.9, 22.6, 29.0, 31.3, 31.7, 31.9, 36.1, 72.3, 127.8, 133.8, 145.7 (one signal for arylcarbon is too broad to be seen due to the quadrupole effect of the adjacent boron atom); IR (KBr) 2961 s, 2930 s, 2855 s, 1611 m, 1481 m, 1419 m, 1380 m, 1306 s, 1248 m, 1130 m cm^{-1}; HRMS (DART-TOF) calcd for $[M + H]^+$ ($C_{17}H_{28}BO_2$) m/z 275.2182, found 275.2185.

*4-Methoxyphenylboronic Acid Neopentylglycol Ester (**3f**).* The general procedure was followed with 4-methoxyphenylboronic acid (1.52 g, 10 mmol), neopentylglycol (1.15 g, 11 mmol), and Et_2O as solvent. Purification by silica gel column chromatography (15:1 hexane/EtOAc) afforded **3f** as a white solid (2.11 g, 96% yield). The spectroscopic data of **3f** are in good agreement with those reported in the literature.[18c]

*4-(N,N-Dimethylamino)phenylboronic Acid Neopentylglycol Ester (**3g**).* The general procedure was followed with 4-(*N,N*-dimethylamino)phenylboronic acid (3.30 g, 5 mmol), neopentylglycol (2.29 g, 22 mmol), and THF as solvent. Purification by silica gel column chromatography (30:1 hexane/EtOAc) afforded **3g** as a white solid (3.64 g, 78% yield). The spectroscopic data of **3g** are in good agreement with those reported in the literature.[18e]

*3-Methylphenylboronic Acid Neopentylglycol Ester (**3h**).* The general procedure was followed with 3-methylphenylboronic acid (6.12 g, 45 mmol), neopentylglycol (5.21 g, 50 mmol), and THF as solvent. Purification by silica gel column chromatography (20:1 hexane/EtOA) afforded **3h** as a white solid (9.15 g, >99% yield). The spectroscopic data of **3h** are in good agreement with those reported in the literature.[18f]

*3,5-Dimethylphenylboronic Acid Neopentylglycol Ester (**3i**).* The general procedure was followed with 3,5-dimethylphenylboronic acid (12.0 g, 80 mmol), neopentylglycol (9.17 g, 88 mmol), and THF as solvent. Purification by silica gel column chromatography (30:1 hexane/EtOAc) afforded **3i** as a white solid (16.4 g, 94% yield). The spectroscopic data of **3i** are in good agreement with those reported in the literature.[18b]

*2-Methylphenylboronic Acid Neopentylglycol Ester (**3j**).* The general procedure was followed with 2-methylphenylboronic acid (1.36 g, 10 mmol), neopentylglycol (1.04 g, 10 mmol), and THF as solvent. Purification by silica gel column chromatography (20:1 hexane/EtOAc) afforded **3j** as a colorless oil (1.90 g, 93% yield). The spectroscopic data of **3j** are in good agreement with those reported in the literature.[18b]

*1-Naphthylboronic Acid Neopentylglycol Ester (**3k**).* The general procedure was followed with 1-naphthylboronic acid (1.72 g, 10 mmol), neopentylglycol (1.25 g, 12 mmol), and THF as solvent. Purification by silica gel column chromatography (30:1 hexane/EtOAc) afforded **3k** as a white solid (2.21 g, 92% yield). The pectroscopic data of **3k** are in good agreement with those reported in the literature.[18g]

*2-Naphthylboronic Acid Neopentylglycol Ester (**3l**).* The general procedure was followed with 2-naphthylboronic acid (8.60 g, 50 mmol), neopentylglycol (5.21 g, 50 mmol) and THF as solvent. Purification by silica gel column chromatography (30:1 hexane/EtOAc) afforded **3l** as a white solid (9.14 g, 76% yield). The spectroscopic

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data of **3l** are in good agreement with those reported in the literature.[18b]

Procedures for Syntheses of Aromatic Nitriles 2b. The Suzuki−Miyaura cross coupling was performed using a procedure similar to the one reported by Camp and co-workers.[19] To a solution of 4-(trifluoromethyl)phenylboronic acid (1.22 g, 6.4 mmol) and K_2CO_3 (1.66 g, 12 mmol) in 22 mL of DME/H_2O (10:1) degassed with nitrogen were added 4-iodo-2-(trifluoromethyl)benzonitrile (1.18 g, 4.0 mmol) and $Pd(PPh_3)_4$ (300 mg, 0.26 mmol). The mixture was stirred for 16 h at 80 °C under nitrogen. After the reaction, the solution evaporated under reduced pressure and then purified by silica gel column chromatography (20:1 hexane/EtOAc) to afford 4-[4-(trifluoromethyl)phenyl]-2trifluoromethylbenzonitrile (**2b**) as a white solid (212.8 mg, 17% yield): mp 115−115.5 °C; ^{1}H NMR ($CDCl_3$, 399.7 MHz) δ 7.75−7.81 (m, 4 H), 7.93−7.99 (m, 2 H), 8.03 (s, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 109.4 (q, J_{C-F} = 1.9 Hz), 115.2, 122.2 (q, J_{C-F} = 273.9 Hz), 123.8 (q, J_{C-F} = 272.4 Hz), 125.5 (q, J_{C-F} = 4.4 Hz), 126.3 (q, J_{C-F} = 3.7 Hz), 127.7, 130.7, 131.4 (q, J_{C-F} = 32.6 Hz), 133.6 (q, J_{C-F} = 32.6 Hz), 135.4, 141.2, 144.6; IR (KBr) 3106 w, 3068 w, 2234 m, 1935 w, 1814 w, 1616 m, 1586 w, 1528 w, 1498 w, 1436 m, 1399 m, 1324 s, 1299 m, 1265 s, 1183 s, 1167 s, 1141 s, 1116 s, 1071 s, 1055 s, 1033 s, 1011 m, 963 w, 911 m, 863 w, 850 m, 837 s, 775 w, 746 w, 702 m, 675 m, 671 w, 620 w, 599 w, 563 w, 517 w cm^{-1}; HRMS (DART-TOF) calcd for $[M + H]^+$ ($C_{15}H_8F_6N$) *m*/*z* 316.0561, found 316.0561.

General Procedures for Ruthenium-Catalyzed C−H Arylation of Aromatic Nitriles. General procedure A: In a glovebox, arylboronate (**3**) (0.8 mmol), 20.9 mg of $RuH_2(CO)\{P(4\text{-}MeC_6H_4)_3\}_3$ (**1e**) (0.02 mmol), and 20.0 mg of $KHCO_3$ (0.2 mmol) were placed in a 6 mL screw cap tube, and then 2-(trifluoromethyl)-benzonitrile (**2a**) (0.2 mmol) and pinacolone (0.2 mL) were added in that order. The mixture was heated at 120 °C for 24 h. The resulting mixture analyzed by GC and GCMS. After removal of the volatile materials by rotary evaporation, the crude material was passed through a basic aluminum oxide column to remove the remaining arylboronate. The arylation product **4** and **5** was isolated by silica gel column chromatography or preparative thin-layer chromatography (PTLC), followed by gel permeation chromatography (GPC) in some cases. General procedure B: In a glovebox, arylboronate (**3**) (2.0 mmol), 45.9 mg of $RuH_2(CO)$ $(PPh_3)_3$ (**1a**) (0.05 mmol), and 50.1 mg of $KHCO_3$ (0.5 mmol) were placed in a 20 mL J. Young tube, and then 2-(trifluoromethyl)benzonitrile (**2a**) (0.5 mmol) and pinacolone (0.5 mL) were added in that order. The mixture was heated at 120 °C for 15 h. The resulting mixture was analyzed by GC and GCMS. After removal of the volatile materials by rotary evaporation, the crude material was passed through a basic aluminum oxide column to remove the remaining arylboronate. The arylation product **4** and **5** was isolated by silica gel column chromatography or preparative thin-layer chromatography (PTLC), followed by gel permeation chromatography (GPC) in some cases.

*6-Phenyl-2-(trifluoromethyl)benzonitrile (**4aa**).* General procedure A was followed with 34.0 mg of **2a** and 153.8 mg of **3a**. PTLC (10:1 hexane/EtOAc) afforded **4aa** as a white solid (40.6 mg, 82% yield): mp 63−64 °C; ^{1}H NMR ($CDCl_3$, 391.8 MHz) δ 7.42−7.55 (m, 5 H), 7.71 (dd, *J* = 7.8 Hz, 1.5 Hz, 1 H), 7.76 (t, *J* = 7.8 Hz, 1 H), 7.80 (dd, *J* = 7.6 Hz, 1.5 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.5 MHz) δ 108.9 (q, J_{C-F} = 1.8 Hz), 114.8, 122.5 (q, J_{C-F} = 274.0 Hz), 125.2 (q, J_{C-F} = 4.9 Hz), 128.8, 128.9, 129.3, 132.4, 133.5 (q, J_{C-F} = 1.1 Hz), 133.9 (q, J_{C-F} = 32.0 Hz), 137.1, 148.3; IR (KBr) 3054 w, 2926 w, 2233 m, 1721 w, 1589 w, 1457 m, 1431 m, 1335 s, 1295 s, 1168 s, 1133 s, 1117 s, 1050 m, 821 s, 763 s, 700 s cm^{-1}; HRMS (ESI-TOF) calcd for $[M + K]^+$ ($C_{14}H_8F_3NK$) *m*/*z* 286.0246. Found 286.0245.

*2-(Trifluoromethyl)-6-[4-(trifluoromethyl)phenyl]benzonitrile (**4ab**).* General procedure A was followed with 33.4 mg of **2a** and 207.2 mg of **3b**. PTLC (10:1 hexane/EtOAc) afforded **4ab** as a white solid (53.6 mg, 87% yield): mp 101−102 °C; ^{1}H NMR ($CDCl_3$, 399.7 MHz) δ 7.67 (d, *J* = 7.6 Hz, 2 H), 7.71 (d, *J* = 7.6 Hz, 1 H), 7.80 (d, *J* = 8.4 Hz, 2 H), 7.82 (dd, *J* = 7.2 Hz, 8.0 Hz, 1 H), 7.87 (d, *J* = 6.8 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 109.2, 114.6, 122.5 (q, J_{C-F} = 274.3 Hz), 123.9 (q, J_{C-F} = 272.3 Hz), 126.1 (q J_{C-F} = 3.8 Hz), 126.1 (q J_{C-F} = 4.6 Hz), 129.6, 131.6 (q, J_{C-F} = 32.8 Hz), 132.9, 133.5, 134.3 (q, J_{C-F} = 31.9 Hz), 140.6, 146.8; IR (KBr) 3366 w, 2357 m, 2339 w, 2231 s, 1621 m, 1465 s, 1451 s, 1403 s, 1324 vs, 1295 vs, 1203 vs, 1176 vs, 1136 vs, 1108 vs, 1070 vs, 1040 vs, 1016 s, 936 m, 832 s, 813 vs, 792 s, 758 vs, 715 vs, 669 vs, 667 vs, 659 s, 637 s, 603 s cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{15}H_7F_6NNa$) *m*/*z* 338.0380, found 338.0377.

*6-(4-Fluorophenyl)-2-(trifluoromethyl)benzonitrile (**4ac**).* General procedure A was followed with 34.4 mg of 2a and 166.2 mg of **3c**. PTLC (4:1 hexane/EtOAc) afforded **4ac** as a white solid (41.1 mg, 77% yield): mp 124−125 °C; ^{1}H NMR ($CDCl_3$, 391.8 MHz) δ 7.21 (t, *J* = 8.6 Hz, 2 H), 7.51−7.54 (m, 2 H), 7.69 (d, *J* = 7.4 Hz, 1 H), 7.75−7.82 (m, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 108.9 (q, J_{C-F} = 2.1 Hz), 114.7, 116.0 (d, J_{C-F} = 21.9 Hz), 122.4 (q, J_{C-F} = 274.2 Hz), 125.3 (q, J_{C-F} = 4.9 Hz), 130.9 (d, J_{C-F} = 8.5 Hz), 132.6, 133.1 (d, J_{C-F} = 3.5 Hz), 133.4, 134.0 (q, J_{C-F} = 32.1 Hz), 147.2, 163.4 (d, J_{C-F} = 250.0 Hz); IR (KBr) 2232 m, 1609 m, 1579 w, 1515 s, 1466 w, 1445 m, 1405 w, 1331 s, 1292 m, 1227 s, 1204 s, 1192 m, 1175 s, 1164 m, 1133 s, 1122 s, 1075 w, 1040 m, 844 m, 816 s, 776 w, 757 m, 722 m, 706 w, 669 w, 584 m, 560 w, 520 m cm^{-1}; HRMS (APCI-TOF) calcd for $[M + H]^+$ ($C_{14}H_8F_4N$) *m*/*z* 266.0593, found 266.0582.

*6-(4-Methylphenyl)-2-(trifluoromethyl)benzonitrile (**4ad**).* General procedure A was followed with 34.2 mg of **2a** and 164.5 mg of **3d**. PTLC (10:1 hexane/EtOAc) afforded **4ad** as a white solid (45.9 mg, 88% yield): mp 85.5−86.5 °C; ^{1}H NMR ($CDCl_3$, 399.7 MHz) δ 2.43 (s, 3 H), 7.32 (d, *J* = 7.6 Hz, 2 H), 7.43 (d, *J* = 8.4 Hz, 2 H), 7.69 (dd, *J* = 7.6 Hz, 1 H), 7.73 (dd, *J* = 8.0 Hz, 1 H), 7.77 (dd, *J* = 7.6 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 21.2, 108.8, 115.0, 122.5 (q, J_{C-F} = 273.3 Hz), 124.9 (q, J_{C-F} = 4.7 Hz), 128.8, 129.5, 132.3, 133.4, 133.9 (q, J_{C-F} = 31.9 Hz), 134.2, 139.4, 148.3; IR (KBr) 3094 w, 2931 w, 2365 w, 2362 w, 2360 m, 2357 w, 2339 w, 2323 w, 2231 s, 1994 w, 1924 w, 1612 s, 1595 m, 1517 m, 1465 s, 1442 s, 1407 w, 1333 vs, 1315 s, 1293 vs, 1213 vs, 1199 vs, 1187 vs, 1173 vs, 1141 vs, 1126 vs, 1098 s, 1075 s, 1042 vs, 999 m, 935 m, 847 s, 832 s, 809 vs, 768 s, 756 s, 723 s, 703 vs cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{15}H_{10}F_3NNa$) *m*/*z* 284.0663, found 284.0663.

*6-(4-n-Hexylphenyl)-2-(trifluoromethy)lbenzonitrile (**4ae**).* General procedure A was followed with 35.0 mg of **2a** and 219.7 mg of **3e**. PTLC (5:1 hexane/EtOAc) afforded **4ae** as a yellow oil (55.7 mg, 82% yield): ^{1}H NMR ($CDCl_3$, 391.8 MHz) δ 0.90 (t, *J* = 7.1 Hz, 3 H), 1.30−1.41 (m, 6 H), 1.62−1.70 (m, 2 H), 2.68 (t, *J* = 7.4 Hz, 2 H), 7.32 (d, *J* = 7.8 Hz, 2 H), 7.46 (d, *J* = 7.8 Hz, 2 H), 7.69 (dd, *J* = 7.4 Hz, 2.0 Hz, 1 H), 7.73 (t, *J* = 7.4 Hz, 1 H), 7.77 (dd, *J* = 7.4 Hz, 2.0 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 14.1, 22.6, 29.1, 31.3, 31.7, 35.8, 108.7 (q, J_{C-F} = 1.9 Hz), 115.0, 122.6 (q, J_{C-F} = 274.4 Hz), 124.9 (q, J_{C-F} = 4.9 H), 128.86, 128.89, 132.4, 133.5, 134.0 (q, J_{C-F} = 31.9 Hz), 134.4, 144.5, 148.4; IR (NaCl) 3029 w, 2929 s, 2857 s, 2231 m, 1612 m, 1516 w, 1467 s, 1448 s, 1408 m, 1333 s, 1293 s, 1201 s, 1174 s, 1140 s, 1076 m, 1042 s, 810 s, 753 w, 723 w, 706 m, 699 m, 667 w, 618 w cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{20}H_{20}F_3NNa$) *m*/*z* 354.1446, found 354.1441.

*6-(4-Methoxylphenyl)-2-(trifluoromethyl)benzonitrile (**4af**).* General procedure A was followed with 33.5 mg of **2a** and 175.4 mg of **3f**. PTLC (10:1 hexane/EtOAc) afforded **4af** as a white solid (48.5 mg, 89% yield): mp 83−84 °C; ^{1}H NMR ($CDCl_3$, 391.8 MHz) δ 3.88 (s, 3 H), 7.04 (d, *J* = 8.6 Hz, 2 H), 7.49 (d, *J* = 8.6 Hz, 2 H), 7.67−7.76 (m, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 55.5, 108.8 (q, J_{C-F} = 1.9 Hz), 114.5, 115.3, 122.7 (q, J_{C-F} = 274.1 Hz), 124.9 (q, J_{C-F} = 4.8 Hz), 129.5, 130.5, 132.5, 133.5, 133.6, 134.1 (q, J_{C-F} = 32.0 Hz), 148.2; IR (KBr) 3010 w, 2972 w, 2944 w, 2842 w, 2227 w, 1614 m, 1574 w, 1520 m, 1468 m, 1448 m, 1334 s, 1312 m, 1295 m, 1259 m, 1208 m, 1176 m, 1140 m, 1112 s, 1074 w, 1046 m, 1022 w, 831 m, 753 m, 705 w, 634 w, 594 m, 558 w, 543 w, 522 w, 467 w, 448 w, 438 w, 424 w, 412 w cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{15}H_{10}F_3NONa$) *m*/*z* 300.0612, found 300.0612.

*6-[4-(N,N-Dimethylamino)phenyl]-2-(trifluoromethyl)benzonitrile (**4ag**).* General procedure A was followed with 34.2 mg of **2a** and 186.2 mg of **3g**. PTLC (4:1 hexane/EtOAc) afforded **4ag** as a yellow solid (46.7 mg, 80% yield): mp 164−165 °C; ^{1}H NMR ($CDCl_3$, 391.8 MHz) δ 3.03 (s, 6 H), 6.80 (d, *J* = 8.6 Hz), 7.46 (d, *J* = 8.6 Hz),

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7.67 (s, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 40.2, 107.8 (q, J_{C-F} = 2.2 Hz), 112.0, 115.6, 122.7 (q, J_{C-F} = 274.0 Hz), 123.9 (q, J_{C-F} = 4.9 Hz), 124.3, 129.9, 132.1, 133.2, 133.9 (q, J_{C-F} = 32.0), 148.6, 150.9; IR (KBr) 3098 w, 2919 m, 2864 m, 2822 m, 2227 m, 1987 w, 1901 w, 1609 s, 1530 s, 1484 m, 1465 m, 1444 s, 1424 w, 1411 m, 1368 s, 1335 s, 1295 s, 1267 w, 1231 m, 1209 s, 1197 s, 1170 s, 1121 s, 1086 m, 1063 m, 1043 s, 998 m, 960 w, 946 m, 928 w, 830 m, 808 s, 792 m, 753 m, 696 s cm^{-1}; HRMS (ESI-TOF) calcd for $[M + H]^+$ ($C_{16}H_{14}F_3N_2$) m/z 291.1109, found 291.1131.

*6-(3-Methylphenyl)-2-(trifluoromethyl)benzonitrile (**4ah**).* General procedure A was followed with 34.3 mg of **2a** and 163.2 mg of **3h**. PTLC (10:1 hexane/EtOAc) afforded **4ah** as a white solid (43.9 mg, 84% yield): mp 77−78 °C; ^1H NMR ($CDCl_3$, 399.7 MHz) δ 1.54 (s, 3 H), 7.29−7.42 (m, 4 H), 7.69 (dd, J = 7.9 Hz, 1.5 Hz, 1 H), 7.74 (t, J = 7.9 Hz, 1 H), 7.79 (dd, J = 7.9 Hz, 1.5 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 21.3, 108.8 (q, J_{C-F} = 1.9 Hz), 114.9, 122.5 (q, J_{C-F} = 274.4 Hz), 125.0 (q, J_{C-F} = 5.6 Hz), 126.0, 126.7, 128.7, 129.6, 130.0, 132.4, 133.8 (q, J_{C-F} = 31.9 Hz), 137.0, 138.5, 148.4; IR (KBr) 3049 w, 2917 w, 2851 w, 2231 m, 1610 w, 1585 w, 1464 w, 1336 s, 1297 s, 1215 m, 1192 m, 1163 m, 1124 s, 1055 m, 1000 w, 940 w, 911 w, 895 w, 821 m, 784 m, 755 m, 712 m, 702 m, 640 w cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{15}H_{10}F_3NNa$) m/z 284.0663, found 284.0665.

*6-(3,5-Dimethylphenyl)-2-(trifluoromethyl)benzonitrile (**4ai**).* General procedure A was followed with 34.4 mg of **2a** and 174.1 mg of **3i**. PTLC (4:1 hexane/EtOAc) afforded **4ai** as a white solid (40.8 mg, 74% yield): mp 114−115 °C; ^1H NMR ($CDCl_3$, 391.8 MHz) δ 2.39 (s, 6 H), 7.13 (s, 3 H), 7.67−7.77 (m, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 21.3, 108.8 (q, J_{C-F} = 1.9 Hz), 114.9, 122.5 (q, J_{C-F} = 274.1 Hz), 124.9 (q, J_{C-F} = 4.9 Hz), 126.7, 130.9, 132.3, 133.4, 133.5 (q, J_{C-F} = 1.2 Hz), 133.8 (q, J_{C-F} = 32.1 Hz), 137.1, 138.4, 148.6; IR (KBr) 3091 w, 3029 w, 2922 m, 2865 w, 2234 m, 1606 m, 1596 m, 1453 m, 1343 s, 1309 s, 1289 m, 1230 m, 1197 m, 1185 s, 1169 s, 1137 s, 1122 s, 1089 s, 1072 s, 1039 w, 908 w, 900 w, 858 s, 816 s, 757 m, 708 s, 675 m, 634 w cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{16}H_{12}F_3NNa$) m/z 298.0820, found 298.0818.

*6-(2-Methylphenyl)-2-(trifluoromethyl)benzonitrile (**4aj**).* General procedure A was followed with 33.9 mg of **2a** and 180.0 mg of **3j**. PTLC (10:1 hexane/EtOAc) afforded **4aj** as a white solid (12.3 mg, 24% yield): mp 82.5−83 °C; ^1H NMR ($CDCl_3$, 399.7 MHz) δ 2.18 (s, 3 H), 7.21 (dd, J = 7.4 Hz, 1.2 Hz, 1 H), 7.30−7.39 (m, 3 H), 7.59 (dd, J = 7.4 Hz, 1.2 Hz, 1 H), 7.77 (td, J = 7.4 Hz, 1.2 Hz, 1 H), 7.81 (dd, J = 7.4 Hz, 1.2 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 19.8, 110.3 (q, J_{C-F} = 1.9 Hz), 114.3, 122.5 (q, J_{C-F} = 274.4 Hz), 125.2 (q, J_{C-F} = 4.6 Hz), 126.1, 129.3, 129.3, 130.6, 132.2, 133.4 (q, J_{C-F} = 31.9 Hz), 133.7, 135.6, 136.9, 148.5; IR (KBr) 3050 w, 2925 w, 2233 s, 1995 w, 1602 w, 1581 w, 1495 w, 1463 w, 1456 s, 1430 m, 1334 s, 1298 s, 1210 s, 1199 s, 1179 s, 1162 s, 1131 s, 1111 s, 1074 s,1053 m, 1031 m, 999 w, 953 w, 933 w, 836 w, 819 s, 800 w, 774 w, 760 s, 755 s, 751 s cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{15}H_{10}F_3NNa$) m/z 284.0663, found 284.0661.

*6-(1-Naphthyl)-2-(trifluoromethyl)benzonitrile (**4ak**).* General procedure A was followed with 33.7 mg of **2a** and 192.0 mg of **3k**. PTLC (10:1 hexane/EtOAc) afforded **4ak** as a white solid (28.7 mg, 49% yield): mp 87.5−89 °C; ^1H NMR ($CDCl_3$, 391.8 MHz) δ 7.42−7.50 (m, 3 H), 7.55 (td, J = 6.7 Hz, 1.6 Hz, 1 H), 7.60 (t, J = 7.1 Hz, 1 H), 7.75 (d, J = 7.8 Hz, 1 H), 7.82 (t, J = 7.8 Hz, 1 H), 7.90 (d, J = 7.8 Hz, 1 H), 7.96 (d, J = 7.8 Hz, 1 H), 8.00 (d, J = 8.2 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 111.0 (q, J_{C-F} = 1.6 Hz), 114.3, 122.5 (q, J_{C-F} = 274.4 Hz), 124.7, 125.2, 125.6 (q, J_{C-F} = 5.3 Hz), 126.4, 127.0, 127.7, 128.7, 129.8, 131.2, 132.0, 133.7, 133.7 (q, J_{C-F} = 32.3 Hz), 134.6, 134.8, 147.2; IR (KBr) 3092 w, 3064 w, 3011 w, 2368 w, 2324 w, 2230 m, 1843 w, 1733 w, 1718 w, 1700 w, 1695 w, 1684 w, 1653 w, 1634 w, 1616 w, 1592 w, 1559 w, 1539 w, 1520 w, 1507 m, 1473 w, 1456 w, 1447 m, 1435 w, 1398 m, 1334 s, 1292 s, 1252 w, 1214 w, 1178 s, 1173 s, 1149 s, 1132 s, 1106 s, 1072 m, 1058 w, 1020 w, 995 w, 981 w, 959 w, 924 w, 855 w, 807 s, 800 s, 792 m, 781 s, 761 m, 749 m, 741 m, 737 m, 703 m cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{18}H_{10}F_3NNa$) m/z 320.0663, found 320.0661.

*6-(2-Naphthyl)-2-(trifluoromethyl)benzonitrile (**4al**).* General procedure A was followed with 32.5 mg of **2a** and 191.7 mg of **3l**. PTLC (10:1 hexane/EtOAc) afforded **4al** as a white solid (49.1 mg, 87% yield): mp 115.5−116 °C; ^1H NMR ($CDCl_3$, 391.8 MHz) δ 7.55−7.60 (m, 2 H), 7.64 (dd, J = 8.6 Hz, 2.0 Hz, 1 H), 7.77−7.85 (m, 3 H), 7.93 (dd, J = 9.0 Hz, 5.5 Hz, 2 H), 7.99 (d, J = 9.0 Hz, 1 H), 8.03 (s, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 109.1 (q, J_{C-F} = 1.9 Hz), 114.9, 122.5 (q, J_{C-F} = 274.4 Hz), 125.2 (q, J_{C-F} = 4.7 Hz), 126.1, 126.9, 127.2, 127.8, 128.4, 128.7, 128.7, 132.5, 133.0, 133.3, 133.8, 134.0 (q, J_{C-F} = 31.9 Hz), 134.4, 148.3; IR (KBr) 3044 m, 2365 w, 2229 s, 1700 w, 1684 w, 1652 w, 1597 w, 1557 w, 1539 w, 1506 w, 1478 m, 1446 m, 1347 s, 1329 s, 1292 s, 1270 w, 1235 w, 1206 s, 1177 s, 1163 s, 1134 s, 1126 s, 1076 s, 1045 s, 1014 w, 1001 w, 947 w, 910 w, 884 w, 860 w, 822 s, 810 s, 769 m, 755 s, 737 s,703 s, 667 s cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{18}H_{10}F_3NNa$) m/z 320.0663, found 320.0661.

*4,6-Diphenyl-2-(trifluoromethyl)benzonitrile (**5aa**).* General procedure B was followed with 83.1 mg of **2a** and 379.9 mg of **3a**. PTLC (5:1 hexane/EtOAc) afforded **5aa** as a white solid (26.2 mg, 17% yield): mp 98.5−99.5 °C; ^1H NMR ($CDCl_3$, 391.8 MHz) δ 7.48−7.56 (m, 6 H), 7.59−7.61 (m, 2 H), 7.64−7.66 (m, 2 H), 7.89 (d, J = 1.6 Hz, 1 H), 7.99 (d, J = 1.6 Hz, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 107.2, 115.0, 122.6 (q, J_{C-F} = 274.4 Hz), 123.9 (q, J_{C-F} = 4.9 Hz), 124.0, 127.4, 128.9, 129.0, 129.4, 129.5, 131.7, 134.5 (q, J_{C-F} = 31.7 Hz), 137.3, 137.8, 145.6, 148.8; IR (KBr) 3063 w, 2923 w, 2349 w, 2228 m, 1605 m, 1578 w, 1496 w, 1458 m, 1437 m, 1405 w, 1360 s, 1289 s, 1264 w, 1249 w, 1190 s, 1164 s, 1153 s, 1118 s, 1078 w, 1063 w, 1049 m, 1000 w, 917 w, 897 m, 832 w, 764 s, 721 w, 696 s, 630 w, 616 w, 583 w, 541 w, 516 w, 477 w, 449 w, 427 w cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{20}H_{12}F_3NNa$) m/z 346.0820, found 346.0821.

*2-(Trifluoromethyl)-4,6-bis[4-(trifluoromethyl)phenyl]benzonitrile (**5ab**).* General procedure B was followed with 86.3 mg of **2a** and 515.1 mg of **3b**. PTLC (10:1 hexane/EtOAc) afforded **5ab** as a white solid (11.5 mg, 5% yield): mp 162−163 °C; ^1H NMR ($CDCl_3$, 399.7 MHz) δ 7.72−7.84 (m, 8 H), 7.89 (s, 1 H), 8.05 (s, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 108.2 (q, J_{C-F} = 1.5 Hz), 114.3, 122.3 (q, J_{C-F} = 274.4 Hz), 123.8 (q, J_{C-F} = 272.4 Hz), 123.8 (q, J_{C-F} = 272.4 Hz), 124.7 (q, J_{C-F} = 4.9 Hz), 125.9 (q, J_{C-F} = 3.6 Hz), 126.4 (q, J_{C-F} = 3.8 Hz), 127.8, 129.5, 131.6 (q, J_{C-F} = 32.8 Hz), 131.6 (q, J_{C-F} = 32.8 Hz), 131.8, 134.9 (q, J_{C-F} = 32.4 Hz), 140.4 (q, J_{C-F} = 1.1 Hz), 140.9 (q, J_{C-F} = 1.1 Hz), 144.5, 147.4; IR (KBr) 3023 w, 2922 w, 2864 w, 2224 s, 1905 w, 1790 w, 1729 w, 1652 w, 1605 s, 1514 m, 1460 m, 1357 s, 1325 m, 1290 s, 1220 w, 1208 w, 1181 s, 1123 s, 1039 s, 1019 w, 895 s, 860 w, 842 w, 812 s, 724 w, 719 w, 709 m, 683 w, 667 m, 665 w, 647 w, 642 w, 619 w, 540 w, 531 w, 525 w, 515 s, 507 w, 504 w, 501 w, 496 w, 493 w, 488 w cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{22}H_{10}F_9NNa$) m/z 482.0567, found 482.0544.

*4,6-Bis(4-methylphenyl)-2-(trifluoromethyl)benzonitrile (**5ad**).* General procedure B was followed with 88.6 mg of **2a** and 407.9 mg of **3d**. PTLC (10:1 hexane/EtOAc) afforded **5ad** as a white solid (14.6 mg, 8% yield): mp 97−98 °C; ^1H NMR ($CDCl_3$, 399.7 MHz) δ 2.43 (s, 3 H), 2.46 (s, 3 H), 7.33 (t, J = 8.0 Hz, 4 H), 7.49 (d, J = 8.4 Hz, 2 H), 7.55 (d, J = 8.0 Hz, 2 H), 7.85 (s, 1 H), 7.95 (s, 1 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 98.5 MHz) δ 21.2, 21.3, 106.6, 115.3, 122.6 (q, J_{C-F} = 274.4 Hz), 123.3 (q, J_{C-F} = 5.6 Hz), 127.1, 127.1, 128.8, 129.5, 130.0, 131.3, 134.3 (q, J_{C-F} = 31.0 Hz), 134.9, 139.4, 139.7, 145.4, 148.8; IR (KBr) 3093 w, 2938 w, 2642 w, 2360 w, 2357 w, 2226 s, 2003 w, 1943 w, 1934 w, 1807 w, 1700 w, 1695 w, 1652 w, 1619 s, 1607 s, 1588 w, 1577 w, 1523 w, 1461 m, 1438 m, 1406 s, 1393 s, 1363 s, 1325 s, 1296 s, 1271 m, 1255 m, 1191 s, 1123 s, 1069 s, 1062 s, 1035 s, 1014 s, 975 m, 961 m, 915 w, 904 s, 846 s, 832 s, 766 w, 742 w, 722 w, 698 w, 654 s, 590 m, 503 w cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{22}H_{16}F_3NNa$) m/z 374.1133, found 374.1141.

*4,6-Bis(4-methoxylphenyl)-2-(trifluoromethyl)benzonitrile (**5af**).* General procedure B was followed with 86.9 mg of **2a** and 441.5 mg

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of **3f**. PTLC (10:1 hexane/EtOAc) afforded **5af** as a white solid (4.1 mg, 2% yield): mp 146.5–148.5 °C; ^{1}H NMR ($CDCl_3$, 399.7 MHz) δ 3.88 (s, 3 H), 3.89 (s, 3 H), 7.04 (t, J = 8.8 Hz, 4 H), 7.54 (d, J = 8.8 Hz, 2 H), 7.60 (d, J = 8.8 Hz, 2 H), 7.81 (s, 1 H), 7.90 (s, 1 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 98.5 MHz) δ 55.4, 55.5, 106.1, 114.3, 114.8, 115.5, 122.6 (q, J_{C-F} = 274.3 Hz), 122.8 (q, J_{C-F} = 5.1 Hz), 128.5, 129.7, 130.1, 130.3, 130.8, 134.4 (q, J_{C-F} = 31.6 Hz), 145.0, 148.4, 160.5, 160.8; IR (KBr) 3063 m, 3037 m, 3012 m, 2972 m, 2945 m, 2918 m, 2849 m, 2225 m, 2035 w, 1876 w, 1844 w, 1604 s, 1576 w, 1515 s, 1461 m, 1436 m, 1419 w, 1413 w, 1362 s, 1333 w, 1318 m, 1307 m, 1290 s, 1257 s, 1245 s, 1207 s, 1179 s, 1174 s, 1164 s, 1118 s, 1060 m, 1044 m, 1024 s, 1014 m, 917 w, 903 m, 960 w, 847 w, 826 s, 820 s, 799 w, 791 w, 777 w, 763 w, 731 w, 725 w, 710 w, 682 w, 667 s, 656 w, 638 w, 620 w, 594 w, 581 w, 568 w, 559 w, 544 w, 536 m, 525 m, 521 m cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{22}H_{16}F_3NO_2Na$) m/z 406.1031, found 406.1031.

*4,6-Bis(3-methylphenyl)-2-(trifluoromethyl)benzonitrile (**5ah**).* General procedure B was followed with 88.1 mg of **2a** and 406.4 mg of **3h**. PTLC (10:1 hexane/EtOAc) afforded **5ah** as a white solid (10.5 mg, 6% yield): mp 165 °C dec; ^{1}H NMR ($CDCl_3$, 400.1 MHz) δ 2.45 (s, 3 H), 2.46 (s, 3 H), 7.30 (t, J = 8.0 Hz, 2 H), 7.38–7.45 (m, 6 H), 7.86 (s, 1 H), 7.96 (s, 1 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 98.5 MHz) δ 21.5, 21.5, 107.0, 115.1, 122.6 (q, J_{C-F} = 274.4 Hz), 123.7 (q, J_{C-F} = 4.6 Hz), 124.5, 126.1, 128.0, 128.8, 129.3, 129.6, 130.1, 130.2, 131.7, 134.3 (q, J_{C-F} = 32.9 Hz), 137.3, 137.8, 138.6, 139.2, 145.7, 148.9; IR (KBr) 3651 w, 3028 w, 2963 w, 2925 w, 2864 w, 2352 w, 2229 w, 1947 w, 1734 m, 1695 m, 1607 m, 1456 m, 1419 m, 1394 m, 1362 s, 1289 s, 1135 s, 957 s, 894 m, 785 s, 705 w, 671 w cm^{-1}; HRMS (ESI-TOF) calcd for $[M + Na]^+$ ($C_{22}H_{16}F_3NNa$) m/z 374.1133, found 374.1120.

Spectroscopic data of 2-methyl-6-phenylbenzonitrile (**4ca**)[20a] and 2,6-diphenylbenzonitrile (**6da**)[20b] are in good agreement with those reported in literature.

Para C–H Arylation of Aromatic Nitrile 7. In a glovebox, phenylboronate (**3a**) (152 mg, 0.8 mmol), $RuH_2(CO)(PPh_3)_3$ (**1a**) (36.7 mg, 0.04 mmol), 2,6-bis(trifluoromethyl)benzonitrile (**7**) (47.8 mg, 0.2 mmol), and $KHCO_3$ (20.0 mg, 0.2 mmol) were placed in a 6 mL screw cap tube, and then pinacolone (0.2 mL) was added to the tube. The mixture was heated at 120 °C for 15 h. After removal of the volatile materials by rotary evaporation, the crude material was passed through a basic aluminum oxide column to remove the remaining arylboronate and then purified by silica gel column chromatography (15:1:5 hexane/EtOAc/toluene) to afford 2,6-bis(trifluoromethyl)-4-phenylbenzonitrile (**8**) as a white solid (8.7 mg, 14% yield): mp 111–112 °C; ^{1}H NMR ($CDCl_3$, 391.8 MHz) δ 7.55–7.59 (m, 3 H), 7.64–7.66 (m, 2 H), 8.19 (s, 2 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 98.5 MHz) δ 106.3 (sep, J_{C-F} = 2.1 Hz), 111.8, 121.8 (q, J_{C-F} = 274.9 Hz), 127.4, 127.9 (qq, J_{C-F} = 4.6 Hz, 0.9 Hz), 129.7, 130.3, 135.9 (q, J_{C-F} = 32.9 Hz), 136.5, 146.7; IR (KBr) 3098 w, 3069 w, 3042 w, 2921 w, 2851 w, 2236 w, 1614 m, 1590 w, 1469 w, 1460 w, 1374 s, 1340 w, 1325 w, 1302 s, 1291 s, 1217 s, 1193 s, 1177 s, 1136 s, 1074 m, 1058 m, 1000 w, 971 w, 927 w, 908 m, 848 w, 762 m, 693 m, 675 w, 671 w cm^{-1}; HRMS (DART-TOF) calcd for $[M]^-$ ($C_{15}H_7F_6N$) m/z 315.0483, found 315.0493.

Procedures for Syntheses of Benzonitrile-d_5 (2d-d_5). Benzonitrile-d_5 was prepared using a procedure similar to the one for synthesis of various aromatic nitriles reported by Friedman and Shechter.[21] A three-neck flask was charged with bromobenzene-d_5 (4.86 g, 30 mmol), CuCN (3.13 g, 35 mmol), and 4.5 mL of DMF. The mixture was heated to reflux for 22 h under nitrogen. The reaction mixture was quenched by addition of NH_3 aq and extracted with Et_2O. The organic layer was washed with 6 M HCl and water, dried over $MgSO_4$, and concentrated. Purification of the crude material by distillation and then by silica gel column chromatography (20:1 hexane/EtOAc) afforded **2d-d_5** as a colorless oil (1.50 g, 46% yield).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02623.

X-ray crystallographic data for **5ab** and NMR spectra for all new compounds (PDF)

X-ray crystallographic data for **5ab** (CIF)

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Notes

The authors declare no competing financial interest.

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