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Formation of Arylboronates by a CuI-Catalyzed Coupling Reaction of Pinacolborane with Aryl Iodides at Room Temperature

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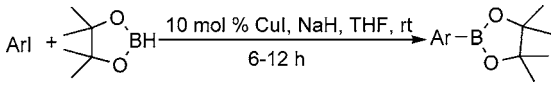
ABSTRACT



The coupling reaction of pinacolborane with aryl iodides under the catalysis of 10 mol % CuI and the action of sodium hydride in THF works at room temperature to provide corresponding arylboronates in good yields. Aryl bromides give poor conversion under these reaction conditions.

Arylboronic acids and their esters have found increasing application in organic synthesis and medical treatments.[1] Traditionally, they were prepared by the reaction of trialkyl borates with Grignard or lithium reagents.[2] The drawback of this methodology is the limitation of substrates available. This prompted research that lead to the Miyaura−Masuda reaction, in which the arylboronates were assembled via a Pd-catalyzed cross-coupling of aryl halides with pinacolborane or dialkoxyborane.[3,4] Mechanistically, this reaction is assumed to proceed through an Ar−Pd^{II}−B(OR)$_2$ intermediate, which results from the ligand exchange of Ar−Pd^{II}−X, an oxidative addition product of Pd(0) with aryl halides, with the boryl anion analogue.[3]

Recently, we have demonstrated that CuI/L-proline is a powerful catalytic system for coupling reactions of aryl halides with some nucleophiles such as azide[5a] and methanesulfinate.[5b] We envisaged that their possible mechanisms might be similar to that of the Miyaura−Masuda reaction, and therefore, a CuI-catalyzed coupling reaction of aryl halides with pinacolborane was explored. Herein, we wish to disclose our results.

Initially, our experiment was conducted by refluxing a mixture of 4-iodoanisole **1a**, pinacolborane **2**, 10 mol % CuI, 20 mol % L-proline sodium salt, and triethylamine in THF. At this time, triethylamine was used as a base, as in the case of the Miyaura−Masuda reaction.[3] However, no desired coupling product was determined from this reaction system

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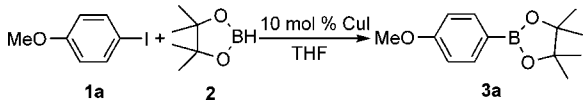
Table 1. CuI-Catalyzed Cross-Coupling Reaction of 4-Iodoanisole **1a** with Pinacolborane **2**[a]



entry	base	additive[b]	temp (°C)/time (h)	yield (%)[c]
1	Et_3N	A	70/24	0
2	*t*-BuOK	A	70/24	10
3	*t*-BuOK	B	70/24	11
4	*t*-BuOK	C	70/24	12
5	*t*-BuOK		70/4	24
6	Cs_2CO_3		70/24	22
7	NaHMDS		70/24	trace
8	NaH		70/4	58
9	NaH		25/4	75

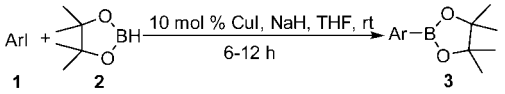
[a] Reaction conditions: 4-iodoanisole **1a** (1 mmol), pinacolborane **2** (1.5 mmol), base (1.5 mmol), CuI (0.1 mmol), additive (0.2 mmol), THF (4 mL). [b] Additive: A, L-proline sodium salt; B, *N*-methylglycine sodium salt; C, *N*,*N*-dimethylglycine sodium salt. [c] Isolated yield.

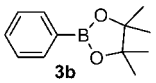
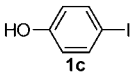
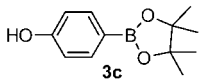
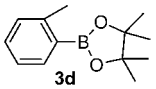
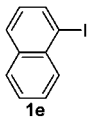
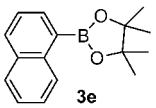
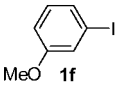
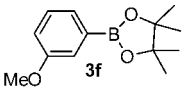
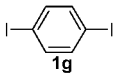
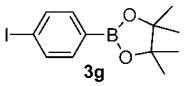
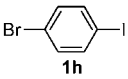
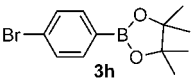
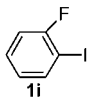
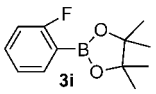
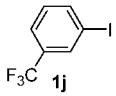
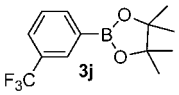
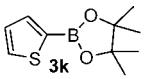
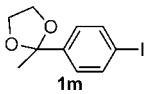
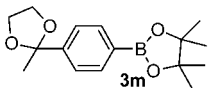
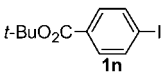
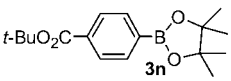
(Table 1, entry 1). We reasoned that triethylamine might be too weak a base for this reaction, and therefore, some stronger bases were attempted. To our delight, when *t*-BuOK was employed, the desired coupling product **3a** was isolated although the yield was only 10% (entry 2). Changing the additive to *N*-methylglycine sodium salt or *N*,*N*-dimethylglycine sodium salt failed to improve the reaction yields (entries 3 and 4), whereas deletion of the additive gave a better yield (entry 5). These results indicated that the amino acid additives were useless for the present coupling reaction. For other bases tested, Cs_2CO_3 delivered a yield similar to that of *t*-BuOK and NaHMDS provided a trace of the coupling product (entries 6 and 7). However, when sodium hydride was used, the yield jumped to 58% under the same reaction temperature (entry 8). Further investigations demonstrated that when this reaction was carried out at room temperature a satisfactory coupling yield was obtained (entry 9).

With the above optimized reaction conditions in hand,[6] the reaction scope was explored by varying the aryl iodides. As shown in Table 2, it was found that both electron-rich and electron-deficient aryl iodides were compatible with these reaction conditions, providing the corresponding coupling products in good yields (entries 2, 5, 8, and 9). The successful couplings of 4-iodophenol, 2-methylphenyl iodide, and naphthyl iodide with pinacolborane indicated that either a free hydroxyl group or steric hindrance did not alter this reaction process greatly (entries 2−4). In the case of 1,4-diiodobenzene, mono-coupling product **3g** was isolated in

(6) The typical procedure for a CuI-catalyzed coupling reaction of aryl iodide with pinacolborane is as follows: To a solution of aryl iodide (2 mmol), CuI (0.2 mmol), and sodium hydride (3 mmol) in THF was added pinacolborane (3 mmol) via syringe under argon atmosphere. The resultant mixture was stirred at room temperature until the aryl iodide disappeared, as monitored by TLC. After the reaction was quenched by adding 10 mL of saturated NH_4Cl, the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine and dried over $MgSO_4$. The solution was concentrated and the residue was chromatographed, eluting with 1:10 ethyl acetate/petroleum ether to afford arylboronate.

Table 2. CuI-Catalyzed Cross-Coupling Reaction of Aryl Iodides with Pinacolborane[a]



entry	ArI	product	yield (%)[b]
1	 1b	 3b	78
2	 1c	 3c	65[c]
3	 1d	 3d	71
4	 1e	 3e	80
5	 1f	 3f	83
6	 1g	 3g	61[d]
7	 1h	 3h	76
8	 1i	 3i	70
9	 1j	 3j	70
10	 1k	 3k	62
11	 1m	 3m	76
12	 1n	 3n	78

[a] Reaction conditions: aryl iodide **1** (2 mmol), pinacolborane **2** (3 mmol), sodium hydride (3 mmol), CuI (0.2 mmol), THF (8 mL). [b] Isolated yield. [c] 5 mmol of sodium hydride was added. [d] The bis coupling product was isolated in about 5% yield.

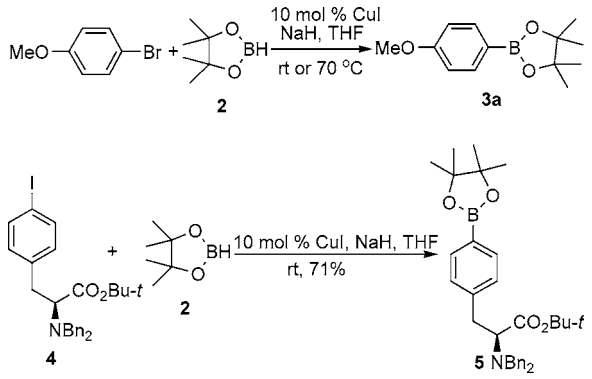
61% yield together with a bis-coupling product in about 5% yield (entry 5). Good selectivity was seen when 4-bromophenyl iodide was used, as only a mono-coupled product **3h** was obtained (entry 6), which meant that coupling with the C−I bond was significantly faster than that with the C−Br bond. Noteworthy is that both 4-hydroxyphenylboronate **3c** and 4-iodophenylboronate **3g** have not been obtained via previous methods.[3,4] Considering the fact that their additional function groups are ready for further transformations, this advantage may find special usage in

organic synthesis. In addition, a heteroaromatic iodide also gave the corresponding coupling product **3k** in 62% yield (entry 10).

The highly reductive ability of the combination of pinacolborane and sodium hydride was found to be troublesome for couplings of some functionalized aryl iodides. For example, when 4-acylphenyl iodide was used, a reduction product, α-hydroxy-4-iodophenylethane, was isolated in 77% yield. This problem was simply solved by employing protected 4-acylphenyl iodide **1m** as a substrate, which produced the desired arylboronate **3m** in 76% yield (entry 11). Similarly, 4-methoxycarbonylphenyl iodide furnished a reduction product, 4-iodobenzyl alcohol, in 69% yield, and reaction of the *tert*-butyl ester **1n** smoothly proceeded to deliver the corresponding arylboronate **3n** in 78% yield, indicating that a bulky *tert*-butyl ester moiety could survive under these reaction conditions (entry 12).

To explore the reaction scope further, a coupling reaction of 4-bromoanisole with pinacolborane was tested. At room temperature after 48 h, this reaction produced **3a** in only 20% yield, with recovery of 61% of 4-bromoanisole (Scheme 1). Raising the reaction temperature to 70 °C did not give

Scheme 1

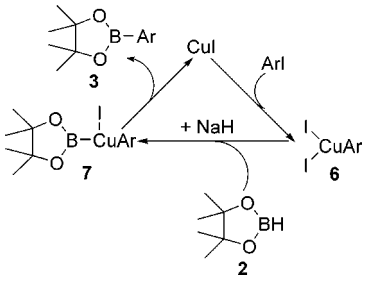


increased conversion. Further experimentation is required to overcome this problem.

To demonstrate the usage of the present coupling reaction further, iodide **4** was prepared from L-phenylalanine according to the known procedure. We were pleased to observe that the coupling reaction of **4** with pinacolborane provided arylboronate **5** in 71% yield (Scheme 1). It is notable that some related arylboronates have already been used in elaboration of natural products and phenylalanine derivatives.[7]

Although a detailed mechanistic investigation of the present reaction awaits further experimentation, tentative proposals are depicted in Scheme 2, which relied on the

Scheme 2



proposed catalytic cycles for Ullmann-type coupling reactions[5d,8] and the Miyaura−Masuda reaction. Oxidative addition of CuI with an aryl iodide afforded a Cu(III) intermediate **6**, which reacted with pinacolborane **2** under the assistance of sodium hydride to produce intermediate **7**. Reductive elimination of **7** would deliver the arylboronate and regenerate the catalyst.

In conclusion, we have demonstrated here a CuI-catalyzed cross-coupling reaction of aryl iodide with pinacolborane. Although it requires more reactive sodium hydride as a base and shows poor conversion for aryl bromides, its inexpensive catalyst and room-temperature reaction condition, as well as its suitability for assembling 4-hydroxyphenylboronate and 4-iodophenylboronate, are attractive for practical usage. In addition, the present results provided another new CuI-catalyzed reaction, which should stimulate the investigations on coupling reactions using CuI as a catalyst.[8a,b] Further studies on the optimization of the reaction conditions to expand the reaction scope are in progress.

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Supporting Information Available: Experimental procedures and copies of ^{1}H NMR spectra for compounds **3** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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