A novel transmetallation of arylzinc species into arylboronates from aryl halides in a barbier procedure†

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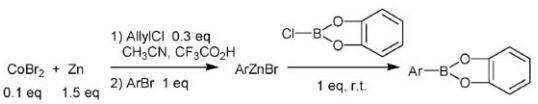
A variety of functionalized arylboronates are obtained in moderate to excellent yield by a one-step chemical procedure from the corresponding halides and a haloboronic ester *via* an intermediate arylzinc species.

Arylboronic acids and their derivatives have become very attractive reagents in modern organic synthesis,[1] and they are used in a wide variety of significant organic transformations. In fact, the availability of these reagents and their mild reaction conditions both contribute to the versatility of their reactions. For example, the Suzuki–Miyaura palladium-catalyzed cross-coupling reaction between organoboron compounds and organic halides or triflates has become a cornerstone of organic synthesis, providing a carbon–carbon bond-forming reaction.[2] The key advantages of boronic derivatives over other organometallic derivatives are the commercial availability of diverse boronic acids, their wide ranging functional group tolerance, and the low toxicity of the reagents and their by-products, especially compared to tin-containing compounds. Arylboronates are playing an increasing prominent role in Suzuki–Miyaura cross-coupling reactions as important alternatives to arylboronic acids, particularly when the corresponding boronic acids are not readily available, as they are as easy to handle as boronic acids. They also continue to attract attention as versatile functional group-tolerant cross-coupling substrates in organic synthesis. However, the difficulty of accessing such compounds constitutes their main drawback. Different approaches to their preparation have been reported in the literature. Generally, they are conventionally prepared from a reaction of arylmagnesium or -lithium reagents with boron halides or trialkylborates.[3] This approach is limited in scope because of its incompatibility with sensitive functionalities. To avoid this drawback, alternative synthetic methodologies, allowing the direct transition metal-catalyzed coupling of aryl halides, triflates or aryldiazonium tetrafluoroborate salts with tetraalkoxydiboranes[4] by the cleavage of the B–B bond or the more readily available dialkoxyboranes,[5] have been successfully performed to afford arylboronic esters. Generally, these methodologies require the use of a base associated with high temperature. Furthermore, transition metal-catalyzed direct borylation of aromatic rings has been achieved using expensive Re, Rh, Ir or other catalysis.[6] In addition to these methods utilizing aromatic precursors, benzannulation or cycloaddition involving unsaturated organoboron reagents has allowed the assembly of highly substituted arylboronic acid frameworks.[7]

During the course of our work, based on the cobalt-catalyzed formation of organometallic compounds, we have found a new method for the preparation of functionalized arylboronic esters from the corresponding arylzinc species.[8] Contrary to arylboronate esters, arylzinc species can neither be stored for a long time nor isolated because of their instability. Recently, we have established that arylzinc compounds[9] are convenient for the facile preparation of arylstannanes from the corresponding arylbromides.[10] In this case, transmetallation between the arylzinc species, formed in the medium, and tributylstannyl chloride occurs, as described in the literature. However, the toxicity of organotin reagents limits the use of such compounds. Unlike these tin-containing compounds, boronic derivatives present a lower toxicity, but to our knowledge, there are no reports in the literature concerning transmetallation between an organozinc species and a boron compound. Conversely, organozinc compounds are prepared *via* a boron–zinc exchange reaction.[11] We supposed that the use of a halogenocatecholborane might transmetallate arylzinc compounds. Therefore, a coupling reaction of arylzinc species, formed *via* cobalt catalysis, with a halogenocatecholborane was explored. Herein, we wish to disclose our results. Initially, we verified that the two-step coupling reaction of arylzinc bromides and chlorocatecholborane led to the corresponding arylboronic ester at room temperature without the further addition of a catalyst (eqn. 1).



(1)

The behaviour of our arylzinc compounds, synthesized *via* a cobalt catalysis in acetonitrile, towards a halogenocatecholborane is similar to that of Bu_3SnCl. For example, *p*-$MeOC_6H_4B$-catechol (70% GC yield) and *p*-EtOCO-C_6H_4B-catechol (80% GC yield) have been readily synthesized in a two-step sequence from the corresponding aryl bromides and chlorocatecholborane using the reaction conditions detailed elsewhere for the preparation of ArZnBr: 0.1 equiv. of $CoBr_2$, 1.5 equiv. of zinc dust activated by 50 ml of trifluoroacetic acid and a 1.5 M aryl bromide solution. Prior to the addition of aryl bromide in acetonitrile, a preliminary step of 5 min stirring in the presence of 0.3 equiv. of allyl chloride (3 equiv. *vs.* cobalt) is required in order to enhance the yield of the organozinc species and to decrease the formation of by-products, especially ArH. Once the organozinc compound has formed,

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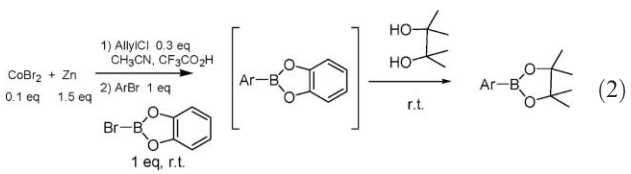
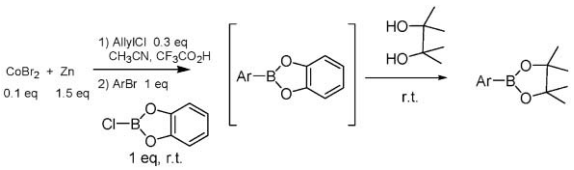
1 equiv. of chlorocatecholborane is added to the solution at room temperature and the mixture stirred for 30 min. Hydrolysis with NH_4Cl, followed by diethyl ether extraction, gives the crude arylboronic ester in good yields. As reported in the case of arylstannanes, it seemed interesting to develop a convenient method for the one-step synthesis of arylboronic esters from aryl bromides or iodides. This procedure follows the protocol already described, but after the usual preliminary stirring in the presence of 0.3 equiv. of allyl chloride, the aryl halide (1 equiv.) and halogenocatecholborane are simultaneously added in acetonitrile at room temperature. The nature of the halogenocatecholborane depends on the substituent on aromatic ring. The mixture is stirred until total consumption of the aryl bromide has taken place (in about 30 min). The corresponding arylboronic ester is rapidly detected by GC using an internal standard (alkane). In several instances, the arylboronate products were accompanied by the formation of a small amount of the reduction product in the reaction mixture. An inert atmosphere is not required. Consequently, we applied this method to various aromatic bromides or iodides bearing electron-donating or -withdrawing groups in the *para*/*meta*/*ortho* series. With an electron-withdrawing group on the aromatic ring, the aryl halide is more reactive with low valency cobalt, and the corresponding arylzinc species is less nucleophilic than an electron-donating group substituent. Therefore, a more reactive halogenocatecholborane, such as bromocatecholborane, has to be used in the one-step coupling. Moreover, the resulting catechol esters are sensitive to moisture and chromatography, whereas the corresponding inert pinacol esters are more stable.[5a] This is the reason why the quantitative transesterification with pinacol was performed at room temperature in 30 min (eqn. 2). On the basis of this result, subsequent experiments with a number of representative aryl halides bearing an electron-withdrawing group were carried out to give the corresponding products. The results are summarized in Table 1.



(2)

These results show that this original method gives the expected arylboronates bearing an electron-withdrawing group. In all cases, the only by-product is that from reduction, contrary to the two-step procedure where the homocoupling product was detected in small amounts. Satisfactory-to-excellent yields are observed when the electron-withdrawing substituent is in *para* or *meta* position. However, it can be pointed out that substituents in the *ortho* position have an important influence on the yields, as revealed in the case of ethyl bromobenzoate (Table 1, entries 1, 2 and 3) and bromobenzonitrile (Table 1, entries 7 and 8). This reflects steric and chelation effects.

In the case where an aromatic ring is substituted by an electron-donating group, the chlorocatecholborane is sufficiently reactive for the transmetallation to occur with the corresponding intermediate arylzinc species (eqn. 3). The results are reported in Table 2.



(3)

Again, satisfactory yields were observed, and the *ortho* position was less compatible with this process (Table 2, entry 2).

In order to confirm that cobalt salts were not involved in transmetallation between the organozinc species and the halogenocatecholborane, benzylzinc bromide was prepared in acetonitrile in the absence of a cobalt catalyst. The organozinc species thus obtained was allowed to react with chlorocatecholborane at room temperature, giving rise almost quantitatively to the benzylboronate ester without supplementary cobalt catalysis.

The standard conditions developed for aromatic halides bearing either electron-donating or -withdrawing groups have also been applied to the conversion of heteroaromatic bromides into the corresponding boronate esters. The resulting products have been isolated and show that the preceding method affords 3-thienylboronate esters from their corresponding 3-bromothiophene in good yield (75% isolated). With a more reactive bromothiophene, such as 2-bromothiophene, the corresponding thienylboronate is detected in small amounts (18%). 2-Thienyl bromide gives a large amount of the reduction product. Unfortunately, results were disappointing with bromopyridines. As already described for organozinc species formed by cobalt catalysis in acetonitrile, no organoboronate ester could be detected from 2- or 3-bromopyridine. These results were not surprising. Indeed, the synthesis of 2-pyridyl organometallics remains a significant problem, probably due to their frequent instability and difficult synthesis.[12]

In conclusion, we have developed a new method to prepare arylboronate esters from the corresponding aryl iodide or bromide *via* an intermediate arylzinc species. To the best of our knowledge, we have shown for the first time that transmetallation between an arylzinc species and a halogenoborane occurs without a transition

Table 1 One-step synthesis at room temperature of arylboronates bearing an electron-withdrawing group from ArBr

Entry	Aryl halide	Isolated yield of ArBP (%)[a]	GC yield (%)
1	2-EtOCOPhBr	47	71
2	3-EtOCOPhBr	95	95
3	4-EtOCOPhBr	90	90
4	4-EtOCOPhI	65	65
5	4-F_3CPhBr	48	61
6	4-MeOCOPhBr	69	80
7	2-NCPhBr	5	33
8	4-NCPhBr	52	79
9	4-ClPhBr	51	88
10	4-MeCOPhBr	50	75

[a] Based on initial ArX. All products gave satisfactory ^1H, ^{13}C NMR and mass spectra.

Table 2 One-step synthesis of arylboronates from ArBr bearing an electron-donating group at room temperature

Entry	Aryl bromide	Isolated yield of ArBP (%)[a]	GC yield (%)
1	4-MeOPhBr	71	80
2	2-MeOPhBr	45	60
3	4-MeSPhBr	56	60
4	4-$(Me)_2$NPhB	43	76

[a] Based on initial ArX. All products gave satisfactory ^1H, ^{13}C NMR and mass spectra.

metal. This versatile process compares favourably with other procedures that use palladium catalysis.

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