New Electrosynthesis of Arylboronic Esters from Aromatic Halides and Pinacolborane

Carine Laza,[a] Elisabet Duñach*[b]

[a] Laboratoire Arômes, Synthèses et Interactions, Université de Nice-Sophia Antipolis, 06108 Nice Cédex 2, France
[b] Laboratoire de Chimie Bio-Organique, CNRS, UMR 6001, Université de Nice-Sophia Antipolis, 06108 Nice Cédex 2, France
Phone: (+33)-4-92-07-61-42, Fax : (+33)-4-92-07-61-51, e-mail: dunach@unice.fr

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Abstract: A novel synthesis of arylboronic esters by a reductive electrochemical coupling reaction between aromatic halides and pinacolborane (HBpin, pin = pinacolate) has been carried out leading to arylboronic esters in moderate to good yields.

Keywords: arylboronic esters; aryl halide; electrosynthesis; pinacolborane; sacrificial anode

Arylboronic acids or esters constitute an important class of compounds, widely used as coupling agents, allowing formation of various C-C[1] and C-heteroatom[2] bonds. The cross-coupling reaction between aryl halides and arylboronic acids, the Suzuki reaction,[3,4] constitutes an efficient and selective method for non-symmetrical Ar-Ar' biaryl synthesis. Numerous applications of this reaction have been reported due to the fact that the biaryl unit is found in natural products, polymers, liquid crystals and advanced materials.

The access to arylboronic acids or esters is almost limited to the reaction of an aryl Grignard[5] or an aryllithium reagent[6] with a trialkyl borate at low temperature. These methods require the previous preparation of the organometallic species, do not allow much functionality and variable yields of arylboronic acids are obtained. The use of trialkyl borates for the electrosynthesis of arylboronic acids has been reported to occur in moderate yields.[7]

We report here a novel coupling reaction, based on the use of pinacolborane (HBpin) as an efficient reagent for the electrochemical functionalisation of aryl halides under mild conditions. To our knowledge, no electrochemical reaction with HBpin or analogous boranes has yet been reported. Dialkoxyboranes are generally used in the hydroboration of alkenes and alkynes.[8] Pinacolborane has been recently reported for the synthesis of arylboronic pinacol esters from hydrocarbon aromatic compounds in presence of iridium[9] or rhodium[10] complexes, or from aryl halides using palladium catalysts at 80 °C.[11,12]

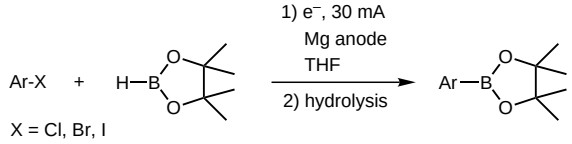
The electrochemical boration with HBpin presented here proceeds through a reductive one-step direct reaction between the aryl halide and pinacolborane, in the absence of any metal catalyst. The electrolyses were carried out in a single-compartment cell in THF, at room temperature and at constant current intensity, according to Scheme 1. Pinacolborane acts as an electrophilic and non-easily reducible borating agent.

The results of the electrosynthesis of several arylboronic pinacol esters are summarised in Table 1.

The electroreduction of phenyl iodide, bromide or chloride in the presence of HBpin afforded 78–83% yields of phenylboronic pinacol ester calculated on converted halides, (entries 1–3, 46–78% isolated yields). Interestingly, as shown in entries 3 to 5, the reaction could be carried out with aryl chlorides, even with electron-donating substituents, such as *p*-methyl or *o*-methoxy groups. These non-activated chlorides could be functionalised to afford the corresponding arylboronic pinacol esters in moderate to good yields, though with low faradic efficiencies (42–77% conversions after 6 F/mol). In all cases the reaction was very clean, the only by-product being the Ar-H derivative, which resulted from the reductive dehalogenation of the starting halide.

Reactions were generally carried out with 3 equivs. of HBpin per aryl halide. If 1 or 2 equivs. of the borane were used, the yields of the corresponding ArBpin were diminished.

Several tests were carried out with *p*-tolyl bromide (entries 6–8). The nature of the electrodes strongly influenced the results. A magnesium anode proved to be more efficient than an aluminium or a zinc one for the synthesis of *p*-tolylboronic pinacol ester (entries 6 and



Scheme 1. Electrosynthesis of arylboronic pinacol esters from aryl halides and pinacolborane.

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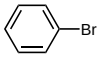
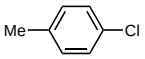
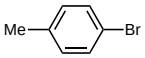
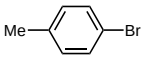
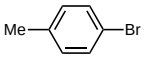
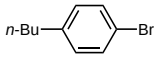
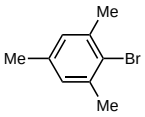
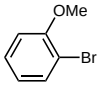
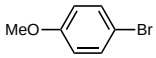
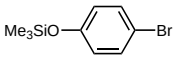
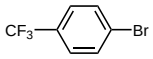
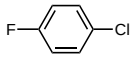
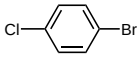
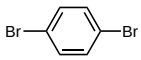
Table 1. Electrosynthesis of arylboronic pinacol esters from aryl halides and pinacolborane.

Entry	Ar-X	Anode	Cathode	F/mol of ArX	Recovered Ar-X [%]	ArBpin Yield [%]
1		Mg	nickel foam	1.5	5	78
2		Mg	nickel foam	2.0	–	78
3		Mg	nickel foam	6.0	45	46
4		Mg	nickel foam	6.0	23	53
5		Mg	nickel foam	6.0	58	22
6		Mg	nickel foam	1.2	7	75
7		Al	stainless steel	4.0	–	19
8		Mg	stainless steel	1.2	–	68
9		Mg	nickel foam	2.0	17	74
10		Mg	nickel foam	2.0	17	67
11		Mg	nickel foam	2.0	41	40
12		Mg	nickel foam	2.0	–	79
13		Mg	nickel foam	2.0	–	65
14		Mg	nickel foam	1.0[a]	66	20
15		Mg	nickel foam	2.0[a]	45	25
16		Mg	nickel foam	1.0	55	34
17		Mg	nickel foam	1.0	68	20

[a] The yield was calculated by ^{19}F-NMR and by GC analysis.

7). The best yield (81% calculated on converted substrate) was obtained using a nickel foam cathode and a magnesium anode (entry 6). The electrolytic system constituted also an important feature; no reaction occurred in DMF or in acetonitrile as the solvents, due to their reactivity with pinacolborane.[13] The use of THF associated with lithium bis(trifluoromethanesulphonyl)imide as the supporting electrolyte afforded the best results, as compared to the use of tetraalkylammonium salts.

Other alkyl-substituted aryl bromides were also selectively functionalised by HBpin. Thus, the electroreduction of *p*-*n*-butylphenyl bromide gave 89% yield (based on halide conversion) of the corresponding

arylboronic ester (entry 9). It is noteworthy that a good yield was also obtained with 2,4,6-trimethylphenyl bromide (entry 10, yield of 81% based on halide conversion), indicating that the reaction was compatible with sterically hindered aryl derivatives.

With either *ortho*- or *para*-methoxy-substituted aryl bromide derivatives (entries 11 and 12) yields of boronic esters of 68 and 79% (based on halide conversion) were obtained, respectively.

The electrolysis of *p*-trimethylsiloxyphenyl bromide afforded the corresponding arylboronic pinacol ester in 65% yield with a neutral work-up. The corresponding *p*-hydroxyphenylboronic pinacol ester (*p*-HOC_6H_4Bpin) could be obtained with the same yield under an acidic work-up (entry 13).

In the case of *p*-trifluoromethylphenyl bromide (entry 14), the *p*-trifluoromethylphenylboronic ester was obtained in 58% yield (calculated on converted halide) after 1 F/mol at a partial conversion. In the presence of the CF_3 groups, the electroreduction of the benzylic C-F bonds occurred as a competitive reaction. When the electrolysis was continued up to 2 F/mol, the yield of *p*-trifluoromethylphenylboronic ester per converted halide was lowered to 48% and *p*-pin$BCH_2C_6H_4Bpin$ was formed as a by-product.

The reduction of other difunctional aromatic halides was also examined (entries 15–17) and allowed the access to haloarylboronic acids in 45–75% yields at partial conversions. Thus, *p*-fluorophenyl-, *p*-chlorophenyl- and *p*-bromophenylboronic esters were obtained in 45, 75 and 60% yields per converted halide, respectively, in entries 15–17, after 1–2 F/mol consumption. The further electroreduction of these derivatives afforded mixtures of phenylboronic pinacol ester and *p*-phenylene-*bis*-boronic pinacol diester.

The yield of arylboronic pinacol esters obtained by electrosynthesis with several aryl bromides are slightly better than those reported by a chemical Pd-catalysed procedure.[11,12]

Concerning the mechanism of this aryl-boron coupling reaction, a first aryl halide reduction is proposed to proceed at the cathode, parallel to the oxidation of the magnesium rod into magnesium ions occurring at the anode. An ate-type complex between a formal ArMgX and pinacolborane is likely to be formed as reaction intermediate, before the final hydrolysis to the arylboronic pinacol ester.

In conclusion, the electrochemical method involving the direct reductive coupling of aryl halides and pinacolborane constitutes a novel alternative for the synthesis of arylboronic pinacol esters. The reaction can be applied to non-activated aryl chlorides as well as to hindered aryl halides. With aryl bromides, the yields of arylboronic esters are in the range of 58–89% based on converted halides. The reaction is carried out under mild conditions, with a very simple electrochemical set-up and presents several advantages: one step, room temperature, no catalyst, no previous preparation of organometallic species. Work is in progress to investigate the reaction mechanism in order to get a better insight into this novel electrochemical reaction.

Experimental Section

General Electrochemical Procedure

Under inert atmosphere in a single-compartment cell fitted with a consumable Mg anode and a nickel foam cathode, the ArX substrate (1 mmol) and HBpin (3 mmol) were added to a distilled THF solution (20 mL) containing $(CF_3SO_2)_2NLi$ (7×10^{-2} M). The electrolysis was carried out at room temperature and at constant current density ($i = 0.03$ A, $j = 0.15$ A $\times$ dm^{-2}), the charge involved during the electrochemical process being calculated by the time of the electrolysis. After electrolysis, the solvent in excess was evaporated under vacuum. The medium was slowly hydrolysed at 0 °C with a 10% H_2SO_4 solution until pH 5. The aqueous phase was saturated with NaCl and extracted with Et_2O (3×60 mL). The organic phases were washed twice with an NaOH solution (pH 8–9) and once with water (pH 7), dried over magnesium sulphate and concentrated under vacuum. In most cases pure pinacol esters were obtained after evaporation of the Ar-H by-products. When necessary, boronic esters were purified by column chromatography on silica gel with pentane-ether mixtures as the eluent. The purity of the arylboronic pinacol esters was checked by ^1H NMR and the products were compared to authentic samples.

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