Novel synthesis of arylboronic acids by electroreduction of aromatic halides in the presence of trialkyl borates

Carine Laza,[a] Elisabet Duñach,*[b] Françoise Serein-Spirau,*†[c] Joël J. E. Moreau[d] and Luc Vellutini[d]

[a] *Laboratoire Arômes, Synthèses et Interactions, Université de Nice-Sophia Antipolis, 06108 Nice cedex 2, France*
[b] *Laboratoire de Chimie Bio-Organique (CNRS UMR 6001), Université de Nice-Sophia Antipolis, 06108 Nice cedex 2, France. E-mail: dunach@unice.fr; Fax: +33 4 92 07 61 51*
[c] *Laboratoire de Chimie Organique et Organométallique (CNRS UMR 5802), Université Bordeaux 1, 33405 Talence cedex, France*
[d] *Laboratoire de Chimie Organométallique (CNRS UMR 5076), Ecole Nationale Supérieure de Chimie de Montpellier, 8, Rue de l'Ecole Normale, 34293 Montpellier cedex, France*

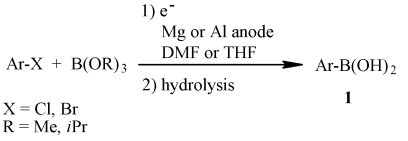
Received (in Strasbourg, France) 1st December 2001, Accepted 15th January 2002
First published as an Advance Article on the web

A novel preparation of aryl and heteroarylboronic acids by an electrochemical coupling reaction is described. It is based on the reductive coupling between aromatic or heteroaromatic halides and a trialkyl borate. The reactions are carried out in DMF or THF with the use of sacrificial aluminium or magnesium anodes in a single-compartment cell. Arylboronic acids are obtained with moderate to good selectivities and isolated yields.

Aryl boronic acids **1** constitute an important class of compounds, widely used in the last decade as coupling agents in the Pd-catalyzed Suzuki reaction.[1] This reaction constitutes an efficient and selective method for Ar–Ar′ reductive coupling between an aryl halide and an arylboronic acid, under mild conditions.[2] Arylboronic acids also participate in various C–C bond formation reactions,[3] including the coupling of vinyl halides[4] and polymerization reactions.[5]

The access to arylboronic acids is essentially limited to the reaction of an aryl Grignard[6] or an aryl lithium reagent[7] with a trialkyl borate at low temperature. Variable yields of arylboronic acids are obtained. These methods require the previous preparation of the organometallic species and only tolerate a restricted number of functional groups, owing to the basic and nucleophilic reaction conditions. On the other hand, the preparation of the ArMgX or ArLi reagents with aryl chloride derivatives is often difficult and the less easily available bromide derivatives are generally required.

We present here our results on the use of electrochemical methodology as a novel strategy for the one-step synthesis of arylboronic acids under mild conditions. The electrochemical coupling was performed in a single-compartment cell fitted with a consumable anode of aluminium or magnesium and an inert cathode of stainless steel or nickel foam.[8,9] The coupling reaction is based on the direct electroreduction of either aryl or heteroaryl chlorides and bromides in the presence of several trialkyl borates, such as $B(OMe)_3$ or $B(O^iPr)_3$, according to eqn. (1).



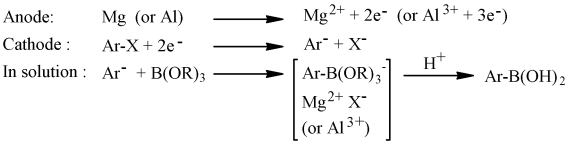
1

No example of such an electrochemical coupling reaction involving trialkyl borates has, to our knowledge, been yet described in the literature.

The reactions at the electrodes are, at the anode, the oxidation of the Al or Mg rods into the corresponding Al^{3+} or Mg^{2+} ions in solution. At the cathode, the reduction of the aryl halide should generate Ar^-, which further reacts with the $B(OR)_3$ electrophile to afford, after hydrolysis, the corresponding arylboronic acid, as shown in Scheme 1.

The electrolyses were carried out either in DMF or in THF, at room temperature and at constant current intensity. The results of the electrosynthesis of several aryl and heteroarylboronic acids are summarized in Table 1.

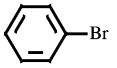
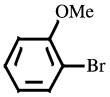
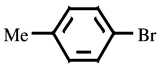
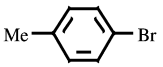
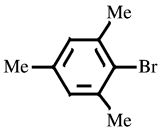
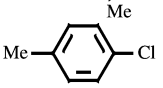
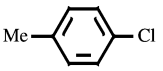
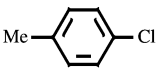
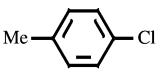
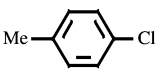
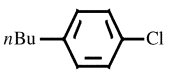
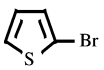
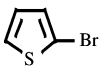
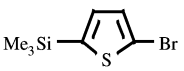
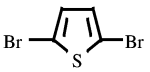
The electroreduction of phenyl bromide in the presence of $B(OMe)_3$ afforded a 45% isolated yield of phenylboronic acid in 82% conversion after passage of 2 F mol^{-1} (entry 1). Similar results were obtained with *o*-methoxy or *p*-methyl substituted aryl bromide derivatives (entries 2–4), in DMF or THF, using either $B(OMe)_3$ or $B(O^iPr)_3$ as electrophiles. Sterically hindered 2,4,6-trimethylphenyl bromide afforded the corresponding arylboronic acid in 40% isolated yield (entry 5). In all cases, the main by-product was the Ar–H derivative, which resulted from the reductive dehalogenation of ArX and which was formed in yields up to 60%. The other by-products were the corresponding phenols, ArOH, which were shown to be formed in the extraction procedure; they could be avoided by a work-up under inert atmosphere. In reactions run in DMF, aldehydes, ArCHO, issued from formylation[8,10] were also formed in 5–20% yield.



Scheme 1

† Present address: Laboratoire de Chimie Organométallique (CNRS UMR 5076), Ecole Nationale Supérieure de Chimie de Montpellier, 8, Rue de l'Ecole Normale, 34293 Montpellier cedex, France. E-mail: fspirau@cit.enscm.fr; Fax: +33 4 67 14 72 12.

Table 1 Electrosynthesis of arylboronic acids

Entry	Ar–X	$B(OR)_3$	Solvent	Anode/cathode	F mol^{-1} of ArX	% conv. of ArX	$ArB(OH)_2$ % yield
1		$B(OMe)_3$	DMF	Mg/stainless steel	2.0	82	45[a]
2		$B(OMe)_3$	DMF	Mg/stainless steel	2.0	89	48[a]
3		$B(OMe)_3$	DMF	Mg/stainless steel	2.5	100	32[a]
4		$B(O^iPr)_3$	THF	Mg/stainless steel	4.0	100	44[a]
5		$B(OMe)_3$	DMF	Mg/stainless steel	2.0	78	40[a]
6		$B(O^iPr)_3$	THF	Mg/stainless steel	4.0	82	46[a]
7		$B(OMe)_3$	THF	Mg/stainless steel	1.6	83	40[a]
8		$B(OMe)_3$	DMF	Mg/stainless steel	4.3	100	36[a]
9		$B(OMe)_3$	DMF	Mg/nickel foam	5.1	100	36[a]
10		$B(OMe)_3$	DMF	Al/nickel foam	8.0	63	41[a]
11		$B(OMe)_3$	DMF	Mg/stainless steel	3.5	100	38[a]
12		$B(OMe)_3$	DMF	Al/stainless steel	2.2	100	56[b]
13		$B(OMe)_3$	DMF	Mg/stainless steel	2.2	100	57[b]
14		$B(OMe)_3$	DMF	Al/stainless steel	2.2	80	57[b]
15		$B(OMe)_3$	DMF	Al/stainless steel	2.2	70	73[b]
16		$B(OMe)_3$	DMF	Al/stainless steel	2.2	100	59[b]

[a] Isolated yield calculated on converted ArX. [b] Selectivity in $ArB(OH)_2$ evaluated by gas chromatography or ^1H NMR. They were isolated as the arylboronic esters in 31 to 53% yields, by esterification of the arylboronic acids with 2,2′-dimethylpropane-1,3-diol.[12]

Some aryl chloride derivatives, though more difficult to reduce, could also be functionalized with $B(OMe)_3$ or $B(O^iPr)_3$ in DMF or THF to afford the corresponding arylboronic acids after acidic hydrolysis, in 36–46% yields (entries 6–11). The nature of the cathode did not strongly influence the results (entries 8, 9), and replacement of the Mg by an Al anode led to a 41% yield of *p*-tolylboronic acid but with incomplete conversion (entries 9, 10).

For thienyl halide derivatives, the aluminium/stainless steel couple seemed also well suited and led to conversions ranging from 70 to 100% after passage of 2.2 F mol^{-1} (entries 12–16). The selectivities in arylboronic acid varied from 56 to 73%, the only by-product of the reaction being the protonation of the starting material. Related observations were made in the reductive electrosilylation of aromatic halides using the sacrificial anode methodology.[11] However, chlorosilanes being more electrophilic than trialkyl borates, the protonation reaction occurs to a lesser extent in electrosilylation.

A high selectivity was found in the reduction of aromatic dihalides (entry 15), allowing the access to haloarylboronic acids, which have proved to be useful monomers in Pd(0) catalyzed polymerization.[5]

In conclusion, the electrochemical method involving the reaction of aryl or heteroaryl halides and trialkyl borates constitutes an alternative for the synthesis of aryl and heteroarylboronic acids. The selectivities of arylboronic acids are in the range of 32–73%. The main by-product, the Ar–H derivative, arising from competitive reduction, is easy to eliminate. The reaction is carried out under mild conditions

(one-step, room temperature) with a simple electrochemical set-up. Although the reaction is still limited in terms of functional group compatibility, work is in progress to widen its scope, to investigate the reaction mechanism in order to gain a better insight into this novel electrochemical reaction and to better control its yield and selectivity.

Experimental

The general electrochemical procedure is the following: in a single-compartment cell fitted with an Al or Mg consumable anode, the substrates ArX (1 mmol) and $B(OR)_3$ (3 mmol) are added to a DMF or THF solution (20 mL) containing either KBr or *n*-Bu_4NBr as supporting electrolyte in DMF (2×10^{-2} M) or $(CF_3SO_2)_2NLi$ in THF (7×10^{-2} M) at room temperature. The electrolysis was carried out at constant current density ($i = 0.06$ to 0.2 A, $j = 0.3$ to 1.0 A dm^{-2}); the charge involved during the electrochemical process was evaluated by the time of the electrolysis. After electrolysis, the solvent and $B(OR)_3$ in excess could be evaporated under vacuum. The medium was slowly hydrolyzed at 0 °C with an HCl (0.1 M) or H_2SO_4 (10%) solution. After extraction with Et_2O (3×20 mL if the solvent was evaporated or 3×60 mL otherwise), the organic phase was dried over sodium or magnesium sulfate and concentrated under vacuum. The purity of the arylboronic acids was evaluated by ^1H NMR spectra. Thienylboronic acids were recrystallized in CH_2Cl_2.

Acknowledgements

We thank Rhodia Organique Fine for financial support of this work. F. Serein-Spirau would like to thank the CNRS for a position "en delegation".

References

1 See, for example: (*a*) N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457–2483 and references therein; (*b*) A. Suzuki, *J. Organomet. Chem.*, 1999, **576**, 147–168 and references therein.

2 See, for example: (*a*) S. Gervat, E. Léonel, J.-Y. Barraud and V. Ratovelomanana, *Adv. Mater.*, 1992, **4**, 747–749; (*b*) A. R. Martin and Y. Youhua, *Acta Chem. Scand.*, 1993, **47**, 221–230; (*c*) J. C. Anderson, H. Namli and C. A. Roberts, *Tetrahedron*, 1997, **53**, 15 123–15 134; (*d*) S. Chowdhury and P. E. Georghiou, *Tetrahedron Lett.*, 1999, **40**, 7599–7603; (*e*) X. Bei, H. W. Turner, W. H. Weinberg and A. S. Giam, *J. Org. Chem.*, 1999, **64**, 6797–6803.

3 (*a*) A. B. Charrette and A. Giroux, *J. Org. Chem.*, 1996, **61**, 8718–8719; (*b*) A. B. Charette and R. P. De Freitas-Gil, *Tetrahedron Lett.*, 1997, **38**, 2809–2812.

4 (*a*) M. Moreno-Manas, F. Pajuelo and R. Pleixats, *J. Org. Chem.*, 1995, **60**, 2396–2397; (*b*) F. Koch and W. Heitz, *Macromol. Chem. Phys.*, 1997, **198**, 1531–1544.

5 (*a*) M. Bouachrine, J.-P. Lère-Porte, J. J. E. Moreau and C. Torreilles, *J. Chim. Phys.*, 1998, **95**, 1176–1179; (*b*) J.-P. Lère-Porte, J. J. E. Moreau and C. Torreilles, *Synth. Met.*, 1999, **101**, 588–589; (*c*) M. Bouachrine, J.-P. Lère-Porte, J. J. E. Moreau, F. Serein-Spirau and C. Torreilles, *J. Mater. Chem.*, 2000, **10**, 263–268.

6 (*a*) R. T. Hawkins, J. Lennarz and H. R. Snyder, *J. Am. Chem. Soc.*, 1960, **82**, 3058–3059; (*b*) W. J. Thompson and J. Gaudino, *J. Org. Chem.*, 1984, **49**, 5237–5243.

7 (*a*) A. J. Seed, K. J. Toyne and J. W. Goodby, *J. Mater. Chem.*, 1995, **5**, 653–661; (*b*) H. Yamashita, K. Amano, S. Shimada and K. Naraska, *Chem. Lett.*, 1996, 537–538.

8 J. Chaussard, J.-C. Folest, J.-Y. Nedelec, J. Perichon, S. Sibille and M. Troupel, *Synthesis*, 1990, **5**, 369–381.

9 J.-Y. Nédélec, J. Périchon and M. Troupel, *Top. Curr. Chem.*, 1997, **185**, 141–262.

10 C. Saboureau, M. Troupel, S. Sibille, E. D'Incan and J. Périchon, *J. Chem. Soc., Chem. Commun.*, 1989, 895–896.

11 (*a*) D. Deffieux, D. Bonafoux, M. Bordeau, C. Biran and J. Dunoguès, *Organometallics*, 1996, **15**, 2041–2046; (*b*) C. Moreau, F. Serein-Spirau, C. Biran, M. Bordeau and P. Gerval, *Organometallics*, 1998, **17**, 2797–2804.

12 S. Guillerez and G. Bidan, *Synth. Met.*, 1998, **93**, 123–126.