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Electrochemical preparation of pinacol allylboronic esters

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ABSTRACT

The electroreduction of allylic halide derivatives in the presence of pinacolborane afforded allylboronic pinacol esters with moderate to good yields (up to 86%) and high regioselectivities. The electrosynthesis was carried out in a single-compartment cell with an Al anode, in THF at room temperature and it constitutes an alternative route for the preparation of allylboronic esters under mild conditions.

1. Introduction

Allylboronic acids and esters constitute important synthetic intermediates in organic chemistry. Allylboronic derivatives can undergo Suzuki-type cross-coupling reactions, similarly to arylboronic acids and esters [1,2]. Allylboronic esters have also been described as partners for the highly stereo- and enantio-selective coupling with carbonyl compounds for the synthesis of homoallylic alcohols [3–7]. Moreover, the low toxicity of boronic acids and their ultimate degradation to boric acid allow these derivatives to be qualified as "green" compounds [8].

The general synthetic access to these intermediates has been reported *via* the corresponding allyl Grignard [9–11] or lithium reagents [12] with trialkyl borates, in two-step reactions at −78 °C (with low functional group compatibility) or *via* palladium- or platinum-catalysed coupling processes with allylic derivatives and pinacolborane or bis(pinacolato)diboron as the borating agents [13–19].

Within our interest in developing the electrochemical methodology for synthetic purposes [20,21] we reported the electrosynthesis of arylboronic acids [22] and esters [23,24]. An alternative electrochemical method for the access to benzylboronic derivatives has also been described [25].

We present here our results on the application of the electrosynthetic methodology for the preparation of allylboronic esters, as a direct synthetic alternative to the transition-metal-catalysed procedures.

2. Experimental

General electrolysis procedure: In a single-compartment cell fitted with a consumable Al anode and a nickel foam cathode [25,26] the allyl halide **1** (1 mmol) and HBpin (3 mmol) were added to a distilled THF solution (20 mL) containing $(CF_3SO_2)_2NLi$ (7×10^{-1} M), under nitrogen atmosphere. The electrolysis was carried out at room temperature and at constant current density ($i = 0.03$ A, $j = 0.15$ A dm^{-2}), the charge involved during the electrochemical process being calculated by the time of the electrolysis. After 2–3 F mol^{-1} electrolysis, the solvent was evaporated under vacuum. The crude reaction mixture was hydrolysed with water (50 mL) and extracted with Et_2O (3× 50 mL). The organic phases were washed with distilled water, then with saturated aqueous NaCl solution, dried over magnesium sulphate and concentrated under vacuum. Boronic esters were purified by column chromatography on silica-gel with petroleum ether-diethyl ether mixtures as the eluents. The ^{1}H and ^{13}C NMR spectra were recorded with BRUKER AC 200 in $CDCl_3$. Mass spectra were recorded on selective mass detector HP 5971 (electronic impact 70 eV).

(*E*)-2-(3,7-dimethylocta-2,6-dienyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, (*E*)-2a mixture with **(*Z*)-2a** (83:17): ^{1}H NMR: $\delta = 1.24$ (s, 12H), 1.58–1.61 (m, 8H), 1.68–1.69 (m, 3H), 1.98–2.08 (m, 4H), 5.08–5.13 (bt, 1H), 5.23–5.26 (bt, 1H) ppm; ^{13}C NMR: $\delta = 16.3$, 18.1, 25.1, 26.8, 27.2, 40.1, 83.4, 118.9, 124.9, 131.5, and 135.5 ppm; MS: *m*/*z* (%): 264 (M^+, 2), 221 (34), 95 (24), 83 (100), 69 (32), 41 (31).

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2-(3,7-dimethylocta-1,6-dien-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, 3a: ^{1}H NMR: δ = 0.76 (s, 3H), 1.24 (s, 12H), 1.59–1.61 (m, 3H), 1.67–1.69 (m, 3H), 1.91–1.98 (m, 2H), 2.00–2.08 (m, 2H), 4.92–4.96 (m, 2H), 5.08–5.14 (bt, 1H), 5.89 (dd, J = 17.5 Hz, 10.5 Hz, 1H) ppm; ^{13}C NMR, δ = 16.3, 18.1, 19.9, 25.0, 38.7, 83.4, 111.4, 125.4, and 145.6 ppm; MS: m/z (%): 264 (M^+, 1), 95 (23), 83 (100), 69 (34), 41 (36).

(*E*)-2-cinnamyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, (*E*)-2c, mixture with **3c** (82:18): ^{1}H NMR: δ = 1.24 (s, 12H), 1.55–1.65 (m, 2H), 6.25–6.40 (m, 2H) ppm; ^{13}C NMR: δ = 24.9, 83.6, 125.6, 126.3, 127.0, 127.1, 128.9, and 136.2 ppm; MS: m/z (%): 244 (M^+, 21), 126 (29), 117 (98), 91 (100), 83 (53), 41 (33).

2-(1-phenylallyl)-1,3,2-dioxaborolane-4,4,5,5-tetramethyl, 3c: ^{1}H NMR: δ = 1.24 (s, 12H), 1.55–1.65 (m, 1H), 5.00–5.10 (m, 2H), 6.02–6.15 (m, 1H) ppm; MS: m/z (%): 244 (M^+, 85), 217 (63), 145 (52), 117 (100), 105 (63), 91 (90), 83 (46).

2-(3-methylbut-2-enyl)-1,3,2-dioxaborolane-4,4,5,5-tetramethyl, 2e, mixture with **3e** (87:13): ^{1}H NMR, δ = 1.23 (s, 12H), 1.58 (s, 3H), 1.58–1.61 (m, 2H), 1.69 (s, 3H), 5.22 (m, 1H) ppm; ^{13}C NMR, δ = 18.0, 23.8, 25.1, 26.1, 83.5, 118.9, and 131.8 ppm; MS: m/z (%): 196 (M^+, 36), 139 (76), 101 (35), 84 (100), 69 (61), 55 (56), 41 (83).

2-(2-methylbut-3-en-2-yl)-1,3,2-dioxaborolane-4,4,5,5-tetramethyl, 3e: ^{1}H NMR: δ = 1.23 (s, 12H), 1.23–1.30 (m, 6H), 4.85–4.94 (m, 2H), 5.88–6.02 (m, 1H) ppm; MS: m/z (%): 196 (M^+, 9), 139 (92), 111 (22), 101 (33), 95 (42), 84 (92), 69 (85), 55 (67), 41 (100).

2-(cyclohex-2-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, 2f: ^{1}H NMR, δ = 1.24 (s, 12H), 1.50–1.90 (m, 5H), 1.95–1.99 (m, 2H), 5.67 (m, 2H) ppm; ^{13}C NMR, δ = 22.9, 24.5, 24.9, 25.0–25.2, 25.3, 83.5, 126.4, and 128.0 ppm; MS: m/z (%): 208 (M^+, 3), 84 (100), 81 (74), 79 (64), 41 (27).

(*E*)-2-hex-2-enyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, (*E*)-2g, mixture with **3g** (85:15): ^{1}H NMR: δ = 0.86 (t, J = 7.2 Hz, 3H), 1.23 (s, 12H), 1.20–1.50 (m, 2H), 1.64 (bs, 2H), 1.90–2.10 (m, 2H), 5.30–5.50 (m, 2H) ppm; ^{13}C NMR: δ = 14.0, 23.1, 25.1, 30.1, 35.2, 83.5, 125.2, and 131.2 ppm; MS: m/z (%): 210 (M^+, 8), 84 (100), 69 (36), 55 (37), 41 (49).

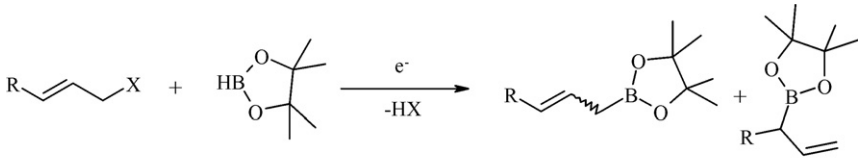
2-(hex-1-ene-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, 3g: ^{1}H NMR: δ = 0.86 (t, J = 7.2 Hz, 3H), 1.23 (s, 12H), 1.20–1.50 (m, 4H), 1.60–1.70 (m, 1H), 4.90–5.00 (m, 2H), 5.70–5.90 (m, 1H) ppm; ^{13}C NMR: δ = 14.5, 22.5, 25.1, 30.1, 83.5, 113.5, and 143.5 ppm; MS: m/z (%): 210 (M^+, 1), 153 (42), 84 (100), 69 (54), 55 (63), 41 (85).

(*E*)-2-(oct-2-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, (*E*)-2h, mixture with **3h** (90:10): ^{1}H NMR: δ = 0.86 (m, 3H), 1.10–1.40 (m, 18H), 1.60–1.70 (m, 2H), 1.90–2.10 (m, 2H), 5.30–5.50 (m, 2H) ppm; ^{13}C NMR: δ = 14.5, 22.9, 29.7, 30.1, 31.7, 33.1, 83.5, 125.0, and 131.5 ppm; MS: m/z (%): 238 (M^+, 5), 84 (100), 69 (24), 55 (32), 41 (41).

2-(oct-1-ene-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, 3h: ^{1}H NMR: δ = 0.86 (m, 3H), 1.10–1.40 (m, 18H), 1.55–1.70 (m, 1H), 4.88–5.01 (m, 2H), 5.65–5.86 (m, 1H) ppm; MS: m/z (%): 238 (M^+, 2), 181 (43), 84 (100), 69 (37), 55 (47), 41 (58).

3. Results and discussion

The general reaction is presented in Eq. (1) and concerns the electroreductive functionalization of an allylic halide **1** (bromide or chloride) in the presence of pinacolborane (HBpin) as the borating agent. The preparative electrolyses were carried out in a single-compartment cell fitted with a consumable anode [26,27]:



1 **2** (*E*, *Z*) **3** (1)

The boration of non-symmetrical allyl halides such as **1** can give rise to two regioisomeric pinacol borates **2** and **3**. In addition, boronic ester **2** may present *E*/*Z* stereochemistry.

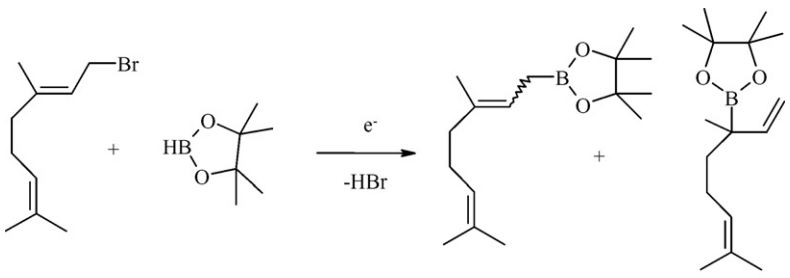
Previous studies indicated that in electrochemical borations, HBpin afforded superior results as compared to the use of trialkylborates such as $B(OMe)_3$ or $B(Oi\text{-}Pr)_3$ [24]. Moreover, the use of HBpin may directly afford the corresponding pinacol boronic esters, which are easier compounds to isolate and purify than the corresponding boronic acids.

The optimisation studies were carried out with geranyl bromide **1a** as the model substrate (Eq. (2)), and the most representative results are presented in Table 1:

Table 1
Electroboration of **1a** in the presence of pinacolborane[a].

Entry	Anode/cathode	F mol^{-1}	Current density (10^{-3} A cm^{-2})	Conversion of **1a**	Yield of boration **2a** + **3a**	Ratio **2a**:**3a**	*E*/*Z* ratio of **2a**
1[b]	Mg/Ni	2	1.5	100%	44%	64:36	(90/10)
2	Mg/Ni	2	1.5	100%	67%	75:25	(92/8)
3	Al/Ni	2	1.5	80%	70%	81:19	(65/35)
4	Zn/Ni	2	1.5	95%	5%	40:60	(65/35)
5	Al/stainless steel	2	1.5	100%	61%	81:19	(82/18)
6	Al/C	2	1.5	94%	25%	74:26	(100/–)
7	Al/Ni	3	1.5	100%	76%	93:7	(63/37)
8	Al/Ni	3	2.3	100%	81%	90:10	(70/30)
9	Al/Ni	3	3	100%	71%	89:11	(68/32)

[a] See general electrolysis conditions. Reaction carried out in THF-TFSILi with slow addition of HBpin (3 equiv.), unless stated.
[b] Addition of HBpin (3 equiv.) at the beginning of the electrolysis.



1a **2a** (*E*, *Z*) **3a** (2)

In a first reaction, the electrolysis of **1a** was run in the presence of 3 equiv. of pinacolborane in THF at room temperature, with Mg/Ni as the couple of electrodes (entry 1). The use of DMF or MeCN was not convenient for these reactions, due to the fact that some solvent reduction occurs in the presence of pinacolborane. As supporting electrolyte, lithium bis(trifluoromethanesulfonyl)imide [$(CF_3SO_2)_2NLi$ or TFSILi] was used, for its high solubility in the THF medium. The reaction monitoring was done by GC. After 2 F mol^{-1}, the consumption of **1a** was of 100% and geranylboronic esters **2a** and **3a** were formed in 44% yield with a **2a**:**3a** ratio of 64:36. The main by-products resulted from the dimerisation of **1a**; R–R products were reductively formed from R–Br in 39% yield. To reduce the formation of such undesired dimers, the electroboration was next run with a slow addition of the substrate during the electrolysis time (2 h). The yields of the coupling products **2a** and **3a** was raised to 67%, with a **2a** to **3a** ratio of 75:25 and a (*E*/*Z*) stereoselectivity for **2a** of 92/8 (entry 2). The amount of R–R dimers was reduced to 22%.

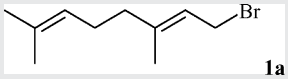
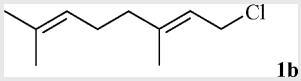
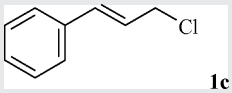
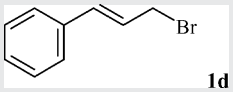
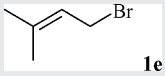
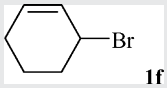
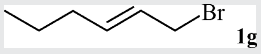
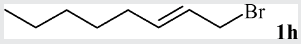
The influence of the anode was examined by using magnesium, aluminum and zinc (entries 2–4). The aluminum anode afforded the best yield of boration of 70%, with a **2a** to **3a** ratio of 81:19. The (*E*/*Z*) stereoselectivity for **2a** was of 65/35. The use of a zinc anode resulted in a low yield of boration with a high ratio of protohehalogenation of **1a**.

With an Al anode, the influence of the nature of the cathode was examined with stainless steel, carbon fiber and nickel foam, with the results shown in entries 3, 5 and 6. The best yields were obtained with Al/Ni electrode combination (entry 3). It is to note that with Al/C as the electrodes (entry 6), although the yield of coupling was only of 25%, the borate **2a** was found exclusively as the (*E*)-isomer.

With Al/Ni as the couple of electrodes, the increase of the amount of current to 3 F mol^{-1} of **1a** allowed its complete consumption with 76% of boration (entry 7). The further change of the current density from 1.5 to 3×10^{-3} A cm^{-2} (intensity from 30 to 60 mA, entries 7–9), gave the best results with an intermediate 0.23×10^{-3} A cm^{-2} current density (entry 8), with a yield of boration of 81% and a **2**:**3** ratio of 90:10. The (*E*/*Z*) stereoselectivity for **2a** resulted in 70/30.

Under the optimised conditions (Table 1, entry 8), the electrochemical boration methodology was then extended to a series of differently substituted allyl chlorides and bromides, and the results are summarised in Table 2.

Table 2
Electrosynthesis of allylboronic pinacol esters from allyl halides and pinacolborane.

Entry	Substrate	Products ratio	*E*/*Z* ratio of **2**	Boration yield (**2** + **3**)
1	 **1a**	**2a:3a**, 90:10	70/30	81%
2	 **1b**	**2a:3a**, 91:9	74/26	86%
3	 **1c**	**2c:3c**, 84:16	96/4	70%
4	 **1d**	**2c:** 7%, **4d:** 90% ($PhCH=CHCH_2)_2$	–	7%
5	 **1e**	**2e:3e**, 79:21	–	76%
6	 **1f**	**2f**	–	65%
7	 **1g**	**2g:3g**, 83:17	100/–	74%
8	 **1h**	**2h:3h**, 68:32	100/–	64%

The electrochemical boration of geranyl chloride **1b** (entry 2) led to similar results as those obtained for bromide **1a**. Boration of **1b** occurred in an overall yield of 86% with a **2a**:**3a** ratio of 91:9. For major regioisomer **2a**, the stereoisomer (*E*/*Z*) ratio was of 74/26.

In contrast, the electrochemical boration of cinnamyl chloride **1c** and cinnamyl bromide **1d** resulted in very different results (entries 3 and 4). Whereas **1c** led to a 70% boration yield with formation of **2c** and **3c** in a 86:16 ratio, the corresponding **2c:3c** was only obtained in 7% yield from bromide **1d**. In this case, the reaction led mainly to the formation of dimer **4d,** [$(PhCH=CHCH_2)_2$], obtained in 90% yield.

Prenyl bromide **1e** afforded borated regioisomers **2e** and **3e** in 76% yield and a 79:21 ratio, respectively (entry 5). The electroboration of 2-cyclohexenyl bromide **1f** afforded a single isomer **2f**, which was isolated in 65% yield (entry 6). The bromoallyl derivative **1g** gave a mixture of **2g** and **3g** in 74% yield and a relative ratio of 83:17 (entry 7). Pinacol ester **2g** was of (*E*)-configuration. Similarly, 1-bromo-2-octene, **1h**, afforded the main boration at the terminal position, with a **2h**:**3h** ratio of 68:32 and an overall yield of 64%. Derivative **2h** was also of (*E*)-configuration.

4. Conclusion

In conclusion, the electrochemical boration of allyl halides with pinacolborane was examined with several examples and led generally to good yields. The electrosynthesis may therefore constitute an interesting synthetic alternative to conventional methods.

The procedure is simple, affords generally good yields with either chlorides or bromides (64–86%), does not need organometallic catalysis and works under mild conditions (room temperature), in a one-step reaction. Among the two possible allylic regioisomers, the less hindered terminal borated compound **2** is obtained preferentially with selectivities of 68–91%; the (*E*)-derivative being the predominant or exclusive stereoisomer.

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