Electronic Supplementary Material (ESI) for Chemical Communications

A practical electromediated *ipso*-hydroxylation of aryl and alkyl boronic acids under air atmosphere

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1. General methods

NMR spectra were acquired on a Varian AS 400 spectrometer, running at 400 MHz for ^{1}H and 100 MHz for ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^{1}H NMR, $CDCl_3$, 77.0 ppm for ^{13}C NMR). The following abbreviations are used to indicate the multiplicity in NMR spectra: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal. Deuterium-exchangeable proton signals (OH signals) are omitted for clarity reasons. ^{13}C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded on a micromass LCT spectrometer using electrospray (ES^+) ionization techniques. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or $KMnO_4$ dip. Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification. For flash chromatography (FC) silica gel (SiO_2 60, 230-400 mesh, Fluka) was used. Cyclic voltammetry and controlled-potential experiments were performed using a CH Instruments Electrochemical Analyzer. A Danica Supply (HTPS 150a) apparatus was used for the constant current bulk electrolysis.

2. Constant current bulk electrolysis of boronic acids

General procedure: A H-cell charged with a magnetic stirring bar and boronic acid **1** (for slightly better isolated yields, employ 0.5 mmol of **1**, 20 mM; for better current efficiency, employ 1 mmol of **1**, 40 mM) in 0.1 M Bu_4NBF_4/DMF as electrolyte. A Pt-net and a C-rod was then lowered into the cell as working and counter electrode, respectively. The divided cell was left open to air and a constant current of 5 mA was applied (under gentle stirring in the working cell). The electrolysis was terminated after 16 h (overnight) and the DMF solutions were collected and treated with 30 mL 2 N HCl (cool if necessary). After 5 min of standing, the solution was transferred to a separation funnel and extracted with Et_2O (3 x 50 mL). The combined organic layers was washed twice with brine, dried over Na_2SO_4 and concentrated in *vacuo*. The obtained crude product was subjected to flash chromatography on silica gel to afford the pure products **2**. All physical and spectroscopic data match those reported in literature.[1]

2a - Phenol (Table 2, entry 1)

Following the general procedure compound **2a** was isolated after FC (pentane/EtOAc 10:1 to 4:1) in 81% yield as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.25 (t, J = 7.9 Hz, 2H), 6.92 (t, J = 7.3 Hz, 1H), 6.83 (d, J = 7.6 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$) δ 155.3, 129.7, 120.7, 115.3 ppm.

2b - 4-Iodophenol (Table 2, entry 2)

Following the general procedure compound **2b** was isolated after FC (pentane/EtOAc 10:1 to 4:1) in 79% yield as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.51 (d, J = 9.1 Hz, 2H), 6.62 (d, J = 9.1 Hz, 2H). ^{13}C NMR (CDCl3): δ 155.2, 138.3, 117.8, 82.7 ppm.

2c - *p*-Cresol (Table 2, entry 3)

Following the general procedure compound **2c** was isolated after FC (pentane/EtOAc 10:1 to 4:1) in 71% yield as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.06 (d, J = 8.2, 2H), 6.73 (d, J = 8.2 Hz, 2H), 2.26 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$) δ 152.8, 130.1, 130.0, 115.1, 20.4 ppm.

2d - 3-*iso*-Propoxyphenol (Table 2, entry 4)

Following the general procedure compound **2d** was isolated after FC (pentane/EtOAc 5:1 to 4:1) in 96% yield as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.11 (t, *J* = 7.8 Hz, 1H), 6.47 (m, 1H), 6.43-

[1] (*a*) Y.-Q. Zou, J.-R. Chen, X.-P. Liu, L.-Q. Lu, R. L. Davis, K. A. Jørgensen and W.-J. Xiao, *Angew. Chem. Int. Ed.*, 2012, **51**, 784; (*b*) K. Yang, Z. Li, Z.-Y. Wang, Z.-Y Yao and S. Jiang, *Org. Lett.*, 2011, **13**, 4340; (*c*) G. A. Molander and L. A. Cavalcanti, *J. Org. Chem.*, 2011, **76**, 623.

6.35 (m, 2H), 4.51 (sept., *J* = 6.0 Hz, 1H) 1.32 (d, *J* = 6.0 Hz, 6H) ppm. ^{13}C NMR ($CDCl_3$): δ 159.7, 157.2, 130.5, 108.7, 108.0, 103.7, 70.4, 22.4 ppm.

2e - 2-Hydroxybenzaldehyde (Table 2, entry 5)

Following the general procedure compound **2e** was isolated after FC (pentane/EtOAc 10:1 to 2:1) in 60% yield as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 9.80 (s, 1H), 7.70 (d, *J* =9.6 Hz, 1H), 7.64-7.40 (m, 1H), 7.24-7.10 (m, 1H), 6.55-6.48 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$) δ 190.2, 162.0, 135.7, 131.0, 122.8, 121.9, 116.3 ppm.

2f - 6-Methoxynaphthalen-2-ol (Table 2, entry 6)

Following the general procedure compound **2f** was isolated after FC (pentane/EtOAc 4:1 to 3:1) in 79% yield as a colorless solid. ^{1}H NMR ($CDCl_3$) δ 7.70 (d, J = 8.6 Hz, 1H), 7.64 (d, J = 8.6 Hz, 1H), 7.20–7.11 (m, 4H), 3.95 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$) δ 156.1, 151.8, 129.9, 129.8, 128.5, 127.9, 119.4, 118.1, 109.8, 106.0, 55.4 ppm.

2g - 2-Phenylethanol (Table 2, entry 7)

Following the general procedure compound **2g** was isolated after FC (pentane/EtOAc 10:1 to 4:1) in 92% yield as a pale yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.31-7.27 (m, 2H), 7.23-7.17 (m, 3H), 3.80 (t, J = 6.4 Hz, 2H), 2.82 (t, J = 6.4 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$) δ 138.6, 129.0, 128.4, 126.4, 63.4, 39.0 ppm

2h - Cyclohexanol (Table 2, entry 8)

Following the general procedure compound **2h** was isolated after FC (pentane/Et_2O 4:1 to 1:1) in 60% yield as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 3.62-3.50 (m, 1H), 1.94-1.78 (m, 2H), 1.77-1.62 (m, 2H), 1.57-1.46 (m, 1H), 1.30-1.10 (m, 5H) ppm. ^{13}C NMR ($CDCl_3$) δ 70.3, 35.4, 25.4, 24.2 ppm.

2i - 4-Hydroxy-*N*,*N*-dimethylbenzamide (Table 2, entry 12)

A modified workup protocol was employed for this substrate. After 16 h of reaction, the electrolysis was stopped and the reaction was quenched with 2 N HCl (as described in the general procedure). The mixed DMF/HCl solution was then transferred to a separation funnel and extracted with EtOAc (3 x 50 mL). The combined organic layers was washed twice with brine

and dried over Na_2SO_4. Excess solvents were reduced under high vacuum at 50 ºC and the yield of **2i**[2] was determined by ^{1}H NMR spectroscopy with an internal standard (*t*BuOMe).

[2] R. Eckardt, E. Carstens and W. Friedler, *Pharmazie*, 1975, **301**, 633.

3. Electrochemical experiments

CV experiments of oxygen reduction in the presence of phenylboronic acid (**1a**):

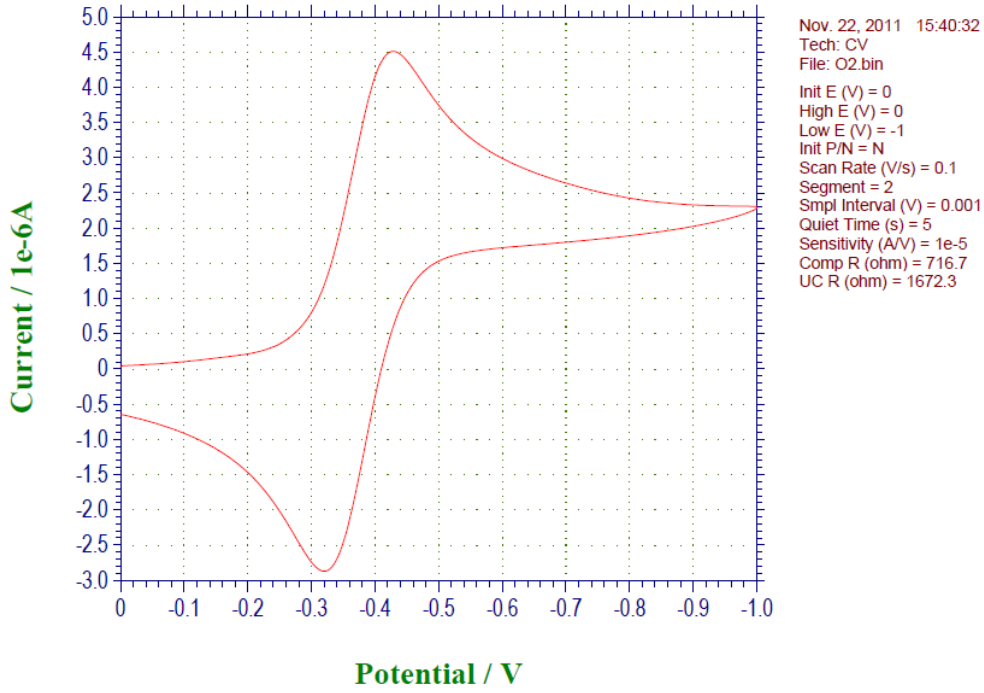


Figure 1. [1a] = 0 mM.

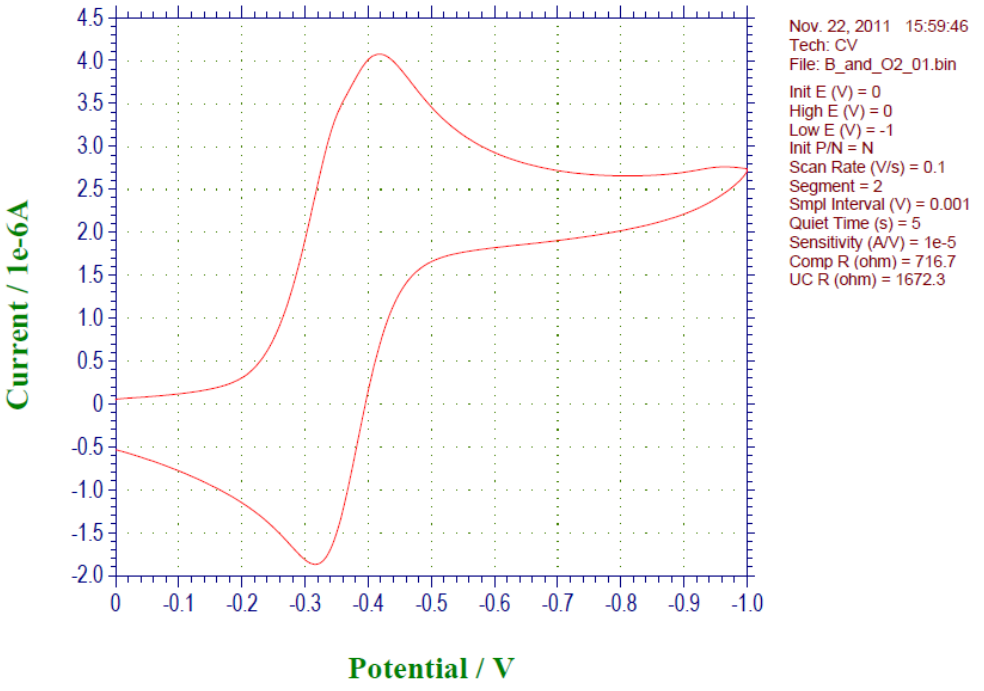


Figure 2. [1a] = 1 mM.

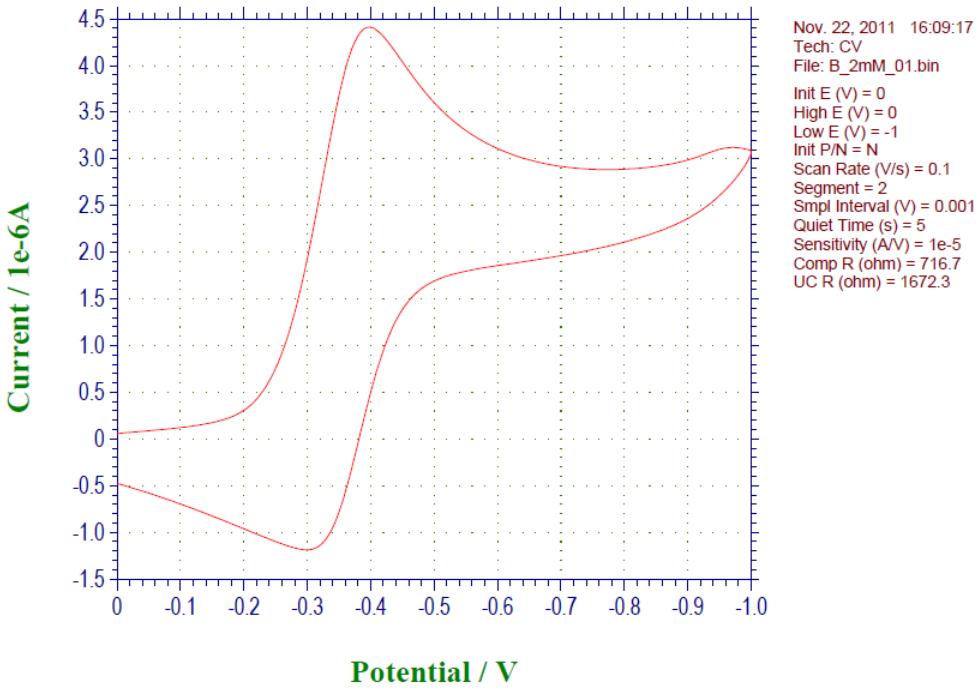


Figure 3. [1a] = 2 mM.

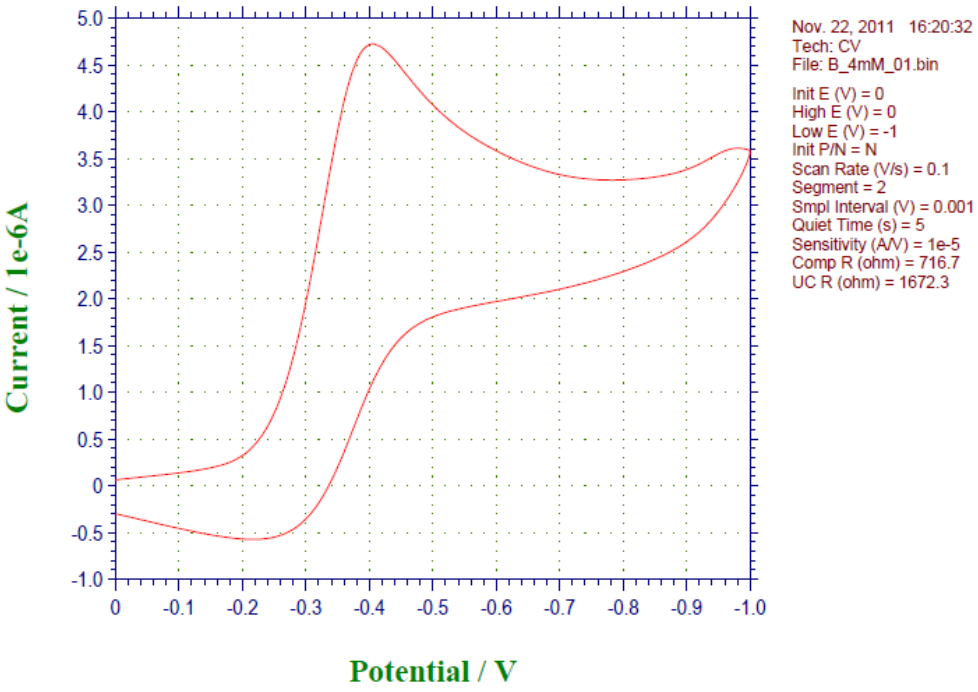
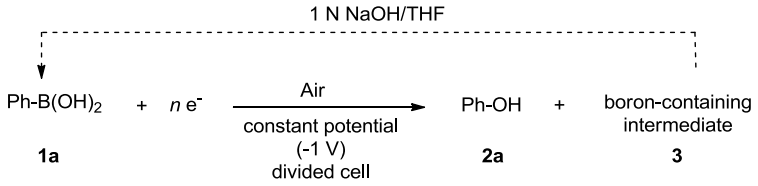


Figure 4. [1a] = 4 mM.

Procedure: In a CV cell open to air atmosphere was added 10 mL of an electrolyte (0.1 M Bu_4NBF_4/DMF) containing phenylboronic acid (**1a**) at different concentrations (0, 1, 2, 4 mM).

The solution was saturated with air by briefly bubbling a flow of air through the media. CV spectra were recorded using glassy carbon as the working electrode, Pt as the counter electrode and Ag/AgI as the reference. As depicted in Figure 1, the anodic peak is increasingly suppressed by raising the concentration of **1a**.

Controlled-potential electrolysis:



n e⁻	**1a** : **2a** : **3** ratio
1 F/mol	63 : 27 : traces
2 F/mol	traces : >70 : <30
3 F/mol	<5 : >90 : <5

A H-cell was filled with 0.1 M Bu_4NBF_4 in DMF as electrolyte, herein 25 mL in the working cell, which was also charged with a magnetic stirring bar and 0.1 mmol of phenylboronic acid **1a** (4 mM concentration). A Pt-net and Ag/AgI electrode were then lowered into the working cell as the working and reference electrode, respectively, while a C-rod was employed as the counter electrode. Electrolysis was carried out with a constant potential of -1 V. After the application of 9.65, 19.3 or 28.94 C (corresponding to 1, 2 and 3 electrons per molecule) the electrolysis was aborted. The solution was stirred for an additional 16 h, worked up following the general procedure and analysed by ^{1}H-NMR spectroscopy.