C–H Activation/Borylation/Oxidation: A One-Pot Unified Route To Meta-Substituted Phenols Bearing Ortho/Para-Directing Groups

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Supporting Information

Methods:

All substrates are subject to purification before use. Solid substrates were sublimed under vacuum. Liquid substrates were stirred or refluxed, depending on the boiling points, over Na, CaH₂, or molecular sieves (4Å) overnight, distilled, and degassed. Cyclohexane was purchased from Aldrich, washed with concentrated H₂SO₄ until the acid layer was colorless. Water and saturated NaHCO₃ solution washes then followed until the water wash was neutral. The cyclohexane was then dried over MgSO₄ before being refluxed over Na, distilled, and degassed. *n*-Hexane was purchased from Baker Inc., refluxed over Na, distilled, and degassed. Pinacolborane (H–BPin) was purchased from Aldrich, stirred over PPh₃ overnight, vacuum transferred into an air-free flask and brought into a dry box. B₂Pin₂ was purchased from Frontier Scientific Discovery Chemicals and used without purification. 1,2-Bis(dimethylphosphino)ethane (dmpe) and 1,2-bis(diphenylphosphino)ethane (dppe) were purchased from Strem and d'pby (4,4'-di-*tert*-butyl-2,2'-bipyridine) from Aldrich. These ligands were used as received. (Ind)Ir(COD) (Ind = indenyl, COD = 1,5-cyclooctadiene) and [Ir(OMe)(COD)]₂ were prepared per literature procedures.^{1,2} Oxone[®] was purchased from Aldrich as 2KHSO₅•KHSO₄•K₂SO₄ and was used as a ~0.3 mol/L aqueous solution. Reagent grade acetone was purchased from CCI and used without purification. (Note: technical grade acetone also worked well.) All borylation reactions were carried out in oven-dried thick-walled air-free flasks, magnetically stirred, and monitored by Varian CP-3800 GC-FID (column type: WCOT Fused silica 30m*0.25mm ID coating CP-SIL 8 CB). Silica gel was supplied by Silicycle as 60 Å (230-400 Mesh). Yields refer to isolated material and have been corrected to discount the added weight of trapped residual solvent. All spectral data reported was obtained from solvent free material. Infrared spectra were obtained on a Nicolet IR/42 spectrometer; ¹H NMR and ¹³C NMR spectra were recorded on a Varian Gemini-300 or a Varian VXP-500 spectrometer (300, 500 MHz for ¹H, respectively, and 75, 125 MHz for ¹³C, respectively), with chemical shifts reported relative to the residue peaks of solvent chloroform (δ 7.24 for ¹H and 77.0 for ¹³C) or acetone (δ 2.04 for ¹H and 29.8 for ¹³C). Melting points were measured on a Thomas-Hoover

capillary melting point apparatus and are uncorrected; GC-MS were recorded by HP 5890 Series II GC with SPB-1 non-polar column, in series with a Trio-1 mass spectrometer; high-resolution mass spectra were obtained at Michigan State University Mass Spectrometry Service Center with a JOEL-AX505 mass spectrometer (resolution 7000); preparative GC was performed with a Varian 920 GC-TCD with packed C₁₈ column. Combustion analyses were performed on a Perkin Elmer Series II 2400 CHNS/O analyzer.

General Procedure:

In a dry box, arene (1.0 mmol), HBPIn (1.5-2.5 mmoles), (Ind)Ir(COD) (8.3 mg, 0.02 mmol, 2 mol %), and dmpe (3.0 mg, 0.02 mmol, 2 mol %) or dppe (8.0 mg, 0.02 mmol, 2 mol %) were transferred into an air-free flask equipped with a stirrer bar. (In cases where cyclohexane was used as a solvent, the reagents were dissolved in 1 mL cyclohexane, and transferred to the air-free flask.) The flask was sealed and brought out of the dry box and placed in an oil bath heated to 150 °C (dmpe) or 100 °C (dppe) until the reaction was judged complete by GC-FID. At that time the reaction was allowed to cool to room temperature. If solvent was used it was removed under reduced pressure. To the crude material (usually a dark orange or brown gel-like liquid or a solid) was added 3.2 mL acetone. After stirring produced a homogeneous solution, an aqueous solution of oxone[®] (6.15 g, 1.0 mmol in 3.2 mL) was added dropwise over 2-4 min. Upon complete addition, the reaction mixture was vigorously stirred for 7 minutes. At that time the reaction was quenched with aqueous NaHSO₃. A layer of dark orange oil was observed. The reaction mixture was extracted three times with ether or CH₂Cl₂. The combined organics were washed with brine followed by water, and concentrated in vacuo. The crude material was dissolved in CH₂Cl₂ or pentane/ether and passed through a plug of silica gel. Evaporation afforded the phenol.

(Note: In the cases of multiple borylations (Tables 1, Entries 15-16), periodic cooling and purging of the H₂ gas formed during that step of the sequence helps to maintain an effective rate of reaction.)

Experimental details, spectroscopic data, and comparisons to previous methods:

3-Bromo-5-chlorophenol³ (1): The general procedure was applied to 3-bromochlorobenzene (192 mg, 1.0 mmol). The borylation step was carried out neat with HBPIn (250 mg, 1.95 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 3.5

hours. The oxidation step was then carried out as described above, after which the crude material was

dissolved in CH_2Cl_2 and passed through a plug of silica gel. Evaporation of solvent gave 183 mg of a white solid containing 171 mg (82%) of **1** and 12 mg of trapped acetone (by ^1H NMR). Preparative GC at 160 °C afforded analytically pure **1** as a white solid; mp 66–68 °C (lit.^{3a} 70). ^1H NMR (300 MHz, CDCl_3): δ 7.08 (t, J = 1.65 Hz, 1 H), 6.89 (dd, J = 2.2, 1.65 Hz, 1 H), 6.78 (t, J = 2.1 Hz, 1 H), 5.0–5.1 (brs, 1 H); ^{13}C NMR (75 MHz, CDCl_3): δ 156.7, 135.6, 124.0, 122.9, 117.9, 115.0; IR (neat): 3293, 1578, 1435, 914, 775 cm^{-1} ; LRMS m/e 206 (M^+), 127, 99. Anal. Calcd for $\text{C}_6\text{H}_4\text{BrClO}$: C, 34.74; H, 1.94. Found C, 34.87; H 2.03.

3,5-Dibromophenol⁴ (2): The general procedure was applied to a solution of 1,3-dibromobenzene (236 mg, 1.0 mmol) in 1.0 mL cyclohexane. The borylation step was carried out with HBPin (256 mg, 2 mmol) and dppe (8.0 mg, 0.02 mmol, 2 mol %) at 100 °C for 18 hours.⁵ After removal of cyclohexane, the oxidation step was then performed as described above, after which the crude material was dissolved in CH_2Cl_2 and passed through a plug of silica gel. Evaporation of solvent gave 250 mg material containing 227 mg phenol **2** (90%), 12 mg water, and 11 mg acetone (by ^1H NMR). Sublimation at 55 °C under 0.08 mm Hg afforded analytically pure **2** as a white solid; mp 78–80 °C (lit.^{4b} 81). ^1H NMR (300 MHz, CDCl_3): δ 7.23 (t, J = 1.4 Hz, 1 H), 6.94 (d, J = 1.4 Hz, 2 H), 4.82 (s, 1 H); ^{13}C NMR (75 MHz, CDCl_3): δ 156.7, 126.7, 123.1, 117.8; IR (neat): 3233, 1576, 1421, 841, 752 cm^{-1} ; LRMS: m/e 250 (M^+), 171, 143. Anal. Calcd for $\text{C}_6\text{H}_4\text{Br}_2\text{O}$: C, 28.61; H, 1.60. Found C, 28.98; H, 1.52.

3-Bromo-5-methylphenol⁷ (3): The general procedure was applied to 3-bromotoluene (171 mg, 1.0 mmol). The borylation step was carried out neat with HBPin (200 mg, 1.55 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 12 hours.

The oxidation step was then performed as described above, after which the crude material was dissolved in CH_2Cl_2 and passed through a plug of silica gel. Evaporation of solvent gave 174 mg material containing 146 mg phenol **3** (78%), 11 mg CH_2Cl_2 , and 17 mg acetone. Preparative GC at 150 °C afforded analytically pure **3** as a white solid; mp 55–57 °C (lit.⁷ 52). ^1H NMR (300 MHz, CDCl_3): δ 6.89 (s, 1 H), 6.80 (s, 1 H), 6.56 (s, 1 H), 4.67 (s, 1 H), 2.26 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3): δ 156.0, 141.4, 124.7, 122.4, 115.8, 115.0, 21.1; IR (neat): 3297, 1579, 1366, 1273, 822 cm^{-1} ; LRMS: m/e 186 (M^+), 107, 77. Anal. Calcd for $\text{C}_7\text{H}_7\text{BrO}$: C, 44.95; H, 3.77. Found C, 45.21; H, 3.93.

3-Chloro-5-methoxyphenol⁸ (4): The general procedure was applied to 3-chloroanisole (143 mg, 1.0 mmol). The borylation step was carried out neat with HBPin (256 mg, 2 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 18 hours. The oxidation step was then performed as described above, after which the crude material was dissolved in CH₂Cl₂ and passed through a plug of silica gel. Evaporation of solvent gave 148 mg material containing 121 mg phenol **4** (76%), 7 mg CH₂Cl₂, and 20 mg acetone. Preparative GC at 170 °C afforded analytically pure **4** as a white solid; mp 94–96 °C.⁸ ¹H NMR (300 MHz, CDCl₃): δ 6.48 (t, *J* = 2.2 Hz, 1 H), 6.43 (t, *J* = 2.2 Hz, 1 H), 6.27 (t, *J* = 2.2 Hz, 1 H), 4.81 (s, 1 H), 3.75 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 161.3, 157.0, 135.4, 108.6, 107.3, 100.4, 55.5; IR (neat): 3378, 1597, 1159 cm⁻¹; LRMS: *m/e* 158 (M⁺), 128. Anal. Calcd for C₇H₇ClO₂: C, 53.02; H, 4.45. Found C, 52.88; H, 4.81.

Methyl 3-Chloro-5-hydroxybenzoate⁹ (5): The general procedure was applied to methyl 3-chlorobenzoate (171 mg, 1.0 mmol). The borylation step was carried out neat with HBPin (200 mg, 1.55 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 3 hours.⁵ The oxidation step was then performed as described above, after which the crude material was dissolved in ether and passed through a plug of silica gel (pentane/ether 2:1). Evaporation of solvent gave 134 mg phenol **5** (72%) with trace water. Sublimation at 85 °C under 0.06 mm Hg afforded analytically pure **5** as a white solid; mp 133–135 °C (lit.⁹ 138–139). ¹H NMR (300 MHz, acetone-*d*₆): δ 9.2 (brs, 1 H), 7.43 (t, *J* = 1.7 Hz, 1 H), 7.40 (dd, *J* = 2.2, 1.7 Hz, 1 H), 7.10 (t, *J* = 2.2 Hz, 1 H), 3.87 (s, 3 H); ¹³C NMR (75 MHz, acetone-*d*₆): δ 165.9, 159.3, 135.3, 133.8, 121.0, 120.6, 115.7, 52.7; IR (neat): 3335, 1690, 1591, 1431, 1350, 1242, 768 cm⁻¹; LRMS: *m/e* 186 (M⁺), 155, 127, 99. Anal. Calcd for C₈H₇ClO₃: C, 51.50; H, 3.78. Found C, 51.78; H, 3.73.

2,6-Dichloro-4-pyridinol¹⁰ (6): The general procedure was applied to 2,6-dichloropyridine (148 mg, 1.0 mmol). The borylation step was carried out with HBPin (200 mg, 1.55 mmol, 1.55 equiv.) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C in cyclohexane for 3 hours.⁵ The oxidation step was then performed after removal of cyclohexane as described above, after which the crude material was dissolved in ether and passed through a plug of silica

gel (pentane/ether 2:1). Evaporation of solvent gave 145 mg material containing 108 mg phenol **6** (66%) and 37 mg water. Sublimation at 110 °C under 0.1 mmHg afforded analytically pure **6** as a white solid; mp 201–202 °C.¹⁰ ¹H NMR (300 MHz, acetone-*d*₆): δ 10.48 (brs, 1 H), 6.88 (s, 2 H); ¹³C NMR (75 MHz, acetone-*d*₆): δ 168.3, 151.5, 111.5; IR (KBr): 3200~2500 (br), 1597, 1576, 1554, 1427, 1294, 1211, 1157, 1092, 993, 966, 847 cm⁻¹; LRMS: *m/e* 163 (M⁺), 128, 100. Anal. Calcd for C₅H₃Cl₂NO: C, 36.62; H, 1.84; N, 8.54. Found C, 36.63; H, 1.98, N, 8.52.

3,4-Dichloro-5-methylphenol¹¹ (**7**): The general procedure was applied to 2,3-dichlorotoluene (161 mg, 1.0 mmol). The borylation step was carried out neat with HBPin (256 mg, 2 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 12 hours.

The oxidation step was then performed as described above, after which the crude material was dissolved in CH₂Cl₂ and passed through a plug of silica gel. Evaporation of solvent gave 154 mg material containing 147 mg phenol **7** (83%) and 7 mg water. Sublimation at 70 °C under 0.07 mmHg afforded analytically pure **7** as a white solid; mp 98–100 °C. ¹H NMR (300 MHz, CDCl₃): δ 6.81 (d, *J* = 2.2 Hz, 1 H), 6.63 (t, *J* = 2.2 Hz, 1 H), 4.61 (s, 1 H), 2.34 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 153.7, 139.1, 133.0, 124.3, 116.4, 115.0, 21.3; IR (neat): 3285, 1580, 1449, 1285, 1151, 886, 646 cm⁻¹; LRMS: *m/e* 176 (M⁺), 141, 77. Anal. Calcd for C₇H₆Cl₂O: C, 47.49; H, 3.42. Found C, 47.72; H, 3.61.

3,5-Dichloro-4-methylphenol¹² (**8**): The general procedure was applied to 2,6-dichlorotoluene (161 mg, 1.0 mmol). The borylation step was carried out neat with HBPin (200 mg, 1.55 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 12 hours. The

oxidation step was then performed as described above, after which the crude material was dissolved in CH₂Cl₂ and passed through a plug of silica gel. Evaporation of solvent gave 176 mg material containing 156 mg phenol **8** (88%), 14 mg water, and 6 mg acetone. Sublimation at 70 °C under 0.08 mmHg afforded analytically pure **8** as a white solid; mp 92–93 °C.¹² ¹H NMR (300 MHz, CDCl₃): δ 6.79 (s, 2 H), 4.67 (s, 1 H), 2.34 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃): δ 153.5, 135.6, 126.6, 115.2, 16.4; IR (neat): 3333, 1608, 1578, 1238, 947, 839 cm⁻¹; LRMS: *m/e* 176 (M⁺), 141, 105, 84, 77. Anal. Calcd for C₇H₆Cl₂O: C, 47.49; H, 3.42. Found C, 47.65; H, 3.45.

2,6-Dichloro-1,4-hydroquinone¹³ (9): The general procedure was applied to 2,6-dichloroanisole (177 mg, 1.0 mmol). The borylation step was carried out neat with HBPIn (320 mg, 2.5 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 16 hours. The oxidation step was then performed, after which the crude material was dissolved in ether and passed through a plug of silica gel (pentane/ether 2:1). Evaporation of solvent gave 140 mg material containing 120 mg hydroquinone **9** (67%) and 20 mg water. Sublimation at 90 °C under 0.08 mmHg or recrystallization from CH₂Cl₂ afforded analytically pure **9** as a white solid; mp 160–161 °C (lit.¹³ 164). ¹H NMR (300 MHz, acetone-*d*₆): δ 8.43 (brs, 1 H), 8.24 (brs, 1 H), 6.83 (s, 2 H); ¹³C NMR (75 MHz, acetone-*d*₆): δ 150.7, 142.3, 122.3, 115.5; IR (KBr): 3349, 1591, 1482, 1213, 953, 791 cm⁻¹; LRMS: *m/e* 178 (M⁺), 142, 114, 86. Anal. Calcd for C₆H₄Cl₂O₂: C, 40.26; H, 2.25. Found C, 40.58; H, 2.17.

3-Bromo-4,5-dimethylphenol¹⁴ (10): The general procedure was applied to a solution of 3-bromo-*o*-xylene (185 mg, 1.0 mmol) in 1.0 mL cyclohexane. The borylation step was carried out with HBPIn (320 mg, 2.5 mmol) and dppe (8.0 mg, 0.02 mmol, 2 mol %) at 100 °C for 50 hours. After removal of the cyclohexane, the oxidation step was then performed as

described above, after which the crude material was dissolved in CH₂Cl₂ and passed through a plug of silica gel. Evaporation of solvent gave 148 mg pure **10** (74%) as a white wax solid; mp 98–99 °C (lit.^{14b} 101–102). ¹H NMR (300 MHz, CDCl₃): δ 6.91 (d, *J* = 2.5 Hz, 1 H), 6.59 (d, *J* = 2.7 Hz, 1 H), 2.25 (s, 6 H); ¹³C NMR (75 MHz, CDCl₃): δ 153.2, 139.3, 128.3, 125.2, 116.9, 116.2, 21.4, 18.3; IR (neat): 3252, 2919, 1606, 1576, 1477, 1451, 1279, 1119, 839 cm⁻¹; LRMS: *m/e* 200 (M⁺), 185, 121, 91; HRMS (EI): *m/z* 199.9839 [(M⁺); calcd for C₈H₉BrO: 199.9837].

4-Bromo-3,5-dichlorophenol¹⁵ (11): The general procedure was applied to a solution of 1-bromo-2,6-dichlorobenzene (226 mg, 1.0 mmol) in 1.0 mL cyclohexane. The borylation step was carried out with HBPIn (256 mg, 2 mmol, 2 equiv.) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 3.5 hours. After removal of solvent, the oxidation step was then performed as described above, after which the crude material was dissolved in CH₂Cl₂ and passed through a plug of silica gel. Evaporation of solvent gave 260 mg material containing 197 mg phenol **11** (81%), 31

mg CH₂Cl₂, and 32 mg acetone. Sublimation at 90 °C under 0.30 mmHg afforded analytically pure **11** as a white solid; mp 117–119 °C.¹⁵ ¹H NMR (300 MHz, CDCl₃): δ 6.90 (s, 2 H), 4.86 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ 154.8, 136.5, 116.2, 114.4; IR (neat): 3366, 1570, 1412, 1129, 845 cm⁻¹. LRMS: *m/e* 240 (M⁺), 162; HRMS (EI): *m/z* 239.8751 [(M⁺); calcd for C₆H₃Cl₂BrO: 239.8744].

3,4,5-Trichlorophenol¹⁶ (**12**): The general procedure was applied to a solution of 1,2,3-trichlorobenzene (182 mg, 1.0 mmol) in 1.0 mL cyclohexane. The borylation step was carried out with HBPIn (226 mg, 1.8 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol%) at

150 °C for 3 hours. After removal of solvent, the oxidation step was then performed as described above, after which the crude material was dissolved in CH₂Cl₂ and passed through a plug of silica gel. Evaporation of solvent gave 212 mg material containing 176 mg phenol **12** (89%), 4 mg CH₂Cl₂, and 32 mg acetone. Sublimation at 70 °C under 0.06 mmHg afforded analytically pure **12** as a white solid; mp 97–99 °C (lit.^{16b} 101). ¹H NMR (300 MHz, CDCl₃): δ 6.89 (s, 2 H), 5.04 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ 154.0, 134.4, 123.3, 116.3; IR (neat): 3312, 1574, 1420, 1144, 947, 818 cm⁻¹; LRMS: *m/e* 196 (M⁺), 160, 133, 97. Anal. Calcd for C₆H₃Cl₃O: C, 36.50; H, 1.53. Found C, 36.73; H, 1.64.

5-Bromo-2-fluorophenol¹⁷ (**13**): The general procedure was applied to 1-bromo-4-fluorobenzene (700 mg, 4.0 mmol). The borylation step was carried out neat with HBPIn (128 mg, 1.0 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 3.5 hours. The

oxidation step was then performed as described above, after which the crude material was dissolved in CH₂Cl₂ and passed through a plug of silica gel. The first fraction collected contained ~500 mg unreacted arene. Evaporation of the second fraction gave 165 mg of material containing 134 mg phenol **13** (70%; H-BPin limiting reagent), 17 mg CH₂Cl₂, and 14 mg acetone. Preparative GC at 110 °C afforded analytically pure **13** as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.12–7.16 (m, 1 H), 6.90–6.96 (m, 2 H), 5.29 (s, 1 H); ¹³C NMR (125 MHz, CDCl₃): δ 150.3 (d, *J* = 239 Hz), 144.4 (d, *J* = 15 Hz), 123.7 (d, *J* = 6 Hz), 120.6, 116.8 (d, *J* = 19 Hz), 116.8 (d, *J* = 3 Hz); IR (neat): 3412, 1611, 1495, 1267 cm⁻¹; LRMS: *m/e* 190 (M⁺), 161, 111, 83. Anal. Calcd for C₆H₄BrFO: C, 37.73; H, 2.11. Found C, 37.58; H, 2.32.

5-Bromo-2-fluororesorcinol¹⁸ (14): The general procedure was applied to a solution of 1-bromo-4-fluorobenzene (175 mg, 1.0 mmol) in 1.0 mL cyclohexane. The borylation step was carried out with HBPIn (580 mg, 4.5 mmol, 4.5 equiv.), (Ind)Ir(COD) (20.6 mg, 0.05 mmol, 5 mol %) and dppe (20.0 mg, 0.05 mmol, 5 mol %) at 110 °C for 53 hours. After removal of solvent, the oxidation step was then performed utilizing 6.5 mL acetone, 6.5 mL aqueous oxone[®] (12.4 g in 6.5 mL, 2 equiv.) at room temperature for 11 min. The crude material was subsequently dissolved in ether and passed through a plug of silica gel (pentane/ether 1.5:1). After evaporation of solvent, the crude product was recrystallized from CH₂Cl₂, giving 165 mg **14** (76%) as a white solid; mp 83–86 °C. *R_f* 0.31 (pentane/ether 2:1). ¹H NMR (300 MHz, CDCl₃): δ 6.72 (d, *J* = 7.1 Hz, 2 H), 5.10 (s, 2 H); ¹³C NMR (75 MHz, acetone-*d*₆): δ 147.5 (d, *J* = 11 Hz), 141.4 (d, *J* = 237 Hz), 115.8 (d, *J* = 5 Hz), 112.3; IR (KBr): 3128, 1617, 1501, 1431, 1331, 1159, 1047 cm⁻¹. LRMS: *m/e* 206 (M⁺), 127, 109, 79; HRMS (EI): *m/z* 205.9378 [(M⁺); calcd for C₆H₄BrFO₂: 205.9379].

2,4,6-Trifluoroglucinol¹⁸ (15): The general procedure was applied to a solution of 1,3,5-trifluorobenzene (132 mg, 1.0 mmol) in 1.0 mL cyclohexane. The borylation step was carried out with HBPIn (640 mg, 5 mmol), (Ind)Ir(COD) (12.5 mg, 0.03 mmol, 3 mol %) and dmpe (4.5 mg, 0.03 mmol, 3 mol %) at 150 °C for 63 hours.⁵ The borylation gives an 1:6 mixture of diborylated and triborylated products. After removal of solvent, the mixture was subjected to the oxidation using 9 mL acetone, 8.5 mL aqueous oxone[®] (17.4 g in 8.5 mL, 2.8 equiv.) at room temperature for 13 min. The crude material was subsequently dissolved in ether and passed through a plug of silica gel (pentane/ether 1:1.5). After evaporation of solvent, the crude product was washed with boiling CH₂Cl₂ and then sublimed at 130 °C under 0.1 mmHg, giving 88 mg **15** (49%) as a slightly yellow solid; mp 260 °C (decomposed). *R_f* 0.43 (pentane/ether 1:1.5). ¹H NMR (300 MHz, acetone-*d*₆): δ 8.66 (brs, 3 H); ¹³C NMR (125 MHz, acetone-*d*₆): δ 137.3 (dt, *J* = 230, 6 Hz) 131.9 (dt, *J* = 14, 5 Hz); IR (KBr): 3324, 1510, 1400–1200 (br), 1132, 980 cm⁻¹; LRMS: *m/e* 180 (M⁺), 151, 104; HRMS (EI): *m/z* 180.0030 [(M⁺); calcd for C₆H₃F₃O₃: 180.0034].

3-Chloro-5-trifluoromethylphenol¹⁸ (16): The general procedure was applied to a solution of 3-chlorobenzotrifluoride (181 mg, 1.0 mmol) in 1.0 mL cyclohexane. The borylation step was carried out with HBPin (200 mg, 1.55 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 3.5 hours. After removal of solvent, the oxidation step was performed as described above, after which the crude material was dissolved in CH₂Cl₂ and passed through a plug of silica gel. Evaporation of solvent gave 185 mg material containing 160 mg phenol **16** (81%) and 25 mg acetone. Preparative GC at 120 °C afforded analytically pure **16** as a colorless oil. *R_f* 0.34 (CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ 7.18 (brs, 1 H), 7.01 (brs, 1 H), 6.96 (brs, 1 H), 5.03 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ 156.5, 135.7, 133.1 (q, *J* = 33 Hz), 123.0 (q, *J* = 273 Hz), 119.2, 118.5 (q, *J* = 4 Hz); IR (KBr): 3384, 1597, 1455, 1335, 1175, 1134, 936 704, 693 cm⁻¹; LRMS: *m/e* 196 (M⁺), 177, 161, 146; HRMS (EI): *m/z* 195.9902 [(M⁺); calcd for C₇H₄ClF₃O: 195.9903].

3-Chloro-5-(dimethylamino)phenol¹⁸ (17): The general procedure was applied to 3-chloro-*N,N*-dimethylaniline (156 mg, 1.0 mmol). The borylation step was carried out neat with HBPin (256 mg, 2 mmol) and dmpe (3.0 mg, 0.02 mmol, 2 mol %) at 150 °C for 18 hours. The oxidation step was then performed at 0 °C for 15 min. The crude material was then passed through a plug of silica gel (pentane/ether 2:1). Evaporation of solvent gave 155 mg material containing 146 mg phenol **17** (85%) and 9 mg ether. Sublimation at 60 °C under 0.10 mmHg afforded analytically pure **17** as a slightly colored solid; mp 86–88 °C. *R_f* 0.30 (pentane/ether, 2:1). ¹H NMR (300 MHz, CDCl₃): δ 6.28 (brs, 1 H), 6.19 (t, *J* = 1.6 Hz, 1 H), 6.03 (t, *J* = 2.2 Hz, 1 H), 5.0-5.3 (brs, 1 H), 2.88 (s, 6 H); ¹³C NMR (75 MHz, CDCl₃): δ 156.8, 152.3, 135.4, 105.6, 104.2, 97.8, 40.4; IR (neat): 3349, 2901, 2812, 1603, 1506, 1443, 1156, 1233, 1019, 916 cm⁻¹; LRMS: *m/e* 171 (M⁺), 170, 128, 99. Anal. Calcd for C₈H₁₀ClNO: C, 55.99; H, 5.87; N, 8.16. Found C, 56.12; H, 5.81; N, 8.11.

3-Bromo-5-iodophenol^{3a} (18): To a solution of 1-bromo-3-iodobenzene (283 mg, 1 mmol) in 5 mL *n*-hexane, was added B₂Pin₂ (154 mg, 0.6 mmol, 1.2 equiv. boron), [Ir(OMe)(COD)]₂ (10.0 mg, 0.015 mmol, 1.5 mol %), and d⁺bpy (8.0 mg, 0.03 mol, 3 mol %).⁶ The mixture was stirred at room temperature for 11 hours. After removal of hexane, the oxidation step was performed as described above. The reaction was extracted with Et₂O (CH₂Cl₂ is to be avoided).

After evaporation of the ethereal layer, the crude material was dissolved in CH₂Cl₂ and passed through a plug of silica gel. Evaporation of solvent gave 244 mg of a solid material containing 236 mg phenol **18** (79%), 5 mg ether, and 3 mg acetone. Sublimation at 50 °C under 0.09 mmHg afforded analytically pure **18** as a white solid; mp 83–84 °C (lit.^{3a} 82.5). ¹H NMR (300 MHz, CDCl₃): δ 7.42 (t, *J* = 1.4 Hz, 1 H), 7.13 (dd, *J* = 1.4, 2.2 Hz, 1 H), 6.96 (dd, *J* = 1.9, 2.2 Hz, 1 H), 4.77 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ 156.4, 132.4, 123.6, 123.2, 118.6, 94.2; IR (neat): 3268, 3071, 1586, 1566, 893, 885, 664 cm⁻¹; LRMS: *m/e* 298 (M⁺), 171, 143. Anal. Calcd for C₆H₄BrIO: C, 24.11; H, 1.35. Found C, 24.26; H, 1.30.

References:

- (1) (a) Merola, J. S.; Kacmarcik, R. T. *Organometallics* **1989**, *8*, 778–784. (b) Crabtree, R. H.; Quirk, J. M. *Synth. React. Inorg. Met.-Org. Chem.* **1982**, *12*, 407–413. (c) Naderer, H.; Siebel, E. *J. Organomet. Chem.* **1996**, *518*, 181–187.
- (2) Uson, R.; Oro, L. A. *Inorg. Synth.* **1985**, *23*, 126–130.
- (3) For a previous preparations see: (a) Hodgson, H. H.; Wignall, J. S. *J. Chem. Soc.* **1926**, 2077–2079 (ten steps from 1,3,5-trinitrotoluene, overall yield not reported). (b) Kohn, M.; Zandman, A. *Montash.* **1926**, *47*, 367–377 (exhaustive bromination of 3-chlorophenol, followed by partial debromination).
- (4) (a) For a previous preparation see: Ishida, Y.; Jikei, M.; Kakimoto, M. *Polymers for Adv. Tech.* **2000**, *11*, 698–704 (debromination of pentabromophenol, 76% yield). (b) see citation 3.
- (5) Ir-catalyzed borylation of the arene was previously described, see Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E., Jr.; Smith, M. R., III *Science* **2002**, *295*, 305–308.
- (6) Ishiyama, T.; Takagi, J.; Hartwig, J. F.; Miyaura, N. *Angew. Chem. Int. Ed.* **2002**, *41*, 3056–3058.
- (7) For a previous preparation see: Brittain, J. M.; de la Mare, P. B. D.; Newman, P. A. *J. Chem. Soc., Perkin Trans. 2* **1981**, 32–41 (four steps from 3-methylphenol, overall yield not reported).
- (8) (a) To the best of our knowledge only one other preparation of this compound has been reported: Testaferri, L.; Tiecco, M.; Tingoli, M.; Chinaelli, D.; Montanucci, M. *Tetrahedron* **1983**, *39*, 193–197 (as a byproduct during the reaction of NaOMe with 1,3,5-trichlorobenzene, 7% yield, no mp reported). However, **5** is available from ICN for \$99.70/g.
- (9) For a previous preparation see: Takahashi, K.; Shimizu, S.; Ogata, M. *Heterocycles* **1985**, *23*, 1483–1491 (three steps from 3,5-dichlorobenzoic acid, 65% overall yield).
- (10) To the best of our knowledge only one other preparation of this compound has been reported: Umemoto, T.; Harasawa, K.; Tomizawa, G.; Kawada, K.; Tomita, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1081–1092 (as a byproduct (mp not reported) during the hydrolysis of an *N*-fluoro-2,6-

dichloropyridinium PF₆⁻ salt that was prepared by the reaction of 2,6-dichloropyridine with F₂ gas, 4% yield).

- (11) To the best of our knowledge no other preparation of this compound has been reported, however it has been used in water treatment experiments (Ben Amor, H.; De Laat, J.; Dore, M. *Water Res.* **1984**, *18*, 1545–1516).
- (12) For a previous preparation see: Wedemeyer, K.; Koppelman, E. *Ger. Offen.* **1975**, DE2344926 (three steps from 4-methylphenol, 54% yield, mp not reported).
- (13) For a previous preparation see: Kulkarni, M. G.; Kate, S. D. *J. Chem. Soc., Perkin. Trans. 1* **2000**, 4242–4244 (photoreduction of 2,6-dichloro-1,4-benzoquinone with a vitamin C derivative, 87% yield). This material is also available from Apin.
- (14) (a) For a previous preparation see: Jacquesy, J.-C.; Jouannetaud, M.-P.; Makani, S. *J. Chem. Soc., Chem. Commun.* **1980**, 110–111 (bromination of 3,4-dimethylphenol in superacid SbF₅-HF, 83% yield). (b) Fischer, A.; Henderson, G. N. *Can. J. Chem.* **1983**, *61*, 1045–1052.
- (15) For a previous preparation see: Soma, T.; Konishi, K. *Takeda Kenkyusho Nenpo* **1996**, *25*, 109–122 (two steps of 3,5-dichloroaniline, overall yield or mp not reported).
- (16) (a) For a previous preparation see: Miles, M. H. *Brit. UK Pat. Appl.* **1973**, GB 13116277 (byproduct of the reaction of 1,2,3,5-tetrachlorobenzene with NaOH, 3.3% yield, mp not reported). This material is also available from AccuStandard (\$12.20 for 10 mg) or Sigma-Aldrich (\$82.20 for 25 mg). (b) We thank AccuStandard for providing us their melting point data on **12**.
- (17) For a previous preparation see: Elliott, M.; Janes, N. F.; Khambay, B. P. S. *Brit. UK Pat. Appl.* **1987**, GB 2187731 (three steps from 2,4-dibromofluorobenzene, 18% overall yield).
- (18) To the best of our knowledge no other preparation of this compound has been reported.