Supporting information

Cu-Catalyzed Regioselective C–H Aerobic Oxidative Cycloetherification of \( o \)-Arylphenols Bearing an Additional Directing Group

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1. Procedures for the preparation of substrates

For substrates 1a-1g, and 1j:

A mixture of substituted 2-iodophenol (2 mmol), 3-acetamidophenylboronic acid (3 mmol, 1.5 equiv, for 1a-1f, and 1j) or 3-(N-Boc-amino)phenylboronic acid (3 mmol, 1.5 equiv, for 1g), Pd(PPh3)2Cl2 (70 mg, 0.1 mmol, 5 mol %) and K2CO3 (828 mg, 6 mmol, 3 equiv) in dioxone/H2O (6 mL/2 mL) was stirred at 100 °C under an argon atmosphere until the starting material was disappeared (typically 20 h). An aqueous solution of HCl (10%, 4 mL) was added to acidify the reaction mixture with vigorous stirring. The mixture was then extracted with EtOAc (15 mL × 2). The combined organic layers were washed with brine, and dried over Na2SO4. The concentrated crude product was purified by column chromatography to afford 2-arylphenol 1.

For substrate 1h:

2-(3-Aminophenyl)-4-nitrophenol (0.5 mmol), obtained by following the above procedure using 3-aminophenylboronic acid as one of the substrates, was dissolved in THF (3 mL). Et3N (0.55 mmol, 1.1 equiv) and benzoyl chloride (0.55 mmol, 1.1 equiv) was added into the above solution at 0 °C. The reaction mixture was warmed gradually to room temperature. After being stirred at rt for 4 h, the mixture was diluted with EtOAc (20 mL). The resulting solution was washed with brine (15 mL) and the organic layer was dried over Na2SO4. The concentrated crude product was purified by column chromatography to afford 1h.

For substrate 1i:

To a solution of 2-(3-aminophenyl)-4-nitrophenol (1 mmol) and Et3N (1.1 mmol, 1.1 equiv) in EtOAc (2.5 mL), was added a solution of 4-chlorobutanoyl chloride (1.05 mmol, 1.05 equiv) in EtOAc (1.3 mL) dropwise at 0 °C. The reaction mixture was warmed to room temperature and it was stirred at rt for 4 h. To the mixture was added EtOAc (20 mL). The resulting solution was washed with brine (15 mL), and dried over Na2SO4. The concentrated residue was purified by column chromatography to afford 2-(3-(4-chlorobutanoyl)aminophenyl)-4-nitrophenol. This product was dissolved in isopropanol (2 mL), and an aqueous solution of NaOH (6%, 2 mL) was added. The mixture was stirred for 11 h at rt before it was acidified with diluted HCl aqueous solution (10%, 4 mL). The mixture was extracted with EtOAc (20 mL) The organic layer was washed with brine (15 mL) and dried over Na2SO4. The concentrated residue was purified by column chromatography to afford 1i.
2. Characterization of substrates

2-(3-acetamidophenyl)-4-nitrophenol (1a)

Pale yellow solid, yield: 55%. \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 11.28 (br, 1H), 10.01 (s, 1H), 8.08-8.14 (m 2H), 7.79 (s, 1H), 7.61 (d, \(J = 6.0\) Hz, 1H), 7.34-7.38 (m, 1 H), 7.26 (s, 1H), 7.11-7.13 (m, 1H), 2.05 (s, 3H); \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \(\delta\) 168.3, 160.9, 139.7, 139.2, 136.6, 128.4, 128.2, 125.8, 124.7, 123.7, 119.6, 118.3, 116.4, 23.9.

2-(3-acetamidophenyl)-4-fluorophenol (1b)

White solid, yield: 75%. \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 9.96 (s, 1H), 9.53 (s, 1H), 7.74 (t, \(J = 1.6\) Hz, 1H), 7.57 (d, \(J = 8.0\) Hz, 1H), 7.31 (t, \(J = 8.0\) Hz, 1H), 7.19 (d, \(J = 7.8\) Hz, 1H), 6.97-7.04 (m, 2H), 6.90-6.93 (m, 1H), 2.05 (s, 3H); \(^{13}\)C NMR (125 MHz, DMSO-d\(_6\)): \(\delta\) 168.3, 156.5, 154.6, 150.6, 139.0, 137.8, 128.7, 128.6, 128.3, 123.8, 119.8, 117.8, 116.9, 116.8, 116.1, 116.0, 114.7, 114.5, 24.0.

2-(3-acetamidophenyl)-4-chlorophenol (1c)

White solid, yield: 72%. \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 9.97 (s, 1H), 9.85 (s, 1H), 7.72 (s, 1H), 7.57 (d, \(J = 8.0\) Hz, 1H), 7.31 (t, \(J = 8.0\) Hz, 1H), 7.18-7.22 (m, 3H), 6.95 (d, \(J = 9.2\) Hz, 1H), 2.04 (s, 3H); \(^{13}\)C NMR (125 MHz, DMSO-d\(_6\)): \(\delta\) 168.4, 153.3, 139.1, 137.6, 129.5, 129.4, 128.4, 128.1, 123.8, 122.8, 119.8, 117.9, 117.7, 24.0.

2-(3-acetamidophenyl)-4-cyanophenol (1d)
White solid, yield: 42%. $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 10.81 (s, 1H), 9.99 (s, 1H), 7.74 (s, 1H), 7.62-7.65 (m, 2H), 7.58 (d, $J$ = 8.8 Hz, 1H), 7.33 (t, $J$ = 8.0 Hz, 1H), 7.19 (d, $J$ = 7.6 Hz, 1H), 7.08 (d, $J$ = 8.8 Hz, 1H), 2.05 (s, 3H); $^{13}$C NMR (125 MHz, DMSO-d$_6$): $\delta$ 168.3, 158.6, 139.1, 136.8, 134.3, 133.0, 129.0, 128.5, 123.8, 119.8, 119.3, 118.1, 117.0, 101.6, 24.0.

2-(3-acetamidophenyl)-4-formylphenol (1e)

White solid, yield: 48%. $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 10.80 (s, 1H), 9.99 (s, 1H), 9.85 (s, 1H), 7.74-7.78 (m, 3H), 7.59 (d, $J$ = 8.0 Hz, 1H), 7.34 (t, $J$ = 8.0 Hz, 1H), 7.23 (d, $J$ = 8.0 Hz, 1H), 7.12 (d, $J$ = 8.4 Hz, 1H), 2.05 (s, 3H); $^{13}$C NMR (125 MHz, DMSO-d$_6$): $\delta$ 191.2, 168.4, 160.2, 139.1, 137.6, 132.6, 130.6, 128.7, 128.4, 128.3, 123.8, 119.8, 117.9, 116.5, 24.0.

methyl 3-(3-acetamidophenyl)-4-hydroxybenzoate (1f)

White solid, yield: 52%. $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 10.56 (s, 1H), 9.99 (s, 1H), 7.79-7.82 (m, 2H), 7.73 (s, 1H), 7.59 (d, $J$ = 8.0 Hz, 1H), 7.33 (t, $J$ = 8.0 Hz, 1H), 7.21 (d, $J$ = 7.6 Hz, 1H), 7.04 (d, $J$ = 8.4 Hz, 1H), 3.80 (s, 3H), 2.05 (s, 3H); $^{13}$C NMR (125 MHz, DMSO-d$_6$): $\delta$ 168.4, 166.0, 158.9, 139.2, 137.8, 131.7, 130.2, 128.4, 127.8, 123.8, 120.7, 119.6, 117.8, 116.1, 51.7, 24.0.

2-(3-(N-Boc-amino)phenyl)-4-nitrophenol (1g)

White solid, yield: 42%. $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 10.81 (s, 1H), 9.99 (s, 1H), 7.74 (s, 1H), 7.62-7.65 (m, 2H), 7.58 (d, $J$ = 8.8 Hz, 1H), 7.33 (t, $J$ = 8.0 Hz, 1H), 7.19 (d, $J$ = 7.6 Hz, 1H), 7.08 (d, $J$ = 8.8 Hz, 1H), 2.05 (s, 3H); $^{13}$C NMR (125 MHz, DMSO-d$_6$): $\delta$ 168.3, 158.6, 139.1, 136.8, 134.3, 133.0, 129.0, 128.5, 123.8, 119.8, 119.3, 118.1, 117.0, 101.6, 24.0.
Pale yellow solid, yield: 40%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.28 (br, 1H), 9.43 (s, 1H), 8.12 (dd, $J = 8.8$, 2.8 Hz, 1H), 8.06 (d, $J = 2.8$ Hz, 1H), 7.71 (s, 1H), 7.44 (d, $J = 7.6$ Hz, 1H), 7.32 (t, $J = 7.8$ Hz, 1H), 7.18 (d, $J = 7.6$ Hz, 1H), 7.11 (d, $J = 8.8$ Hz, 1H), 1.48 (s, 9H); $^{13}$C NMR (100 MHz, DMSO-$d_6$): 160.9, 152.8, 139.8, 139.4, 136.7, 128.5, 128.4, 125.8, 124.7, 122.8, 118.8, 117.5, 116.3, 79.0, 28.1.

$N$-(3-(2-hydroxy-5-nitrophenyl)phenyl)benzamide (1h)

Pale yellow solid, yield: 79%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.32 (br, 1H), 10.33 (s, 1H), 8.13-8.16 (m, 2H), 7.97-8.01 (m, 3H), 7.84 (d, $J = 8.0$ Hz, 1H), 7.58-7.62 (m, 1H), 7.52-7.56(m, 2H), 7.44 (t, $J = 7.8$ Hz, 1H), 7.36 (d, $J = 7.8$ Hz, 1H), 7.14 (d, $J = 8.8$ Hz, 1H); $^{13}$C NMR (125 MHz, DMSO-$d_6$): 165.6, 161.0, 139.8, 139.1, 136.6, 134.9, 131.6, 128.4, 128.3, 128.3, 127.6, 125.9, 124.9, 124.5, 121.0, 119.6, 116.4.

1-(3-(2-hydroxy-5-nitrophenyl)phenyl)pyrrolidin-2-one (1i)

Pale yellow solid, yield: 40%. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.32 (br, 1H), 8.13 (dd, $J = 8.8$, 2.8 Hz, 1H), 8.10 (d, $J = 2.8$ Hz, 1H), 7.88 (t, $J = 1.8$ Hz, 1H), 7.64 (d, $J = 8.4$ Hz, 1H), 7.44 (t, $J = 8.0$ Hz, 1H), 7.35 (d, $J = 7.8$ Hz, 1H), 7.12 (d, $J = 8.8$ Hz, 1H), 3.88 (t, $J = 7.0$ Hz, 2H), 2.50 (m, 2H), 2.04-2.11 (m, 2H); $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 173.9, 161.1, 139.7, 139.5, 136.7, 128.4, 128.2, 126.1, 124.9, 124.7, 120.1, 118.7, 116.4, 48.1, 32.3, 17.4.

2-(3-acetamidophenyl)-phenol (1j)

White solid, yield: 58 %. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 9.93 (s, 1H), 9.48 (s, 1H),
7.71 (s, 1H), 7.54 (d, \( J = 8.0 \) Hz, 1H), 7.29 (t, \( J = 7.8 \) Hz, 1H), 7.13-7.21 (m, 3H), 
6.93 (d, \( J = 7.4 \) Hz, 1H), 6.84-6.88 (m, 1H), 2.04 (s, 3H); \(^{13}\text{C} \text{NMR} \) (100 MHz, 
DMSO-\( d_6 \)): \( \delta \) 168.0, 154.1, 138.9, 138.8, 130.0, 128.3, 127.9, 127.6, 123.7, 119.8, 
119.2, 117.3, 115.9, 23.8.

3. Copies of \(^1\text{H} \) and \(^{13}\text{C} \) NMR spectra of 2