

Supporting Information

Regioselective C-H Chlorination: Towards the Sequential difunctionalization of Phenol Derivatives and Late-Stage Chlorination of Bioactive Compounds

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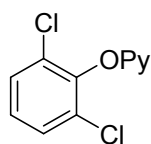
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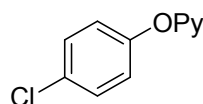
Characterization of Products in Details

2-(2,6-dichlorophenoxy)pyridine (3a)



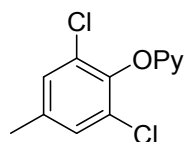
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (40 mg, 83 % yield). **¹H NMR** (500 MHz, CDCl₃): δ 8.10 (d, *J* = 3.5 Hz, 1H), 7.73 (t, *J* = 7.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.14 (t, *J* = 8.5 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 7.00 (t, *J* = 6.0 Hz, 1H); **¹³C NMR** (125 MHz, CDCl₃): δ 162.0, 147.4, 146.4, 139.6, 129.8, 128.8, 126.4, 118.7, 110.6; **HRMS** (TIC): calcd for C₁₁H₈Cl₂NO [M + H]⁺ 239.9978, found 239.9976.

2-(4-chlorophenoxy)pyridine (3a')



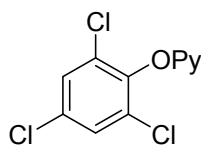
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (37 mg, 90 % yield). **¹H NMR** (500 MHz, CDCl₃): δ 8.16 - 8.15 (m, 1H), 7.66 (t, *J* = 7.3 Hz, 1H), 7.33 (d, *J* = 8.6 Hz, 2H), 7.06 (d, *J* = 8.5 Hz, 2H), 6.97 (t, *J* = 5.6 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H); **¹³C NMR** (125 MHz, CDCl₃): δ 163.4, 152.7, 147.6, 139.6, 129.8, 129.6, 122.6, 118.8, 111.7; **HRMS** (TIC): calcd for C₁₁H₈ClNO [M + H]⁺ 206.0367, found 206.0365.

2-(2,6-dichloro-4-methylphenoxy)pyridine (3b)



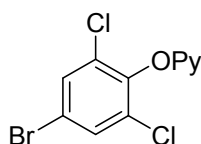
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (35.1 mg, 69 % yield). **¹H NMR** (500 MHz, CDCl₃): δ 8.03 (d, *J* = 4.5 Hz, 1H), 7.65 (t, *J* = 7.0 Hz, 1H), 7.13 (s, 2H), 6.97 - 6.91 (m, 2H), 2.26 (s, 3H); **¹³C NMR** (125 MHz, CDCl₃): δ 161.1, 146.4, 142.9, 138.5, 135.7, 128.3, 128.1, 117.6, 109.6, 19.7; **HRMS** (TIC): calcd for C₁₂H₁₀Cl₂NO [M + H]⁺ 254.0134, found 254.0131.

2-(2,4,6-trichlorophenoxy)pyridine (3c)



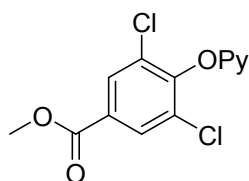
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (35.1 mg, 69 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.08 (d, $J = 4.5$ Hz, 1H), 7.74 (t, $J = 6.5$ Hz, 1H), 7.40 (s, 2H), 7.08 - 7.01 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3): δ 161.7, 147.3, 145.4, 139.8, 131.0, 130.4, 128.7, 128.1, 121.7, 118.9, 110.7; **HRMS** (TIC): calcd for $\text{C}_{11}\text{H}_7\text{Cl}_3\text{NO}$ $[\text{M} + \text{H}]^+$ 273.9588 found 273.9591.

2-(4-bromo-2,6-dichlorophenoxy)pyridine (3d)



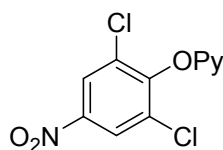
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (59.6 mg, 94 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.09 (d, $J = 4.5$ Hz, 1H), 7.75 (t, $J = 7.5$ Hz, 1H), 7.55 (s, 2H), 7.07 (d, $J = 8.0$ Hz, 1H), 7.03 (t, $J = 5.5$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 162.0, 147.4, 146.4, 139.6, 129.8, 128.8, 128.1, 126.4, 121.7, 118.7, 110.6; **HRMS** (TIC): calcd for $\text{C}_{11}\text{H}_7\text{BrCl}_2\text{NO}$ $[\text{M} + \text{H}]^+$ 317.9083, found 317.9085.

methyl 3,5-dichloro-4-(pyridin-2-yloxy)benzoate (3e)



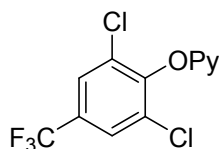
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid (59.1 mg, 99 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.07 (s, 3H), 7.76 (t, $J = 8.0$ Hz, 1H), 7.09 (d, $J = 8.0$ Hz, 1H), 7.03 (t, $J = 5.0$ Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 164.6, 161.7, 150.2, 147.3, 139.9, 130.1, 130.0, 128.6, 119.1, 110.8, 52.7; **HRMS** (TIC): calcd for $\text{C}_{13}\text{H}_{10}\text{Cl}_2\text{NO}_3$ $[\text{M} + \text{H}]^+$ 298.0032, found 298.0030.

2-(2,6-dichloro-4-nitrophenoxy)pyridine (3f)



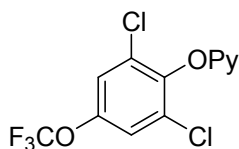
Following the general procedure, using 5:1 petroleum ether-EtOAc as the eluant afforded a white liquid (56.2 mg, 99 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.30 (s, 2H), 8.04 (d, $J = 6.0$ Hz, 1H), 7.80 (t, $J = 8.5$ Hz, 1H), 7.14 (d, $J = 8.0$ Hz, 1H), 7.07 (t, $J = 7.0$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 161.4, 152.1, 147.2, 144.8, 140.1, 131.1, 124.2, 119.5, 110.8; **HRMS** (TIC): calcd for $\text{C}_{11}\text{H}_7\text{Cl}_2\text{N}_2\text{O}_3$ $[\text{M} + \text{H}]^+$ 284.9828, found 284.9825.

2-(2,6-dichloro-4-(trifluoromethyl)phenoxy)pyridine (3g)



Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (56.2 mg, 92 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.07 (d, $J = 5.0$ Hz, 1H), 7.77 (t, $J = 6.5$ Hz, 1H), 7.67 (s, 2H), 7.11 (d, $J = 8.0$ Hz, 1H), 7.04 (t, $J = 7.0$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 161.5, 149.5, 147.3, 140.0, 130.8, 128.9 (q, $J_{\text{F}} = 33.8$ Hz), 126.0 (q, $J_{\text{F}} = 3.8$ Hz), 122.7 (q, $J_{\text{F}} = 271.2$ Hz), 119.2, 110.8. ^{19}F NMR (470 MHz, CDCl_3): δ -62.6(s, 1F); **HRMS** (TIC): calcd for $\text{C}_{12}\text{H}_7\text{Cl}_2\text{F}_3\text{NO}$ $[\text{M} + \text{H}]^+$ 307.9852, found 307.9850.

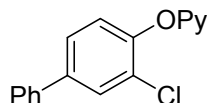
2-(2,6-dichloro-4-(trifluoromethoxy)phenoxy)pyridine (3h)



Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid (59.3 mg, 92 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.09 (d, $J = 6.5$ Hz, 1H), 7.75 (t, $J = 7.0$ Hz, 1H), 7.30 (s, 2H), 7.08 (d, $J = 8.5$ Hz, 1H), 7.03 (t, $J = 7.0$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 161.7, 147.3, 145.7 (q, $J_{\text{F}} = 1.2$ Hz), 145.5, 139.8, 130.6, 121.6, 120.3 (q, $J_{\text{F}} = 256.2$ Hz), 119.1, 110.7; ^{19}F NMR (470 MHz, CDCl_3): δ -58.1(s, 3F); **HRMS** (TIC): calcd for $\text{C}_{12}\text{H}_7\text{Cl}_2\text{F}_3\text{NO}_2$ $[\text{M}$

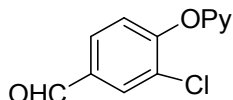
+ H]⁺ 323.9801, found 323.9800.

2-((3-chloro-[1,1'-biphenyl]-4-yl)oxy)pyridine (3i)



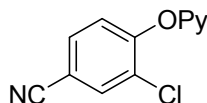
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (45.6 mg, 81 % yield). ¹H NMR (500 MHz, CDCl₃): δ 8.13 (d, *J* = 6.0 Hz, 1H), 7.75 (t, *J* = 8.5 Hz, 1H), 7.60 - 7.54 (m, 4H), 7.46 - 7.37 (m, 4H), 7.10 - 7.01 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 172.2, 162.1, 147.4, 145.5, 140.0, 137.7, 138.3, 129.9, 129.0, 128.2, 127.4, 127.0, 121.5, 118.8, 110.7; **HRMS** (TIC): calcd for C₁₇H₁₃ClNO [M + H]⁺ 282.0680, found 282.0684.

3-chloro-4-(pyridin-2-yloxy)benzaldehyde (3j)



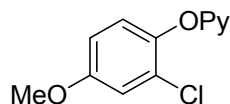
Following the general procedure, using 4:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid (21.3 mg, 46 % yield). ¹H NMR (500 MHz, CDCl₃): δ 9.96 (s, 1H), 8.16 (d, *J* = 3.0 Hz, 1H), 8.01 (s, 1H), 7.84 - 7.76 (m, 2H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.09 - 7.06 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 189.8, 162.2, 154.9, 147.1, 140.4, 133.6, 131.4, 129.2, 128.3, 123.7, 119.5, 111.8; **HRMS** (TIC): calcd for C₁₂H₉ClNO₂ [M + H]⁺ 234.0317, found 234.0315.

3-chloro-4-(pyridin-2-yloxy)benzonitrile (3k)



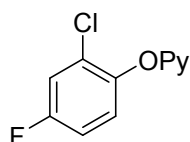
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a white liquid (23.3 mg, 51 % yield). ¹H NMR (500 MHz, CDCl₃): δ 8.14 (d, *J* = 3.5 Hz, 1H), 7.79 - 7.76 (m, 2H), 7.61 - 7.59 (m, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 7.09 - 7.07 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 162.0, 154.0, 147.4, 140.0, 134.3, 131.7, 128.3, 124.2, 119.6, 117.4, 111.8, 109.6; **HRMS** (TIC): calcd for C₁₂H₈ClN₂O [M + H]⁺ 231.0320, found 231.0321.

2-(2-chloro-4-methoxyphenoxy)pyridine (3l).



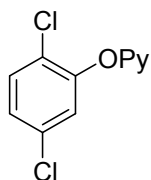
Following the general procedure, using 5:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (29.4 mg, 63 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.14 (d, $J = 4.0$ Hz, 1H), 7.68 (t, $J = 7.5$ Hz, 1H), 7.13 (d, $J = 9.0$ Hz, 1H), 7.01 (s, 1H), 6.98 - 6.93 (m, 2H), 6.85 (d, $J = 8.5$ Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 162.4, 156.8, 147.4, 140.0, 139.5, 129.8, 118.6, 114.5, 110.7, 110.5, 102.0, 55.9; **HRMS** (TIC): calcd for $\text{C}_{12}\text{H}_{11}\text{ClNO}_2$ $[\text{M} + \text{H}]^+$ 236.0473, found 236.0470.

2-(2-chloro-4-fluorophenoxy)pyridine (3m)



Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (51.4 mg, 76 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.18 - 8.12 (m, 1H), 7.72 - 7.66 (m, 1H), 7.23 - 7.17 (m, 1H), 7.10 - 6.97 (m, 3H), 6.90 (d, $J = 8.5$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 163.3 (d, $J_F = 98.8$ Hz), 160.4 (d, $J_F = 22.5$ Hz), 158.5 (d, $J_F = 26.2$ Hz), 147.5 (d, $J_F = 26.2$ Hz), 139.5 (d, $J_F = 15.0$ Hz), 124.7 (d, $J_F = 10.0$ Hz), 122.7 (d, $J_F = 8.8$ Hz), 118.6 (d, $J_F = 20.0$ Hz), 117.6 (d, $J_F = 26.2$ Hz), 116.2 (d, $J_F = 22.5$ Hz), 111.2 (d, $J_F = 46.2$ Hz); ^{19}F NMR (470 MHz, CDCl_3): δ -118.5(s, 1F); **HRMS** (TIC): calcd for $\text{C}_{11}\text{H}_8\text{ClFNO}$ $[\text{M} + \text{H}]^+$ 224.0273, found 224.0275.

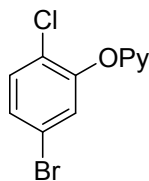
2-(2,5-dichlorophenoxy)pyridine (3n)



Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (38.1 mg, 80 % yield). ^1H NMR (400 MHz, CDCl_3): δ 8.26 - 8.21 (m, 1H), 7.73 (d, $J = 8.4$ Hz, 1H), 7.54 - 7.26 (m, 3H), 7.04 - 6.95 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3): δ 162.5, 150.4, 147.5, 139.8, 133.0, 131.1, 128.3, 126.2, 124.2, 119.0, 111.3; **HRMS** (TIC): calcd for $\text{C}_{11}\text{H}_8\text{Cl}_2\text{NO}$ $[\text{M} + \text{H}]^+$ 239.9978, found

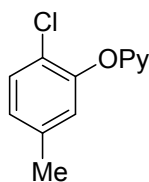
239.9976.

2-(5-bromo-2-chlorophenoxy)pyridine (3o)



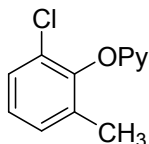
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (49.7 mg, 88 % yield). ¹H NMR (400 MHz, CDCl₃): δ 8.19 (s, 1H), 7.77 (t, *J* = 7.2 Hz, 1H), 7.42 (s, 1H), 7.39 - 7.34 (m, 2H), 7.06 - 7.04 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 162.5, 150.3, 147.5, 139.8, 131.5, 129.1, 127.0, 126.6, 120.4, 119.1, 111.5; **HRMS** (TIC): calcd for C₁₁H₈BrClNO [M + H]⁺ 283.9473, found 283.9474.

2-(2-chloro-5-methylphenoxy)pyridine (3p)



Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (34.8 mg, 79 % yield). ¹H NMR (400 MHz, CDCl₃): δ 8.27 - 8.22 (m, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.41 - 7.32 (m, 1H), 7.09 - 7.02 (m, 3H), 6.95 (d, *J* = 8.0 Hz, 1H), 2.43 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 162.1, 148.4, 146.5, 138.4, 137.2, 129.1, 125.9, 123.3, 123.1, 117.4, 110.0, 20.0; **HRMS** (TIC): calcd for C₁₂H₁₁ClNO [M + H]⁺ 220.0524, found 220.0523.

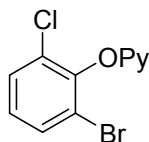
2-(2-chloro-6-methylphenoxy)pyridine (3q)



Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (35.5 mg, 81 % yield). ¹H NMR (400 MHz, CDCl₃): δ 8.17 (s, 1H), 7.74 (t, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.30 (s, 1H), 7.16 - 7.12 (m, 1H), 7.01 - 6.99 (m, 2H), 2.23 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 161.5, 147.0,

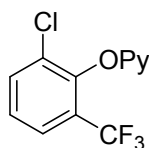
146.5, 138.5, 132.7, 128.4, 126.9, 126.8, 124.9, 117.2, 109.2, 15.8; **HRMS** (TIC): calcd for $C_{12}H_{11}ClNO$ $[M + H]^+$ 220.0524, found 220.0523.

2-(2-bromo-6-chlorophenoxy)pyridine (3r)



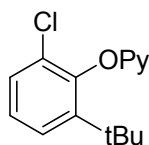
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (40.1 mg, 71 % yield). 1H NMR (500 MHz, $CDCl_3$): δ 8.10 (d, $J = 4.5$ Hz, 1H), 7.74 (t, $J = 7.0$ Hz, 1H), 7.55 (d, $J = 8.5$ Hz, 1H), 7.43 (d, $J = 8.0$ Hz, 1H), 7.09 - 6.99 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.9, 147.5, 147.3, 139.6, 131.8, 129.7, 129.5, 126.9, 118.9, 118.7, 110.7; **HRMS** (TIC): calcd for $C_{11}H_8BrClNO$ $[M + H]^+$ 283.9473, found 283.9474.

2-(2-chloro-6-(trifluoromethyl)phenoxy)pyridine (3s)



Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded yellow liquid (25.7 mg, 47 % yield). 1H NMR (400 MHz, $CDCl_3$): δ 8.14 (s, 1H), 7.79 (t, $J = 7.2$ Hz, 1H), 7.70 (t, $J = 8.4$ Hz, 2H), 7.38 - 7.32 (m, 2H), 7.12 (d, $J = 8.0$ Hz, 1H), 7.06 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.1, 151.8, 147.5, 139.6, 138.4, 132.9, 127.1 (q, $J_F = 5.0$ Hz), 124.5, 123.6, 123.0 (q, $J_F = 151.2$ Hz), 119.0; ^{19}F NMR (470 MHz, $CDCl_3$): δ -61.8(s, 3F); **HRMS** (TIC): calcd for $C_{12}H_8ClF_3NO$ $[M + H]^+$ 274.0241, found 274.0240.

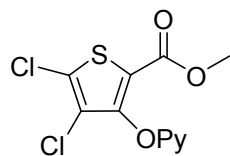
2-(2-(tert-butyl)-6-chlorophenoxy)pyridine (3t)



Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a brown liquid (40.1 mg, 77 % yield). 1H NMR (500 MHz, $DMSO-d_6$): δ 8.17 (d, $J = 4.5$ Hz, 1H), 7.85 (t, $J = 7.5$ Hz, 1H), 7.41 (d, $J = 7.5$ Hz, 1H), 7.22 (d, $J = 7.5$ Hz, 1H), 7.15 - 7.10 (m, 2H), 7.01 - 6.91 (m, 1H), 1.31 (s, 9H); ^{13}C NMR (125

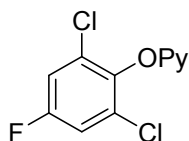
MHz, CDCl₃): δ 162.0, 147.1, 146.6, 143.7, 138.3, 128.0, 127.4, 124.9, 124.6, 116.9, 109.7, 34.3, 29.5, 28.2, 17.4; **HRMS** (TIC): calcd for C₁₅H₁₇ClNO [M + H]⁺ 262.0993, found 262.0990.

methyl-4,5-dichloro-3-(pyridin-2-yloxy)thiophene-2-carboxylate (3u)



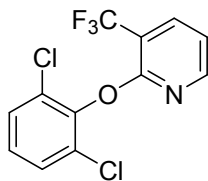
Following the general procedure, using 8:1 petroleum ether-EtOAc as the eluant afforded a brown liquid (42.3.3 mg, 70 % yield). ¹H NMR (500 MHz, CDCl₃): δ 8.01 (d, *J* = 5.0 Hz, 1H), 7.66 (t, *J* = 6.5 Hz, 1H), 7.33 (s, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 6.93 (t, *J* = 7.0 Hz, 1H), 3.65 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 161.5, 159.4, 148.7, 146.2, 138.6, 123.5, 121.4, 118.6, 117.8, 109.8, 51.1; **HRMS** (TIC): calcd for C₁₁H₈Cl₂NO₃S [M + H]⁺ 303.9597, found 303.9595.

2-(2,6-dichloro-4-fluorophenoxy)pyridine (3v)



Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid (48.4 mg, 92 % yield). ¹H NMR (500 MHz, CDCl₃): δ 8.00 (d, *J* = 4.0 Hz, 1H), 7.66 (t, *J* = 7.0 Hz, 1H), 7.08 (t, *J* = 8.0 Hz, 2H), 6.99 - 6.92 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 160.8, 158.7, 156.7, 146.2, 142.1, 138.7, 129.3 (d, *J*_F = 12.5 Hz), 117.9, 115.2 (d, *J*_F = 25.0 Hz), 109.6; ¹⁹F NMR (470 MHz, CDCl₃): δ -113.9(s, 1F); **HRMS** (TIC): calcd for C₁₁H₇Cl₂FNO [M + H]⁺ 257.9883, found 257.9885.

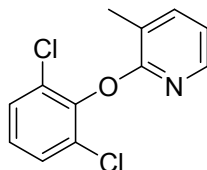
2-(2,6-dichlorophenoxy)-3-(trifluoromethyl)pyridine (5a)



Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (14.1 mg, 23 % yield). ¹H NMR (500 MHz, CDCl₃): δ 8.25

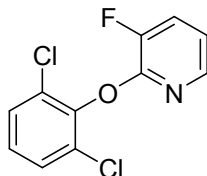
(d, $J = 4.5$ Hz, 1H), 8.01 (d, $J = 8.0$ Hz, 1H), 7.49 (d, $J = 7.0$ Hz, 1H), 7.42 - 7.33 (m, 1H), 7.25 - 7.22 (m, 1H), 7.11 - 7.09 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 159.6, 150.7, 149.0, 137.1 (q, $J_{\text{F}} = 5.0$ Hz), 130.6, 128.1 (q, $J_{\text{F}} = 108.8$ Hz), 127.9, 126.7, 120.0 (q, $J_{\text{F}} = 271.2$ Hz), 117.9; ^{19}F NMR (470 MHz, CDCl_3): δ -63.4(s, 3F); **HRMS** (TIC): calcd for $\text{C}_{12}\text{H}_7\text{Cl}_2\text{F}_3\text{NO}$ $[\text{M} + \text{H}]^+$ 307.9852, found 307.9850.

2-(2,6-dichlorophenoxy)-3-methylpyridine (5b)



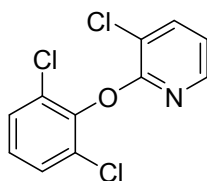
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (41.1 mg, 81 % yield). ^1H NMR (500 MHz, CDCl_3): δ 7.81 (d, $J = 5.0$ Hz, 1H), 7.45 (d, $J = 7.5$ Hz, 1H), 7.30 (d, $J = 8.0$ Hz, 2H), 7.04 (t, $J = 8.0$ Hz, 1H), 6.84 - 6.82 (m, 1H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 159.3, 145.9, 143.4, 138.7, 128.7, 127.6, 125.1, 119.8, 117.8, 14.8; **HRMS** (TIC): calcd for $\text{C}_{12}\text{H}_{10}\text{Cl}_2\text{NO}$ $[\text{M} + \text{H}]^+$ 254.0134, found 254.0131.

2-(2,6-dichlorophenoxy)-3-fluoropyridine (5c)



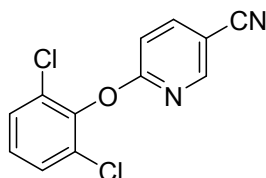
Following the general procedure, using 10:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid (40.8 mg, 79 % yield). ^1H NMR (500 MHz, CDCl_3): δ 7.84 (s, 1H), 7.26 - 7.18 (m, 1H), 7.11 (t, $J = 8.5$ Hz, 3H), 7.00 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 155.7 (d, $J_{\text{F}} = 6.2$ Hz), 150.6 (d, $J_{\text{F}} = 200.0$ Hz), 144.0 (d, $J_{\text{F}} = 75$ Hz), 143.1, 129.9 (d, $J_{\text{F}} = 45$ Hz), 126.8 (d, $J_{\text{F}} = 81.2$ Hz), 124.4 (d, $J_{\text{F}} = 8.8$ Hz), 123.4 (d, $J_{\text{F}} = 31.2$ Hz), 118.8 (d, $J_{\text{F}} = 18.8$ Hz); ^{19}F NMR (470 MHz, CDCl_3): δ -137.7(s, 1F); **HRMS** (TIC): calcd for $\text{C}_{11}\text{H}_7\text{Cl}_2\text{FNO}$ $[\text{M} + \text{H}]^+$ 257.9883, found 257.9885.

3-chloro-2-(2,6-dichlorophenoxy)pyridine (5d)



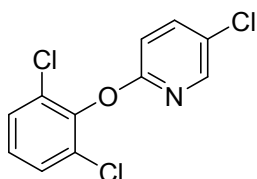
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid (40.1 mg, 73 % yield). ^1H NMR (500 MHz, CDCl_3): δ 7.96 (d, $J = 3.5$ Hz, 1H), 7.79 (d, $J = 9.0$ Hz, 1H), 7.40 (d, $J = 8.0$ Hz, 2H), 7.17 (t, $J = 8.0$ Hz, 1H), 7.01 - 6.98 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 157.3, 146.3, 144.9, 139.5, 129.6, 128.8, 126.7, 119.8, 118.3; **HRMS** (TIC): calcd for $\text{C}_{11}\text{H}_7\text{Cl}_3\text{NO}$ $[\text{M} + \text{H}]^+$ 273.9588, found 273.9591.

6-(2,6-dichlorophenoxy)nicotinonitrile (5e)



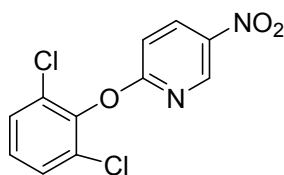
Following the general procedure, using 5:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (40.4 mg, 76 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.40 (d, $J = 2.0$ Hz, 1H), 7.99 (d, $J = 6.5$ Hz, 1H), 7.42 (d, $J = 8.0$ Hz, 2H), 7.22 - 7.19 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3): δ 163.7, 151.9, 142.6, 129.4, 128.9, 127.2, 122.0, 120.9, 116.5, 111.5; **HRMS** (TIC): calcd for $\text{C}_{12}\text{H}_7\text{Cl}_2\text{N}_2\text{O}$ $[\text{M} + \text{H}]^+$ 264.9930, found 264.9927.

5-chloro-2-(2,6-dichlorophenoxy)pyridine (5f)



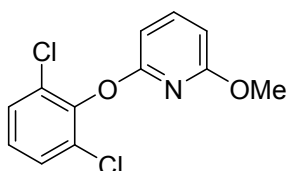
Following the general procedure, using 15:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid (53.3 mg, 98 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.03 (d, $J = 2.0$ Hz, 1H), 7.71 - 7.68 (m, 1H), 7.39 (d, $J = 8.0$ Hz, 2H), 7.16 (t, $J = 8.0$ Hz, 1H), 7.03 (d, $J = 9.0$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 160.3, 146.1, 145.7, 139.6, 129.7, 128.8, 126.7, 126.3, 111.7; **HRMS** (TIC): calcd for $\text{C}_{11}\text{H}_7\text{Cl}_3\text{NO}$ $[\text{M} + \text{H}]^+$ 273.9588, found 273.9591.

2-(2,6-dichlorophenoxy)-5-nitropyridine (5g)



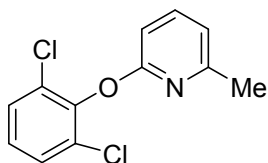
Following the general procedure, using 5:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid (18.7 mg, 33 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.98 (d, $J = 2.5$ Hz, 1H), 8.55 (d, $J = 6.0$ Hz, 1H), 7.43 (d, $J = 8.5$ Hz, 2H), 7.24 - 7.21 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3): δ 164.8, 145.6, 144.8, 141.0, 135.3, 129.3, 128.9, 127.3, 111.0; **HRMS** (TIC): calcd for $\text{C}_{11}\text{H}_7\text{Cl}_2\text{N}_2\text{O}_3$ $[\text{M} + \text{H}]^+$ 284.9828, found 284.9825.

2-(2,6-dichlorophenoxy)-6-methoxypyridine (5h)



Following the general procedure, using 2:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (35.0 mg, 65 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.06 (d, $J = 3.5$ Hz, 1H), 7.60 (t, $J = 7.5$ Hz, 1H), 7.05 (d, $J = 9.0$ Hz, 1H), 6.93 (d, $J = 3.0$ Hz, 2H), 6.90 - 6.76 (m, 2H), 3.72 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 156.0, 154.9, 153.6, 140.7, 129.2, 124.8, 121.1, 110.6, 109.2, 54.6; **HRMS** (TIC): calcd for $\text{C}_{12}\text{H}_{10}\text{Cl}_2\text{NO}_2$ $[\text{M} + \text{H}]^+$ 270.0083, found 270.0084.

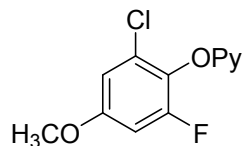
2-(2,6-dichlorophenoxy)-6-methylpyridine (5i)



Following the general procedure, using 5:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (36.6 mg, 68 % yield). ^1H NMR (400 MHz, CDCl_3): δ 7.56 (t, $J = 7.2$ Hz, 1H), 7.41 (t, $J = 6.4$ Hz, 2H), 7.22 - 7.15 (m, 3H), 6.90 (d, $J = 6.8$ Hz, 1H), 6.60 (d, $J = 8.0$ Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 161.3, 154.4, 139.7, 129.7, 124.9, 124.6, 122.1, 120.2, 109.4, 22.4; **HRMS** (TIC): calcd for

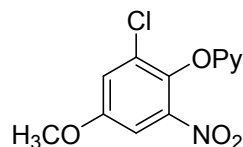
$C_{12}H_{10}Cl_2NO$ $[M + H]^+$ 254.0134, found 254.0131.

2-(2-chloro-6-fluoro-4-methoxyphenoxy)pyridine (7a)



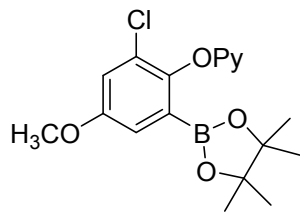
A 25 mL Schlenk tube equipped with a stir bar was charged with 3l (0.2 mmol), NFSI (3.0 equiv), $Pd(OAc)_2$ (10 mol %), EtOAc (2.0 mL), 110 °C, under N_2 , 6 h, using 10:1 petroleum ether -EtOAc as the eluant afforded a light yellow liquid (26.7 mg, 53 % yield). 1H NMR (500 MHz, $CDCl_3$): δ 8.12 (d, J = 4.5 Hz, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.05 - 7.00 (m, 2H), 6.95 (s, 1H), 6.82 - 6.68 (m, 1H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.2, 155.8, 146.3 (d, J_F = 3.8 Hz), 138.6 (d, J_F = 7.5 Hz), 134.5, 128.7 (d, J_F = 23.8 Hz), 127.4, 117.7 (d, J_F = 15.0 Hz), 113.5, 109.6 (d, J_F = 27.5 Hz), 101.0 (d, J_F = 22.5 Hz), 54.9; ^{19}F NMR (470 MHz, $CDCl_3$): δ -123.4 (s, 1F); **HRMS** (TIC): calcd for $C_{12}H_{10}ClFNO_2$ $[M + H]^+$ 254.0379, found 254.0382.

2-(2-chloro-4-methoxy-6-nitrophenoxy)pyridine (7b)



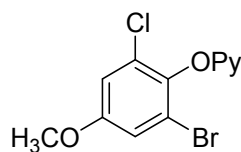
A 25 mL Schlenk tube equipped with a stir bar was charged with 3l (0.2 mmol), $AgNO_2$ (2.0 equiv), $Pd(OAc)_2$ (10 mol %), $K_2S_2O_8$ (2.0 equiv), DCE (2.0 mL), 110 °C, under N_2 , 48 h, using 5:1 petroleum ether- EtOAc as the eluant afforded a light yellow liquid (35.3 mg, 68 % yield). 1H NMR (500 MHz, $CDCl_3$): δ 8.06 (d, J = 4.5 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.05 (d, J = 9.0 Hz, 1H), 6.93 - 6.87 (m, 2H), 6.78 - 6.76 (m, 1H), 3.72 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 155.8, 146.4, 138.9, 138.5, 128.8, 124.4, 117.6, 113.5, 112.5, 109.5, 54.9; **HRMS** (TIC): calcd for $C_{12}H_{10}ClN_2O_4$ $[M + H]^+$ 281.0324, found 281.0323.

2-(2-chloro-4-methoxy-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)pyridine (7c)



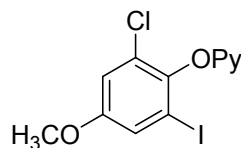
A 25 mL Schlenk tube equipped with a stir bar was charged with 3l (0.2 mmol), B₂pin₂ (2.0 equiv), Cp*Rh(III) (5 mol %), PCy₃ (30 mol %), EtOAc (2.0 mL), 100 °C, under N₂, 24 h, using 10:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid (41.1 mg, 57 % yield). ¹H NMR (500 MHz, CDCl₃): δ 8.05 (d, *J* = 4.5 Hz, 1H), 7.66 (t, *J* = 8.5 Hz, 1H), 6.96 - 6.92 (m, 2H), 6.88 (s, 2H), 3.74 (s, 3H), 1.51 (s, 6H), 1.18 (s, 6H); ¹³C NMR (125 MHz, CDCl₃): δ 162.3, 156.8, 147.5, 140.0, 139.5, 129.8, 126.1, 125.4, 118.6, 114.5, 113.6, 110.6, 83.5, 65.6, 56.7, 55.9, 25.0, 24.6; **HRMS** (TIC): calcd for C₁₈H₂₂BClNO₄ [M + H]⁺ 362.1325, found 362.1323.

2-(2-bromo-6-chloro-4-methoxyphenoxy)pyridine (7d)



A 25 mL Schlenk tube equipped with a stir bar was charged with 3l (0.2 mmol), NBS (3.0 equiv), Pd(OAc)₂ (10 mol %), TsOH (10 mol %), EtOAc (2.0 mL), 110 °C, under N₂, 6 h using 10:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid (32.3 mg, 52 % yield). ¹H NMR (500 MHz, CDCl₃): δ 8.11 (s, 1H), 7.71 (t, *J* = 8.0 Hz, 1H), 7.04 - 6.98 (m, 2H), 6.94 (s, 2H), 3.80 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 162.3, 156.8, 147.4, 139.9, 139.5, 129.8, 125.4, 118.6, 114.5, 111.0, 110.6, 55.9; **HRMS** (TIC): calcd for C₁₂H₁₀BrClNO₂ [M + H]⁺ 313.9578, found 313.9580.

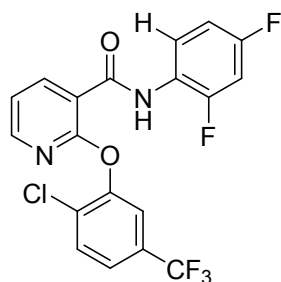
2-(2-chloro-6-iodo-4-methoxyphenoxy)pyridine (7e)



A 25 mL Schlenk tube equipped with a stir bar was charged with 3l (0.2 mmol), NIS (3.0 equiv), Pd(OAc)₂ (10 mol %), TsOH (10 mol %), EtOAc (2.0 mL), 110 °C, under N₂, 6 h, using 10:1 petroleum ether-EtOAc as the eluant afforded a light yellow liquid

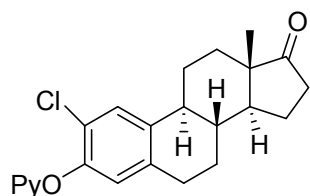
(25.3 mg, 35 % yield). ^1H NMR (500 MHz, CDCl_3): δ 8.05 (d, $J = 5.0$ Hz, 1H), 7.66 (t, $J = 7.5$ Hz, 1H), 6.97 - 6.93 (m, 2H), 6.88 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 163.4, 157.2, 147.5, 143.3, 139.4, 127.8, 124.4, 118.3, 115.6, 113.7, 110.8, 55.8; **HRMS** (TIC): calcd for $\text{C}_{12}\text{H}_{11}\text{ClINO}_2$ $[\text{M} + \text{H}]^+$ 361.9439, found 361.9437.

2-(2-chloro-5-(trifluoromethyl)phenoxy)-N-(2,4-difluorophenyl)nicotinamide (8a)



Following the general procedure, using 8:1 petroleum ether-EtOAc as the eluant afforded a light brown liquid (80.7 mg, 94 % yield). ^1H NMR (500 MHz, CDCl_3): δ 9.82 (s, 1H), 8.71-8.69 (m, 1H), 8.52 - 8.47 (m, 1H), 8.24 - 8.22 (m, 1H), 7.68 - 7.55 (m, 3H), 7.29 - 7.26 (m, 1H), 6.95 - 6.87 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3): δ 161.0, 158.8 (dd, $J_F = 245.0$, 11.2 Hz), 158.6, 152.9 (dd, $J_F = 246.2$, 11.2 Hz), 150.4, 148.5, 142.9, 131.4, 131.2, 130.6 (q, $J_F = 33.8$ Hz), 124.2, 123.9 (q, $J_F = 3.8$ Hz), 123.1 (d, $J_F = 7.5$ Hz), 122.8 (dd, $J_F = 10.0$, 3.8 Hz), 122.0 (q, $J_F = 3.8$ Hz), 120.4, 116.6, 111.3 (dd, $J_F = 21.2$, 3.8 Hz), 103.6 (dd, $J_F = 26.2$, 23.8 Hz); ^{19}F NMR (470 MHz, CDCl_3): δ -125.3 (s, 1F), -114.5 (s, 1F), -62.5 (s, 3F). **HRMS** (TIC): calcd for $\text{C}_{19}\text{H}_{11}\text{ClF}_5\text{N}_2\text{O}_2$ $[\text{M} + \text{H}]^+$ 429.0424, found 429.0423.

(8R,9S,13S,14S)-2-chloro-8,9,13,14-tetramethyl-3-(pyridin-2-yloxy)-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (8b)



Following the general procedure, using 10:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (46.5 mg, 55 % yield). ^1H NMR (400 MHz, CDCl_3): δ 8.22 (s, 1H), 7.77 (t, $J = 6.8$ Hz, 1H), 7.39 (s, 1H), 7.05 - 7.01 (m, 3H), 3.06 - 3.03 (m, 1H),

2.93 (s, 2H), 2.59 - 2.52 (m, 1H), 2.46 - 2.41 (m, 2H), 2.19 - 2.09 (m, 2H), 1.94 - 1.90 (m, 2H), 1.74 - 1.52 (m, 4H), 1.30 (s, 1H), 1.17 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 205.6, 162.9, 147.4, 147.2, 139.9, 137.4, 136.3, 127.4, 124.3, 123.8, 118.5, 111.2, 82.9, 47.3, 45.8, 45.7, 43.8, 36.5, 32.3, 28.7, 26.2, 25.2, 15.8; **HRMS** (TIC): calcd for $\text{C}_{26}\text{H}_{31}\text{ClNO}_2$ $[\text{M} + \text{H}]^+$ 424.2038, found 424.2039.

