Supporting Information
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Copper-Catalyzed Aromatic C–H Bond Halogenation Using Lithium Halides as Halogenating Reagents

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Supporting Information

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I. General procedures

Cu-catalyzed C–H halogenation of 2-arylpyridines was performed in sealed vials. Substrates 1, 2, 9, 11, 12, and 13 were purchased from Alfa Aesar or Acros and used without purification, substrates 3, 4, 5, 6, 7, 8, and 10 were synthesized according to the literature reported methods. The HOAc and Ac2O were purified prior to use following the guidelines of Perrin and Armarego. The Reactions were monitored by thin-layer chromatography (TLC). 1H and 13C NMR spectra were obtained on a MERCURY plus 400 at 400 MHz and 100 MHz, respectively. Data for 1H NMR spectra are reported as follows: chemical shift (δ shift), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling

constant (Hz), and assignment. Data for $^{13}$C NMR are reported in terms of chemical shift (δ ppm). Mass spectra were recorded on an AMD 402/3 or a HP 5989A mass selective detector. Infrared spectra were recorded on a AVATAR 370 machine.

II. The synthesis of 2-Methoxy-6-(3-nitrophenyl)pyridine$^{1b}$

Under air, a mixture of 2-bromo-6-methoxypyridine (945 mg, 5 mmol), (3-nitrophenyl)boronic acid (1098.5 mg, 6.5 mmol), Pd(OAc)$_2$ (11.2 mg, 0.05 mmol), PEG (1 g, 0.5 mmol), K$_2$CO$_3$ (1.38 g, 10 mmol), THF (8 mL) and H$_2$O (8 mL) was stirred for 3 days at 80 °C. Then the mixture was diluted with H$_2$O and extracted with EtOAc (3 x 50 mL). The extract was washed with brine (2 x 50 mL) and dried over Na$_2$SO$_4$. After evaporation, the residue was purified via chromatography on silica gel with petroleum ether/EtO (20/1 (v/v)) as the eluent to afford the white solid in 35% yield; m.p.: 102-104 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 4.06 (s, 3H), 6.79 (d, $J = 8.4$ Hz, 1H), 7.42 (d, $J = 7.2$ Hz, 1H), 7.63 (t, $J = 8.0$ Hz, 1H), 7.70 (t, $J = 8.0$ Hz, 1H), 8.23-8.25 (m, 1H), 8.39 (d, $J = 7.6$ Hz, 1H), 8.90 (t, $J = 2.0$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 53.4, 110.8, 113.1, 121.5, 123.3, 129.5, 132.4, 139.4, 140.7, 148.7, 151.9, 164.0; IR (KBr): ν 1575, 1523, 1469, 1429, 1248, 794, 739 cm$^{-1}$; MS (EI) m/z: 230.1 (M$^+$), 229.1 (M-1)$^+$, 200.1, 184.1, 155.1, 154.1, 153.1, 141.1, 140.1, 127.1, 114.0, 77.0; HRMS (EI) Calcd for C$_{12}$H$_{10}$N$_2$O$_3$: 230.0691, Found: 230.0685.
III. The optimization for the C-H halogenation

**Table 1.** Screening of Solvents for the Cu-Catalyzed C-H Halogenation

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Yield (%) (1a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMP</td>
<td>N.R.</td>
</tr>
<tr>
<td>2</td>
<td>DMSO</td>
<td>N.R.</td>
</tr>
<tr>
<td>3</td>
<td>DMF</td>
<td>N.R.</td>
</tr>
<tr>
<td>4</td>
<td>CH₃CN</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>THF</td>
<td>N.R.</td>
</tr>
<tr>
<td>6</td>
<td>CH₃NO₂</td>
<td>N.R.</td>
</tr>
<tr>
<td>7</td>
<td>1,4-dioxane</td>
<td>30</td>
</tr>
<tr>
<td>8</td>
<td>iPrOH</td>
<td>N.R.</td>
</tr>
<tr>
<td>9</td>
<td>acetone</td>
<td>N.R.</td>
</tr>
<tr>
<td>10</td>
<td>toluene</td>
<td>31</td>
</tr>
</tbody>
</table>

*a* Conditions: 1 (31 mg, 0.2 mmol), Cu(NO₃)₂·3H₂O (9.7 mg, 20 mol%), PPh₃ (21 mg, 40 mol%), LiCl (34 mg, 0.8 mmol), CrO₃ (80 mg, 0.8 mmol), solvent (1.5 mL), 150 °C. *b* GC yield with *n*-dodecane as an internal standard.

**Table 2.** Screening of Ligands for the Cu-Catalyzed C-H Halogenation

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Yield (%) (1a)</th>
<th>Yield (%) (1b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2,2-bipyridine</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>L-proline</td>
<td>33</td>
<td>34</td>
</tr>
<tr>
<td>3</td>
<td>1,2-Diaminocyclohexane</td>
<td>24</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>dppp</td>
<td>26</td>
<td>29</td>
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<tr>
<td>5</td>
<td>dppe</td>
<td>11</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>dppf</td>
<td>&lt;5</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>TEMDA</td>
<td>52</td>
<td>13</td>
</tr>
<tr>
<td>8</td>
<td>1,10-phenanthroline</td>
<td>23</td>
<td>42</td>
</tr>
</tbody>
</table>
a Conditions: 1 (31 mg, 0.2 mmol), Cu(NO$_3$)$_2$•3H$_2$O (9.7 mg, 20 mol%), LiCl (34 mg, 0.8 mmol), CrO$_3$ (24 mg, 0.24 mmol), HOAc (1.5 mL), ligand (20 mol%), 150 °C.  

GC yield with $n$-dodecane as internal standard.

IV. Representative procedure for Cu-catalyzed C-H bond chlorination

Synthesis of 2-(2,6-dichlorophenyl)pyridine (1b)$^3$ as a typical example:

In a sealed tube, a solution of substrate 1 (31 mg, 0.2 mmol), LiCl (34 mg, 0.8 mmol), Cu(NO$_3$)$_2$•3H$_2$O (9.7 mg, 0.04 mmol), CrO$_3$ (40 mg, 0.4 mmol), Ac$_2$O (102 mg, 1.0 mmol) in HOAc (1.5 mL) was stirred at 150 °C for 2 days. Then the mixture was neutralized with NaHCO$_3$ (saturated solution) and extracted with EtOAc (3 x 15 mL). The extract was washed with brine (2 x 15 mL) and dried over Na$_2$SO$_4$. After evaporation, the residue was purified via chromatography on silica gel with petroleum ether.

ether/Et₂O (2/1 (v/v)) as the eluent to afford oil 1b in 71% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.28 (t, J = 8.0 Hz, 1H), 7.34-7.37 (m, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.82 (td, J = 2.0, 7.6 Hz, 1H), 8.76 (d, J = 4.8 Hz, 1H); IR (KBr): ν 2929, 1593, 1566, 1422, 1191, 1116, 773, 747 cm⁻¹; MS (EI) m/z: 227.0 [M⁺ (³⁷Cl³⁷Cl)] (3.43), 225.0 [(M-1)⁺ (³⁷Cl³⁷Cl)] (20.26), 223.0 [M⁺ (³⁵Cl³⁵Cl)] (32.07), 190.0, 188.0, 161.0, 153.1, 152.1.

2-(2-Chlorophenyl)pyridine (1a)

![Structure of 1a]

The separative method of product (1a) is the same as that of 1b. Oil, ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.32 (m, 1H), 7.32-7.39 (m, 2H), 7.48 (dd, J = 1.6, 7.2 Hz, 1H), 7.60 (dd, J = 2.0, 7.6 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.77 (td, J = 1.6, 7.6 Hz, 1H), 8.73 (d, J = 4.8 Hz, 1H); IR (KBr): ν 2919, 1573, 1421, 1128, 751 cm⁻¹; MS (EI) m/z: 191.0 [M⁺ (³⁷Cl)] (19.72), 189.0 [M⁺ (³⁵Cl)] (51.25), 188.0, 155.1, 154.1, 153.0, 128.0, 127.0, 126.0.

2-(2-Chloro-4-methylphenyl)pyridine (2a)

![Structure of 2a]

In a sealed tube, a solution of substrate 2 (67.6 mg, 0.4 mmol), LiCl (67.2 mg, 1.6 mmol), Cu(NO₃)₂·3H₂O (19.4 mg, 0.08 mmol), CrO₃ (80 mg, 0.8 mmol), Ac₂O (204 mg, 2 mmol) in HOAc (3 ml) was stirred at 150 °C for 6 days. Then the mixture was neutralized with NaHCO₃ (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na₂SO₄. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/Et₂O (2/1 (v/v)) as the eluent to afford oil 2a in 32% yield; ¹H NMR (400 MHz, CDCl₃) δ 2.38 (s, 3H), 7.17 (d, J = 7.6 Hz, 1H), 7.26 (d, J = 6.0 Hz, 1H), 7.30 (s, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.74 (t,
$J = 8.0 \text{ Hz, 1H)$, 8.71 (d, $J = 5.2 \text{ Hz, 1H}$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 20.9, 122.1, 124.8, 127.8, 130.5, 131.3, 131.7, 135.7, 136.2, 139.9, 149.4, 156.8; IR (KBr): $\nu$ 2924, 1609, 1585, 1463, 874, 783 cm$^{-1}$; MS (EI) m/z: 205.1 [M$^+$ ($^{37}$Cl)] (19.72), 203.1 [M$^+$ ($^{35}$Cl)] (66.28), 169.1, 168.1, 167.1, 153.1. HRMS (EI) Calcd for C$_{12}$H$_{10}$ClN: 203.0502, Found: 203.0505.

2-(2,6-Dichloro-4-methylphenyl)pyridine (2b)$^3$

The separative method of product (2b) is the same as that of 2a. Oil, 30% yield; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.30 (s, 3H), 7.16 (s, 2H), 7.31-7.35 (m, 2H), 7.73 (td, $J = 1.6, 7.6 \text{ Hz, 1H}$), 8.68 (d, $J = 4.8 \text{ Hz, 1H}$); IR (KBr): $\nu$ 2923, 1731, 1600, 1494, 1452, 736, 696 cm$^{-1}$; MS (EI) m/z: 241.0 [M$^+$ ($^{37}$Cl$^{37}$Cl)] (3.10), 239.0 [M$^+$ ($^{37}$Cl$^{35}$Cl)] (19.70), 237.0 [M$^+$ ($^{35}$Cl$^{35}$Cl)] (30.51), 205.0, 204.0, 202.0, 167.1, 166.1, 139.1, 138.0.

2-(3-Chloro-4-methoxyphenyl)pyridine (3a)

In a sealed tube, a solution of subtrate 3 (74 mg, 0.4 mmol), LiCl (67.2 mg, 1.6 mmol), Cu(NO$_3$)$_2$·3H$_2$O (19.4 mg, 0.08 mmol), CrO$_3$ (80 mg, 0.8 mmol), Ac$_2$O (204 mg, 2 mmol) in HOAc (3 ml) was stirred at 150 °C for 19 hours. Then the mixture was neutralized with NaHCO$_3$ (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na$_2$SO$_4$. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/1,4-dioxane (15/1 (v/v)) as the eluent to afford yellow oil 3a in 24% yield; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.96 (s, 3H), 7.02 (d, $J = 8.8 \text{ Hz, 1H}$), 7.20-7.22 (m, 1H), 7.65 (d, $J = 8.0 \text{ Hz, 1H}$), 7.73 (td, $J = 2.0, 7.6 \text{ Hz, 1H}$), 7.88 (dd, $J = 2.2, 8.8 \text{ Hz, 1H}$), 8.06 (d, $J = 2.2 \text{ Hz, 1H}$), 8.66 (d, $J = 4.8 \text{ Hz, 1H}$); $^{13}$C NMR (100
MHz, CDCl$_3$) $\delta$ 56.2, 112.0, 119.8, 122.9, 126.2, 128.7, 132.5, 136.8, 149.6, 155.6, 155.7; IR (KBr): v 2922, 1595, 1507, 1463, 1274, 1058, 774 cm$^{-1}$; MS (EI) m/z: 221.0 [M$^+$ (37Cl)] (23.53), 219.0 [M$^+$ (35Cl)] (100.00), 206.0, 204.0, 176.0, 169.1, 141.1, 78.0; HRMS (EI) Caled for C$_{12}$H$_{10}$ClNO: 219.0451, Found: 219.0456.

2-(2,5-Dichloro-4-methoxyphenyl)pyridine (3b)

![Chemical Structure of 3b]

The separative method of product (3b) is the same as that of 3a. Yellow solid, 35% yield; m.p.: 118-120 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.95 (s, 3H), 7.02 (s, 1H), 7.26-7.29 (m, 1H), 7.65 (d, $J$ = 8.0 Hz, 1H), 7.68 (s, 1H), 7.75 (td, $J$ = 2.0, 8.0 Hz, 1H), 8.70 (d, $J$ = 4.8 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 56.5, 113.5, 121.5, 122.4, 124.8, 130.9, 132.2, 132.5, 135.9, 149.6, 155.2, 155.4; IR (KBr): v 2916, 1591, 1489, 1461, 1282, 1068, 746 cm$^{-1}$. MS (EI) m/z: 257.0 [M$^+$ (37Cl$_3$7Cl)] (9.92), 256.0 [(M-1)$^+$ (37Cl$_3$7Cl)] (8.21), 255.0 [M$^+$ (37Cl$_3$5Cl)] (62.80), 254.0 [(M-1)$^+$ (37Cl$_3$5Cl)] (13.21), 253.0 [M$^+$ (35Cl$_3$5Cl)] (100.00), 240.0, 238.0, 220.0, 218.0, 203.0, 177.0, 175.0, 140.1, 99.0; HRMS (EI) Caled for C$_{12}$H$_{9}$Cl$_2$NO: 253.0061, Found: 253.0054.

2-(2-Chloro-4-(trifluoromethyl)phenyl)pyridine (4a)

![Chemical Structure of 4a]

In a sealed tube, a solution of subtrate 4 (44.6 mg, 0.2 mmol), LiCl (34 mg, 0.8 mmol), Cu(NO$_3$)$_2$3H$_2$O (9.7 mg, 0.04 mmol), CrO$_3$ (40 mg, 0.4 mmol), Ac$_2$O (102 mg, 1 mmol) in HOAc (1.5 ml) was stirred at 150 °C for 2 days. Then the mixture was neutralized with NaHCO$_3$ (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na$_2$SO$_4$. After evaporation, the residue was purified via chromatography on silica gel with petroleum ether/Et$_2$O (2/1 (v/v)) as the eluent to afford yellow oil 4a in 23%
yield; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.34-7.37 (m, 1H), 7.63 (d, $J = 8.0$ Hz, 1H), 7.68 (d, $J = 8.0$ Hz, 1H), 7.75 (d, $J = 10.8$ Hz, 2H), 7.81 (td, $J = 2.0$, $8.0$ Hz, 1H), 8.75 (d, $J = 4.8$ Hz, 1H); IR (KBr): $\nu$ 2924, 1654, 1560, 1508, 1458, 1395, 1324, 1134 cm$^{-1}$; MS (EI) m/z: 259.0 [M$^+$ (37Cl)] (13.65), 257.0 [M$^+$ (35Cl)] (43.92), 223.0, 222.0, 191.1, 91.1, 71.1.

2-(2,6-Dichloro-4-(trifluoromethyl)phenyl)pyridine (4b)$^3$

![Image of 4b]

The separative method of product (4b) is the same as that of 4a. Oil, 58% yield; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.34 (d, $J = 8.0$ Hz, 1H), 7.38-7.41 (m, 1H), 7.68 (s, 2H), 7.85 (td, $J = 1.6$, 7.6 Hz, 1H), 8.77-8.78 (m, 1H); IR (KBr): $\nu$ 2925, 1587, 1558, 1486, 1384, 1316, 1137, 1101 cm$^{-1}$; MS (EI) m/z: 295.0 [M$^+$ (37Cl$_3$)] (2.73), 293.0 [M$^+$ (37Cl$_5$Cl)] (17.57), 291.0 [M$^+$ (35Cl$_3$Cl)] (27.46), 258.0, 257.0, 256.0, 236.0, 191.1, 78.0.

2-(2,6-Dichloro-3-methoxyphenyl)pyridine (5a)

![Image of 5a]

In a sealed tube, a solution of substrate 5 (55.5 mg, 0.3 mmol), LiCl (50.4 mg, 1.2 mmol), Cu(NO$_3$)$_2$·3H$_2$O (14.5 mg, 0.06 mmol), CrO$_3$ (60 mg, 0.6 mmol), Ac$_2$O (153 mg, 1.5 mmol) in HOAc (2.25 ml) was stirred at 150 °C for 19 hours. Then the mixture was neutralized with NaHCO$_3$ (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na$_2$SO$_4$. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/1,4-dioxane (5/1 (v/v)) as the eluent to afford oil 5a in 38% yield; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.93 (s, 3H), 6.94 (d, $J = 9.2$ Hz, 1H), 7.30-7.36 (m, 3H), 7.81 (td, $J = 2.0$, 8.0 Hz, 1H), 8.76 (d, $J = 4.8$ Hz,
1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 56.6, 112.3, 122.9, 123.2, 124.9, 125.4, 128.1, 136.4, 139.3, 149.6, 154.2, 155.6; IR (KBr): ν 2938, 1565, 1457, 1427, 1297, 1027, 771 cm$^{-1}$. MS (EI) m/z: 257.0 [M$^+$ (37Cl37Cl)] (5.37), 256.0 [(M-1)$^+$ (37Cl37Cl)] (4.79), 255.0 [M$^+$ (37Cl35Cl)] (36.58), 254.0 [(M-1)$^+$ (37Cl35Cl)] (7.63), 253.0 [M$^+$ (35Cl35Cl)] (58.88), 220.0, 218.0, 203.0, 175.0, 140.1; HRMS (EI) Calcd for C$_{12}$H$_9$ClNO: 253.0061, Found: 253.0061.

2-(2-Chloro-5-(trifluoromethyl)phenyl)pyridine (6a)$^4$

In a sealed tube, a solution of subtrate 6 (89.2 mg, 0.4 mmol), LiCl (67.2 mg, 1.6 mmol), Cu(NO$_3$)$_2$·3H$_2$O (19.4 mg, 0.08 mmol), CrO$_3$ (80 mg, 0.8 mmol), Ac$_2$O (204 mg, 2 mmol) in HOAc (3 ml) was stirred at 150 °C for 4.5 days. Then the mixture was neutralized with NaHCO$_3$ (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na$_2$SO$_4$. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/Et$_2$O (5/1 (v/v)) as the eluent to afford bright yellow oil 6a in 44% yield; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.33-7.36 (m, 1H), 7.58-7.63 (m, 2H), 7.68 (dt, $J = 1.2, 8.0$ Hz, 1H), 7.81 (td, $J = 2.0, 7.6$ Hz, 1H), 7.90 (s, 1H), 8.76 (ddd, $J = 0.8, 1.6, 4.8$ Hz, 1H); IR (KBr): ν 2962, 1612, 1587, 1462, 1403, 1337, 1129, 826, 788 cm$^{-1}$; MS (EI) m/z: 259.0 [M$^+$ (37Cl)] (15.19), 257.0 [M$^+$ (35Cl)] (48.25), 223.1, 222.1, 202.1, 188.0, 99.0, 71.1, 43.1.

3-Chloro-6-methoxy-2-(3-nitrophenyl)pyridine (7a)

In a sealed tube, a solution of subtrate 7 (69 mg, 0.3 mmol), LiCl (50.4 mg, 1.2 mmol),

Cu(NO₃)₂·3H₂O (14.5 mg, 0.06 mmol), CrO₃ (60 mg, 0.6 mmol), Ac₂O (153 mg, 1.5 mmol) in HOAc (2.25 ml) was stirred at 150 °C for 22 hours. Then the mixture was neutralized with NaHCO₃ (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na₂SO₄. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/Et₂O (15/1 (v/v)) as the eluent to afford white solid 7a in 28% yield; m.p.: 138-140 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.97 (s, 3H), 6.76 (d, J = 8.6 Hz, 1H), 7.63 (t, J = 8.4 Hz, 1H), 7.67 (d, J = 8.6 Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 8.26-8.29 (m, 1H), 8.70 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 53.9, 112.0, 121.7, 123.4, 124.6, 128.8, 135.4, 139.6, 141.0, 148.0, 149.8, 162.2; IR (KBr): ν 2977, 1586, 1526, 1463, 1410, 1251, 1027, 734 cm⁻¹; MS (EI) m/z: 266.0 [M⁺ (³⁷Cl)] (26.84), 265.0 [(M-1)⁺ (³⁷Cl)] (37.36), 264.0 [M⁺ (³⁵Cl)] (100.00), 263.0 [(M-1)⁺ (³⁵Cl)] (84.25), 235.0, 218.0, 217.0, 203.0, 140.1; HRMS (EI) Calcd for C₁₂H₉ClN₂O₃: 264.0302, Found: 264.0295.

3,5-Dichloro-2-methoxy-6-(3-nitrophenyl)pyridine (7b)

![3,5-Dichloro-2-methoxy-6-(3-nitrophenyl)pyridine (7b)](image)

The separative method of product (7b) is the same as that of 7a. White solid, 17% yield; m.p.: 131-132 °C; ¹H NMR (400 MHz, CDCl₃) δ 4.07 (s, 3H), 7.65 (t, J = 8.0 Hz, 1H), 7.80 (s, 1H), 8.16 (d, J = 7.6 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H), 8.69 (t, J = 2.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 55.0, 118.8, 121.7, 123.9, 124.8, 129.2, 135.6, 135.7, 138.9, 140.3, 148.3, 157.8; IR (KBr): ν 2954, 1530, 1463, 1404, 1350, 1249, 731 cm⁻¹; MS (EI) m/z: 302.0 [M⁺ (³⁷Cl³⁷Cl)] (10.16), 301.0 [(M-1)⁺ (³⁷Cl³⁷Cl)] (13.74), 300.0 [M⁺ (³⁷Cl³⁵Cl)] (61.04), 299.0 [(M-1)⁺ (³⁷Cl³⁵Cl)] (50.71), 298.0 [M⁺ (³⁵Cl³⁵Cl)] (100.00), 297.0 [(M-1)⁺ (³⁵Cl³⁵Cl)] (65.29), 271.0, 269.0, 239.0, 237.0, 174.0; HRMS (EI) Calcd for C₁₂H₈Cl₂N₂O₃: 297.9912, Found: 297.9906.
3-Chloro-6-methoxy-2-(3-(trifluoromethyl)phenyl)pyridine (8a)\(^5\)

![8a]

In a sealed tube, a solution of subtrate 8 (101.2 mg, 0.4 mmol), LiCl (67.2 mg, 1.6 mmol), Cu(NO\(_3\))\(_2\)·3H\(_2\)O (19.4 mg, 0.08 mmol), CrO\(_3\) (80 mg, 0.8 mmol), Ac\(_2\)O (204 mg, 2 mmol) in HOAc (3 ml) was stirred at 150 °C for 14 hours. Then the mixture was neutralized with NaHCO\(_3\) (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na\(_2\)SO\(_4\). After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether as the eluent to afford oil 8a in 30% yield; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.96 (s, 3H), 6.72 (d, \(J = 8.8\) Hz, 1H), 7.58 (t, \(J = 7.6\) Hz, 1H), 7.64-7.69 (m, 2H), 8.01 (d, \(J = 8.0\) Hz, 1H), 8.09 (s, 1H); IR (KBr): v 2922, 1581, 1463, 1408, 1330, 1125, 701 cm\(^{-1}\); MS (EI) m/z: 289.0 [M\(^+\) (37Cl)] (19.53), 288.0 [(M-1)\(^+\) (37Cl)] (29.75), 287.0 [M\(^+\) (35Cl)] (72.09), 286.0 [(M-1)\(^+\) (35Cl)] (100.00), 258.0, 222.0, 202.0.

3,5-Dichloro-2-methoxy-6-(3-(trifluoromethyl)phenyl)pyridine (8b)

![8b]

The separative method of product (8b) is the same as that of 8a. Yellow solid, 33% yield; m.p.: 50-52 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.05 (s, 3H), 7.58 (t, \(J = 7.6\) Hz, 1H), 7.69 (d, \(J = 8.0\) Hz, 1H), 7.77 (s, 1H), 7.99 (d, \(J = 8.0\) Hz, 1H), 8.06 (s, 1H); \(^1\)H NMR (100 MHz, CDCl\(_3\)) \(\delta\) 54.7, 117.9, 121.3, 125.57, 125.61, 126.32, 126.36, 128.5, 132.7, 137.9, 139.9, 149.1, 157.5; IR (KBr): v 2953, 1570, 1467, 1405, 1326, 1248, 1128, 751 cm\(^{-1}\); MS (EI) m/z: 325.0 [M\(^+\) (37Cl\(^37\)Cl)] (9.56), 324.0 [(M-1)\(^+\) (37Cl\(^37\)Cl)] (15.91), 323.0 [M\(^+\) (37Cl\(^35\)Cl)] (59.97), 322.0 [(M-1)\(^+\) (37Cl\(^35\)Cl)] (66.37), 321.0 [M\(^+\) (35Cl\(^35\)Cl)] (100.00), 320.0 [(M-1)\(^+\) (35Cl\(^35\)Cl)] (86.36), 294.0, 292.0, 256.0, 236.0;

HRMS (EI) Calcd for C_{13}H_{8}Cl_{2}F_{3}NO: 320.9935, Found: 320.9923.

2-(2-Chlorophenyl)-3-methylpyridine (9a)

![9a]

In a sealed tube, a solution of substrate 9 (67.6 mg, 0.4 mmol), LiCl (67.2 mg, 1.6 mmol), Cu(NO_{3})_{2}:3H_{2}O (19.4 mg, 0.08 mmol), CrO_{3} (80 mg, 0.8 mmol), Ac_{2}O (204 mg, 2 mmol) in HOAc (3 ml) was stirred at 150 °C for 6 days. Then the mixture was neutralized with NaHCO_{3} (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na_{2}SO_{4}. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/Et_{2}O (2/1 (v/v)) as the eluent to afford oil 9a in 32% yield; $^{1}$H NMR (400 MHz, CDCl_{3}) δ 2.17 (s, 3H), 7.25 (dd, $J = 4.8$, 7.6 Hz, 1H), 7.30-7.36 (m, 3H), 7.46-7.48 (m, 1H), 7.60 (dd, $J = 1.2$, 8.0 Hz, 1H), 8.53 (dd, $J = 0.8$, 4.8 Hz, 1H); IR (KBr): ν 2923, 1569, 1430, 1080, 1021, 792, 755 cm^{-1}; MS (EI) m/z: 205.0 [M^+ (^{37}Cl)] (17.68), 204.0 [(M-1)^+ (^{37}Cl)] (37.19), 203.0 [M^+ (^{35}Cl)] (53.60), 202.0 [(M-1)^+ (^{35}Cl)] (100.00), 168.1, 167.1.

2-(2-Chlorophenyl)-6-methoxypyridine (10a)

![10a]

In a sealed tube, a solution of substrate 10 (74 mg, 0.4 mmol), LiCl (67.2 mg, 1.6 mmol), Cu(NO_{3})_{2}:3H_{2}O (19.4 mg, 0.08 mmol), CrO_{3} (80 mg, 0.8 mmol), Ac_{2}O (204 mg, 2 mmol) in HOAc (3 ml) was stirred at 150 °C for 14 hours. Then the mixture was neutralized with NaHCO_{3} (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na_{2}SO_{4}. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/1,4-dioxane (5/1 (v/v)) as the eluent to afford oil 10a in 21% yield; $^{1}$H NMR (400 MHz, CDCl_{3}) δ 3.83 (s, 3H), 6.89 (dd, $J = 2.8$, 8.8 Hz, 1H), 7.14 (d, $J = 3.2$ Hz, 1H), 7.28-7.31 (m, 1H), 7.36 (d, $J = 8.8$ Hz, 1H), 7.66 (d, $J = 8.0$ Hz, 1H).
Hz, 1H), 7.77 (td, J = 1.6, 7.6 Hz, 1H), 8.72 (d, J = 4.0 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 55.6, 116.0, 116.1, 122.5, 123.4, 124.9, 130.8, 135.8, 139.8, 149.4, 156.8, 158.4; IR (KBr): $\nu$ 2928, 1734, 1585, 1460, 1224, 1034, 787 cm$^{-1}$; MS (EI) m/z: 221.0 [M$^+$ ($^{37}$Cl)] (16.59), 220.0 [(M-1)$^+$ ($^{37}$Cl)] (34.80), 219.0 [M$^+$ ($^{35}$Cl)] (58.71), 218.0 [(M-1)$^+$ ($^{35}$Cl)] (100.00), 190.0, 189.0, 154.1, 78.0; HRMS (EI) Calcd for C$_{12}$H$_{10}$ClNO: 219.0451, Found: 219.0446.

4-Chloro-2-(2-chlorophenyl)-6-methoxypyridine (10b)

The separative method of product (10b) is the same as that of 10a. Yellow solid, 18% yield; m.p.: 94-95 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.94 (s, 3H), 7.22 (s, 1H), 7.30-7.33 (m, 1H), 7.50 (s, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.78 (t, J = 8.0 Hz, 1H), 8.73 (d, J = 4.8 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 56.4, 114.5, 122.7, 123.3, 123.4, 124.9, 131.1, 136.0, 138.3, 149.6, 154.0, 155.8; IR (KBr): $\nu$ 2921, 1735, 1560, 1458, 1370, 1245 cm$^{-1}$; MS (EI) m/z: 257.0 [M$^+$ ($^{37}$Cl$_3$Cl)] (5.10), 256.0 [(M-1)$^+$ ($^{37}$Cl$_3$Cl)] (13.32), 255.0 [M$^+$ ($^{37}$Cl$_3$Cl)] (31.47), 254.0 [(M-1)$^+$ ($^{37}$Cl$_3$Cl)] (66.55), 253.0 [M$^+$ ($^{37}$Cl$_3$Cl)] (49.75), 252.0 [(M-1)$^+$ ($^{37}$Cl$_3$Cl)] (100.00), 224.0, 188.0, 78.0; HRMS (EI) Calcd for C$_{12}$H$_9$Cl$_2$NO: 253.0061, Found: 253.0059.

3-Chloro-6-(2-chlorophenyl)-2-methoxypyridine (10c)

The separative method of product (10c) is the same as that of 10a. Oil, 36% yield; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.93 (s, 3H), 6.93 (d, J = 8.8 Hz, 1H), 7.31-7.37 (m, 1H), 7.80 (td, J = 2.0, 8.0 Hz, 1H), 8.74 (d, J = 4.4 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 56.6, 112.3, 122.9, 123.2, 124.9, 125.4, 128.1, 136.4, 139.3, 149.6, 154.2, 155.6; IR (KBr): $\nu$ 2935, 1565, 1457, 1427, 1297, 1241, 1080, 1027, 772 cm$^{-1}$; MS (EI) m/z:
257.0 [M⁺ (³⁷Cl³⁷Cl)] (5.76), 256.0 [(M-1)⁺ (³⁷Cl³⁷Cl)] (4.63), 255.0 [M⁺ (³⁷Cl³⁵Cl)] (35.30), 254.0 [(M-1)⁺ (³⁷Cl³⁵Cl)] (7.51), 253.0 [M⁺ (³⁵Cl³⁵Cl)] (56.45), 220.0, 218.0, 203.0, 175.0, 78.0; HRMS (EI) Calcd for C₁₂H₉Cl₂NO: 253.0061, Found: 253.0068.

1-(2-Chlorophenyl)isoquinoline (11a)⁶

\[
\text{N} \quad \text{Cl} \\
\text{11a}
\]

In a sealed tube, a solution of subtrate 11 (41 mg, 0.2 mmol), LiCl (34 mg, 0.8 mmol), Cu(NO₃)₂·3H₂O (9.7 mg, 0.04 mmol), MnO₂ (69.6 mg, 0.8 mmol) in HOAc (1.5 mL) was stirred at 150 °C for 4 days. Then the mixture was neutralized with NaHCO₃ (saturated solution) and extracted with EtOAc (3 x 15 mL). The extract was washed with brine (2 x 15 mL) and dried over Na₂SO₄. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/ethyl acetate (10/1 (v/v)) as the eluent to afford oil 11a in 33% yield; ¹H NMR (400 MHz, Acetone-D₆) δ 7.36-7.51 (m, 6H), 7.64-7.67 (m, 1H), 7.74 (d, \(J = 5.6\) Hz, 1H), 7.92 (d, \(J = 8.4\) Hz, 1H), 8.47 (dd, \(J = 0.8, 5.6\) Hz, 1H); IR (KBr): \(\nu\) 1582, 1430, 1388, 1357, 1051, 826, 754 cm⁻¹; MS (EI) m/z: 241.0 [M⁺ (³⁷Cl)] (15.29), 240.0 [(M-1)⁺ (³⁷Cl)] (30.52), 239.0 [M⁺ (³⁵Cl)] (53.66), 238.0 [(M-1)⁺ (³⁵Cl)] (100.0), 204.1, 202.1, 201.1, 177.1, 176.1, 175.1, 71.1, 43.0.

2-(2-Chlorophenyl)quinoline (12a)⁷

\[
\text{Cl} \\
\text{N} \\
\text{12a}
\]

In a sealed tube, a solution of subtrate 12 (61.5 mg, 0.3 mmol), LiCl (50.4 mg, 1.2 mmol), Cu(NO₃)₂·3H₂O (14.5 mg, 0.06 mmol), CrO₃ (60 mg, 0.6 mmol), Ac₂O (153 mg, 1.5 mmol) in HOAc (2.25 ml) was stirred at 150 °C for 5.5 days. Then the mixture was neutralized with NaHCO₃ (saturated solution) and extracted with EtOAc

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(3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na₂SO₄. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/Et₂O (20/1 (v/v)) as the eluent to afford oil 12a in 21% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.36-7.43 (m, 2H), 7.50-7.52 (m, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.70 (dd, J = 2.0, 7.2 Hz, 1H), 7.73-7.77 (m, 2H), 7.87 (d, J = 8.0 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H); IR (KBr): ν 1597, 1506, 1486, 1455, 760 cm⁻¹; MS (EI) m/z: 241.0 [M⁺ (⁰Cl)] (14.39), 239.0 [M⁺ (³⁵Cl)] (44.87), 238.0 [(M-1)+ (³⁵Cl)] (7.48), 205.1, 204.1, 203.1, 176.1.

8-Chloro-2-phenylquinoline (12b)

The separative method of product (12b) is the same as that of 12a. Oil, 28% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.43 (t, J = 8.0 Hz, 1H), 7.46-7.56 (m, 3H), 7.74-7.75 (m, 1H), 7.83-7.85 (m, 1H), 7.97 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 8.8 Hz, 1H), 8.28-8.30 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 119.3, 126.3, 126.5, 127.5, 127.7, 128.4, 128.9, 129.7, 133.9, 137.2, 139.0, 144.3, 157.4; IR (KBr): ν 1744, 1567, 1416, 1123, 762 cm⁻¹; MS (EI) m/z: 241.0 [M⁺ (⁰Cl)] (30.23), 240.0 [(M-1)+ (³⁵Cl)] (26.90), 239.0 [M⁺ (³⁵Cl)] (100.00), 238.0 [(M-1)+ (³⁵Cl)] (40.66), 204.1, 203.1; HRMS (EI) Calcd for C₁₅H₁₀ClN: 239.0502, Found: 239.0495.

5-Chlorobenzo[h]quinoline (13a)

In a sealed tube, a solution of substrate 13 (53.7 mg, 0.3 mmol), LiCl (50.4 mg, 1.2 mmol), Cu(NO₃)₂·3H₂O (14.5 mg, 0.06 mmol), CrO₃ (60 mg, 0.6 mmol), Ac₂O (153 mg, 1.5 mmol) in HOAc (2.25 ml) was stirred at 150 °C for 5.5 days. Then

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mixture was neutralized with NaHCO₃ (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na₂SO₄. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/Et₂O (2/1 v/v) as the eluent to afford yellow solid 13a in 36% yield; m.p.: 110-112 °C (lit. m.p.: 113.6-115.0 °C); ¹H NMR (400 MHz, CDCl₃) δ 7.61 (dd, J = 4.4, 8.0 Hz, 1H), 7.67-7.74 (m, 2H), 7.81 (d, J = 7.2 Hz, 1H), 7.90 (s, 1H), 8.62 (d, J = 8.0 Hz, 1H), 9.03 (d, J = 4.4 Hz, 1H), 9.24 (d, J = 7.2 Hz, 1H); IR (KBr): ν 2922, 1586, 1565, 1444, 1398, 935, 757 cm⁻¹; MS (EI) m/z: 215.0 [M⁺ (³⁷Cl)] (26.83), 214.0 [(M-1)+ (³⁷Cl)] (14.88), 213.0 [M⁺ (³⁵Cl)] (100.00), 212.0 [(M-1)+ (³⁵Cl)] (11.71), 178.1, 151.1.

Representative procedure for the Cu-catalyzed C-H bond bromination

Synthesis of 2-(2-bromophenyl)pyridine (1c)³ as a typical example:

2-(2-Bromophenyl)pyridine (1c)³

\[ \text{Br} \]
\[ \text{N} \]
\[ \text{1c} \]

In a sealed tube, a solution of substrate 1 (31 mg, 0.2 mmol), LiBr (69 mg, 0.8 mmol), Cu(NO₃)₂·3H₂O (9.7 mg, 0.04 mmol), CrO₃ (40 mg, 0.4 mmol), Ac₂O (102 mg, 1 mmol) in HOAc (1.5 mL) was stirred at 150 °C for 19 hours. Then the mixture was neutralized with NaHCO₃ (saturated solution) and extracted with EtOAc (3 x 15 mL). The extract was washed with brine (2 x 15 mL) and dried over Na₂SO₄. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/Et₂O (2/1 v/v) as the eluent to afford oil 1c in 22% yield; ¹H NMR (400 MHz, CDCl₃) δ 7.24-7.31 (m, 2H), 7.41 (td, J = 1.2, 7.2 Hz, 1H), 7.54 (dd, J = 1.6, 7.6 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.68 (dd, J = 0.8, 8.0 Hz, 1H), 7.77 (td, J = 1.6, 7.6 Hz, 1H), 8.72 (d, J = 4.8 Hz, 1H); IR (KBr): ν 2926, 1636, 1566, 1415, 1114 cm⁻¹; MS (EI) m/z: 235.0 [M⁺ (⁸¹Br)] (23.53), 234.0 [(M-1)+ (⁸¹Br)] (12.80), 233.0 [M⁺ (⁷⁹Br)] (24.63), 232.0 [(M-1)+ (⁷⁹Br)] (10.77), 154.1, 127.1, 43.0.
2-(2,6-Dibromophenyl)pyridine (1d)

The separative method of product (1d) is the same as that of 1c. Yellow solid, 48\% yield; m.p.: 63-65 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.13 (t, J = 8.0 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.34-7.37 (m, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.82 (td, J = 1.6, 7.6 Hz, 1H), 8.75 (d, J = 4.8 Hz, 1H); IR (KBr): ν 2927, 1635, 1567, 1415, 1106 cm⁻¹; MS (EI) m/z: 314.9 [M⁺ (⁸¹Br⁸¹Br)] (11.08), 312.9 [M⁺ (⁸¹Br⁷⁹Br)] (21.96), 310.9 [M⁺ (⁷⁹Br⁷⁹Br)] (11.55), 234.0, 232.0, 153.1, 126.0.

2-(3-Bromo-4-methoxyphenyl)pyridine (3c)

In a sealed tube, a solution of subtrate 3 (55.5 mg, 0.3 mmol), LiBr (104 mg, 1.2 mmol), CuO(nano) (4.8 mg, 0.06 mmol), CrO₃ (60 mg, 0.6 mmol), Ac₂O (153 mg, 1.5 mmol) in HOAc (2.3 mL) was stirred at 150 °C for 17 hours. Then the mixture was neutralized with NaHCO₃ (saturated solution) and extracted with EtOAc (3 x 15 mL). The extract was washed with brine (2 x 15 mL) and dried over Na₂SO₄. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/Et₂O (2/1 (v/v)) as the eluent to afford white solid 3c in 51\% yield; m.p.: 77-78 °C; ¹H NMR (400 MHz, CDCl₃) δ 3.94 (s, 3H), 6.97 (d, J = 8.8 Hz, 1H), 7.17-7.21 (m, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.71 (td, J = 1.6, 7.6 Hz, 1H), 7.92 (dd, J = 2.4, 8.8 Hz, 1H), 8.23 (d, J = 2.4 Hz, 1H), 8.65 (d, J = 4.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 56.2, 111.7, 112.0, 119.8, 121.9, 126.9, 131.7, 133.2, 136.7, 149.5, 155.5, 156.4; IR (KBr): ν 1598, 1506, 1464, 1279, 1054, 773 cm⁻¹; MS (EI) m/z: 265.0 [M⁺ (⁸¹Br)] (96.78), 263.0 [M⁺ (⁷⁹Br)] (100.00), 250.0, 169.1, 154.1, 141.1; HRMS (EI) Calcd for C₁₂H₁₀BrNO: 262.9946, Found: 262.9940.
2-(2,5-Dibromo-4-methoxyphenyl)pyridine (3d)

The separative method of product (3d) is the same as that of 3c. Yellow solid, 13% yield; m.p.: 127-128 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.95 (s, 3H), 7.17 (s, 1H), 7.27-7.30 (m, 1H), 7.60 (d, \(J = 7.6\) Hz, 1H), 7.75 (d, \(J = 7.6\) Hz, 1H), 7.77 (s, 1H), 8.70 (s, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 56.6, 111.0, 116.4, 120.8, 122.4, 124.8, 134.8, 135.4, 135.9, 149.5, 156.2, 156.8; IR (KBr): \(\nu\) 2926, 1596, 1458, 1430, 1056 cm\(^{-1}\); MS (EI) m/z: 344.9 [M\(^+\) (\(^{81}\)Br\(^{81}\)Br)] (28.31), 342.9 [M\(^+\) (\(^{81}\)Br\(^{79}\)Br)] (72.17), 340.9 [M\(^+\) (\(^{79}\)Br\(^{79}\)Br)] (33.77), 264.0, 262.0, 247.0, 221.0, 140.1; HRMS (EI) Calcd for C\(_{12}\)H\(_9\)Br\(_2\)NO: 340.9051, Found: 340.9092.

2-(2,3-Dibromo-4-methoxyphenyl)pyridine (3e)

The separative method of product (3e) is the same as that of 3c. Yellow solid, 10% yield; m.p.: 139-141 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.96 (s, 3H), 6.98 (d, \(J = 8.6\) Hz, 1H), 7.56 (d, \(J = 8.6\) Hz, 1H), 7.85 (dd, \(J = 2.4, 8.4\) Hz, 1H), 7.91 (dd, \(J = 2.0, 8.4\) Hz, 1H), 8.20 (d, \(J = 2.0\) Hz, 1H), 8.70 (d, \(J = 2.4\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 56.6, 112.1, 112.5, 119.2, 121.1, 127.1, 131.9, 132.3, 139.6, 150.9, 154.27, 154.34; IR (KBr): \(\nu\) 2924, 1557, 1422, 1290, 1056, 801 cm\(^{-1}\); MS (EI) m/z: 344.9 [M\(^+\) (\(^{81}\)Br\(^{81}\)Br)] (45.26), 342.9 [M\(^+\) (\(^{81}\)Br\(^{79}\)Br)] (100.00), 340.9 [M\(^+\) (\(^{79}\)Br\(^{79}\)Br)] (50.05), 327.9, 247.0, 221.0, 140.1; HRMS (EI) Calcd for C\(_{12}\)H\(_9\)Br\(_2\)NO: 340.9051, Found: 340.9092.

2-(2-Bromo-5-methoxyphenyl)pyridine (5b)

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In a sealed tube, a solution of substrate 5 (55.5 mg, 0.3 mmol), LiBr (104 mg, 1.2 mmol), CuO(nano) (4.8 mg, 0.06 mmol), CrO₃ (60 mg, 0.6 mmol), Ac₂O (153 mg, 1.5 mmol) in HOAc (2.3 ml) was stirred at 150 °C for 17 hours. Then the mixture was neutralized with NaHCO₃ (saturated solution) and extracted with EtOAc (3 x 15 mL). The combined organic layers was washed with brine (2 x 15 mL) and dried over Na₂SO₄. After evaporation, the residue was purified via thin-layer chromatography (TLC) with petroleum ether/ethyl acetate (5/1 (v/v)) as the eluent to afford yellow oil 5b in 40% yield; ¹H NMR (400 MHz, CDCl₃) δ 3.82 (s, 3H), 6.83 (dd, J = 3.2, 8.8 Hz, 1H), 7.09 (d, J = 3.2 Hz, 1H), 7.28-7.31 (m, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.76 (td, J = 2.0, 7.6 Hz, 1H), 8.71-8.72 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 55.5, 112.1, 116.2, 116.3, 122.4, 124.7, 133.9, 135.8, 141.8, 149.3, 158.1, 158.9; IR (KBr): ν 2926, 1636, 1567, 1415, 1112 cm⁻¹; MS (EI) m/z: 265.0 [M⁺ (⁸¹Br)] (62.51), 264.0 [(M-1)⁺ (⁸¹Br)] (96.51), 263.0 [M⁺ (⁷⁹Br)] (56.06), 262.0 [(M-1)⁺ (⁷⁹Br)] (100.00), 184.1, 154.1, 141.1; HRMS (EI) Calcd for C₁₂H₁₀BrNO: 262.9946, Found: 262.9940.

2-(2,6-Dibromo-3-methoxyphenyl)pyridine (5c)

The separative method of product (5c) is the same as that of 5b. Yellow oil, 17% yield; ¹H NMR (400 MHz, CDCl₃) δ 3.93 (s, 3H), 6.85 (d, J = 8.8 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.33-7.36 (m, 1H), 7.58 (d, J = 8.8 Hz, 1H), 7.82 (td, J = 2.0, 7.6 Hz, 1H), 8.75 (d, J = 4.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 55.5, 109.7, 112.7, 113.9, 122.9, 124.6, 131.9, 136.5, 142.8, 149.4, 155.7, 158.9; IR (KBr): ν 2924, 1559, 1423, 1293, 1024, 799 cm⁻¹. MS (EI) m/z: 344.9 [M⁺ (⁸¹Br₂Br)] (14.91), 342.9 [M⁺ (⁸¹Br⁷⁹Br)] (32.02), 340.9 [M⁺ (⁷⁹Br₂⁷⁹Br)] (16.57), 264.0, 262.0, 247.0, 140.1; HRMS
(EI) Calcd for C_{12}H_{9}Br_{2}NO: 340.9051, Found: 340.9054.

2-(2,4-Dibromo-5-methoxyphenyl)pyridine (5d)

The separative method of product (5d) is the same as that of 5b. White solid, 26% yield; m.p.: 109-111 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.92 (s, 3H), 7.12 (s, 1H), 7.31-7.34 (m, 1H), 7.65 (d, \(J = 8.0\) Hz, 1H), 7.78 (td, \(J = 1.6, 7.6\) Hz, 1H), 7.84 (s, 1H), 8.72 (d, \(J = 4.4\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 56.5, 112.1, 114.4, 122.7, 124.8, 135.9, 136.8, 141.1, 149.5, 155.4, 157.3, 168.8; IR (KBr): v 2924, 1457, 1363, 1226, 1055, 786 cm\(^{-1}\); MS (EI) m/z: 344.9 [M\(^{+}\) (\(^{81}\)Br\(^{81}\)Br)] (19.94), 343.9 [(M-1)\(^{+}\) (\(^{81}\)Br\(^{81}\)Br)] (38.62), 342.9 [M\(^{+}\) (\(^{81}\)Br\(^{79}\)Br)] (46.07), 341.9 [(M-1)\(^{+}\) (\(^{81}\)Br\(^{79}\)Br)] (100.00), 340.9 [M\(^{+}\) (\(^{79}\)Br\(^{79}\)Br)] (24.49), 339.9 [(M-1)\(^{+}\) (\(^{79}\)Br\(^{79}\)Br)] (42.96), 232.0, 140.1; HRMS (EI) Calcd for C\(_{12}\)H\(_{9}\)Br\(_{2}\)NO: 340.9051, Found: 340.9058.
IV. Spectral data of NMR

\[
\begin{align*}
7.74 & \quad 6.795 \\
7.253 & \\
7.412 & \\
7.430 & \\
7.609 & \\
7.628 & \\
7.496 & \\
7.676 & \\
7.665 & \\
7.175 & \\
7.253 & \\
8.219 & \\
8.223 & \\
8.247 & \\
8.223 & \\
8.277 & \\
8.395 & \\
8.590 & \\
8.685 & \\
8.900 & \\
9.00 &
\end{align*}
\]
\[
\begin{align*}
\text{CF}_3 & \quad \text{O} \\
\text{Cl} & \quad \text{Cl} \\
\text{Cl} & \quad \text{O} \\
\text{CF}_3 & \quad 8b
\end{align*}
\]