Supporting Information

For
Pd(II)-Catalyzed C-H Arylation of Aryl and Benzyl Weinreb Amides

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General Information:

Unless otherwise noted, all the reagents were commercially available, and used as received. NMR spectra were recorded on Bruker-400 (400 MHz for $^1$H; 100 MHz for $^{13}$C) instruments internally referenced to SiMe$_4$ signal. Chemical shifts are reported in δ ppm. High resolution mass spectra were recorded on P-SIMS-Gly of Bruker Daltonics Inc. using ESI-TOF (electrospray ionization-time of flight) or Micromass GCT using EI (electron impact).
Tables of the Optimization of Reaction Conditions

Table S1. Silver Salts Screening:

![Chemical reaction diagram]

<table>
<thead>
<tr>
<th>entry</th>
<th>silver salt (equiv)</th>
<th>yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ag&lt;sub&gt;2&lt;/sub&gt;O (1)</td>
<td>N. R.</td>
</tr>
<tr>
<td>2</td>
<td>Ag&lt;sub&gt;2&lt;/sub&gt;CO&lt;sub&gt;3&lt;/sub&gt; (1)</td>
<td>N. R.</td>
</tr>
<tr>
<td>3</td>
<td>AgTFA (2)</td>
<td>N. R.</td>
</tr>
<tr>
<td>4</td>
<td>AgOAc (2)</td>
<td>N. R.</td>
</tr>
<tr>
<td>5</td>
<td>AgOTf (2)</td>
<td>69 (4)</td>
</tr>
</tbody>
</table>

<sup>a</sup>GC yield using dodecane as the internal standard, yield of diarylation product was given in the parentheses.

Table S2. Solvent Screening:

![Chemical reaction diagram]

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhMe</td>
<td>67 (6)</td>
</tr>
<tr>
<td>2</td>
<td>t-AmlyOH</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>dioxane</td>
<td>50 (3)</td>
</tr>
<tr>
<td>4</td>
<td>DMF</td>
<td>N. R.</td>
</tr>
<tr>
<td>5</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;CN</td>
<td>N. R.</td>
</tr>
<tr>
<td>6</td>
<td>DMSO</td>
<td>N. R.</td>
</tr>
<tr>
<td>7</td>
<td>acetone</td>
<td>complex</td>
</tr>
<tr>
<td>8</td>
<td>DCE</td>
<td>69 (4)</td>
</tr>
</tbody>
</table>

<sup>a</sup>GC yield using dodecane as the internal standard, yield of diarylation product was given in the parentheses.
Table S3. Additive Screening:

\[
\begin{align*}
\text{entry} & \quad \text{additive} & \quad \text{yield (\%)}^a \\
1 & \quad \text{HOTf} & \quad 89 (5), 91^b \\
2 & \quad \text{HOAc} & \quad 66 (19) \\
3 & \quad \text{TFA} & \quad 75 (21) \\
4 & \quad \text{PiOH} & \quad 70 (20) \\
5 & \quad \text{TsoH} & \quad 74 (17) \\
6 & \quad \text{HBF}_4 & \quad 62 (18)
\end{align*}
\]

*aGC yield using dodecane as the internal standard, yield of diarylation product was given in the parentheses. ^bisolated yield.

Table S4. Other conditions:

\[
\begin{align*}
\text{entry} & \quad \text{Pd (mol \%)} & \quad \text{AgOTf (equiv)} & \quad \text{yield(\%)}^a \\
1 & \quad \text{Pd(OAc)}_2 (5) & \quad \text{AgOTf (1.0)} & \quad 77 (3) \\
2^b & \quad \text{Pd(OAc)}_2 (5) & \quad \text{AgOTf (2)} & \quad 80 (6) \\
3^c & \quad \text{Pd(OAc)}_2 (5) & \quad \text{AgOTf (2)} & \quad 76 (3) \\
4 & \quad \text{Pd(PPh}_3\text{P)}_4 (5) & \quad \text{AgOTf (2)} & \quad 90 (6) \\
5 & \quad \text{Pd}_2(\text{dba})_3 (2.5) & \quad \text{AgOTf (2)} & \quad 56 (1) \\
6 & \quad \text{AgOTf (2)} & \quad \text{N. R.} \\
7 & \quad \text{Pd(OAc)}_2 (1) & \quad \text{AgOTf (2)} & \quad 81 (4)
\end{align*}
\]

*aGC yield using dodecane as the internal standard, yield of diarylation product was given in the parentheses. ^bPhl (1.1 equiv). ^c60 °C.
**Preparation of Substrates:**

Weinreb amides 1a-1g, 10-1p and 4a-4l were prepared according to the known methods, respectively. [D₃]-N-methoxy-N-methylbenzamide ([D₃]-1a) was prepared from D₃-Benzene according to the literature. All the aryl iodides were commercially available and used as received.

**General Procedure for Pd(II)-Catalyzed C–H Arylation of Aryl and Benzyl Weinreb Amides:**

1a (33.0 mg, 0.2 mmol), Pd(OAc)$_2$ (2.2 mg, 5 mol%), AgOTf (102.8 mg, 2 equiv), PhI (40.8 mg, 2 equiv), DCE (1 mL) and HTOf (15 mg, 0.5 equiv) were sequentially added to a 35 mL sealed tube. The reaction mixture was then placed into a preheated oil bath at 80 °C for 24 h. After cooling to room temperature, the mixture was diluted with ethyl acetate, filtered through a plug of silica. The filtrate was concentrated under vacuum, and the residue was purified by flash column chromatography on silica gel (petroleum ether : EtOAc = 5:1) to give monoarylation product 3a (91% yield) as a white solid with minor diarylation product (5% yield) (determined by $^1$H NMR and GC-MS) (Note: Arylation products 3a-3l were showed as mixture in the NMR spectra because of the C-N bond rotation of the amide bond. Substrates 1a-1h, 1j, 1k, 1m afforded monoarylation product majorly along with minor diarylation product which were detected by crude $^1$H NMR, $^{13}$C NMR and GC-MS.)

3a: Purification by flash chromatography (petroleum ether/ EtOAc = 5:1) on silica gel to give 3a (91% yield) as a white solid and minor diarylation product (5% yield) (The yields were determined by $^1$H NMR and GC). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.49-7.26 (m, 9H), 3.49 (br s, 1.2H), 3.26 (br s, 1.8H), 3.09 (br s, 1.8H), 2.66 (br s, 1.2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.90, 167.05, 140.49, 139.45, 139.18, 134.85, 134.28, 129.90, 129.35, 128.41, 128.29, 127.68, 127.57, 127.36, 126.84, 61.00, 59.74, 35.76, 32.37. HRMS EI (m/z): [M + Na]$^+$ calcd. for C$_{15}$H$_{15}$NO$_2$Na: 264.1000, found: 264.1001.
**3b:** Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 3b (93% yield) as a yellow oil and minor diarylation product (6% yield) (determined by $^1$H NMR). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.31 (m, 2H), 7.24-7.21 (m, 4H), 7.09-7.05 (m, 2H), 3.34 (br s, 1.3H), 3.12 (br s, 1.9H), 2.94 (br s, 1.9H), 2.54 (br s, 1.3H), 2.27 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.86, 167.06, 140.42, 139.67, 139.08, 131.74, 131.35, 129.87, 128.07, 127.35, 127.16, 126.73, 60.76, 59.43, 35.55, 32.17, 21.11. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{16}$H$_{17}$NO$_2$Na: 278.1157, found: 278.1159.

**3c:** Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 3c (71% yield) as a yellow oil and minor diarylation product (8% yield) (determined by $^1$H NMR and GC). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.31-7.10 (m, 6H), 7.08-6.94 (m, 2H), 3.38 (br s, 1.2H), 3.12 (br s, 2H), 2.95 (br s, 1.9H), 2.53 (br s, 0.9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.86, 166.12, 162.84 (d, $J = 251.0$ Hz), 142.06, 141.67, 139.28, 138.16, 128.84, 128.33, 127.81, 116.22, 116.01, 114.55, 113.78, 113.57, 60.87, 59.77, 35.66, 32.27. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{15}$H$_{14}$NO$_2$NaF: 282.0926, found: 282.0916.

**3d:** Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 3d (88% yield) as a yellow oil and minor diarylation product (9% yield) (determined by $^1$H NMR and GC). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.50 (d, $J = 2.0$ Hz, 1H), 7.45 (d, $J = 8.4$ Hz, 1H), 7.33-7.11 (m, 6H), 3.41 (br s, 1.2H), 3.18 (br s, 1.8H), 2.99 (br s, 2H), 2.58 (br s, 0.8H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.95, 141.69, 140.79, 139.19, 134.73, 133.83, 132.38, 130.81, 130.66, 129.98, 129.81, 129.39, 128.52, 128.42, 128.03, 127.10, 126.89, 123.39, 61.23, 59.95, 35.91, 32.50. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{15}$H$_{14}$NO$_2$NaBr: 342.0104, found: 342.0106.
3e: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 3e (91% yield) as a white solid and minor diarylation product (4% yield) (determined by $^1$H NMR and GC). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.51-7.49 (m, 4H), 7.41-7.39 (m, 3H), 7.33-7.21 (m, 6H), 3.37 (br s, 1.2H), 3.16 (br s, 1.8H), 2.98 (br s, 1.8H), 2.58 (br s, 1.2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.76, 166.95, 142.73, 142.21, 140.48, 140.06, 133.70, 133.14, 130.98, 130.53, 129.90, 128.85, 128.48, 128.38, 128.19, 127.79, 127.52, 127.12, 126.95, 126.81, 126.55, 126.21, 125.50, 61.08, 59.80, 35.92, 32.41. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{21}$H$_{19}$NO$_2$Na: 340.1313, found: 340.1314.

3f: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 3f (93% yield) as a yellow oil and minor diarylation product (4% yield) (determined by $^1$H NMR). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.49-7.40 (m, 2H), 7.39-7.25 (m, 6H), 3.49 (br s, 1.7H), 3.22 (br s, 1.9H), 3.08 (br s, 1.8H), 2.65 (br s, 1.5H), 2.39 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 172.11, 167.29, 140.51, 139.41, 137.66, 136.73, 136.33, 134.64, 134.09, 130.78, 130.17, 129.46, 129.28, 128.64, 128.39, 127.62, 127.44, 127.31, 127.15, 61.05, 59.80, 35.68, 32.39, 20.98. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{16}$H$_{17}$NO$_2$NaCl: 278.1157, found: 278.1166.

3g: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 3g (92% yield) as a yellow oil and minor diarylation product (3% yield) (determined by $^1$H NMR and GC). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.52-7.27 (m, 8H), 3.49 (br s, 1.1H), 3.27 (br s, 1.8H), 3.08 (br s, 1.9H), 2.67 (br s, 0.9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.31, 165.60, 135.75, 133.88, 133.17, 132.96, 131.06, 130.81, 130.73, 130.13, 129.91, 129.79, 129.46, 128.45, 128.37, 128.22, 127.97, 127.76, 127.06, 126.88, 126.72, 126.53, 126.23, 59.91, 35.88, 32.44. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{15}$H$_{14}$NO$_2$NaCl: 298.0611, found: 298.0616.
**3h:** Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 3h (88% yield) as a yellow oil and minor diarylation product (8% yield) (determined by $^1$H NMR). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.29-7.17 (m, 6H), 7.06 (m, 2H), 3.40 (br s, 1.2H), 3.11 (br s, 1.8H), 2.97 (br s, 1.9H), 2.52 (br s, 1.2H), 2.22 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.79, 166.83, 139.11, 138.87, 137.35, 136.69, 134.57, 134.00, 129.61, 129.05, 128.80, 128.01, 127.25, 127.17, 126.46, 126.33, 60.70, 59.82, 35.49, 32.09. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{16}$H$_{17}$NO$_2$Na: 278.1157, found: 278.1160.

**3i:** Purification by flash chromatography (petroleum ether/EtOAc = 2:1) on silica gel to give 3i (39.1 mg, 72%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.24-7.14 (m, 6H), 6.76 (d, $J$ =8.4, 2H), 3.60 (s, 3H), 3.38 (br s, 1.2H), 3.07 (br s, 1.7H), 2.94 (br s, 1.7H), 2.49 (br s, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.56, 166.68, 158.87, 158.60, 138.51, 138.27, 134.57, 134.00, 129.25, 129.05, 128.78, 127.04, 126.72, 126.19, 125.90, 113.30, 60.44, 59.33, 54.62, 35.18, 31.80. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{16}$H$_{17}$NO$_3$Na: 294.1106, found: 294.1113.

**3j:** Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 3j (51.8 mg, 94%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.28-7.17 (m, 8H), 3.37 (br s, 0.9H), 3.09 (br s, 2H), 2.93 (br s, 2H), 2.53 (br s, 0.9H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.05, 166.20, 138.63, 137.68, 134.47, 132.99, 129.42, 129.03, 128.81, 128.04, 127.65, 126.81, 126.41, 60.57, 59.42, 35.46, 31.90. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{15}$H$_{14}$NO$_2$NaCl: 298.0611, found: 298.0617.

**3k:** Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 3k (90% yield) as a yellow oil and minor diarylation product (4% yield) (determined by $^1$H
NMR and GC. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40 (d, $J = 7.6$ Hz, 2H), 7.34-7.31 (m, 2H), 7.28-7.27 (m, 1H), 7.24-7.19 (m, 3H), 3.42 (br s, 0.9H), 3.15 (br s, 2H), 2.98 (br s, 2H), 2.59 (br, 0.8H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.23, 166.50, 139.23, 137.91, 134.52, 131.19, 129.91, 129.25, 128.95, 127.80, 127.04, 126.63, 121.80, 121.49, 60.81, 59.61, 35.56, 32.16. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{15}$H$_{14}$NO$_2$NaBr: 342.0106, found: 342.0104.

3l: Purification by flash chromatography (petroleum ether/EtOAc = 4:1) on silica gel to give 3l (51.2 mg, 89%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.26 (d, $J = 8.4$ Hz, 2H), 7.61-7.56 (m, 2H), 7.56-7.47 (m, 3H), 7.43 (d, $J = 7.2$ Hz, 1H), 7.27 (s, 1H), 3.69-3.33 (br, 3H), 3.11-2.67 (br, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.98, 147.42, 137.41, 135.01, 129.85, 129.42, 129.28, 128.42, 127.32, 123.68, 61.25, 32.47, 29.83. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{15}$H$_{14}$N$_2$O$_2$Na: 309.0851, found: 309.0852.

3m: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 3m (89% yield) as a yellow oil and minor diarylation product (9% yield) (determined by $^1$H NMR). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.12-7.10 (m, 3H), 6.98 (s, 1H), 3.32 (br s, 1.3H), 3.09 (br s, 1.8H), 2.93 (br s, 1.7H), 2.48 (br, 1.2H), 2.20 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.69, 166.50, 140.05, 139.09, 137.33, 134.58, 133.93, 129.46, 128.93, 127.76, 127.14, 126.27, 125.09, 60.53, 59.13, 35.35, 31.99, 21.00. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{16}$H$_{17}$NO$_2$Na: 278.1157, found: 278.1165.

3n: Purification by flash chromatography (petroleum ether/EtOAc = 3:1) on silica gel to give 3n (55.0 mg, 96%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.08 (s, 1H), 7.93 (d, $J = 7.2$, 1H), 7.55 (d, $J = 4.4$ Hz, 1H), 7.35 (t, $J = 7.6$ Hz, 1H), 7.27-7.20 (m, 4H), 3.33-3.16 (br, 3H), 2.90-2.66 (br, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.53, 165.69, 147.60, 141.50, 136.36, 134.61, 134.08, 129.20, 128.94, 128.81, 127.50, 126.44, 122.58, 121.71, 60.56, 59.42, 35.40, 31.73.
HRMS ESI (m/z): [M+Na]^+ calcd. for C_{13}H_{14}N2O_{4}Na: 309.0851, found: 309.0853.

**5a:** Purification by flash chromatography (petroleum ether/ EtOAc = 8:1) on silica gel to give 5a (27.2 mg, 43%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.38-7.29 (m, 8H), 7.28-7.25 (m, 1H), 3.71 (s, 2H), 3.34(s, 3H), 3.12 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ142.44, 141.59, 132.68, 130.35, 130.12, 129.43, 128.24, 127.62, 127.13, 126.93, 60.99, 37.02, 32.41.

HRMS ESI (m/z): [M+Na]^+ calcd. for C_{16}H_{17}NO_{2}Na: 278.1157, found: 278.1168.

**5a':** Purification by flash chromatography (petroleum ether/ EtOAc =8:1) on silica gel to give 5a' (18.1 mg, 27%) as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.31-7.28 (m, 8H), 7.28-7.22 (m, 3H), 7.19 (s, 1H), 7.18-7.17 (m, 1H), 3.45 (s, 2H), 3.02 (s, 3H), 2.91 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ173.18, 143.70, 142.18, 130.93, 129.45, 129.30, 128.14, 127.10, 126.57, 60.56, 35.12, 32.32. HRMS ESI (m/z): [M+Na]^+ calcd. for C_{22}H_{21}NO_{2}Na: 354.1470, found: 354.1458.

**5b:** Purification by flash chromatography (petroleum ether/ EtOAc =10:1) on silica gel to give 5b (21.0 mg, 39%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.41-7.37 (m, 2H), 7.34-7.29 (m, 3H), 7.26-7.23 (m, 1H), 7.16-7.10 (m, 1H), 7.09 (s, 1H), 3.66 (s, 2H), 3.34 (s, 3H), 3.11 (s, 3H), 2.36 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ142.26, 141.75, 136.49, 130.88, 130.24, 129.58, 129.41, 128.42, 128.20, 127.05, 36.47, 32.07, 21.18. HRMS ESI (m/z): [M+Na]^+ calcd. for C_{17}H_{19}NO_{2}Na: 292.1313, found: 292.1324.

**5b':** Purification by flash chromatography (petroleum ether/ EtOAc = 10:1) on silica gel to give 5b' (19.5 mg, 28%) as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.37-7.28 (m, 10H), 7.08 (s, 2H), 3.48 (s, 2H), 3.09 (s, 3H), 2.95 (s, 3H), 2.38 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ143.56, 142.33, 136.04, 130.14, 129.43, 128.11, 127.87, 127.01, 60.50, 34.68, 32.33,

5c: Purification by flash chromatography (petroleum ether/EtOAc = 10:1) on silica gel to give 5c (26.3 mg, 45%) as a yellow oil. \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.35-7.25 (m, 3H), 7.24-7.19 (m, 5H), 3.58 (s, 2H), 3.28 (s, 3H), 3.05 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 172.56, 143.99, 140.26, 132.53, 131.85, 131.24, 129.97, 129.21, 128.39, 127.64, 61.04, 36.37, 32.41.

HRMS ESI (m/z): [M+Na]^+ calcd. for C_{16}H_{16}NO_2NaCl: 312.0767, found: 312.0764.

5c’: Purification by flash chromatography (petroleum ether/EtOAc = 10:1) on silica gel to give 5c’ (17.9 mg, 24%) as a white solid. \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.33-7.24 (m, 10H), 7.19 (s, 2H), 3.39 (s, 2H), 3.01 (s, 3H), 2.91 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 172.86, 145.14, 140.85, 132.01, 129.72, 129.19, 129.06, 128.27, 127.55, 60.55, 34.66, 32.22.

HRMS ESI (m/z): [M+Na]^+ calcd. for C_{22}H_{20}NO_2NaCl: 388.1080, found: 388.1083.

5d: Purification by flash chromatography (petroleum ether/EtOAc = 10:1) on silica gel to give 5d (43.8 mg, 81%) as a yellow solid. \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.29-7.28 (m, 2H), 7.23-7.22 (m, 3H), 7.16-7.12 (m, 2H), 7.03 (m, 1H), 3.60 (s, 2H), 3.35 (s, 3H), 3.09 (s, 3H), 2.82 (s, 2H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 172.76, 143.35, 142.36, 138.00, 131.55, 129.48, 129.31, 128.15, 127.71, 126.97, 126.72, 60.99, 34.45, 32.56, 20.35.

HRMS ESI (m/z): [M+Na]^+ calcd. for C_{17}H_{19}NO_2Na: 292.1313, found: 292.1311.

5e: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 5e (35.6mg, 61%) as a yellow oil. \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.32-7.29 (m, 2H), 7.25-7.21 (m, 3H), 7.12 (d, \(J=8.4\text{Hz}, 1\text{H}\)), 6.84 (d, \(J=2.4\text{Hz}, 1\text{H}\)), 6.78 (dd, \(J=8.4, 2.8\text{Hz}, 1\text{H}\)), 3.76 (s, 3H), 3.61 (s, 2H), 3.27 (s, 3H), 3.04 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 172.74, 158.95, 157.72, 132.18, 131.82, 131.18, 129.31, 128.27, 127.71, 120.95, 36.95, 32.91, 31.98, 20.35.
5f: Purification by flash chromatography (petroleum ether/ EtOAc = 10:1) on silica gel to give 5f (48.6 mg, 84%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.42-7.38 (m, 2H), 7.36-7.32 (m, 2H), 7.29-7.27 (m, 3H), 7.19 (d, $J$ =8.0 Hz, 1H), 3.67 (s, 2H), 3.36 (s, 3H), 3.13 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) 172.25, 140.94, 140.37, 134.52, 133.28, 131.28, 130.37, 129.30, 128.34, 127.44, 127.10, 61.04, 36.75, 32.38.

5g: Purification by flash chromatography (petroleum ether/ EtOAc = 5:1) on silica gel to give 5g (47.9 mg, 72%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.42 (d, $J$=2.0 Hz, 1H), 7.36-7.32 (m, 2H), 7.31-7.25 (m, 2H), 7.21-7.18 (m, 2H), 7.05 (d, $J$ =8.4 Hz, 1H), 3.58 (s, 2H), 3.28 (s, 3H), 3.05 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) 8172.16, 141.37, 140.32, 134.85, 133.27, 131.56, 130.03, 129.21, 128.34, 127.46, 121.44, 61.03, 36.69, 32.42. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{16}$H$_{16}$NO$_2$NaCl: 321.0767, found: 321.0767.

5h: Purification by flash chromatography (petroleum ether/ EtOAc =10:1) on silica gel to give 5h (39.4 mg, 73%) as a yellow solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.33-7.27 (m, 2H), 7.24-7.22 (m, 3H), 7.16-7.09 (m, 2H), 7.05-7.01 (m, 1H), 3.60 (s, 2H), 3.35 (s, 3H), 3.08 (s, 3H), 2.23 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) 8172.74, 143.34, 142.36, 137.99, 131.55, 129.48, 129.31, 128.15, 127.71, 126.96, 126.71, 60.89, 34.45, 32.53, 20.28. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{17}$H$_{19}$NO$_2$Na: 292.1313, found: 292.1317.
5i: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 5i (36.5 mg, 67%) as a yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.34-7.31 (m, 1H), 7.30-7.29 (m, 1H), 7.28-7.26 (m, 1H), 7.26-7.24 (m, 1H), 7.24-7.22 (m, 1H), 7.21-7.17 (m, 1H), 3.64 (s, 2H), 3.01 (s, 3H), 3.00 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 171.75, 161.86 (d, \(J = 246.44\) Hz), 144.91 (d, \(J = 4.14\) Hz), 140.28 (d, \(J = 2.63\) Hz), 129.25, 128.34, 128.12 (d, \(J = 9.09\) Hz), 127.53, 125.55 (d, \(J = 9.80\) Hz), 120.86 (d, \(J = 16.16\) Hz), 114.07 (d, \(J = 16.16\) Hz), 61.07, 32.47, 30.63. HRMS ESI (m/z): [M+Na]\(^+\) calcd. for C\(_{16}\)H\(_{16}\)NO\(_2\)NaF: 296.1063, found: 296.1068.

5j: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 5j (36.3 mg, 63%) as a yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.33-7.31 (m, 2H), 7.29-7.26 (m, 2H), 7.25-7.23 (m, 2H), 7.19-7.15 (m, 1H), 7.11-7.09 (dd, \(J = 7.6, 0.8\) Hz, 1H), 3.74 (s, 2H), 3.48 (s, 3H), 3.11 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 171.70, 145.13, 141.08, 135.82, 131.53, 129.13, 128.53, 128.34, 127.87, 127.53, 61.09, 35.35, 32.52. HRMS ESI (m/z): [M+Na]\(^+\) calcd. for C\(_{16}\)H\(_{16}\)NO\(_2\)NaCl: 312.0767, found: 312.0766.

5k: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 5k (38.1 mg, 59%) as a yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.37 (s, 1H), 7.35-7.33 (m, 1H), 7.32-7.26 (m, 3H), 7.20-7.19 (m, 1H), 7.18-7.17 (m, 1H), 3.56 (s, 2H), 3.30 (s, 3H), 3.05 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 171.77, 142.42, 139.29, 132.90, 132.32, 131.60, 131.39, 130.77, 129.13, 128.48, 127.89, 61.27, 36.18, 32.40. HRMS ESI (m/z): [M+Na]\(^+\) calcd. for C\(_{16}\)H\(_{15}\)NO\(_2\)NaCl\(_2\): 346.0378, found: 346.0376.

5l: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 5l (27.2 mg, 45%) as a yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.45-7.40 (m,
3H), 7.39-7.36 (m, 1H), 7.36-7.29 (m, 2H), 7.26-7.23 (m, 1H), 7.17 (d, \(J = 8.4\) Hz, 1H), 4.08 (m, 1H), 3.06 (br, 6H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 174.71, 141.29, 140.53, 139.80, 133.80, 129.33, 128.37, 127.49, 127.29, 126.86, 60.16, 38.05, 32.36, 19.92. HRMS ESI (m/z): [M+Na]\(^+\) calcd. for C\(_{17}\)H\(_{18}\)NO\(_2\)NaCl: 326.0924, found: 326.0923.

**5m**: Purification by flash chromatography (petroleum ether/ EtOAc = 5:1) on silica gel to give 5m (48.0 mg, 79%) as a yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.25 (t, \(J = 2.0\) Hz, 1H), 7.17 (dd, \(J = 8.0, 2.0\) Hz, 1H), 7.20 (d, \(J = 8.0\) Hz, 2H), 7.11-7.06 (m, 3H), 3.60 (s, 2H), 3.31 (s, 3H), 3.05 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 172.35, 140.90, 137.38, 137.11, 134.54, 133.05, 131.36, 130.22, 129.14, 129.01, 127.04, 61.04, 36.78, 32.36, 21.25. HRMS ESI (m/z): [M+Na]\(^+\) calcd. for C\(_{17}\)H\(_{18}\)NO\(_2\)NaCl: 326.0921.

**5n**: Purification by flash chromatography (petroleum ether/ EtOAc = 5:1) on silica gel to give 5n (52.2 mg, 71%) as a yellow solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.65-7.61 (m, 4H), 7.48-7.44 (m, 2H), 7.38-7.35 (m, 4H), 7.29 (dd, \(J = 8.4, 2.4\) Hz, 1H), 7.24-7.22 (m, 1H), 3.72 (s, 2H), 3.39 (s, 3H), 3.14 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 172.25, 140.65, 140.56, 140.27, 139.36, 134.60, 133.38, 131.32, 130.46, 129.77, 128.98, 127.58, 127.20, 127.13, 127.03, 61.09, 36.78, 32.41. HRMS ESI (m/z): [M+Na]\(^+\) calcd. for C\(_{22}\)H\(_{20}\)NO\(_2\)NaCl: 388.1080, found: 388.1083.

**5o**: Purification by flash chromatography (petroleum ether/ EtOAc = 5:1) on silica gel to give 5o (44.7 mg, 69%) as a yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.30 (t, \(J = 2.4\) Hz, 1H), 7.28 (t, \(J = 2.4\) Hz, 1H), 7.25 (d, \(J = 2.0\) Hz, 1H), 7.20 (dd, \(J = 6.0, 2.0\) Hz, 1H), 7.16 (t, \(J = 2.4\) Hz, 1H), 7.14 (t, \(J = 2.0\) Hz, 1H), 7.07 (d, \(J = 8.4\) Hz, 1H), 3.57 (s, 2H), 3.37 (s, 3H), 3.06 (s, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 171.98, 139.74, 138.78, 134.52, 133.64, 133.57,
131.20, 130.66, 130.54, 128.51, 127.25, 61.14, 36.61, 32.40. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{16}$H$_{15}$NO$_2$NaCl$_2$: 346.0378, found: 346.0374.

**5p**: Purification by flash chromatography (petroleum ether/ EtOAc = 5:1) on silica gel to give 5p (52.9 mg, 72%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.45 (d, $J = 8.4$ Hz, 2H), 7.25 (d, $J = 1.0$ Hz, 1H), 7.20 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.08 (t, $J = 8.4$ Hz, 3H), 3.57 (s, 2H), 3.37 (s, 3H), 3.06 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 172.05, 139.76, 139.29, 134.47, 133.70, 131.49, 131.15, 131.02, 130.57, 127.29, 121.76, 61.17, 36.62, 32.46. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{16}$H$_{15}$NO$_2$NaCl$_2$Br: 389.9872, found: 389.9872.

**5q**: Purification by flash chromatography (petroleum ether/ EtOAc = 5:1) on silica gel to give 5q (41.9 mg, 69%) as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.26 (d, $J = 2.4$ Hz, 1H), 7.22-7.17 (m, 2H), 7.11-7.00 (m, 3H), 6.99 (d, $J = 8.0$ Hz, 2H), 3.59 (s, 2H), 3.29 (s, 3H), 3.06 (s, 3H), 2.30 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 172.30, 141.03, 140.28, 137.94, 134.50, 133.13, 131.22, 130.35, 129.98, 128.31, 128.14, 127.03, 126.25, 60.98, 36.80, 32.37, 21.51. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{17}$H$_{18}$NO$_2$NaCl: 326.0924, found: 326.0925.

**5r**: Purification by flash chromatography (petroleum ether/ EtOAc = 5:1) on silica gel to give 5r (46.3 mg, 75%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.31-7.25 (m, 2H), 7.21-7.18 (m, 1H), 7.09 (d, $J = 8.0$ Hz, 1H), 7.00-6.91 (m, 3H), 3.58 (s, 2H), 3.35 (s, 3H), 3.06 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.97, 162.56 (d, $J =$251.5 Hz), 142.52 (d, $J =$7.7 Hz), 139.66, 134.50, 133.75, 131.10, 130.60, 129.90 (d, $J =$8.1 Hz), 127.23, 125.13 (d, $J =$3.0 Hz), 116.35 (d, $J =$21.6 Hz), 114.38 (d, $J =$10.9 Hz), 61.09, 36.63, 32.39. HRMS ESI (m/z): [M+Na]$^+$ calcd. for C$_{16}$H$_{15}$NO$_2$NaClF: 330.0673, found: 330.0677.
5s: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 5s (39.9 mg, 66%) as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.30-7.29 (d, J = 2.0 Hz, 2H), 7.22-7.16 (m, 3H), 7.15-7.10 (m, 1H), 7.02-6.99 (m, 2H), 3.42 (d, J = 8.0 Hz, 1H), 3.35 (d, J = 8.0 Hz, 1H), 3.21 (s, 3H), 3.00 (s, 3H), 1.20 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.72, 140.17, 139.65, 136.21, 135.07, 133.13, 130.92, 130.22, 130.09, 129.79, 127.82, 127.03, 125.68, 60.93, 36.40, 32.13, 20.02. HRMS ESI (m/z): [M+Na]⁺ calcd. for C₁₇H₁₈NO₂NaCl: 326.0924, found: 326.0920.

5t: Purification by flash chromatography (petroleum ether/EtOAc = 5:1) on silica gel to give 5t (35.5 mg, 54%) as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.31 (d, J = 2.0 Hz, 1H), 7.22 (dd, J = 10.4, 2.4 Hz, 1H), 7.19-7.13 (m, 1H), 7.08 (d, J = 8.0 Hz, 1H), 6.88-6.84 (m, 1H), 6.84-6.80 (m, 1H), 3.53 (s, 2H), 3.35 (s, 3H), 3.02 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.65, 162.73 (dd, J = 250.5, 12.1 Hz), 159.60 (dd, J = 249.5, 12.1 Hz), 135.83, 134.32, 133.56, 132.75 (dd, J = 9.1, 5.1 Hz), 131.85, 130.36, 127.26, 123.63 (dd, J = 16.2, 4.4 Hz), 123.63 (dd, J = 16.2, 4.0 Hz), 104.06 (t, J = 25.3 Hz), 61.15, 36.65, 32.36. HRMS ESI (m/z): [M+Na]⁺ calcd. for C₁₆H₁₄NO₂NaClF₂: 348.0579, found: 348.0581.

4l: ¹H NMR (400 MHz, CDCl₃) δ 7.33 (s, 1H), 7.23-7.13 (m, 3H), 4.14 (m, 1H), 3.34 (s, 3H), 3.12 (s, 3H), 1.41 (d, J = 8.0 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 173.90, 143.47, 133.74, 129.43, 127.29, 126.45, 125.53, 60.69, 41.01, 31.77, 18.96. HRMS ESI (m/z): [M+Na]⁺ calcd. for C₁₁H₁₄NO₂NaCl: 250.0611, found: 250.0619.
Mechanistic Investigation:
Deuterium Kinetic Isotope Effect Experiment (KIE)

Control Experiments
References:


Copies of $^1$H and $^{13}$C Spectra
3j

N-OMe

N

O

Cl

3j

N-OMe

N

O

Cl

3j
NOMe

\[ \text{3n} \]

\[ \begin{array}{c}
\text{NOMe} \\
\text{\(2\text{NO}_2\)}
\end{array} \]

S32
Kinetic isotope effect (KIE)

N^OMe

H/D/D4

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0