

# Palladium-Catalyzed Highly Practicable Oxygenation of C(sp<sup>2</sup>)-H and C(sp<sup>3</sup>)-H Bonds under Assistance of Oxalyl Amide

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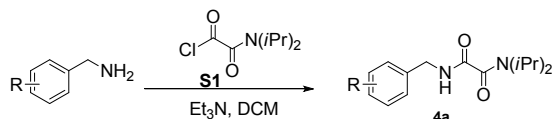
## General Information and Procedure for the Reaction

### General information:

**1. Reagents:** Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Column chromatography purifications were performed using 300–400 mesh silica gel.

**2. Instruments:** NMR spectra were recorded on Varian Inova-400 MHz, Inova-300 MHz, Bruker DRX-400 or Bruker DRX-500 instruments and calibrated using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, br = broad singlet, m = multiplet. HRMS analyses were carried out using a Bruker micrOTOF-Q instrument or a TOF-MS instrument.

### 3. Preparation of oxalamide substrates



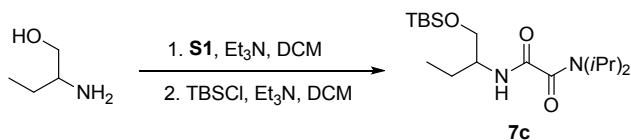
#### 3.1. Preparation of N, N–Diisopropyl oxamoyl chloride S1<sup>[1,2]</sup>

A solution of Diisopropylamine (7.01 mL, 50 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) was added dropwise to a solution of oxalyl chloride (6.44 mL, 75 mmol, 1.5 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) at 0 °C, after stirring for 5 min, triethylamine (7.30 mL, 52.5 mmol, 1.05 equiv) was added dropwise. The solution was warmed to room temperature and stirred for 6 hours. The excess of oxalyl chloride and the solvent were removed under reduce pressure and CH<sub>2</sub>Cl<sub>2</sub> (30 mL) was added and evaporated. This operation was performed twice to give S1 as a pale yellow solid. The crude product was used in the next step without any purification.

#### 3.2. General procedures for the preparation of oxalamide substrates (4a–4n, 7a–7f, except 7c–7e)<sup>[3]</sup>

A solution of amine (20 mmol, 1.0 eq) in CH<sub>2</sub>Cl<sub>2</sub> (40 mL) was added dropwise to a solution of N,N–Diisopropyl oxamoyl chloride S1 (25 mmol, 1.25 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) at 0 °C, after stirring for 5 min, triethylamine (2.92 mL, 21 mmol, 1.05 equiv) was added dropwise and then the mixture was stirred for 6 hours at room temperature before quenched by water (50 mL). The organic layer was separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL × 2). The combined organic phase was washed with brine (30 mL), and then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Evaporation and column chromatography on silica gel afforded corresponding amide substrates as white solid with good yields.

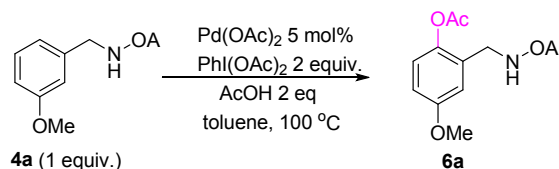
#### 3.3. preparation of oxalamide substrates 7c<sup>[4]</sup>





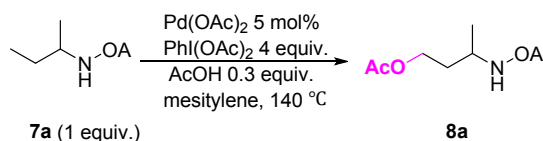
in a 25 mL glass vial (sealed with PTFE cap) was heated at 60-110 °C with vigorous stirring for 8-22 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the alkoxylation product **5a** in 83% yield.

#### 4.2 Standard procedure for Pd-catalyzed C(sp<sup>2</sup>)-H acetoxylation of Benzylamines



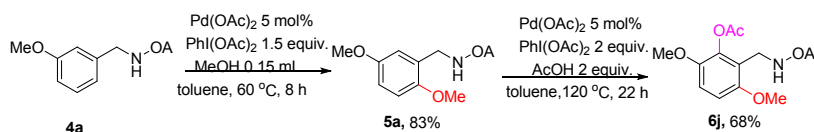
A mixture of benzylamine **4a** (87.6 mg, 0.3 mmol), Pd(OAc)<sub>2</sub> (3.3 mg, 0.015 mmol, 0.05 equiv.), PhI(OAc)<sub>2</sub> (193 mg, 0.6 mmol, 2 equiv.) and AcOH (36 mg, 0.6 mmol, 2 equiv.) in anhydrous toluene (0.9 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 100 °C with vigorous stirring for 22 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the acetoxylation product **6a** in 58% yield.

#### 4.3 Standard procedure for Pd-catalyzed C(sp<sup>3</sup>)-H acetoxylation of alkylamides



A mixture of alkylamide **7a** (68.4 mg, 0.3 mmol), Pd(OAc)<sub>2</sub> (3.3 mg, 0.015 mmol, 0.05 equiv.), PhI(OAc)<sub>2</sub> (387 mg, 1.2 mmol, 4 equiv.) and AcOH (5.4 mg, 0.9 mmol, 0.3 equiv.) in anhydrous mesitylene (0.9 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 140 °C with vigorous stirring for 22 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the acetoxylation product **8a** in 68% yield.

### 5. Synthesis of compound **6j** by sequential C-H alkoxylation/acetoxylation reaction

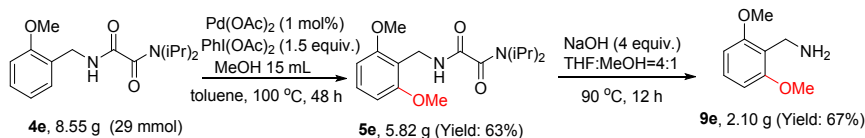


Compound **5a**: A mixture of m-methoxybenzylamine **4a** (87.6 mg, 0.3 mmol), MeOH (0.15 mL), Pd(OAc)<sub>2</sub> (3.3 mg, 0.015 mmol, 0.05 equiv.), and PhI(OAc)<sub>2</sub> (144.9 mg, 0.45 mmol, 1.5 equiv.) in anhydrous toluene (0.9 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 60 °C with vigorous stirring for 8 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the alkoxylation product **5a** in 83% yield.

Compound **6j**: A mixture of Compound **5a** (87.6 mg, 0.3 mmol), Pd(OAc)<sub>2</sub> (3.3 mg, 0.015 mmol, 0.05 equiv.), PhI(OAc)<sub>2</sub> (193.2 mg, 0.6 mmol, 2 equiv.) and AcOH (36 mg, 0.6 mmol, 2 equiv.) in anhydrous toluene (0.9 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 100 °C

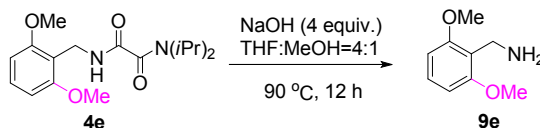
with vigorous stirring for 22 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the product **6j** in 68% yield.

## 6. Gram Reaction



A mixture of **4e** (8.55 g, 29 mmol, 1.0 equiv.),  $\text{Pd}(\text{OAc})_2$  (64 mg, 0.01 equiv.),  $\text{PhI}(\text{OAc})_2$  (1.5 equiv.) and toluene (30 mL) in a 100 mL boiling flask (sealed with vacuum plug) was heated at 100 °C with vigorous stirring for 48 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give **9e** as pale yellow solid in 67% yield.

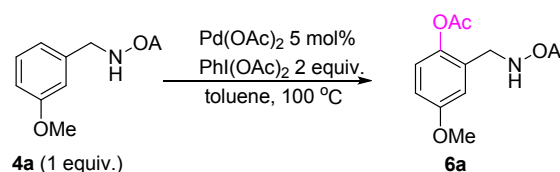
## 7. Removal of the Directing Group



Compound **4e** (0.16g, 0.5 mmol, 1.0 equiv.) was dissolved in a mixture of THF/MeOH (0.4/0.1 mL); NaOH (80 mg, 2.0 mmol, 4.0 equiv.) was then added. The mixture was heated to 90 °C with vigorous stirring and stirred for 12 hours. Water was added and the mixture was extracted with DCM. The combined organic layers was washed with water and brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give the desired product **9e** in 88% yield.

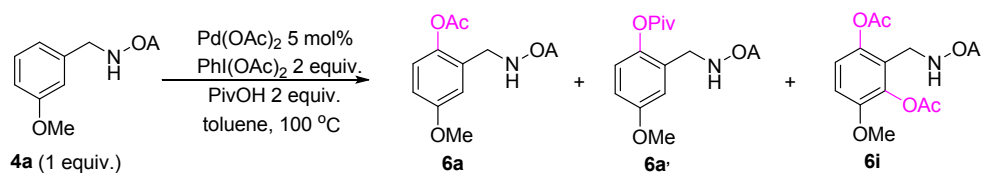
## 8. Experiments about the mechanism

### 8.1 Pd-catalyzed C(sp<sup>2</sup>)-H acetoxylation of Benzylamines without AcOH



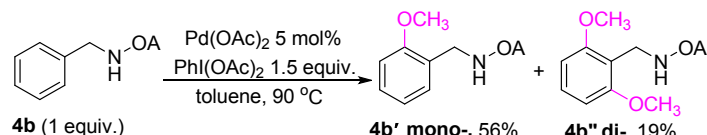
A mixture of benzylamine **4a** (87.6 mg, 0.3 mmol),  $\text{Pd}(\text{OAc})_2$  (3.3 mg, 0.015 mmol, 0.05 equiv.),  $\text{PhI}(\text{OAc})_2$  (193 mg, 0.6 mmol, 2 equiv.) in anhydrous toluene (0.9 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 100 °C with vigorous stirring for 22 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the acetoxylation product **6a** in 45% yield.

### 8.2 Pd-catalyzed C(sp<sup>2</sup>)-H acetoxylation of Benzylamines with PivOH



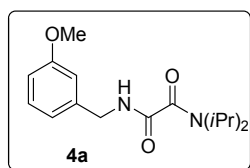
As predicted by GC-MS, the result gave ratio of 6a:6a':6i was 21:12:1, so acetic acid might be acted as a stabilizer during the catalytic cycle.

### 9. Selectivity of an un-substituted phenyl derivative

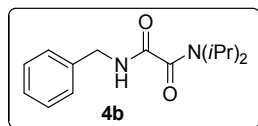


The un-substituted phenyl derivative afforded a mixture mono and di alkoxyated products without selectivity. The mono-alkoxyated product was in 56% yield, and di-alkoxyated product in 19% yield.

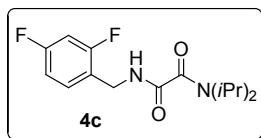
## Analytic Data of Products



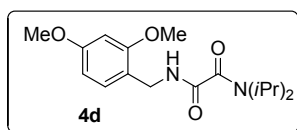
Yield: 82% (4.79g).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 (br, 1H), 7.21 (t,  $J = 7.8$  Hz, 1H), 6.86 (d,  $J = 7.6$  Hz, 1H), 6.79 (m, 2H), 4.74–4.64 (m, 1H), 4.39 (d,  $J = 6.0$  Hz, 2H), 3.76 (s, 3H), 3.52–3.45 (m, 1H), 1.38 (d,  $J = 6.8$  Hz, 6H), 1.21 (d,  $J = 6.7$  Hz, 6H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  163.23, 163.17, 163.09, 159.94, 139.17, 139.12, 129.81, 129.79, 120.07, 113.35, 113.22, 55.28, 49.76, 49.75, 46.61, 46.57, 43.30, 43.27, 20.93, 20.19, 20.12. HRMS Calcd for  $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}_3$  [ $\text{M}+\text{Na}$ ]: 315.1685; Found: 315.1673.



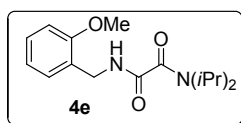
Yield: 93% (4.87g).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39–7.27 (m, 5H), 7.20 (br, 1H), 4.87–4.80 (m, 1H), 4.46 (d,  $J = 6.0$  Hz, 2H), 3.56–3.49 (m, 1H), 1.42 (d,  $J = 6.8$  Hz, 6H), 1.24 (d,  $J = 6.7$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.16, 163.04, 137.53, 128.84, 127.90, 127.70, 49.75, 46.69, 43.41, 20.97, 20.15. HRMS Calcd for  $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_2$  [ $\text{M}+\text{Na}$ ]: 285.1579; Found: 285.1579.



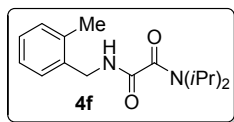
Yield: 90% (5.36g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.52 (s, 1H), 7.34–7.28 (m, 1H), 6.83–6.75 (m, 2H), 4.71–4.65 (m, 1H), 4.44 (d, *J* = 6.1 Hz, 2H), 3.52–3.45 (m, 1H), 1.37 (d, *J* = 6.8 Hz, 6H), 1.20 (d, *J* = 6.7 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.88, 163.76, 163.25, 162.95, 162.34, 162.22, 161.41, 161.29, 159.87, 159.75, 131.17, 131.11, 131.07, 131.01, 120.79, 120.75, 120.64, 120.60, 111.58, 111.54, 111.36, 111.33, 104.26, 104.00, 103.75, 49.78, 46.67, 36.79, 36.75, 20.91, 20.10. HRMS Calcd for C<sub>15</sub>H<sub>20</sub>F<sub>2</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]: 321.1391; Found: 321.1394.



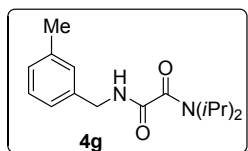
Yield: 85% (5.47g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.18 (m, 2H), 6.43 (m, 2H), 4.80–4.73 (m, 1H), 4.38 (d, *J* = 6.0 Hz, 2H), 3.82 (s, 3H), 3.79 (s, 3H), 3.52–3.45 (m, 1H), 1.40 (d, *J* = 6.8 Hz, 6H), 1.21 (d, *J* = 6.7 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.20, 162.85, 160.73, 158.70, 130.50, 118.09, 103.98, 98.59, 55.44, 55.42, 49.59, 46.49, 38.76, 20.90, 20.12. HRMS Calcd for C<sub>17</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]: 345.1790; Found: 345.1783.



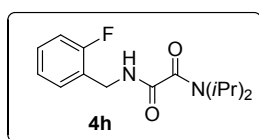
Yield: 78% (4.56g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.37 (br, 1H), 7.26 (m, 2H), 6.89 (m, 2H), 4.79–4.69 (m, 1H), 4.46 (d, *J* = 5.8 Hz, 2H), 3.85 (s, 3H), 3.53–3.45 (m, 1H), 1.41 (d, *J* = 6.6 Hz, 6H), 1.21 (d, *J* = 6.5 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.12, 162.91, 157.63, 129.69, 129.07, 125.49, 120.61, 110.30, 55.37, 49.60, 46.49, 39.13, 20.88, 20.10. HRMS Calcd for C<sub>16</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub> [M+Na]: 315.1685; Found: 315.1678.



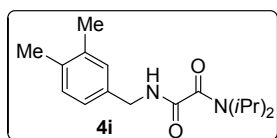
Yield: 91% (5.02g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.29–7.26 (m, 1H), 7.23–7.17 (m, 3H), 7.13 (br, 1H), 4.83–4.76 (m, 1H), 4.47 (d, *J* = 5.7 Hz, 2H), 3.57–3.50 (m, 1H), 2.36 (s, 3H), 1.43 (d, *J* = 6.8 Hz, 6H), 1.26 (d, *J* = 6.7 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.02, 162.98, 136.51, 135.18, 130.65, 128.62, 128.01, 126.38, 49.76, 46.70, 41.59, 20.99, 20.17, 19.12. HRMS Calcd for C<sub>16</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub> [M+Na]: 299.1735; Found: 299.1729.



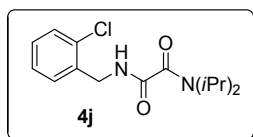
Yield: 81% (4.47g).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 (br, 1H), 7.22 (m, 1H), 7.09 (m, 3H), 4.81–4.73 (m, 1H), 4.41 (d,  $J = 5.9$  Hz, 2H), 3.55–3.47 (m, 1H), 2.34 (s, 3H), 1.41 (d,  $J = 6.8$  Hz, 6H), 1.24 (d,  $J = 6.7$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.10, 163.04, 138.53, 137.38, 128.73, 128.65, 128.45, 124.95, 49.75, 46.66, 43.39, 21.47, 20.96, 20.14. HRMS Calcd for  $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}_2$  [ $\text{M}+\text{Na}$ ]: 299.1735; Found: 299.1731.



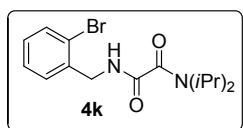
Yield: 87% (4.87g).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36–7.32 (m, 1H), 7.31–7.26 (m, 2H), 7.13–7.09 (m, 1H), 7.07–7.02 (m, 1H), 4.83–4.76 (m, 1H), 4.52 (d,  $J = 6.2$  Hz, 2H), 3.55–3.49 (m,  $J = 13.6, 6.8$  Hz, 1H), 1.42 (d,  $J = 6.8$  Hz, 6H), 1.23 (d,  $J = 6.7$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.19, 162.76, 135.93, 131.42, 128.36, 127.87, 126.18, 125.98, 49.77, 46.78, 39.93, 20.97, 20.16. HRMS Calcd for  $\text{C}_{15}\text{H}_{21}\text{FN}_2\text{O}_2$  [ $\text{M}+\text{Na}$ ]: 303.1485; Found: 303.1485.



Yield: 87% (5.05g).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25 (br, 1H), 7.08–6.95 (m, 3H), 4.79–4.68 (m, 1H), 4.33 (d,  $J = 5.7$  Hz, 2H), 3.50–3.43 (m, 1H), 2.20 (s, 6H), 1.36 (d,  $J = 6.8$  Hz, 6H), 1.19 (d,  $J = 6.6$  Hz, 6H);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  163.04, 137.05, 136.02, 134.87, 130.02, 129.26, 125.36, 49.70, 46.66, 43.21, 20.98, 20.16, 19.82, 19.51. HRMS Calcd for  $\text{C}_{17}\text{H}_{26}\text{N}_2\text{O}_2$  [ $\text{M}+\text{Na}$ ]: 313.1892; Found: 313.1877.

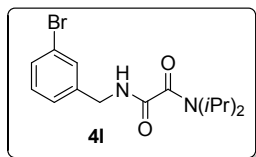


Yield: 92% (5.45g).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 (br, 1H), 7.40–7.31 (m, 2H), 7.25–7.18 (m, 2H), 4.73–4.63 (m, 1H), 4.54 (d,  $J = 6.2$  Hz, 2H), 3.53–3.44 (m, 1H), 1.38 (d,  $J = 6.8$  Hz, 6H), 1.20 (d,  $J = 6.7$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.20, 162.95, 134.95, 133.68, 129.89, 129.62, 129.08, 127.16, 49.76, 46.61, 41.22, 20.90, 20.11. HRMS Calcd for  $\text{C}_{15}\text{H}_{21}\text{ClN}_2\text{O}_2$  [ $\text{M}+\text{Na}$ ]: 319.1189; Found: 319.1188.

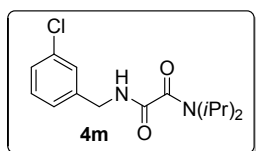




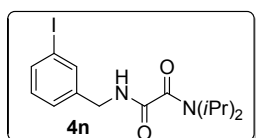
Yield: 85% (5.78g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.56–7.54 (m, 1H), 7.40–7.37 (m, 1H), 7.35 (br, 1H), 7.31–7.24 (m, 1H), 7.17–7.13 (m, 1H), 4.79–4.73 (m, 1H), 4.54 (d, *J* = 6.3 Hz, 2H), 3.55–3.48 (m, 1H), 1.41 (d, *J* = 6.8 Hz, 6H), 1.22 (d, *J* = 6.7 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.14, 162.82, 136.64, 133.00, 130.15, 129.44, 127.89, 123.85, 49.75, 46.75, 43.70, 20.99, 20.18. HRMS Calcd for C<sub>15</sub>H<sub>21</sub>BrN<sub>2</sub>O<sub>2</sub> [M+Na]: 363.0684; Found: 363.0677.



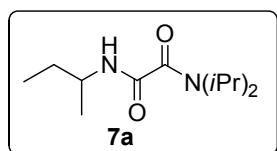
Yield: 82% (5.58g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.44 (br, 1H), 7.42–7.39 (m, 2H), 7.25–7.16 (m, 2H), 4.82–4.75 (m, 1H), 4.42 (d, *J* = 6.1 Hz, 2H), 3.56–3.49 (m, 1H), 1.41 (d, *J* = 6.8 Hz, 6H), 1.24 (d, *J* = 6.7 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.25, 163.01, 140.01, 130.81, 130.77, 130.38, 126.46, 122.81, 49.84, 46.72, 42.70, 20.96, 20.15. HRMS Calcd for C<sub>15</sub>H<sub>21</sub>BrN<sub>2</sub>O<sub>2</sub> [M+Na]: 363.0684; Found: 363.0677.



Yield: 86% (5.09g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.28–7.27 (m, 2H), 7.27–7.24 (m, 2H), 7.20–7.16 (m, 1H), 4.87–4.80 (m, 1H), 4.44 (d, *J* = 6.1 Hz, 2H), 3.57–3.50 (m, 1H), 1.43 (d, *J* = 6.8 Hz, 6H), 1.25 (d, *J* = 6.7 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.22, 162.89, 139.69, 134.67, 130.12, 127.92, 127.88, 125.97, 49.82, 46.78, 42.80, 20.98, 20.16. HRMS Calcd for C<sub>15</sub>H<sub>21</sub>ClN<sub>2</sub>O<sub>2</sub> [M+Na]: 319.1189; Found: 319.1173.

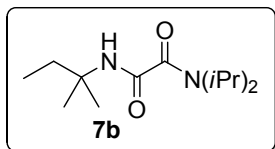


Yield: 85% (6.60g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.66 (m, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.28 (d, *J* = 6.6 Hz, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 4.74–4.67 (m, 1H), 4.39 (d, *J* = 6.1 Hz, 2H), 3.56–3.49 (m, 1H), 1.41 (d, *J* = 6.8 Hz, 6H), 1.25 (d, *J* = 6.7 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.24, 163.07, 140.06, 136.70, 130.52, 127.12, 94.63, 49.86, 46.68, 42.55, 20.95, 20.14. HRMS Calcd for C<sub>15</sub>H<sub>21</sub>IN<sub>2</sub>O<sub>2</sub> [M+Na]: 411.0545; Found: 411.0551.

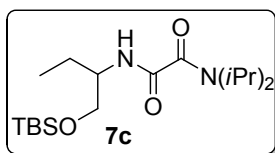


Yield: 84% (3.83g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.85 (br, 1H), 4.75–4.68 (m, 1H), 3.89–3.81 (m, 1H), 3.52–3.45 (m, 1H), 1.53–1.46 (m, 2H), 1.40 (d, *J* = 6.8 Hz, 6H), 1.21 (d, *J* = 6.7 Hz, 6H), 1.15 (d, *J* = 6.6 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.51, 162.77, 49.71, 46.85,

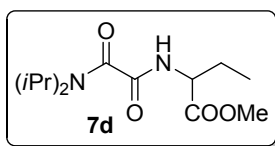
46.57, 29.49, 20.22, 20.18, 20.13, 10.45. HRMS Calcd for C<sub>12</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub> [M+Na]: 251.1735; Found: 251.1740.



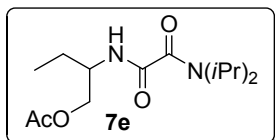
Yield: 87% (4.21g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.60 (br, 1H), 4.74-4.64 (m, 1H), 3.52-3.42 (m, 1H), 1.76-1.70 (m, 2H), 1.40 (d, *J* = 6.8 Hz, 6H), 1.31 (s, 6H), 1.21 (d, *J* = 6.7 Hz, 6H), 0.85 (t, *J* = 7.5 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.82, 162.76, 54.35, 49.68, 46.45, 32.63, 26.14, 20.91, 20.15, 8.39. HRMS Calcd for C<sub>13</sub>H<sub>26</sub>N<sub>2</sub>O<sub>2</sub> [M+Na]: 265.1892; Found: 265.1891.



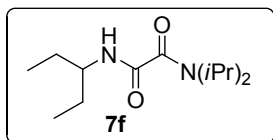
Yield: 74% (5.29g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.82 (d, *J* = 8.8 Hz, 1H), 4.71-4.65 (m, 1H), 3.87 – 3.80 (m, 1H), 3.66-3.59 (m, 2H), 3.55-3.45 (m, 1H), 1.68 – 1.61 (m, 1H), 1.55-1.48 (m, 1H), 1.43-1.41 (m, 6H), 1.22 (t, *J* = 6.2 Hz, 6H), 0.93 (t, *J* = 7.5 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.38, 163.17, 64.06, 52.30, 49.75, 46.57, 26.00, 24.29, 21.02, 20.22, 18.42, 10.58, -5.32, -5.35. HRMS Calcd for C<sub>18</sub>H<sub>38</sub>IN<sub>2</sub>O<sub>3</sub>Si [M+Na]: 381.2549; Found: 381.2555.



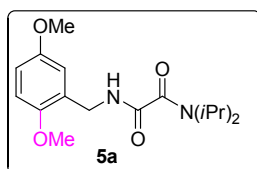
Yield: 68% (3.69g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.29 (d, *J* = 7.2 Hz, 1H), 4.65-4.58 (m, 1H), 4.51-4.46 (m, 1H), 3.73 (s, 3H), 3.54-3.45 (m, 1H), 1.94-1.88 (m, 1H), 1.82-1.71 (m, 1H), 1.40 (d, *J* = 6.8 Hz, 6H), 1.20 (dd, *J* = 6.6, 2.6 Hz, 6H), 0.93 (t, *J* = 7.5 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 175.38, 163.67, 163.20, 52.03, 49.80, 46.50, 41.50, 39.36, 20.89, 20.12, 14.93. HRMS Calcd for C<sub>13</sub>H<sub>24</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]: 295.1634; Found: 295.1638.



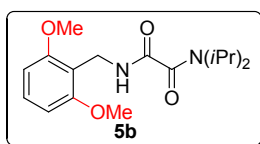
Yield: 71% (4.06g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.99 (d, *J* = 7.8 Hz, 1H), 4.73-4.63 (m, 1H), 4.13-4.10 (m, 2H), 4.07-4.01 (m, 1H), 3.54-3.47 (m, 1H), 2.05 (s, 3H), 1.64-1.51 (m, 2H), 1.41 (d, *J* = 6.8 Hz, 6H), 1.21 (dd, *J* = 6.6, 3.8 Hz, 6H), 0.95 (t, *J* = 7.4 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 171.02, 163.21, 163.09, 65.39, 49.83, 46.66, 24.47, 20.96, 20.94(-CH<sub>3</sub>, -CH<sub>3</sub>), 20.91, 20.23, 20.16, 10.43. HRMS Calcd for C<sub>14</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub> [M+H]: 287.1971; Found: 287.1969.



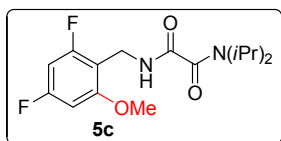
Yield: 89% (4.31g). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.88 (br, 1H), 4.64–4.57 (m, 1H), 3.75–3.66 (m, 1H), 3.51–3.41 (m, 1H), 1.59–1.52 (m, 2H), 1.44–1.37 (m, 8H), 1.19 (d, *J* = 6.7 Hz, 6H), 0.88 (t, *J* = 7.4 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.90, 163.48, 52.35, 49.82, 46.42, 27.39, 20.89, 20.18, 10.40. HRMS Calcd for C<sub>13</sub>H<sub>26</sub>N<sub>2</sub>O<sub>2</sub> [M+H]: 243.2073; Found: 243.2069.



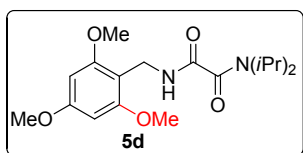
Yield: 83% (80.2 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.30 (br, 1H), 6.85 (s, 1H), 6.77 (s, *J* = 1.5 Hz, 2H), 4.76–4.68 (m, 1H), 4.42 (d, *J* = 6.1 Hz, 2H), 3.80 (s, 3H), 3.74 (s, 3H), 3.55–3.34 (m, 1H), 1.40 (d, *J* = 6.8 Hz, 6H), 1.21 (d, *J* = 6.7 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.19, 162.79, 158.38, 138.48, 128.70, 123.96, 123.01, 108.16, 55.67, 49.66, 46.60, 35.13, 21.01, 20.20, 19.68. HRMS Calcd for C<sub>17</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]: 345.1790; Found: 345.1789.



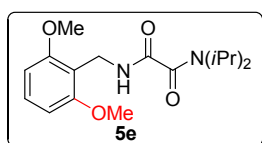
Yield: 87% (84.0 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.20 (t, *J* = 8.4 Hz, 1H), 7.11 (br, 1H), 6.53 (d, *J* = 8.4 Hz, 2H), 4.82–4.72 (m, 1H), 4.56 (d, *J* = 5.7 Hz, 2H), 3.82 (s, 6H), 3.52–3.42 (m, 1H), 1.38 (d, *J* = 6.8 Hz, 6H), 1.20 (d, *J* = 6.7 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.40, 162.69, 158.72, 129.29, 113.26, 103.80, 55.94, 49.60, 46.49, 32.20, 20.97, 20.17. HRMS Calcd for C<sub>17</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub> [M+H]: 323.1971; Found: 323.1979.



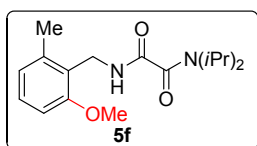
Yield: 66% (64.9 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.18 (br, 1H), 6.48–6.40 (m, 2H), 4.85–4.77 (m, 1H), 4.47 (d, *J* = 5.9 Hz, 2H), 3.84 (s, 3H), 3.53–3.44 (m, 1H), 1.39 (d, *J* = 6.8 Hz, 6H), 1.21 (d, *J* = 6.7 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 164.58, 164.42, 162.89, 162.83, 162.74, 162.60, 162.12, 161.96, 160.44, 160.28, 160.07, 159.97, 159.84, 109.28, 109.24, 109.09, 109.05, 96.43, 96.42, 95.48, 95.22, 56.40, 49.66, 46.73, 31.44, 31.39, 21.01, 20.19. HRMS Calcd for C<sub>16</sub>H<sub>22</sub>F<sub>2</sub>N<sub>2</sub>O<sub>3</sub> [M+Na]: 351.1496; Found: 351.1497.



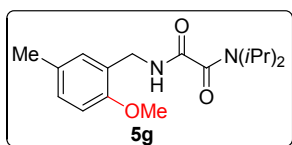
Yield: 86% (83.2 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.99 (br, 1H), 6.10 (s, 2H), 4.82–4.72 (m, 1H), 4.47 (d, *J* = 5.6 Hz, 2H), 3.81 (d, *J* = 3.8 Hz, 9H), 3.52–3.42 (m, 1H), 1.39 (d, *J* = 6.8 Hz, 6H), 1.21 (d, *J* = 6.7 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.52, 162.72, 161.17, 159.46, 105.96, 90.56, 55.91, 55.50, 49.64, 46.50, 32.07, 21.00, 20.21. HRMS Calcd for C<sub>18</sub>H<sub>28</sub>N<sub>2</sub>O<sub>5</sub> [M+H]: 353.2076; Found: 353.2079.



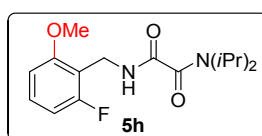
Yield: 82% (79.2 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.20 (t, *J* = 8.4 Hz, 1H), 7.11 (br, 1H), 6.53 (d, *J* = 8.4 Hz, 2H), 4.82–4.72 (m, 1H), 4.56 (d, *J* = 5.7 Hz, 2H), 3.82 (s, 6H), 3.52–3.42 (m, 1H), 1.38 (d, *J* = 6.8 Hz, 6H), 1.20 (d, *J* = 6.7 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.40, 162.69, 158.72, 129.29, 113.26, 103.80, 55.94, 49.60, 46.49, 32.20, 20.97, 20.17. HRMS Calcd for C<sub>17</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub> [M+H]: 323.1971; Found: 323.1979.



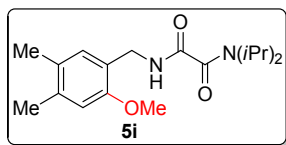
Yield: 98% (90.0 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.16 (t, *J* = 7.9 Hz, 1H), 7.09 (br, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 4.84–4.74 (m, 1H), 4.53 (d, *J* = 5.8 Hz, 2H), 3.84 (s, 3H), 3.53–3.44 (m, 1H), 2.41 (s, 3H), 1.40 (d, *J* = 6.8 Hz, 6H), 1.22 (d, *J* = 6.7 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.19, 162.79, 158.38, 138.48, 128.70, 123.96, 123.01, 108.16, 55.67, 49.66, 46.60, 35.13, 21.01, 20.20, 19.68. HRMS Calcd for C<sub>17</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub> [M+H]: 307.2022; Found: 307.2024.



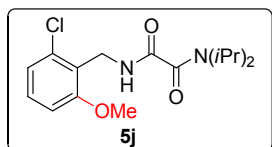
Yield: 81% (74.4 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.30 (br, 1H), 7.09–7.03 (m, 2H), 6.75 (d, *J* = 8.2 Hz, 1H), 4.79–4.69 (m, 1H), 4.41 (d, *J* = 6.1 Hz, 2H), 3.81 (s, 3H), 3.54–3.43 (m, 1H), 2.25 (s, 3H), 1.40 (d, *J* = 6.8 Hz, 6H), 1.21 (d, *J* = 6.7 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 163.19, 162.90, 155.60, 130.52, 129.86, 129.29, 125.18, 110.29, 55.51, 49.65, 46.54, 39.22, 20.92, 20.47, 20.14, 20.11. HRMS Calcd for C<sub>17</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub> [M+H]: 307.2022; Found: 307.2027.



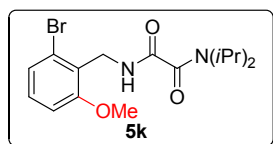
Yield: 68% (63.2 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25–7.19 (m, 2H), 6.74–6.63 (m, 2H), 4.86–4.80 (m, 1H), 4.54 (d,  $J = 5.9$  Hz, 2H), 3.87 (s, 3H), 3.53–3.46 (m, 1H), 1.39 (d,  $J = 6.8$  Hz, 6H), 1.21 (d,  $J = 6.7$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  162.93, 162.73, 162.60, 160.28, 159.30, 159.23, 129.68, 129.57, 113.12, 112.94, 108.35, 108.12, 106.35, 106.33, 56.18, 49.63, 46.67, 31.77, 31.72, 21.01, 20.20. HRMS Calcd for  $\text{C}_{16}\text{H}_{23}\text{FN}_2\text{O}_3$  [ $\text{M}+\text{Na}$ ]: 333.1590; Found: 333.1582.



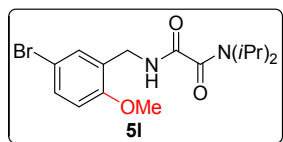
Yield: 81% (84.7 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.24 (br, 1H), 7.02 (s, 1H), 6.66 (s, 1H), 4.82–4.72 (m, 1H), 4.39 (d,  $J = 6.1$  Hz, 2H), 3.82 (s, 3H), 3.52–3.43 (m, 1H), 2.24 (s, 3H), 2.17 (s, 3H), 1.40 (d,  $J = 6.8$  Hz, 6H), 1.21 (d,  $J = 6.7$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.16, 162.82, 155.79, 137.34, 131.25, 128.36, 122.60, 112.18, 55.60, 49.66, 46.62, 39.06, 21.00, 20.20, 20.16, 18.79. HRMS Calcd for  $\text{C}_{18}\text{H}_{28}\text{N}_2\text{O}_3$  [ $\text{M}+\text{H}$ ]: 321.2178; Found: 321.2178.



Yield: 81% (84.7 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.18 (t,  $J = 8.2$  Hz, 1H), 7.11 (br, 1H), 6.97 (d,  $J = 8.1$  Hz, 1H), 6.78 (d,  $J = 8.3$  Hz, 1H), 4.82–4.72 (m, 1H), 4.66 (d,  $J = 5.8$  Hz, 2H), 3.84 (s, 3H), 3.53–3.42 (m, 1H), 1.38 (d,  $J = 6.8$  Hz, 6H), 1.20 (d,  $J = 6.7$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.10, 162.64, 159.12, 135.39, 129.64, 129.61, 123.60, 121.90, 109.20, 56.10, 49.67, 46.58, 35.60, 20.96, 20.15. HRMS Calcd for  $\text{C}_{16}\text{H}_{23}\text{ClN}_2\text{O}_3$  [ $\text{M}+\text{H}$ ]: 327.1475; Found: 327.1487.

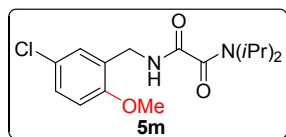


Yield: 80% (88.8 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.15–7.08 (m, 3H), 6.81 (d,  $J = 7.9$  Hz, 1H), 4.81–4.71 (m, 1H), 4.67 (d,  $J = 5.7$  Hz, 2H), 3.83 (s, 3H), 3.52–3.41 (m, 1H), 1.37 (d,  $J = 6.8$  Hz, 6H), 1.20 (d,  $J = 6.7$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.11, 162.59, 159.07, 130.06, 125.09, 109.81, 56.08, 49.66, 46.54, 38.33, 20.96, 20.14. HRMS Calcd for  $\text{C}_{16}\text{H}_{23}\text{BrN}_2\text{O}_3$  [ $\text{M}+\text{H}$ ]: 371.0970; Found: 371.0970.

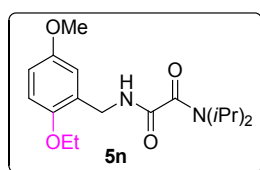


Yield: 59% (64.5 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38–7.34 (m, 2H), 7.32 (br, 1H), 6.74 (d,  $J = 8.5$  Hz, 1H), 4.81–4.72 (m, 1H), 4.41 (d,  $J = 6.3$  Hz, 2H), 3.83 (s, 3H), 3.56–3.45 (m, 1H), 1.41 (d,  $J = 6.8$  Hz, 6H), 1.23 (d,  $J = 6.7$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  162.95, 162.88, 156.81, 132.32,

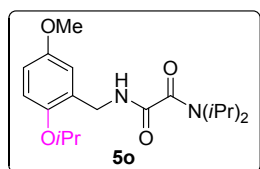
131.73, 127.82, 112.85, 112.14, 55.80, 49.74, 46.74, 38.73, 21.01, 20.21. HRMS Calcd for  $C_{16}H_{23}BrN_2O_3$  [M+H]: 371.0970; Found: 371.0975.



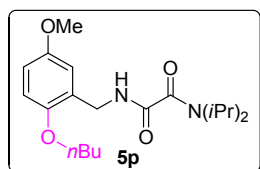
Yield: 73% (71.4 mg).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.32 (br, 1H), 7.24–7.19 (m, 2H), 6.78 (d,  $J$  = 8.6 Hz, 1H), 4.82–4.72 (m, 1H), 4.41 (d,  $J$  = 6.3 Hz, 2H), 3.84 (s, 3H), 3.56–3.46 (m, 1H), 1.41 (d,  $J$  = 6.8 Hz, 6H), 1.23 (d,  $J$  = 6.7 Hz, 6H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  162.98, 162.90, 156.29, 129.48, 128.69, 127.41, 125.57, 111.61, 55.84, 49.72, 46.72, 38.75, 21.00, 20.20. HRMS Calcd for  $C_{16}H_{23}ClN_2O_3$  [M+H]: 327.1475; Found: 327.1478.



Yield: 85% (85.6 mg).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.31 (br, 1H), 6.84 (d,  $J$  = 2.5 Hz, 1H), 6.76–6.75 (m, 2H), 4.77–4.69 (m, 1H), 4.43 (d,  $J$  = 6.1 Hz, 2H), 4.03–3.98 (m, 2H), 3.73 (s, 3H), 3.54–3.44 (m, 1H), 1.42–1.38 (m, 9H), 1.21 (d,  $J$  = 6.7 Hz, 6H);  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  163.11, 162.98, 153.51, 151.20, 126.71, 115.66, 113.46, 112.47, 64.29, 55.85, 49.67, 46.60, 39.37, 20.97, 20.15, 15.11. HRMS Calcd for  $C_{18}H_{28}N_2O_4$  [M+H]: 337.2127; Found: 337.2133.

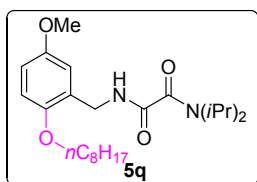


Yield: 69% (72.5 mg).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.28 (br, 1H), 6.85 (d,  $J$  = 2.5 Hz, 1H), 6.78–6.73 (m, 2H), 4.78–4.68 (m, 1H), 4.44 (d,  $J$  = 6.1 Hz, 2H), 3.90 (t,  $J$  = 6.5 Hz, 2H), 3.74 (s, 3H), 3.54–3.44 (m, 1H), 1.85–1.76 (m, 2H), 1.40 (d,  $J$  = 6.8 Hz, 6H), 1.21 (d,  $J$  = 6.7 Hz, 6H), 1.03 (t,  $J$  = 7.4 Hz, 3H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  163.09, 163.00, 153.50, 151.32, 126.66, 115.65, 113.44, 112.35, 70.22, 55.85, 49.64, 46.58, 39.34, 22.80, 20.96, 20.13, 10.77. HRMS Calcd for  $C_{19}H_{30}N_2O_4$  [M+H]: 351.2284; Found: 351.2282.

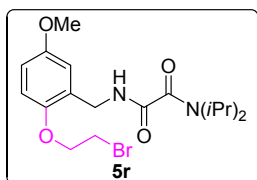


Yield: 76% (83.0 mg).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.28 (br, 1H), 6.84 (s, 1H), 6.78–6.73 (m, 2H), 4.76–4.68 (m, 1H), 4.43 (d,  $J$  = 6.0 Hz, 2H), 3.93 (t,  $J$  = 6.4 Hz, 2H), 3.73 (s, 3H), 3.54–3.44 (m, 1H), 1.79–1.72 (m, 2H), 1.51–1.45 (m, 2H), 1.40 (d,  $J$  = 6.8 Hz, 6H), 1.20 (d,  $J$  = 6.6 Hz, 6H), 0.96 (t,  $J$  =

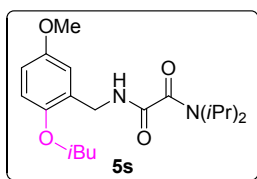
7.4 Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.10, 163.02, 153.47, 151.33, 126.63, 115.63, 113.43, 112.30, 68.40, 55.87, 49.68, 46.60, 39.35, 31.53, 20.97, 20.15, 19.48, 13.99. HRMS Calcd for  $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_4$  [M+H]: 365.2440; Found: 365.2444.



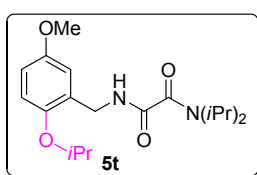
Yield: 58% (73.1 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29 (br, 1H), 6.85 (d,  $J = 2.4$  Hz, 1H), 6.78–6.73 (m, 2H), 4.81–4.71(m,1H), 4.44 (d,  $J = 6.1$  Hz, 2H), 3.93 (t,  $J = 6.5$  Hz, 2H), 3.74 (s, 3H), 3.54–3.44 (m, 1H), 1.81–1.74 (m, 2H), 1.51–1.43 (m, 2H), 1.40 (d,  $J = 6.8$  Hz, 6H), 1.33–1.27(m, 8H), 1.21 (d,  $J = 6.7$  Hz, 6H), 0.88 (t,  $J = 6.9$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.01, 162.97, 153.47, 151.36, 126.66, 115.62, 113.44, 112.32, 68.76, 55.88, 49.64, 46.62, 39.36, 31.96, 29.51, 29.36, 26.27, 22.78, 20.99, 20.17, 14.23. HRMS Calcd for  $\text{C}_{24}\text{H}_{40}\text{N}_2\text{O}_4$  [M+H]: 421.3066; Found: 421.3066.



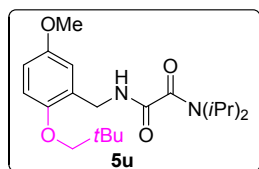
Yield: 50% (62.2 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33 (br, 1H), 6.88 (s, 1H), 6.76 (d,  $J = 1.5$  Hz, 2H), 4.67–4.58 (m, 1H), 4.47 (d,  $J = 6.2$  Hz, 2H), 4.29 (t,  $J = 5.8$  Hz, 2H), 3.75 (s, 3H), 3.67 (t,  $J = 5.8$  Hz, 2H), 3.54–3.44 (m, 1H), 1.40 (d,  $J = 6.7$  Hz, 6H), 1.21 (d,  $J = 6.7$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.29, 163.25, 154.24, 150.32, 127.35, 115.99, 113.62, 112.84, 68.54, 55.89, 49.75, 46.55, 39.32, 30.00, 20.99, 20.18. HRMS Calcd for  $\text{C}_{18}\text{H}_{27}\text{BrN}_2\text{O}_4$  [M+H]: 415.1232; Found: 415.1241.



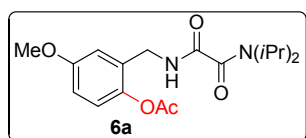
Yield: 65% (71.0 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.26 (s, 1H), 6.85 (s, 1H), 6.76 (d,  $J = 2.1$  Hz, 2H), 4.79–4.69(m, 1H), 4.46 (d,  $J = 6.0$  Hz, 2H), 3.75 (s, 3H), 3.71 (d,  $J = 6.4$  Hz, 2H), 3.53–3.44 (m, 1H), 2.13–2.06 (m,1H), 1.40 (d,  $J = 6.8$  Hz, 6H), 1.21 (d,  $J = 6.7$  Hz, 6H), 1.03 (d,  $J = 6.7$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.07, 163.04, 153.47, 151.36, 126.54, 115.64, 113.42, 112.19, 75.02, 55.88, 49.66, 46.59, 39.34, 28.48, 20.96, 20.13, 19.48. HRMS Calcd for  $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_4$  [M+H]: 365.2440; Found: 365.2442.



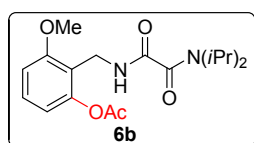
Yield: 60% (63.0 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28(br, 1H), 6.84–6.75(m, 3H), 4.74–4.71(m, 1H), 4.48–4.41(m, 1H), 4.42 (d,  $J$  = 6.1 Hz, 2H), 3.74 (s, 3H), 3.54–3.44(m, 1H), 1.40 (d,  $J$  = 6.8 Hz, 6H), 1.32 (d,  $J$  = 6.1 Hz, 6H), 1.21 (d,  $J$  = 6.7 Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.12, 163.02, 153.53, 150.02, 127.77, 115.48, 114.56, 113.68, 71.12, 55.84, 49.66, 46.59, 39.47, 22.34, 20.98, 20.15. HRMS Calcd for  $\text{C}_{19}\text{H}_{30}\text{N}_2\text{O}_4$  [M+H]: 351.2284; Found: 351.2284.



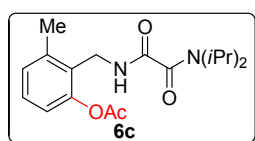
Yield: 54% (61.6 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.23(br, 1H), 6.85 (s, 1H), 6.75 (s, 2H), 4.77–4.68 (m, 1H), 4.47 (d,  $J$  = 6.0 Hz, 2H), 3.74 (s, 3H), 3.57 (s, 2H), 3.47–3.43 (m, 1H), 1.39 (d,  $J$  = 6.8 Hz, 6H), 1.20 (d,  $J$  = 6.7 Hz, 6H), 1.04 (s, 9H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.10, 163.02, 153.46, 151.47, 126.45, 115.58, 113.37, 112.04, 78.47, 55.88, 49.64, 46.56, 39.31, 32.05, 26.86, 20.95, 20.10. HRMS Calcd for  $\text{C}_{21}\text{H}_{34}\text{N}_2\text{O}_4$  [M+H]: 379.2597; Found: 379.2607.



Yield: 58% (60.9 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22 (br, 1H), 6.96 (d,  $J$  = 8.8 Hz, 1H), 6.88 (d,  $J$  = 3.0 Hz, 1H), 6.83–6.80 (m, 1H), 4.69–4.59 (m, 1H), 4.34 (d,  $J$  = 6.1 Hz, 2H), 3.76 (s, 3H), 3.54–3.43 (m, 1H), 2.30 (s, 3H), 1.39 (d,  $J$  = 6.8 Hz, 6H), 1.21 (d,  $J$  = 6.7 Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  170.05, 163.17, 157.64, 142.38, 130.46, 123.39, 114.92, 114.19, 55.70, 49.78, 46.59, 38.47, 20.96, 20.91, 20.11. HRMS Calcd for  $\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}_5$  [M+H]: 351.1920; Found: 351.1927.



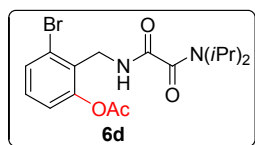
Yield: 96% (100.8 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29 (d,  $J$  = 8.3 Hz, 1H), 6.99 (br, 1H), 6.79 (d,  $J$  = 8.3 Hz, 1H), 6.70 (d,  $J$  = 8.2 Hz, 1H), 4.64–4.54 (m, 1H), 4.46 (d,  $J$  = 6.1 Hz, 2H), 3.87 (s, 3H), 3.52–3.42 (m, 1H), 2.36 (s, 3H), 1.39 (d,  $J$  = 6.8 Hz, 6H), 1.20 (d,  $J$  = 6.7 Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.89, 163.42, 162.87, 159.04, 149.80, 129.32, 118.41, 115.05, 108.24, 55.96, 49.66, 46.42, 32.22, 21.05, 20.88, 20.13. HRMS Calcd for  $\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}_5$  [M+H]: 351.1920; Found: 351.1929.



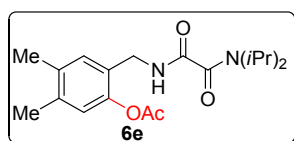
Yield: 65% (65.1 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22 (t,  $J$  = 7.8 Hz, 1H), 7.08 (d,  $J$  = 7.6 Hz, 1H), 6.91–6.86 (m, 2H), 4.68–4.59 (m, 1H), 4.41 (d,  $J$  = 5.6 Hz, 2H), 3.52–3.42 (m, 1H), 2.38 (s, 3H), 2.33 (s, 3H), 1.38 (d,  $J$  = 6.8 Hz, 6H), 1.22 (d,  $J$  = 6.7 Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  170.10,



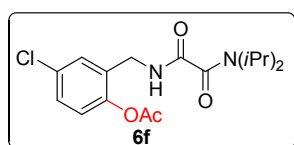
163.03, 162.99, 149.92, 139.37, 128.95, 128.53, 127.61, 120.20, 49.76, 46.57, 35.11, 21.09, 20.94, 20.13, 19.44. HRMS Calcd for  $C_{18}H_{26}N_2O_4$  [M+H]: 335.1971; Found: 335.1972.



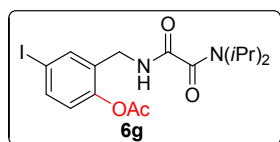
Yield: 72% (86.0 mg).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.49–7.47 (m, 1H), 7.21 (t,  $J$  = 8.1 Hz, 1H), 7.05–7.03 (m, 1H), 6.98 (br, 1H), 4.64–4.57 (m, 3H), 3.53–3.42 (m, 1H), 2.37 (s, 3H), 1.39 (d,  $J$  = 6.8 Hz, 6H), 1.20 (d,  $J$  = 6.7 Hz, 6H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  169.74, 163.00, 162.85, 150.25, 130.80, 130.14, 129.84, 125.88, 122.50, 49.76, 46.60, 37.74, 21.11, 20.93, 20.16. HRMS Calcd for  $C_{17}H_{23}BrN_2O_4$  [M+H]: 399.0919; Found: 399.0923.



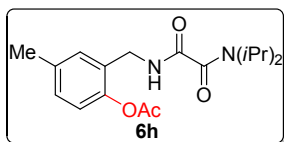
Yield: 72% (75.2 mg).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.10 (s, 2H), 6.82 (s, 1H), 4.70–4.64 (m, 1H), 4.31 (d,  $J$  = 6.0 Hz, 2H), 3.51–3.43 (m, 1H), 2.30 (s, 3H), 2.21 (d,  $J$  = 3.1 Hz, 6H), 1.39 (d,  $J$  = 6.8 Hz, 6H), 1.21 (d,  $J$  = 6.7 Hz, 6H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  169.99, 163.04, 146.79, 137.86, 135.00, 131.12, 126.38, 123.44, 49.72, 46.56, 38.09, 21.00, 20.92, 20.11, 19.66, 19.24. HRMS Calcd for  $C_{19}H_{28}N_2O_4$  [M+H]: 349.2127; Found: 349.2120.



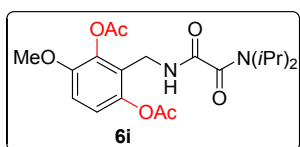
Yield: 77% (81.8 mg).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.68 (br, 1H), 7.34 (d,  $J$  = 2.3 Hz, 1H), 7.23 (d,  $J$  = 8.6 Hz, 1H), 6.99 (d,  $J$  = 8.6 Hz, 1H), 4.55–4.50 (m, 1H), 4.33 (d,  $J$  = 6.1 Hz, 2H), 3.50–3.44 (m, 1H), 2.30 (s, 3H), 1.37 (d,  $J$  = 6.7 Hz, 6H), 1.20 (d,  $J$  = 6.6 Hz, 6H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  169.28, 163.31, 147.30, 131.62, 129.61, 128.79, 123.93, 49.90, 46.51, 37.74, 20.92, 20.81, 20.05. HRMS Calcd for  $C_{17}H_{23}ClN_2O_4$  [M+H]: 355.1425; Found: 355.1438.



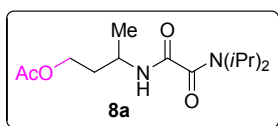
Yield: 68% (91.0 mg).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.68 (d,  $J$  = 2.1 Hz, 1H), 7.62–7.60 (m, 1H), 7.32 (br, 1H), 6.83 (d,  $J$  = 8.5 Hz, 1H), 4.70–4.59 (m, 1H), 4.34 (d,  $J$  = 6.2 Hz, 2H), 3.55–3.45 (m, 1H), 2.32 (s, 3H), 1.40 (d,  $J$  = 6.8 Hz, 6H), 1.23 (d,  $J$  = 6.7 Hz, 6H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  169.22, 163.15, 162.88, 148.88, 138.65, 138.07, 132.15, 124.74, 90.54, 49.85, 46.69, 37.77, 21.03, 20.96, 20.15. HRMS Calcd for  $C_{17}H_{23}IN_2O_4$  [M+H]: 447.0781; Found: 447.0783.



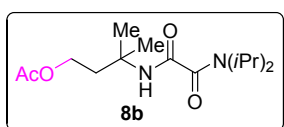
Yield: 73% (73.2 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.16–7.09 (m, 3H), 6.94 (d,  $J$  = 8.2 Hz, 1H), 4.73–4.63 (m, 1H), 4.35 (d,  $J$  = 6.0 Hz, 2H), 3.54–3.44 (m, 1H), 2.31 (s, 6H), 1.40 (d,  $J$  = 6.8 Hz, 6H), 1.22 (d,  $J$  = 6.7 Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.88, 163.08, 163.00, 146.78, 136.35, 130.60, 129.74, 129.05, 122.36, 49.75, 46.62, 38.37, 21.03, 20.96, 20.93, 20.13. HRMS Calcd for  $\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}_4$  [M+H]: 335.1971; Found: 335.1978.



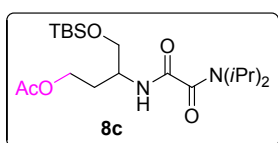
Yield: 54% (61.6 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.95–6.88 (m, 2H), 6.83 (br, 1H), 4.52–4.42 (m, 1H), 4.34 (d,  $J$  = 6.1 Hz, 2H), 3.79 (s, 3H), 3.49–3.40 (m, 1H), 2.32 (d,  $J$  = 9.4 Hz, 6H), 1.37 (d,  $J$  = 6.8 Hz, 6H), 1.18 (d,  $J$  = 6.7 Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  170.11, 168.97, 163.23, 162.99, 149.51, 142.63, 139.16, 124.19, 120.28, 111.87, 56.29, 49.73, 46.41, 32.64, 20.96, 20.82, 20.61, 20.08. HRMS Calcd for  $\text{C}_{20}\text{H}_{28}\text{N}_2\text{O}_7$  [M+H]: 409.1975; Found: 409.1986.



Yield: 68% (58.4 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.02 (d,  $J$  = 8.5 Hz, 1H), 4.80–4.70 (m, 1H), 4.13–4.10 (m, 3H), 3.53–3.45 (m, 1H), 2.05 (s, 3H), 1.85–1.80 (m, 2H), 1.40 (d,  $J$  = 6.8 Hz, 6H), 1.22 (d,  $J$  = 6.7 Hz, 9H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.19, 163.06, 162.63, 61.52, 49.73, 46.70, 42.97, 35.21, 21.08, 20.99, 20.94(- $\text{CH}_3$ , - $\text{CH}_3$ ), 20.57, 20.20, 20.15(- $\text{CH}_3$ , - $\text{CH}_3$ ). HRMS Calcd for  $\text{C}_{14}\text{H}_{26}\text{N}_2\text{O}_4$  [M+H]: 287.1971; Found: 287.1980.

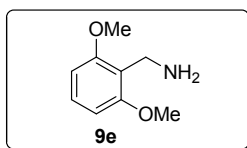


Yield: 76% (68.4 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.99 (br, 1H), 4.78–4.68 (m, 1H), 4.14 (t,  $J$  = 6.7 Hz, 2H), 3.52–3.44 (m, 1H), 2.10 (t,  $J$  = 6.7 Hz, 2H), 2.04 (s, 3H), 1.40 (d,  $J$  = 7.0 Hz, 12H), 1.23 (d,  $J$  = 6.7 Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.18, 163.41, 162.75, 61.24, 53.18, 49.77, 46.70, 38.11, 26.96, 21.11, 20.99, 20.17. HRMS Calcd for  $\text{C}_{15}\text{H}_{28}\text{N}_2\text{O}_4$  [M+H]: 301.2127; Found: 301.2131.





3.41 (m, 1H), 2.34 (s, 3H), 1.37 (d,  $J = 6.8$  Hz, 6H), 1.17 (d,  $J = 6.7$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.23, 163.39, 162.82, 152.29, 145.77, 139.15, 119.96, 111.87, 107.82, 56.54, 56.04, 49.69, 46.45, 32.41, 20.91, 20.70, 20.16. HRMS Calcd for  $\text{C}_{19}\text{H}_{28}\text{N}_2\text{O}_6$  [M+Na]: 403.1845; Found: 403.1851.



Yield: 88% (73.5mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22 (t,  $J = 8.4$  Hz, 1H), 6.56 (d,  $J = 8.4$  Hz, 2H), 4.53 (d,  $J = 5.3$  Hz, 2H), 3.84 (s, 6H), 1.94 (s, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.62, 158.75, 129.18, 114.16, 103.96, 55.99, 32.68, 23.59.

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## NMR Spectra

