Trimethylchlorosilane Mediated Mild α-Chlorination of 1,3-Dicarbonyl Compounds Promoted by Phenylidonium Diacetate

Siying Chong; Yingpeng Su,* Lili Wu; Weigang Zhang; Junyan Ma; Xiaowei Chen; Danfeng Huang; Ke-Hu Wang and Yulai Hu*

College of Chemistry and Chemical Engineering, Northwest Normal University 967 Anning East Road, Lanzhou 730070, P. R. China
State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, P. R. China
E-mail: suyp51@nwnu.edu.cn, huyl@nwnu.edu.cn
Supporting Information

Contents

1. Experimental Procedure .................................................................................................................. 5
   1.1 General Methods ........................................................................................................................... 5
   1.2 General procedure: preparation of β-ketoesters. ........................................................................... 5
      1.2.1 General procedure A: preparation of β-ketoesters 1a. ........................................................... 5
      1.2.2 General procedure B: preparation of β-ketoesters 1b. ............................................................ 6
      1.2.3 General procedure C: preparation of β-diketones 1c. ............................................................. 6
      1.2.4 General procedure D: preparation of β-diketones 1c. ............................................................. 7
   1.3 General procedure E: chlorinations of 1,3-dicarbonyle compounds .......................................... 7
   1.4 General procedure F: modified chlorinations of 1,3-dicarbonyle compounds .......................... 7
   1.5 General procedure G: bromination of 1aa and 1ba. ................................................................. 8
   1.6 General procedure H: bromination of 1cg. .................................................................................. 8

2. Data of new compounds ..................................................................................................................... 9
   Compound 4aa ................................................................................................................................... 9
   Compound 4aa' .............................................................................................................................. 11
   Compound 4ab .............................................................................................................................. 13
   Compound 4ac .............................................................................................................................. 15
   Compound 4ad .............................................................................................................................. 17
   Compound 4ae .............................................................................................................................. 19
   Compound 4af .............................................................................................................................. 21
   Compound 4ag .............................................................................................................................. 23
   Compound 4ah .............................................................................................................................. 25
   Compound 4ai .............................................................................................................................. 27
Compound 4aj..................................................................................................................29
Compound 4ak..................................................................................................................31
Compound 4al......................................................................................................................33
Compound 4am......................................................................................................................35
Compound 4an .....................................................................................................................37
Compound 4ao .....................................................................................................................39
Compound 4ba ....................................................................................................................41
Compound 4ba' ..................................................................................................................43
Compound 4bb ....................................................................................................................45
Compound 4bc ....................................................................................................................47
Compound 4bc' ..................................................................................................................49
Compound 4bd ....................................................................................................................51
Compound 4be ....................................................................................................................53
Compound 4be' ..................................................................................................................55
Compound 4bf ....................................................................................................................57
Compound 4bg ....................................................................................................................59
Compound 4bh' ..................................................................................................................61
Compound 4bi ....................................................................................................................63
Compound 4bi' ..................................................................................................................65
Compound 4bj ....................................................................................................................67
Compound 4bj' ..................................................................................................................69
Compound 4bl ....................................................................................................................71
Compound 4ca ....................................................................................................................73
Compound 4cb ....................................................................................................................75
Compound 4cc ....................................................................................................................77
1. Experimental Procedure

1.1 General Methods

All reactions were performed in flame-dried glassware with magnetic stirring bar and sealed with a rubber septum. The solvents were distilled by standard methods. Reagents were obtained from commercial suppliers and used without further purification unless otherwise noted. Flash column chromatography was carried out using Qingdao silica Gel 60 (230–400 mesh). Analytical thin layer chromatography (TLC) was done using Qingdao silica Gel (silica gel 60 F254). TLC plates were analyzed by an exposure to ultraviolet (UV) light and/or submersion in phosphomolybdic acid solution or in I2. NMR experiments were carried out in deuterochloroform (CDCl3). 1H NMR, 13C NMR spectra were recorded at 400 MHz or 600 MHz and 100 MHz or 150 MHz spectrometers Varian (Varian Mercury 400 plus, 400 MHz) and Agilent (Agilent DD2-600, 600 MHz), respectively. Chemical shifts are reported as δ values relative to internal TMS(δ 0.00 for 1H NMR) and chloroform (δ 77.0 for 13C NMR) in parts per million (ppm). The following abbreviations are used for the multiplicities: s: singlet, d: doublet, dd: doublet of doublet, t: triplet, q: quadruplet, m: multiplet, br: broad signal for proton spectra; Coupling constants (J) are reported in Hertz (Hz). Melting points were uncorrected. Infrared spectra were recorded on an IR spectrometer (Perkin Elmer BX FT-IR), and absorption frequencies were reported in reciprocal centimeters (cm⁻¹).

1.2 General procedure: preparation of β-ketoesters.

1.2.1 General procedure A: preparation of β-ketoesters 1a.

\[ \text{NaH (60\% suspension in mineral oil, 2.86g, 71.5mmol) and THF(40 mL) were added into a flame-dried round-bottom flask equipped with a stir bar under argon atmosphere. Then dimethyl carbonate (14.4 mL, 171.6 mmol) was added, and the mixture was warmed to 60 °C. A solution of 1-indanone (3.78 g, 28.6 mmol) in THF (40 mL) was added dropwise into the flask over 1 h. The mixture was refluxed until TLC indicated the total consumption of the 1-indanone. After cooled to room} \]
temperature, it was quenched by 2 M HCl (60 mL). The mixture was extracted with DCM. The combined organic phases were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (petroleum ether /EtOAc = 5/1) to afford the desired compound.

\[
\text{R}^1\text{C} = \text{O} \quad \text{R}^2\text{OH} \quad \text{Dibutyl tin oxide} \quad \text{Toluene, reflux} \quad \text{R}^1\text{C} = \text{O} \quad \text{R}^2\text{Me}
\]

Methyl 1-indanone-2-carboxylate (1.00 g, 5.26 mmol), the alcohol (10 mL) and dibutyl tin oxide (131 mg, 0.526 mmol) were dissolved into toluene. The mixture was then refluxed until completion of the reaction, and then cooled to room temperature. After concentrated in vacuo, the residue was purified by flash column chromatography (petroleum ether /EtOAc = 5/1) to afford the desired compound.

1.2.2 General procedure B: preparation of \(\beta\)-ketoesters 1b.

\[
\text{R}^1\text{Me} + \text{NaH} + \text{MeO} = \text{O} \quad \text{Toluene, reflux} \quad \text{R}^1\text{Me} + \text{NaH} + \text{R} = \text{O} = \text{Me} \quad \text{THF, reflux} \quad \text{R}^1\text{R} = \text{O} = \text{Me}
\]

All the enamine carboxylic esters were prepared adapted from a previously reported procedure with some modification. To a solution of ketone (20 mmol) in toluene (80 mL) was added methyl dicarbonate (60 mmol) and NaH (40 mmol, 60%). The reaction mixture was refluxed for 5 h until TLC indicated the total consumption of the ketone. After cooling, the reaction mixture was poured into ice-water (100 mL), acidified with 3 M HCl to pH 2-3 and extracted with EtOAc (100 mL x 3). The combined organic layer was dried over Na$_2$SO$_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether /EtOAc = 10/1) to afford the desired compound.

1.2.3 General procedure C: preparation of \(\beta\)-diketones 1c.
To a solution of NaH (40 mmol, 60%) in THF (80 mL) was added ketone (20 mmol.). After the reaction mixture was stirred at 0 °C for around 1 h, the ester was added dropwise at the same temperature. Then the mixture was stirred at room temperature until TLC indicated the total consumption of the ketone. The reaction mixture was poured into ice-water (100 mL), acidified with aqueous HCl (3 M) to pH 2-3 and extracted with EtOAc (100 mLx3). The combined organic layer was dried over Na₂SO₄ and evaporated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc = 10/1) to afford the desired compound.

1.2.4 General procedure D: preparation of β-diketones 1c.

\[ \text{R}^{1}\text{Me} + \text{NaH} + \text{R}^{2}\text{O}\text{Me} \xrightarrow{\text{THF, reflux}} \text{R}^{1}\text{R}^{2} \]

To a solution of NaH (40 mmol, 60%) in THF (80 mL) was added ketone (20 mmol.). After the reaction mixture was stirred at 0 °C for around 1 h, the ester was added dropwise at the same temperature. Then the mixture was stirred at room temperature until TLC indicated the total consumption of the ketone. The reaction mixture was poured into ice-water (100 mL), acidified with aqueous HCl (3 M) to pH 2-3 and extracted with EtOAc (100 mLx3). The combined organic layer was dried over Na₂SO₄ and evaporated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc = 5/1) to afford the desired compound.

1.3 General procedure E: chlorinations of 1,3-dicarboxylic compounds.

To a solution of 1,3-dicarboxylic compound (0.26 mmol, 1 eq.) in MeCN (3 mL) was added TMSCl (1.04 mmol, 4 eq.). After the reaction mixture was stirred at r.t. for 10 min, the PhI(OAc)₂ (0.26 mmol, 1 eq.) was added. The mixture was stirred at r.t. and monitored by thin layer chromatography (TLC) until the starting material was not detected. The reaction mixture was poured into ice-water (10 mL), then extracted with DCM. The combined organic phases were dried over Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography to afford the desired compound.

1.4 General procedure F: modified chlorinations of 1,3-dicarboxylic compounds.

To a solution of 1,3-dicarboxylic compound (0.26 mmol, 1 eq.) in MeCN (3 mL) was added TMSCl (0.26 mmol, 1 eq.). After the reaction mixture was stirred at r.t. for 10
min, the PhI(OAc)$_2$ (0.26 mmol, 1 eq.) was added. The mixture was stirred at r.t. and monitored by thin layer chromatography (TLC) until the starting material was not detected. The reaction mixture was poured into ice-water (10 mL), then extracted with DCM. The combined organic phases were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography to afford the desired compound.

1.5 General procedure G: bromination of 1aa and 1ba.

To a solution of 1,3-dicarboxyle compound (0.26 mmol, 1 eq.) in MeCN (3 mL) was added TMSBr (1.04 mmol, 4 eq.). After the reaction mixture was stirred at r.t. for 10 min, the PhI(OAc)$_2$ (0.26 mmol, 1 eq.) was added. The mixture was stirred at r.t. After TLC indicated the disappearance of starting material, the reaction mixture was poured into ice-water (10 mL). The mixture was extracted with DCM. The combined organic phases were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography to afford the desired compound.

1.6 General procedure H: bromination of 1cg.

To a solution of 1cg (0.26 mmol, 1 eq.) in MeCN (3 mL) was added TMSBr (0.26 mmol, 1 eq.). After the reaction mixture was stirred at r.t. for around 10 min, the PhI(OAc)$_2$ (0.26 mmol, 1 eq.) was added. The mixture was stirred at r.t. After TLC indicated the disappearance of starting material, the reaction mixture was poured into ice-water (10 mL). The mixture was extracted with DCM. The combined organic phases were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (petroleum ether/EtOAc = 40/1) to afford the desired compound 4cg'
2. Data of new compounds

Compound 4aa

Following the general procedure E, 4aa was purified by silica gel chromatography (EA/PE = 1/15); Compound 4aa: 58 mg (96%); yellow oil; IR (neat) ν (cm$^{-1}$): 3440, 2956, 1759, 1730, 1600, 1286, 1246, 1017, 867, 754; $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm): 7.86 (d, $J = 7.6$ Hz, 1H), 7.73-7.70 (m, 1H), 7.51-7.46 (m, 2H), 4.12 (d, $J = 18.0$ Hz, 1H), 3.82 (s, 3H), 3.58 (d, $J = 17.6$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 194.9, 167.5, 150.5, 136.5, 132.3, 128.6, 126.3, 125.9, 67.8, 54.0, 43.3; HRMS (ESI): caleed for C$_{11}$H$_{13}$ClNO$_3$ [M + NH$_4$]$^+$ 242.0578; found 242.0575.
NMR copies of major product of compound 4aa:

$\text{4aa }^{1}H \text{ NMR } 400 \text{ MHz, CDCl}_3$

$\text{4aa }^{13}C \text{ NMR } 100 \text{ MHz, CDCl}_3$
**Compound 4aa'**

Following the general procedure G, 4aa' was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4aa'**: 67 mg (96%); yellow oil;

**IR** (neat) ν (cm⁻¹): 3434, 2954, 1760, 1712, 1595, 1463, 1277, 1244, 1037, 959, 754;

**¹H NMR** (400 MHz, CDCl₃) δ (ppm): 7.87 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.48 (d, J = 6.0 Hz, 2H), 4.23 (d, J = 18.4 Hz, 1H), 3.83 (s, 3H), 3.69 (d, J = 18.4 Hz, 1H);

**¹³C NMR** (100 MHz, CDCl₃) δ (ppm): 195.0, 167.6, 150.1, 136.3, 132.1, 128.6, 126.3, 126.0, 58.1, 54.3, 43.8;

**HRMS (ESI)**: calced for C₁₁H₁₃BrNO₃ [M + NH₄]⁺ 286.0073; found 286.0076.
NMR copies of major product of compound 4aa':

4aa' $^1$H NMR 400 MHz, CDCl$_3$

4aa' $^{13}$C NMR 100 MHz, CDCl$_3$
**Compound 4ab**

Following the general procedure E, 4ab was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4ab**: 59 mg (96%); yellow oil;

**IR** (neat) ν (cm⁻¹): 3440, 2983, 1761, 1716, 1600, 1463, 1280, 1243, 1025, 886;

**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 7.86 (d, J = 7.2 Hz, 1H), 7.71 (t, J = 7.2 Hz, 1H), 7.50-7.46 (m, 2H), 4.28 (q, J = 7.2 Hz, 2H), 4.10 (d, J = 18.0 Hz, 1H), 3.57 (d, J = 18.0 Hz, 1H), 1.265 (t, J = 7.2 Hz, 3H);

**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 195.0, 167.0, 150.5, 136.3, 132.4, 128.5, 126.2, 125.8, 67.9, 63.3, 43.3, 13.9;

**HRMS (ESI)**: caled for C₁₂H₁₅ClNO₃ [M + NH₄]⁺ 256.0735; found 256.0732.
NMR copies of major product of compound 4ab:

4ab $^1$H NMR 600 MHz, CDCl$_3$

4ab $^{13}$C NMR 150 MHz, CDCl$_3$
Compound 4ac

Following the general procedure E, 4ac was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4ac:** 62 mg (95%); yellow oil;

**IR (neat) v (cm\(^{-1}\)):** 3440, 2983, 1759, 1730, 1600, 1465, 1276, 1100, 1000, 922;

**\(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) (ppm):** 7.86 (d, \(J = 7.2\) Hz, 1H), 7.70 (t, \(J = 7.2\) Hz, 1H), 7.50-7.46 (m, 2H), 5.13-5.07 (m, 1H), 4.06 (d, \(J = 17.4\) Hz, 1H), 3.55 (d, \(J = 18.0\) Hz, 1H), 1.25 (d, \(J = 2.4\) Hz, 3H), 1.24 (d, \(J = 2.4\) Hz, 3H);

**\(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) (ppm):** 195.1, 166.5, 150.5, 136.2, 128.5, 126.2, 125.8, 71.4, 68.1, 43.3, 21.4, 21.3;

**HRMS (ESI):** Caled for C\(_{13}\)H\(_{17}\)ClNO\(_3\) [M + NH\(_4\)]\(^+\) 270.0891; found 270.0888.
NMR copies of major product of compound 4ac:
Compound 4ad

Following the general procedure E, 4ad was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4ad**: 61 mg (88%); white solid; mp 75-76 °C;

**IR** (neat) ν (cm⁻¹): 3433, 2980, 1749, 1708, 1600, 1452, 1369, 1250, 1153, 1007, 831;

**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 7.85 (d, J = 7.2 Hz, 1H), 7.69 (t, J = 7.2 Hz, 1H), 7.49-7.45 (m, 2H), 4.02 (d, J = 18.0 Hz, 1H), 3.54 (d, J = 17.4 Hz, 1H), 1.40 (s, 9H);

**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 195.5, 165.8, 150.6, 136.1, 132.7, 128.4, 126.2, 125.7, 84.3, 68.7, 43.5, 27.6;

**HRMS (ESI)**: caleed for C₁₄H₁₉ClNO₃ [M + NH₄]⁺ 284.1048; found 284.1051.
NMR copies of major product of compound 4ad:
Compound 4ae

Following the general procedure E, 4ae was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4ae**: 64 mg (82%); yellow oil;

**IR** (neat) ν (cm\(^{-1}\)) : 3455, 3052, 1757, 1722, 1605, 1452, 1273, 1170, 1096, 1022;

**\(^1\)H NMR** (400 MHz, CDCl\(_3\)) \(\delta\) (ppm): 7.84 (d, \(J = 7.6\) Hz, 1H), 7.67 (t, \(J = 7.6\) Hz, 1H), 7.44 (t, \(J = 7.2\) Hz, 2H), 7.32-7.26 (m, 5H), 5.22 (dd, \(J = 19.6, 12.8\) Hz, 2H), 4.06 (d, \(J = 18.0\) Hz, 1H), 3.54 (d, \(J = 17.6\) Hz, 1H);

**\(^{13}\)C NMR** (150 MHz, CDCl\(_3\)) \(\delta\) (ppm): 194.8, 166.9, 150.4, 136.4, 134.7, 132.4, 128.6, 128.5, 128.4, 127.8, 126.3, 125.8, 68.5, 68.0, 43.3;

**HRMS (ESI)**: caled for C\(_{17}\)H\(_{17}\)ClNO\(_3\) [M + NH\(_4\)]\(^+\) 318.0891; found 318.0888.
NMR copies of major product of compound 4ae:

4ae $^1$H NMR 400 MHz, CDCl$_3$

4ae $^{13}$C NMR 150 MHz, CDCl$_3$
Compound 4af

Following the general procedure E, 4af was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4af:** 61 mg (92%); white solid; mp 95-97 °C;
**IR** (neat) ν (cm⁻¹): 3484, 2958, 1757, 1708, 1490, 1301, 1170, 1105, 852;
**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 7.37 (d, J = 8.4 Hz 1H), 7.30-7.26 (m, 2H), 4.02 (d, J = 17.4 Hz, 1H), 3.86 (s, 3H), 3.81 (s, 3H), 3.49 (d, J = 17.4 Hz, 1H);
**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 194.9, 167.6, 160.2, 143.4, 133.6, 127.0, 126.0, 106.7, 68.5, 55.7, 54.0, 42.8;
**HRMS (ESI):** called for C₁₂H₁₂ClO₄ [M + H]^+ 255.0419; found 255.0422.
NMR copies of major product of compound 4af:
Compound 4ag

Following the general procedure E, 4ag was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4ag**: 58 mg (93%); white solid; mp 81-82 °C;

**IR** (neat) v (cm⁻¹): 3425, 2954, 1766, 1715, 1620, 1492, 1413, 1249, 1017, 931, 831;

**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 7.65 (s, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.37 (d, J = 7.8 Hz, 1H), 4.05 (t, J = 17.4 Hz, 1H), 3.80 (s, 3H), 3.51 (d, J = 17.4 Hz, 1H), 2.43 (s, 3H);

**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 194.9, 167.6, 147.9, 138.8, 137.7, 132.5, 125.9, 125.7, 68.3, 54.0, 43.1, 21.0;

**HRMS (ESI)**: caled for C₁₂H₁₂ClO₃ [M + H]^+ 239.0469; found 239.0470.
NMR copies of major product of compound 4ag:

$^1$H NMR 600 MHz, CDCl$_3$

$^{13}$C NMR 150 MHz, CDCl$_3$
**Compound 4ah**

Following the general procedure E, 4ah was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4ah**: 59 mg (88%); white solid; mp 119-120 °C;

**IR** (neat) ν (cm\(^{-1}\)):

- 3441,
- 2596,
- 1762,
- 1720,
- 1598,
- 1423,
- 1249,
- 1012,
- 889;

**\(^1\)H NMR** (600 MHz, CDCl\(_3\)) δ (ppm):

- 7.72 (d, \(J = 8.4\) Hz, 1H),
- 7.68 (s, 1H),
- 7.62 (d, \(J = 7.8\) Hz, 1H),
- 4.10 (d, \(J = 18.0\) Hz, 1H),
- 3.82 (s, 3H),
- 3.55 (d, \(J = 18.0\) Hz, 1H);

**\(^13\)C NMR** (150 MHz, CDCl\(_3\)) δ (ppm):

- 193.7,
- 167.2,
- 151.9,
- 132.4,
- 132.1,
- 131.3,
- 129.6,
- 127.0,
- 67.7,
- 54.2,
- 42.9;

**HRMS (ESI)**: C\(_{11}\)H\(_8\)Cl\(_2\)O\(_3\)K [M + K]\(^+\) 296.9482; found 296.9481.
NMR copies of major product of compound 4ah:
Compound 4ai

Following the general procedure E, 4ai was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4ai**: 72 mg (92%); white solid; mp 118-119 °C;

**IR** (neat) ν (cm⁻¹): 3421, 2956, 1764, 1720, 1600, 1420, 1249, 1205, 1182, 1014, 844;

**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 7.79 (d, J = 7.8 Hz, 1H), 7.49 (s, 1H), 7.46 (d, J = 8.4 Hz, 1H), 4.10 z (d, J = 17.4 Hz, 1H), 3.82 (s, 3H), 3.54 (d, J = 18.0 Hz, 1H);

**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 193.5, 167.2, 151.9, 143.2, 130.8, 129.5, 127.0, 126.5, 67.7, 54.2, 43.0;

**HRMS (ESI)**: caled for C₁₁H₁₂BrClNO₃ [M + NH₄]^⁺ 319.9684; found 319.9680.
NMR copies of major product of compound 4ai:

4ai $^1$H NMR 600 MHz, CDCl$_3$

4ai $^{13}$C NMR 150 MHz, CDCl$_3$
Compound 4aj

Following the general procedure E, 4aj was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4aj**: 66 mg (81%); yellow oil;
**IR** (neat) \( \nu \) (cm\(^{-1}\)): 3452, 2924, 1762, 1728, 1617, 1478, 1278, 1166, 1087, 1017, 821;
**\(^1\)H NMR** (600 MHz, CDCl\(_3\)) \( \delta \) (ppm): 7.65 (s, 1H), 7.50 (d, \( J = 6.0 \) Hz, 1H), 7.34-7.28 (m, 6H), 5.23 (dd, \( J = 26.4, 12.0 \) Hz, 2H), 4.01 (d, \( J = 17.4 \) Hz, 1H), 3.50 (d, \( J = 17.4 \) Hz, 1H), 2.42 (s, 3H);
**\(^{13}\)C NMR** (100 MHz, CDCl\(_3\)) \( \delta \) (ppm): 194.8, 167.0, 147.8, 138.8, 137.7, 134.8, 132.6, 128.6, 128.4, 127.9, 125.9, 128.8, 68.5, 68.4, 43.0, 21.1;
**HRMS (ESI)**: caled for C\(_{18}\)H\(_{19}\)ClNO\(_3\) [M + NH\(_4\)]\(^+\) 332.1048; found 332.1051.
NMR copies of major product of compound 4aj:
Compound 4ak

Following the general procedure E, 4ak was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4ak**: 72 mg (83%); white solid; mp 84-85 °C;
**IR** (neat) ν (cm⁻¹): 3425, 2918, 1759, 1725, 1595, 1255, 1183, 1023, 886, 833, 737;
**¹H NMR** (400 MHz, CDCl₃) δ (ppm): 7.78 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 10.4 Hz, 2H), 7.36-7.28 (m, 5H), 5.24 (dd, J = 19.2, 12.0 Hz, 2H), 4.04 (d, J = 17.6 Hz, 1H), 3.52 (d, J = 18.0 Hz, 1H);
**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 193.4, 166.6, 151.8, 143.2, 134.6, 130.9, 129.5, 128.6, 128.5, 128.0, 127.0, 126.6, 68.8, 67.9, 43.0;
**HRMS (ESI)**: caled for C₁₇H₁₆Cl₂NO₃ [M + NH₄]⁺ 352.0502; found 352.0507.
NMR copies of major product of compound 4ak:

4ak $^1$H NMR 400 MHz, CDCl$_3$

4ak $^{13}$C NMR 150 MHz, CDCl$_3$
Compound 4al

Following the general procedure E, 4al was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4al**: 81 mg (82%); white solid; mp 86-87 °C

**IR** (neat) ν (cm⁻¹): 3437, 3052, 1761, 1590, 1435, 1247, 1184, 1022, 875, 742;

**¹H NMR** (400 MHz, CDCl₃) δ (ppm): 7.71-7.57 (m, 3H), 7.34-7.27 (m, 5H), 5.27-5.20 (m, 2H), 4.04 (d, J = 18.0, 1H), 3.52 (d, J = 18.0, 1H);

**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 193.6, 166.5, 151.9, 134.6, 132.3, 132.1, 131.3, 129.6, 128.6, 128.5, 128.0, 127.0, 68.8, 67.8, 42.8.

**HRMS (ESI)**: caled for C₁₇H₁₆BrClNO₃ [M + NH₄]⁺ 395.9997; found 396.0001.
NMR copies of major product of compound 4al:

$^1$H NMR 400 MHz, CDCl$_3$

$^1$C NMR 150 MHz, CDCl$_3$
Compound 4am

Following the general procedure E, 4am was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4am**: 59 mg (95%); yellow oil;
**IR** (neat) ν (cm⁻¹): 2954, 1767, 1689, 1600, 1447, 1302, 1256, 1217, 1044, 956, 730;
**¹H NMR** (400 MHz, CDCl₃) δ (ppm): 8.10 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 7.4 Hz, 1H), 3.85 (s, 3H), 3.32-3.25 (m, 1H), 3.05-2.97 (m, 2H), 2.57-2.51 (m, 1H);
**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 187.5, 168.0, 142.5, 134.4, 129.5, 129.0, 128.7, 127.3, 70.7, 53.8, 35.0, 25.5;
**HRMS (ESI)**: calced for C₁₂H₁₂ClO₃ [M + H]⁺ 239.0469; found 239.0472.
NMR copies of major product of compound 4am:
**Compound 4an**

Following the general procedure E, **4an** was purified by silica gel chromatography (EA/PE = 1/20);

**Compound 4an**: 42 mg (91%); yellow oil;

IR (neat) ν (cm⁻¹): 3380, 1654, 1400, 1078;

¹H NMR (400 MHz, CDCl₃) δ (ppm): 3.84 (s, 3H), 2.80-2.73 (m, 1H), 2.62-2.54 (m, 1H), 2.45-2.36 (m, 2H), 2.23-2.08 (m, 2H);

¹³C NMR (100 MHz, CDCl₃) δ (ppm): 206.0, 167.7, 69.5, 53.8, 38.4, 35.3, 19.1;

HRMS (ESI): calcd for C₇H₁₀ClO₃ [M + H]⁺ 177.0313; found 177.0309.
NMR copies of major product of compound 4an:
Following the general procedure E, 4ao was purified by silica gel chromatography (EA/PE = 1/20);

**Compound 4ao:** 46 mg (93%); yellow oil;

**IR (neat) v (cm\(^{-1}\)):** 3454, 2956, 1741, 1447, 1243, 1211, 1072, 958, 754;

**\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm):** 3.85 (s, 3H), 2.92-2.84 (m, 1H), 2.83-2.76 (m, 1H), 2.47-2.40 (m, 1H), 2.20-2.14 (m, 1H), 2.02-1.87 (m, 3H), 1.81-1.73 (m, 1H);

**\(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) (ppm):** 199.6, 167.8, 73.3, 53.6, 39.5, 38.6, 26.6, 21.9;

**HRMS (ESI):** caled for C\(_8\)H\(_{11}\)ClO\(_3\)Na [M + Na]\(^+\) 213.0289; found 213.0285.
NMR copies of major product of compound 4ao:

$\text{O} \quad \text{O} \quad \text{OMe}$

$\text{4ao} \quad ^1H\text{NMR} \ 400\text{MHz, CDCl}_3$

$\text{O} \quad \text{O} \quad \text{Cl}$

$\text{4ao} \quad ^1C\text{NMR} \ 170\text{MHz, CDCl}_3$
Compound 4ba

Following the general procedure E, 4ba was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4ba**: 54 mg (91%); yellow oil;
**IR** (neat) ν (cm\(^{-1}\)): 2985, 1767, 1678, 1595, 1442, 1295, 1162, 1022, 823, 683;
**\(^1\)H NMR** (400 MHz, CDCl\(_3\)) δ (ppm): 8.00 (dd, \(J = 8.0, 0.8\) Hz, 2H), 7.64 (t, \(J = 7.2\) Hz, 1H), 7.51 (d, \(J = 8.0\) Hz, 2H), 5.63 (s, 1H), 4.29 (q, \(J = 7.2\) Hz, 2H), 1.24 (t, \(J = 7.2\) Hz, 3H);
**\(^{13}\)C NMR** (100 MHz, CDCl\(_3\)) δ (ppm): 188.2, 165.2, 134.3, 133.3, 129.2, 128.8, 63.1, 57.9, 13.8;
**HRMS (ESI)**: caledd for C\(_{11}\)H\(_{12}\)ClO\(_3\) [M + H]\(^+\) 227.0469; found 227.0466.
NMR copies of major product of compound 4ba:

4ba $^1$H NMR 400 MHz, CDCl$_3$

4ba $^{13}$C NMR 100 MHz, CDCl$_3$
**Compound 4ba’**

![Chemical Structure of Compound 4ba'](image)

Following the general procedure G, 4ba’ was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4ba’:** 65 mg (93%); yellow oil;

**IR (neat) ν (cm⁻¹):** 3504, 2970, 1794, 1685, 1590, 1457, 1303, 1264, 1187, 1031, 936, 798;

**¹H NMR (400 MHz, CDCl₃) δ:** 8.00 (d, J = 7.6 Hz, 2H), 7.63 (t, J = 7.2 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 5.68 (s, 1H), 4.28 (q, J = 7.2 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H);

**¹³C NMR (100 MHz, CDCl₃) δ (ppm):** 188.1, 165.1, 134.2, 133.3, 129.1, 128.8, 63.2, 46.3, 13.8;

**HRMS (ESI):** calced for C₁₁H₁₅BrNO₃ [M + NH₄]⁺ 288.0230; found 288.0234.
NMR copies of major product of compound 4ba':

4ba$^1$H NMR 400 MHz, CDCl$_3$

4ba$^{13}$C NMR 100 MHz, CDCl$_3$
Following the general procedure E, 4bb was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4bb**: 51 mg (87%); yellow oil;

**IR (neat) v (cm$^{-1}$):** 3447, 2956, 1774, 1678, 1612, 1442, 1273, 1162, 1003, 846, 712;

**$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm):** 7.89 (d, $J = 7.8$ Hz, 2H), 7.30 (d, $J = 7.2$ Hz, 2H), 5.64 (s, 1H), 3.82 (s, 3H), 2.43 (s, 3H);

**$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ (ppm):** 187.7, 165.8, 145.6, 130.7, 129.6, 129.3, 57.6, 53.7, 21.7;

**HRMS (ESI):** caled for C$_{11}$H$_{15}$ClNO$_3$ [M + NH$_4$]$^+$ 244.0735; found 244.0736.
NMR copies of major product of compound 4bb:

$\text{Me} \quad \text{Cl} \quad \text{OMe}$

$\text{4bb} \, ^1\!H \!\text{NMR } 600 \text{ MHz, CDCl}_3$

$\text{Me} \quad \text{Cl} \quad \text{OMe}$

$\text{4bb} \, ^1\!C \!\text{NMR } 150 \text{ MHz, CDCl}_3$
Following the general procedure F, 4bc was purified by silica gel chromatography (EA/PE = 1/40);

**Compound 4bc:** 48 mg (82%); yellow oil;

**IR (neat) ν (cm⁻¹):** 3447, 2956, 1768, 1447, 1293, 1165, 976, 831, 764, 728;

**¹H NMR (5:1 tautomer ratio, asterisk denotes minor tautomer peaks, 600 MHz, CDCl₃) δ (ppm):** 12.44* (s, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 7.2 Hz, 1H), 7.35-7.29 (m, 2H), 7.26-7.23* (m, 2H), 5.61 (s, 1H), 3.93* (s, 3H), 3.81 (s, 3H), 2.52 (s, 3H), 2.36* (s, 3H);

**¹³C NMR (5:1 tautomer ratio, asterisk denotes minor tautomer peaks, 150 MHz, CDCl₃) δ (ppm):** 190.8, 171.5*, 170.0*, 165.8, 140.4, 135.8*, 133.7, 133.3*, 132.7, 132.4, 130.3*, 129.9*, 128.9, 128.0*, 125.8, 125.5*, 59.3, 53.7, 53.0*, 21.2, 19.1*;

**HRMS (ESI):** caled for C₁₁H₁₅ClNO₃ [M + NH₄]^+ 244.0735; found 244.0732.
NMR copies of major product of compound 4bc:
Compound 4bc'

Following the general procedure E, 4bc' was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4bc':** 59 mg (87%); yellow oil;

**IR** (neat) ν (cm\(^{-1}\)): 2956, 1770, 1715, 1600, 1435, 1242, 1003, 852, 720, 631;

**\(^1\)H NMR** (600 MHz, CDCl\(_3\)) δ (ppm): 7.75 (d, \(J = 7.8\) Hz, 1H), 7.42 (t, \(J = 7.8\) Hz, 1H), 7.31 (d, \(J = 7.8\) Hz, 1H), 7.24 (t, \(J = 7.8\) Hz, 1H), 3.87 (s, 3H), 2.46 (s, 3H);

**\(^{13}\)C NMR** (100 MHz, CDCl\(_3\)) δ (ppm): 188.0, 164.5, 139.8, 132.4,132.2, 132.0, 128.0, 125.2, 81.7, 54.9, 21.0;

**HRMS (ESI):** caled for C\(_{11}\)H\(_{11}\)Cl\(_2\)O\(_3\) [M + H]\(^+\) 261.0034; found 261.0033.
NMR copies of major product of compound 4bc:

4bc \textsuperscript{1}H NMR 600 MHz, CDCl$_3$

4bc \textsuperscript{13}C NMR 100 MHz, CDCl$_3$
**Compound 4bd**

Following the general procedure E, 4bd was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4bd**: 57 mg (90%); yellow oil;

IR (neat) ν (cm⁻¹): 2956, 2836, 1759, 1683, 1590, 1508, 1265, 1170, 1027, 983, 843;

**¹H NMR (400 MHz, CDCl₃) δ (ppm)**: 7.99 (d, J = 8.8 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 5.61 (s, 1H), 3.89 (s, 3H), 3.83 (s, 3H);

**¹³C NMR (150 MHz, CDCl₃) δ (ppm)**: 186.6, 165.9, 164.5, 131.8, 126.1, 114.2, 57.6, 55.6, 53.7;

**HRMS (ESI)**: caleed for C₁₁H₁₂ClO₄ [M + H]⁺ 243.0419; found 243.0418.
NMR copies of major product of compound 4bd:

4bd $^1$H NMR 400 MHz, CDCl$_3$

4bd $^{13}$C NMR 150 MHz, CDCl$_3$
Compound 4be

Following the general procedure F, 4be was purified by silica gel chromatography (EA/PE = 1/40);

**Compound 4be**: 55 mg (88%); yellow oil;

**IR** (neat) ν (cm⁻¹): 3494, 3024, 2965, 1745, 1595, 1452, 1305, 1163, 1016, 910, 761;

**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 7.91 (dd, J = 7.8 1.8 Hz, 1H), 7.56 (dt, J = 7.8 1.8 Hz, 1H), 7.07 (dt, J = 7.8 1.2Hz, 1H), 6.99 (d, J = 8.4 Hz, 1H), 5.73 (s, 1H), 3.91 (s, 3H), 3.79 (s, 3H);

**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 188.2, 166.2, 158.6, 135.4, 131.9, 123.9, 121.3, 111.6, 62.4, 55.4, 53.3;

**HRMS (ESI)**: caled for C₁₁H₁₂ClO₄ [M + H]⁺ 243.0419; found 243.0418.
NMR copies of major product of compound 4be:

4be $^1$H NMR 600 MHz, CDCl₃

4be $^{13}$C NMR 150 MHz, CDCl₃
Following the general procedure E, 4be' was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4be'**: 72 mg (89%); yellow oil;

**IR (neat) v (cm⁻¹)**: 2954, 1772, 1708, 1582, 1487, 1391, 1281, 1194, 1007, 852, 816, 639;

**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 7.87 (d, J = 2.4 Hz, 1H), 7.51 (dd, J = 9.0, 2.4 Hz, 1H), 6.93 (d, J = 9.0Hz, 1H), 3.85 (s, 3H), 3.82 (s, 3H);

**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 183.1, 163.7, 156.1, 135.0, 132.2, 126.9, 123.6, 113.4, 84.8, 55.4, 54.4;

**HRMS (ESI)**: caled for C₁₁H₇Cl₃O₄Na [M + Na]⁺ 334.9430; found 334.9431.
NMR copies of major product of compound 4be':

4be' $^1$H NMR 600 MHz, CDCl$_3$

4be' $^{13}$C NMR 150 MHz, CDCl$_3$
Compound 4bf

Following the general procedure E, 4bf was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4bf**: 59 mg (78%); yellow oil;

**IR (neat) ν (cm$^{-1}$)**: 3457, 2956, 1769, 1686, 1579, 1447, 1265, 1192, 1071, 986, 843;

**$^1$H NMR** (20:1 tautomer ratio, asterisk denotes minor tautomer peaks, 600 MHz, CDCl$_3$) δ (ppm): 12.76* (s, 1H), 7.87 (d, $J = 7.2$ Hz, 2H), 7.66 (d, $J = 6.6$ Hz, 2H), 5.57 (s, 1H), 3.927* (s, 3H), 3.84 (s, 3H);

**$^{13}$C NMR** (150 MHz, CDCl$_3$) δ (ppm): 187.2, 165.5, 132.3, 131.9, 130.7, 129.9, 57.7, 53.9;

**HRMS (ESI)**: caled for C$_{10}$H$_{12}$BrClNO$_3$ [M + NH$_4$]$^+$ 307.9684; found 307.9681.
NMR copies of major product of compound 4bf:
Compound 4bg

Following the general procedure E, 4bg was purified by silica gel chromatography (EA/PE = 1/15);

Compound 4bg: 59 mg (78%); yellow oil;
IR (neat) ν (cm⁻¹): 2951, 1766, 1683, 1563, 1414, 1290, 1199, 993, 863;
¹H NMR (400 MHz, CDCl₃) δ (ppm): 8.13 (s, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.78-7.75 (m, 1H), 7.40 (t, J = 8.0 Hz, 1H), 5.58 (s, 1H), 3.85 (s, 3H);
¹³C NMR (150 MHz, CDCl₃) δ (ppm): 186.9, 165.3, 137.2, 134.9, 132.2, 130.4, 127.7, 123.2, 57.5, 53.9;
NMR copies of major product of compound 4bg:

4bg $^1$H NMR 400 MHz, CDCl$_3$

4bg $^{13}$C NMR 150 MHz, CDCl$_3$
Compound 4bh'

Following the general procedure E, 4bh' was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4bh':** 65 mg (77%); yellow oil;

**IR** (neat) ν (cm⁻¹): 3447, 2961, 1770, 1722, 1579, 1452, 1246, 1022, 838, 764;

**¹H NMR** (400 MHz, CDCl₃) δ (ppm): 7.70-7.63 (m, 2H), 7.41-7.35 (m, 2H), 3.94 (s, 3H);

**¹³C NMR** (100 MHz, CDCl₃) δ (ppm): 188.5, 163.9, 136.0, 133.9, 132.3, 128.3, 126.8, 120.6, 80.8, 55.1;

**HRMS (ESI):** caled for C₁₀H₁₁BrCl₂NO₃ [M + NH₄]^+ 341.9294; found 341.9297.
NMR copies of major product of compound 4bh':

4bh' $^1$H NMR 400 MHz, CDCl$_3$

4bh' $^{13}$C NMR 100 MHz, CDCl$_3$
Compound 4bi

Following the general procedure F, 4bi was purified by silica gel chromatography (EA/PE = 1/40);

**Compound 4bi:** 60 mg (90%); yellow oil;

**IR** (neat) ν (cm\(^{-1}\)): 3484, 2964, 1771, 1633, 1584, 1388, 1290, 1192, 1005, 839, 702;

**\(^1\)H NMR** (600 MHz, CDCl\(_3\)) \(\delta\) (ppm): 7.89 (d, \(J = 9.6\) Hz, 2H), 6.66 (d, \(J = 9.0\) Hz, 2H), 5.61 (s, 1H), 3.81 (s, 3H), 3.09 (s, 6H);

**\(^{13}\)C NMR** (150 MHz, CDCl\(_3\)) \(\delta\) (ppm): 185.7, 166.4, 154.1, 131.7, 120.6, 110.8, 57.4, 53.5, 39.9;

**HRMS (ESI):** caled for C\(_{12}\)H\(_{15}\)ClNO\(_3\) [M + H]\(^+\) 256.0735; found 256.0732.
NMR copies of major product of compound 4bi:

\[ \text{4bi} {^1}\text{H NMR 600 MHz, CDCl}_3 \]

\[ \text{4bi} {^{13}}\text{C NMR 150 MHz, CDCl}_3 \]
Compound 4bi'

Following the general procedure E, 4bi' was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4bi':** 67 mg (89%); yellow oil;

**IR (neat) v (cm⁻¹):** 3428, 2954, 2845, 1771, 1591, 1515, 1430, 1293, 1170, 971, 949, 740;  

**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 7.98 (d, J = 2.4 Hz, 1H), 7.82 (dd, J = 8.4, 2.4 Hz, 1H), 6.99 (d, J = 8.4 Hz, 1H), 5.56 (s, 1H), 3.84 (s, 3H), 2.99 (s, 6H);  

**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 185.7, 165.8, 155.1, 132.7, 129.0, 126.1, 125.6, 118.2, 57.4, 53.8, 42.9;  

**HRMS (ESI):** caled for C₁₂H₁₄Cl₂NO₃ [M + H]⁺ 290.0345; found 290.0346.
NMR copies of major product of compound 4bi':

\[ \text{4bi'} \text{ }\]^1H NMR 600 MHz, CDCl\textsubscript{3} \\

\[ \text{4bi'} \text{ }\]^{13}C NMR 150 MHz, CDCl\textsubscript{3}
Following the general procedure F, 4bj was purified by silica gel chromatography (EA/PE = 1/15).

**Compound 4bj**: 47 mg (90%); yellow oil;
**IR** (neat) ν (cm⁻¹): 3137, 2963, 1766, 1679, 1567, 1466, 1289, 1168, 1015, 767, 685;
**¹H NMR** (400 MHz, CDCl₃) δ (ppm): 7.69 (dd, J = 0.8, 1.6 Hz, 1H), 7.43 (dd, J = 0.8, 3.6 Hz, 1H), 6.64 (dd, J = 1.6, 3.6 Hz, 1H), 5.51 (s, 1H), 3.84 (s, 3H);
**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 176.6, 165.3, 149.6, 147.9, 120.4, 113.1, 57.5, 53.8;
**HRMS (ESI)**: calcd for C₈H₁₁ClNO₄ [M + NH₄]⁺ 220.0368; found 220.0371.
NMR copies of major product of compound 4bj:

4bj $^1$H NMR 400 MHz, CDCl$_3$

4bj $^1$C NMR 150 MHz, CDCl$_3$
**Compound 4bj**

Following the general procedure E, 4bj was purified by silica gel chromatography (EA/PE = 1/15).

**Compound 4bj**: 46 mg (75%); yellow oil;

**IR (neat) v (cm⁻¹)**: 3137, 2972, 1769, 1700, 1569, 1460, 1261, 1234, 1015, 864, 764, 697, 658;

**¹H NMR (600 MHz, CDCl₃) δ (ppm)**: 7.65 (d, J = 1.2 Hz, 1H), 7.49 (d, J = 3.6 Hz, 1H), 6.62 (dd, J = 1.2, 3.6 Hz, 1H), 3.89 (s, 3H);

**¹³C NMR (150 MHz, CDCl₃) δ (ppm)**: 171.9, 164.0, 147.9, 147.2, 122.0, 113.0, 80.9, 54.9;

**HRMS (ESI)**: calcd for C₈H₆Cl₂O₄Na [M + Na]⁺ 258.9535; found 258.9537.
NMR copies of major product of compound 4bj':

4bj$^{1}$H NMR 600 MHz, CDCl$_3$

4bj$^{13}$C NMR 150 MHz, CDCl$_3$
Compound 4bl

Following the general procedure F, 4bl was purified by silica gel chromatography (EA/PE = 1/15);

**Compound 4bl**: 41 mg (72%); yellow oil;
**IR** (neat) ν (cm⁻¹): 3463, 2945, 2866, 1775, 1734, 1445, 1246, 1005, 858, 843;
**¹H NMR** (3:1 tautomer ratio, asterisk denotes minor tautomer peaks, 400 MHz, CDCl₃) δ (ppm): 12.46* (d, J = 1.2 Hz, 1H), 4.93(s, 1H), 3.83(s, 3H), 2.86-2.79 (m, 1H), 1.91-1.79 (m, 4H), 1.75-1.68* (m, 4H), 1.54-1.17 (m, 6H);
**¹³C NMR** (3:1 tautomer ratio, asterisk denotes minor tautomer peaks, 100 MHz, CDCl₃) δ (ppm): 201.5, 165.6, 59.4, 53.6, 52.7*, 47.6, 41.0*, 28.8, 28.6, 28.4*, 25.8*, 25.7*, 25.5, 25.4, 25.3;
NMR copies of major product of compound 4bl:

4bl $^1$H NMR: 400 MHz, CDCl$_3$

4bl $^{13}$C NMR: 100 MHz, CDCl$_3$
Compound 4ca

Following the general procedure E, 4ca was purified by silica gel chromatography (EA/PE = 1/10);

**Compound 4ca**: 74 mg (95%); white solid; mp 98-99 °C;

**IR** (neat) ν (cm\(^{-1}\)): 3064, 2930, 1744, 1600, 1473, 1265, 1177, 1022, 858, 757, 594;

**\(^1\)H NMR** (600 MHz, CDCl\(_3\)) \(\delta\) (ppm): 8.16 (d, \(J = 9.0\) Hz, 2H), 7.83 (d, \(J = 7.8\) Hz, 1H), 7.68 (t, \(J = 7.8\) Hz, 1H), 7.49 (d, \(J = 7.8\) Hz, 1H), 7.45 (t, \(J = 7.8\) Hz, 1H), 6.92 (d, \(J = 9.0\) Hz, 2H), 4.37 (d, \(J = 16.8\) Hz, 1H), 3.86 (s, 3H), 3.58 (d, \(J = 17.4\) Hz, 1H);

**\(^{13}\)C NMR** (150 MHz, CDCl\(_3\)) \(\delta\) (ppm): 196.3, 189.7, 163.8, 150.3, 136.3, 133.1, 133.0, 128.5, 126.1, 125.9, 125.7, 113.5, 73.6, 55.5, 43.3;

**HRMS (ESI)**: calcd for C\(_{17}\)H\(_{14}\)ClO\(_3\) [M + H]\(^+\) 301.0626; found 301.0623.
NMR copies of major product of compound 4ca:
**Compound 4cb**

![Chemical structure of Compound 4cb](image)

Following the general procedure E, **4cb** was purified by silica gel chromatography (EA/PE = 1/10);

**Compound 4cb**: 70 mg (94%); white solid; mp 93-95 °C;
**IR** (neat) ν (cm⁻¹): 3410, 2935, 1681, 1656, 1595, 1447, 1296, 1221, 1170, 1044, 809, 698;
**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 8.05 (d, J = 7.8 Hz, 1H), 7.96 (d, J = 7.8 Hz, 2H), 7.53 (q, J = 7.8 Hz, 2H), 7.41 (t, J = 7.8 Hz, 2H), 7.35 (t, J = 7.8 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 3.32-3.27 (m, 1H), 3.21-3.10 (m, 2H), 2.60-2.56 (m, 1H);
**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 192.8, 190.2, 142.5, 134.4, 134.3, 133.1, 130.7, 130.1, 128.8, 128.7, 128.2, 127.3, 75.0, 35.7, 26.1;
**HRMS (ESI)**: caled for C₁₇H₁₄ClO₂ [M + H]⁺ 285.0677; found 285.0676.
NMR copies of major product of compound 4cb:

$^1$H NMR 600 MHz, CDCl$_3$

$^1$C NMR 150 MHz, CDCl$_3$
Following the general procedure E, 4cc was purified by silica gel chromatography (EA/PE = 1/20);

**Compound 4cc:** 58 mg (95%); yellow oil;

**IR** (neat) ν (cm⁻¹): 3462, 2949, 1732, 1685, 1584, 1448, 1244, 1122, 883, 683;

**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 7.97 (d, J = 7.2 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 7.8 Hz, 2H), 3.07-3.04 (m, 1H), 2.81-2.78 (m, 1H), 2.24-2.19 (m, 1H), 2.14 – 2.09 (m, 1H), 2.01-1.98 (m, 1H), 1.96-1.83 (m, 3H);

**¹³C NMR** (100 MHz, CDCl₃) δ (ppm): 203.4, 190.7, 134.2, 133.6, 130.0, 128.5, 77.1, 41.3, 41.1, 28.3, 22.9;

**HRMS (ESI):** caled for C₁₃H₁₄ClO₂ [M + H]⁺ 237.0677; found 237.0674.
NMR copies of major product of compound 4cc:

4cc $^1$H NMR 600 MHz CDCl$_3$

4cc $^{13}$C NMR 100 MHz CDCl$_3$
**Compound 4cd**

![Chemical structure of Compound 4cd](attachment:image.png)

Following the general procedure E, **4cd** was purified by silica gel chromatography (EA/PE = 1/20);

**Compound 4cd**: 61 mg (94%); yellow oil;

**IR** (neat) ν (cm\(^{-1}\)): 3381, 2931, 1732, 1693, 1596, 1448, 1236, 1126, 941, 865, 759, 698;

**\(^1\)H NMR** (600 MHz, CDCl\(_3\)) δ (ppm): 7.93 (d, \(J = 7.8\) Hz, 2H), 7.54 (t, \(J = 7.8\) Hz, 1H), 7.42 (t, \(J = 7.8\) Hz, 2H), 3.02-3.00 (m, 1H), 2.62-2.57 (m, 1H), 2.49-2.44 (m, 1H), 2.42-2.38 (m, 1H) 1.96-1.82 (m, 4H), 1.78-1.71 (m, 1H), 1.44-1.40 (m, 1H);

**\(^13\)C NMR** (100 MHz, CDCl\(_3\)) δ (ppm): 205.3, 191.7, 133.6, 133.2, 130.1, 128.3, 79.3, 40.2, 37.3, 27.7, 24.2, 23.8;

**HRMS (ESI)**: caled for C\(_{14}\)H\(_{16}\)ClO\(_2\) [M + H]\(^+\) 251.0833; found 251.0836.
NMR copies of major product of compound 4cd:
Compound 4ce

Following the general procedure F, 4ce was purified by silica gel chromatography (EA/PE = 1/10);

**Compound 4ce**: 58 mg (86%); white solid; mp 71-72.5 °C;

**IR** (neat) ν (cm⁻¹): 3450, 3041, 1707, 1681, 1579, 1447, 1290, 1261, 1212, 1163, 938, 831, 752, 694;

**¹H NMR** (400 MHz, CDCl₃) δ (ppm): 8.00 (d, J = 7.6 Hz, 4H), 7.60 (t, J = 7.6 Hz, 2H), 7.47 (t, J = 8.0 Hz, 4H), 6.42 (s, 1H);

**¹³C NMR** (100 MHz, CDCl₃) δ (ppm): 189.3, 134.3, 133.8, 129.3, 129.0, 62.9;

**HRMS (ESI)**: caled for C₁₅H₁₅ClNO₂ [M + NH₄]⁺ 276.0786; found 276.0789.
NMR copies of major product of compound 4ce:

\[ \text{4ce} \text{ } ^1H \text{NMR 400 MHz, CDCl}_3 \]

\[ \text{4ce} \text{ } ^1^3C \text{NMR 100 MHz, CDCl}_3 \]
Compound 4ce'

Following the general procedure E, 4ce' was purified by silica gel chromatography (EA/PE = 1/10);

**Compound 4ce':** 68 mg (90%); yellow oil;

**IR (neat) ν (cm\(^{-1}\)):** 3396, 3071, 1699, 1595, 1442, 1238, 1207, 1180, 1000, 821, 685, 636;

**\(^1\)H NMR (600 MHz, CDCl\(_3\)) δ (ppm):** 7.97 (d, \(J = 7.8\) Hz, 4H), 7.54 (t, \(J = 7.8\) Hz, 2H), 7.40 (t, \(J = 7.8\) Hz, 4H);

**\(^13\)C NMR (150 MHz, CDCl\(_3\)) δ (ppm):** 185.3, 134.2, 131.5, 130.4, 128.7, 87.5;

**HRMS (ESI):** Caled for C\(_{15}\)H\(_{10}\)Cl\(_2\)O\(_2\)Na [M + Na]\(^+\) 314.9950; found 314.9954.
NMR copies of major product of compound 4ce':

4ce' $^1$H NMR 600 MHz, CDCl$_3$

4ce' $^{13}$C NMR 150 MHz, CDCl$_3$
Compound 4cf

Following the general procedure F, 4cf was purified by silica gel chromatography (EA/PE = 1/10);

Compound 4cf: 63 mg (89%); white solid; mp 77-79 °C;

IR (neat) ν (cm⁻¹): 3450, 2933, 1730, 1656, 1600, 1508, 1413, 1261, 1027, 864, 752, 588;

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.99 (d, J = 7.2 Hz, 2H), 7.90 (d, J = 8.4 Hz, 2H), 7.59 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 6.40 (s, 1H), 2.40 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ (ppm): 189.3, 188.9, 145.6, 134.2, 133.8, 131.3, 129.7, 129.4, 129.2, 128.9, 63.0, 21.8;

HRMS (ESI): caled for C₁₆H₁₇ClNO₂ [M + NH₄]⁺ 290.0942; found 290.0939.
NMR copies of major product of compound 4cf:

4cf $^1$H NMR 400 MHz, CDCl$_3$

4cf $^{13}$C NMR 100 MHz, CDCl$_3$
Compound 4cf<sup>*</sup>

Following the general procedure E, 4cf was purified by silica gel chromatography (EA/PE = 1/10);

**Compound 4cf**: 73 mg (92%); yellow oil;

**IR** (neat) v (cm<sup>-1</sup>): 3727, 2918, 1695, 1604, 1442, 1244, 1192, 1000, 838, 698;

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ (ppm): 7.96 (d, <i>J</i> = 7.2 Hz, 2H), 7.87 (d, <i>J</i> = 8.4 Hz, 2H), 7.53 (t, <i>J</i> = 7.2 Hz, 1H), 7.39 (t, <i>J</i> = 8.4 Hz, 2H), 7.19 (d, <i>J</i> = 8.4 Hz, 2H), 2.36 (s, 3H);

**<sup>13</sup>C NMR** (150 MHz, CDCl<sub>3</sub>) δ (ppm): 185.3, 184.9, 145.5, 134.1, 131.5, 130.6, 130.4, 129.4, 128.8, 128.6, 87.9, 21.7;

**HRMS (ESI)**: caled for C<sub>16</sub>H<sub>12</sub>Cl<sub>2</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup> 329.0107; found 329.0109.
NMR copies of major product of compound 4cf:
Compound 4cg

Following the general procedure F, 4cg was purified by silica gel chromatography (EA/PE = 1/40);

**Compound 4cg**: 55 mg (89%); white solid; mp 95-96 °C;

**IR** (neat) ν (cm⁻¹): 3440, 2970, 1733, 1669, 1595, 1457, 1314, 1180, 1053, 989, 835, 716, 676;

**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 8.01 (d, J = 7.8 Hz, 2H), 7.63 (t, J = 7.8 Hz, 1H), 7.51 (t, J = 7.8 Hz, 2H), 6.04 (s, 1H), 4.04 (s, 9H);

**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 203.9, 189.8, 134.2, 133.8, 129.3, 128.9, 59.4, 44.8, 26.8;

**HRMS (ESI)**: calcd for C₁₃H₁₉ClNO₂ [M + NH₄]⁺ 256.1099; found 256.1098.
NMR copies of major product of compound 4cg:

\[ \text{4cg} \quad ^1H \text{NMR 600 MHz, CDCl}_3 \]

\[ \text{4cg} \quad ^13C \text{NMR 150 MHz, CDCl}_3 \]
Following the general procedure E, 4cg' was purified by silica gel chromatography (EA/PE = 1/40); 

**Compound 4cg'**: 63 mg (89%); yellow oil; 
**IR** (neat) ν (cm⁻¹): 3429, 2974, 2913, 1718, 1706, 1597, 1457, 1226, 1064, 835, 681; 
**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 8.01 (d, J = 7.8 Hz, 2H), 7.62 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 1.26 (s, 9H); 
**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 199.4, 185.0, 134.3, 131.8, 130.5, 128.8, 88.5, 45.4, 29.1; 
**HRMS (ESI)**: caled for C₁₃H₁₈Cl₂N₂O₂ [M + NH₄]^+ 290.0709; found 290.0710.
NMR copies of major product of compound 4cg':

4cg$^1$H NMR 600 MHz, CDCl$_3$

4cg$^{13}$C NMR 150 MHz, CDCl$_3$
Following the general procedure H, 4cg" was purified by silica gel chromatography (EA/PE = 1/40);

**Compound 4cg"**

Following the general procedure H, 4cg" was purified by silica gel chromatography (EA/PE = 1/40);

**Compound 4cg"**: 66 mg (90%); white solid; mp 101-103 °C;

- **IR** (neat) ν (cm$^{-1}$): 3451, 2971, 1731, 1668, 1589, 1306, 1056, 997, 685;
- **$^1$H NMR** (400 MHz, CDCl$_3$) δ (ppm): 8.03 (d, $J = 7.2$ Hz, 2H), 7.64 (t, $J = 7.2$ Hz, 1H), 7.51 (t, $J = 7.2$ Hz, 2H), 6.19 (s, 1H), 1.22 (s, 9H);
- **$^{13}$C NMR** (100 MHz, CDCl$_3$) δ (ppm): 203.2, 189.5, 134.2, 133.7, 129.2, 128.9, 49.1, 44.7, 26.9;

**HRMS (ESI)**: caled for C$_{13}$H$_{19}$BrNO$_2$ [M + NH$_4$]$^+$ 300.0594; found 300.0591.
NMR copies of major product of compound **4cg**: 

**$^1$H NMR 400 MHz, CDCl$_3$**

**$^{13}$C NMR 100 MHz, CDCl$_3$**
Compound 4ch

Following the general procedure F, 4ch was purified by silica gel chromatography (EA/PE = 1/40);

**Compound 4ch**: 60 mg (91%); white solid; mp 93-94 °C;

**IR** (neat) v (cm\(^{-1}\)): 3443, 2968, 2924, 1723, 1673, 1306, 1190, 1067, 994, 846;

**\(^1\)H NMR** (600 MHz, CDCl\(_3\)) \(\delta\) (ppm): 7.91 (d, \(J = 8.4\) Hz, 2H), 7.30 (d, \(J = 7.8\) Hz, 2H), 6.00 (s, 1H), 2.43 (s, 3H), 1.21 (s, 9H);

**\(^13\)C NMR** (150 MHz, CDCl\(_3\)) \(\delta\) (ppm): 203.9, 189.4, 145.4, 131.3, 129.6, 129.5, 59.6, 44.8, 26.9, 21.8;

**HRMS (ESI)**: caled for \(C_{14}H_{17}ClO_2Na\) [M + Na]\(^+\) 275.0809; found 275.0811.
NMR copies of major product of compound 4ch:
Compound 4ci

Following the general procedure F, 4ci was purified by silica gel chromatography (EA/PE = 1/40);

**Compound 4ci**: 71 mg (86%); white solid; mp 96-97 °C;

**IR** (neat) v (cm⁻¹): 3440, 2968, 1723, 1673, 1576, 1395, 1287, 1183, 1067, 996, 852;

**¹H NMR** (600 MHz, CDCl₃) δ (ppm): 7.89 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 7.8 Hz, 2H), 5.92 (s, 1H), 1.21 (s, 9H);

**¹³C NMR** (150 MHz, CDCl₃) δ (ppm): 203.8, 189.1, 132.5, 132.2, 130.88, 129.7, 59.6, 45.0, 26.8;

**HRMS (ESI)**: calcd for C₁₃H₁₄BrClO₂Na [M + Na]⁺ 338.9758; found 338.9761.
NMR copies of major product of compound 4ci: