Supporting Information for

Copper/O₂-mediated direct sp³ C-H/N-H cross-dehydrogen coupling reaction of acylated amines with N-aryl glycine esters

Bin Sun, a Yao Wang b, Deyu Li b, Can Jin, *a,b and WeiKe Su *a,b

a Collaborative Innovation Center of Yangtze River Delta Region Green Pharmaceuticals, Zhejiang University of Technology, Hangzhou, P. R. China.
b College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou, P. R. China.

Email: jincan@zjut.edu.cn; pharmlab@zjut.edu.cn

Content

General Information

General Procedure for the Synthesis of 3

Characterization Data for Products

Copies of NMR Spectra
**General Information**

Melting points were determined using a digital melting point apparatus and uncorrected. $^1$H NMR spectra were recorded at 500 and 600 MHz using TMS as internal standard, $^{13}$C NMR spectra were recorded at 125 and 150 MHz using TMS as internal standard. All chemical shifts were reported as $\delta$ values (ppm) relative to TMS and observed coupling constants ($J$) are given in Hertz (Hz). Mass spectra were measured with a HRMS-ESI instrument. All chemical reagents were purchased from commercial source and without prior purification. Column Chromatography was performed on silica gel (200-300 mesh) and the elution was performed with $n$-hexane/ethyl acetate. $N$-aryl glycine esters 1 were prepared according to reported protocols.$^1$

**General Procedure for the Synthesis of 3**

$N$-aryl glycine esters 1 (0.6 mmol) and acylated amines 2 (0.5 mmol) were dissolved in CH$_3$CN, CuCl (0.025 mmol) was then added in one portion under stirring. The reactions were performed under an oxygen atmosphere (oxygen ballon) at 50 °C for 24 h. Next, the reaction mixture was concentrated in vacuum, and the residues were purified by silica gel column chromatography ($n$-hexane-EtOAc) to afford the desired product 3.

Characterization Data for Products

3aa: yellow solid; yield 81% (137 mg); m.p. 113.8-116.5 °C; ^1H NMR (600 MHz, CDCl₃): δ 7.87-7.84 (m, 2H), 7.75-7.72 (m, 2H), 7.01 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 7.8 Hz, 2H), 6.23 (s, 1H), 5.23 (br. s, 1H), 4.33 (q, J = 7.2 Hz, 2H), 2.22 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H). ^13C NMR (150 MHz, CDCl₃) δ 167.5, 167.2, 141.6, 134.4, 131.7, 130.0, 128.8, 123.7, 114.0, 63.0, 60.4, 20.4, 14.1. HRMS: C₁₉H₁₈N₂NaO₄ [M+Na]^+; calculated: 361.1159, found: 361.1144.

3ba: yellow solid; yield 86% (145 mg); m.p. 115.1-117.2 °C; ^1H NMR (600 MHz, CDCl₃): δ 7.85-7.83 (m, 2H), 7.72-7.70 (m, 2H), 7.07 (t, J = 7.8 Hz, 1H), 6.66-6.60 (m, 3H), 6.21 (s, 1H), 5.27 (br. s, 1H), 4.32 (q, J = 7.2 Hz, 2H), 2.26 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H). ^13C NMR (150 MHz, CDCl₃) δ 167.5, 167.2, 143.9, 139.4, 134.4, 131.7, 129.4, 123.7, 120.5, 114.7, 110.6, 63.0, 59.9, 21.6, 14.1. HRMS: C₁₉H₁₈N₂NaO₄ [M+Na]^+; calculated: 361.1159, found: 361.1141.

3ca: yellow solid; yield 56% (95 mg); m.p. 94.2-97.3 °C; ^1H NMR (600 MHz, CDCl₃): δ 7.85-7.84 (m, 2H), 7.73-7.72 (m, 2H), 7.10 (t, J = 7.8 Hz, 1H), 7.06 (d, J = 7.2 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 6.72 (t, J = 7.2 Hz, 1H), 6.25 (s, 1H), 5.27 (br. s, 1H), 4.32 (q, J = 7.2 Hz, 2H), 2.26 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H). ^13C NMR (150 MHz, CDCl₃) δ 167.5, 167.3, 142.1, 134.4, 131.7, 130.7, 127.3, 123.7, 123.3, 119.2, 110.9, 63.1, 59.9, 17.4, 14.1. HRMS: C₁₉H₁₉N₂O₄ [M+H]^+; calculated: 339.1339, found: 339.1339.

3da: yellow solid; yield 78% (126 mg); m.p. 112.6-114.6 °C; ^1H NMR (600 MHz, CDCl₃): δ 7.89-7.86 (m, 2H), 7.77-7.74 (m, 2H), 7.23-7.20 (m, 2H), 6.85
(d, J = 7.8 Hz, 2H), 6.81 (t, J = 7.2 Hz, 1H), 6.24 (s, 1H), 5.31 (br. s, 1H), 4.33 (q, J = 7.2 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H). 13C NMR (150 MHz, CDCl3) δ 167.5, 167.1, 143.9, 134.4, 131.7, 129.5, 123.7, 119.6, 113.7, 63.1, 59.9, 14.1. HRMS: C18H16N2O4 [M+Na]+; calculated: 347.1002, found: 347.0993.

3ea: yellow solid; yield 80% (130 mg); m.p. 144.3-146.1 °C; 1H NMR (600 MHz, CDCl3): δ 7.88-7.84 (m, 2H), 7.76-7.73 (m, 2H), 7.02 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.4 Hz, 2H), 6.25 (s, 1H), 3.85 (s, 3H), 2.23 (s, 3H). 13C NMR (150 MHz, CDCl3) δ 167.7, 167.5, 141.4, 134.4, 131.7, 130.0, 129.0, 123.7, 114.0, 60.2, 53.6, 20.4. HRMS: C18H17N2O4 [M+H]+; calculated: 325.1183, found: 325.1183.

3fa: yellow solid; yield 82% (133 mg); m.p. 108.4-111.3 °C; 1H NMR (600 MHz, CDCl3): δ 7.87-7.84 (m, 2H), 7.73-7.71 (m, 2H), 7.07 (t, J = 7.8 Hz, 1H), 6.65-6.60 (m, 3H), 6.24 (s, 1H), 5.19 (br. s, 1H), 3.83 (s, 3H), 2.26 (s, 3H). 13C NMR (150 MHz, CDCl3) δ 167.7, 167.5, 143.8, 134.4, 131.7, 129.4, 123.7, 120.5, 114.8, 110.7, 59.8, 53.7, 21.6. HRMS: C18H17N2O4 [M+H]+; calculated: 325.1183, found: 325.1169.

3ga: yellow solid; yield 52% (84 mg); m.p. 116.0-118.9 °C; 1H NMR (600 MHz, CDCl3): δ 7.86-7.84 (m, 2H), 7.74-7.72 (m, 2H), 7.11-7.06 (m, 2H), 6.87 (d, J = 7.8 Hz, 1H), 6.74-6.71 (m, 1H), 6.28 (d, J = 8.4 Hz, 1H), 5.26 (d, J = 9.0 Hz, 1H), 3.85 (s, 3H), 2.26 (s, 3H). 13C NMR (150 MHz, CDCl3) δ 167.9, 167.5, 142.0, 134.4, 131.7, 130.7, 127.3, 123.8, 123.4, 119.3, 110.9, 59.6, 53.7, 17.4. HRMS: C18H16N2NaO4 [M+Na]+; calculated: 347.1002, found: 347.1016.
**3ha:** yellow solid; yield 76% (118 mg); m.p. 117.2-119.8 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.87-7.83 (m, 2H), 7.75-7.71 (m, 2H), 7.20-7.18 (m, 2H), 6.83 (d, $J = 8.4$ Hz, 2H), 6.79 (t, $J = 7.8$ Hz, 1H), 6.24 (s, 1H), 5.31 (br. s, 1H), 3.83 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.7, 167.5, 143.8, 134.5, 131.7, 129.5, 123.8, 119.6, 113.8, 59.7, 53.7. HRMS: C$_{17}$H$_{14}$N$_2$O$_4$ [M+Na]$^+$; calculated: 333.0846, found: 333.0852.

![3ia](image)

**3ia:** yellow solid; yield 86% (151 mg); m.p. 106.3-109.1 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.84-7.83 (m, 2H), 7.72-7.71 (m, 2H), 6.99 (d, $J = 7.8$ Hz, 2H), 6.74 (d, $J = 8.4$ Hz, 2H), 6.15 (d, $J = 9.0$ Hz, 1H), 5.22-5.12 (m, 2H), 2.20 (s, 3H), 1.28 (d, $J = 6.6$ Hz, 3H), 1.19 (d, $J = 6.0$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.5, 166.7, 141.6, 134.4, 131.7, 130.0, 128.8, 123.7, 114.0, 71.1, 60.5, 21.6, 21.5, 20.4. HRMS: C$_{20}$H$_{21}$N$_2$O$_4$ [M+H]$^+$; calculated: 353.1496, found: 353.1479.

![3ja](image)

**3ja:** yellow solid; yield 83% (146 mg); m.p. 117.0-120.3 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.85-7.82 (m, 2H), 7.73-7.70 (m, 2H), 7.07 (t, $J = 7.8$ Hz, 1H), 6.66-6.64 (m, 2H), 6.60 (d, $J = 7.2$ Hz, 1H), 6.17 (s, 1H), 5.25 (br. s, 1H), 5.18-5.12 (m, 1H), 2.26 (s, 3H), 1.28 (d, $J = 6.0$ Hz, 3H), 1.19 (d, $J = 6.6$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.5, 166.7, 144.0, 139.4, 134.4, 131.7, 129.4, 123.7, 120.4, 114.7, 110.6, 71.1, 60.1, 21.6, 21.5. HRMS: C$_{20}$H$_{20}$N$_2$O$_4$ [M+Na]$^+$; calculated: 375.1315, found: 375.1324.

![3ka](image)

**3ka:** yellow solid; yield 51% (90 mg); m.p. 110.0-112.1 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.89-7.86 (m, 2H), 7.77-7.74 (m, 2H), 7.14-7.11 (m, 1H), 7.09 (d, $J = 7.2$ Hz, 1H), 6.91 (d, $J = 7.8$ Hz, 1H), 6.76-6.73 (m, 1H), 6.23 (s, 1H), 5.29 (br. s, 1H), 5.22-5.16 (m, 1H), 2.28 (s, 3H), 1.31 (d, $J = 6.0$ Hz, 3H), 1.23 (d, $J = 6.0$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.5, 166.8, 142.2, 134.4, 131.7, 130.6, 127.3, 123.7, 123.2, 119.1, 110.9, 71.2, 60.0, 21.6, 21.5, 17.4. HRMS: C$_{20}$H$_{20}$N$_2$O$_4$ [M+H]$^+$; calculated: 375.1315, found: 375.1334.
3la: yellow solid; yield 82% (139 mg); m.p. 118.0-120.2 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 7.87-7.84 (m, 2H), 7.75-7.72 (m, 2H), 7.20-7.18 (m, 2H), 6.83 (d, \(J = 7.8\) Hz, 2H), 6.78 (t, \(J = 7.2\) Hz, 1H), 6.17 (s, 1H), 5.19-5.13 (m, 1H), 1.28 (d, \(J = 6.0\) Hz, 3H), 1.19 (d, \(J = 6.6\) Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 167.5, 166.6, 144.0, 134.4, 131.7, 129.5, 123.7, 119.5, 113.5, 71.2, 60.0, 21.6. HRMS: \(\text{C}_{19}\text{H}_{18}\text{N}_{2}\text{O}_{4}\) \([\text{M+Na}]^+\); calculated: 361.1159, found: 361.1162.

3ma: yellow solid; yield 59% (101 mg); m.p. 92.2-95.0 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 7.90-7.86 (m, 2H), 7.79-7.75 (m, 2H), 6.93-6.89 (m, 2H), 6.81-6.77 (m, 2H), 6.15 (s, 1H), 4.33 (q, \(J = 7.2\) Hz, 2H), 1.28 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 167.5, 166.6, 144.0, 134.4, 131.6, 123.8, 116.0 (d, \(J_{C-F} = 22.4\) Hz), 115.0 (d, \(J_{C-F} = 7.5\) Hz), 63.1, 60.6, 14.1. HRMS: \(\text{C}_{18}\text{H}_{15}\text{F}_{2}\text{N}_{2}\text{O}_{4}\) \([\text{M+Na}]^+\); calculated: 365.0908, found: 365.0911.

3na: yellow solid; yield 52% (93 mg); m.p. 108.7-111.0 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 7.87-7.84 (m, 2H), 7.76-7.74 (m, 2H), 7.13 (d, \(J = 9.0\) Hz, 2H), 6.75 (d, \(J = 9.0\) Hz, 2H), 6.14 (s, 1H), 5.32 (br. s, 1H), 4.30 (q, \(J = 7.2\) Hz, 2H), 1.25 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 167.4, 166.9, 142.6, 134.5, 131.6, 129.4, 124.4, 123.8, 115.0, 63.2, 59.8, 14.1. HRMS: \(\text{C}_{18}\text{H}_{15}\text{Cl}_{2}\text{N}_{2}\text{O}_{4}\) \([\text{M+Na}]^+\); calculated: 381.0613, found: 381.0627.
167.4, 166.9, 143.1, 134.5, 132.2, 131.6, 123.8, 115.4, 111.5, 63.2, 59.7, 14.1.

HRMS: C_{18}H_{15}BrN_{2}NaO_{4} [M+Na]^+; calculated: 425.0107, found: 425.0125.

(3pa)

3pa: yellow solid; yield 49% (84 mg); m.p. 127.3-130.5 °C; ¹H NMR (600 MHz, CDCl₃): δ 7.87-7.85 (m, 2H), 7.76-7.74 (m, 2H), 7.13 (d, J = 8.4 Hz, 2H), 6.75 (d, J = 9.0 Hz, 2H), 6.17 (d, J = 8.4 Hz, 1H), 5.31 (d, J = 9.0 Hz, 1H), 3.84 (s, 3H).

(3qa)

3qa: yellow solid; yield 43% (83 mg); m.p. 155.9-158.8 °C; ¹H NMR (600 MHz, CDCl₃): δ 7.78-7.76 (m, 2H), 7.67-7.65 (m, 2H), 7.19-7.17 (m, 2H), 6.62 (d, J = 9.0 Hz, 2H), 6.09 (s, 1H), 5.27 (br. s, 1H), 3.75 (s, 3H).

(3ra)

3ra: yellow solid; yield 62% (115 mg); m.p. 127.0-129.7 °C; ¹H NMR (600 MHz, CDCl₃): δ 7.87-7.85 (m, 2H), 7.75-7.74 (m, 2H), 7.13 (d, J = 9.0 Hz, 2H), 6.76 (d, J = 9.0 Hz, 2H), 6.10 (s, 1H), 5.18-5.14 (m, 1H), 1.28 (d, J = 6.6 Hz, 3H), 1.19 (d, J = 6.0 Hz, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 167.5, 166.4, 142.6, 134.5, 131.6, 129.4, 124.3, 123.8, 115.0, 71.3, 59.8, 21.6, 21.5. HRMS: C_{17}H_{13}ClN_{2}NaO_{4} [M+Na]^+; calculated: 410.9951, found: 410.9927.

(3sa)

3sa: yellow solid; yield 58% (120 mg); m.p. 125.8-128.9 °C; ¹H NMR (600 MHz, CDCl₃): δ 7.87-7.85 (m, 2H), 7.75-7.74 (m, 2H), 7.26 (d, J = 9.0 Hz, 2H), 6.71 (d, J = 9.0 Hz, 2H), 6.10 (s, 1H), 5.18-5.14 (m, 1H), 1.28 (d, J = 6.6 Hz,
$^3$H), 1.19 (d, $J = 6.0$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.4, 166.3, 143.1, 134.5, 132.2, 131.6, 123.8, 115.4, 111.4, 71.4, 59.8, 21.6, 21.5. HRMS: C$_{19}$H$_{17}$ BrN$_2$NaO$_4$ [M+Na]$^+$; calculated: 439.0264, found: 439.0244.

3ta: yellow solid; yield 62% (115 mg); m.p. 144.3-147.1 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.89-7.88 (m, 2H), 7.77-7.76 (m, 2H), 6.92-6.88 (m, 2H), 6.79-6.77 (m, 2H), 6.04 (s, 1H), 1.47 (s, 9H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 167.6, 165.9, 156.9 (d, $J_{C-F} = 235.7$ Hz), 140.6, 134.4, 131.6, 123.7, 116.0 (d, $J_{C-F} = 22.5$ Hz), 114.9 (d, $J_{C-F} = 7.5$ Hz), 84.2, 61.0, 27.8. HRMS: C$_{20}$H$_{19}$FN$_2$NaO$_4$ [M+Na]$^+$; calculated: 393.1221, found: 393.1232.

3bb: yellow glass; yield 72% (150 mg); $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 8.00 (s, 1H), 7.88 (d, $J = 7.8$ Hz, 1H), 7.73 (d, $J = 8.4$ Hz, 1H), 7.10 (t, $J = 7.8$ Hz, 1H), 6.66-6.63 (m, 3H), 6.21 (d, $J = 9.0$ Hz, 1H), 5.25 (d, $J = 9.0$ Hz, 1H), 4.32 (q, $J = 7.2$ Hz, 2H), 2.28 (s, 3H), 1.28 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 166.9, 166.7, 166.2, 143.8, 139.4, 137.4, 133.3, 130.2, 129.4, 127.1, 125.0, 120.6, 114.7, 110.6, 63.1, 60.2, 21.6, 14.1. HRMS: C$_{19}$H$_{17}$BrN$_2$NaO$_4$ [M+Na]$^+$; calculated: 439.0264, found: 439.0243.

3db: yellow solid; yield 70% (141 mg); m.p. 120.9-123.1 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.88 (s, 1H), 7.76 (d, $J = 7.8$ Hz, 1H), 7.61 (d, $J = 7.8$ Hz, 1H), 7.10-7.08 (m, 2H), 6.72-6.68 (m, 3H), 6.11 (d, $J = 9.0$ Hz, 1H), 5.23 (d, $J = 9.0$ Hz, 1H), 4.22 (q, $J = 7.2$ Hz, 2H), 1.17 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 164.8, 164.6, 164.0, 141.7, 135.4, 131.2, 128.1, 127.4, 127.3, 125.0, 123.0, 117.6, 111.6, 61.1, 58.0, 12.0. HRMS: C$_{18}$H$_{15}$BrN$_2$NaO$_4$ [M+Na]$^+$; calculated: 425.0107, found: 425.0095.
3eb: yellow solid; yield 75% (151 mg); m.p. 142.2-144.1 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta 7.98\) (s, 1H), 7.87 (d, \(J = 7.8\) Hz, 1H), 7.72 (d, \(J = 7.8\) Hz, 1H), 7.01 (d, \(J = 8.4\) Hz, 2H), 6.73 (d, \(J = 8.4\) Hz, 2H), 6.22 (d, \(J = 9.6\) Hz, 1H), 5.19 (d, \(J = 9.6\) Hz, 1H), 3.85 (s, 3H), 2.22 (s, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \(\delta 167.5, 166.7, 166.2, 141.2, 137.4, 133.3, 130.2, 129.4, 129.2, 127.1, 125.0, 114.0, 60.5, 53.7, 20.3\). HRMS: \(\text{C}_{18}\text{H}_{15}\text{BrN}_{2}\text{NaO}_4 [M+Na]^+\); calculated: 425.0107, found: 425.0090.

3ac: yellow solid; yield 83% (146 mg); m.p. 46.8-49.0 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta 7.73\) (d, \(J = 7.5\) Hz,1H), 7.65 (s, 1H), 7.51 (d, \(J = 7.5\) Hz, 1H), 7.00 (d, \(J = 8.0\) Hz, 2H), 6.75 (d, \(J = 8.5\) Hz, 2H), 6.19 (s, 1H), 5.20 (br. s, 1H), 4.31 (q, \(J = 7.0\) Hz, 2H), 2.50 (s, 3H), 2.21 (s, 3H), 1.27 (t, \(J = 7.0\) Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta 167.7, 167.6, 167.3, 145.8, 141.6, 134.9, 132.1, 129.9, 129.1, 128.9, 124.2, 123.6, 114.0, 62.9, 60.2, 22.0, 20.4, 14.1\). HRMS: \(\text{C}_{18}\text{H}_{15}\text{BrN}_{2}\text{NaO}_4 [M+Na]^+\); calculated: 375.1315, found: 375.1305.

3ad: glass; yield 66% (100 mg); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta 6.90\) (d, \(J = 8.4\) Hz, 2H), 6.60-6.58 (m, 3H), 4.96 (br. s, 1H), 4.20-4.11 (m, 2H), 2.55 (t, \(J = 6.6\) Hz, 4H), 2.15 (s, 3H), 1.83-1.80 (m, 2H), 1.18 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \(\delta 172.6, 168.1, 142.3, 129.9, 128.9, 124.2, 123.6, 114.0, 62.9, 60.2, 22.0, 20.4, 14.1\). HRMS: \(\text{C}_{16}\text{H}_{20}\text{N}_{2}\text{NaO}_4 [M+Na]^+\); calculated: 327.1315, found: 327.1328.

3bd: glass; yield 57% (87 mg); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta 7.11-7.08\) (m, 1H), 6.70 (s, 1H), 6.64 (d, \(J = 7.8\) Hz, 1H), 6.62-6.60 (m, 2H), 4.30-4.24 (m, 2H), 2.69-2.67 (m, 4H), 2.29 (s, 3H), 1.97-1.93 (m, 2H), 1.29 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \(\delta 172.5, 168.0, 144.6, 139.3, 129.3, 120.2, 108.0\).
114.8, 110.7, 62.4, 61.5, 32.6, 21.6, 16.9, 14.1. HRMS: C_{16}H_{20}N_{2}NaO_{4} [M+Na]^+; calculated: 327.1315, found: 327.1317.

(3rd)

3rd: white solid; yield 41% (70 mg); m.p. 89.2-92.3 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 7.13 (d, \(J = 9.0\) Hz, 2H), 6.70 (d, \(J = 9.0\) Hz, 2H), 6.59 (d, \(J = 10.2\) Hz, 1H), 5.16 (d, \(J = 10.2\) Hz, 1H), 5.11-5.07 (m, 1H), 2.71-2.63 (m, 4H), 1.95-1.91 (m, 2H), 1.29 (d, \(J = 6.0\) Hz, 3H), 1.22 (d, \(J = 6.0\) Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 172.5, 167.1, 143.4, 129.3, 123.9, 115.1, 70.5, 61.6, 32.6, 21.7, 21.6, 16.9. HRMS: C_{16}H_{19}ClN_{2}NaO_{4} [M+Na]^+; calculated: 361.0926, found: 361.0918.

(3ae)

3ae: yellow solid; yield 82% (118 mg); m.p. 141.0-142.3 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 7.02 (d, \(J = 8.4\) Hz, 2H), 6.72-6.69 (m, 4H), 6.01 (s, 1H), 5.09 (br. s, 1H), 4.34-4.27 (m, 2H), 2.25 (s, 3H), 1.30 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 169.9, 167.0, 141.4, 134.4, 130.0, 129.0, 114.0, 63.0, 60.2, 20.4, 14.1. HRMS: C_{15}H_{16}N_{2}NaO_{4} [M+Na]^+; calculated: 311.1002, found: 311.1010.

(3re)

3re: yellow solid; yield 61% (98 mg); m.p. 118.0-120.1 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 7.16 (d, \(J = 9.0\) Hz, 2H), 6.74 (s, 2H), 6.71 (d, \(J = 9.0\) Hz, 2H), 5.92 (d, \(J = 8.4\) Hz, 1H), 5.21 (d, \(J = 9.0\) Hz, 1H), 5.18-5.14 (m, 1H), 1.30 (d, \(J = 6.6\) Hz, 3H), 1.24 (d, \(J = 6.0\) Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 169.7, 166.1, 142.5, 134.4, 129.4, 124.5, 115.0, 71.4, 59.8, 21.6, 21.5. HRMS: C_{15}H_{15}ClN_{2}NaO_{4} [M+Na]^+; calculated: 345.0613, found: 345.0601.

(3af)

3af: yellow solid; yield 85% (145 mg); m.p. 103.8-106.0 °C; \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 7.00 (d, \(J = 8.4\) Hz, 2H), 6.65 (d, \(J = 8.4\) Hz, 2H), 5.99 (s, 1H), 5.80-5.74 (m, 2H), 4.33-4.22 (m, 2H), 3.09-3.04 (m, 2H), 2.58-2.52 (m, 2H), 2.25-2.19 (m, 5H), 1.28 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\)

![3ff](image)

**3ff:** yellow solid; yield 77% (126 mg); m.p. 120.6-122.9 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.09-7.07 (m, 1H), 6.65 (d, $J$ = 7.8 Hz, 1H), 6.56-6.53 (m, 2H), 6.04 (s, 1H), 5.78-5.73 (m, 2H), 5.13 (br. s, 1H), 3.81 (s, 3H), 3.22-3.18 (m, 2H), 2.28 (s, 3H), 2.25-2.17 (m, 2H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 179.9, 179.2, 179.2, 167.2, 143.7, 139.2, 129.3, 127.3, 127.2, 120.6, 115.1, 111.1, 60.6, 53.4, 39.2, 39.1, 23.4, 23.3, 21.5. HRMS: $\text{C}_{19}\text{H}_{21}\text{ClN}_2\text{NaO}_4 [\text{M+Na}]^+$; calculated: 351.1315, found: 351.1327.

![3rf](image)

**3rf:** yellow solid; yield 56% (105 mg); m.p. 128.7-131.0 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.13 (d, $J$ = 9.0 Hz, 2H), 6.66 (d, $J$ = 9.0 Hz, 2H), 5.89 (d, $J$ = 9.0 Hz, 1H), 5.81-5.76 (m, 2H), 5.22 (d, $J$ = 9.0 Hz, 1H), 5.14-5.08 (m, 1H), 3.11-3.04 (m, 2H), 2.59-2.53 (m, 2H), 2.26-2.18 (m, 2H), 1.27 (d, $J$ = 6.0 Hz, 3H), 1.22 (d, $J$ = 6.0 Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 179.4, 179.2, 167.2, 143.7, 139.2, 129.3, 127.3, 127.2, 120.6, 115.1, 111.1, 60.6, 53.4, 39.2, 39.1, 23.4, 23.3, 21.5. HRMS: $\text{C}_{19}\text{H}_{21}\text{ClN}_2\text{NaO}_4 [\text{M+Na}]^+$; calculated: 399.1082, found: 399.1088.

![3ag](image)

**3ag:** yellow solid; yield 80% (116 mg); m.p. 113.0-116.5 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.00 (d, $J$ = 8.4 Hz, 2H), 6.67 (d, $J$ = 8.4 Hz, 2H), 6.03 (s, 1H), 5.10 (br. s, 1H), 4.29 (q, $J$ = 7.2 Hz, 2H), 2.72-2.65 (m, 4H), 2.23 (s, 3H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 176.4, 166.8, 141.5, 130.0, 129.0, 113.9, 63.0, 61.0, 28.1, 20.4, 14.1. HRMS: $\text{C}_{15}\text{H}_{18}\text{N}_2\text{NaO}_4 [\text{M+Na}]^+$; calculated: 313.1159, found: 313.1149.
**3eg:** yellow solid; yield 55% (80 mg); m.p. 132.9-134.8 °C; $^1$H NMR (600 MHz, CDCl$_3$): δ 7.12-7.07 (m, 2H), 6.78-6.74 (m, 2H), 6.09 (d, J = 7.8 Hz, 1H), 5.18 (d, J = 7.8 Hz, 1H), 4.34-4.26 (m, 2H), 2.75-2.65 (m, 4H), 2.22 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 176.3, 166.9, 142.1, 130.7, 127.3, 123.3, 119.3, 110.9, 63.1, 60.5, 28.1, 17.3, 14.1. HRMS: C$_{15}$H$_{18}$N$_2$NaO$_4$ [M+Na]$^+$; calculated: 313.1159, found: 313.1149.

![3eg](image)

**3eg:** yellow solid; yield 70% (97 mg); m.p. 144.4-147.1 °C; $^1$H NMR (600 MHz, CDCl$_3$): δ 6.92 (d, J = 7.2 Hz, 2H), 6.59 (d, J = 7.8 Hz, 2H), 5.97 (d, J = 10.2 Hz, 1H), 5.04 (d, J = 10.2 Hz, 1H), 3.74 (s, 3H), 2.64-2.54 (m, 4H), 2.15 (s, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 176.5, 167.4, 141.4, 130.0, 129.0, 114.0, 60.8, 53.6, 28.1, 20.4. HRMS: C$_{14}$H$_{16}$N$_2$NaO$_4$ [M+Na]$^+$; calculated: 299.1002, found: 299.0996.

![3jg](image)

**3jg:** yellow solid; yield 86% (131 mg); m.p. 111.0-113.4 °C; $^1$H NMR (600 MHz, CDCl$_3$): δ 7.08 (t, J = 7.8 Hz, 1H), 6.63 (d, J = 7.2 Hz, 1H), 6.59-6.57 (m, 2H), 6.00 (s, 1H), 5.26 (br. s, 1H), 4.31 (q, J = 7.2 Hz, 2H), 2.80-2.70 (m, 4H), 1.31 (t, J = 7.2 Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 176.4, 166.2, 144.0, 139.4, 129.4, 120.4, 114.7, 110.6, 71.1, 60.7, 28.1, 21.7, 21.6, 21.5. HRMS: C$_{16}$H$_{20}$N$_2$NaO$_4$ [M+Na]$^+$; calculated: 327.1315, found: 327.1302.

![3ng](image)

**3ng:** yellow solid; yield 40% (62 mg); m.p. 150.5-152.9 °C; $^1$H NMR (600 MHz, CDCl$_3$): δ 7.17 (d, J = 9.0 Hz, 2H), 6.71 (d, J = 8.4 Hz, 2H), 6.00 (s, 1H), 5.26 (br. s, 1H), 4.31 (q, J = 7.2 Hz, 2H), 2.80-2.70 (m, 4H), 1.31 (t, J = 7.2 Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 176.3, 166.4, 142.5, 129.4, 124.5, 115.0, 63.2, 60.4, 28.1, 14.1. HRMS: C$_{14}$H$_{15}$ClN$_2$NaO$_4$ [M+Na]$^+$; calculated: 333.0613, found: 333.0612.
3ai: yellow solid; yield 62% (97 mg); m.p. 139.2-141.9 °C; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.75 (d, $J = 7.2$ Hz, 2H), 7.52-7.49 (m, 1H), 7.42 (t, $J = 7.8$ Hz, 2H), 7.01 (d, $J = 8.4$ Hz, 2H), 6.72-6.68 (m, 3H), 6.09 (d, $J = 7.8$ Hz, 1H), 4.31 (q, $J = 7.2$ Hz, 2H), 2.23 (s, 3H), 1.32 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 170.0, 167.3, 141.7, 133.4, 132.0, 130.0, 128.9, 128.6, 127.1, 114.3, 62.6, 61.3, 20.4, 14.1. HRMS: C$_{18}$H$_{20}$N$_2$NaO$_3$ [M+Na]$^+$; calculated: 335.1366, found: 335.1369.

![Chemical Structure](3ai.png)

3oi: yellow solid; yield 49% (92 mg); m.p. 166.7-168.2 °C; $^1$H NMR (600 MHz, DMSO-$d_6$): $\delta$ 9.32 (d, $J = 7.2$ Hz, 1H), 7.86 (d, $J = 7.8$ Hz, 2H), 7.56-7.54 (m, 1H), 7.47 (t, $J = 7.8$ Hz, 2H), 7.25 (d, $J = 9.0$ Hz, 2H), 6.80-6.78 (m, 2H), 6.51 (d, $J = 8.4$ Hz, 1H), 5.79-5.75 (m, 1H), 4.24-4.16 (m, 2H), 1.21 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 169.2, 166.8, 145.6, 133.8, 132.2, 131.9, 128.8, 127.9, 115.6, 108.8, 61.9, 60.8, 14.5. HRMS: C$_{17}$H$_{17}$BrN$_2$NaO$_3$ [M+Na]$^+$; calculated: 399.0315, found: 399.0309.