Supporting Information

For

One-pot regioselective synthesis of 2,4-disubstituted quinolines via copper(II)-catalyzed cascade annulation

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General Methods and Materials

Cu(OTf)$_2$, HOTf and Tf$_2$O were purchased from Energy Chemical and used without further purification. Other chemicals were purchased from commercial suppliers, further dried and purified if necessary. The water used was re-distillated and ion-free. $^1$H and $^{13}$C NMR spectra were achieved on a Bruker AVANCE 400 MHz spectrometer ($^1$H 400 MHz; $^{13}$C 100 MHz) in CDCl$_3$. Abbreviations for data quoted are s-singlet; brs-broad singlet; d-doublet; t-triplet; dd-doublet of doublets; m-multiplet. High-resolution mass spectra were measured on a Waters Micromass GCT facility. Thin-layer chromatographies were done on pre-coated silica gel 60F254 plates (Merck). Silica gel 60H (200-300 mesh) manufactured by Qingdao Haiyang Chemical Group Co. (China) was used for general chromatography.
General catalytic procedure for the synthesis of quinolines

A seal tube (30 mL) was charged with aniline (1.0 mmol, 1.0 equiv.), alkyne ester (2.2 mmol, 2.2 equiv.), then the Cu(OTf)$_2$ (0.05 mmol), CH$_3$CN (2 mL) and HOTf (0.1 mmol) were added. The mixture was stirred at 120 °C for 24 hours, the mixture was quenched by sat. aq. NaHCO$_3$, and diluted with 20 mL of dichloromethane and washed with 10 mL of H$_2$O. The aqueous layer was extracted twice with dichloromethane (10 mL) and the combined organic phase was dried over Na$_2$SO$_4$. After evaporation of the solvents, the residue was purified by silica gel chromatography (hexane/AcOEt = 7:1) to afford the corresponding quinoline products. All other compounds are synthesized in a similar manner, with the yields listed in the main text calculated from the isolated, pure products.

A seal tube (30 mL) was charged with aniline (1.0 mmol, 1.0 equiv.), alkyne ester (1.0 mmol, 1.0 equiv.) and ketone (1.2 mmol, 1.2 equiv.), then the Cu(OTf)$_2$ (0.05 mmol), CH$_3$CN (2 mL) and HOTf (0.1 mmol) were added. The mixture was stirred at 120 °C for 24 hours. After the reaction finished, the mixture was quenched by sat. aq. NaHCO$_3$, and diluted with 20 mL of dichloromethane and washed with 10 mL of H$_2$O. The aqueous layer was extracted twice with dichloromethane (10 mL) and the combined organic phase was dried over Na$_2$SO$_4$. After evaporation of the solvents, the residue was purified by silica gel chromatography (hexane/AcOEt = 2:1) to afford the corresponding quinoline products. All other compounds are synthesized in a similar manner, with the yields listed in the main text calculated from the isolated, pure products.
A seal tube (30 mL) was charged with aniline (1.0 mmol, 1.0 equiv.), alkyne ester (1.0 mmol, 1.0 equiv.) and phenylacetylene (1.2 mmol, 1.2 equiv.), then the Cu(OTf)$_2$ (0.05 mmol), CH$_3$CN (2 mL) and HOTf (0.1 mmol) were added. The mixture was stirred at 120 °C for 24 hours. After the reaction finished, the mixture was quenched by sat. aq. NaHCO$_3$, and diluted with 20 mL of dichloromethane and washed with 10 mL of H$_2$O. The aqueous layer was extracted twice with dichloromethane (10 mL) and the combined organic phase was dried over Na$_2$SO$_4$. After evaporation of the solvents, the residue was purified by silica gel chromatography (hexane/ACOEt = 10:1) to afford the product 5a in 52% yield.
To two separate pressure tubes were charged with \( p \)-toluidine (0.5 mmol, 1.0 equiv) or \( p \)-Toluidine-\( d_2 \) (0.5 mmol, 1.0 equiv), alkyne ester (1.1 mmol, 2.2 equiv.), then the Cu(OTf)\(_2\) (0.05 mmol), CH\(_3\)CN (2 mL) and HOTf (0.05 mmol) were added. The mixture was stirred at 120 °C for 10 hours. Next, the two reaction mixtures were combined, then diluted with 30 mL of dichloromethane and washed with 10 mL of H\(_2\)O. The aqueous layer was extracted twice with dichloromethane (10 mL) and the combined organic phase was dried over Na\(_2\)SO\(_4\). After evaporation of the solvents, the residue was purified by silica gel chromatography (hexane/AcOEt = 7:1) to afford quinoline (217.6 mg, 84% yield).
To two separate pressure tubes were charged with *p*-toluidine (0.5 mmol, 1.0 equiv) or *p*-Toluidine-*d*₂ (0.5 mmol, 1.0 equiv), alkyne (0.5 mmol, 1.0 equiv), and ketone (1.2 mmol), then the Cu(OTf)₂ (0.05 mmol), CH₃CN (2 mL) and HOTf (0.05 mmol) were added. The mixture was stirred at 120 °C for 10 hours. Next, the two reaction mixtures were combined, then diluted with 30 mL of dichloromethane and washed with 10 mL of H₂O. The aqueous layer was extracted twice with dichloromethane (10 mL) and the combined organic phase was dried over Na₂SO₄. After evaporation of the solvents, the residue was purified by silica gel chromatography (hexane/AcOEt = 3:1) to afford quinoline (202.9 mg, 73% yield).
The experimental investigation for the Reaction Mechanism

For the synthesis of the enamine 6 from the procedure (a):
A sealed tube (30 mL) was charged with aniline (1a, 1.0 mmol), and dimethyl acetylenedicarboxylate (2a, 1.0 mmol) in CH$_3$CN (2 mL). The mixture was stirred at room temperature for 10 minutes, then evaporated in vacuo. The obtained residue was purified by flash column chromatography using a mixture of PE and EA as the eluent to afford the enamine 6 in 96% yield: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 9.66 (s, 1H), 7.26 - 7.30 (m, 2H), 7.07 - 7.11 (t, 1H), 6.90 (d, $J$ = 8.0 Hz, 2H), 3.74 (s, 3H), 3.69 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 169.9, 164.9, 148.0, 140.3, 129.2, 124.2, 120.7, 93.6, 52.7, 51.2; HRMS (ESI-TOF) m/z calcd for C$_{12}$H$_{14}$NO$_4$ [M + H]$^+$ 236.0917, found 236.0920.

For the synthesis of 3a from the procedure (b):
A sealed tube (30 mL) was charged with the enamine (6, 1.0 mmol), alkyne ester (2a, 1.1 mmol, 1.1 equiv.), then the Cu(OTf)$_2$ (0.05 mmol), CH$_3$CN (2 mL) and HOTf (0.1 mmol) were added. The mixture was stirred at 120 °C for 24 hours, the mixture was quenched by sat. aq. NaHCO$_3$, and diluted with 20 mL dichloromethane and washed with 10 mL H$_2$O. The aqueous layer was extracted twice with dichloromethane (10 mL) and the combined organic phase was dried over Na$_2$SO$_4$. 
After evaporation of the solvents, the residue was purified by silica gel chromatography (hexane/AcOEt = 7:1) to afford the quinoline product 3a in 92% yield.

**For the synthesis of 5a from the procedure (c):**

A sealed tube (30 mL) was charged with the enamine (6, 1.0 mmol), and ketone (4a, 1.1 mmol), then the Cu(OTf)$_2$ (0.05 mmol), HOTf (0.1 mmol) and CH$_3$CN (2 mL) were added. The mixture was stirred at 100 °C for 24 hours. After the reaction finished, the mixture was quenched by sat. aq. NaHCO$_3$, and diluted with 20 mL of dichloromethane and washed with 10 mL of H$_2$O. The aqueous layer was extracted twice with dichloromethane (10 mL) and the combined organic phase was dried over Na$_2$SO$_4$. After evaporation of the solvents, the residue was purified by silica gel chromatography (hexane/AcOEt = 2:1) to afford the quinoline product 5a in 91% yield.
Characterization data for products

Quinoline-2,4-dicarboxylic acid dimethyl ester (3a):

Obtained as a yellow solid (223.0 mg, 91% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.86 (d, J = 8.4 Hz, 1H), 8.70 (s, 1H), 8.38 (d, J = 8.4 Hz, 1H), 7.84 - 7.88 (t, 1H), 7.76 - 7.80 (t, 1H), 4.12 (s, 3H), 4.08 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 166.6, 165.3, 148.6, 147.5, 136.0, 131.3, 130.6, 130.3, 126.3, 125.5, 122.3, 53.4, 52.9; HRMS (ESI-TOF) m/z Calcd. for C$_{13}$H$_{11}$NO$_4$ [M + H]$^+$ 246.0761. Found: m/z 246.0782.

6-Methyl-quinoline-2,4-dicarboxylic acid dimethyl ester (3b): Obtained as a gray solid (248.6 mg, 96% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.63 (d, J = 18.4 Hz, 2H), 8.25 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 4.10 (s, 3H), 4.07 (s, 3H), 2.62 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 166.2, 165.4, 147.3, 146.5, 141.1, 135.1, 132.9, 130.9, 126.4, 124.3, 122.4, 53.4, 52.9, 22.3; HRMS (ESI-TOF) m/z Calcd. for C$_{14}$H$_{13}$NO$_4$ [M + H]$^+$ 260.0917. Found: m/z 260.0942.

6-Methoxy-quinoline-2,4-dicarboxylic acid dimethyl ester (3c): Obtained as a light yellow solid (258.5 mg, 94% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.74 (s, 1H), 8.32 (d, J = 2.8 Hz, 1H), 8.25 (d, J = 9.6 Hz, 1H), 7.49 (dd, J = 9.2 Hz, 1H), 4.10 (s, 3H), 4.06 (s, 3H), 4.10 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 166.2, 165.5, 161.1, 145.2, 144.6, 133.2, 132.8, 128.5, 123.9, 103.0, 55.8, 53.2, 52.7; HRMS (ESI-TOF) m/z Calcd. for C$_{14}$H$_{13}$NO$_5$ [M + H]$^+$ 276.0867. Found: m/z 276.0894.

6-Fluoro-quinoline-2,4-dicarboxylic acid dimethyl ester (3d): Obtained as a light yellow solid (189.4 mg, 72% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.63 (d, J =
18.4 Hz, 2H), 8.25 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 4.10 (s, 3H), 4.07 (s, 3H), 2.62 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 165.6, 165.1, 164.3, 161.8, 146.9, 145.9, 135.1, 133.9 (d, J = 10 Hz), 127.6 (d, J = 11 Hz), 123.3, 121.2 (d, J = 26 Hz), 109.7 (d, J = 25 Hz), 53.4, 53.0; HRMS (ESI-TOF) m/z Calcd. for C$_{13}$H$_{10}$FNO$_4$ [M + H]$^+$ 264.0667. Found: m/z 264.0772.

6-Chloro-quinoline-2,4-dicarboxylic acid dimethyl ester (3e): Obtained as a light yellow solid (231.5 mg, 83% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.76 (s, 1H), 8.62 (dd, J = 10.4 Hz, 1H), 8.38 (d, d, J = 9.6, 9.2 Hz, 1H), 7.63 (m, 1H), 4.12 (s, 3H), 4.08 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 165.5, 165.0, 147.7, 147.0, 137.0, 134.9, 132.6, 131.7, 126.9, 124.7, 123.3, 53.4, 53.0; HRMS (ESI-TOF) m/z Calcd. for C$_{13}$H$_{10}$ClNO$_4$ [M + H]$^+$ 280.0371. Found: m/z 280.0381.

6-Bromo-quinoline-2,4-dicarboxylic acid dimethyl ester (3f): Obtained as a light yellow solid (274.5 mg, 85% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 9.12 (d, J = 2.4 Hz, 2H), 8.73 (s, 1H), 8.22 (d, J = 9.2 Hz, 1H), 7.93 (dd, J = 9.2, 8.8 Hz, 1H), 4.12 (s, 3H), 4.08 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 165.5, 165.0, 147.8, 147.2, 134.8, 134.9, 132.6, 128.0, 127.2, 125.6, 123.2, 53.5, 53.1; HRMS (ESI-TOF) m/z Calcd. for C$_{13}$H$_{10}$BrNO$_4$ [M + H]$^+$ 323.9866. Found: m/z 323.9880.

6-Trifluoromethyl-quinoline-2,4-dicarboxylic acid dimethyl ester (3g): Obtained as a Brownish-black solid (200.3 mg, 64% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 9.27 (s, 1H), 8.78 (s, 1H), 8.48 (d, J = 9.2 Hz, 1H), 8.01 (dd, J = 1.6, 8.8 Hz, 1H), 4.14 (s, 3H), 4.11 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 165.2, 164.8, 149.6, 149.4, 136.7, 132.3, 131.5 (q, J = 10 Hz), 126.3 (q, J = 11 Hz), 125.4 (q,
$J = 8.8 \text{ Hz}$, 125.0, 123.8 ($q, J = 9.2, 8.8 \text{ Hz}$), 123.4, 53.4, 53.0; **HRMS (ESI-TOF)**
m/z Calcd. for $\text{C}_{14}\text{H}_{10}\text{F}_{3}\text{NO}_{4} [\text{M + H}]^+$ 314.0635. Found: m/z 314.0669.

**8-Methyl-quinoline-2,4-dicarboxylic acid dimethyl ester (3h):** Obtained as a light yellow solid (230.5 mg, 89% yield);
$^1\text{H NMR (400 MHz, CDCl}_3$ $\delta$ ppm: $\delta$ 8.63 - 8.65 (m, 2H),
7.65 - 7.68 (m, 2H), 4.09 (s, 3H), 4.06 (s, 3H), 2.92 (s, 3H);
$^{13}\text{C NMR (100 MHz, CDCl}_3$ $\delta$ ppm: $\delta$ 166.4, 135.6, 147.8, 146.2, 139.3, 136.2, 130.6, 130.1, 126.3, 123.3, 121.9, 53.1, 52.8, 18.3; **HRMS (ESI-TOF)** m/z Calcd. for $\text{C}_{14}\text{H}_{13}\text{NO}_{4} [\text{M + H}]^+$ 260.0917. Found: m/z 260.0918.

**8-Fluoro-quinoline-2,4-dicarboxylic acid dimethyl ester (3i):** Obtained as a light yellow solid (178.8 mg, 68% yield);
$^1\text{H NMR (400 MHz, CDCl}_3$ $\delta$ ppm: $\delta$ 8.75 (s, 1H), 8.66 (d, $J$ = 8.8 Hz, 1H), 7.70 - 7.75 (q, 1H), 7.52 - 7.57 (t, 1H), 4.11 (s, 3H), 4.08 (s, 3H);
$^{13}\text{C NMR (100 MHz, CDCl}_3$ $\delta$ ppm: $\delta$ 165.6, 165.0, 159.7, 157.1, 147.7, 139.2 (d, $J$ = 19.7 Hz), 136.0, 130.3 (d, $J$ = 8.1 Hz), 127.5, 123.2, 121.4 (d, $J$ = 5.1 Hz), 114.6 (d, $J$ = 18.5 Hz), 53.4, 53.0; **HRMS (ESI-TOF)** m/z Calcd. for $\text{C}_{13}\text{H}_{10}\text{FNO}_{4} [\text{M + H}]^+$ 264.0667. Found: m/z 264.0668.

**8-Iodo-quinoline-2,4-dicarboxylic acid dimethyl ester (3j):**
Obtained as a yellow solid (259.7 mg, 70% yield); $^1\text{H NMR (400 MHz, CDCl}_3$ $\delta$ ppm: $\delta$ 8.85 (d, $J$ = 8.4 Hz, 1H), 8.71 (s, 1H), 8.49 (d, $J$ = 7.2 Hz, 1H), 7.43 - 7.47 (t, 1H), 4.11 (s, 3H), 4.07 (s, 3H);
$^{13}\text{C NMR (100 MHz, CDCl}_3$ $\delta$ ppm: $\delta$ 165.5, 164.9, 148.3, 147.3, 141.4, 136.9, 131.1, 127.1, 126.3, 123.1, 105.4, 53.4, 53.1; **HRMS (ESI-TOF)** m/z Calcd. for $\text{C}_{13}\text{H}_{10}\text{INO}_{4} [\text{M + H}]^+$ 371.9727. Found: m/z 371.9729.
7-Methyl-quinoline-2,4-dicarboxylic acid dimethyl ester (3k): Obtained as a light yellow solid (238.3 mg, 92% yield); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: $\delta$ 8.74 (d, $J = 8.8$ Hz, 1H), 8.63 (s, 1H), 8.15 (s, 1H), 7.60 (d, $J = 8.8$ Hz, 1H), 4.10 (s, 3H), 4.06 (s, 3H), 2.60 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: $\delta$ 166.1, 165.5, 148.9, 147.4, 141.1, 135.7, 132.7, 130.1, 125.1, 124.4, 121.5, 53.3, 52.8, 21.6; HRMS (ESI-TOF) m/z Calcd. for C$_{14}$H$_{13}$NO$_4$ [M + H]$^+$ 260.0917. Found: m/z 260.0918.

7-Fluoro-quinoline-2,4-dicarboxylic acid dimethyl ester (3l): Obtained as a white solid (181.5 mg, 69% yield); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: $\delta$ 8.86 (d, $J = 9.2$ Hz, 1H), 8.69 (s, 1H), 8.37 (d, $J = 2.0$ Hz, 1H), 7.60 (dd, $J = 9.2$, 2.0 Hz, 1H), 4.12 (s, 3H), 4.08 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: $\delta$ 165.5, 165.0, 149.0, 148.6, 136.8, 136.0, 131.2, 129.9, 127.0, 124.7, 122.5, 53.5, 53.0; HRMS (ESI-TOF) m/z Calcd. for C$_{13}$H$_{10}$FNO$_4$ [M + H]$^+$ 264.0667. Found: m/z 264.0668.

7-Trifluoromethyl-quinoline-2,4-dicarboxylic acid dimethyl ester (3m): Obtained as a light yellow solid (274.5 mg, 85% yield); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: $\delta$ 8.86 (d, $J = 9.2$ Hz, 1H), 8.69 (s, 1H), 8.37 (d, $J = 2.0$ Hz, 1H), 7.60 (dd, $J = 9.2$, 2.0 Hz, 1H), 4.12 (s, 3H), 4.08 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: $\delta$ 165.3, 164.7, 149.0, 147.6, 136.0, 132.3 (q, $J = 67$ Hz), 128.8 (q, $J = 9$ Hz), 127.7, 127.2, 125.6 (q, $J = 3$ Hz), 124.0, 122.1, 53.5, 53.1; HRMS (ESI-TOF) m/z Calcd. for C$_{14}$H$_{10}$F$_3$NO$_4$ [M + H]$^+$ 314.0635. Found: m/z 314.0636.

7-Chloro-6-methoxy-quinoline-2,4-dicarboxylic acid
**dimethyl ester (3n):** Obtained as a light yellow solid (287.4 mg, 93% yield); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm: \(8.73\) (s, 1H), \(8.45\) (s, 1H), \(7.39\) (s, 1H), \(4.10\) (s, 3H), \(4.10\) (s, 3H), \(4.06\) (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm: \(165.9, 165.2, 156.5, 145.7, 144.7, 133.1, 131.8, 129.5, 127.0, 123.2, 103.9, 56.6, 53.3, 52.8; HRMS (ESI-TOF) m/z Calcd. for C\(_{14}\)H\(_{12}\)ClNO\(_5\) [M + H]\(^+\) 310.0477. Found: m/z 310.0447.

**6,8-Dimethyl-quinoline-2,4-dicarboxylic acid dimethyl ester (3o):** Obtained as a light yellow solid (259.4 mg, 95% yield); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm: \(8.60\) (s, 1H), \(8.40\) (s, 1H), \(7.53\) (s, 1H), \(4.07\) (s, 3H), \(4.05\) (s, 3H), \(2.87\) (s, 3H), \(2.56\) (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm: \(166.5, 165.7, 146.5, 145.2, 140.7, 138.8, 135.2, 133.0, 126.4, 122.1, 121.9, 53.0, 52.7, 22.3, 18.2; HRMS (ESI-TOF) m/z Calcd. for C\(_{15}\)H\(_{15}\)NO\(_4\) [M + H]\(^+\) 274.1074. Found: m/z 274.1074.

**Quinoline-2,4-dicarboxylic acid diethyl ester (3p):** Obtained as a light red solid (237.5 mg, 87% yield); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm: \(8.82\) (d, \(J = 8.4\) Hz, 1H), \(8.65\) (s, 1H), \(8.37\) (d, \(J = 8.4\) Hz, 1H), \(7.82\) - \(7.86\) (t, 1H), \(7.73\) - \(7.78\) (t, 1H), \(4.52\) - \(4.62\) (m, 4H), \(1.48\) - \(1.53\) (m, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm: \(165.7, 164.9, 148.6, 147.9, 136.5, 131.3, 130.4, 130.1, 126.2, 125.5, 122.1, 62.5, 62.1, 14.4, 14.3; HRMS (ESI-TOF) m/z Calcd. for C\(_{15}\)H\(_{15}\)NO\(_4\) [M + H]\(^+\) 274.1074. Found: m/z 274.1074.

**4-Phenyl-quinoline-2-carboxylic acid methyl ester (5a):** Obtained as a light yellow solid (192.0 mg, 73% yield); \(^1\)H NMR (400 MHz, CDCl\(_3\))
δ ppm: 8.38 (d, J = 8.8 Hz, 1H), 8.16 (s, 1H), 7.98 (d, J = 8.8 Hz, 1H), 7.77 - 7.81 (t, 1H), 7.53 - 7.62 (m, 6H), 4.10 (s, 3H); 13C NMR (100 MHz, CDCl3) δ ppm: 166.0, 149.9, 148.2, 147.5, 137.5, 131.1, 130.1, 129.6, 128.8, 128.7, 128.7, 127.9, 125.8, 121.3, 53.2; HRMS (ESI-TOF) m/z calcd for C17H14NO2 [M + H]+ 264.1079, found 264.0985.

![Structure](image)

4-p-Tolyl-quinoline-2-carboxylic acid methyl ester (5b):

Obtained as a light yellow solid (216.1 mg, 78% yield); 1H NMR (400 MHz, CDCl3) δ ppm: 8.37 (d, J = 8.8 Hz, 1H), 8.14 (s, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.76 - 7.80 (t, 1H), 7.57 - 7.61 (t, 1H), 7.43 (d, J = 7.6 Hz, 2H), 7.35 (d, J = 7.6 Hz, 2H), 4.09 (s, 3H), 2.47 (s, 3H); 13C NMR (100 MHz, CDCl3) δ ppm: 166.1, 150.0, 149.6, 148.2, 147.4, 138.8, 134.6, 131.1, 130.0, 129.5, 129.4, 128.5, 128.0, 125.8, 121.2, 53.2, 21.3; HRMS (ESI-TOF) m/z calcd for C18H16NO2 [M + H]+ 278.1176, found 278.1177.

![Structure](image)

4-(4-Methoxy-phenyl)-quinoline-2-carboxylic acid methyl ester (5c): Obtained as a yellow solid (222.5 mg, 76% yield); 1H NMR (400 MHz, CDCl3) δ ppm: δ 8.36 (d, J = 8.4 Hz, 1H), 8.14 (s, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.97 - 7.81 (t, 1H), 7.58 - 7.62 (t, 1H), 7.49 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 4.10 (s, 3H), 3.91 (s, 3H); 13C NMR (100 MHz, CDCl3) δ ppm: δ 166.1, 160.1, 149.6, 148.2, 147.4, 131.1, 130.9, 130.0, 128.5, 127.9, 125.8, 121.2, 114.2, 55.4, 53.1; HRMS (ESI-TOF) m/z Calcd. for C18H15NO3 [M + H]+ 294.1125. Found: m/z 294.1127.
4-(4-Fluoro-phenyl)-quinoline-2-carboxylic acid methyl ester (5d): Obtained as a light yellow solid (196.7 mg, 70% yield); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: 8.38 (d, $J = 8.4$ Hz, 1H), 8.13 (s, 1H), 7.93 (d, $J = 8.4$ Hz, 1H), 7.78 - 7.82 (t, 1H), 7.60 - 7.63 (t, 1H), 7.50 - 7.53 (m, 2H), 7.23 - 7.28 (m, 2H), 4.10 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: 166.0, 163.1 (d, $J = 247.4$), 148.5 (d, $J = 68$), 147.4, 133.4 (d, $J = 3.6$), 131.4, 131.3, 131.2, 130.2, 128.8, 127.8, 125.5, 121.3, 115.8 (d, $J = 21.6$), 53.2; HRMS (ESI-TOF) m/z calcd for C$_{17}$H$_{13}$FNO$_2$ [M + H]$^+$ 282.0925, found 282.0953.

4-Pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5e):
Obtained as a gray solid (235.0 mg, 89% yield); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm: $\delta$ 8.86 (d, $J = 4.8$ Hz, 1H), 8.39 (d, $J = 8.4$ Hz, 1H), 8.33 (s, 1H), 8.24 (d, $J = 8.4$ Hz, 1H), 7.91 - 7.95 (td, 1H), 7.80 - 7.84 (m, 1H), 7.64 - 7.71 (m, 2H), 7.44 - 7.47 (m, 1H), 4.11 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm: $\delta$ 165.8, 156.1, 149.8, 148.4, 147.5, 137.0, 131.0, 130.2, 129.1, 127.1, 125.6, 124.9, 123.4, 121.3, 53.2; HRMS (ESI-TOF) m/z Calcd. for C$_{16}$H$_{12}$N$_2$O$_2$ [M + H]$^+$ 265.0972. Found: m/z 265.0969.

6-Methyl-4-pyridin-2-yl-quinoline-2-carboxylic acid
methyl ester (5f): Obtained as a light yellow solid (269.7 mg, 97% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.85 (d, J = 4.0 Hz, 1H), 8.28 (d, J = 9.6 Hz, 1H), 8.27 (s, 1H), 7.90 - 7.95 (m, 2H), 7.63 - 7.68 (m, 2H), 7.43 - 7.46 (m, 1H), 4.09 (s, 3H), 2.53 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 165.9, 156.4, 149.8, 146.6, 146.5, 139.6, 137.0, 132.6, 132.4, 130.8, 127.2, 124.9, 124.3, 123.3, 121.5, 53.1, 22.1; HRMS (ESI-TOF) m/z Calcd. for C$_{17}$H$_{14}$N$_2$O$_2$ [M + H]$^+$ 279.1128. Found: m/z 279.1125.

![Image](image_url)

6-Methoxy-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5g): Obtained as a light yellow solid (273.4 mg, 93% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.85 (d, J = 4.0 Hz, 1H), 8.26 - 8.28 (m, 2H), 7.91 - 7.94 (t, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.57 (s, 1H), 7.43 - 7.47 (m, 2H), 4.08 (s, 3H), 3.86 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 165.9, 159.9, 156.6, 149.7, 145.4, 144.9, 144.6, 137.1, 132.5, 128.5, 124.7, 123.3, 123.0, 121.9, 103.3, 55.4, 53.0; HRMS (ESI-TOF) m/z Calcd. for C$_{17}$H$_{14}$N$_2$O$_3$ [M + H]$^+$ 295.1083. Found: m/z 295.1075.

![Image](image_url)

6-Fluoro-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5h): Obtained as a light yellow solid (203.0 mg, 72% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.86 (d, J = 4.8 Hz, 1H), 8.37 - 8.41 (m, 1H), 8.34 (s, 1H), 7.92 - 7.97 (m, 2H), 7.70 (d, J = 7.6 Hz, 1H), 7.57 - 7.61 (m, 1H), 7.45 - 7.48 (m, 2H), 4.10 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 165.6, 160.9, 155.8, 149.9, 146.9 (d, J = 2.9 Hz), 146.7 (d, J = 6.0 Hz), 145.6, 137.2, 133.7 (d, J = 9.4 Hz), 128.2 (d, J = 10.5 Hz), 124.7, 123.6, 121.9, 120.7 (d, J = 26.1 Hz), 109.4 (d, J = 23.8 Hz), 53.0; HRMS (ESI-TOF) m/z Calcd. for C$_{17}$H$_{14}$F$_2$N$_2$O$_2$ [M + H]$^+$ 299.0798. Found: m/z 299.0792.
53.2; **HRMS (ESI-TOF)** m/z Calcd. for C_{16}H_{11}FN_{2}O_{2} [M + H]^+ 283.0883. Found: m/z 283.0876.

![Image of 6-Chloro-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester](image)

6-Chloro-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5i): Obtained as a light gray solid (223.5 mg, 75% yield); **^1H NMR (400 MHz, CDCl₃)** δ ppm: δ 8.87 (d, J = 4.0 Hz, 1H), 8.28 - 8.33 (m, 3H), 7.92 - 7.96 (t, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.46 - 7.49 (m, 1H), 4.10 (s, 3H); **^13C NMR (100 MHz, CDCl₃)** δ ppm: δ 165.5, 155.6, 149.9, 147.6, 146.8, 146.5, 137.2, 135.4, 132.5, 131.3, 127.7, 124.79, 124.76, 123.6, 122.1, 53.3; **HRMS (ESI-TOF)** m/z Calcd. for C_{16}H_{11}ClN_{2}O_{2} [M + H]^+ 299.0582. Found: m/z 299.0579.

![Image of 6-Bromo-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester](image)

6-Bromo-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5j): Obtained as a gray solid (266.7 mg, 78% yield); **^1H NMR (400 MHz, CDCl₃)** δ ppm: δ 8.86 (d, J = 4.0 Hz, 1H), 8.45 (s, 1H), 8.32 (s, 1H), 8.24 (d, J = 9.2 Hz, 1H), 7.92 - 7.96 (t, 1H), 7.88 (d, J = 9.2 Hz, 1H), 7.69 (d, J = 7.6 Hz, 1H), 7.46 - 7.49 (t, 1H), 4.11 (s, 3H); **^13C NMR (100 MHz, CDCl₃)** δ ppm: δ 165.5, 155.6, 150.0, 147.8, 147.0, 146.5, 137.3, 133.9, 132.6, 128.2, 128.1, 124.8, 123.9, 123.7, 122.1, 53.3; **HRMS (ESI-TOF)** m/z Calcd. for C_{16}H_{11}BrN_{2}O_{2} [M + H]^+ 343.0077. Found: m/z 343.0076.

![Image of 6-Methylsulfanyl-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester](image)

6-Methylsulfanyl-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5k): Obtained as a gray solid (228.7 mg, 75% yield); **^1H NMR (400 MHz, CDCl₃)** δ ppm: δ 8.91 (d, J = 4.0 Hz, 1H), 8.51 (d, J = 9.2 Hz, 1H), 8.34 (s, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.73 (t, 1H), 7.69 - 7.72 (m, 1H), 4.11 (s, 3H); **^13C NMR (100 MHz, CDCl₃)** δ ppm: δ 165.5, 155.6, 149.9, 147.6, 146.8, 146.5, 137.2, 135.4, 132.5, 131.3, 127.7, 124.79, 124.76, 123.6, 122.1, 53.3; **HRMS (ESI-TOF)** m/z Calcd. for C_{16}H_{11}SBrN_{2}O_{2} [M + H]^+ 359.9577. Found: m/z 359.9576.
**acid methyl ester (5k):** Obtained as a yellow solid (285.2 mg, 92% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.85 (d, J = 4.8 Hz, 1H), 8.29 (s, 1H), 8.24 (d, J = 9.2 Hz, 1H), 8.00 (s, 1H), 7.91 - 7.94 (t, 1H), 7.65 - 7.71 (m, 2H), 7.43 - 7.46 (m, 1H), 4.09 (s, 3H), 2.51 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 165.7, 156.1, 149.7, 146.5, 146.2, 145.4, 141.3, 137.0, 130.9, 129.2, 127.4, 123.4, 122.0, 119.6, 53.1, 15.1; HRMS (ESI-TOF) m/z Calcd. for C$_{17}$H$_{14}$N$_2$O$_2$S [M + H]$^+$ 311.0849. Found: m/z 311.0848.

![Image: 5k](attachment:image.png)

**7-Methyl-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5l):** Obtained as a dark red solid (261.3 mg, 94% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.81 (d, J = 2.8 Hz, 1H), 8.25 (s, 1H), 8.15 (s, 1H), 8.10 (d, J = 8.4 Hz, 1H), 7.85 - 7.88 (t, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.39 - 7.41 (t, 1H), 4.08 (s, 3H), 2.56 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 165.8, 156.2, 149.8, 148.6, 147.3, 147.1, 140.5, 136.9, 131.4, 129.9, 125.19, 125.14, 124.8, 123.3, 120.6, 53.0, 21.6; HRMS (ESI-TOF) m/z Calcd. for C$_{17}$H$_{14}$N$_2$O$_2$ [M + H]$^+$ 279.1128. Found: m/z 279.1126.

![Image: 5l](attachment:image.png)

**7-Methoxy-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5m):** Obtained as a yellow solid (267.5 mg, 91% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.84 (d, J = 4.4 Hz, 1H), 8.20 (s, 1H), 8.13 (d, J = 9.2 Hz, 1H), 7.89 - 7.93 (t, 1H), 7.69 (s, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.42 - 7.45 (t, 1H), 7.30 (d, J = 9.2 Hz, 1H), 4.10 (s, 3H), 3.98 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 166.0, 161.1, 156.4, 150.5, 149.8, 147.7, 147.2, 137.0, 126.7, 124.9, 123.4, 122.6, 122.5, 119.6, 108.5, 55.7, 53.2; HRMS (ESI-TOF) m/z Calcd. for C$_{17}$H$_{14}$N$_2$O$_3$ [M +
8-Methyl-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5n): Obtained as a light yellow solid (250.1 mg, 90% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 8.84 (d, J = 4.4 Hz, 1H), 8.28 (s, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.88 - 7.92 (t, 1H), 7.66 (d, J = 7.2 Hz, 2H), 7.51 - 7.55 (t, 1H), 7.42 - 7.45 (t, 1H), 4.07 (s, 3H), 2.95 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 166.1, 156.3, 149.8, 147.6, 147.5, 146.3, 139.1, 136.8, 130.3, 128.8, 127.2, 125.0, 123.4, 123.2, 121.2, 52.9, 18.3; HRMS (ESI-TOF) m/z Calcd. for C$_{17}$H$_{14}$N$_2$O$_2$ [M + H]$^+$ 279.1128. Found: m/z 279.1128.

7-Chloro-6-methoxy-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5o): Obtained as a yellow solid (275.5 mg, 84% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 8.85 (d, J = 4.4 Hz, 1H), 8.42 (s, 1H), 8.28 (s, 1H), 7.93 - 7.97 (t, 1H), 7.71 - 7.74 (m, 2H), 7.45 - 7.48 (m, 1H), 4.09 (s, 3H), 3.95 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: 165.7, 164.6, 162.1, 150.0, 149.9, 148.7, 136.1, 128.1, 128.0, 123.4, 121.7, 120.9, 120.7, 114.7, 114.5, 53.4, 53.0; HRMS (ESI-TOF) m/z Calcd. for C$_{17}$H$_{13}$ClN$_2$O$_3$ [M + H]$^+$ 329.0687. Found: m/z 329.0664.

6-Morpholin-4-yl-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5p): Obtained as a yellow solid (293.2 mg, 84% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: 8.84 (d, J = 4.4 Hz, 1H), 8.23 - 8.25 (t, 2H), 7.90 - 7.94 (t, 1H), 7.69 (d, J = 7.6 Hz, 1H), 7.54 - 7.56 (m, 1H), 7.41 - 7.47
(m, 2H), 4.07 (s, 3H), 3.85 - 3.87 (t, 2H), 3.27 - 3.29 (t, 2H); 13C NMR (100 MHz, CDCl3) δ ppm: δ 166.0, 156.8, 150.9, 149.6, 144.8, 144.1, 143.9, 137.0, 131.9, 128.6, 124.6, 123.2, 122.1, 121.9, 105.5, 66.5, 52.9, 48.3; HRMS (ESI-TOF) m/z Calcd. for C20H19N3O3 [M + H]+ 350.1499. Found: m/z 350.1496.

6,8-Dimethyl-4-pyridin-2-yl-quinoline-2-carboxylic acid methyl ester (5q): Obtained as a light yellow solid (265.7 mg, 91% yield); 1H NMR (400 MHz, CDCl3) δ ppm: δ 8.84 (d, J = 4.8 Hz, 1H), 8.23 (s, 1H), 7.88 - 7.92 (t, 1H), 7.73 (s, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.50 (s, 1H), 7.41 - 7.44 (t, 1H), 4.16 (s, 3H), 2.91 (s, 3H), 2.47 (s, 3H); 13C NMR (100 MHz, CDCl3) δ ppm: δ 166.2, 156.9, 149.8, 146.7, 146.3, 145.4, 139.1, 138.6, 136.8, 132.7, 127.3, 124.9, 123.1, 122.1, 121.3, 52.9, 22.1, 18.2; HRMS (ESI-TOF) m/z Calcd. for C18H16N2O2 [M + H]+ 293.1285. Found: m/z 293.1288.

4-(6-Bromo-pyridin-2-yl)-quinoline-2-carboxylic acid methyl ester (5r): Obtained as a light yellow solid (301.0 mg, 88% yield); 1H NMR (400 MHz, CDCl3) δ ppm: δ 8.39 (d, J = 8.4 Hz, 1H), 8.31 (s, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.76 - 7.85 (m, 2H), 7.64 - 7.71 (m, 3H), 4.11 (s, 3H); 13C NMR (100 MHz, CDCl3) δ ppm: δ 165.6, 156.8, 148.3, 147.4, 145.5, 142.1, 139.2, 131.1, 130.3, 129.4, 127.9, 126.7, 125.2, 123.7, 121.4, 53.2; HRMS (ESI-TOF) m/z Calcd. for C16H11BrN2O2 [M + H]+ 343.0077. Found: m/z 343.0077.
4-Pyridin-2-yl-quinoline-2-carboxylic acid ethyl ester (5s):
Obtained as a light yellow solid (241.9 mg, 87% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.85 (d, J = 4.4 Hz, 1H), 8.40 (d, J = 8.4 Hz, 1H), 8.30 (s, 1H), 8.21 (d, J = 8.4 Hz, 1H), 7.90 - 7.94 (t, 1H), 7.79 - 7.83 (t, 1H), 7.63 - 7.70 (m, 2H), 7.43 - 7.46 (m, 1H), 4.55 - 4.61 (q, 2H), 1.48 - 1.52 (t, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 165.3, 156.2, 149.9, 148.4, 147.9, 147.4, 136.9, 131.2, 130.0, 129.0, 127.1, 125.6, 124.9, 123.3, 121.3, 62.2, 14.4; HRMS (ESI-TOF) m/z Calcd. for C$_{17}$H$_{14}$N$_2$O$_2$ [M + H]$^+$ 279.1128. Found: m/z 279.1114.

7,8,9,10-Tetrahydro-phenanthridine-6-carboxylic acid methyl ester (5t): Obtained as a red solid (209.7 mg, 87% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.15 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.66 - 7.70 (t, 1H), 7.58 - 7.62 (t, 1H), 4.10 (s, 3H), 3.18 - 3.19 (t, 2H), 3.04 - 3.07 (t, 2H), 1.95 - 1.98 (m, 2H), 1.85 - 1.90 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 167.4, 150.4, 144.8, 143.5, 130.4, 128.7, 128.2, 128.1, 127.7, 127.4, 52.7, 26.5, 25.6, 22.1, 21.8; HRMS (ESI-TOF) m/z Calcd. for C$_{15}$H$_{15}$NO$_2$ [M + H]$^+$ 242.1176. Found: m/z 242.1175.

2-Methyl-7,8,9,10-tetrahydro-phenanthridine-6-carboxylic acid methyl ester (5u): Obtained as a light yellow solid (232.1 mg, 91% yield); $^1$H NMR (400 MHz, CDCl$_3$) δ ppm: δ 8.03 (d, J = 8.4 Hz, 1H), 7.70 (s, 1H), 7.50 (d, J = 8.4 Hz, 1H), 4.02 (s, 3H), 3.12 - 3.15 (t, 2H), 3.03 - 3.06 (t, 2H), 2.55 (s, 3H), 1.92 - 1.98 (m, 2H), 1.83 - 1.88 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm: δ 167.5149.3, 149.3, 146.4, 130.4, 128.7, 128.2, 128.1, 127.7, 127.4, 52.7, 26.5, 25.6, 22.1, 21.8; HRMS (ESI-TOF) m/z Calcd. for C$_{15}$H$_{15}$NO$_2$ [M + H]$^+$ 242.1175. Found: m/z 242.1175.
2,3-Dihydro-1H-cyclopenta[c]quinoline-4-carboxylic acid methyl ester (5w): Obtained as a light yellow solid (186.1 mg, 82% yield); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm: \(\delta\) 7.43 - 7.53 (m, 2H), 7.23 (d, J = 7.2 Hz, 2H), 7.13 (t, 1H), 3.91 (s, 3H), 3.08 - 3.11 (t, 2H), 2.48 - 2.52 (t, 2H), 1.99 - 2.07 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm: \(\delta\) 165.7, 163.4, 152.0, 138.8, 138.5, 129.6, 129.0, 127.0, 120.2, 117.3, 52.5, 33.1, 31.1, 22.2; HRMS (ESI-TOF) m/z Calcd. for C\(_{14}\)H\(_{13}\)NO\(_2\) [M + H] \(^+\) 228.1019. Found: m/z 228.0978.

2-Trifluoromethyl-7,8,9,10-tetrahydro-phenanthridine-6-carboxylic acid methyl ester (5v): Obtained as a yellow solid (234.8 mg, 76% yield); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm: \(\delta\) 8.26 - 8.28 (m, 2H), 7.84 - 7.87 (dd, J = 8.8, 1.6 Hz, 1H), 4.05 (s, 3H), 3.21 - 3.24 (t, 2H), 3.04 - 3.07 (t, 2H), 1.98 - 2.04 (m, 2H), 1.87 - 1.93 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm: \(\delta\) 166.9, 152.6, 145.9, 144.7, 131.5, 129.2 (q), 127.2 (q), 125.4, 124.3 (q), 122.7, 120.6 (q), 52.8, 26.3, 25.6, 21.9, 21.5; HRMS (ESI-TOF) m/z Calcd. for C\(_{16}\)H\(_{17}\)NO\(_2\) [M + H] \(^+\) 256.1332. Found: m/z 256.1332.
Copies of $^1$H and $^{13}$C NMR spectra of products

Product 3a

$^{13}$C NMR

$^1$H NMR
Product 3c
Product 3e
Product 3f

The image contains two chemical structures labeled as Product 3f. The first structure is a chemical compound with a bromine (Br) atom and a methyl (COOCH₃) group attached. The second structure is similar but without the bromine atom. The images also show corresponding NMR spectra, indicating the chemical shifts and multiplicities for each atom.
Product 3g
Product 3h

\[ \text{COOCH}_3 \]

\[ 3h \]

\[ \text{COOCH}_3 \]
Product 3i

\[
\text{F} \quad \text{COOCH}_3 \\
\text{3i} \quad \text{COOCH}_3
\]
Product 3j

\[ \text{I} \quad \text{COOCH}_3 \]

\[ \text{3j} \quad \text{COOCH}_3 \]

\[ \text{I} \quad \text{COOCH}_3 \]

\[ \text{3j} \quad \text{COOCH}_3 \]

\[ \text{106.36} \quad \text{71.35} \quad \text{53.36} \]

\[ \text{108.90} \quad \text{121.40} \quad \text{124.04} \]

\[ \text{122.42} \quad \text{124.26} \quad \text{127.06} \]

\[ \text{1.10} \quad \text{1.10} \quad \text{1.10} \]
Product 3k
Product 3l

[Chemical structure of 3l]

**$^{1}H$ NMR (CDCl$_3$):**
- δ 10.35 (s, 1H)
- δ 1.89 (s, 3H)
- δ 1.40 (s, 3H)
- δ 1.33 (s, 3H)
- δ 1.20 (s, 3H)
- δ 1.16 (s, 3H)
- δ 0.76 (s, 3H)
- δ 0.04 (s, 3H)

**$^{13}C$ NMR (CDCl$_3$):**
- δ 162.98 (s)
- δ 148.57 (d)
- δ 118.55 (d)
- δ 118.29 (d)
- δ 113.58 (d)
- δ 113.36 (d)
- δ 112.46 (d)
- δ 53.40 (s)
- δ 53.02 (s)
Product 3m
Product 3o

![Chemical structure and spectrum diagram for Product 3o. The diagram shows the chemical structure of 3o with COOH3 groups and two separate spectra, one with δ values ranging from 9.5 to 0.0 ppm and the other with δ values ranging from 210 to 0 ppm. The spectrum details include various δ values such as 8.403, 3.004, 3.039, -2.858, etc.]
Product 3p
Product 5a
Product 5b

[Chemical structures and spectra]
Product 5d

5d

COOCH₃

F

5d

COOCH₃

F
Product 5e

![NMR Spectrum of Product 5e](image)

- COOCH₃
- Structure 5e

![NMR Spectrum of Product 5e](image)
Product 5f

$\text{COOCH}_3$

5f

$\text{COOCH}_3$

5f
Product 5g

\[
\text{5g}
\]

\[
\text{5g}
\]
Product 5h

\[
\begin{align*}
\text{COOCH}_3 \\
\text{F} \\
\text{5h}
\end{align*}
\]
Product 5j

\[
\text{Br} \quad \begin{array}{c}
\text{COOCH}_3 \\
\text{N}
\end{array} \quad \text{5j}
\]

\[
\text{Br} \quad \begin{array}{c}
\text{COOCH}_3 \\
\text{N}
\end{array} \quad \text{5j}
\]
Product 5k

[Chemical structure and spectra images]

51
Product 5l
Product 5m

\[
\begin{align*}
\text{Product } & 5m \\
\text{Structure:} & \\
\text{Chemical Shifts:} & \\
\text{NMR Spectrum:} & 
\end{align*}
\]
Product 5p

![Chemical Structure of 5p](image)

**1H NMR**

![NMR Spectrum of 5p](image)

**13C NMR**

![NMR Spectrum of 5p](image)
Product 5q
Product 5r

\[
\text{COOCH}_3 \quad 5r \quad \text{Br}
\]
Product 5s

\[
\begin{align*}
\text{COOEt} \\
5s
\end{align*}
\]
Product 5t

5t

\[
\begin{align*}
\text{COOCH}_3
\end{align*}
\]
Product 5u

[Chemical structure and spectra images]
Product 5v
Product 5w