Synthesis of 2-trifluoromethylquinolines via copper-mediated intramolecular oxidative cyclization of $N$-(2-alkenylaryl) enamines

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Supporting Information

1. $^1$H and $^{13}$C NMR data of compounds 2-4. (P2-9)
2. $^1$H and $^{13}$C NMR spectra of compounds 2-4. (P10-47)
General procedure for copper-catalyze intramolecular oxidative cyclization of N-(2-alkenylaryl)enamines (1a-r): To a 25 mL tube containing a magnetic stir bar, was added N-(2-alkenylaryl) enamine 1 (0.2 mmol), CuCl₂ (10 mol%), and DMAc (2 mL). The resulting mixture was stirred at 60 °C in air for overnight (monitored by TLC). After being cooling to room temperature, evaporation of the solvent under reduced pressure followed purification by silica gel chromatography using petroleum ether/ethyl acetate (10:1) as eluent to provide the desired products 2 or 3a.

Ethyl 4-(2-butoxy-2-oxoethyl)-2-(trifluoromethyl)quinoline-3-carboxylate (2a):
Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a yellow solid (61.0 mg, 80% yield), mp: 62-64 °C. ¹H NMR (400 MHz, CDCl₃) δ 0.77 (t, J = 7.4 Hz, 3H), 1.13-1.22 (m, 2H), 1.35 (t, J = 7.2 Hz, 3H), 1.43-1.50 (m, 2H), 4.02 (t, J = 6.6 Hz, 2H), 4.16 (s, 2H), 4.41 (q, J = 7.2 Hz, 2H), 7.69 (t, J = 7.6 Hz, 1H), 7.81 (t, J = 7.6 Hz, 1H), 8.03 (d, J = 8.2 Hz, 1H), 8.18 (d, J = 8.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 13.5, 13.8, 18.9, 30.4, 35.1, 62.6, 65.5, 121.2 (q, ¹J_C-F = 275.1 Hz), 124.2, 125.2, 127.4, 129.7, 130.8, 131.4, 140.8 143.7 (q, ²J_C-F = 34.1 Hz), 146.3, 166.1, 168.8; HRMS (ESI): m/z [M + H]⁺ calcld for C₁₉H₂₁F₃NO₄: 384.1417, Found: 384.1411

Ethyl 4-(2-(tert-butoxy)-2-oxoethyl)-2-(trifluoromethyl)quinoline-3-carboxylate (2b):
Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a yellow solid (66.0 mg, 86% yield), mp: 70-72 °C; ¹H NMR (400 MHz, CDCl₃) δ 1.29 (s, 9H), 1.33 (t, J = 7.2 Hz, 3H), 4.05 (s, 2H), 4.39 (q, J = 7.2 Hz, 2H), 7.64 (t, J = 8.0 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 8.10 (d, J = 8.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 13.9, 27.8, 36.4, 62.5, 82.3, 121.2 (q, ¹J_C-F = 274.6 Hz), 124.3, 125.2, 127.6, 129.6, 130.8, 131.3, 141.3, 143.5 (q, ²J_C-F = 33.8 Hz), 146.4, 166.2, 167.8; HRMS
(ESI): \( m/z [M + Na]^+ \) calcd for C_{19}H_{20}F_{3}NaO_{4}: 406.1237, Found: 406.1275.

Ethyl 4-(2-ethoxy-2-oxoethyl)-2-(trifluoromethyl)quinoline-3-carboxylate (2c):
Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a yellow solid (55.2 mg, 77% yield), mp: 62-64 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 1.21 (t, \( J = 7.2 \) Hz, 3H), 1.42 (t, \( J = 7.2 \) Hz, 3H), 4.16 (q, \( J = 7.2 \) Hz, 2H), 4.23 (s, 2H), 4.49 (q, \( J = 7.2 \) Hz, 2H), 7.76 (t, \( J = 7.6 \) Hz, 1H), 7.87 (t, \( J = 7.6 \) Hz, 1H), 8.09 (d, \( J = 8.0 \) Hz, 1H), 8.24 (d, \( J = 8.0 \) Hz, 1H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 13.9, 14.0, 35.2, 61.7, 62.7, 121.2 (q, \( ^1J_{C-F} = 275.0 \) Hz), 124.2, 125.2, 127.5, 129.8, 130.9, 131.4, 140.74, 143.9 (q, \( ^2J_{C-F} = 34.2 \) Hz), 146.4, 166.1, 168.7; HRMS (ESI): \( m/z \) [M + Na]\(^+\) calcd for C_{17}H_{16}F_{3}NaO_{4}: 378.0924, Found: 378.0888.

Ethyl 4-(2-methoxy-2-oxoethyl)-2-(trifluoromethyl)quinoline-3-carboxylate (2d):
Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a yellow solid (48.4 mg, 71% yield), mp: 82-84 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 1.42 (t, \( J = 7.2 \) Hz, 3H), 3.70 (s, 3H), 4.24 (s, 2H), 4.48 (q, \( J = 7.2 \) Hz, 2H), 7.77 (t, \( J = 7.6 \) Hz, 1H), 7.88 (t, \( J = 7.6 \) Hz, 1H), 8.08 (d, \( J = 8.0 \) Hz, 1H), 8.25 (d, \( J = 8.4 \) Hz, 1H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 13.8, 34.9, 52.6, 62.7, 121.2 (q, \( ^1J_{C-F} = 274.7 \) Hz), 124.2, 125.3, 127.5, 129.9, 131.0, 131.5, 140.5, 143.9 (q, \( ^2J_{C-F} = 34.1 \) Hz), 146.5, 166.1, 169.2; HRMS (ESI): \( m/z \) [M + Na]\(^+\) calcd for C_{17}H_{16}F_{3}NaO_{4}: 364.0767, Found: 364.0730.

Ethyl 4-(2-butoxy-2-oxoethyl)-6-methyl-2-(trifluoromethyl)quinoline-3-carboxylate (2e):
Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a yellow solid (67.5 mg, 85% yield), mp: 74-76 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 0.85 (t, \( J = 7.2 \) Hz, 3H), 1.21-1.30 (m, 2H), 1.41 (t, \( J = 7.0 \) Hz, 3H), 1.51-1.58 (m, 2H), 2.59 (s, 3H), 4.10 (t, \( J = 7.2 \) Hz, 2H), 7.67 (t, \( J = 7.6 \) Hz, 1H), 7.88 (t, \( J = 7.6 \) Hz, 1H), 8.08 (d, \( J = 8.0 \) Hz, 1H), 8.25 (d, \( J = 8.4 \) Hz, 1H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 13.8, 34.9, 52.6, 62.7, 121.2 (q, \( ^1J_{C-F} = 274.7 \) Hz), 124.2, 125.3, 127.5, 129.9, 131.0, 131.5, 140.5, 143.9 (q, \( ^2J_{C-F} = 34.1 \) Hz), 146.5, 166.1, 169.2; HRMS (ESI): \( m/z \) [M + Na]\(^+\) calcd for C_{18}H_{14}F_{3}NaO_{4}: 380.0924, Found: 380.0888.
Ethyl 4-(2-(tert-butoxy)-2-oxoethyl)-6-methyl-2-(trifluoromethyl)quinoline-3-carboxylate (2f): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a yellow solid (64.3 mg, 81% yield), mp: 68-70 °C; 1H NMR (400 MHz, CDCl₃) δ 1.40 (s, 9H), 1.41 (t, J = 7.2 Hz, 3H), 2.60 (s, 3H), 4.11 (s, 3H), 4.02 (s, 2H), 4.48 (q, J = 7.2 Hz, 2H), 7.68 (d, J = 8.4 Hz, 1H), 7.83 (s, 1H), 8.11 (d, J = 8.4 Hz, 2H); 13C NMR (100 MHz, CDCl₃) δ 13.9, 22.2, 27.9, 36.4, 62.5, 82.2, 121.3 (q, J = 273.5 Hz), 123.2, 125.2, 127.6, 130.5, 133.6, 140.1, 140.3, 142.9 (q, J = 34.3 Hz), 145.0, 166.4, 168.0; HRMS (ESI): m/z [M + H]⁺ calcd for C₂₀H₂₄F₃NO₄: 398.1574, Found: 398.1577.

Ethyl 4-(2-methoxy-2-oxoethyl)-6-methyl-2-(trifluoromethyl)quinoline-3-carboxylate (2g): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a yellow solid (64.6 mg, 95% yield), mp: 127-129 °C; 1H NMR (400 MHz, CDCl₃) δ 1.41 (t, J = 7.0 Hz, 3H), 2.60 (s, 3H), 3.70 (s, 3H), 4.20 (s, 2H), 4.41 (q, J = 7.2 Hz, 2H), 7.68 (d, J = 8.2 Hz, 1H), 7.80 (s, 1H), 8.11 (d, J = 8.2 Hz, 1H); 13C NMR (100 MHz, CDCl₃) δ 13.8, 22.2, 34.8, 52.6, 62.6, 121.3 (q, J = 274.3 Hz), 125.4, 127.5, 130.6, 133.8, 139.6, 140.4, 142.9 (q, J = 34.0 Hz), 145.1, 166.3, 169.3; HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₇H₁₆F₃NNaO₄: 378.0929, Found: 378.0920.

Ethyl 6-bromo-4-(2-butoxy-2-oxoethyl)-2-(trifluoromethyl)quinoline-3-carboxylate
(2i): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a white solid (67.5 mg, 73% yield), mp: 84-86 °C; ¹H NMR (400 MHz, CDCl₃) δ 0.87 (t, J = 8.0 Hz, 3H), 1.23-1.31 (m, 2H), 1.42 (t, J = 7.2, 3H), 1.53-1.60 (m, 2H), 4.12 (t, J = 6.6 Hz, 2H), 4.17 (s, 2H), 4.48 (q, J = 7.2 Hz, 2H), 7.92 (d, J = 8.8 Hz, 1H), 8.10 (d, J = 8.8 Hz, 1H), 8.25 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 12.5, 12.8, 18.0, 29.4, 34.2, 61.8, 64.7, 120.0 (q, J C-F = 274.2 Hz), 123.5, 125.1, 125.8, 127.7, 131.4, 134.0, 138.9, 143.2 (q, J C-F = 35.1 Hz), 144.0, 166.7, 167.3; HRMS (ESI): m/z [M + H]⁺ calcd for C₁₉H₂₀BrF₃NO₄: 462.0522, Found: 462.0526.

Ethyl 4-(2-butoxy-2-oxoethyl)-6-chloro-2-(trifluoromethyl)quinoline-3-carboxylate (2j): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a yellow solid (66.7 mg, 80% yield), mp: 86-84 °C; ¹H NMR (400 MHz, CDCl₃) δ 0.78 (t, J = 7.2 Hz, 3H), 1.17-1.23 (m, 2H), 1.33 (t, J = 7.0 Hz, 2H), 1.47-1.50 (m, 2H), 4.03 (t, J = 6.4 Hz, 3H), 4.08 (s, 2H), 4.41 (q, J = 7.0 Hz, 2H), 7.71 (d, J = 8.8 Hz, 1H), 7.99 (s, 1H), 8.09 (d, J = 8.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 13.6, 13.9, 19.0, 30.4, 35.2, 62.9, 65.7, 121.0 (q, J C-F = 274.2 Hz), 123.4, 126.0, 128.3, 132.4, 132.5, 136.2, 140.0, 144.09 (q, J C-F = 33.4 Hz), 144.8, 165.8, 168.4; HRMS (ESI): m/z [M + H]⁺ calcd for C₁₉H₂₀ClF₃NO₄: 418.1027, Found: 418.1028.

Ethyl 4-(2-butoxy-2-oxoethyl)-6-fluoro-2-(trifluoromethyl)quinoline-3-carboxylate (2k): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a white solid (58.5 mg, 73% yield), mp: 77-79 °C; ¹H NMR (400 MHz, CDCl₃) δ 0.77 (t, J = 7.4 Hz, 3H), 1.14-1.23 (m, 2H), 1.33 (t, J = 7.2 Hz, 3H), 1.46-1.51 (m, 2H), 4.02 (t, J = 6.8 Hz, 2H), 4.40 (q, J = 7.2 Hz, 2H), 7.53-7.57 (m, 1H), 7.61 (d, J = 7.2 Hz, 1H), 8.16 (dd, J = 5.6, 9.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 13.4, 13.8, 18.9, 30.4, 35.3, 62.8, 65.6, 108.2 (d, J C-F = 23.0 Hz), 121.1 (q, J C-F = 274.7 Hz), 121.9 (d, J C-F = 25.8 Hz),
125.9, 128.8 (d, $^3J_{C\text{-}F} = 10.1$ Hz), 133.7 (d, $^3J_{C\text{-}F} = 9.5$ Hz), 140.2, 143.3 (q, $^2J_{C\text{-}F} = 35.1$ Hz), 143.5, 162.5 (d, $^1J_{C\text{-}F} = 252.0$ Hz), 165.8, 168.4; HRMS (ESI): $m/z$ [M + H]$^+$ calcd for C$_{19}$H$_{20}$F$_4$NO$_4$: 402.1323, Found: 402.1334.

Ethyl 4-(2-butoxy-2-oxoethyl)-6-(trifluoromethoxy)-2-(trifluoromethyl)quinoline-3-carboxylate (2l): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a white solid (69 mg, 74% yield), mp: 74-76°C; $^1$H NMR (400 MHz, CDCl$_3$) δ 0.86 (t, $J = 7.4$ Hz, 3H), 1.21-1.31 (m, 2H), 1.42 (t, $J = 8.0$ Hz, 3H), 1.52-1.59 (m, 2H), 4.11 (t, $J = 8.0$ Hz, 2H), 4.19 (s, 2H), 4.49 (q, $J = 7.2$ Hz, 2H), 7.73 (d, $J = 9.2$ Hz, 1H), 7.91 (s, 1H), 8.31 (d, $J = 9.2$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 13.3, 13.7, 18.8, 30.4, 35.3, 62.8, 65.7, 114.7, 120.4 (q, $^1J_{C\text{-}F} = 258.0$ Hz), 120.9 (q, $^1J_{C\text{-}F} = 274.7$ Hz), 125.2, 126.2, 128.2, 133.3, 140.8, 144.4 (q, $^2J_{C\text{-}F} = 34.7$ Hz), 144.6, 149.4, 165.6, 168.2; HRMS (ESI): $m/z$ [M + H]$^+$ calcd for C$_{20}$H$_{20}$F$_6$NO$_5$: 468.1240, Found: 468.1234.

Ethyl 4-(2-butoxy-2-oxoethyl)-6-nitro-2-(trifluoromethyl)quinoline-3-carboxylate (2m): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a white solid (69.3 mg, 81% yield), mp: 80-82°C; $^1$H NMR (400 MHz, CDCl$_3$) δ 0.88 (t, $J = 7.2$ Hz, 3H), 1.26-1.33 (m, 2H), 1.44 (t, $J = 7.0$ Hz, 3H), 1.58-1.63 (m, 2H), 4.14 (t, $J = 6.4$ Hz, 2H), 4.30 (s, 2H), 4.51 (q, $J = 7.2$ Hz, 2H), 8.42 (d, $J = 8.8$ Hz, 1H), 8.63 (d, $J = 7.2$ Hz, 1H), 9.07 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 13.5, 13.8, 19.0, 30.4, 35.3, 63.1, 66.0, 120.7 (q, $^1J_{C\text{-}F} = 275.3$ Hz), 121.3, 124.7, 126.9, 127.1, 133.0, 143.4, 147.1 (q, $^2J_{C\text{-}F} = 35.1$ Hz), 147.5, 148.3, 165.1, 168.0; HRMS (ESI): $m/z$ [M + H]$^+$ calcd for C$_{19}$H$_{20}$F$_3$N$_2$O$_6$: 429.1268, Found: 429.1278.

ethyl 4-(cyanomethyl)-2-(trifluoromethyl)quinoline-3-carboxylate (2n): Isolated (Rf =
0.5, EtOAc–petroleum ether = 1:10) as a yellow solid (46.8 mg, 76% yield), mp: 117-
119 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.46 (t, \(J = 7.2\) Hz, 3H), 4.24 (s, 2H), 4.53 (q, 
\(J = 7.2\) Hz, 2H), 7.90 (t, \(J = 8.4\) Hz, 1H), 7.97 (t, \(J = 8.0\) Hz, 1H), 8.17 (d, \(J = 8.4\) Hz,
1H), 8.31 (d, \(J = 8.2\) Hz, 1H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 13.8, 17.8, 63.4, 115.1,
120.9 (q, \(^1^J_{C,F} = 274.4\) Hz), 123.2, 125.1, 126.0, 130.8, 131.5, 132.2, 136.2, 144.07 (q,
\(^2^J_{C,F} = 34.6\) Hz), 146.5, 165.5; HRMS (ESI): \(m/z [M + Na]^+\) calcd for
C\(_{15}\)H\(_{11}\)F\(_3\)N\(_2\)NaO\(_2\): 331.0665, Found: 331.0666.

Ethyl 4-(1-methoxy-1-oxopropan-2-yl)-2-(trifluoromethyl)quinoline-3-carboxylate
(3a): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a white solid, mp: 64-66
\(^\circ\)C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.45 (t, \(J = 7.2\) Hz, 3H), 4.48 (q, \(J = 7.2\) Hz, 2H),
7.74 (t, \(J = 7.2\) Hz, 1H), 7.91 (t, \(J = 7.2\) Hz, 1H), 7.97 (d, \(J = 8.0\) Hz, 1H), 8.25 (d, \(J = 8.4\) Hz,
1H), 8.69 (s, 1H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 13.9, 62.5, 121.1 (q, \(^1^J_{C,F} = 274.5\) Hz), 124.1,
127.5, 128.2, 129.5, 130.1, 132.1, 140.1, 144.7 (q, \(^2^J_{C,F} = 34.9\) Hz), 146.9, 165.5; HRMS (ESI): \(m/z [M + H]^+\) calcd for
C\(_{13}\)H\(_{11}\)F\(_3\)NO\(_4\): 270.0736, Found: 270.0755.

**General procedure for copper-catalyze intramolecular oxidative cyclization of N-(2-
alkenylaryl) enamines (1s-v):** To a 25 mL tube containing a magnetic stir bar, was
added N-(2-alkenylaryl) enamine 1 (0.2 mmol), CuI (10 mol%), and DCE (2 mL).
The resulting mixture was stirred at 60 °C in air for overnight (monitored by TLC).
After being cooling to room temperature, evaporation of the solvent under reduced
pressure followed purification by silica gel chromatography using petroleum
ether/ethyl acetate (10:1) as eluent to provide the desired products 3b-e.

Ethyl 6-methyl-2-(trifluoromethyl)quinoline-3-carboxylate (3b): Isolated (Rf = 0.5,
EtOAc–petroleum ether = 1:10) as a white solid (38.5 mg, 68% yield), mp: 49-50 °C;
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.44 (t, \(J = 6.6\) Hz, 3H), 2.59 (s, 3H), 4.47 (q, \(J = 6.8\) Hz,
Hz, 2H), 7.70 (s, 1H), 7.72 (t, \( J = 8.4 \) Hz, 1H), 8.11 (d, \( J = 8.4 \) Hz, 1H), 8.57 (s, 1H);
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 14.0, 21.8, 62.4, 121.3 (q, \( ^{1}J_{C,F} = 273.9 \) Hz), 124.0, 126.9, 127.5, 129.7, 134.8, 140.1, 143.8 (q, \( ^{2}J_{C,F} = 34.5 \) Hz), 145.5, 165.7;
HRMS (ESI): \( m/z \) [M + Na]\(^+\) calecd for C\(_{14}\)H\(_{12}\)F\(_3\)NNaO\(_2\): 306.0712; found: 306.0719.

![Structure of Ethyl 6-fluoro-2-(trifluoromethyl)quinoline-3-carboxylate (3c)](image)

Ethyl 6-fluoro-2-(trifluoromethyl)quinoline-3-carboxylate (3c): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a white solid (29.8 mg, 52% yield), mp: 78-79 °C;
\(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 1.44 (t, \( J = 7.2 \) Hz, 3H), 4.48 (q, \( J = 7.2 \) Hz, 2H), 7.59 (d, \( J = 8.0 \) Hz, 1H), 7.67 (t, \( J = 8.4 \) Hz, 1H), 8.27 (dd, \( J = 5.2, 9.2 \) Hz, 1H), 8.63 (s, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 13.9, 62.7, 111.3 (d, \( ^{1}J_{C,F} = 22.1 \) Hz), 121.0 (q, \( ^{1}J_{C,F} = 273.8 \) Hz), 122.9 (d, \( ^{2}J_{C,F} = 25.9 \) Hz), 124.9, 128.5 (d, \( ^{3}J_{C,F} = 10.7 \) Hz), 132.9 (d, \( ^{3}J_{C,F} = 9.4 \) Hz), 139.3, 144.0, 144.1 (q, \( ^{2}J_{C,F} = 35.9 \) Hz), 162.1 (d, \( ^{1}J_{C,F} = 252.3 \) Hz), 165.3; HRMS (ESI): \( m/z \) [M + Na]\(^+\) calecd for C\(_{13}\)H\(_{9}\)F\(_{4}\)NNaO\(_2\): 310.0462; found: 310.0471.

![Structure of Ethyl 6-chloro-2-(trifluoromethyl)quinoline-3-carboxylate (3d)](image)

Ethyl 6-chloro-2-(trifluoromethyl)quinoline-3-carboxylate (3d): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a white solid (34.5 mg, 57% yield), mp: 81-82 °C;
\(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 1.45 (t, \( J = 7.0 \) Hz, 3H), 4.48 (q, \( J = 7.2 \) Hz, 2H), 7.84 (d, \( J = 9.2 \) Hz, 2H), 7.95 (s, 1H), 8.19 (d, \( J = 9.2 \) Hz, 1H), 8.60 (s, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 13.9, 62.7, 121.0 (q, \( ^{1}J_{C,F} = 272.9 \) Hz), 125.0, 126.7, 128.1, 131.7, 133.4, 135.7, 139.0, 144.9 (q, \( ^{2}J_{C,F} = 35.2 \) Hz), 145.2, 165.2; HRMS (ESI): \( m/z \) [M + Na]\(^+\) calecd for C\(_{13}\)H\(_{9}\)ClF\(_{3}\)NNaO\(_2\): 326.0166; found: 326.0191.

![Structure of Ethyl 6-(trifluoromethoxy)-2-(trifluoromethyl)quinoline-3-carboxylate (3e)](image)

Ethyl 6-(trifluoromethoxy)-2-(trifluoromethyl)quinoline-3-carboxylate (3e): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a white solid (46.6 mg, 66% yield), mp: 76-77 °C; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 1.45 (t, \( J = 7.0 \) Hz, 3H), 4.49 (q, \( J = 7.2 \) Hz, 2H), 7.75 (d, \( J = 8.8 \) Hz, 1H), 7.79 (s, 1H), 8.31 (d, \( J = 9.2 \) Hz, 1H), 8.70 (s, 1H); \(^{13}\)C
NMR (100 MHz, CDCl$_3$) $\delta$ 13.9, 62.7, 117.4, 120.4 (q, $^1J_{C,F} = 258.0$ Hz), 120.9 (q, $^1J_{C,F} = 274.2$ Hz), 125.2, 126.3, 127.9, 132.6, 139.8, 145.0, 145.2 (q, $^2J_{C,F} = 35.5$ Hz), 149.1, 165.1; HRMS (ESI): $m/z$ [M + Na]$^+$ calcd for C$_{14}$H$_9$F$_6$NNaO$_3$: 376.0739, Found: 376.0769.

Ethyl 4-(2-butoxy-2-oxoethyl)-2-(trifluoromethyl)-3,4-dihydroquinoline-3-carboxylate (4a): Isolated (Rf = 0.5, EtOAc–petroleum ether = 1:10) as a yellow solid, mp: 68-70 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.88 (t, $J = 7.2$ Hz, 3H), 1.23-1.33 (m, 5H), 1.48-1.55 (m, 2H), 2.47 (dd, $J = 8.8, 14.4$ Hz, 2H), 2.61 (dd, $J = 8.8, 14.4$ Hz, 2H), 3.98 (t, $J = 6.8$ Hz, 3H), 4.25 (q, $J = 7.2$ Hz, 2H), 4.45-4.48 (m, 1H), 6.86 (d, $J = 7.6$ Hz, 1H), 7.04 (t, $J = 7.6$ Hz, 1H), 7.14-7.20 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 13.6, 13.9, 19.0, 30.5, 35.8, 41.8, 60.9, 64.4, 102.6, 115.2, 121.9 (q, $^1J_{C,F} = 274.0$ Hz), 122.9, 124.5, 127.7, 128.5, 135.4 (q, $^2J_{C,F} = 33.7$ Hz), 135.6, 164.8, 171.2; HRMS (ESI): $m/z$ [M + H]$^+$ calcd for C$_{19}$H$_{23}$F$_3$NO$_4$: 386.1574, Found: 386.1579.