

Supporting Information

Ligand-free Cu-catalyzed [3+2] Cyclization for the Synthesis of Pyrrolo[1,2-*a*]quinolines with Ambient Air as Terminal Oxidant

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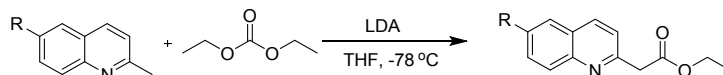
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1. General Information

Unless otherwise noted, all reagents were obtained commercially and used without further purification. Unless otherwise specified, all other reagents were purchased from Acros, Aldrich, Fisher, Adamas-beta Co. Ltd. or TCI and used without further purification. ^1H NMR spectra was recorded at 400 MHz, ^{13}C NMR spectra was recorded at 100 MHz. ^1H NMR spectra was recorded with tetramethylsilane ($\delta = 0.00$ ppm) as internal reference; ^{13}C NMR spectra was recorded with CDCl_3 ($\delta = 77.00$ ppm) or $\text{DMSO}-d_6$ ($\delta = 39.51$ ppm) as internal reference. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br).

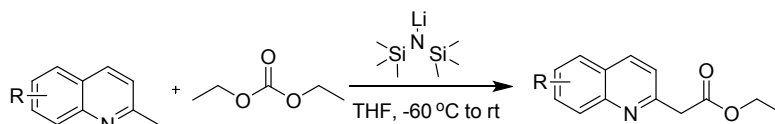
2. General Procedure for the Synthesis of Ethyl 2-(quinolin-2-yl)acetate derivatives

Procedure A¹



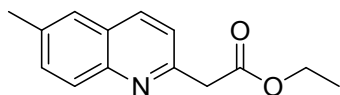
To a solution of 2-merhylquinoline (716 mg, 5 mmol) and diethyl carbonate (2.24 mL, 18.5 mmol) in anhydrous THF (8 mL), LDA (2.0 M, tetrahydrofuran solution) (7 mL, 14 mmol) was added dropwise under nitrogen atmosphere at - 78 °C. The resulting solution was stirred at - 78 °C for 1.5 h. After completion of the reaction, 5 mL water was added and the mixture was warmed gradually to rt. Then, 50 mL water was added again and the solution was extracted with ethyl acetate. The organic layer was washed with saturated sodium bicarbonate solution and brine, then dried over sodium sulfate. The solvent was removed under reduced pressure. The obtained residue was purified by column chromatography to give the compound as yellow liquid (940 mg, 87%).

Procedure B²

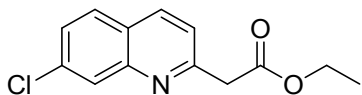


To a solution of 6-bromo-2-methylquinoline (1.11 g, 5 mmol) in anhydrous THF (20 mL), lithium hexamethyldisilazide (1 M, tetrahydrofuran solution) (20 mL, 20 mmol) was added dropwise under nitrogen atmosphere at -60 °C. The resulting solution was stirred below -60 °C for 30 min. To the reaction solution, diethyl carbonate (1.34 mL, 11 mmol) was added. Then the mixture was stirred at rt for 3 h. After the completion of the reaction, 1 N HCl was added. The reaction solution was extracted with ethyl acetate. The organic layer was washed with saturated sodium bicarbonate solution and brine, then dried over sodium sulfate. The solvent was removed under reduced pressure. The obtained residue was purified by column chromatography to give compound (1.51 g, 76%).

Characterization Data for Substrates

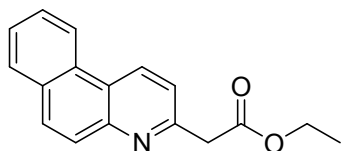


Ethyl 2-(6-Methylquinolin-2-yl)acetate (1h). The title compound was prepared according to general procedure **A** using 2,6-dimethylquinoline as the starting material in 70% yield as yellow liquid. ¹H NMR (400 MHz, CDCl₃): δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.55 (s, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 4.01 (s, 2H), 2.52 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 170.8, 154.0, 146.6, 136.3, 136.1, 132.0, 128.9, 127.2, 126.5, 121.8, 61.2, 44.9, 21.7, 14.3; HRMS (EI) *m/z* calcd for C₁₄H₁₅NO₂ [M]⁺: 229.1103; found: 229.1105.



Ethyl 2-(7-Chloroquinolin-2-yl)acetate (1i). The title compound was prepared according to general procedure **B** using 7-chloro-2-methylquinoline as the starting material in 72% yield as yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 8.11 (d, *J* = 8.0 Hz, 1H), 8.06 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 4.21 (q, *J* = 6.8 Hz, 2H), 4.02 (s, 2H), 1.27 (t, *J* = 6.8 Hz, 3H); ¹³C NMR

(100 MHz, CDCl₃): δ 170.4, 156.2, 148.4, 136.5, 135.6, 128.9, 128.4, 127.6, 125.5, 122.1, 61.4, 44.9, 14.3; HRMS (EI) m/z calcd for C₁₃H₁₂ClNO₂ [M]⁺: 249.0557; found: 249.0555.



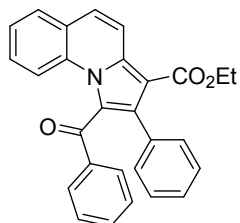
Ethyl 2-(benzo[f]quinolin-3-yl)acetate (11). The title compound was prepared according to general procedure A using 3-methylbenzo[f]quinoline as the starting material in 75% yield as yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 8.89 (d, J = 8.4 Hz, 1H), 8.57 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 2.0 Hz, 2H), 7.91 (d, J = 7.2 Hz, 1H), 7.61 - 7.69 (m, 2H), 7.58 (d, J = 8.8 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 4.08 (s, 2H), 1.27 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 170.7, 154.4, 147.9, 131.7, 131.4, 131.1, 129.6, 128.8, 128.0, 127.3, 127.2, 124.2, 122.7, 121.9, 61.2, 44.6, 14.3; HRMS (EI) m/z calcd for C₁₇H₁₅NO₂ [M]⁺: 265.1103; found: 265.1104.

3. General Procedure for Synthesis of [3+2] Products

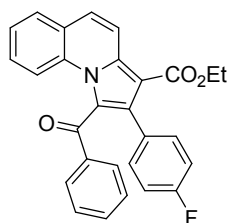
General procedure for synthesis of compounds **3a-3f**, **3i-3l**, **5e**, **5f**, **5h**: To a solution of **1** (0.2 mmol) and **2** (0.4 mmol) in DMSO (1.0 mL) was added the Cu(OAc)₂ (0.06 mmol) and DBU (0.4 mmol). The resulting solution was stirred for 18 h at 75 °C in air. After the reaction was cooled to ambient temperature, the mixture was diluted with ethyl acetate, washed sequentially with saturated aq. NH₄Cl and water. The organic layer was dried over Na₂SO₄, filtered and evaporated under reduced pressure. The crude reaction mixture was directly purified by Al₂O₃ (PE/EA = 50:1-20:1) to give the corresponding product.

General procedure for synthesis of compounds **3g**, **3h**, **5a-5d**, **5g**: To a solution of **1** (0.2 mmol) and **2** (0.4 mmol) in DMSO (1.0 mL) was added CuCl (0.06 mmol) and TBD (0.4 mmol). The resulting solution was stirred for 12 h at 75 °C in air. After the reaction was cooled to ambient temperature, the mixture was diluted with ethyl acetate, washed sequentially with saturated aq. NH₄Cl and water. The organic layer

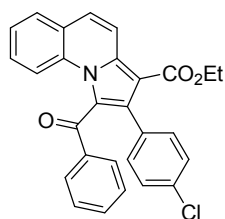
was dried over Na₂SO₄, filtered and evaporated under reduced pressure. The crude reaction mixture was directly purified by Al₂O₃ (PE/EA = 50:1-20:1) to give the corresponding product.



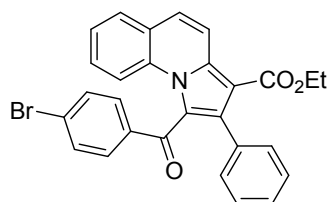
Ethyl 1-benzoyl-2-phenylpyrrolo[1,2-a]quinoline-3-carboxylate (3a). 81% yield, yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.30 (d, *J* = 9.6 Hz, 1H), 7.97 (m, 1H), 7.83 (d, *J* = 9.6 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.47 (m, 4H), 7.33-7.30 (t, *J* = 7.6 Hz, 2H), 7.16 (br, 5H), 4.10 (q, *J* = 7.0 Hz, 2H), 1.00 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 190.2, 164.6, 138.1, 137.1, 135.6, 133.7, 133.3, 132.5, 130.5, 129.9, 129.1, 128.7, 128.3, 127.1, 127.0, 126.7, 126.1, 125.1, 125.0, 118.7, 118.4, 106.7, 59.8, 13.9. HRMS (ESI) *m/z* calcd for C₂₈H₂₁NO₃ (M+1)⁺ 420.1600, found 420.1606.



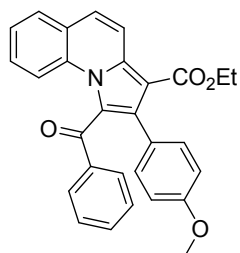
Ethyl 1-benzoyl-2-(4-fluorophenyl)pyrrolo[1,2-a]quinoline-3-carboxylate (3b). 67% yield, yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 8.39 (d, *J* = 9.2 Hz, 1H), 7.78 (d, *J* = 6.4 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 7.43-7.37 (m, 3H), 7.26-7.15 (m, 4H), 6.84 (t, *J* = 8.4 Hz, 2H), 4.21 (q, *J* = 6.8 Hz, 2H), 1.12 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 190.2, 164.5, 162.1(d, *J*_{C-F} = 245 Hz), 138.1, 137.1, 134.5, 133.5, 132.5, 132.2 (d, *J*_{C-F} = 8.1 Hz), 129.8, 129.6, 129.5, 129.1, 128.4, 126.9, 126.2, 125.1, 125.0, 118.7, 118.3, 114.0 (d, *J*_{C-F} = 21.4 Hz), 106.7, 59.8, 14.0. HRMS(ESI) *m/z* calcd for C₂₈H₂₀FN₃ (M+1)⁺ 438.1505, found 438.1502.



Ethyl 1-benzoyl-2-(4-chlorophenyl)pyrrolo[1,2-a]quinoline-3-carboxylate (3c). 74% yield, yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 8.39 (d, $J = 9.6$ Hz, 1H), 7.78-7.76 (m, 1H), 7.69 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.2$ Hz, 2H), 7.60-7.57 (m, 2H), 7.44-7.34 (m, 3H), 7.27-7.23 (m, 2H), 7.16-7.09 (m, 4H), 4.21 (q, $J = 7.2$ Hz, 2H), 1.13 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.1, 164.4, 138.0, 137.0, 134.1, 133.5, 133.2, 132.5, 132.2, 131.9, 129.8, 129.1, 128.8, 128.5, 127.2, 126.9, 126.1, 125.1, 125.1, 118.7, 118.3, 106.6, 59.9, 14.0. HRMS(ESI), calcd for $\text{C}_{28}\text{H}_{20}\text{ClNO}_3$ ($\text{M}+1$) $^+$ 454.1210, found 454.1213.

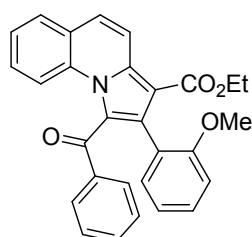


Ethyl 1-(3-bromobenzoyl)-2-phenylpyrrolo[1,2-a]quinoline-3-carboxylate (3d). 65% yield, yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 8.40 (d, $J = 9.6$ Hz, 1H), 7.79-7.77 (m, 1H), 7.60-7.54 (m, 4H), 7.42-7.34 (m, 4H), 7.19-7.13 (m, 5H), 4.19 (q, $J = 7.2$ Hz, 2H), 1.07 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 188.9, 164.5, 137.4, 137.0, 136.1, 133.5, 132.4, 131.6, 131.2, 130.5, 129.2, 128.8, 128.4, 127.3, 127.1, 127.0, 125.6, 125.2, 125.1, 118.6, 118.4, 106.8, 59.8, 13.9. HRMS(ESI), calcd for $\text{C}_{28}\text{H}_{20}\text{BrNO}_3$ ($\text{M}+1$) $^+$ 498.0705, found 498.0708.



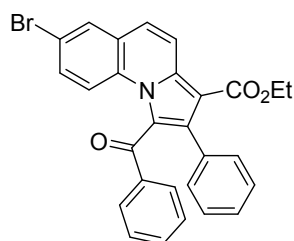
Ethyl 1-benzoyl-2-(4-methoxyphenyl)pyrrolo[1,2-a]quinoline-3-carboxylate (3e).

57% yield, yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 8.38 (d, $J = 9.6$ Hz, 1H), 7.77-7.68 (m, 3H), 7.60-7.54 (m, 2H), 7.40-7.34 (m, 3H), 7.26-7.21 (m, 2H), 7.15 (d, $J = 6.8$ Hz, 2H), 6.69 (d, $J = 8.8$ Hz, 2H), 4.23 (q, $J = 7.0$ Hz, 2H), 3.72 (s, 3H), 1.15 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.4, 164.7, 158.7, 138.1, 136.9, 135.3, 133.3, 132.5, 131.8, 129.8, 129.0, 128.6, 128.3, 126.6, 126.1, 125.7, 125.1, 124.9, 118.7, 118.4, 112.6, 106.7, 59.8, 55.2, 14.1. HRMS (ESI) m/z calcd for $\text{C}_{29}\text{H}_{23}\text{NO}_4(\text{M}+1)^+$ 450.1705, found 450.1706.



Ethyl 1-benzoyl-2-(2-methoxyphenyl)pyrrolo[1,2-a]quinoline-3-carboxylate (3f)

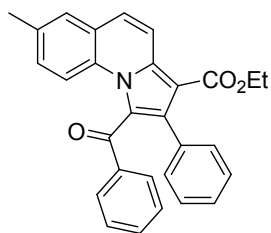
. 48% yield, yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 8.39 (d, $J = 9.6$ Hz, 1H), 7.78-7.76 (m, 3H), 7.64-7.56 (m, 2H), 7.40-7.34 (m, 3H), 7.22-7.18 (m, 2H), 7.09-7.00 (m, 2H), 6.74-6.71 (m, 1H), 6.60 (d, $J = 8.4$ Hz, 1H), 4.14 (q, $J = 7.2$ Hz, 2H), 3.62 (s, 3H), 1.03 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 189.5, 164.6, 156.8, 138.2, 137.7, 133.1, 132.9, 132.6, 131.6, 129.7, 129.0, 128.9, 128.5, 127.9, 126.8, 126.2, 125.1, 124.8, 123.3, 119.6, 119.1, 118.4, 109.6, 107.4, 59.5, 55.0, 13.9. HRMS(ESI), calcd for $\text{C}_{29}\text{H}_{23}\text{NO}_4(\text{M}+1)^+$ 450.1705, found 450.1707.



Ethyl 1-benzoyl-7-bromo-2-phenylpyrrolo[1,2-a]quinoline-3-carboxylate (3g)

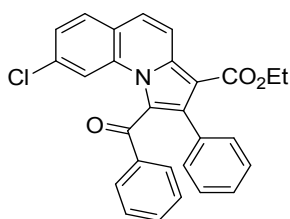
. 64% yield, yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 8.42 (d, $J = 9.6$ Hz, 1H), 7.90 (br, 1H), 7.70 (d, $J = 7.6$ Hz, 2H), 7.49-7.37 (m, 4H), 7.26-7.10 (m, 7H), 4.18 (q, $J = 7.2$ Hz, 2H), 1.07 (t, $J = 6.8$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.1, 164.4, 137.9, 136.8, 135.8, 133.5, 133.4, 131.4, 131.3, 131.1, 130.5, 129.9, 128.4, 127.2,

127.0, 126.8, 126.2, 125.4, 120.3, 119.6, 118.2, 107.3, 59.9, 13.9. HRMS(ESI), calcd for $C_{28}H_{20}BrNO_3$ ($M+1$)⁺ 498.0705, found 498.0709.



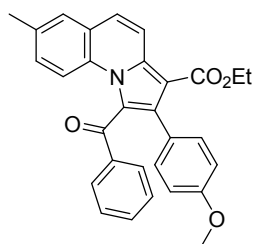
Ethyl 1-benzoyl-7-methyl-2-phenylpyrrolo[1,2-a]quinoline-3-carboxylate (3h).

78% yield, yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 8.36 (d, *J* = 9.6 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.54-7.47 (m, 3H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.26-7.09 (m, 8H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.42 (s, 3H), 1.07 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 190.2, 164.7, 138.2, 136.9, 135.5, 134.7, 133.8, 133.2, 130.6, 130.5, 130.0, 129.9, 128.7, 128.3, 127.0, 126.9, 126.6, 125.9, 125.2, 118.5, 118.3, 106.5, 59.7, 20.9, 13.9. HRMS(ESI), calcd for $C_{29}H_{23}NO_3$ ($M+1$)⁺ 434.1756, found 434.1754.



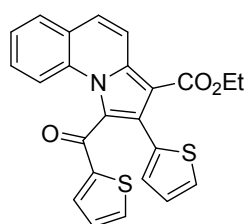
Ethyl 1-benzoyl-8-chloro-2-phenylpyrrolo[1,2-a]quinoline-3-carboxylate (3i).

47% yield, yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.33 (d, *J* = 9.6 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 7.88 (d, *J* = 9.2 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.59-7.47 (m, 3H), 7.36-7.32 (m, 2H), 7.17 (m, 5H), 4.11 (q, *J* = 6.4 Hz, 2H), 1.01 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 189.8, 164.4, 138.0, 137.2, 136.2, 134.3, 133.4, 133.3, 133.0, 130.5, 130.0, 129.8, 128.3, 127.2, 127.0, 126.3, 126.0, 125.6, 123.6, 118.8, 118.6, 107.2, 59.9, 13.9. HRMS(ESI), calcd for $C_{28}H_{20}ClNO_3$ ($M+1$)⁺ 454.1210, found 454.1212.

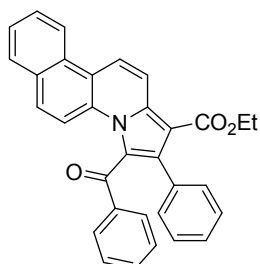


Ethyl 1-benzoyl-2-(4-methoxyphenyl)-7-methylpyrrolo[1,2-a]quinoline-3-

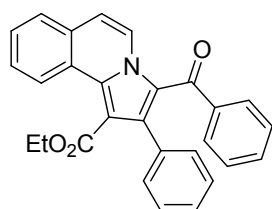
Carboxylate (3j). 53% yield, yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 8.33 (d, $J = 9.2$ Hz, 1H), 7.71 (d, $J = 7.2$ Hz, 2H), 7.54-7.47 (m, 3H), 7.39 (t, $J = 7.6$ Hz, 1H), 7.26-7.09 (m, 5H), 6.67 (d, $J = 8.4$ Hz, 2H) 4.18 (q, $J = 7.2$ Hz, 2H), 3.71 (s, 3H), 2.43 (s, 3H), 1.07 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.4, 164.7, 158.7, 138.2, 136.8, 135.2, 134.7, 133.2, 131.8, 130.6, 130.0, 129.8, 128.6, 128.3, 126.5, 126.0, 125.8, 125.1, 118.5, 118.3, 112.5, 106.5, 59.7, 55.2, 20.9, 14.1. HRMS(ESI), calcd for $\text{C}_{30}\text{H}_{25}\text{NO}_4$ ($\text{M}+1$) $^+$ 464.1862, found 464.1859.



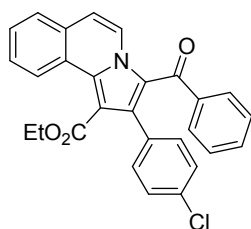
Ethyl 2-(thiophen-2-yl)-1-(thiophene-2-carbonyl)pyrrolo[1,2-a]quinoline-3-carboxylate (3k). 50% yield, yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 8.35 (d, $J = 9.2$ Hz, 1H), 7.77 (m, 2H), 7.62 (d, $J = 4.4$ Hz, 1H), 7.54 (d, $J = 9.6$ Hz, 1H), 7.40 (br, 3H), 7.24 (d, $J = 4.8$ Hz, 1H), 6.95 (d, $J = 12.0$ Hz, 2H), 6.84 (br, 1H), 4.29 (q, $J = 6.8$ Hz, 2H), 1.22 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 182.5, 164.3, 144.9, 136.6, 135.7, 135.5, 133.6, 132.4, 129.5, 129.2, 128.9, 128.1, 126.7, 126.5, 126.4, 126.2, 126.1, 125.2, 125.1, 118.3, 118.2, 107.2, 60.0, 14.1. HRMS(ESI), calcd for $\text{C}_{24}\text{H}_{17}\text{NO}_3\text{S}_2$ ($\text{M}+1$) $^+$ 432.0728, found 432.0728.



Ethyl 3-benzoyl-2-phenylbenzo[*f*]pyrrolo[1,2-*a*]quinoline-1-carboxylate (3l). 70% yield, yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 8.62-8.58 (m, 2H), 8.50 (d, *J* = 10.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.78-7.56 (m, 6H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.25-7.11 (m, 7H), 4.21 (q, *J* = 6.8 Hz, 2H), 1.09 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 189.6, 164.6, 138.3, 137.5, 136.9, 133.8, 133.1, 131.0, 130.5, 130.4, 129.9, 129.9, 129.6, 128.8, 128.3, 127.7, 127.1, 127.0, 126.5, 125.9, 122.9, 121.7, 120.7, 118.4, 118.3, 106.0, 59.8, 13.9. HRMS(ESI), calcd for C₃₂H₂₃NO₃ (M+1)⁺ 470.1756, found 470.1761.

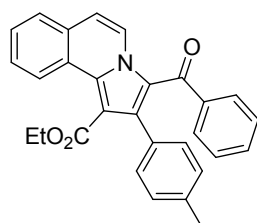


Ethyl 3-benzoyl-2-phenylpyrrolo[2,1-*a*]isoquinoline-1-carboxylate (5a). 63% yield, yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 9.15 (d, *J* = 7.6 Hz, 1H), 8.67-8.64 (m, 1H), 7.74-7.72 (m, 1H), 7.61-7.56 (m, 2H), 7.47 (dd, *J*₁ = 8.0 Hz, *J*₂ = 1.2 Hz, 2H), 7.21-7.01 (m, 9H), 4.18 (q, *J* = 7.2 Hz, 2H), 0.95 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 188.2, 167.4, 139.1, 136.6, 134.1, 132.4, 131.6, 130.6, 129.8, 129.6, 128.6, 127.9, 127.5, 127.3, 127.1, 127.0, 125.2, 124.4, 124.1, 122.5, 114.4, 111.1, 61.2, 13.6. HRMS(ESI), calcd for C₂₈H₂₁NO₃ (M+1)⁺ 420.1600, found 420.1598.

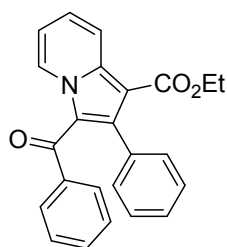


Ethyl 3-benzoyl-2-(4-chlorophenyl)pyrrolo[2,1-*a*]isoquinoline-1-carboxylate (5b). 63% yield, yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 9.14 (d, *J* = 7.6 Hz, 1H), 8.66-8.64 (m, 1H), 7.75-7.73 (m, 1H), 7.62-7.56 (m, 2H), 7.44 (dd, *J*₁ = 8.0 Hz, *J*₂ = 1.2 Hz, 2H), 7.29-7.25 (m, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.10-6.99 (m, 6H), 4.21 (q, *J* = 7.0 Hz, 2H), 1.02 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 188.1, 167.1,

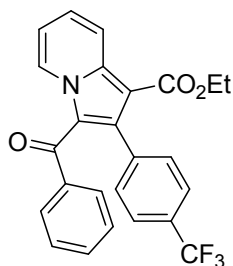
139.0, 135.3, 133.2, 132.7, 132.6, 131.8, 131.7, 129.9, 129.5, 128.7, 128.0, 127.7, 127.5, 127.2, 125.3, 124.4, 124.1, 122.6, 114.6, 111.0, 61.3, 13.7. HRMS(ESI), calcd for $C_{28}H_{20}ClNO_3$ ($M+1$)⁺ 454.1210, found 454.1207.



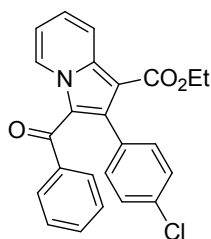
Ethyl 3-benzoyl-2-(p-tolyl)pyrrolo[2,1-a]isoquinoline-1-carboxylate (5c). 57% yield, yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 9.14 (d, *J* = 7.6 Hz, 1H), 8.62-8.60 (m, 1H), 7.74-7.71 (m, 1H), 7.60-7.55 (m, 2H), 7.46 (dd, *J*₁ = 8.0 Hz, *J*₂ = 1.2 Hz, 2H), 7.22-7.18 (m, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.06-7.02 (m, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 7.6 Hz, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 2.18 (s, 3H), 1.01 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 188.3, 167.5, 139.1, 136.7, 136.6, 132.2, 131.3, 130.9, 130.5, 129.8, 129.6, 128.5, 128.0, 127.8, 127.5, 127.1, 125.1, 124.5, 124.1, 122.5, 114.2, 111.1, 61.2, 21.0, 13.6. HRMS(ESI), calcd for $C_{29}H_{23}NO_3$ ($M+1$)⁺ 434.1756, found 434.1752.



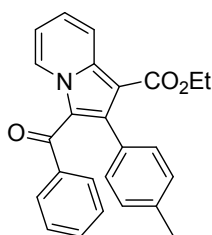
Ethyl 3-benzoyl-2-phenylindolizine-1-carboxylate³ (5d). 81% yield, yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.45 (d, *J* = 6.8 Hz, 1H), 8.39 (d, *J* = 8.8 Hz, 1H), 7.62-7.58 (m, 1H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.26-7.21 (m, 2H), 7.09-6.99 (m, 7H), 4.09 (q, *J* = 7.0 Hz, 2H), 1.02 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 187.9, 163.8, 139.4, 139.3, 138.6, 134, 131.6, 131.5, 129.5, 128.3, 127.9, 127.3, 127.0, 122.3, 119.5, 115.8, 104.2, 100.0, 59.7, 14.2.



Ethyl 3-benzoyl-2-(4-(trifluoromethyl)phenyl)indolizine-1-carboxylate (5e). 77% yield, yellow solid. ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 9.53 (d, $J = 7.2$ Hz, 1H), 8.41 (d, $J = 8.8$ Hz, 1H), 7.65-7.61 (m, 1H), 7.31-7.27 (m, 7H), 7.21-7.18 (m, 1H), 7.06-7.02 (m, 2H), 4.07 (q, $J = 7.0$ Hz, 2H), 0.98 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 188.0, 164.0, 139.3, 139.2, 138.3, 138.2, 131.5, 131.1, 129.1($q, ^1J_{\text{C-F}} = 30\text{Hz}$), 128.9, 128.3, 127.6, 127.5, 124.0 ($q, ^2J_{\text{C-F}} = 270$ Hz), 123.6 ($q, ^3J_{\text{C-F}} = 3.7\text{Hz}$), 122.4, 119.8, 115.3, 104.8, 59.9, 13.9. HRMS(ESI), calcd for $\text{C}_{25}\text{H}_{18}\text{F}_3\text{NO}_3$ ($\text{M}+1$) $^+$ 438.1317, found 438.1317.

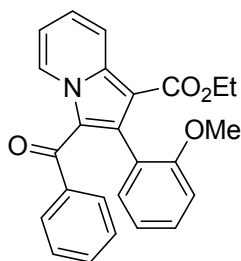


Ethyl 3-benzoyl-2-(4-chlorophenyl)indolizine-1-carboxylate³ (5f). 68% yield, yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 9.62 (d, $J = 7.0$ Hz, 1H), 8.46 (d, $J = 9.0$ Hz, 1H), 7.42 (t, $J = 7.5$ Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.22 (t, $J = 7.5$ Hz, 1H), 7.06-6.94 (m, 7H), 4.18 (q, $J = 7.0$ Hz, 2H), 1.12 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 188.2, 164.1, 139.3, 139.2, 139.1, 133.1, 132.5, 132.4, 131.1, 129.1, 128.2, 127.7, 127.5, 126.9, 122.4, 119.9, 115.1, 104.6, 59.7, 13.9.



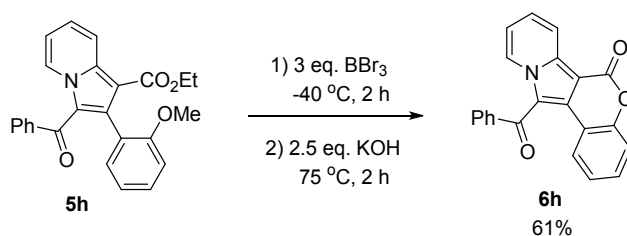
Ethyl 3-benzoyl-2-(p-tolyl)indolizine-1-carboxylate (5g). 52% yield, yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 9.62 (d, $J = 6.8$ Hz, 1H), 8.45 (d, $J = 8.8$ Hz, 1H),

7.43-7.39 (m, 1H), 7.34 (dd, $J_1 = 8.4$ Hz, $J_2 = 1.2$ Hz, 2H), 7.18-7.14 (m, 1H), 7.04-6.95 (m, 5H), 6.78 (d, $J = 8.0$ Hz, 2H), 4.22 (q, $J = 7.2$ Hz, 2H), 2.17 (s, 3H), 1.16 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 188.5, 164.4, 140.7, 139.4, 139.2, 136.7, 131.1, 130.7, 130.6, 129.2, 128.1, 127.5, 127.4, 127.1, 122.4, 119.8, 114.8, 104.7, 59.7, 21.1, 14.1. HRMS(ESI), calcd for $\text{C}_{25}\text{H}_{21}\text{NO}_3$ ($\text{M}+1$) $^+$ 384.1600, found 384.1601.



Ethyl 3-benzoyl-2-(2-methoxyphenyl)indolizine-1-carboxylate (5h). 48% yield, yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 9.65 (d, $J = 7.2$ Hz, 1H), 8.46 (d, $J = 9.2$ Hz, 1H), 7.42-7.37 (m, 3H), 7.17-7.13 (m, 1H), 7.03-6.97 (m, 4H), 6.92 (d, $J = 8.8$ Hz, 1H), 6.65-6.61 (m, 1H), 6.49 (d, $J = 8.4$ Hz, 1H), 4.15 (q, $J = 7.2$ Hz, 2H), 3.65 (s, 3H), 1.05 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 188.2, 164.4, 156.5, 139.5, 139.3, 136.7, 132.2, 130.9, 129.0, 128.7, 128.2, 127.1, 126.8, 123.7, 122.1, 119.7, 119.5, 114.7, 109.4, 105.4, 59.5, 55.0, 13.9. HRMS(ESI), calcd for $\text{C}_{25}\text{H}_{21}\text{NO}_4$ ($\text{M}+1$) $^+$ 400.1549, found 400.1553.

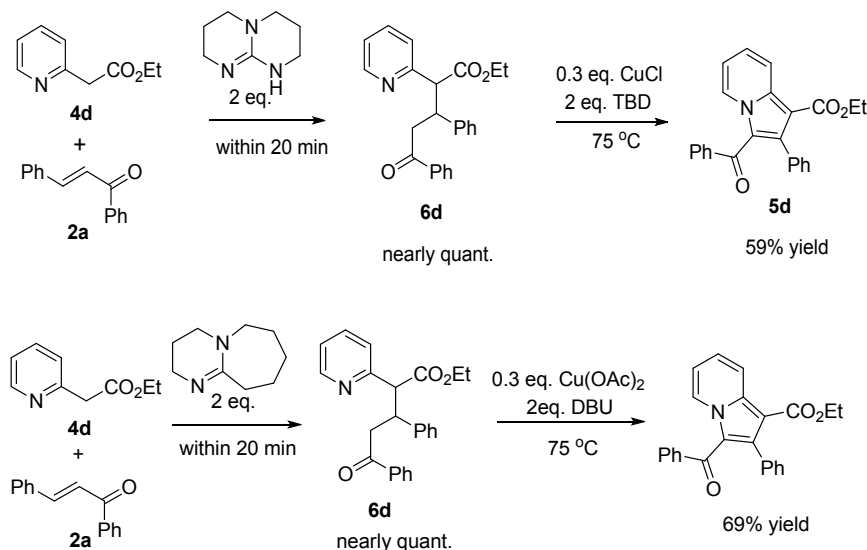
4. Synthesis of polycyclic compound 6H-chromeno[3,4-a]indolizin-6-one (6h)



To a solution of ethyl 3-benzoyl-2-(2-methoxyphenyl)indolizine-1-carboxylate (**5h**, 1 mmol, 40 mg) in the solvent of dichloromethane (2 mL) was added BBr_3 (3 eq. 30 μL) dropwise for 15 min at -40 °C. The mixture was stirred for 2 h at the same

temperature. After the reaction was completed, excess BBr_3 was quenched by water at $-40\text{ }^\circ\text{C}$. Then the reaction was diluted with ethyl acetate in room temperature, washed sequentially with water. The organic layer was dried over Na_2SO_4 , filtered and evaporated under reduced pressure. The residue was added 2.5 mL aq. KOH (1 mol/mL) and stirred for 2 h at $75\text{ }^\circ\text{C}$. The mixture was diluted with ethyl acetate, washed with water followed by brine. The organic layer was dried over Na_2SO_4 , filtered and evaporated under reduced pressure and the residue was purified by Al_2O_3 (PE/EA = 50:1-20/1) to give **6h** as a yellow solid in 61% yield. ^1H NMR (400 MHz, CDCl_3): δ 9.30 (d, $J = 7.2$ Hz, 1H), 8.60 (d, $J = 8.8$ Hz, 1H), 7.88 (dd, $J_1 = 8.4$ Hz, $J_2 = 1.2$ Hz, 2H), 7.62-7.53 (m, 2H), 7.46-7.43 (m, 2H), 7.38-7.27 (m, 2H), 7.18-7.14 (m, 1H), 7.00 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.2$ Hz, 1H), 6.79-6.75 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 187.8, 158.4, 153.2, 139.1, 137.4, 133.6, 130.5, 130.0, 130.0, 129.2, 128.0, 127.8, 127.7, 123.2, 119.6, 117.8, 117.4, 116.6, 115.0, 99.1. HRMS(ESI), calcd for $\text{C}_{22}\text{H}_{13}\text{NO}_3$ ($\text{M}+1$) $^+$ 340.0974, found 340.0970.

5. Synthesis of intermediate ethyl 5-oxo-3,5-diphenyl-2-(pyridin-2-yl)pentanoate and mechanism study



To a solution of **4d** (0.2 mmol) and **2a** (0.4 mmol) in DMSO (1.0 mL) was added TBD or DBU (0.4 mmol). The resulting solution was stirred for 20 min at room temperature. The mixture was diluted with ethyl acetate, washed sequentially with

saturated aq. NH_4Cl and water. The organic layer was dried over Na_2SO_4 , filtered and evaporated under reduced pressure. The crude reaction mixture was directly purified by Al_2O_3 (PE/EA = 20:1-4:1) to give the intermediate **6d** with nearly quantitative yield (dr = 1:0.42). ^1H NMR (400 MHz, CDCl_3): δ 8.52 (d, J = 4.4 Hz, 1H), 8.35 (d, J = 4.4 Hz, 0.42H), 7.84 (d, J = 8.0Hz, 0.84H), 7.69-7.52 (m, 4H), 7.49-7.23 (m, 6H), 7.22-7.12 (m, 4H), 7.12-7.03 (m, 1.42H), 7.03 -6.90 (m, 2.26H), 4.27-4.17 (m, 2.84), 4.10 (q, J = 6.4Hz, 0.84H), 3.80 (q, J = 7.8Hz, 2H), 3.43-3.53 (m, 0.84H), 3.28-3.20 (m, 1H), 2.92 (d, J = 8.8Hz, 1H), 1.28 (t, J = 6.4Hz, 1.26H), 0.80 (t, J = 7.8Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 198.1, 198.0, 172.1, 171.5, 157.0, 156.9, 149.5, 149.2, 141.6, 140.7, 137.1, 137.0, 136.9, 136.2, 132.9, 132.8, 132.8, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 126.9, 126.5, 123.7, 123.2, 122.8, 122.0, 61.2, 60.7, 60.3, 59.6, 44.2, 44.0, 43.3, 42.7, 14.2, 13.8. HRMS(ESI), calcd for $\text{C}_{24}\text{H}_{24}\text{NO}_3$. 374.1753, found 374.1756.

To a solution of **6d** in DMSO (1.0 mL) was added CuCl (0.06 mmol) and TBD (0.4 mmol). The resulting solution was stirred for 12 h at 75 °C in air. After the reaction was cooled to ambient temperature, the mixture was diluted with ethyl acetate, washed sequentially with saturated aq. NH_4Cl and water. The organic layer was dried over Na_2SO_4 , filtered and evaporated under reduced pressure. The crude reaction mixture was directly purified by Al_2O_3 (PE/EA = 50:1-20:1) to give **5d** in 59% yield.

To a solution of **6d** in DMSO (1.0 mL) was added $\text{Cu}(\text{OAc})_2$ (0.06 mmol) and DBU (0.4 mmol). The resulting solution was stirred for 12 h at 75 °C in air. After the reaction was cooled to ambient temperature, the mixture was diluted with ethyl acetate, washed sequentially with saturated aq. NH_4Cl and water. The organic layer was dried over Na_2SO_4 , filtered and evaporated under reduced pressure. The crude reaction mixture was directly purified by Al_2O_3 (PE/EA = 50:1-20:1) to give **5d** in 69% yield.

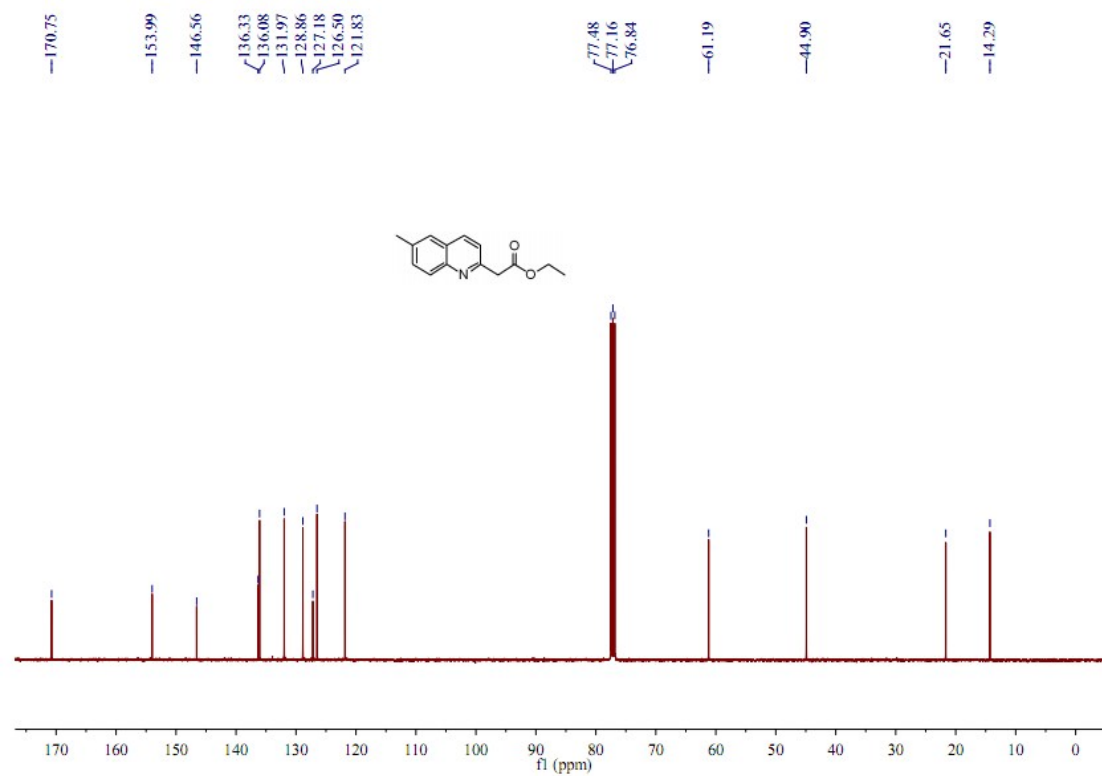
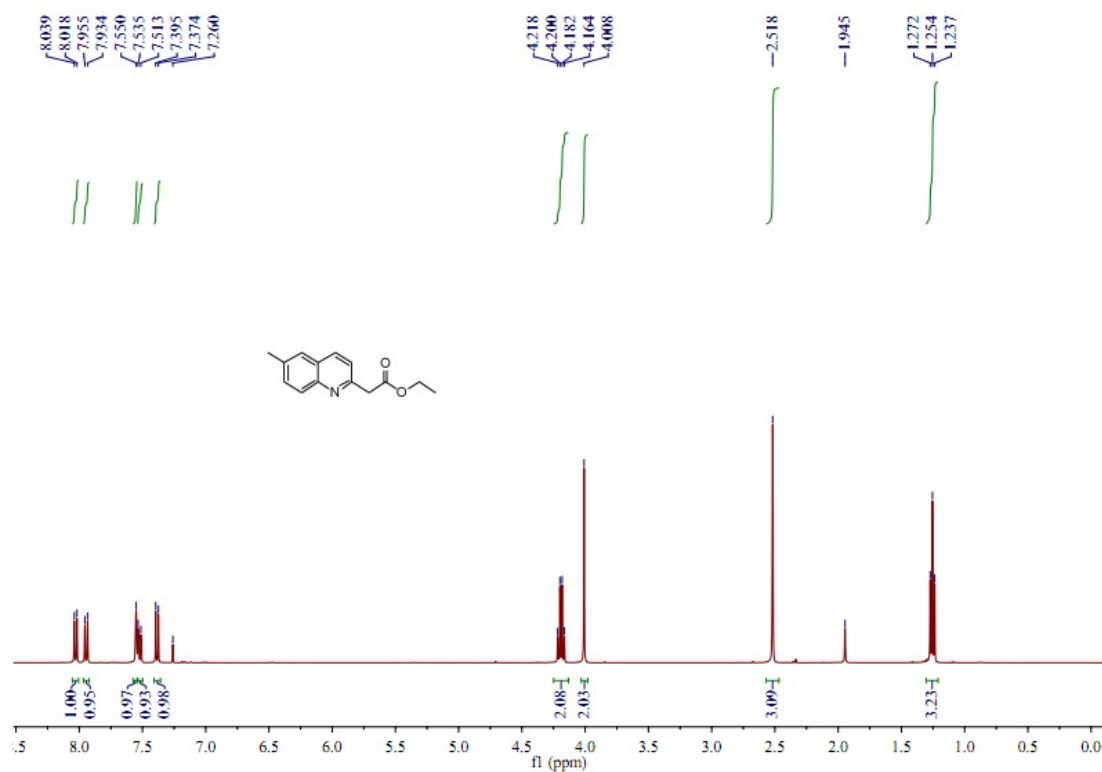
6. References

- (1) Z.-H. Zhang, G.-L. Zhou, Y.-T. Song, WO 2011097946A1.
- (2) M. Koji, K. Shiro, Y. Naoki, K. Manabu, K. Terukazu, N. Mado, K. Eiichi, Y. Mitsuhiro, US 20140323722A1.

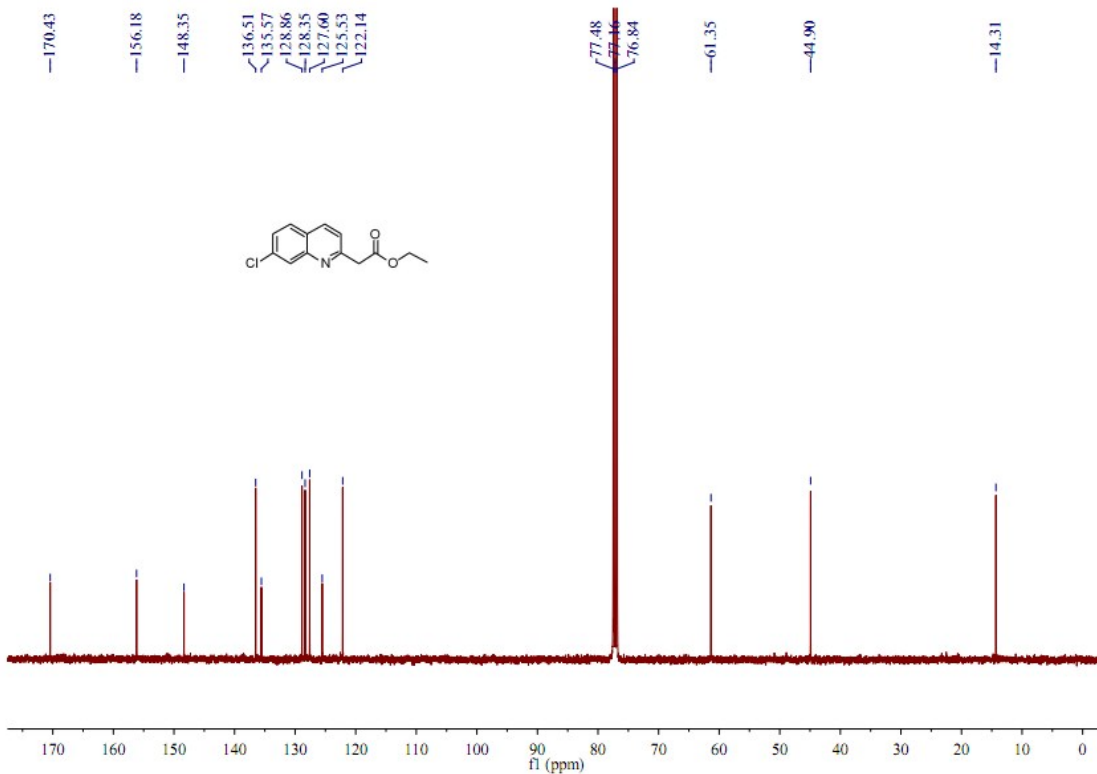
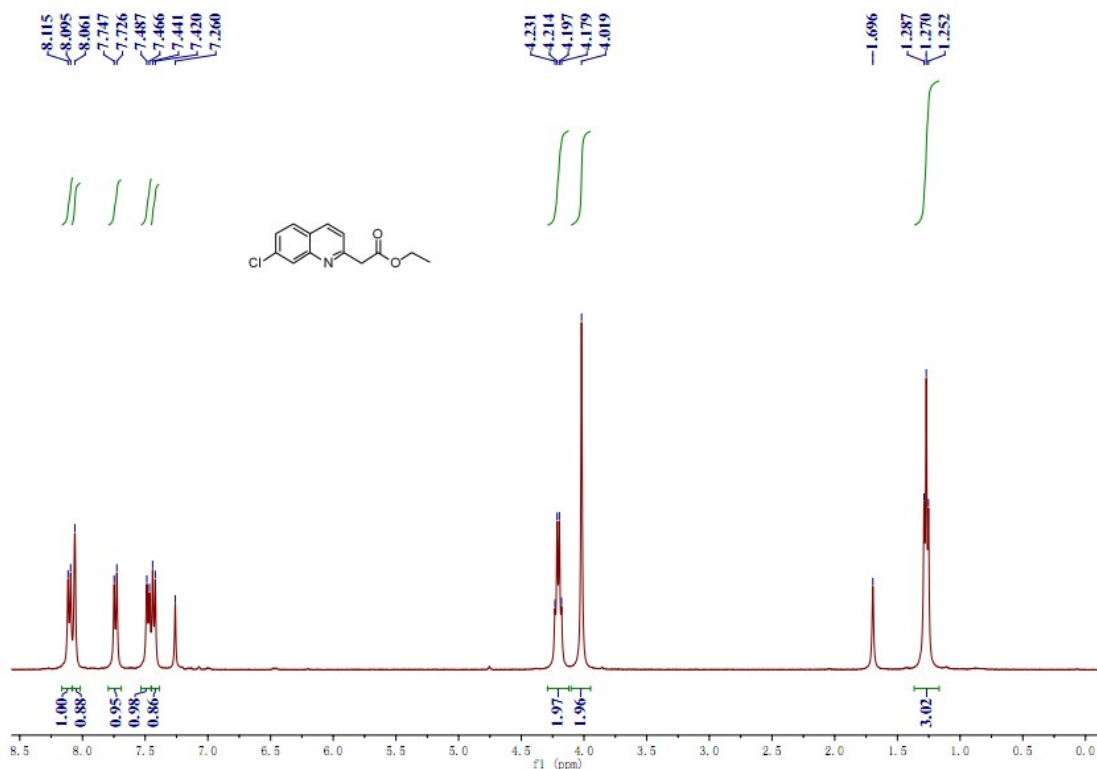
(3) D. C. Mohan, C. Ravi, V. Pappula, S. Adimurthy, *J. Org. Chem.* 2015, **80**, 6846.

7. ^1H and ^{13}C -NMR spectra data

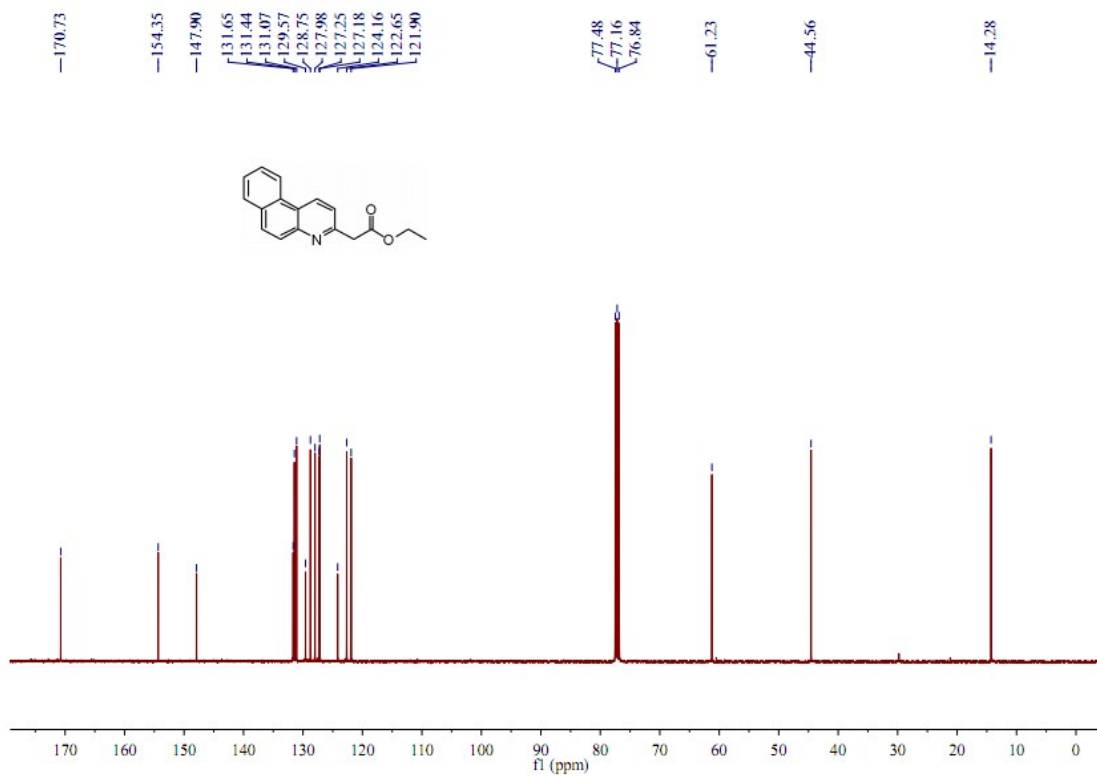
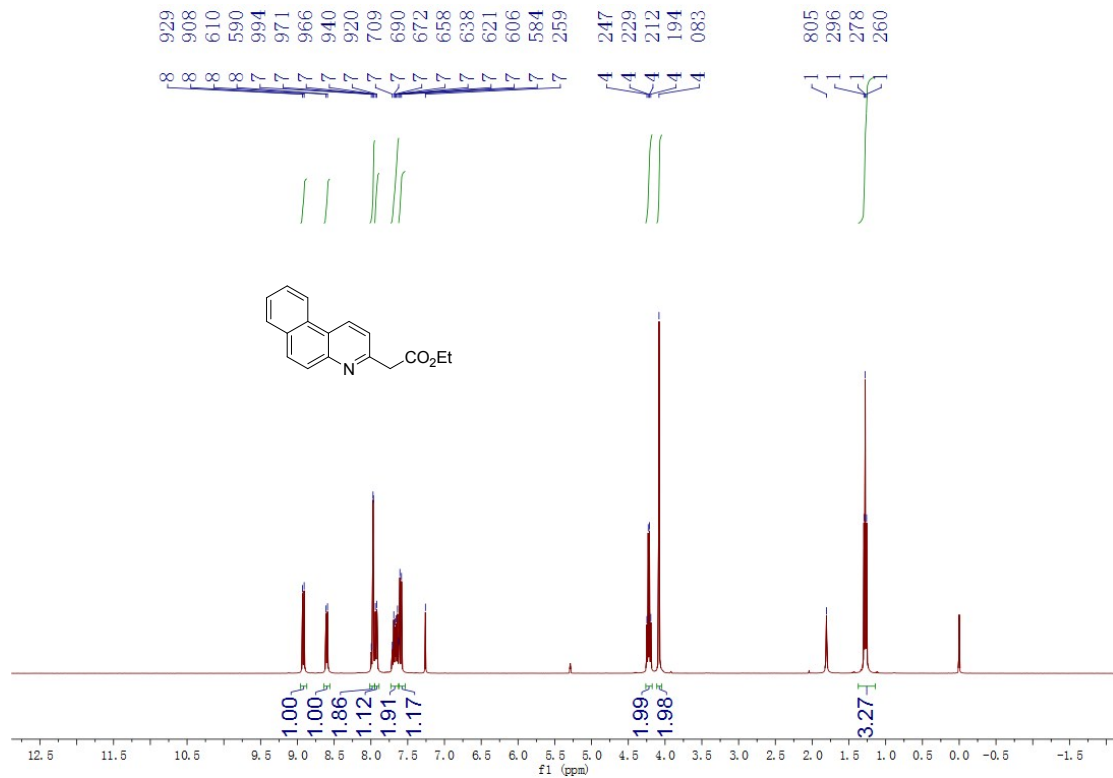
Ethyl 2-(6-methylquinolin-2-yl)acetate (**1h**)



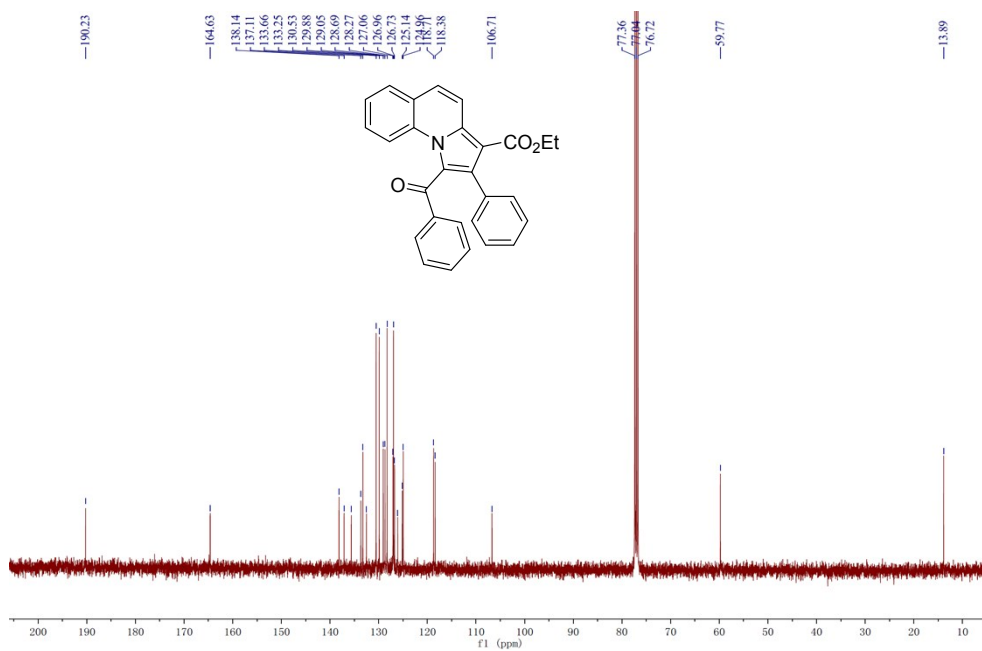
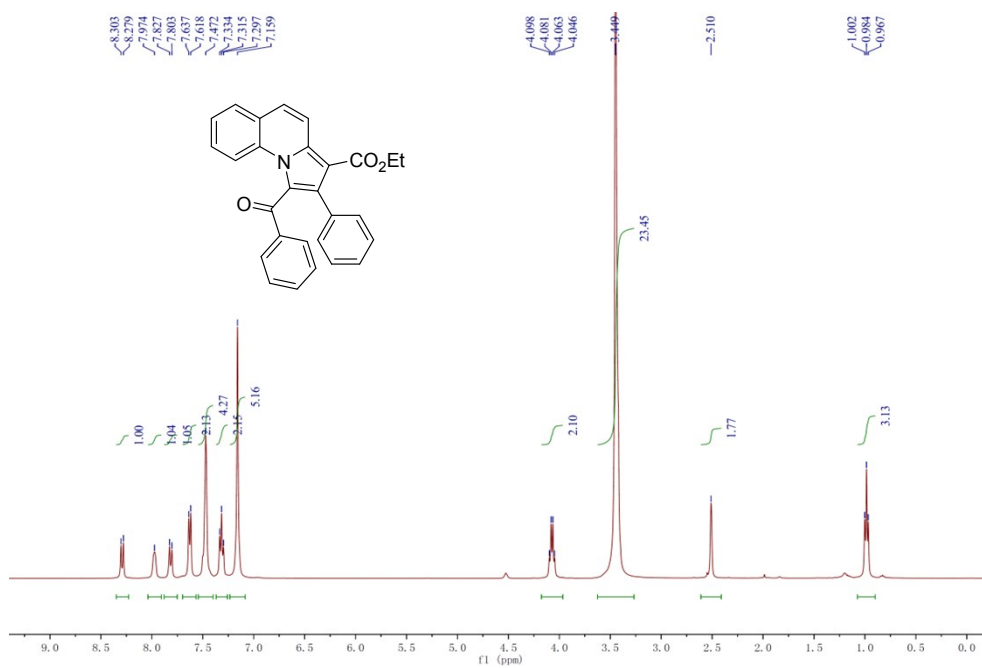
Ethyl 2-(7-chloroquinolin-2-yl)acetate (1i)



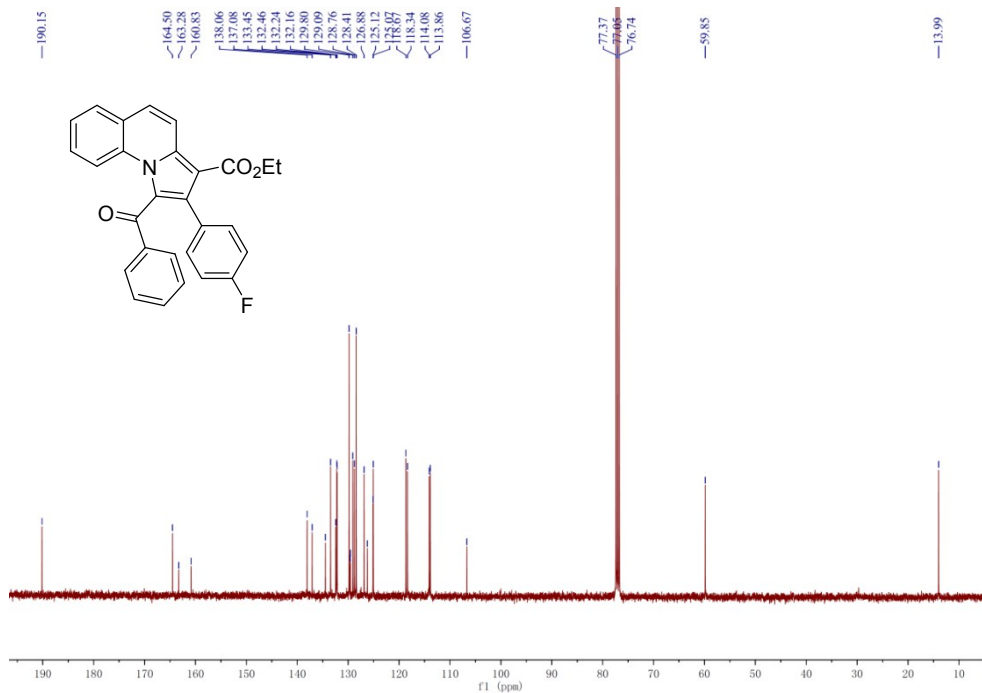
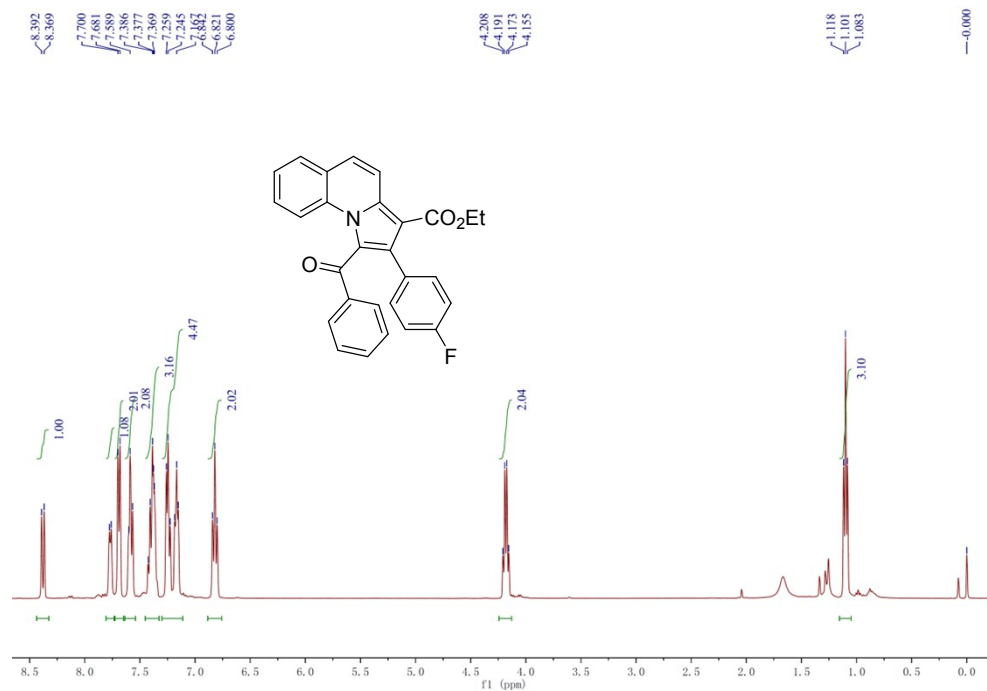
Ethyl 2-(benzo[f]quinolin-3-yl)acetate (11)



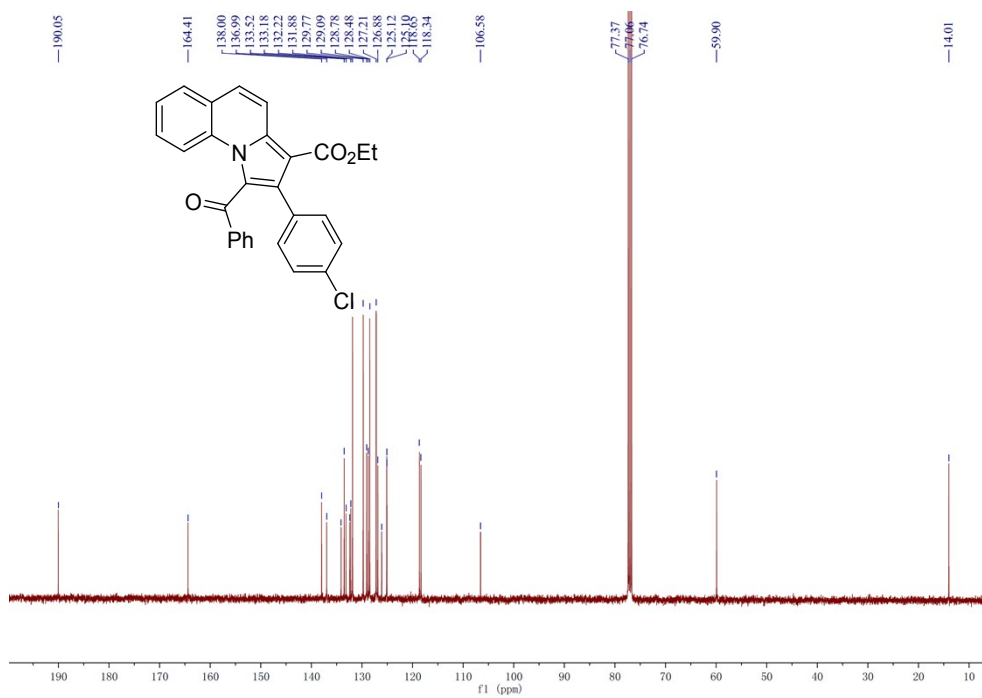
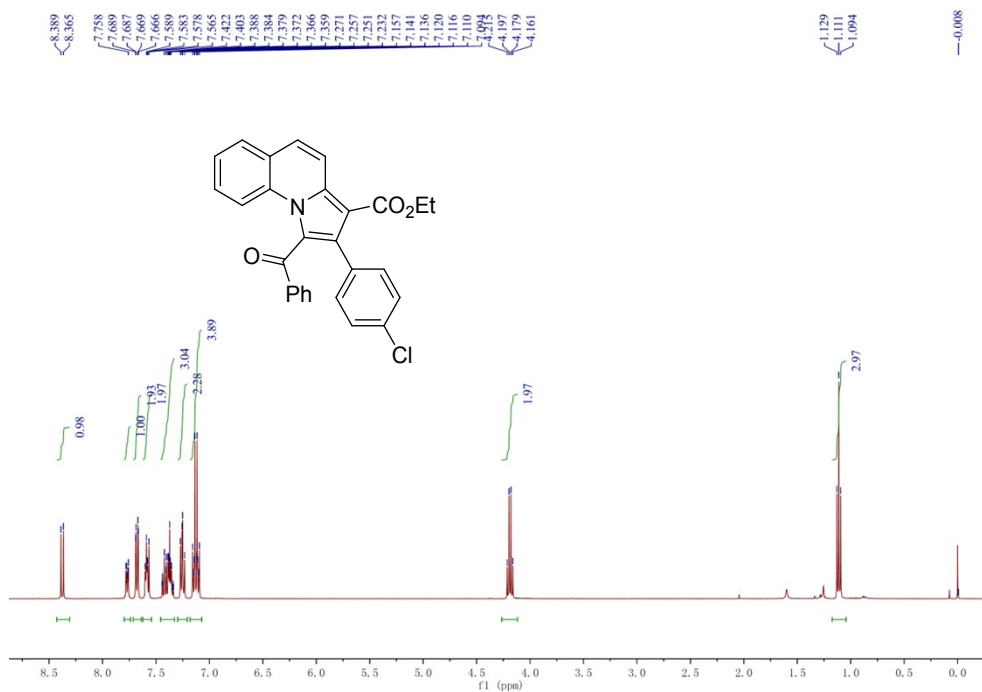
Ethyl 1-benzoyl-2-phenylpyrrolo[1,2-a]quinoline-3-carboxylate. (3a)



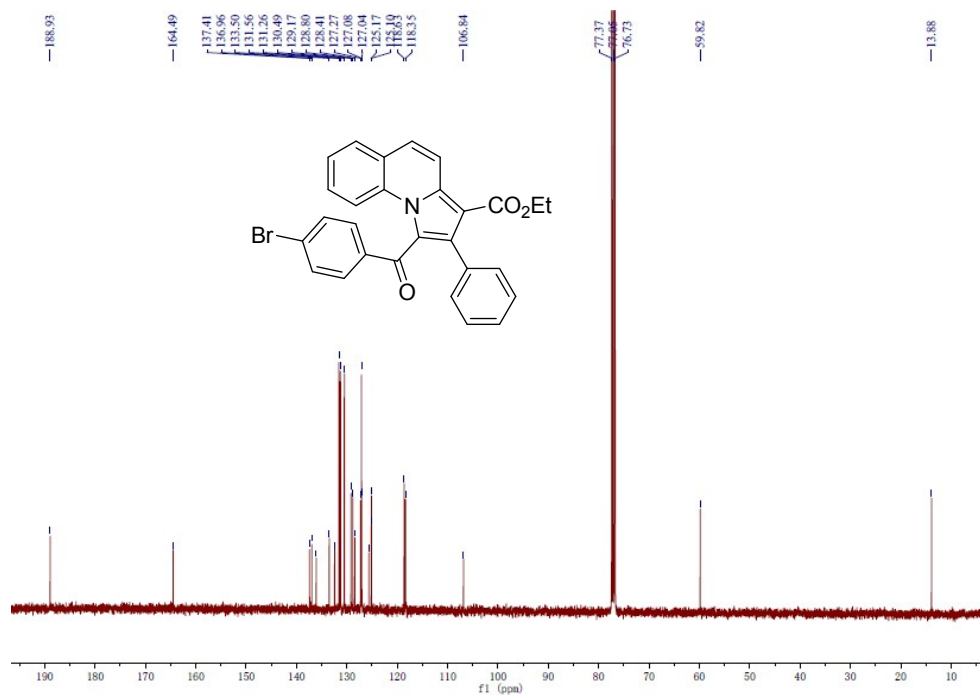
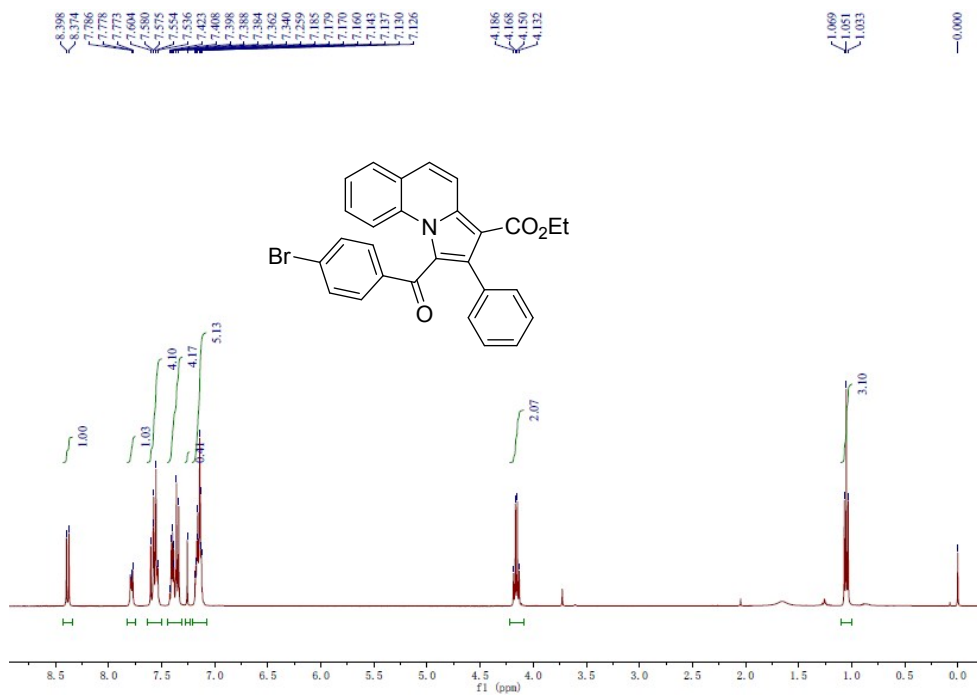
Ethyl 1-benzoyl-2-(4-fluorophenyl)pyrrolo[1,2-a]quinoline-3-carboxylate (3b)



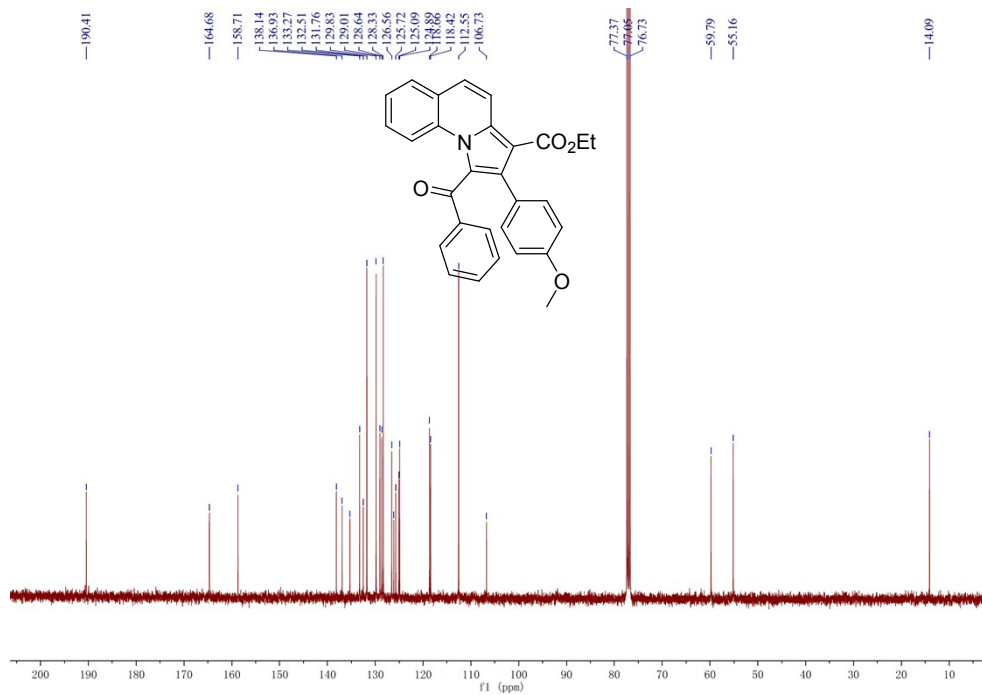
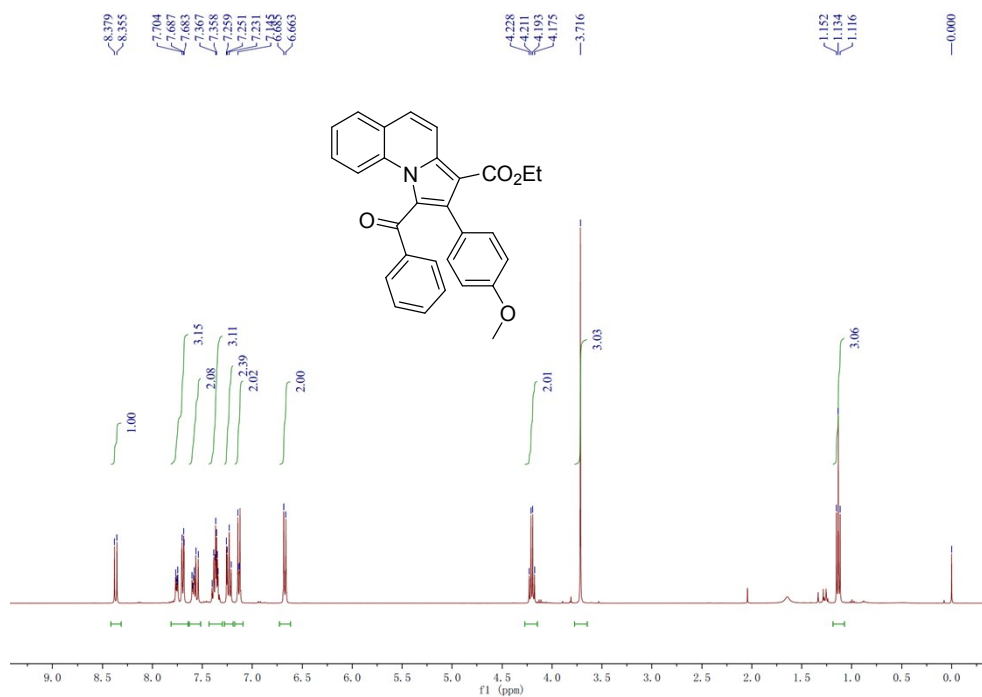
Ethyl 1-benzoyl-2-(4-chlorophenyl)pyrrolo[1,2-a]quinoline-3-carboxylate (3c).



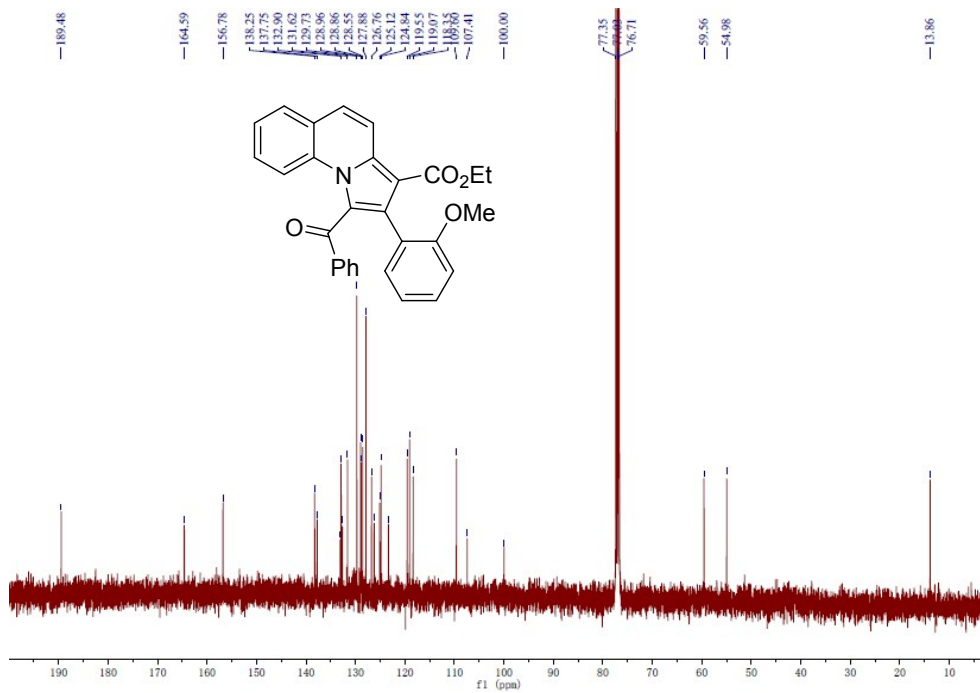
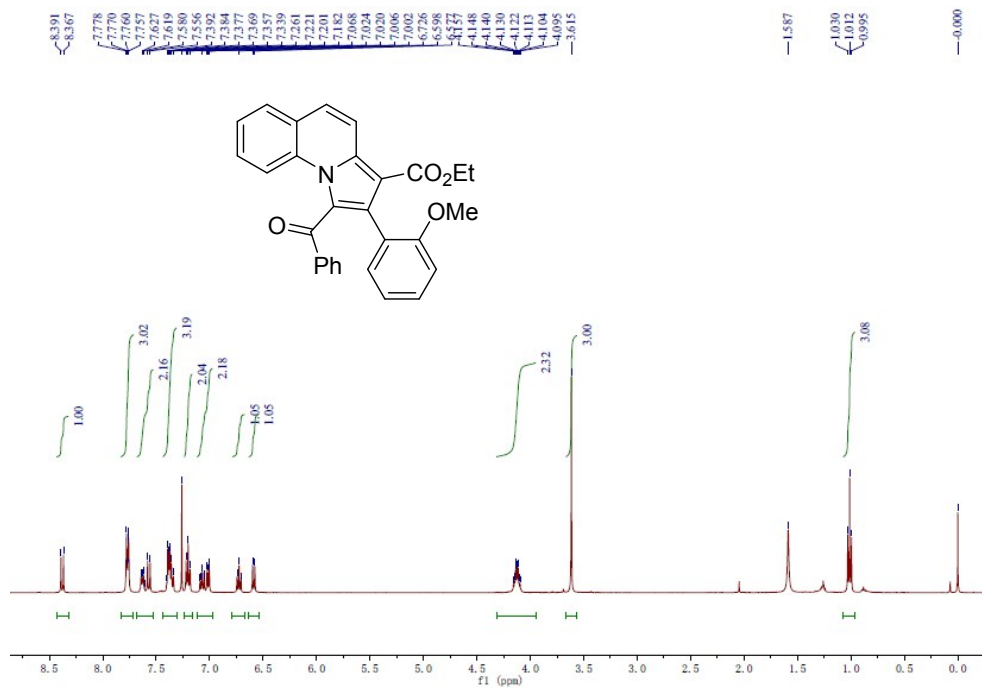
Ethyl 1-(3-bromobenzoyl)-2-phenylpyrrolo[1,2-a]quinoline-3-carboxylate (3d).



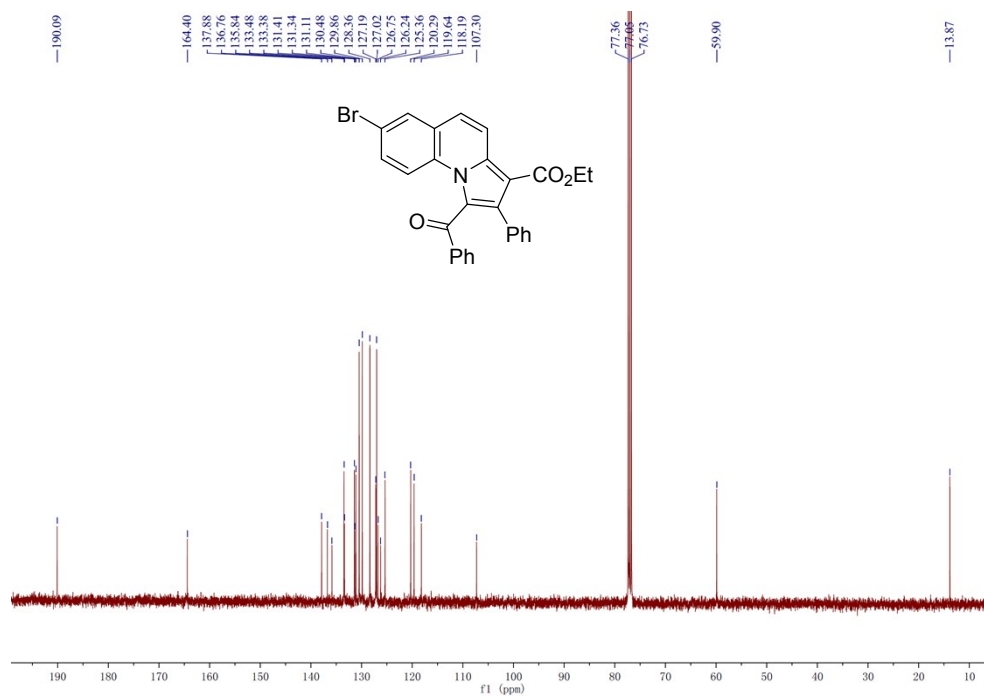
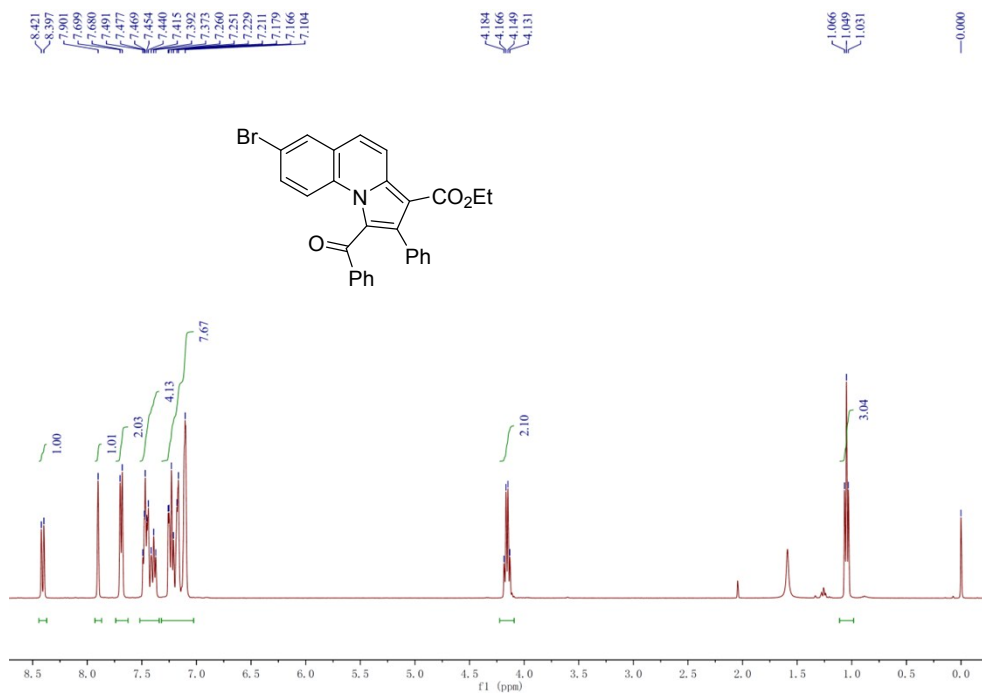
Ethyl 1-benzoyl-2-(4-methoxyphenyl)pyrrolo[1,2-a]quinoline-3-carboxylate (3e).



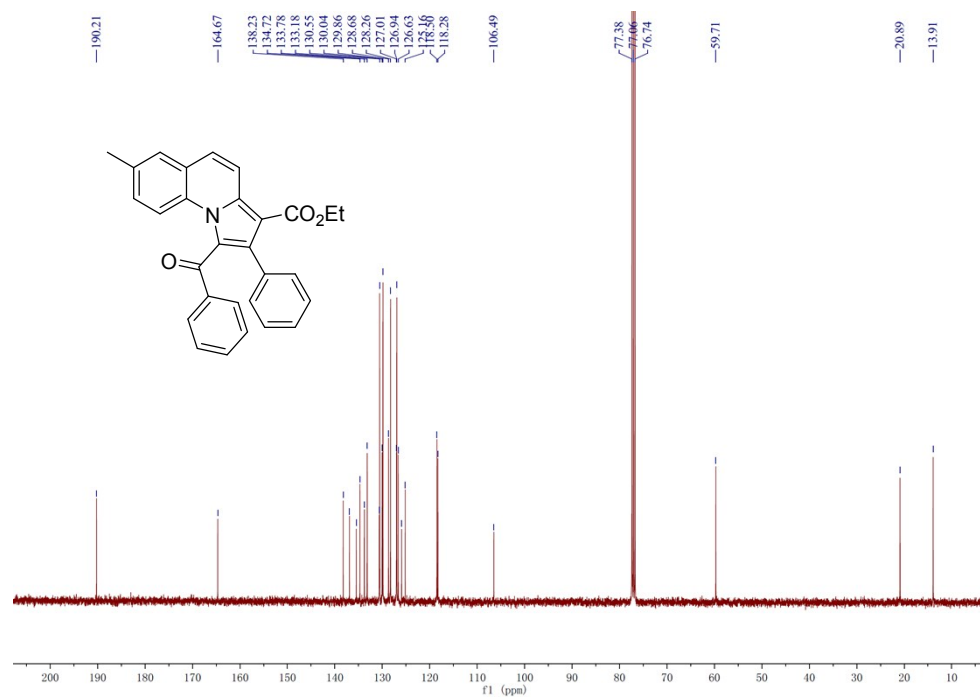
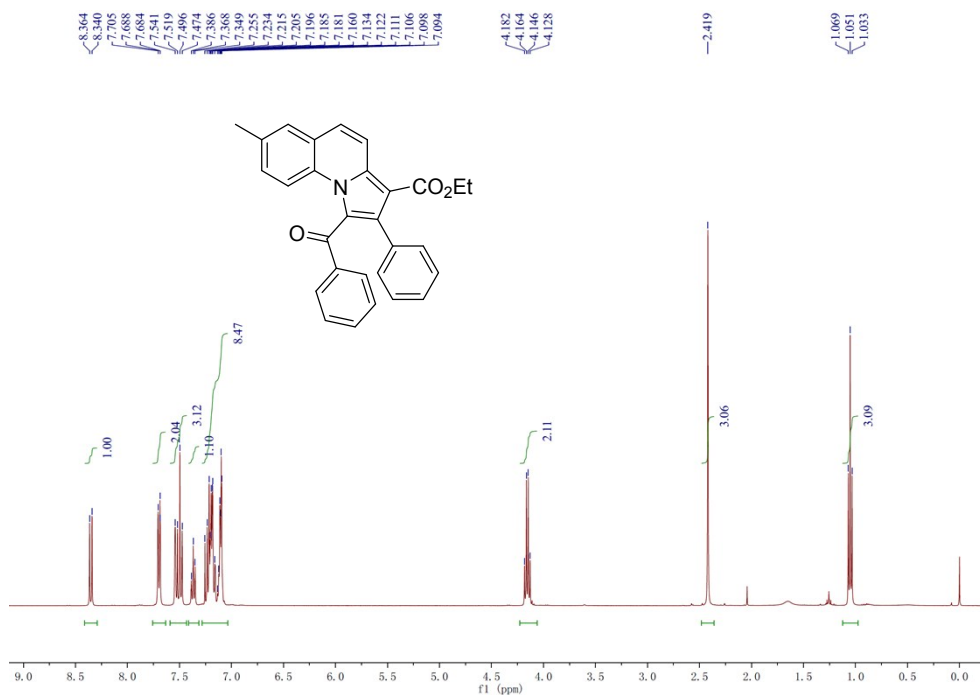
Ethyl 1-benzoyl-2-(2-methoxyphenyl)pyrrolo[1,2-a]quinoline-3-carboxylate (3f) .



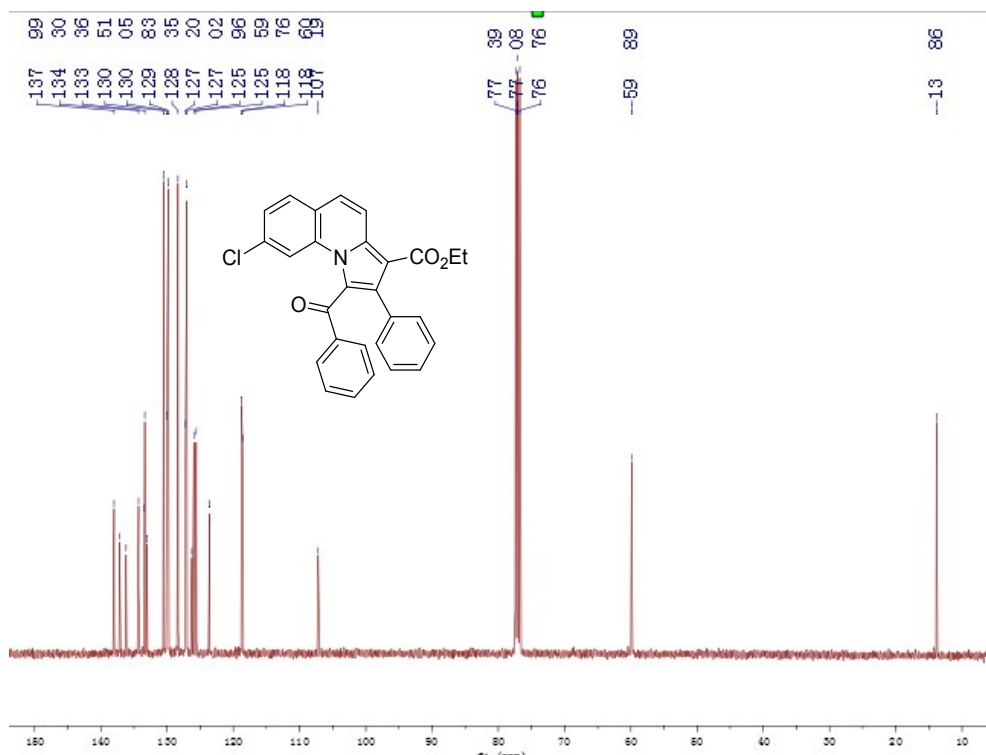
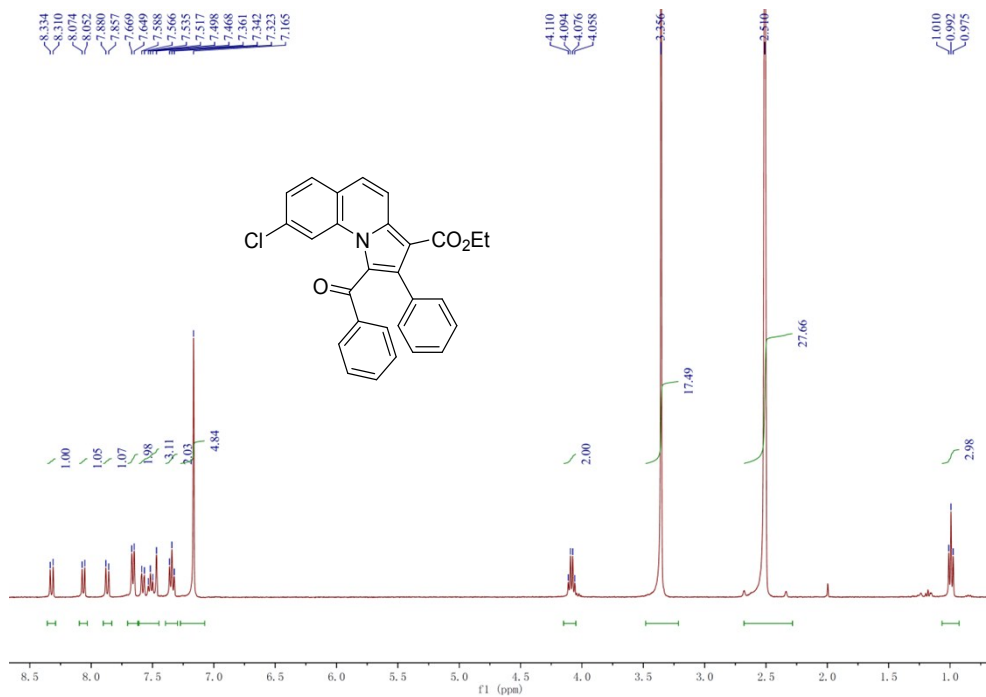
Ethyl 1-benzoyl-7-bromo-2-phenylpyrrolo[1,2-a]quinoline-3-carboxylate (3g).



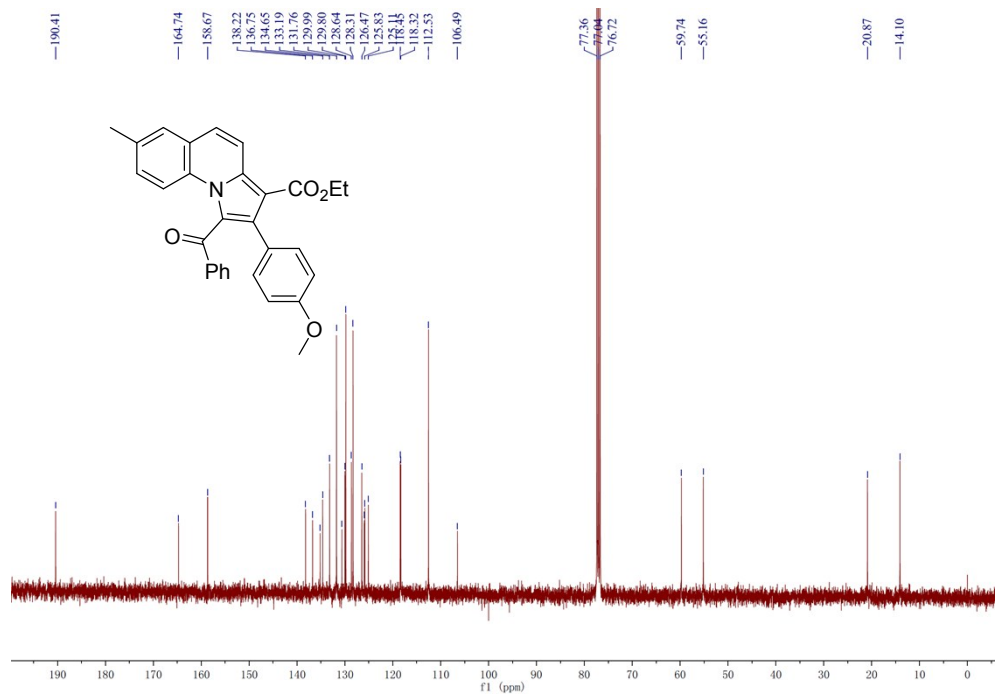
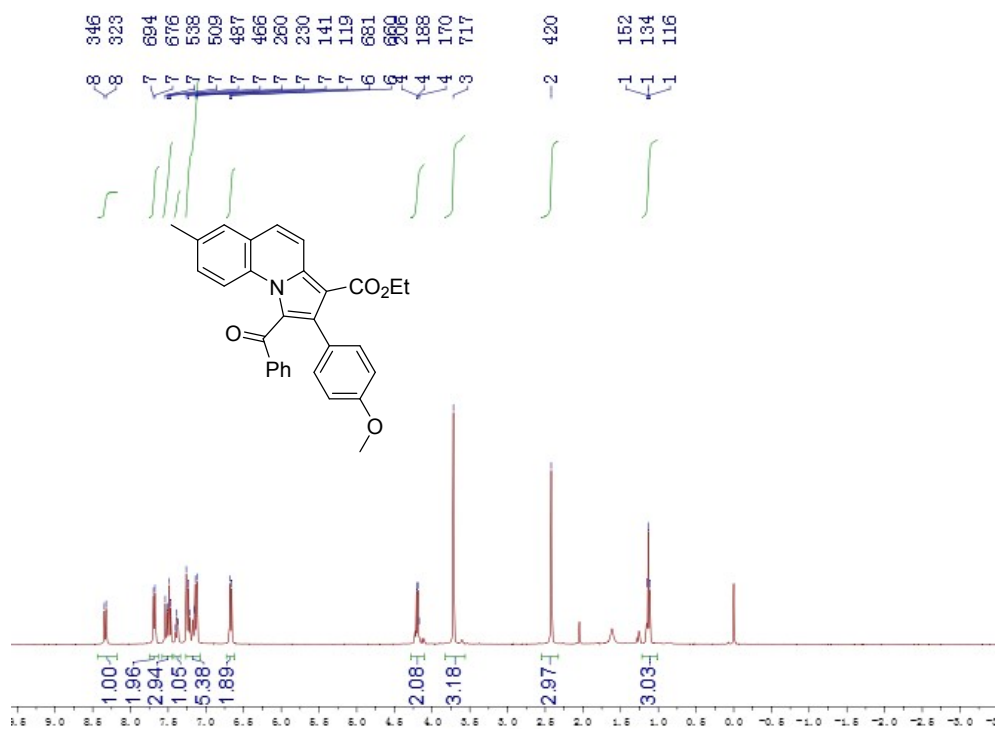
Ethyl 1-benzoyl-7-methyl-2-phenylpyrrolo[1,2-a]quinoline-3-carboxylate (3h).



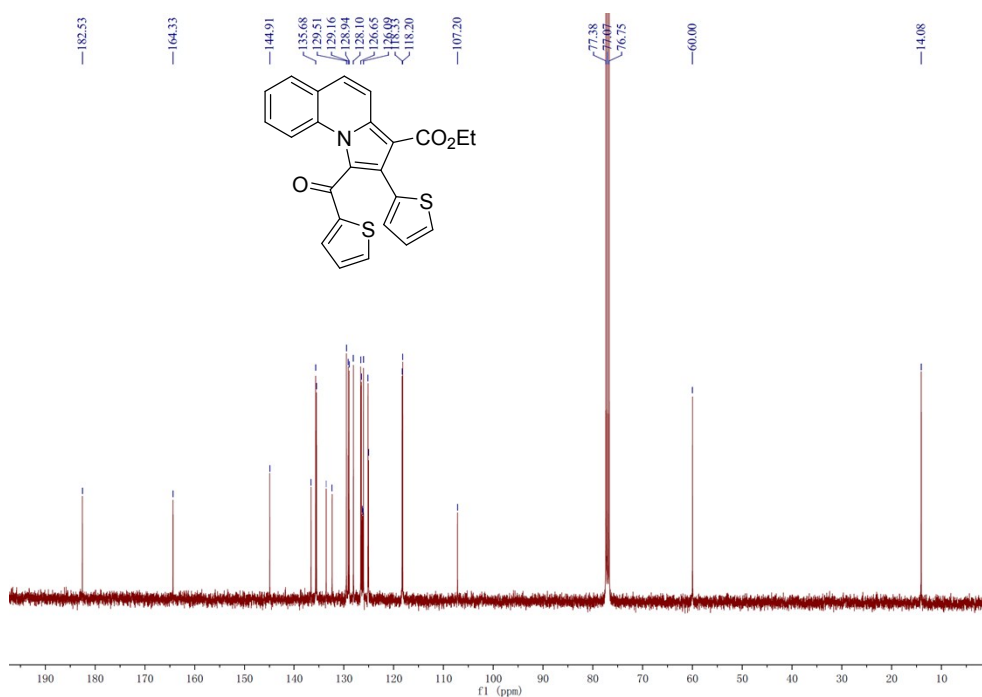
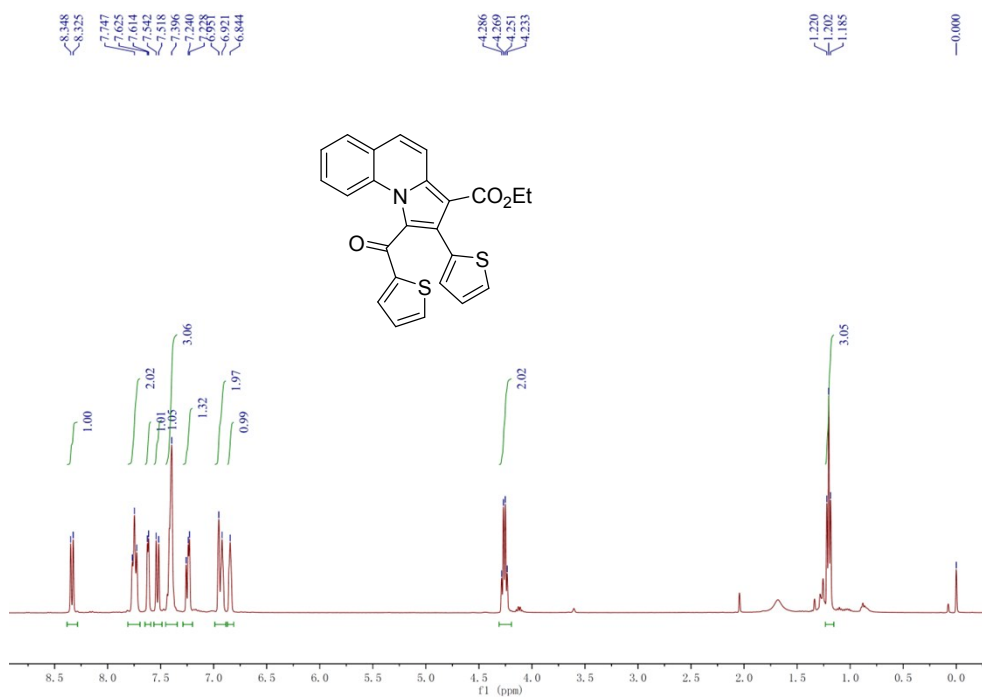
Ethyl 1-benzoyl-8-chloro-2-phenylpyrrolo[1,2-a]quinoline-3-carboxylate (3i).



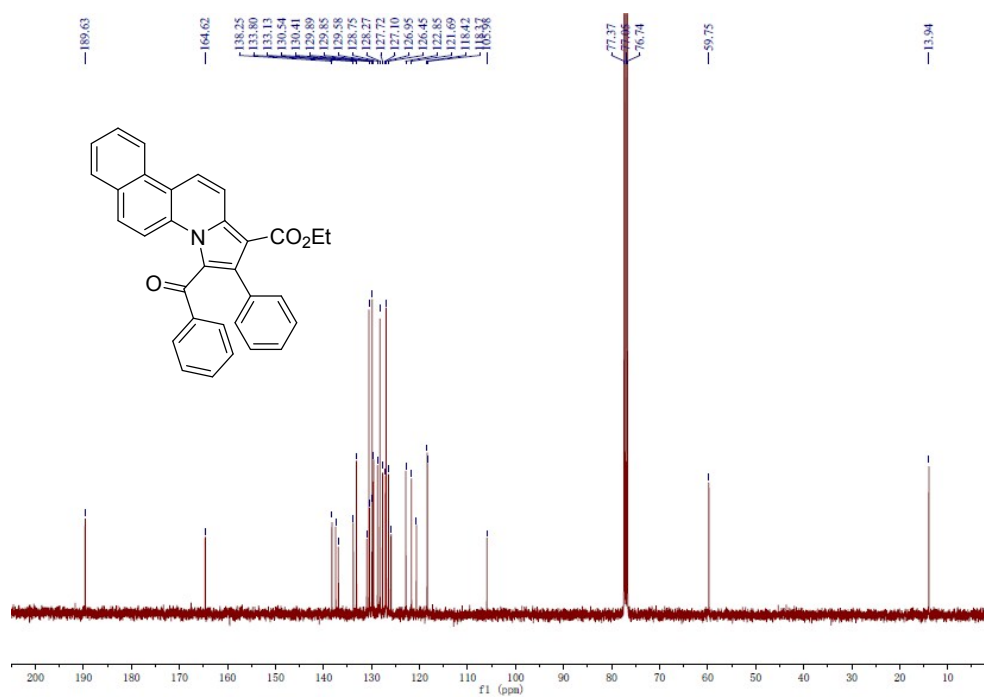
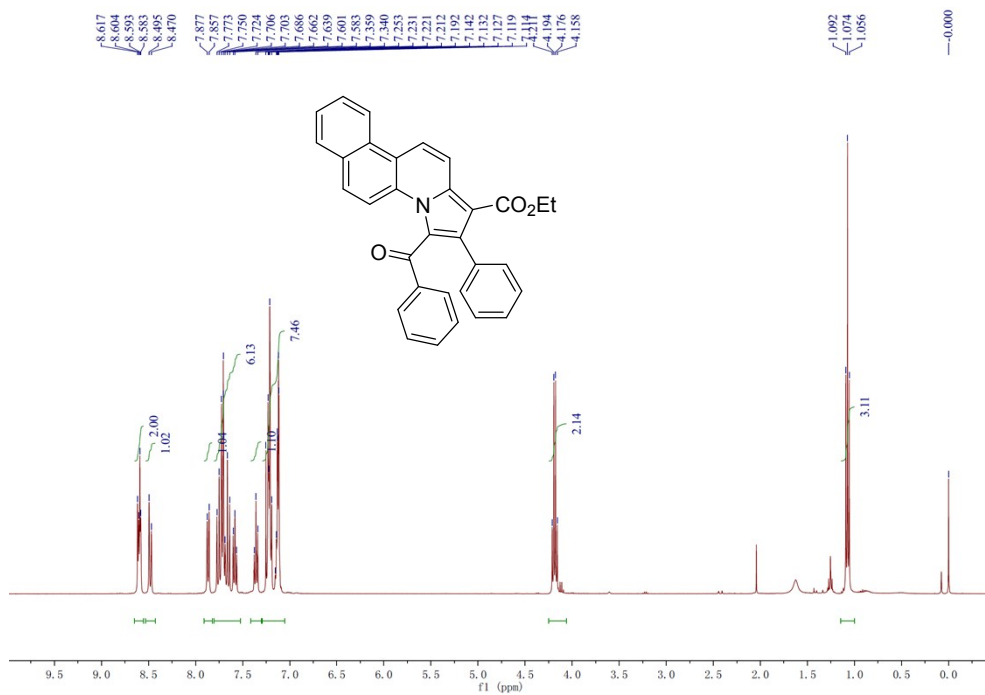
Ethyl 1-benzoyl-2-(4-methoxyphenyl)-7-methylpyrrolo[1,2-a]quinoline-3-Carboxylate (3j).



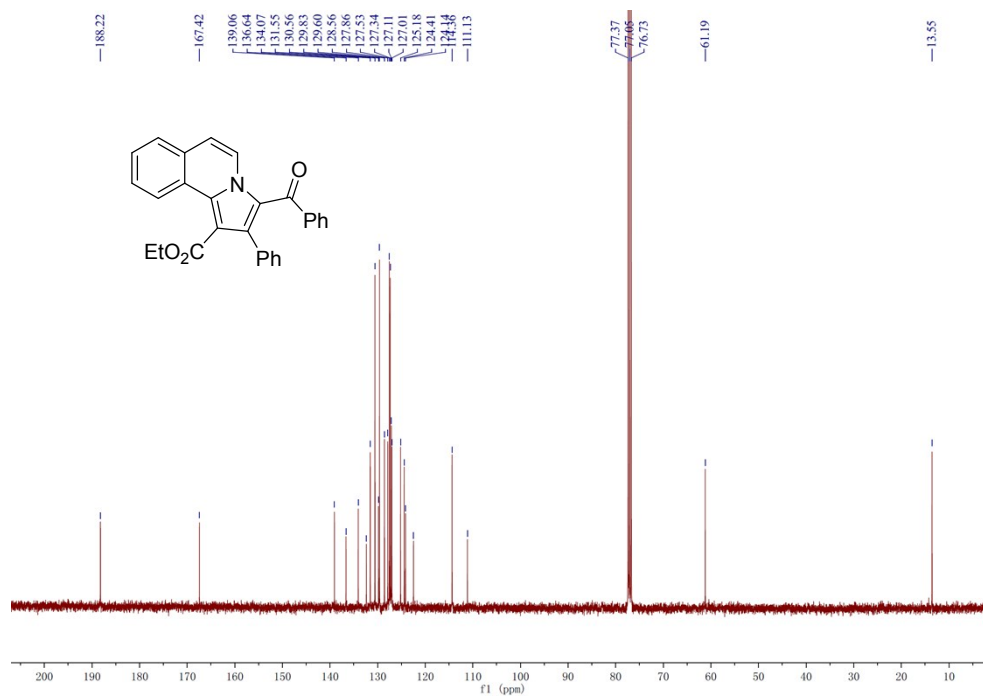
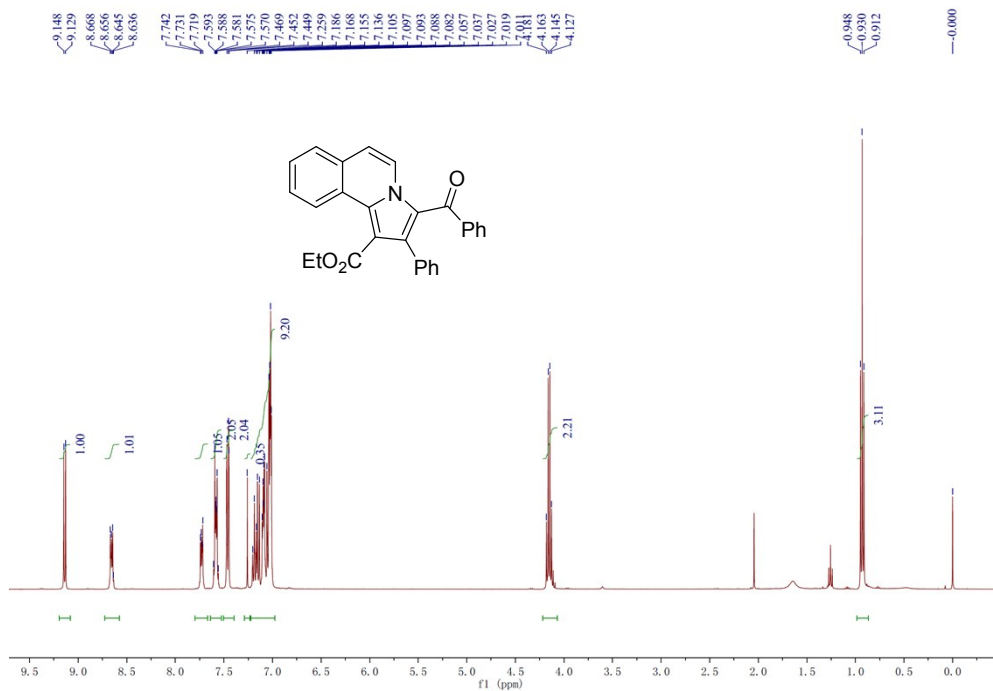
Ethyl 2-(thiophen-2-yl)-1-(thiophene-2-carbonyl)pyrrolo[1,2-a]quinoline-3-carboxylate (3k).



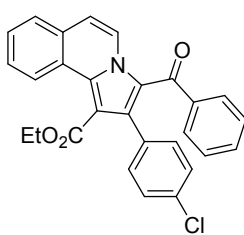
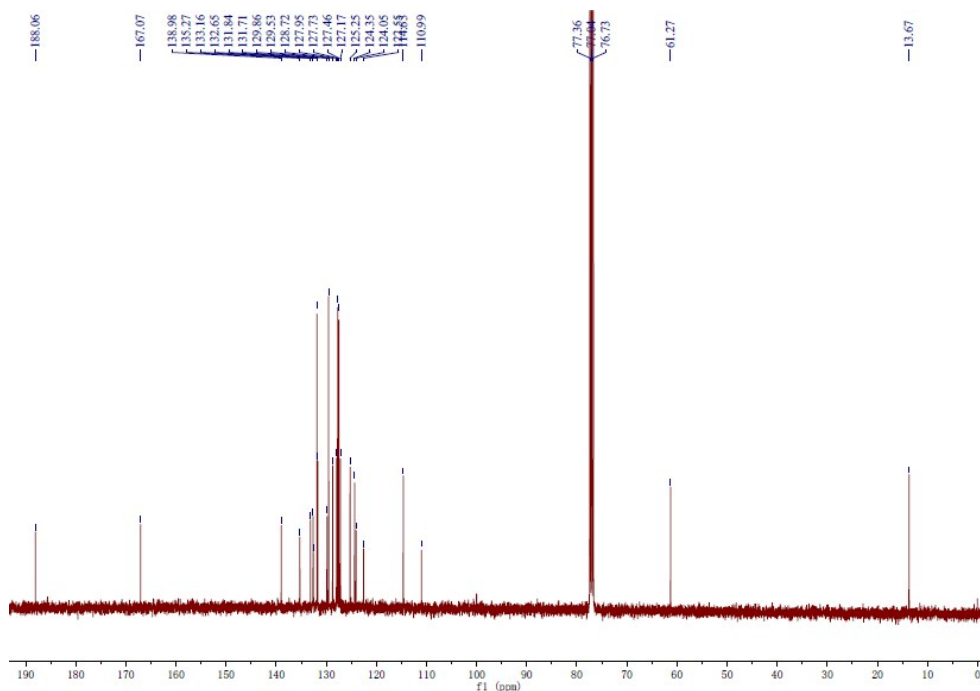
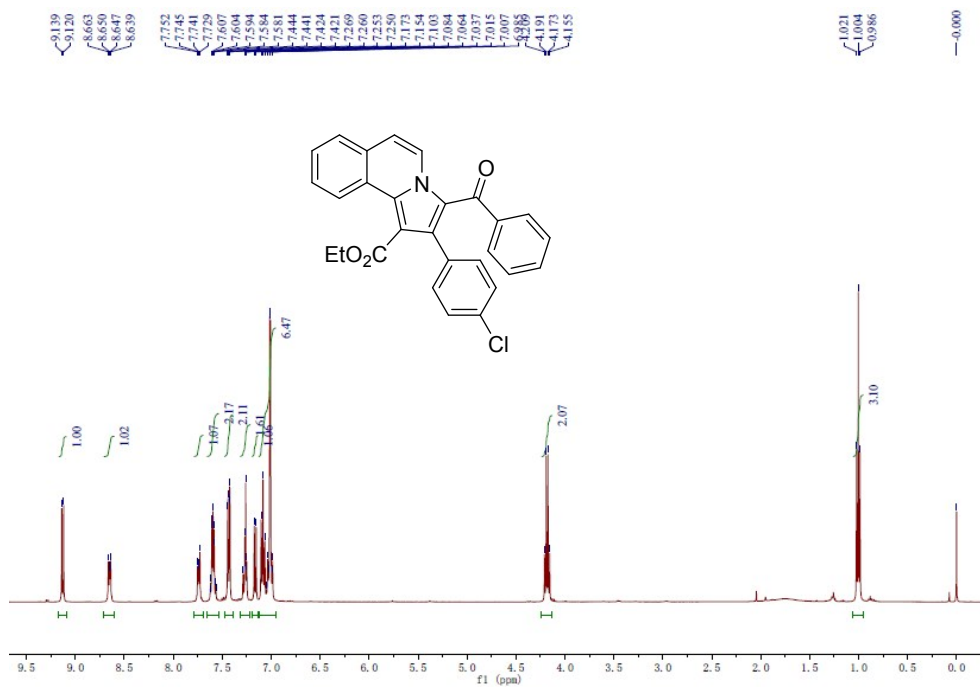
Ethyl 3-benzoyl-2-phenylbenzo[f]pyrrolo[1,2-a]quinoline-1-carboxylate (31).



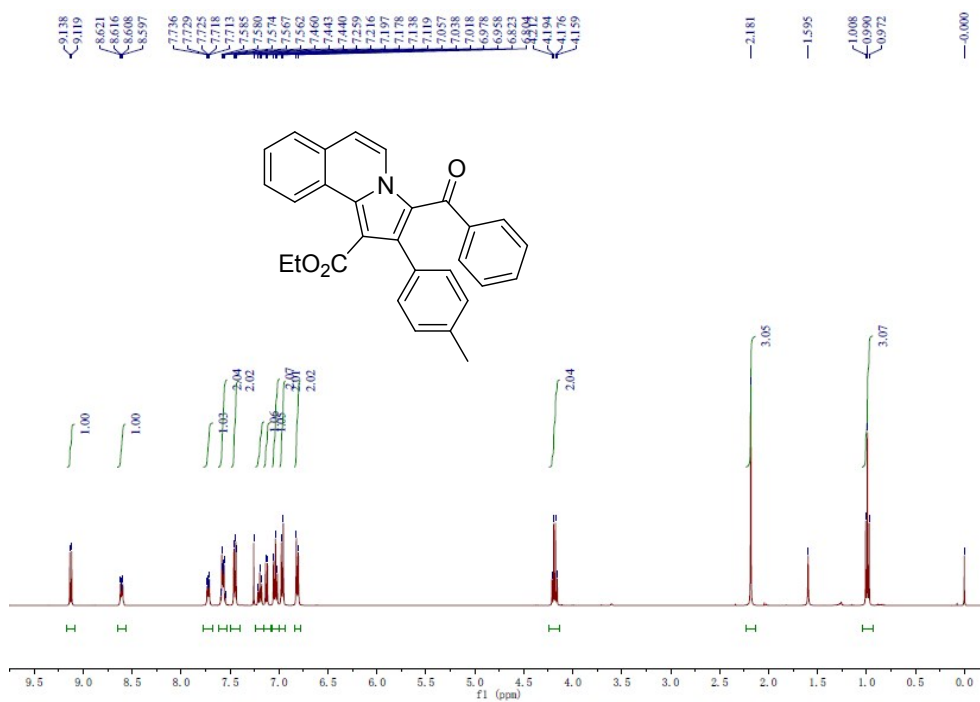
Ethyl 3-benzoyl-2-phenylpyrrolo[2,1-a]isoquinoline-1-carboxylate (5a).

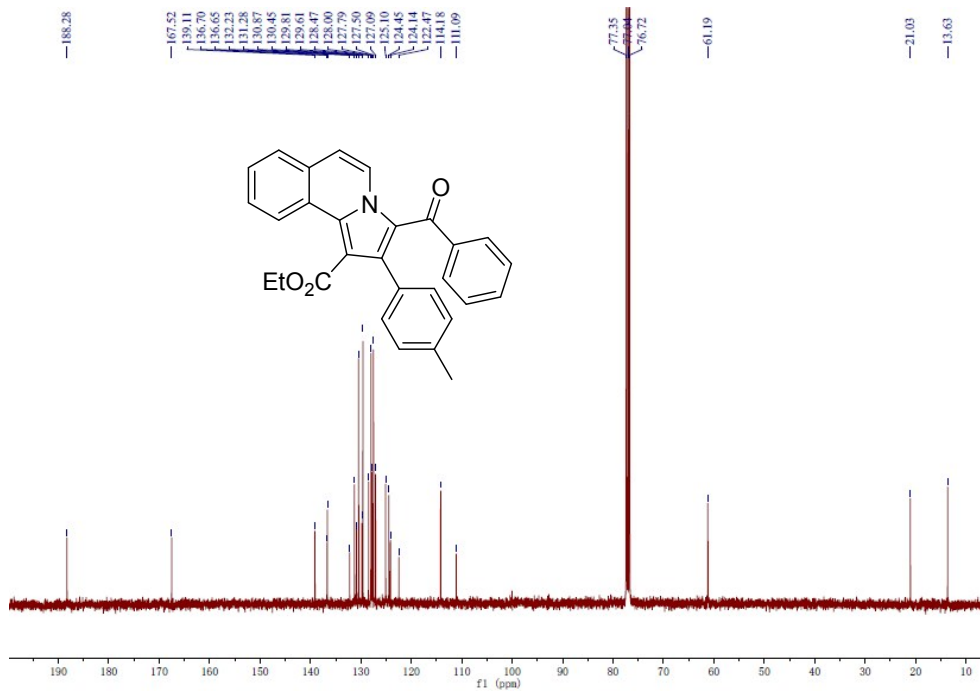


Ethyl 3-benzoyl-2-(4-chlorophenyl)pyrrolo[2,1-a]isoquinoline-1-carboxylate (5b).

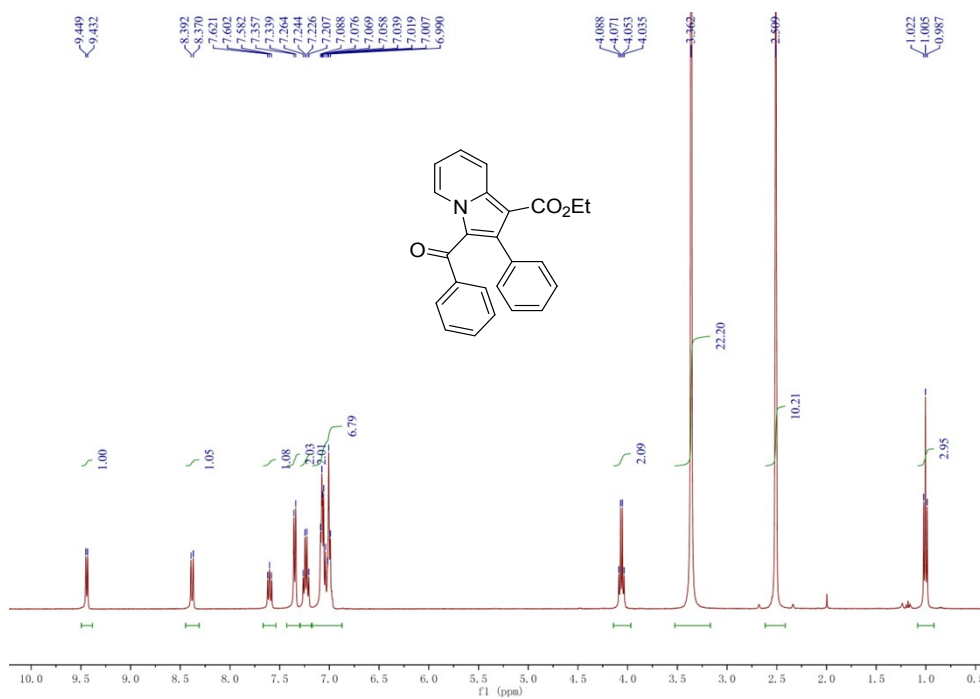


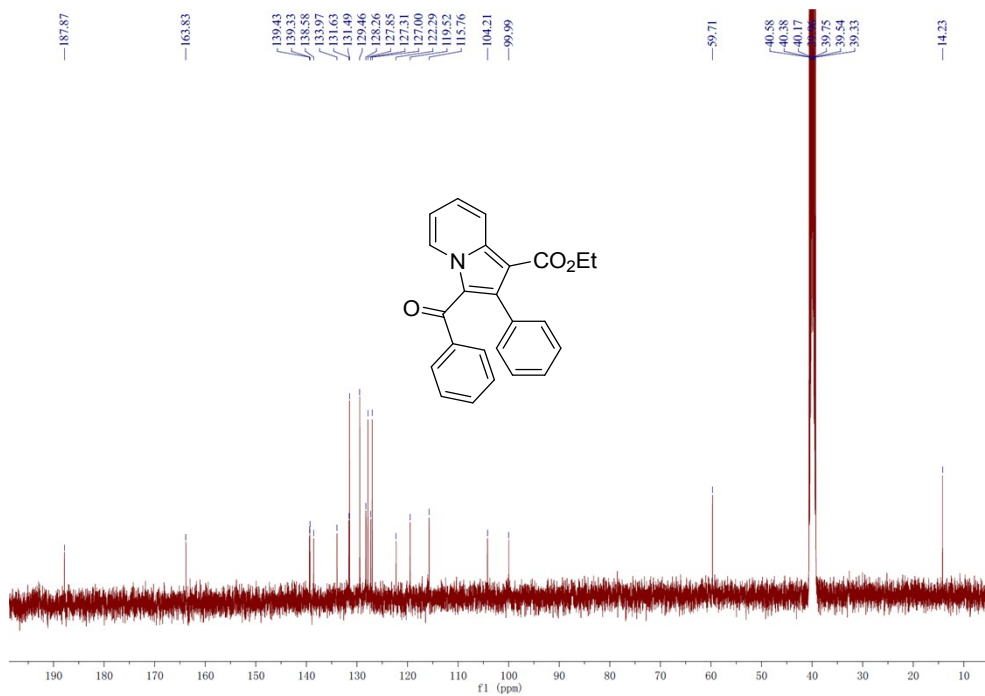
Ethyl 3-benzoyl-2-(p-tolyl)pyrrolo[2,1-a]isoquinoline-1-carboxylate (5c).



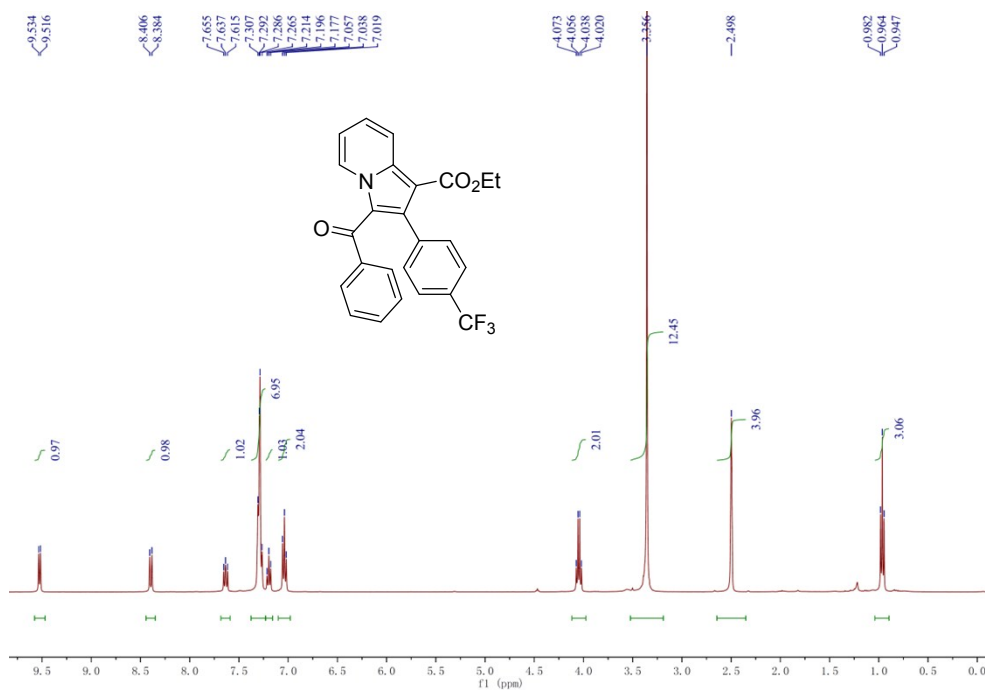


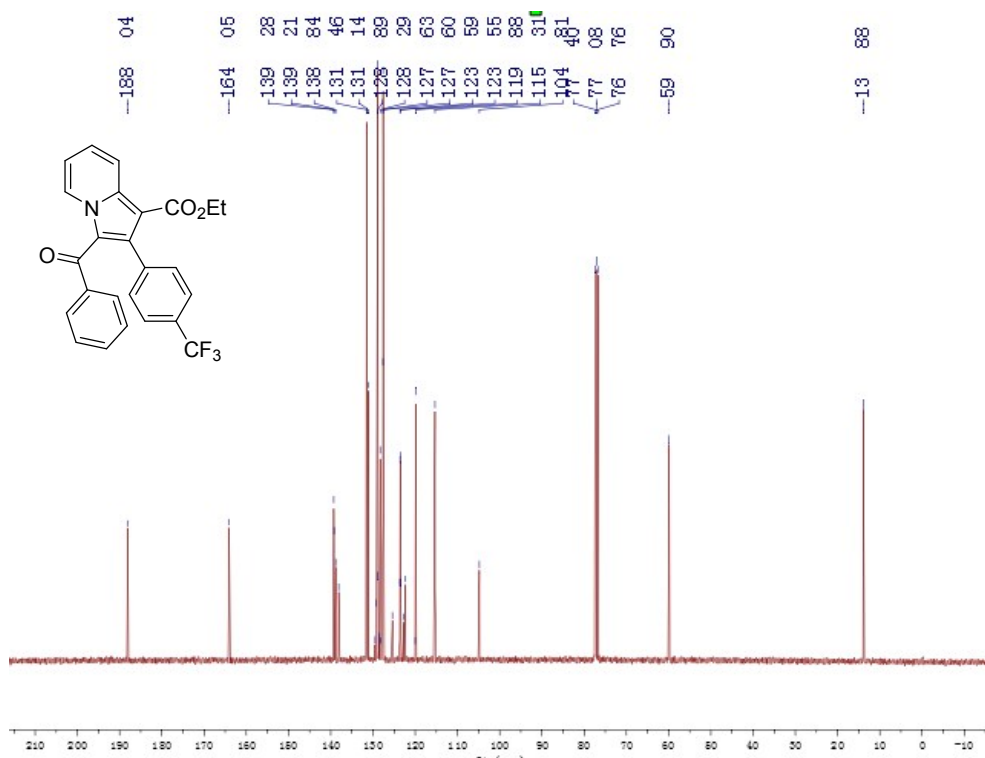
Ethyl 3-benzoyl-2-phenylindolizine-1-carboxylate (5d).



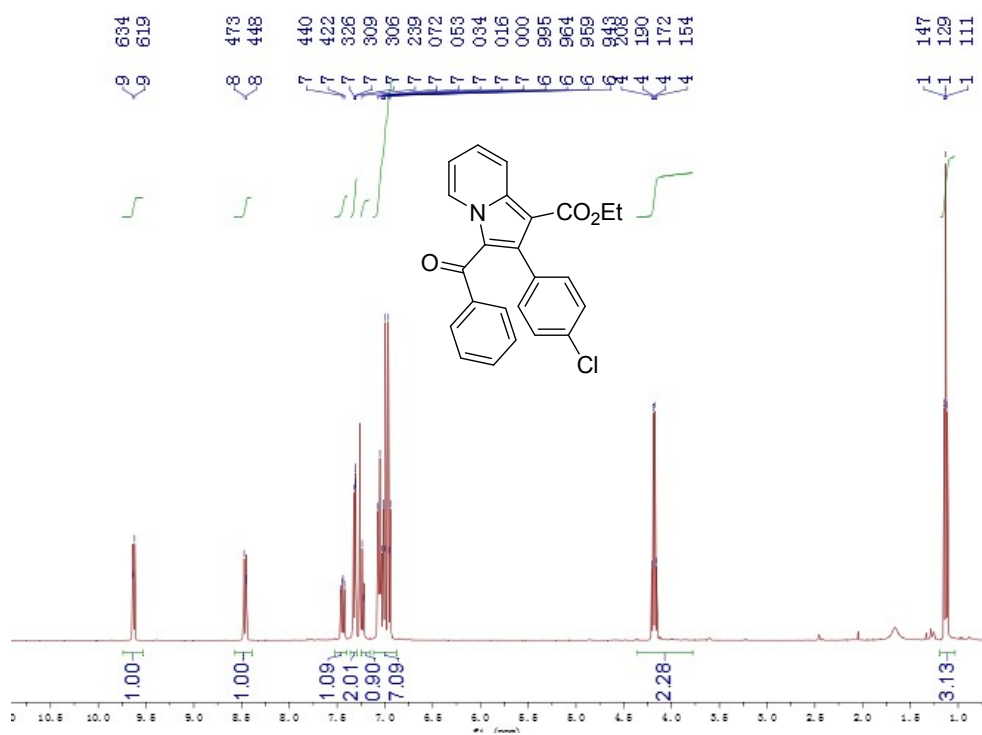


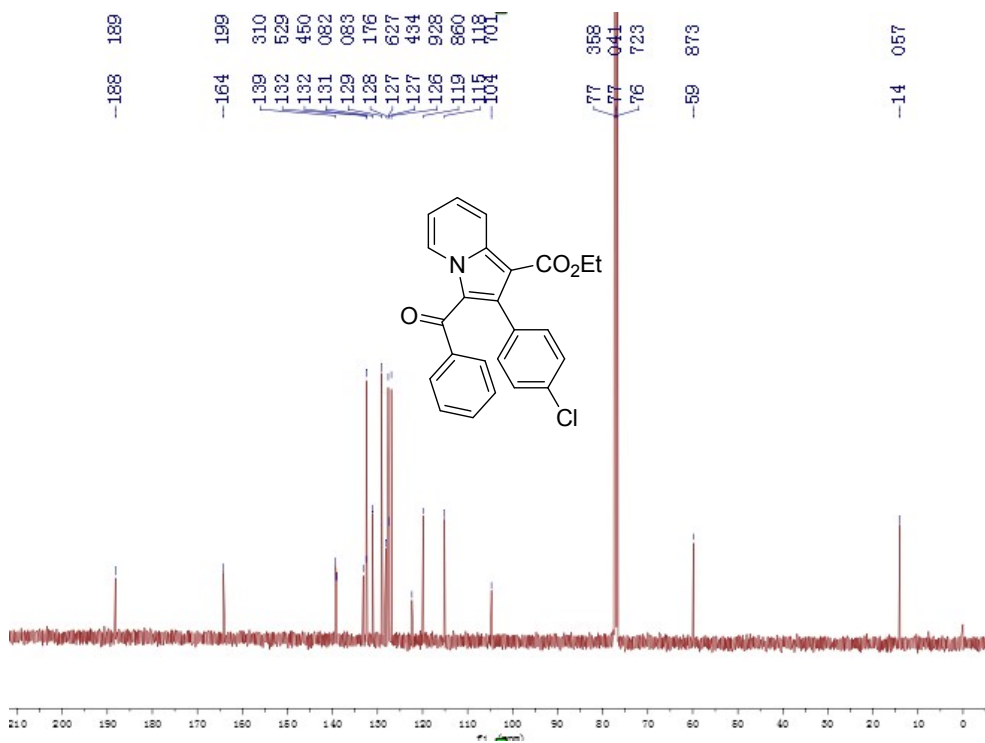
Ethyl 3-benzoyl-2-(4-(trifluoromethyl)phenyl)indolizine-1-carboxylate (5e).



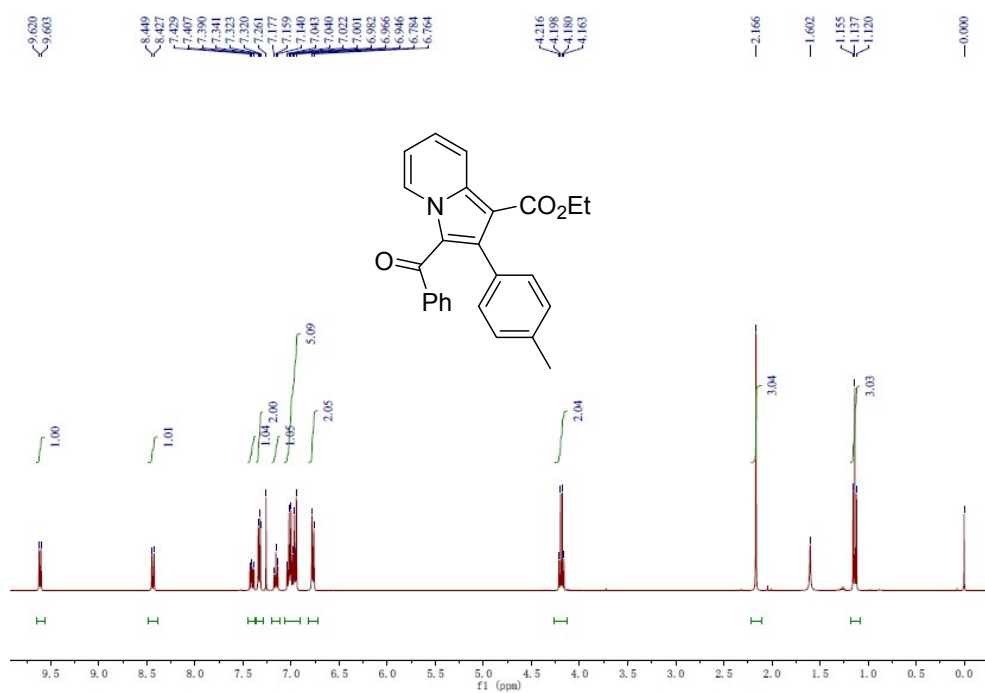


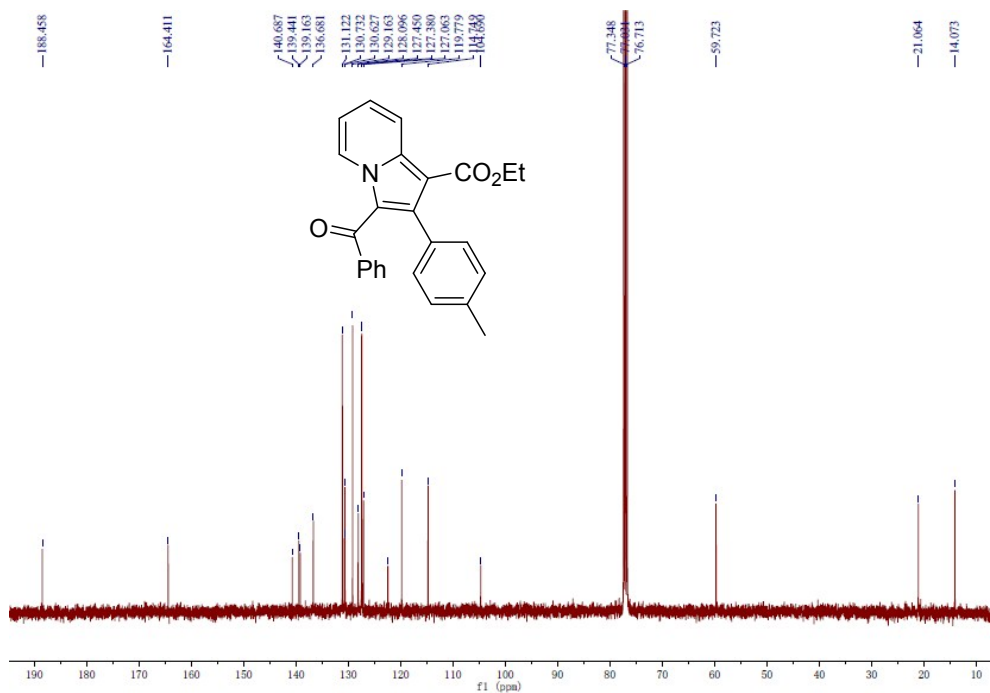
Ethyl 3-benzoyl-2-(4-chlorophenyl)indolizine-1-carboxylate (5f).



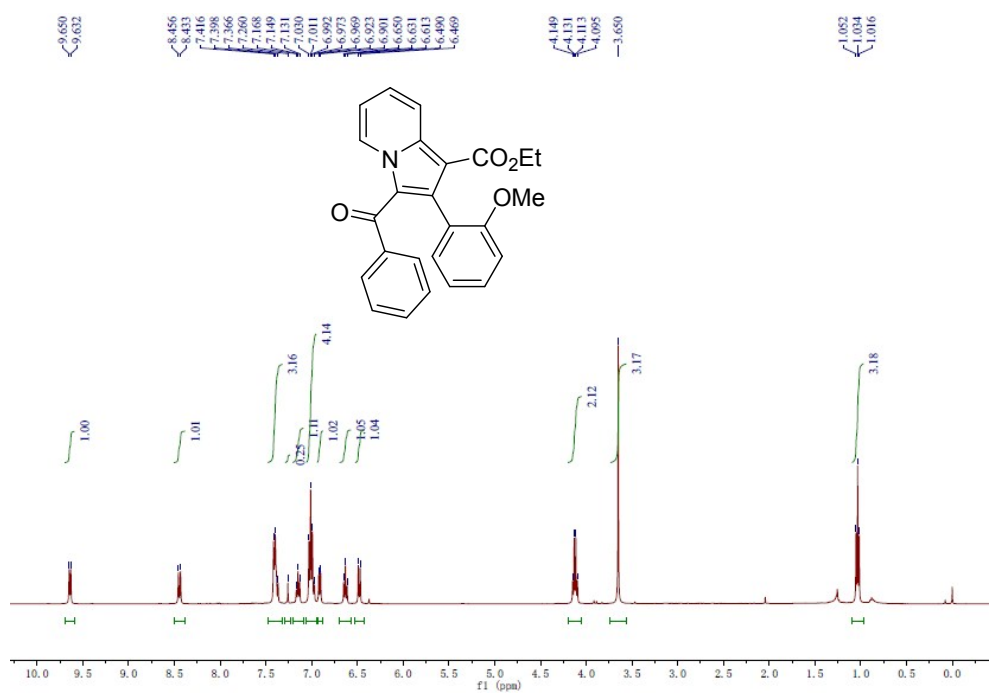


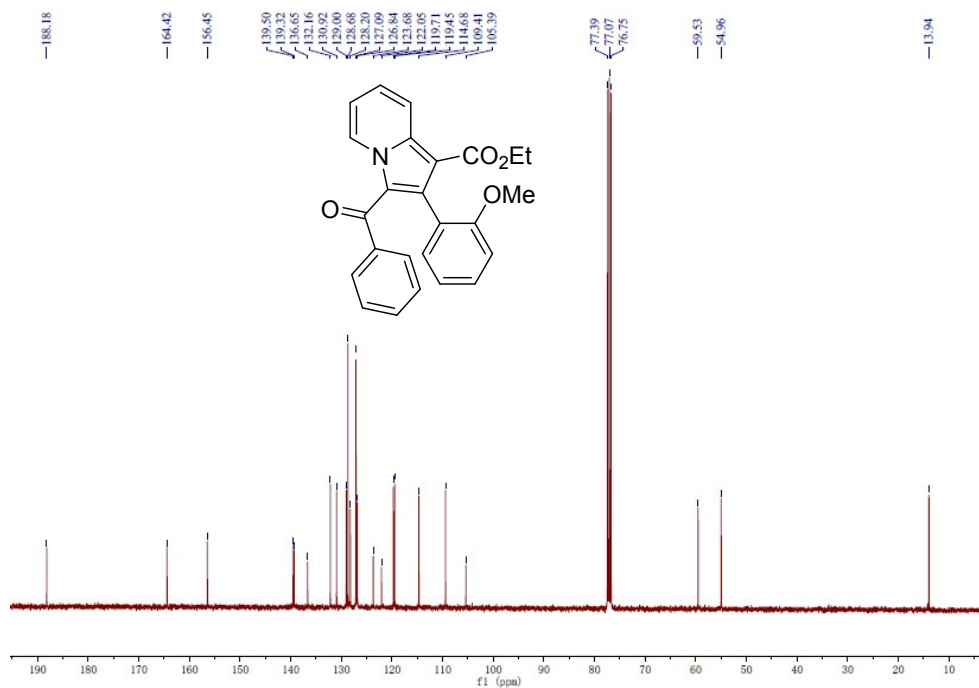
Ethyl 3-benzoyl-2-(p-tolyl)indolizine-1-carboxylate (5g).



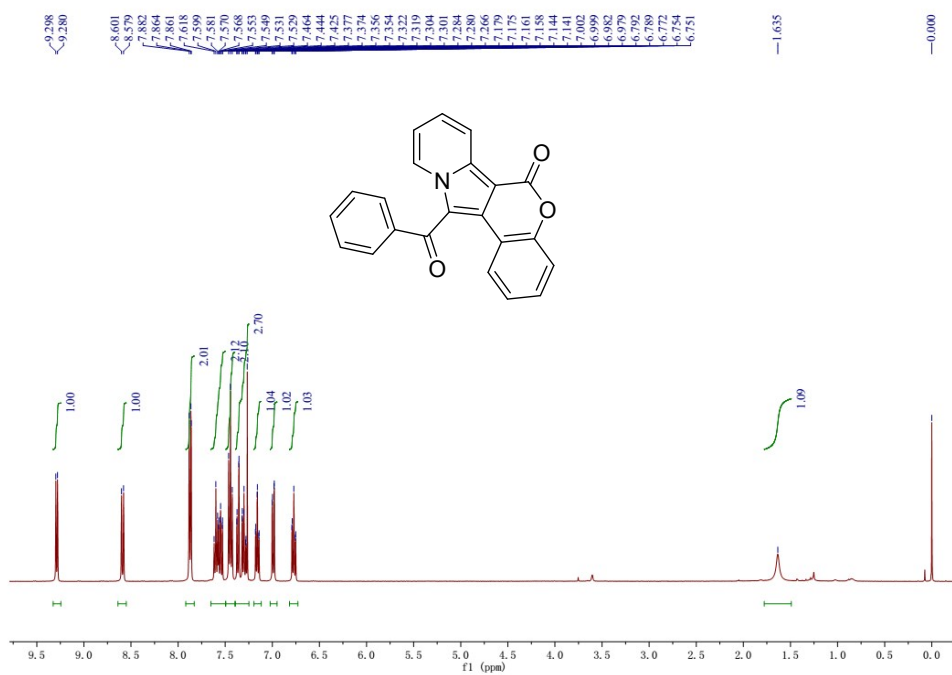


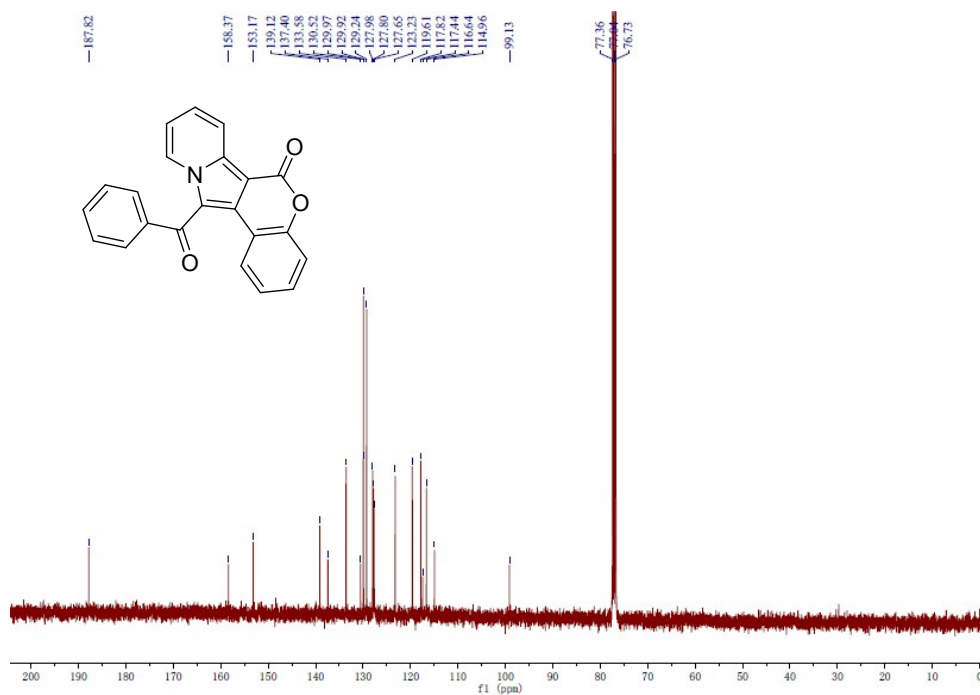
Ethyl 3-benzoyl-2-(2-methoxyphenyl)indolizine-1-carboxylate (5h).





6H-chromeno[3,4-a]indolizin-6-one (6h)





Ethyl 5-oxo-3,5-diphenyl-2-(pyridin-2-yl)pentanoate (6d)

