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Supporting Information

Rh(III)-Catalyzed Redox-Neutral Annulation of Azo and Diazo Compounds: One-step Access to Cinnolines

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1. General Information

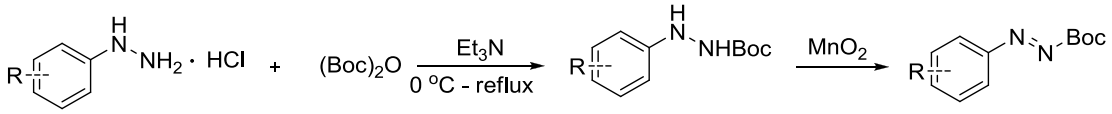
Reagents and Solvents: Rh, Pd and Cu catalysts, bases and additives were commercially available. PE refers to petroleum ether (b.p. 60-90 °C) and EA refers to ethyl acetate. All other starting materials and solvents were commercially available and were used without further purification unless otherwise stated.

Chromatography: Flash column chromatography was carried out using commercially available 200-300 mesh under pressure unless otherwise indicated. Gradient flash chromatography was conducted eluting with PE/EA or DCM/MeOH, they are listed as volume/volume ratios.

Data collection: ^{1}H and ^{13}C NMR spectra were collected on BRUKER AV-300 (300 MHz) spectrometer using $CDCl_3$ or DMSO-d_6 as solvent. Chemical shifts of ^{1}H NMR were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ = 0.00 ppm) with the solvent resonance as the internal standard ($CDCl_3$: δ = 7.26 ppm; DMSO-d_6: δ = 2.50 ppm). Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad single), coupling constant (Hz), and integration. Chemical shifts of ^{13}C NMR were reported in ppm with the solvent as the internal standard ($CDCl_3$: δ = 77.0 ppm; DMSO-d_6: δ = 40.5 ppm). Infrared spectra (IR) were recorded on a Thermo Scientific iS10 FT/IR spectrometer; absorptions are reported in reciprocal centimeters. High Resolution Mass measurement was performed on Agilent QTOF 6520 mass spectrometer with electron spray ionization (ESI) as the ion source. Melting point (mp) was measured on a microscopic melting point apparatus.

2. Preparation of Azo Substrates and Diazo Substrates

Azo substrates were synthesized from the corresponding phenylhydrazine hydrochloride as shown in **Scheme S1**.



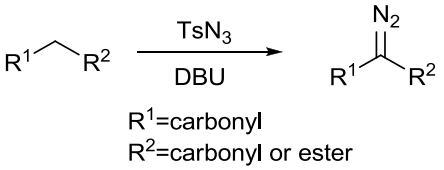
Scheme S1. Preparation of Azo Substrates

General Procedure:

10 mmol phenylhydrazine hydrochloride were dissolved in 20 mL DCM in a 100 mL round bottom flask, then 10 mL 1 mol/L Boc-anhydride solution in DCM were added at 0 °C. The reaction mixture was heated to reflux for 2 hours. After cooling to room temperature, the residue was extracted with DCM for 3 times. The combined organic layers were washed with water, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography on silica gel to afford the corresponding Boc-phenylhydrazine product in 80-90% yields. 5 mmol

Boc-phenylhydrazine were dissolved in 10 mL DCM, then 3.0 equivalent of activated MnO_2 was added at room temperature, the reaction mixture was stirred for 1 hour. The residue was filtrated and the filtrate was collected and concentrated at reduced pressure to afford corresponding azo substrates in 90-100% yields.

Diazo substrates were synthesized from the corresponding ketonic esters or 1,3 di-ketones as shown in **Scheme S2**.



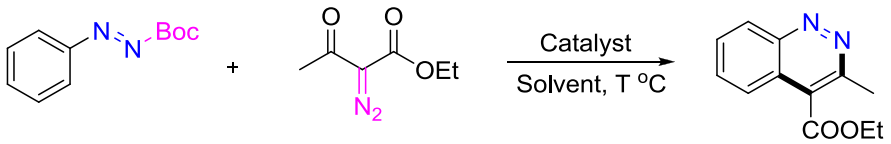
Scheme S2. Preparation of Diazo Substrates

To a solution of ketonic ester or 1,3 di-ketone (5 mmol) in CH_3CN, 6 mmol TsN_3 was added. Then the reaction mixture was cooled to 0 °C and a solution of DBU (6 mmol) in 10 mL CH_3CN was added dropwise. Next, the reaction temperature was raised to room temperature. After stirring for 3 hours, the residue was extracted with EA for 3 times. The combined organic layers were washed with water and brine sequentially, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography on silica gel to afford the corresponding product in 70-90% yields.

3. Optimization of Reaction Conditions

The reaction temperature and additives were screened as shown in **Table S1**.

Table S1.Optimization of Reaction Conditions.[a]

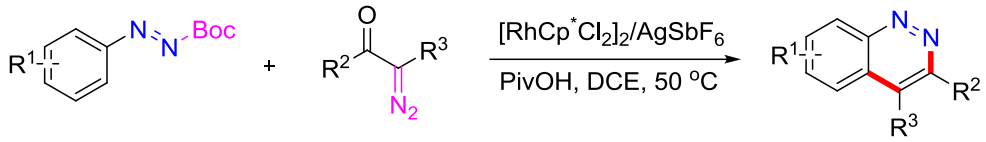


1c **2a** **3ca**

Entry	Catalyst	T (°C)	solvent	Yield (%)[b]
1	$(RhCp^*Cl_2)_2/AgSbF_6$	50	PivOH/tolune(1:4)	45
2	$(RhCp^*Cl_2)_2/AgSbF_6$	50	PivOH/DMF(1:4)	24
3	$(RhCp^*Cl_2)_2/AgSbF_6$	50	PivOH/DMSO(1:4)	28
4	$(RhCp^*Cl_2)_2/AgSbF_6$	50	PivOH/Oxane(1:4)	49
5	$(RhCp^*Cl_2)_2/AgSbF_6$	50	PivOH/CH_3CN(1:4)	51
6	$(RhCp^*Cl_2)_2/AgSbF_6$	50	PivOH/MeOH(1:4)	trace
7	$(RhCp^*Cl_2)_2/AgSbF_6$	25	PivOH/DCE(1:4)	57
8	$(RhCp^*Cl_2)_2/AgSbF_6$	75	PivOH/DCE(1:4)	65
9	$(RhCp^*Cl_2)_2/AgSbF_6$	100	PivOH/DCE(1:4)	43

[a] Reaction conditions: **1c** (0.75 mmol, 1.5 equiv); **2a** (0.5 mmol, 1.0 equiv); $(Cp^*RhCl_2)_2$ (0.0125 mmol, 2.5 mol%), Ag salts (0.1 mmol, 20 mol%), solvent (2 mL), 24 hours under air atmosphere. [b] Yields were determined by ^1H NMR.

4. *General Procedure for Rhodium-Catalyzed Annulations*



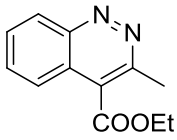
1 2 3

a) General Procedure:

A sealed tube was charged with azo substrate (0.75 mmol, 1.5 equiv), $(RhCp^*Cl_2)_2$ (0.0125 mmol, 2.5 mol%), $AgSbF_6$ (0.1 mmol, 0.2 equiv), diazo (0.5 mmol, 1.0 equiv), 2 mL PivOH/DCE (v:v = 1: 20). The reaction mixture was vigorously stirred at 50 °C (oil temperature) for 24 hours. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and filtered through a plug of celite. The mixture was concentrated *in vacuo* and purified by flash chromatography on silica gel to afford the desired product.

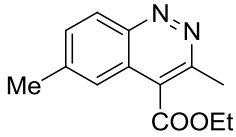
b) Characterization of theProducts

ethyl 3-methylcinnoline-4-carboxylate (3ca)



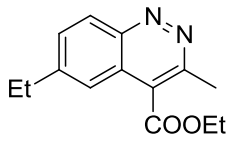
Yield 86%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 – 8.42 (m, 1H), 7.92 – 7.82 (m, 1H), 7.81 – 7.68 (m, 2H), 4.56 (q, *J* = 7.2 Hz, 2H), 2.98 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 149.6, 149.2, 132.2, 130.2, 129.9, 129.1, 123.6, 122.0, 62.4, 20.7, 14.2 ppm; IR (KBr) 3061, 2979, 2932, 1807, 1731, 1450, 1300, 1118, 1032 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{12}N_2O_2+H]^+$ 217.0972, found 217.0971.

ethyl 3,6-dimethylcinnoline-4-carboxylate (3fa)



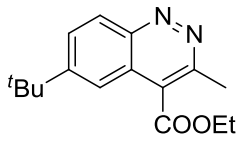
Yield 83%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.6 Hz, 1H), 7.75 – 7.45 (m, 2H), 4.60 (q, *J* = 7.1 Hz, 2H), 2.98 (s, 3H), 2.56 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 149.5, 148.4, 143.2, 132.4 129.7, 124.1, 122.3, 121.8, 62.2, 22.3, 20.7, 14.2 ppm; IR (KBr) 2979, 2932, 2896, 1727, 1623, 1484, 1375, 1233, 1106, 1071 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{14}N_2O_2+H]^+$ 231.1128, found 231.1130.

ethyl 6-ethyl-3-methylcinnoline-4-carboxylate (3ga)



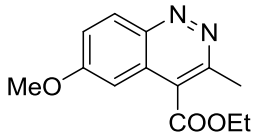
Yield 85%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, *J* = 9.2 Hz, 1H), 7.77 – 7.51 (m, 2H), 4.58 (q, *J* = 7.2 Hz, 2H), 2.97 (s, 3H), 2.84 (q, *J* = 7.6 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.6 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 149.5, 148.6, 131.4, 129.9, 124.2, 122.4, 120.5, 62.2, 29.4, 20.7, 14.7, 14.2 ppm; IR (KBr) 2979, 2930, 2867, 1728, 1625, 1376, 1231, 1055 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{16}N_2O_2+H]^+$ 245.1285, found 245.1283.

ethyl 6-tert-butyl-3-methylcinnoline-4-carboxylate (3ha)



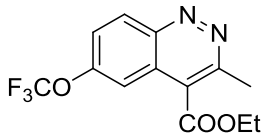
Yield 82% ; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (d, *J* = 9.0 Hz, 1H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.74 (s, 1H), 4.54 (q, *J* = 7.1 Hz, 2H), 2.93 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H), 1.35 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 155.5, 149.7, 148.4, 129.6, 129.2, 124.6, 122.1, 117.9, 62.1, 35.6, 30.6, 20.7, 14.3 ppm; IR (KBr) 2966, 2902, 2873, 1729, 1620, 1483, 1466, 1287, 1264, 1100, 1064 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{20}N_2O_2+H]^+$ 273.1598, found 273.1595.

ethyl 6-methoxy-3-methylcinnoline-4-carboxylate (3ia)



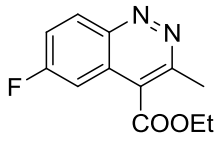
Yield 93%; Light yellow solid, m.p. 81-83 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, *J* = 9.3 Hz, 1H), 7.38 (dd, *J* = 9.3, 2.6 Hz, 1H), 7.08 (d, *J* = 2.5 Hz, 1H), 4.58 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 2.96 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 161.9, 150.0, 146.8, 131.8, 124.5, 123.9, 123.2, 99.7, 62.0, 55.7, 20.9, 14.2 ppm; IR (KBr) 3414, 2981, 2925, 1712, 1619, 1467, 1240, 1019 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{14}N_2O_3+H]^+$ 247.1077, found 247.1078.

ethyl 3-methyl-6-(trifluoromethoxy)cinnoline-4-carboxylate (3ja)



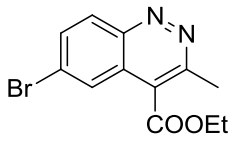
Yield 80%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, *J* = 9.3 Hz, 1H), 7.76 (d, *J* = 0.9 Hz, 1H), 7.61 (dd, *J* = 9.3, 2.0 Hz, 1H), 4.57 (q, *J* = 7.1 Hz, 2H), 3.01 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 151.0, 147.4, 133.2, 123.8, 123.1, 122.0, 118.5, 112.8, 62.6, 21.0, 14.1 ppm; IR (KBr) 3097, 2985, 2938, 1730, 1625, 1484, 1446, 1376, 1261, 1096, 1070 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{11}F_3N_2O_3+H]^+$ 301.0795, found 301.0797.

ethyl 6-fluoro-3-methylcinnoline-4-carboxylate (3ka)



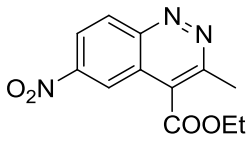
Yield 88%; Light yellow solid, m.p. 54-56 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 – 8.48 (m, 1H), 7.62 – 7.47 (m, 2H), 4.56 (q, *J* = 7.1 Hz, 2H), 2.99 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 165.4, 162.3, 162.0, 150.4, 147.0, 133.7, 133.6, 123.9, 121.2, 120.9, 115.6, 115.3, 114.1, 114.0, 107.2, 106.9, 62.5, 21.0, 14.2 ppm; IR (KBr) 3086, 2985, 2932, 2850, 1718, 1624, 1486, 1375, 1265, 1233, 1189, 1070 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{11}FN_2O_2+H]^+$ 235.0877, found 235.0879.

ethyl 6-bromo-3-methylcinnoline-4-carboxylate (3la)



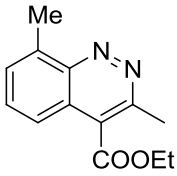
Yield 83%; Light yellow solid, m.p. 79-84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (d, *J* = 9.0 Hz, 1H), 8.07 (d, *J* = 1.8 Hz, 1H), 7.80 (dd, *J* = 9.0, 1.9 Hz, 1H), 4.54 (q, *J* = 7.1 Hz, 2H), 2.96 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 150.6, 147.7, 133.7, 131.8, 127.6, 126.0, 123.1, 123.0, 62.6, 21.0, 14.3 ppm; IR (KBr) 3091, 2979, 2902, 1724, 1599, 1470, 1411, 1366, 1264, 1098, 1076, 1023 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{11}BrN_2O_2+H]^+$ 295.0077, found 295.0076.

ethyl 3-methyl-6-nitrocinnoline-4-carboxylate (3ma)



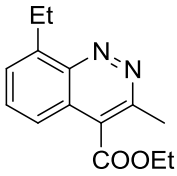
Yield 37%; Light yellow solid, m.p. 186-188 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (d, *J* = 2.3 Hz, 1H), 8.75 (d, *J* = 9.3 Hz, 1H), 8.53 (dd, *J* = 9.3, 2.3 Hz, 1H), 4.64 (q, *J* = 7.1 Hz, 2H), 3.10 (s, 3H), 1.52 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 152.0, 149.0, 148.8, 132.8, 127.1, 125.8, 123.3, 121.5, 63.1, 21.1, 14.3 ppm; IR (KBr) 3014, 1716, 1602, 1558, 1372, 1347, 1346, 1291, 1214, 1134, 1053, 997, 813 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{11}N_3O_4+H]^+$ 262.0822, found 262.0822.

ethyl 3,8-dimethylcinnoline-4-carboxylate (3na)



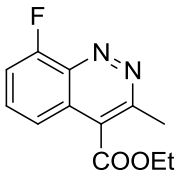
Yield 91%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.3 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 6.7 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 2.86 (d, *J* = 1.8 Hz, 6H), 1.33 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 149.1, 148.2, 138.6, 132.1, 129.7, 124.7, 122.0, 121.3, 62.2, 20.6, 17.6, 14.2 ppm; IR (KBr) 2991, 2956, 2920, 1721, 1540, 1452, 1371, 1293, 1267, 1251, 1230, 1107 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{14}N_2O_2+H]^+$ 231.1128, found 231.1129.

ethyl 8-ethyl-3-methylcinnoline-4-carboxylate (3oa)



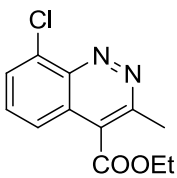
Yield 96%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 6.6 Hz, 1H), 4.50 (q, *J* = 7.1 Hz, 2H), 3.46 (q, *J* = 7.5 Hz, 2H), 2.93 (s, 3H), 1.42 – 1.34 (m, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 149.1, 147.6, 144.4, 132.4, 128.2, 124.9, 122.1, 121.3, 62.2, 24.3, 20.6, 15.3, 14.2 ppm; IR (KBr) 2973, 2926, 2879, 1729, 1370, 1274, 1239, 1129, 1105 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{16}N_2O_2+H]^+$ 245.1285, found 245.1284.

ethyl 8-fluoro-3-methylcinnoline-4-carboxylate (3pa)



Yield 80%; Light yellow solid, m.p. 53-55 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 – 7.49 (m, 2H), 7.41 – 7.27 (m, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 2.90 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 160.2, 156.7, 150.7, 140.3, 132.5, 132.4, 124.0, 123.4, 119.5, 119.5, 113.8, 113.5, 62.6, 20.7, 14.2 ppm; IR (KBr) 3086, 3015, 2985, 1717, 1627, 1444, 1376, 1256, 1109 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{11}FN_2O_2+H]^+$ 235.0877, found 235.0878.

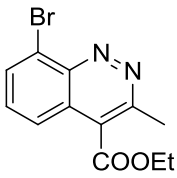
ethyl 8-chloro-3-methylcinnoline-4-carboxylate (3qa)



Yield 82%; Light yellow solid, m.p. 60-62 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.3, 0.9 Hz, 1H), 7.67 (dd, *J* = 8.5, 0.9 Hz, 1H), 7.53 (dd, *J* = 8.5, 7.5 Hz, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 2.90 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 150.6, 145.3, 135.2, 132.0, 130.0, 124.4, 123.6, 122.8, 62.6, 20.7, 14.2

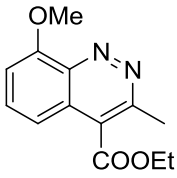
ppm; IR (KBr) 2997, 2962, 2938, 1731, 1608, 1530, 1369, 1287, 1259, 1228, 1198, 1106 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{11}ClN_2O_2+H]^+$ 251.0582, found 251.0581.

ethyl 8-bromo-3-methylcinnoline-4-carboxylate (3ra)



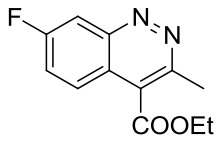
Yield 91%; Light yellow solid, m.p. 57-59 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.3, 0.6 Hz, 1H), 7.76 (dd, *J* = 8.5, 0.8 Hz, 1H), 7.50 (dd, *J* = 8.4, 7.5 Hz, 1H), 4.50 (q, *J* = 7.1 Hz, 2H), 2.94 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 150.6, 146.0, 133.7, 132.3, 126.2, 123.8, 123.6, 62.6, 20.7, 14.2 ppm; IR (KBr) 3074, 2985, 2950, 1730, 1523, 1369, 1271, 1120, 1169, 1064 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{11}BrN_2O_2+H]^+$ 295.0077, found 295.0079.

ethyl 8-methoxy-3-methylcinnoline-4-carboxylate (3sa)



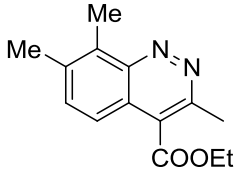
Yield 95%; Light yellow solid, m.p. 75-77 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 – 7.36 (m, 1H), 7.21 (d, *J* = 8.5 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 4.51 – 4.31 (m, 2H), 3.98 (d, *J* = 1.7 Hz, 3H), 2.83 (d, *J* = 1.6 Hz, 3H), 1.30 (td, *J* = 7.1 Hz, 1.8 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 156.2, 150.1, 142.3, 133.0, 124.4, 123.3, 114.6, 107.5, 62.2, 56.2, 20.6, 14.2 ppm; IR (KBr) 3027. 2985, 2926, 1717, 1637, 1531, 1384, 1269, 1054 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{14}N_2O_3+H]^+$ 247.1077, found 247.1079.

ethyl 7-fluoro-3-methylcinnoline-4-carboxylate (3ta)



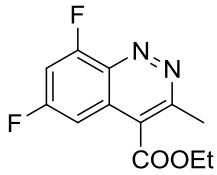
Yield 81%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.6 Hz, 1H), 7.73 (td, *J* = 8.2, 5.4 Hz, 1H), 7.46 – 7.32 (m, 1H), 4.52 (q, *J* = 7.1 Hz, 2H), 2.93 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 157.2, 153.8, 149.7, 149.4, 129.7, 129.6, 126.3, 126.3, 121.4, 115.5, 115.3, 62.7, 19.7, 14.0 ppm; IR (KBr) 2979, 2932, 1736, 1632, 1569, 1450, 1375, 1300, 1248, 1220, 1024 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{11}FN_2O_2+H]^+$ 235.0877, found 235.0878.

ethyl 3,7,8-trimethylcinnoline-4-carboxylate (3ua)



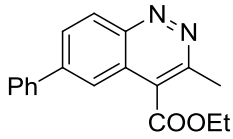
Yield 93%; Light yellow solid, m.p. 62-64 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.7 Hz, 1H), 7.43 (d, *J* = 8.7 Hz, 1H), 4.49 (q, *J* = 7.1 Hz, 2H), 2.90 (s, 3H), 2.86 (s, 3H), 2.40 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 148.3, 148.2, 137.6, 135.5, 135.4, 124.6, 120.5, 120.2, 62.1, 20.4, 20.2, 14.2, 13.0 ppm; IR (KBr) 3086, 2979, 2926, 1725, 1393, 1369, 1266, 1226, 1110, 1011 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{16}N_2O_2+H]^+$ 245.1285, found 245.1286.

ethyl 6,8-difluoro-3-methylcinnoline-4-carboxylate (3va)



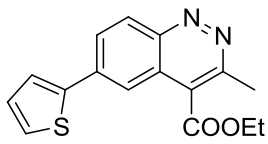
Yield 79%; Light yellow solid, m.p. 73-75 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 1H), 7.24 (td, *J* = 9.1, 2.5 Hz, 1H), 4.53 (q, *J* = 7.2 Hz, 2H), 2.97 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H) ppm ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 165.0, 164.8, 161.9, 161.7, 161.6, 158.3, 158.1, 151.7, 106.4, 106.1, 106.0, 105.7, 103.5, 103.4, 103.2, 103.1, 62.7, 21.0, 14.2 ppm; IR (KBr) 3109, 3044, 3015, 2856, 1731, 1636, 1579, 1423, 1382, 1276, 1161, 1149 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{10}F_2N_2O_2+H]^+$ 253.0783, found 253.0784.

ethyl 3-methyl-6-phenylcinnoline-4-carboxylate (3wa)



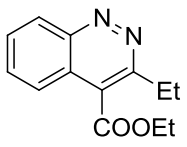
Yield 90%; Light yellow solid, m.p. 73-75 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (dd, *J* = 8.8, 0.6 Hz, 1H), 8.03 (d, *J* = 1.2 Hz, 1H), 7.99 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.68 – 7.61 (m, 2H), 7.50 – 7.36 (m, 3H), 4.57 (q, *J* = 7.1 Hz, 2H), 2.98 (s, 3H), 1.46 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 150.1, 148.6, 144.7, 139.2, 130.6, 129.9, 129.1, 128.8, 127.6, 124.5, 122.5, 120.9, 62.4, 20.9, 14.3 ppm; IR (KBr) 3062, 2968, 2920, 1724, 1708, 1618, 1474, 1378, 1295, 1212, 1072 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{16}N_2O_2+H]^+$ 293.1285, found 293.1283.

ethyl 3-methyl-6-(thiophen-2-yl)cinnoline-4-carboxylate (3xa)



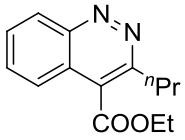
Yield 87%; Light yellow solid, m.p. 90-92 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (dd, *J* = 8.7, 0.6 Hz, 1H), 8.05 – 7.95 (m, 2H), 7.48 (dd, *J* = 3.7, 1.0 Hz, 1H), 7.39 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.10 (dd, *J* = 5.1, 3.7 Hz, 1H), 4.58 (q, *J* = 7.1 Hz, 2H), 2.95 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 150.5, 148.7, 142.3, 137.7, 130.8, 128.7, 128.4, 127.6, 125.9, 124.0, 122.9, 118.7, 62.3, 20.9, 14.4 ppm; IR (KBr) 3062, 2968, 2920, 1724, 1708, 1618, 1474, 1378, 1295, 1212, 1072 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{14}N_2O_2S+H]^+$ 299.0849, found 299.0848.

ethyl 3-ethylcinnoline-4-carboxylate (3cb)



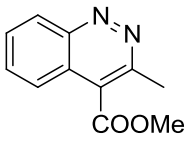
Yield 81%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.96 – 7.84 (m, 1H), 7.84 – 7.69 (m, 2H), 4.60 (q, *J* = 7.1 Hz, 2H), 3.30 (q, *J* = 7.5 Hz, 2H), 1.59 – 1.38 (m, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 154.3, 149.2, 132.0, 130.2, 129.9, 124.3, 123.7, 122.2, 62.4, 28.0, 14.7, 14.2 ppm; IR (KBr) 2973, 2938, 2879, 1729, 1443, 1375, 1284, 1226, 1104 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{14}N_2O_2+H]^+$ 231.1128, found 231.1127.

ethyl 3-isopropylcinnoline-4-carboxylate (3cc)



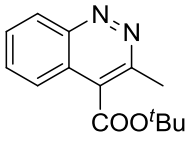
Yield 70%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.87 – 7.80 (m, 1H), 7.80 – 7.66 (m, 2H), 4.55 (q, *J* = 7.1 Hz, 2H), 3.33 – 3.04 (m, 2H), 2.02 – 1.81 (m, 2H), 1.44 (t, *J* = 7.1 Hz, 3H), 1.01 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 153.1, 149.1, 132.0, 130.2, 129.8, 124.6, 123.7, 122.1, 62.3, 36.4, 23.6, 14.2, 14.0 ppm; IR (KBr) 3415, 3068, 2964, 3934, 1729, 1280, 1219, 1037 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{16}N_2O_2+H]^+$ 245.1285, found 245.1286.

methyl 3-methylcinnoline-4-carboxylate (3cd)



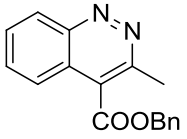
Yield 93%; Light yellow solid, m.p. 89-91 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 – 8.45 (m, 1H), 7.88 – 7.82 (m, 1H), 7.81 – 7.66 (m, 2H), 4.05 (s, 3H), 2.96 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 149.8, 149.3, 132.2, 130.2, 129.9, 129.1, 123.6, 122.1, 52.9, 20.8 ppm; IR (KBr) 3372, 2956, 2932, 2378, 2256, 1731, 1639, 1619, 1237, 1217 cm^{-1}; HRMS (ESI) calcd for $[C_{11}H_{10}N_2O_2+H]^+$ 203.0815, found 203.0814.

tert-butyl 3-methylcinnoline-4-carboxylate (3ce)



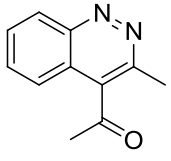
Yield 78%; Light yellow solid, m.p. 69-71 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 – 8.36 (m, 1H), 7.82 (dt, *J* = 6.4, 2.7 Hz, 1H), 7.76 – 7.59 (m, 2H), 2.93 (s, 3H), 1.62 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 149.3, 149.0, 132.0, 130.0, 129.8, 125.7, 123.4, 121.9, 84.4, 28.2, 20.4 ppm; IR (KBr) 3003, 2979, 2932, 1720, 1561, 1368, 1285, 1241, 1160, 1141, 1067 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{16}N_2O_2+H]^+$ 245.1285, found 245.1286.

benzyl 3-methylcinnoline-4-carboxylate (3cf)



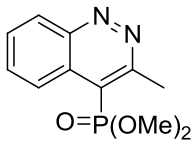
Yield 62%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (dd, *J* = 7.7, 0.9 Hz, 1H), 7.84 (dd, *J* = 8.2, 0.8 Hz, 1H), 7.81–7.66 (m, 2H), 7.54 – 7.46 (m, 2H), 7.45 – 7.36 (m, 3H), 5.54 (s, 2H), 2.94 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 149.7, 149.3, 134.7, 132.3, 130.2, 129.9, 129.0, 128.8, 124.3, 123.6, 122.1, 68.1, 20.8 ppm; IR (KBr) 3068, 3032, 2968, 1729, 1561, 1452, 1375, 1216, 1061 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{14}N_2O_2+H]^+$ 279.1128, found 279.1129.

1-(3-methylcinnolin-4-yl)ethanone (3cg)



Yield 90%; Light yellow solid, m.p. 120-121 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 – 8.38 (m, 1H), 7.86 – 7.64 (m, 2H), 7.64 – 7.47 (m, 1H), 2.86 (s, 3H), 2.64 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.1, 149.1, 146.8, 132.3, 132.1, 130.4, 130.0, 122.8, 121.0, 32.3, 20.1 ppm; IR (KBr) 3050, 3003, 2914, 1728, 1702, 1614, 1376, 1204, 1093 cm^{-1}; HRMS (ESI) calcd for $[C_{11}H_{10}N_2O+H]^+$ 187.0866, found 187.0868.

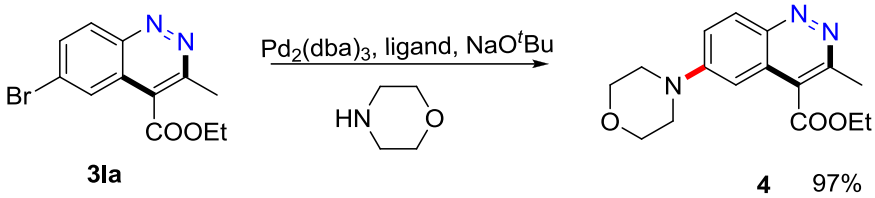
dimethyl 3-methylcinnolin-4-ylphosphonate (3ch)



Yield 76%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.97 – 8.73 (m, 1H), 8.62 – 8.41 (m, 1H), 7.88 – 7.65 (m, 2H), 3.83 (s, 3H), 3.79 (s, 3H), 3.21 (d, *J* = 2.0 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 155.9, 149.3, 149.2, 146.3, 132.5, 130.8, 130.7, 129.7, 126.7, 125.9, 125.8, 125.8, 121.6, 118.3, 116.4, 116.0, 115.0, 52.8, 52.8, 23.4 ppm; IR (KBr) 2956, 1552, 1508, 1263, 1702, 1240, 1054, 1020, 778 cm^{-1}; HRMS (ESI) calcd for $[C_{11}H_{13}N_2O_3P+H]^+$ 253.0737, found 253.0735.

5.Further Functionalization of Generated Cinnolines

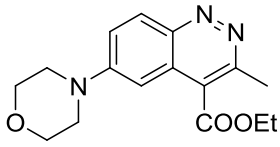
5.1 Cross Coupling of 3la with Morpholine



Scheme S3. Cross Coupling of 3la with Morpholine

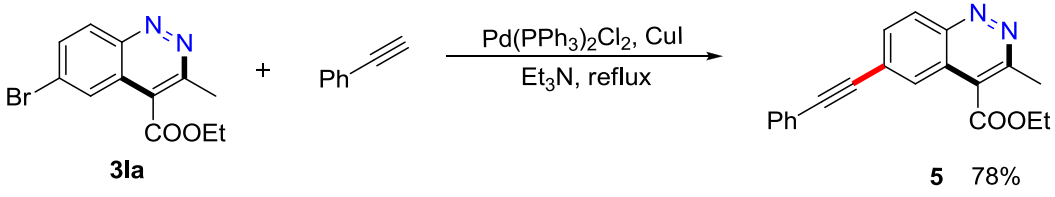
A sealed tube was charged with **3la** (0.2 mmol, 1.0 equiv), $Pd_2(dba)_3$ (0.01 mmol, 5 mol%), XantPhos (0.02 mmol, 10 mol%), NaO^{t}Bu (0.4 mmol, 2.0 equiv), morpholine (0.4 mmol, 2.0 equiv) and tolune 2 mL.(1) The reaction mixture was then vigorously stirred at 80 °C (oil temperature) for 12 hours. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and filtered through a plug of celite. The mixture was concentrated *in vacuo* and purified by flash chromatography on silica gel to afford the desired product **4** in 97% yield.

ethyl 3-methyl-6-morpholinocinnoline-4-carboxylate (4)



Yield 97%; Light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (d, *J* = 9.5 Hz, 1H), 7.51 (dd, *J* = 9.5, 2.6 Hz, 1H), 6.93 (d, *J* = 2.6 Hz, 1H), 4.56 (q, *J* = 7.1 Hz, 2H), 3.99 – 3.76 (m, 4H), 3.54 – 3.28 (m, 4H), 2.91 (s, 3H), 1.48 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 152.5, 150.0, 146.2, 131.4, 124.7, 122.3, 121.5, 101.0, 66.4, 61.9, 47.7, 21.0, 14.3 ppm; IR (KBr) 3448, 3416, 2979, 2826, 2360, 1720, 1615, 1492, 1243, 1122 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{19}N_3O_3+H]^+$ 302.1499, found 302.1502.

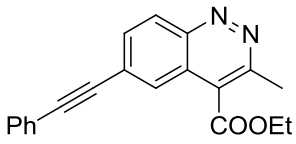
5.2 Cross Coupling of 3la with phenylacetylene



Scheme S4. Cross Coupling of 3la with phenylacetylene

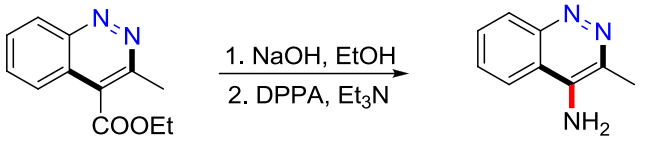
A sealed tube was charged with **3la** (0.2 mmol, 1.0 equiv), $Pd(PPh_3)_2Cl_2$ (0.002 mmol, 1 mol%), CuI (0.004 mmol, 2 mol %), phenylacetylene (0.4 mmol, 2.0 equiv) and Et_3N (2 mL).[(2)] The reaction mixture was then vigorously stirred at 90 °C (oil temperature) for 4 hours. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and filtered through a plug of celite. The mixture was concentrated *in vacuo* and purified by flash chromatography on silica gel to afford the desired product **5** in 78% yield.

ethyl 3-methyl-6-(phenylethynyl)cinnoline-4-carboxylate (5)



Yield 78%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.8 Hz, 1H), 8.03 (d, *J* = 1.0 Hz, 1H), 7.81 (dd, *J* = 8.8, 1.0 Hz, 1H), 7.55 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.35 (dd, *J* = 6.6, 3.0 Hz, 3H), 4.57 (q, *J* = 7.1 Hz, 2H), 2.96 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 150.4, 148.1, 132.6, 131.9, 130.2, 129.2, 128.5, 127.5, 126.6, 123.7, 122.2, 122.1, 94.1, 88.5, 62.5, 20.9, 14.3 ppm; IR (KBr) 3422, 2985, 2920, 2195, 1726, 1613, 1496, 1221, 1095 cm^{-1}; HRMS (ESI) calcd for $[C_{20}H_{16}N_2O_2+H]^+$ 317.1285, found 317.1283.

5.3 Transformation of Ester

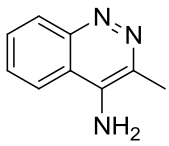


3ca **6** 76%

Scheme S5. Transformation of Ester

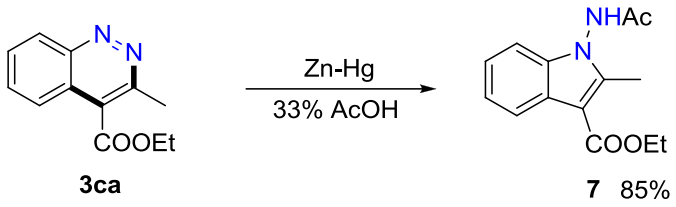
A 25 mL round bottom flask was charged with 0.5 mmol **3ca**, 1 mmol NaOH, 5 mL EtOH, heated to reflux for 2 hours. 6 N HCl was added until the pH = 7, the residue was concentrated *in vacuo* to give white solid. 0.5 mmol DPPA, 0.5 mmol Et_3N and 3 mL *t*-BuOH were added and reacted at 90 °C for 24 hours.[(3)] Solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired product **6** in 76% yield.

3-methylcinnolin-4-amine (6)



Yield 76%; White solid, m.p. 80-82 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.20 (d, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.78 – 7.57 (m, 1H), 7.57 – 7.36 (m, 1H), 6.90 (bs, 2H), 2.56 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 148.5, 140.1, 138.8, 129.8, 128.1, 127.4, 122.1, 114.6, 18.9 ppm; IR (KBr) 2924, 2844, 1637, 1629, 1561, 1194, 1106, 618 cm^{-1}; HRMS (ESI) calcd for $[C_9H_9N_3+H]^+$ 160.0869, found 160.0870.

5.4 Ring-contraction Reaction

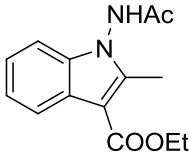


Scheme S7. Ring-contraction Reaction

Ring contract reaction was conducted to offer indole products **7** as shown in Scheme S7.[4]

A 25 mL round bottom flask was charged with 0.5 mmol **3ca**, 0.4 g Zn-Hg and 33% AcOH (5 mL) then the mixture was heated to reflux for 6 hours. The resulted mixture was cooled to room temperature and then filtered, the filtrates was extracted with ethyl acetate 10 mL for 3 times, the combined organic layer were dried with anhydrous $NaSO_4$ and concentrated in reduced pressure. The crude product was purified by flash chromatography on silica gel to afford the desired product **7** in 85% yield.

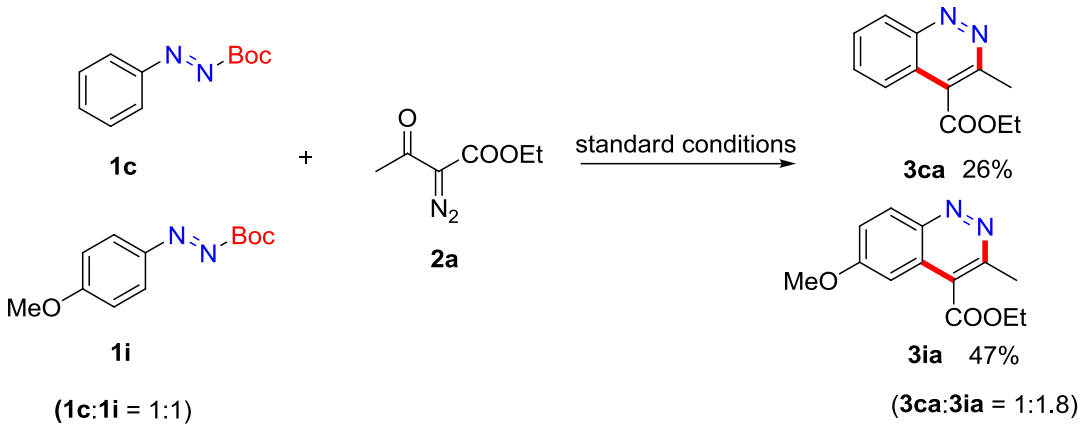
ethyl 1-formylbenzofuro[2,3-c]pyridine-4-carboxylate(7)



Yield 85%; White solid, m.p. 162-164 ºC; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.23 (s, 1H), 7.97 (dd, *J* = 5.7, 3.1 Hz, 1H), 7.26 (dd, *J* = 6.0, 3.1 Hz, 1H), 7.18 (dd, *J* = 6.0, 3.1 Hz, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.50 (s, 3H), 2.14 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.6, 169.2, 149.8, 139.8, 128.4, 127.0, 126.5, 125.1, 113.6, 63.6, 24.9, 18.9, 15.2 ppm; IR (KBr) 3252, 1701, 1671, 1558, 1458, 1405, 1213, 1167 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{16}N_2O_3+H]^+$ 261.1234, found 261.1232.

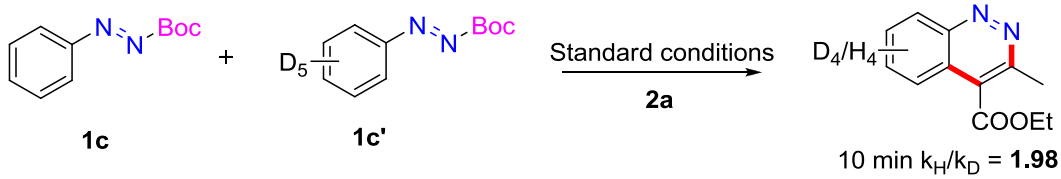
6. *Mechanism Study*

6.1 Competitive Reaction



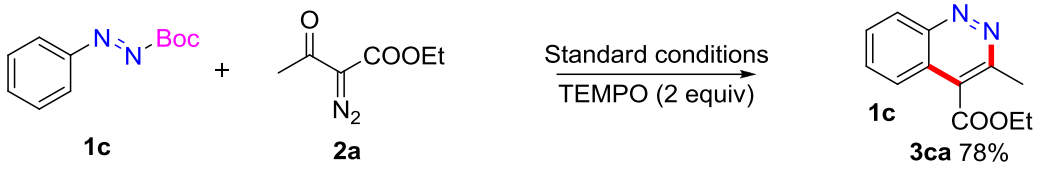
A sealed tube was charged with **1c** (0.375 mmol, 0.75 equiv), **1i** (0.375 mmol, 0.75 equiv), $(RhCp^*Cl_2)_2$ (0.0125 mmol, 2.5 mol%), $AgSbF_6$ (0.1 mmol, 0.2 equiv), **2a** (0.5 mmol, 1.0 equiv), 2 mL PivOH/DCE (v:v = 1: 20). The reaction mixture was vigorously stirred at 50 °C (oil temperature) for 24 hours. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and filtered through a plug of celite. The mixture was concentrated *in vacuo* and the yields of corresponding products **3ca** and **3ia** were determined by ^1H NMR with using dibromomethane (δ = 4.80) as an internal standard. **3ca** and **3ia** were obtained in the ratio of 1:1.8, which indicated that the high electron-density of the phenyl ring played good effect to the reaction.

6.2 Kinetic Isotope Effect Study



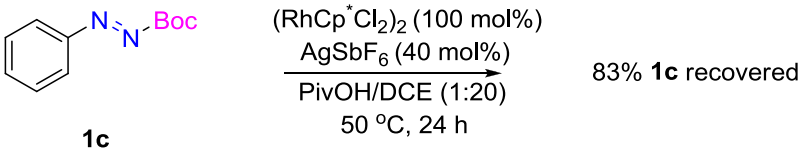
A sealed tube was charged with **1c** (0.375 mmol, 0.75 equiv), **1c'** (0.375 mmol, 0.75 equiv), $(RhCp^*Cl_2)_2$ (0.0125 mmol, 2.5 mol%), $AgSbF_6$ (0.1 mmol, 0.2 equiv), **2a** (0.5 mmol, 1.0 equiv), 2 mL PivOH/DCE (v:v = 1: 20). The reaction mixture was vigorously stirred at 50 °C (oil temperature) for 10 minutes. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and filtered through a plug of celite. The mixture was concentrated *in vacuo* and the yields of products and conversion rate were determined by ^1H NMR. The initial rate of **1c** was compared to those of **1c**-D_5 (by ^1H NMR), which indicated that k_H/k_D should be 1.98 in 10 minutes.

6.3 Radical Reaction



A sealed tube was charged with **1c** (0.375 mmol, 0.75 equiv), $(RhCp^*Cl_2)_2$ (0.0125 mmol, 2.5 mol%), $AgSbF_6$ (0.1 mmol, 0.2 equiv), **2a** (0.5 mmol, 1.0 equiv), TEMPO (1 mmol, 2.0 equiv), 2 mL PivOH/DCE (v:v = 1: 20). The reaction mixture was vigorously stirred at 50 °C (oil temperature) for 24 hours. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and filtered through a plug of celite. The mixture was concentrated *in vacuo* and the yields of **3ca** was determined by ^1H NMR with using dibromomethane (δ = 4.80) as an internal standard. 78% **3ca** was obtained to suggest that this procedure should not be a radical relevant process.

6.4 Control Reaction



A sealed tube was charged with **1c** (0.1 mmol, 1.0 equiv), $(RhCp^*Cl_2)_2$ (0.1 mmol, 100 mol%), $AgSbF_6$ (0.04 mmol, 0.4 equiv), 2 mL PivOH/DCE (v:v = 1: 20). The reaction mixture was vigorously stirred at 50 °C (oil temperature) for 24 hours. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and filtered through a plug of celite. The mixture was concentrated *in vacuo* and the conversion rate was determined by ^1H NMR with using dibromomethane (δ = 4.80) as an internal standard. **1c** was recovered in the yield of 83% and no de-Boc product was detected, which revealed that the Boc group was not removed before the C-H activation step.

7. References

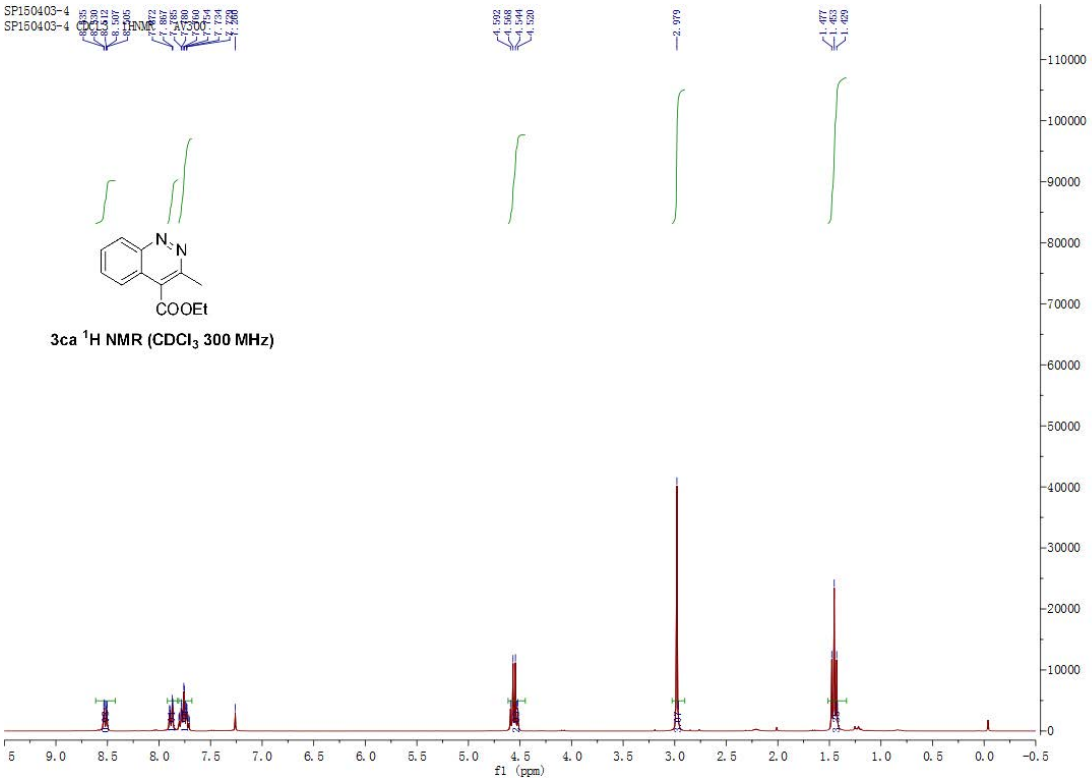
(1) D. Cheng, D. Han, W. Gao, Q. Jing, J. Jiang, Y. Wan, N. P. Englund, T. Tuntland, X. Wu, S. Pan, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 6573-6576.

(2) L. W. Hardy, M. L. R. Heffernan, F. X. Wu, K. L. Spear, L. D. Saraswat. *WO 2011075699.*

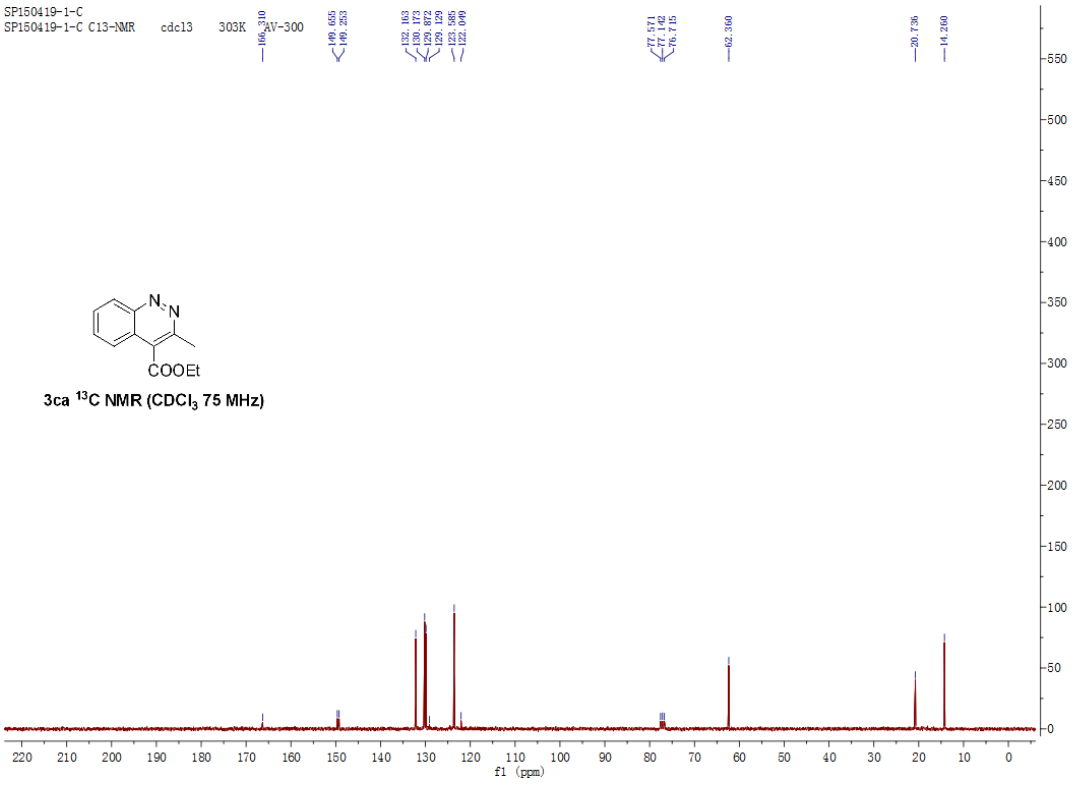
(3) a) S. Sunami, T. Sagara, M. Ohkubo, H. Morishima, *Tetrahedron Lett.* **1999**, *40*, 1721-1724; b) R. G. Wallace, J. M. Barker, M. L. Wood, *Synthesis* **1990**, *12*, 1143-1144.

(4) L. S. Besford, J. M. Bruce, *J. Chem. Soc.* **1964**, 4037-4044.

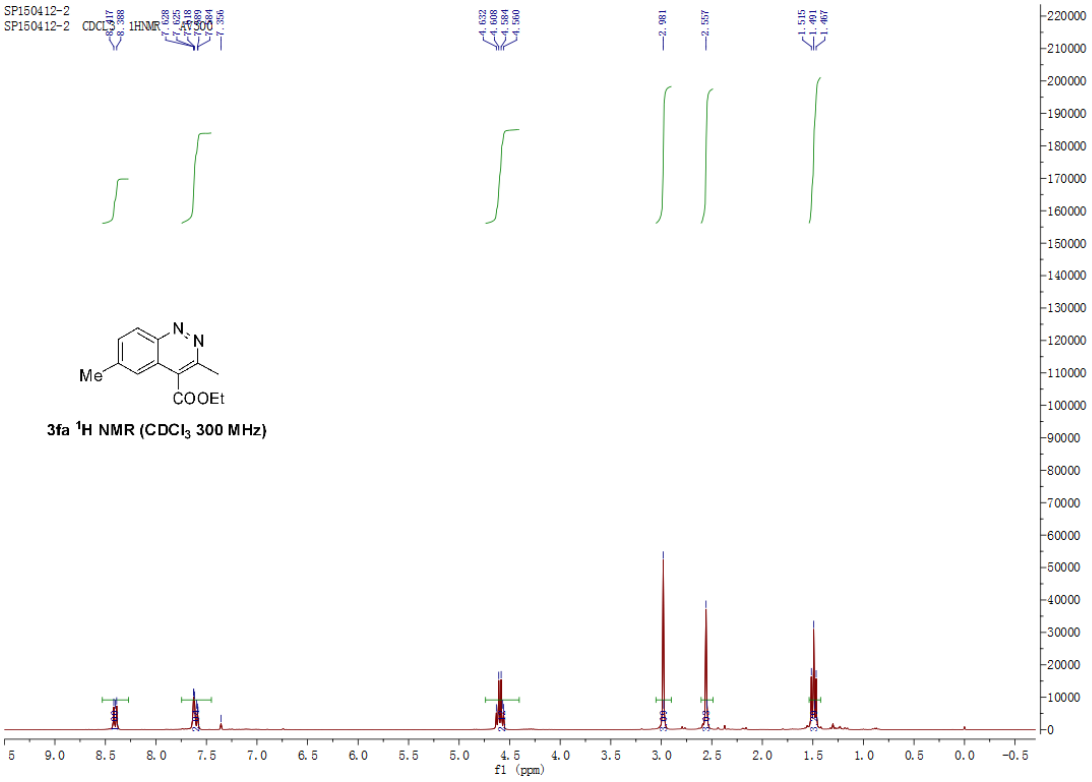
8. ^{1}H and ^{13}C-NMR Spectra of Title Compounds



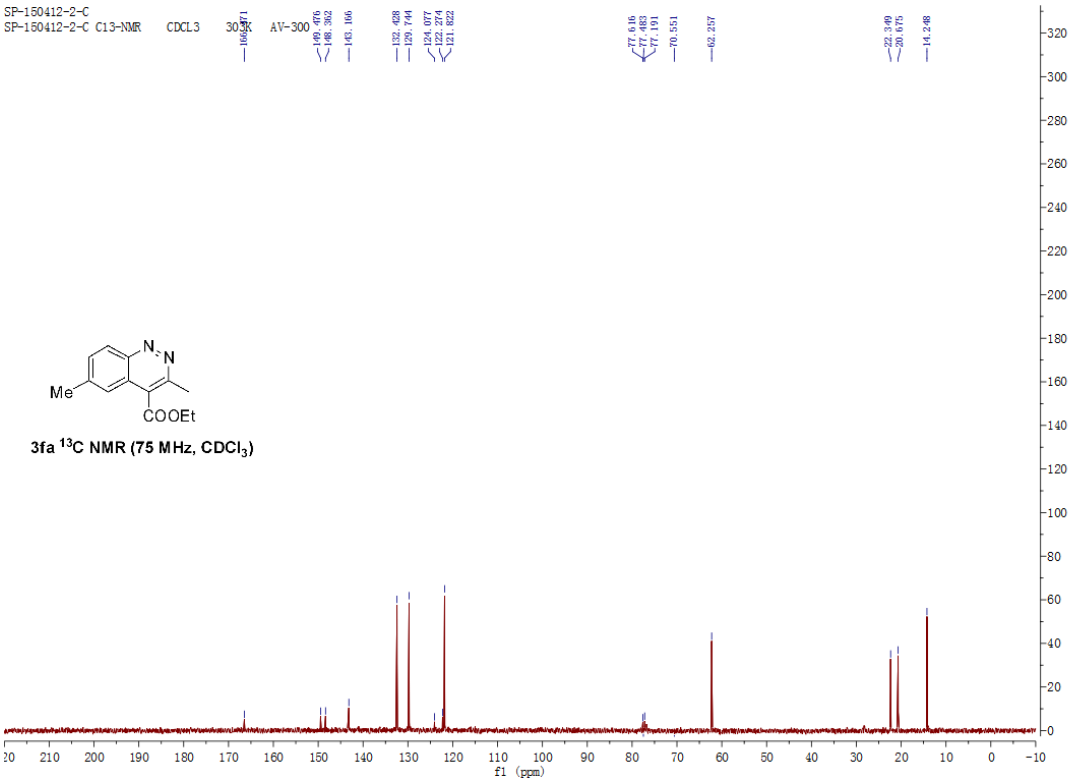
3ca ^{1}H NMR ($CDCl_3$ 300 MHz)



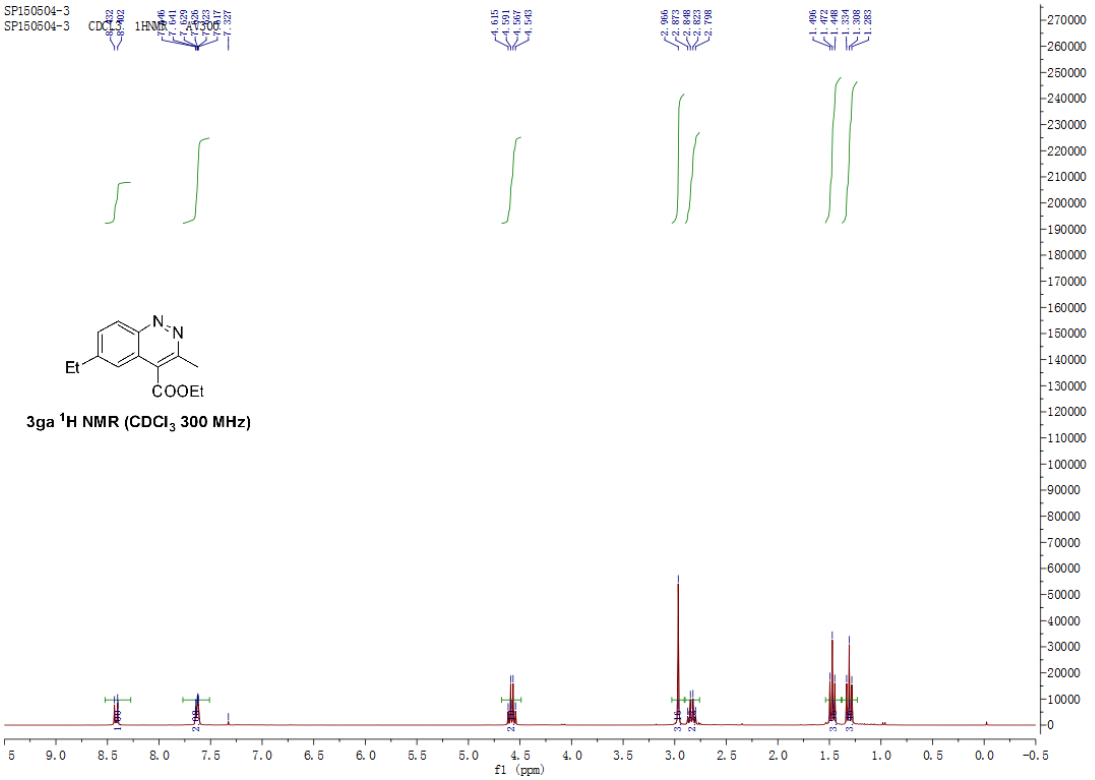
3ca ^{13}C NMR ($CDCl_3$ 75 MHz)



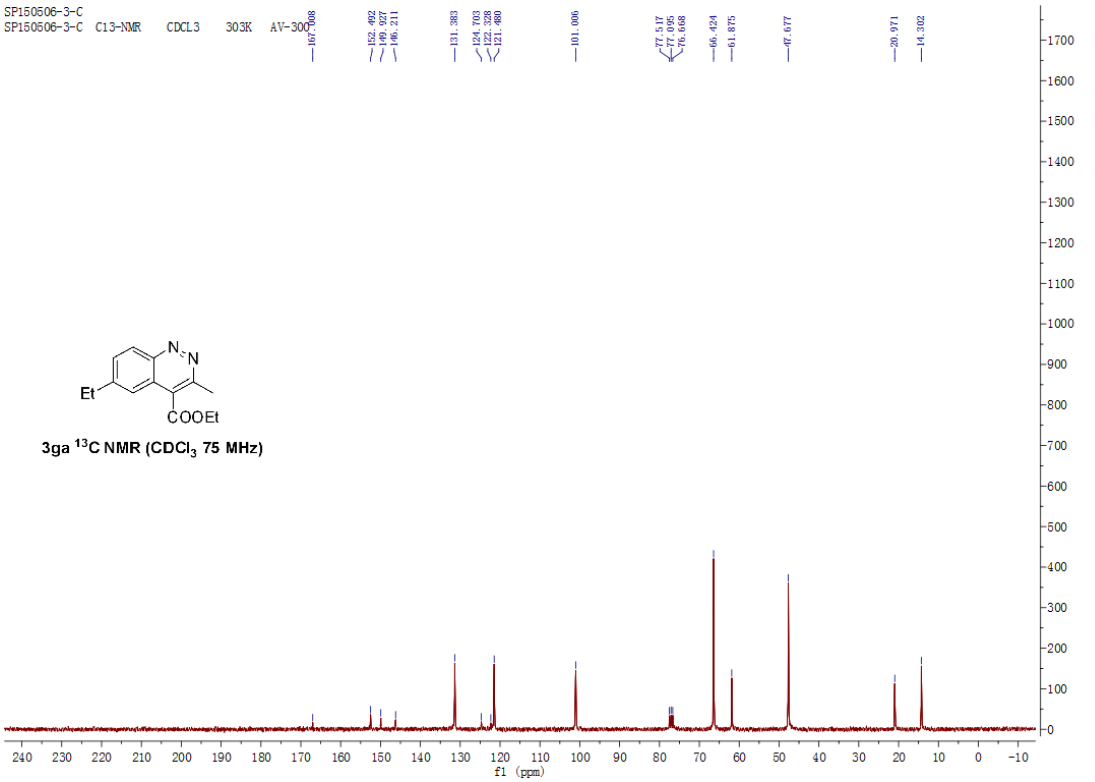
3fa ^{1}H NMR ($CDCl_3$ 300 MHz)



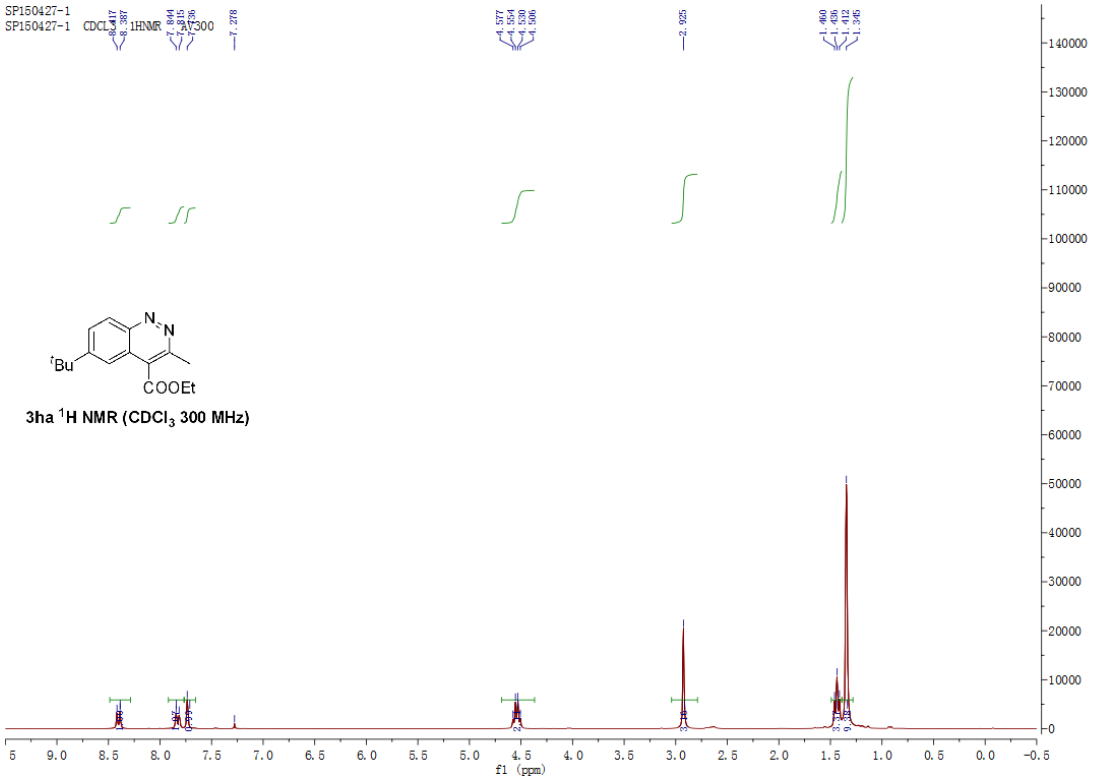
3fa ^{13}C NMR (75 MHz, $CDCl_3$)



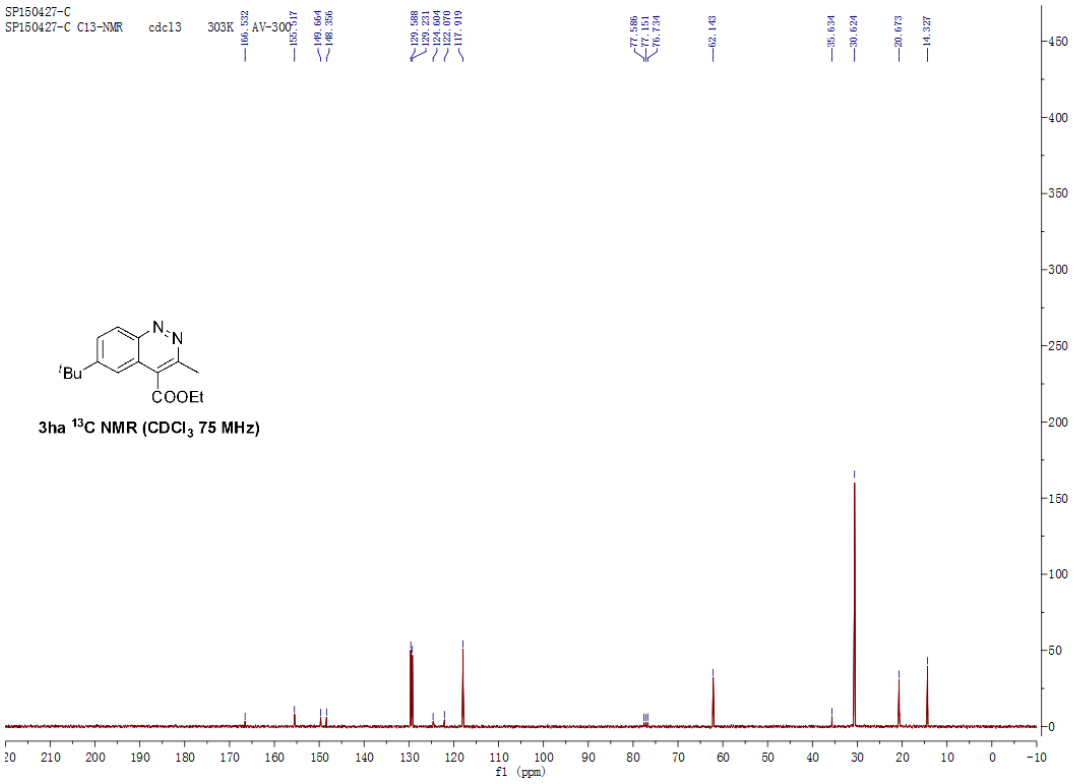
3ga ^{1}H NMR ($CDCl_3$ 300 MHz)



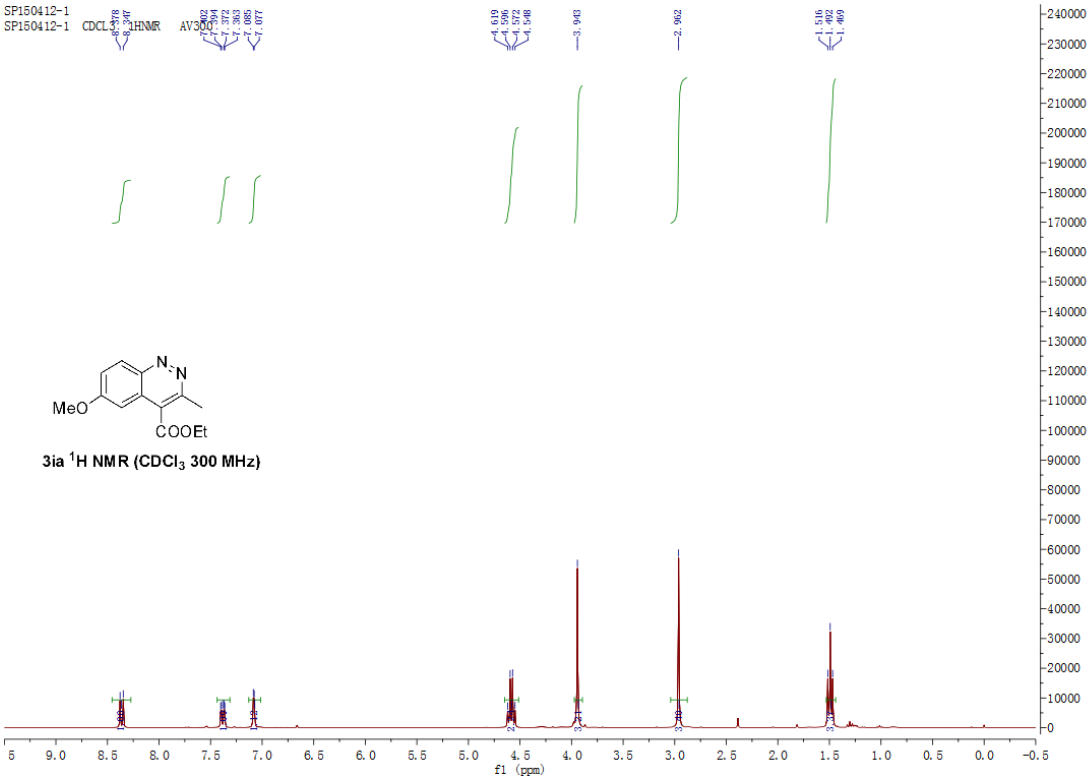
3ga ^{13}C NMR ($CDCl_3$ 75 MHz)



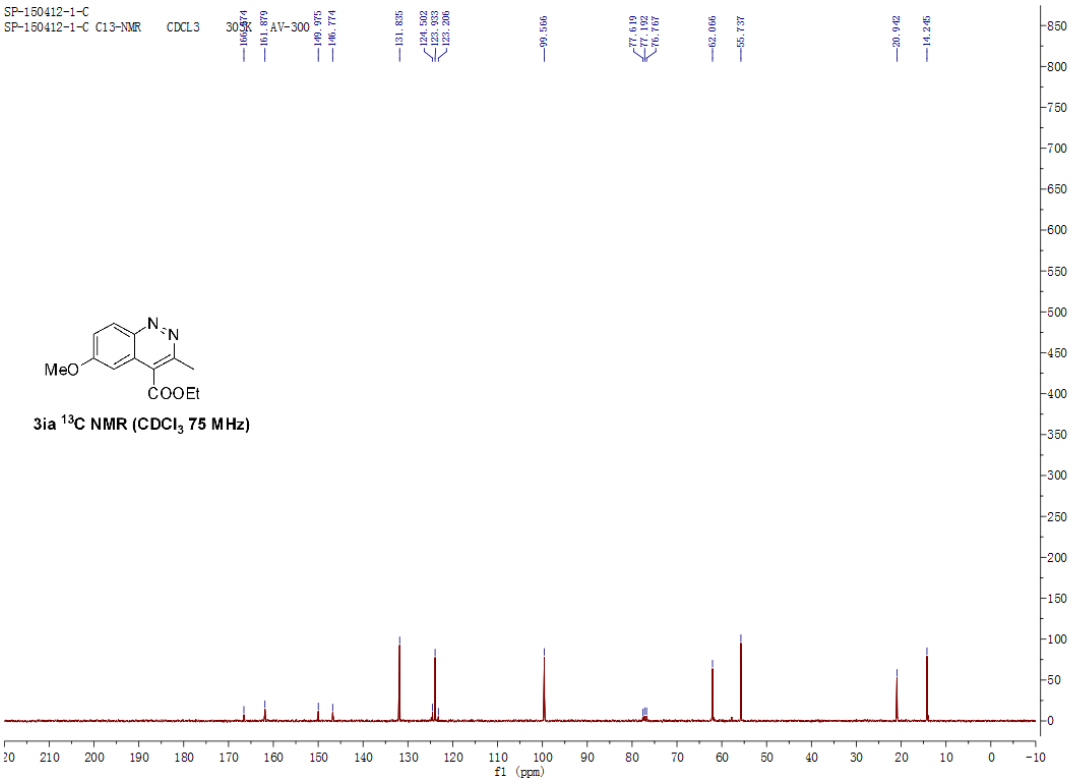
3ha ^{1}H NMR ($CDCl_3$ 300 MHz)



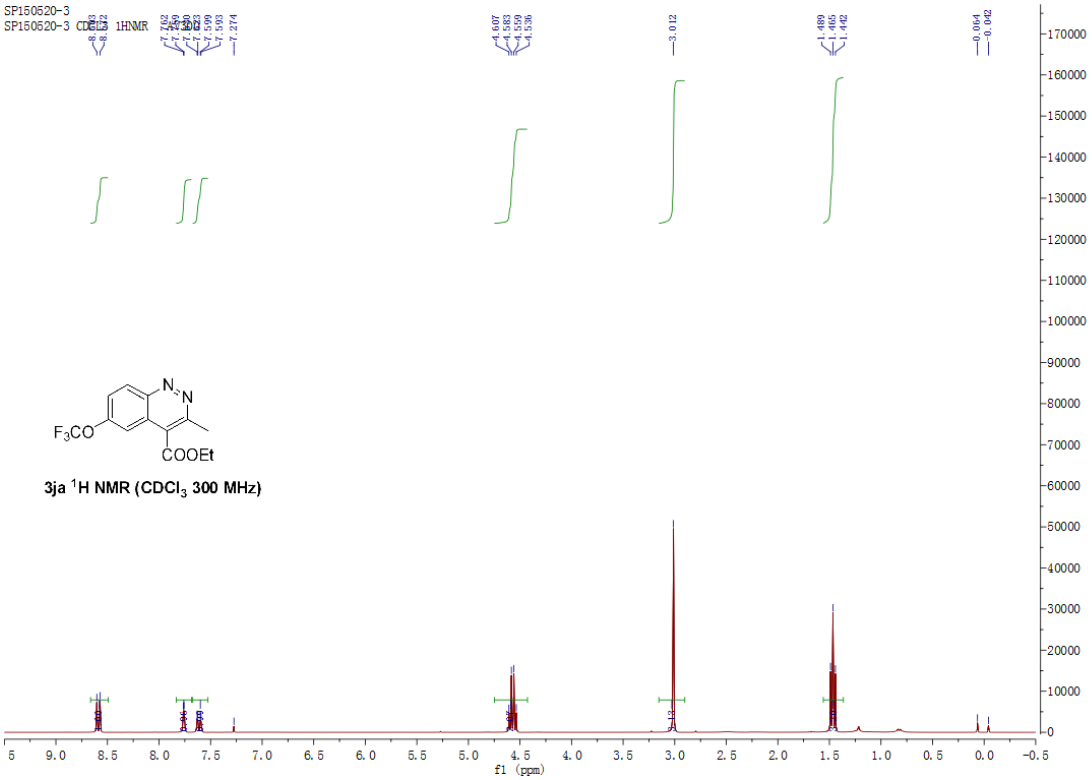
3ha ^{13}C NMR ($CDCl_3$ 75 MHz)



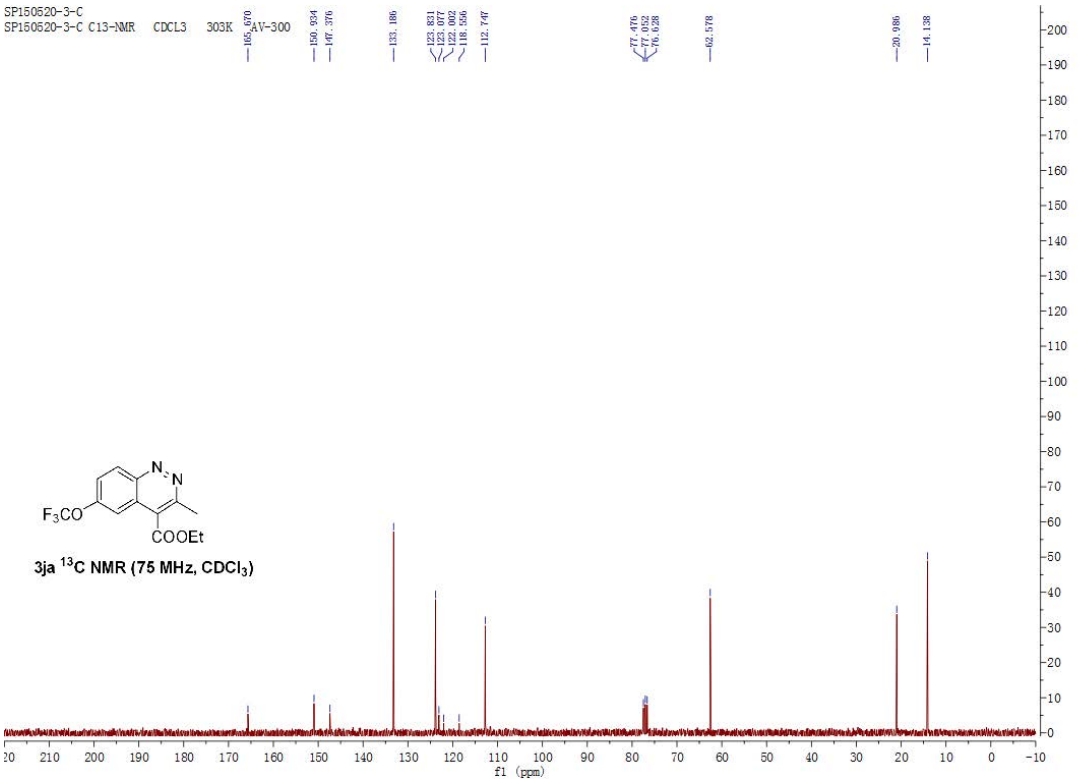
3ia ^{1}H NMR ($CDCl_3$ 300 MHz)



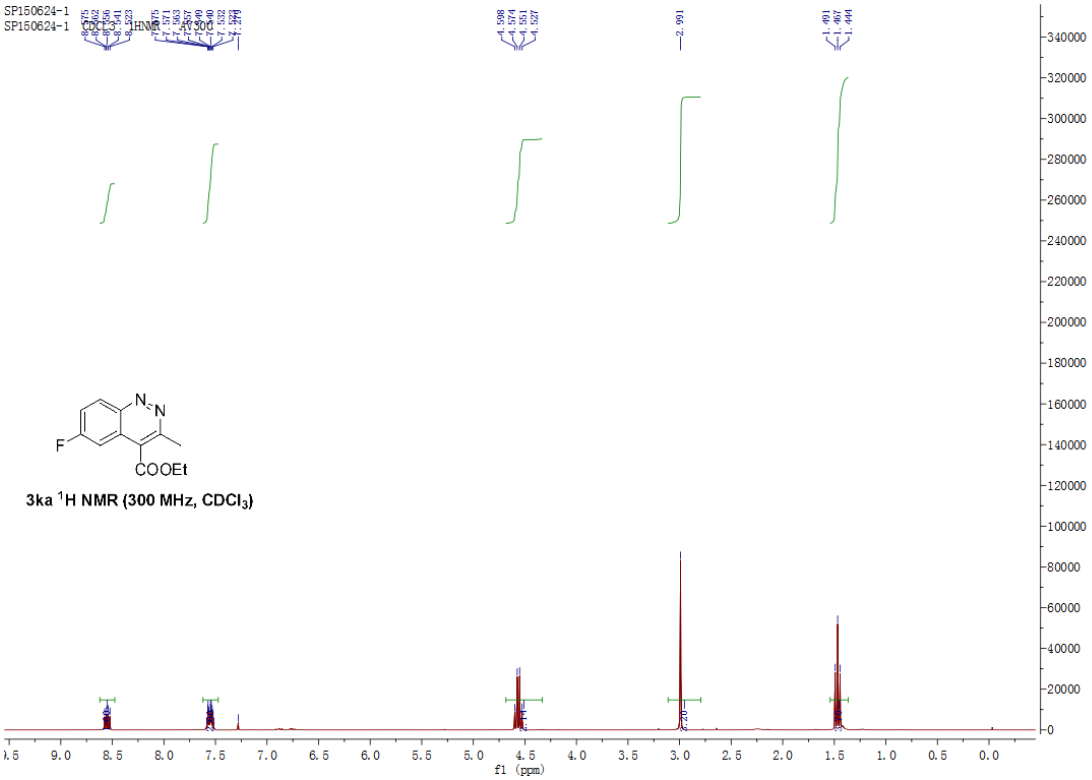
3ia ^{13}C NMR ($CDCl_3$ 75 MHz)



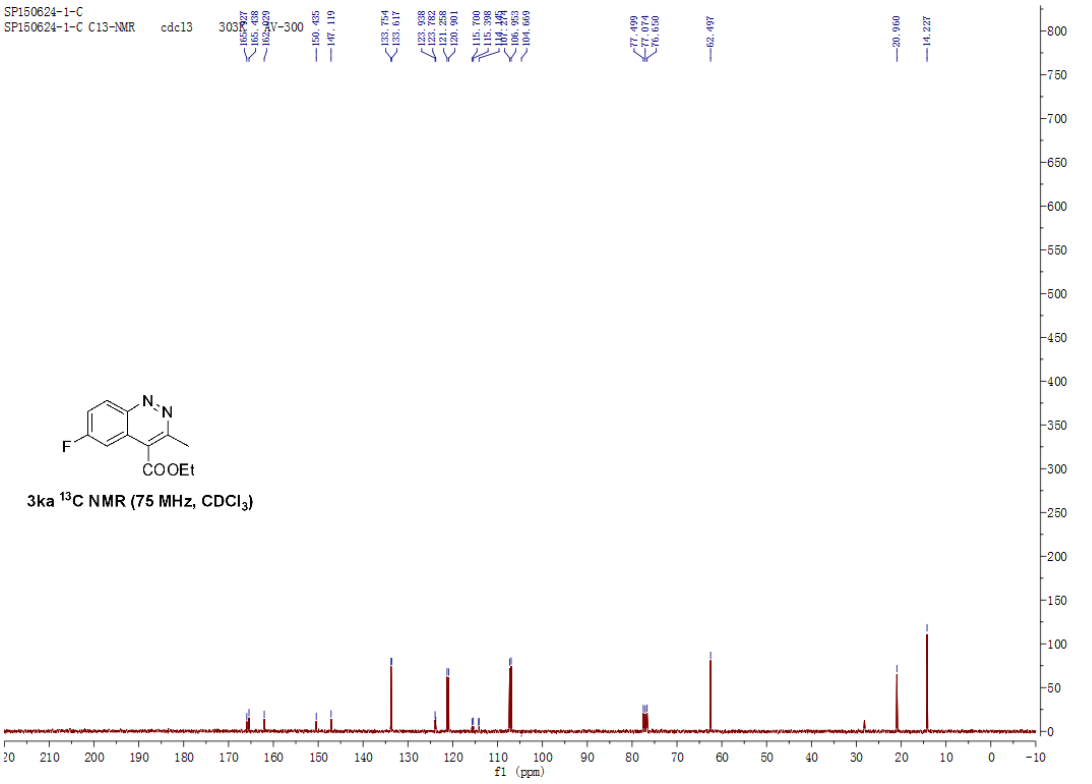
3ja ^{1}H NMR ($CDCl_3$ 300 MHz)



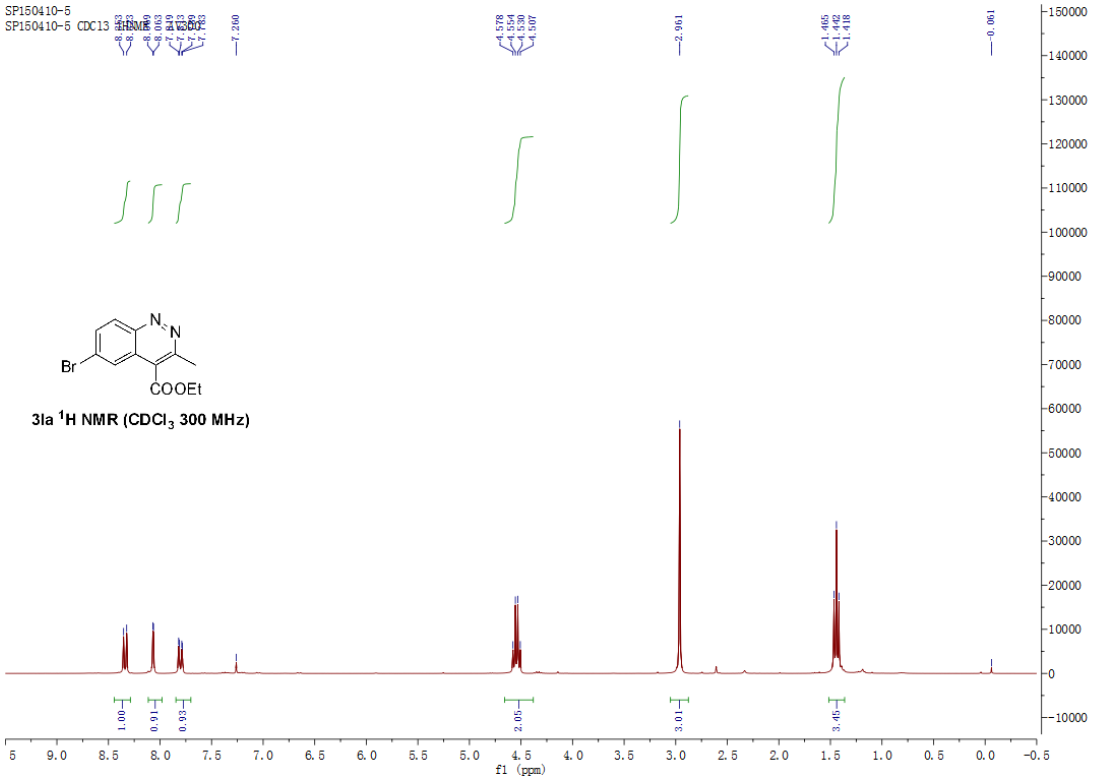
3ja ^{13}C NMR (75 MHz, $CDCl_3$)



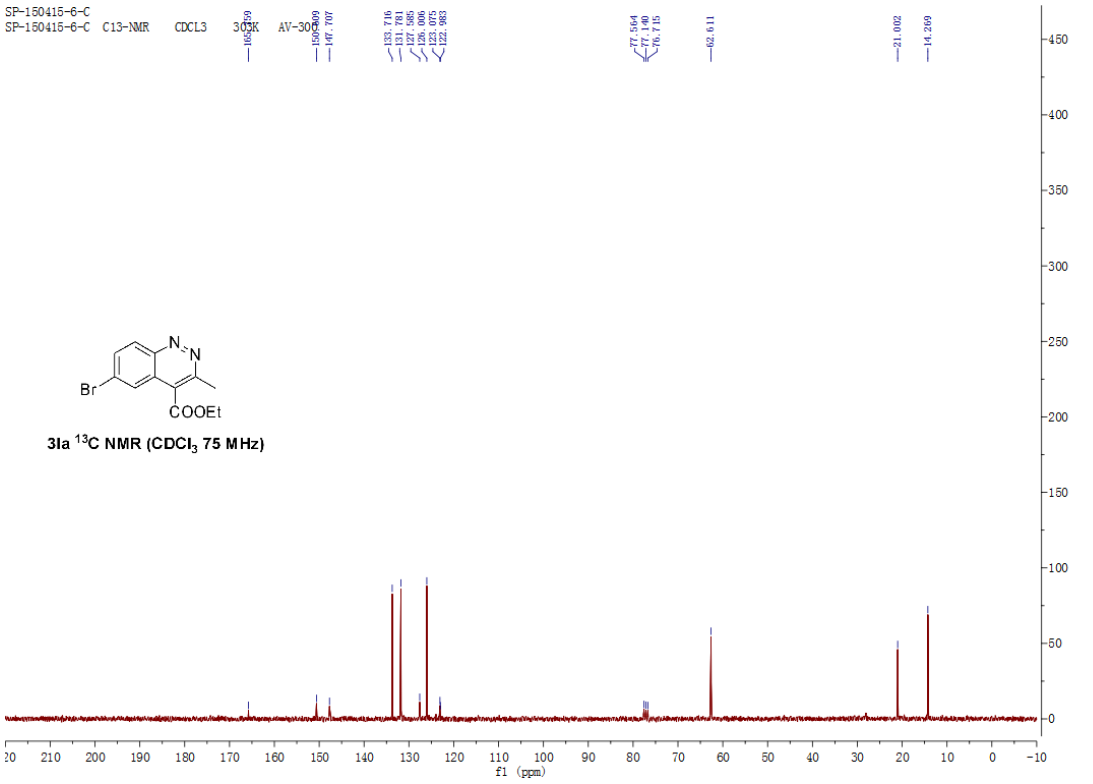
3ka ^{1}H NMR (300 MHz, $CDCl_3$)



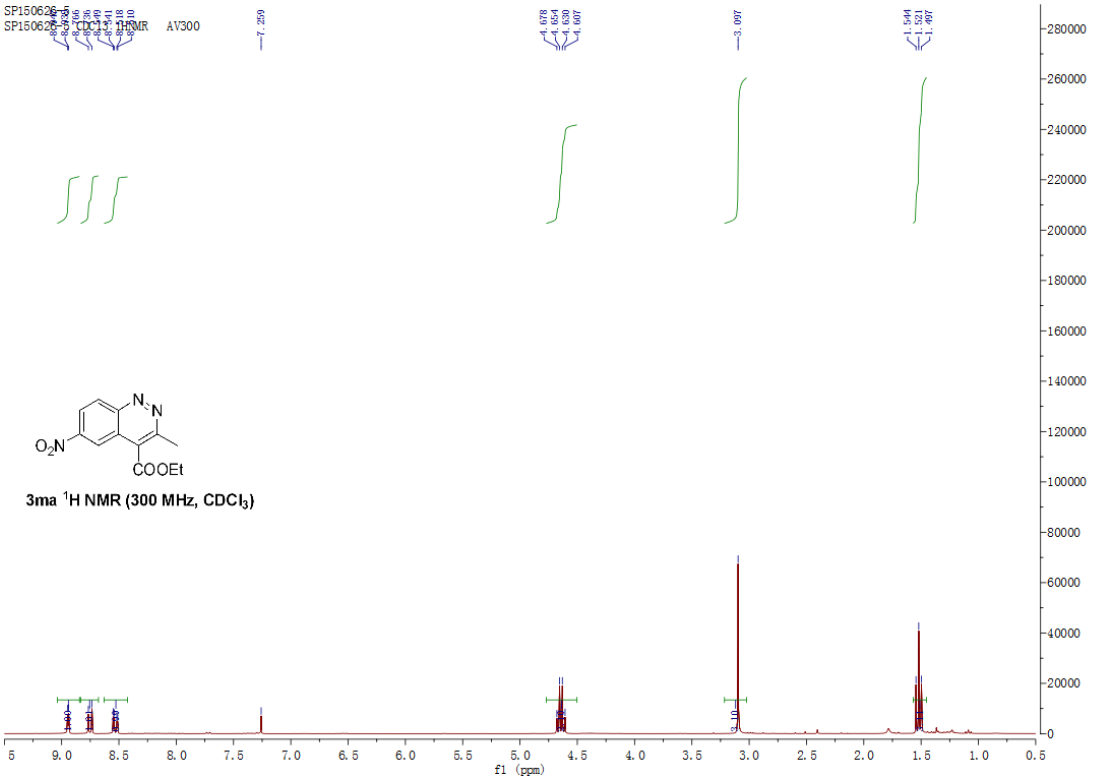
3ka ^{13}C NMR (75 MHz, $CDCl_3$)



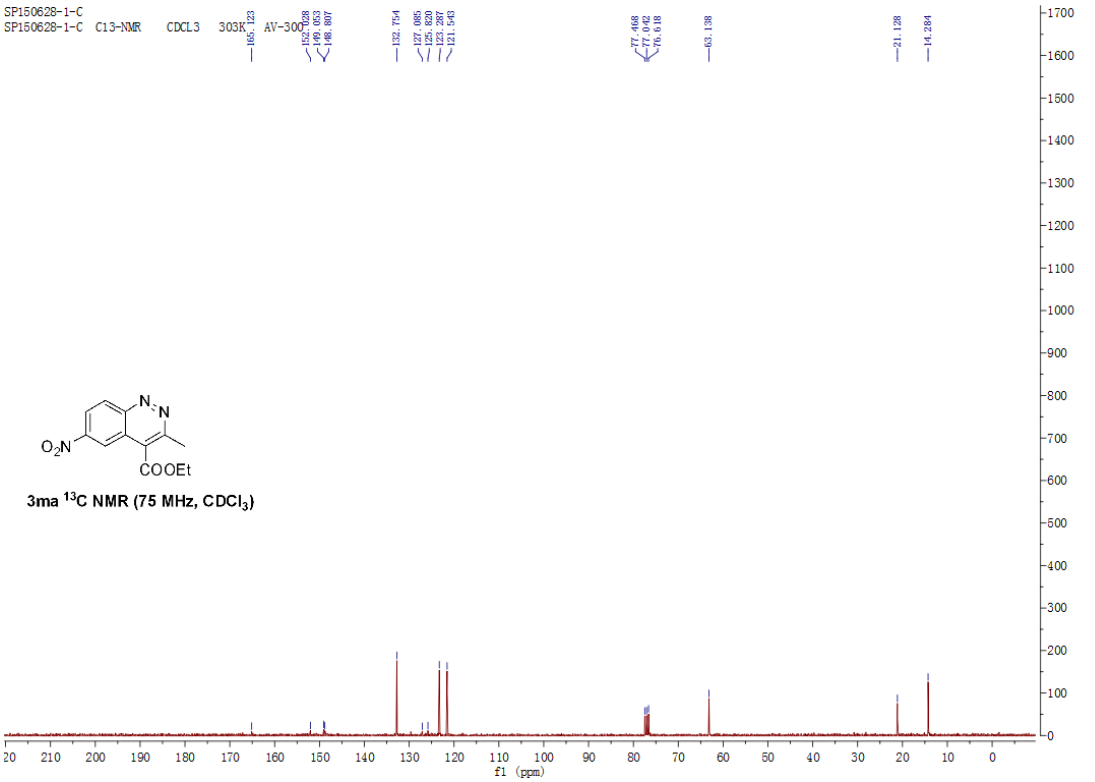
3Ia ^{1}H NMR ($CDCl_3$ 300 MHz)



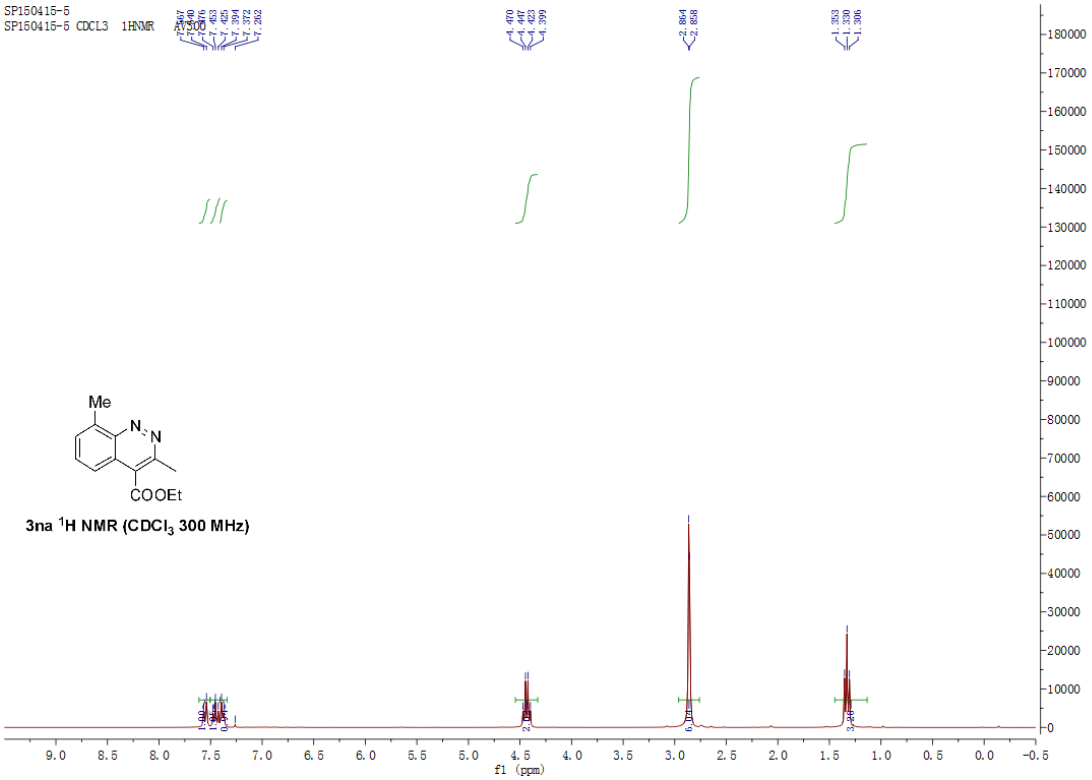
3Ia ^{13}C NMR ($CDCl_3$ 75 MHz)



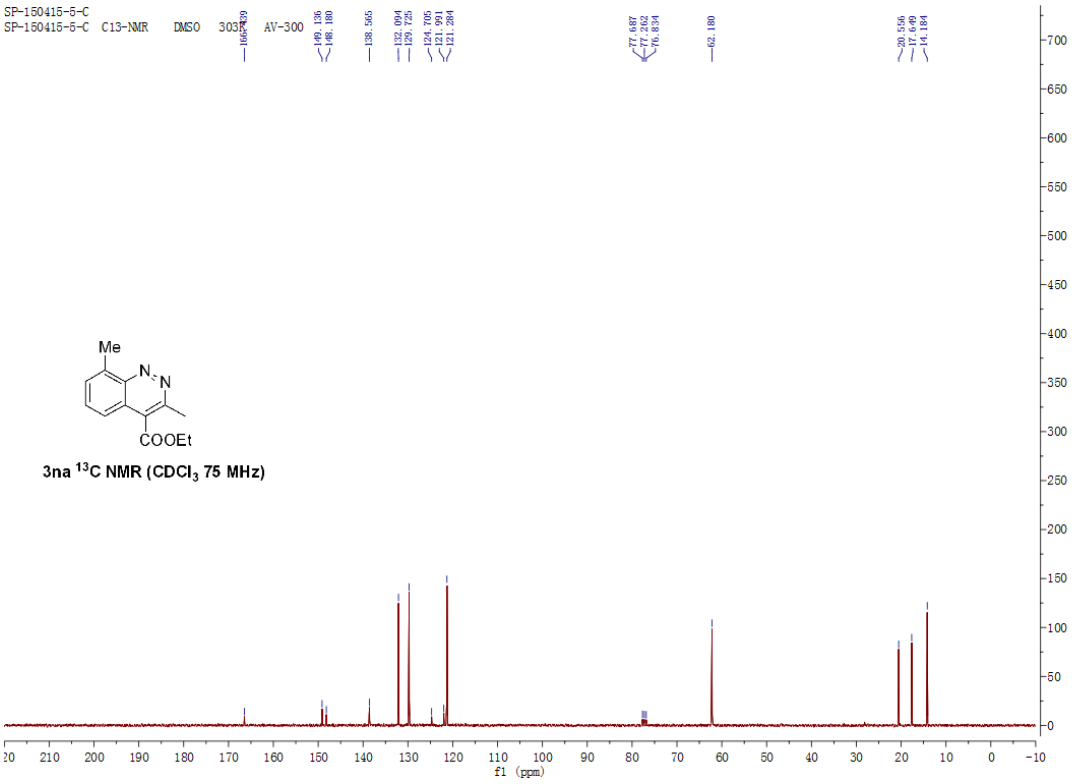
3ma ^{1}H NMR (300 MHz, $CDCl_3$)



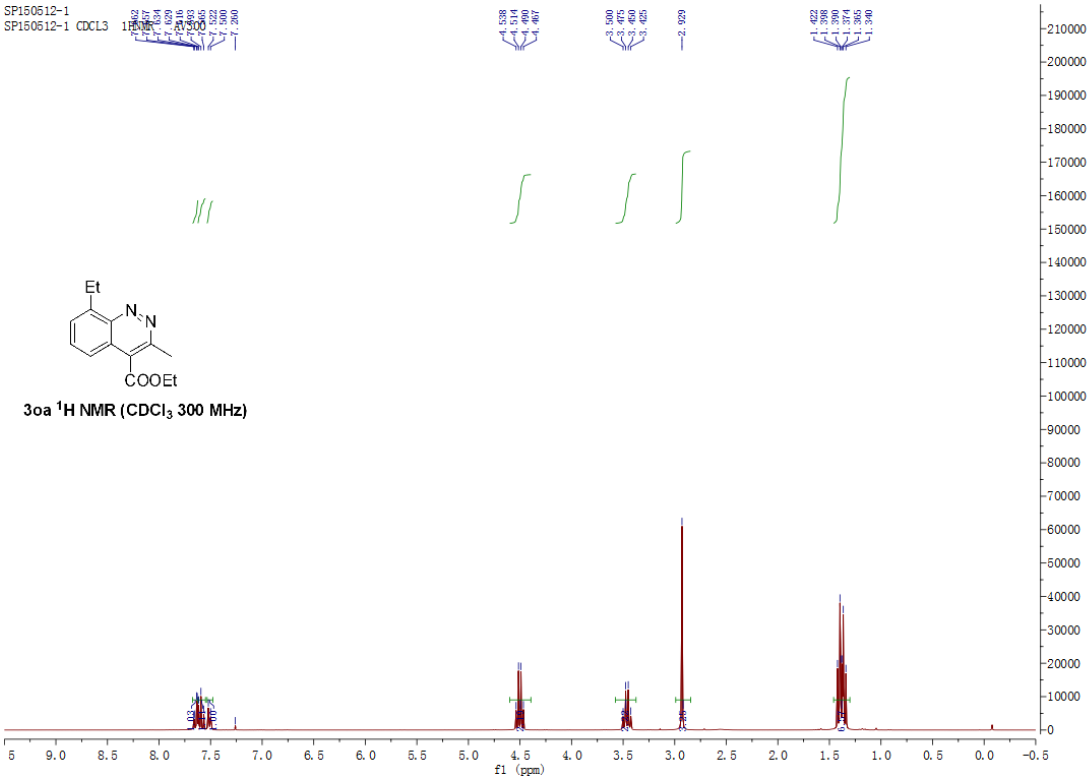
3ma ^{13}C NMR (75 MHz, $CDCl_3$)



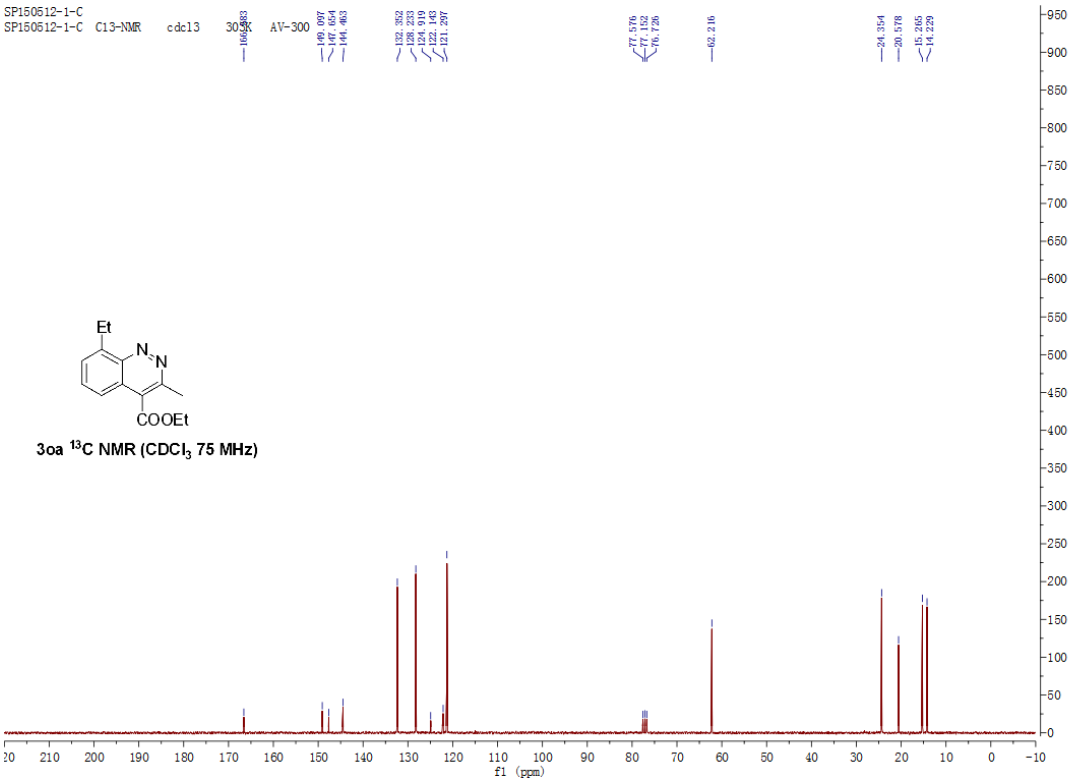
3na ^{1}H NMR ($CDCl_3$ 300 MHz)



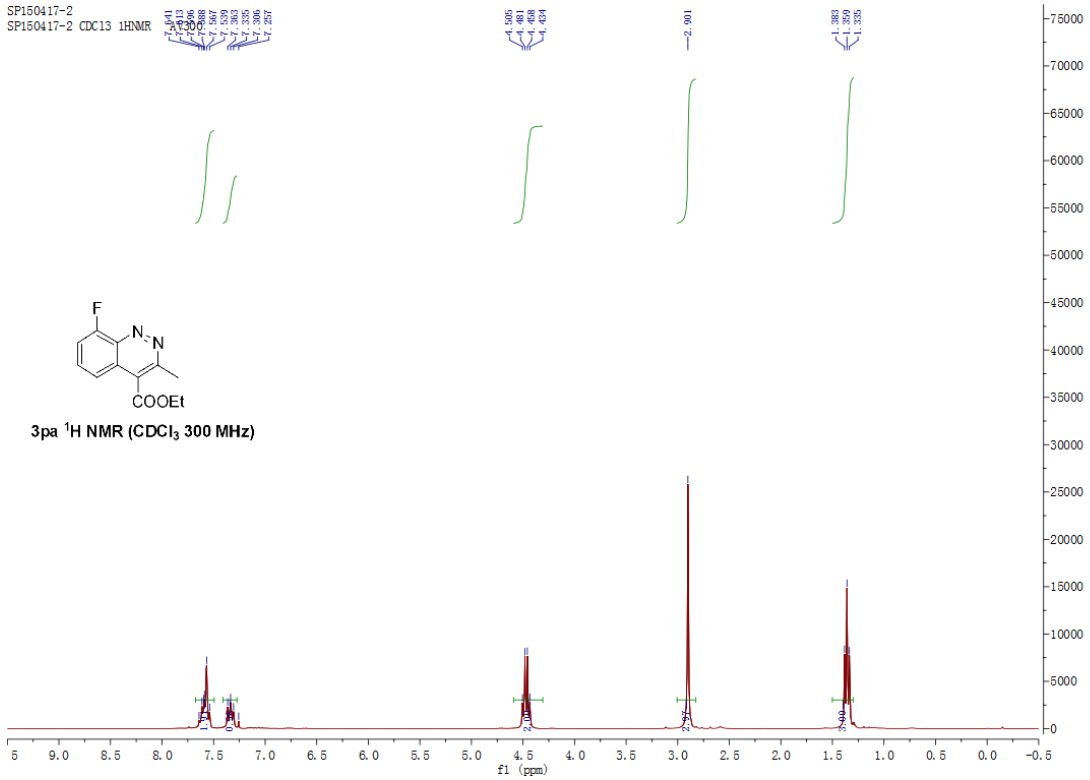
3na ^{13}C NMR ($CDCl_3$ 75 MHz)



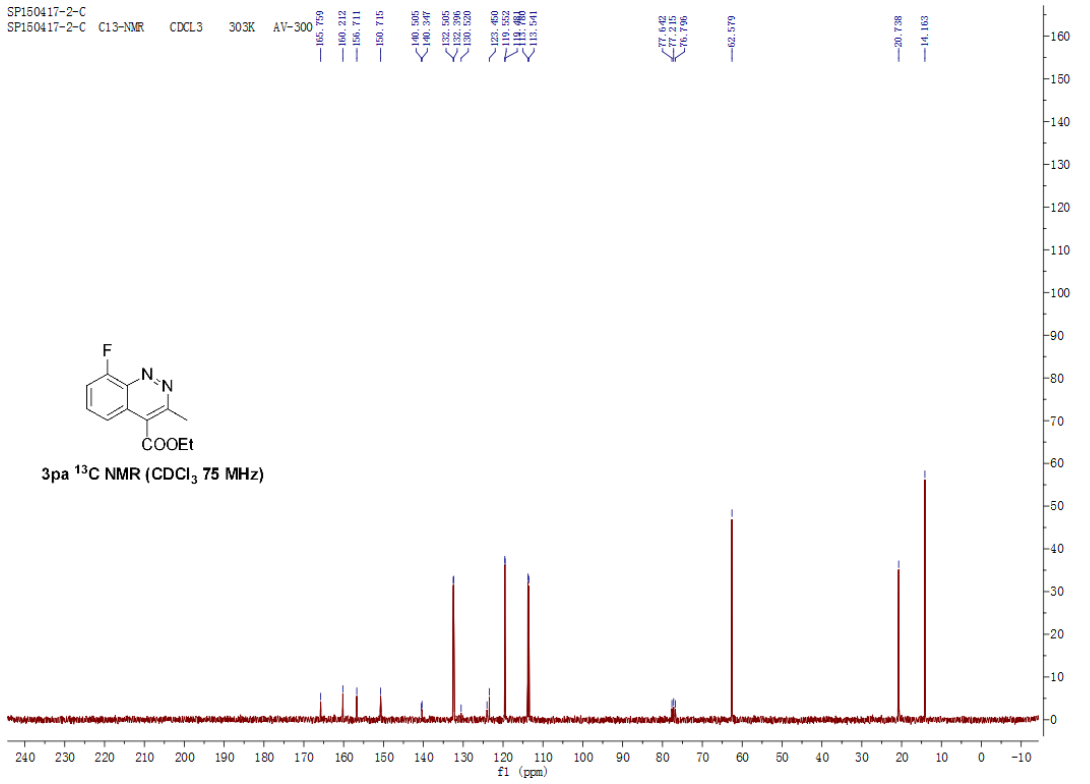
3oa ^{1}H NMR ($CDCl_3$ 300 MHz)



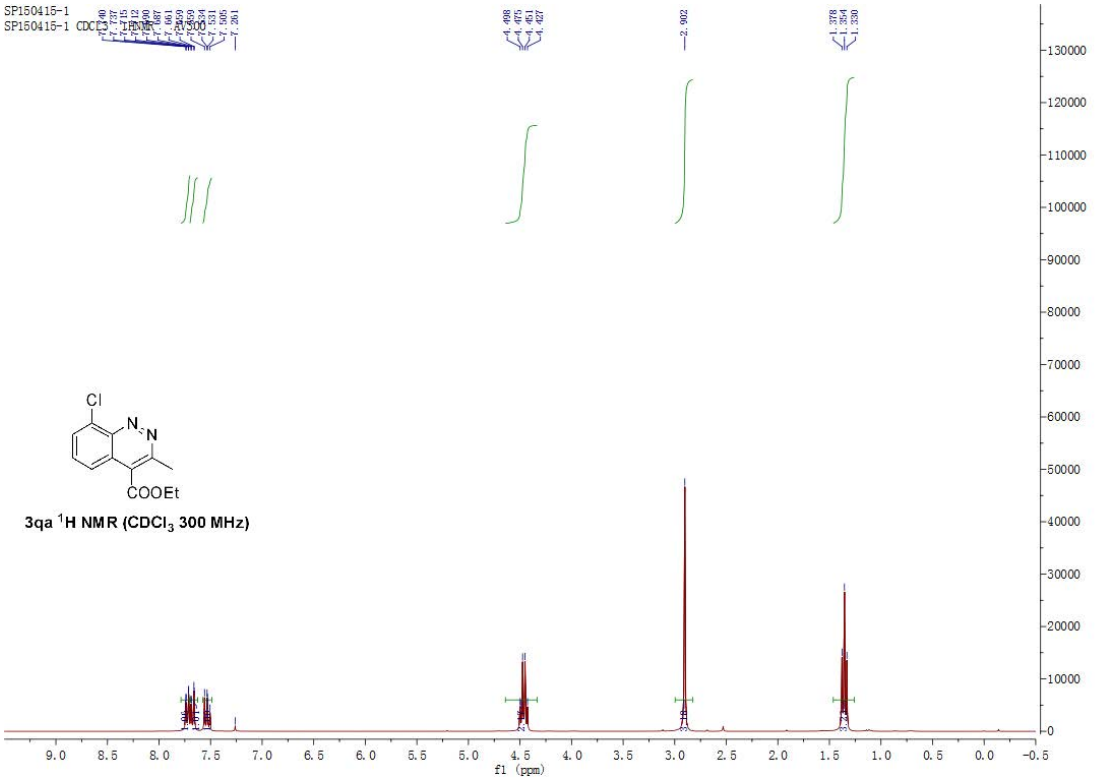
3oa ^{13}C NMR ($CDCl_3$ 75 MHz)



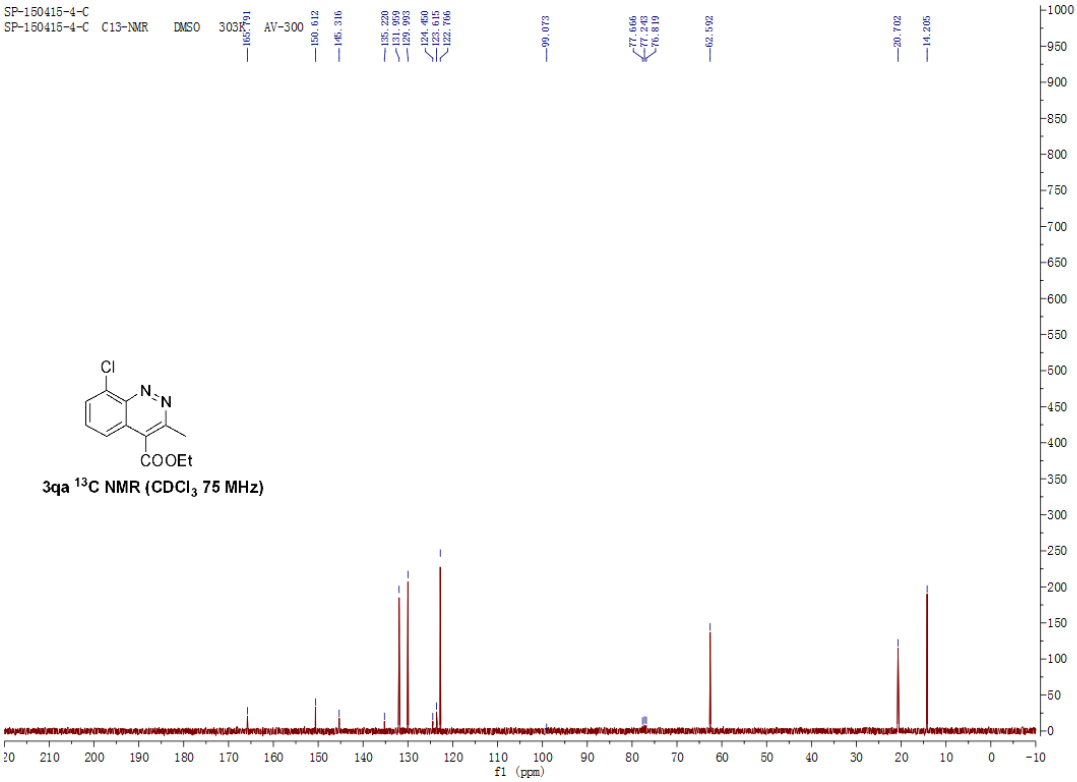
3pa ^{1}H NMR ($CDCl_3$ 300 MHz)



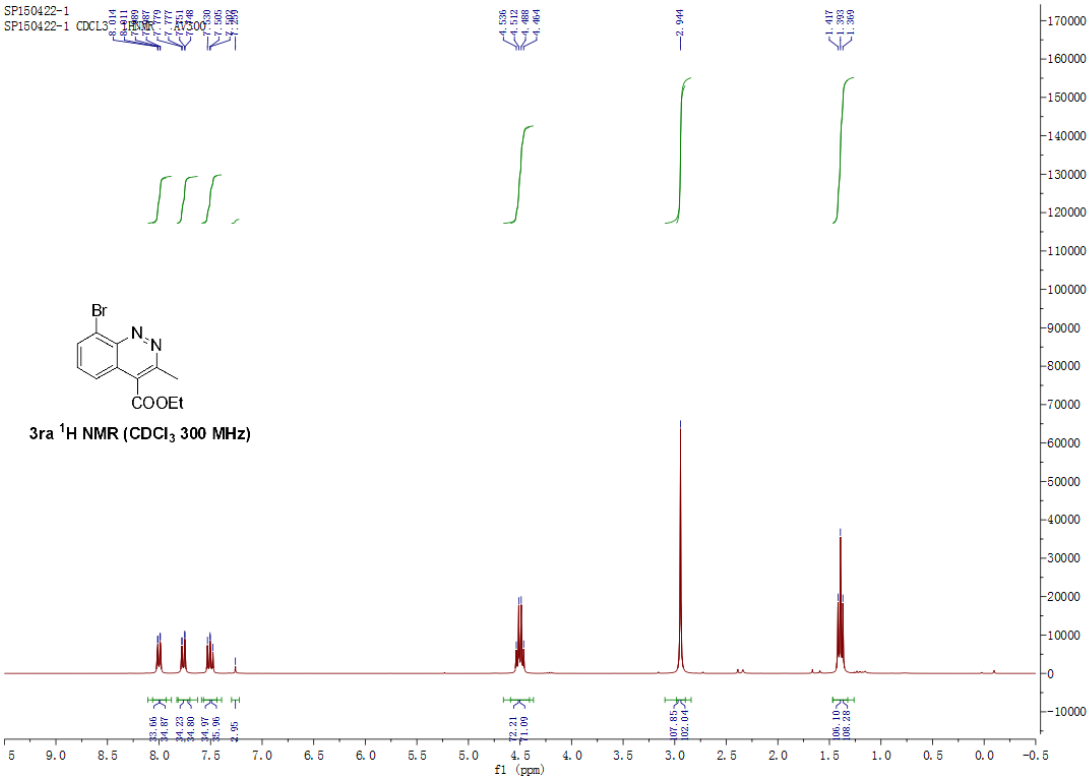
3pa ^{13}C NMR ($CDCl_3$ 75 MHz)



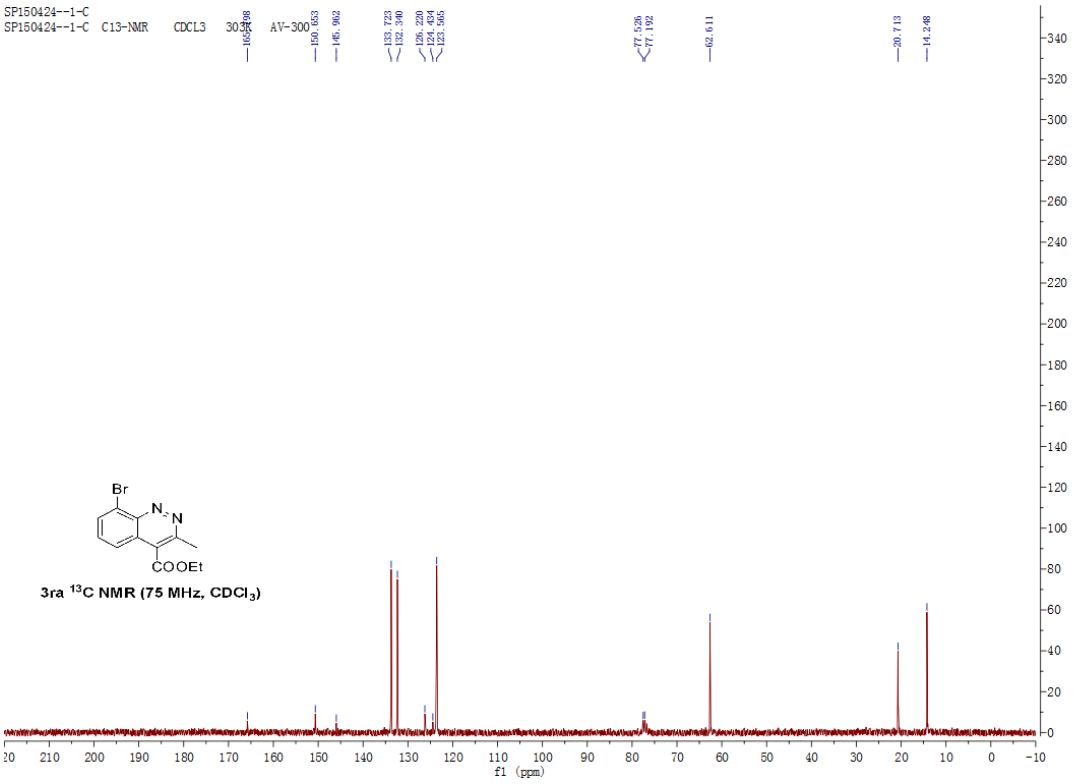
3qa ^{1}H NMR ($CDCl_3$ 300 MHz)



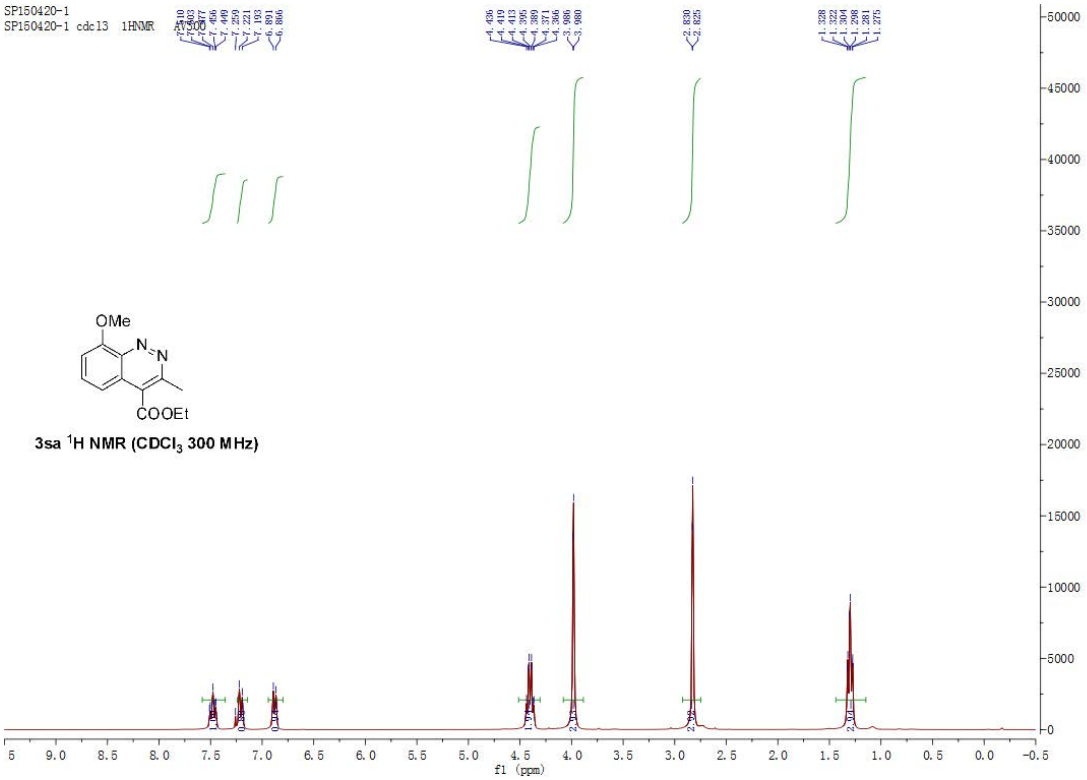
3qa ^{13}C NMR ($CDCl_3$ 75 MHz)



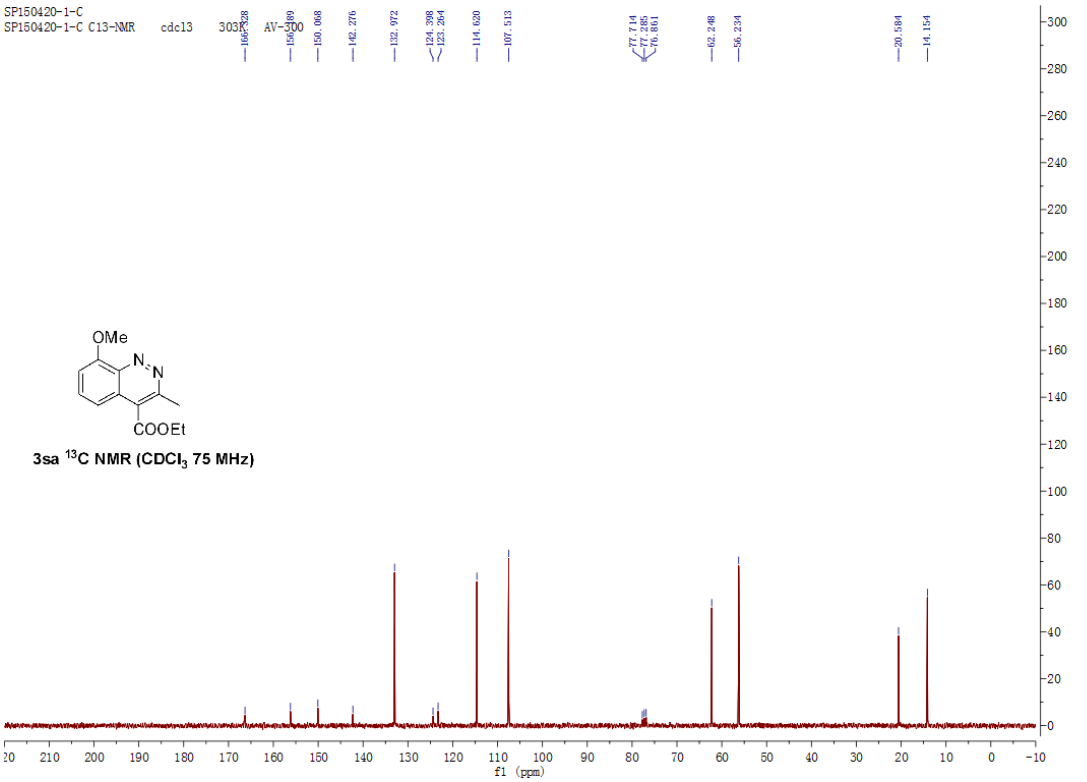
3ra ^{1}H NMR ($CDCl_3$ 300 MHz)



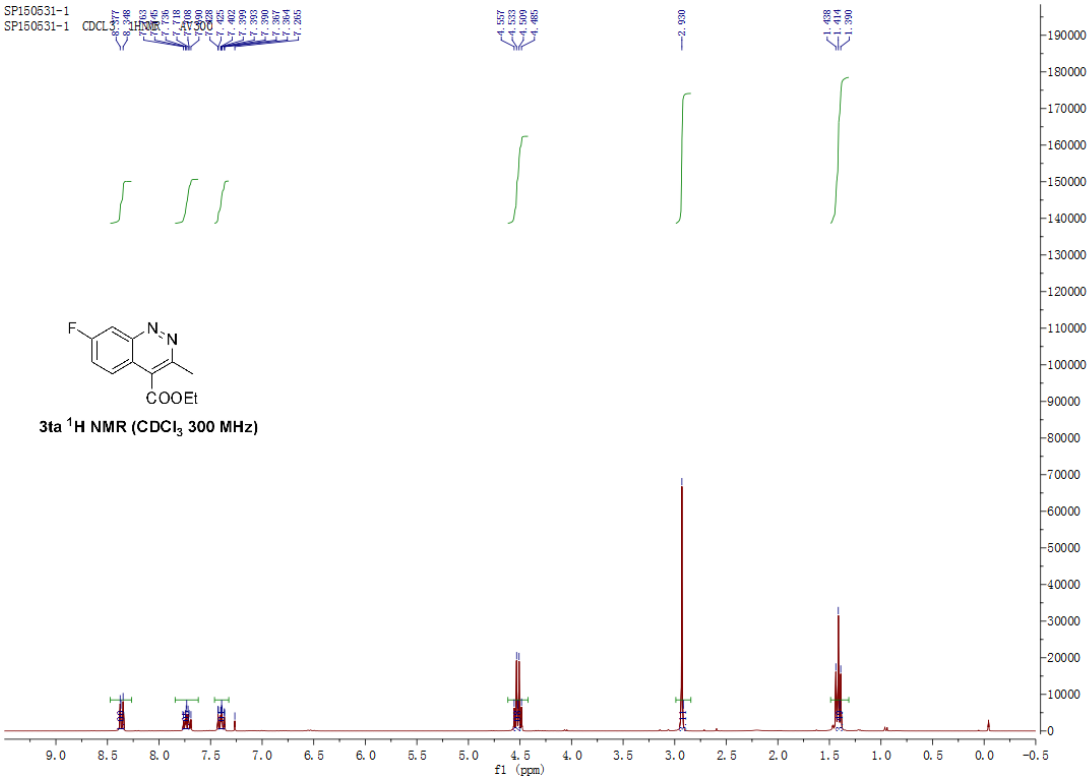
3ra ^{13}C NMR (75 MHz, $CDCl_3$)



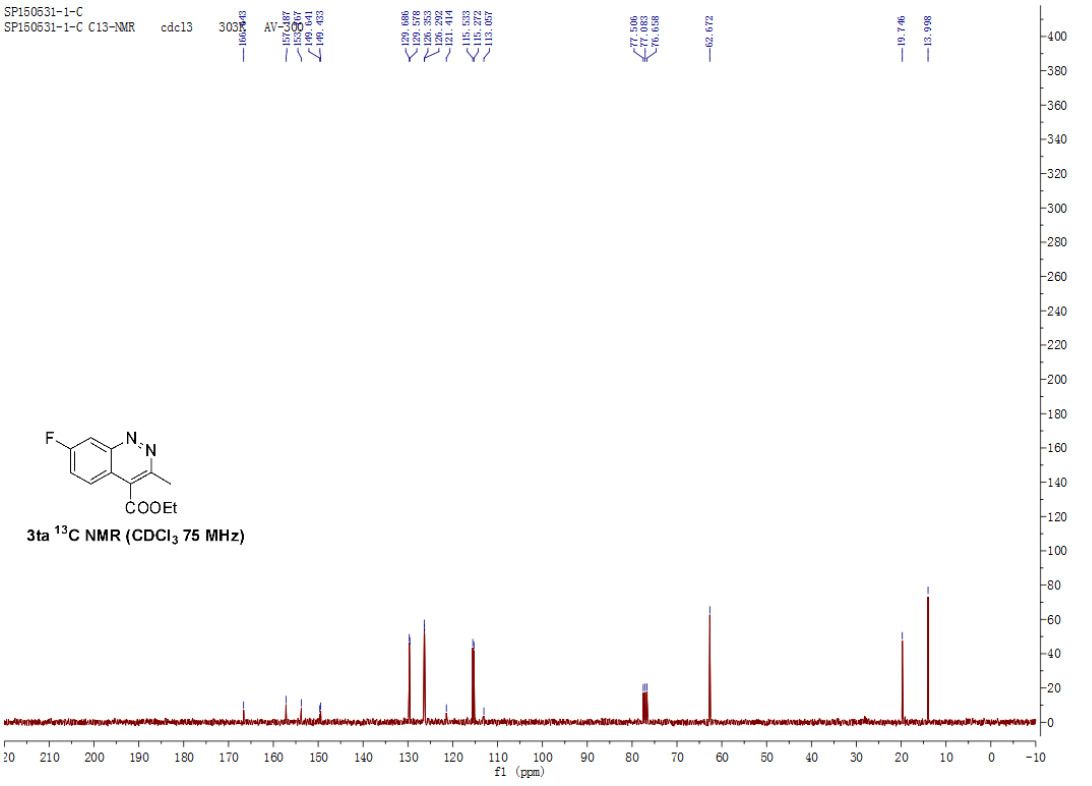
3sa ^{1}H NMR ($CDCl_3$ 300 MHz)



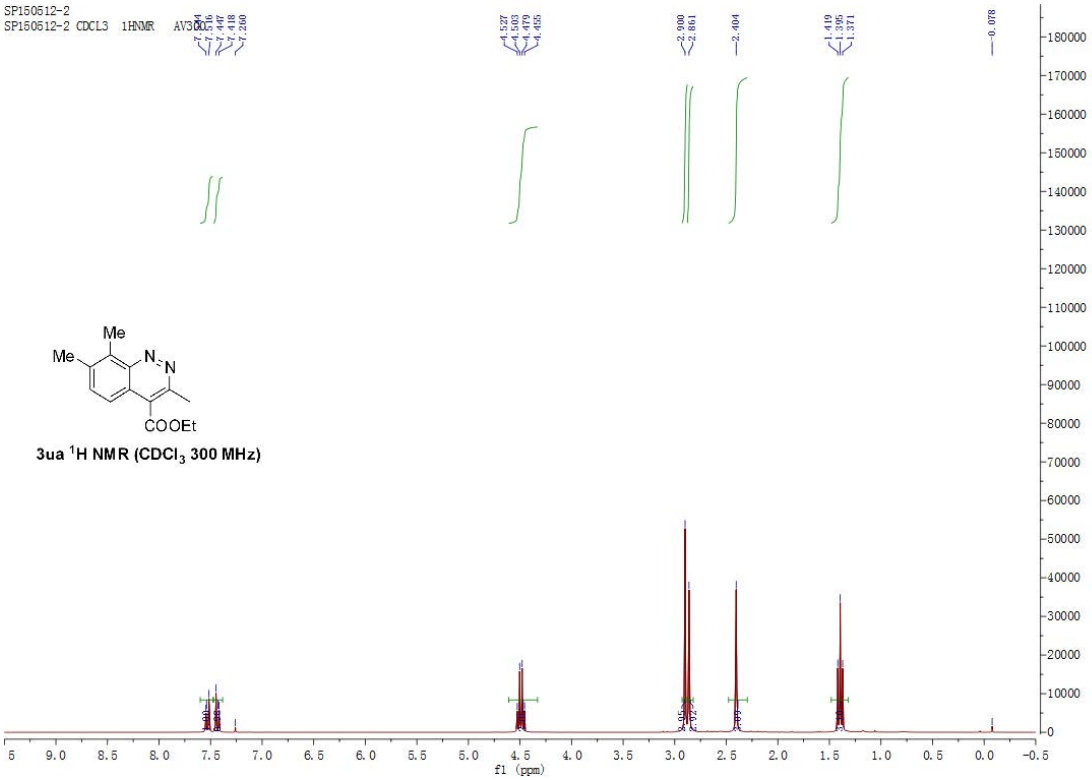
3sa ^{13}C NMR ($CDCl_3$ 75 MHz)



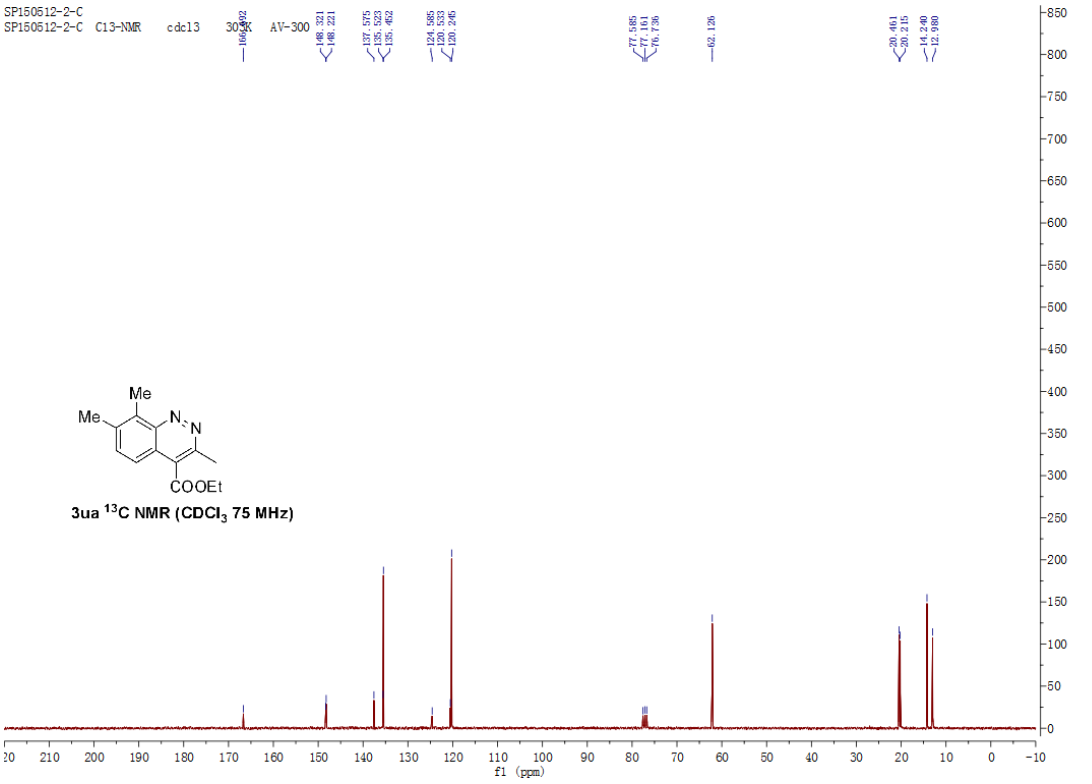
3ta ^{1}H NMR ($CDCl_3$ 300 MHz)



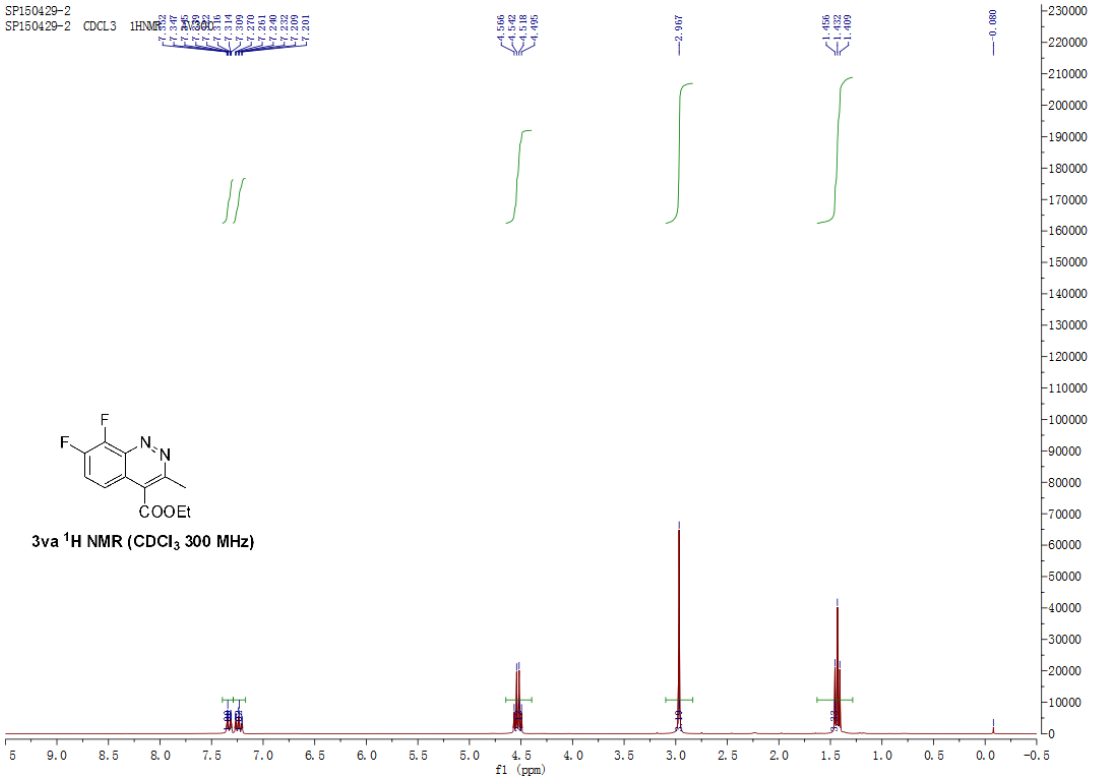
3ta ^{13}C NMR ($CDCl_3$ 75 MHz)



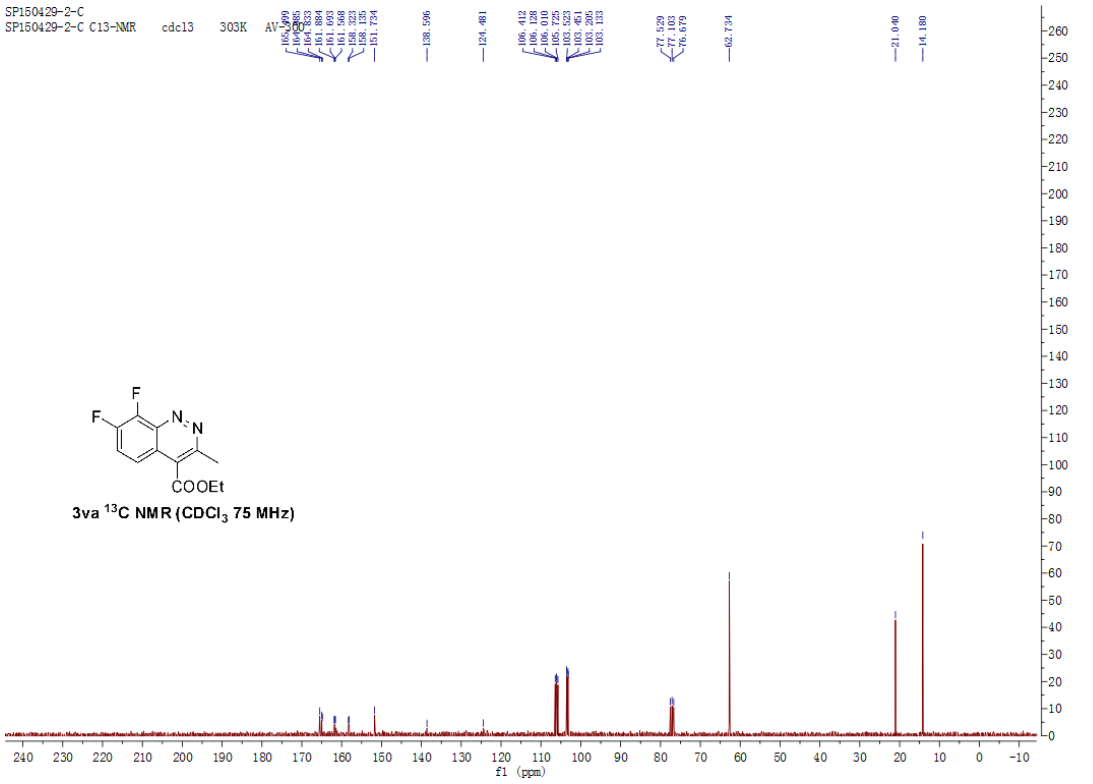
3ua ^{1}H NMR ($CDCl_3$ 300 MHz)



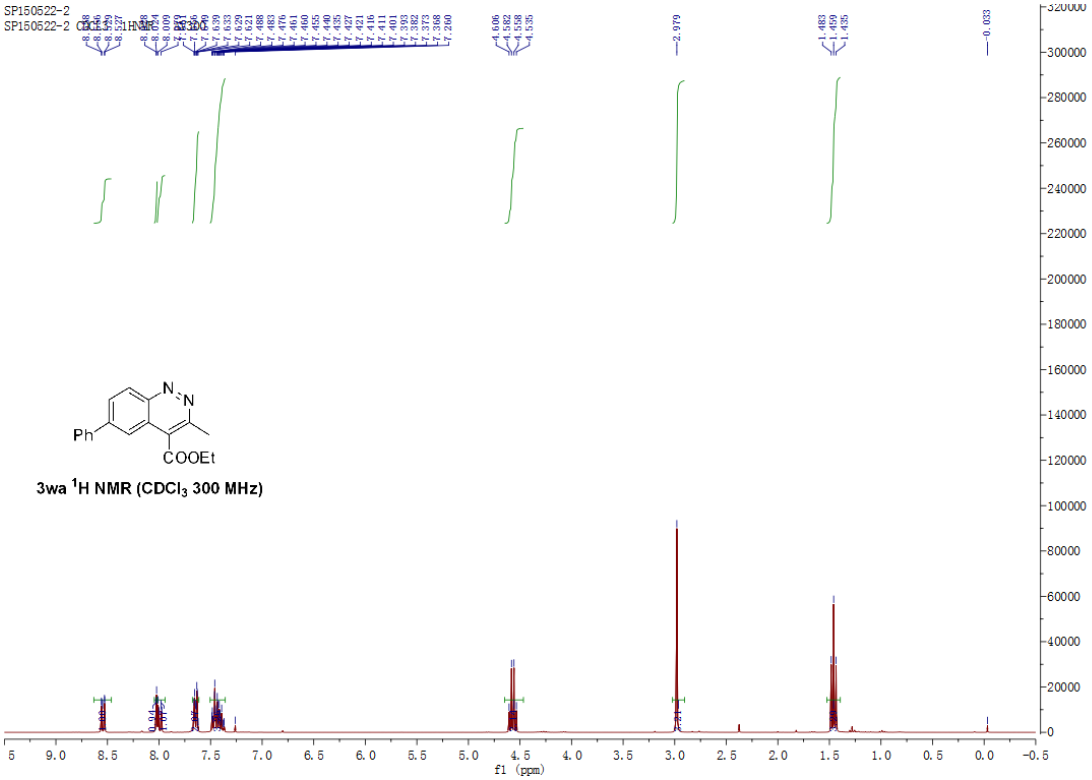
3ua ^{13}C NMR ($CDCl_3$ 75 MHz)



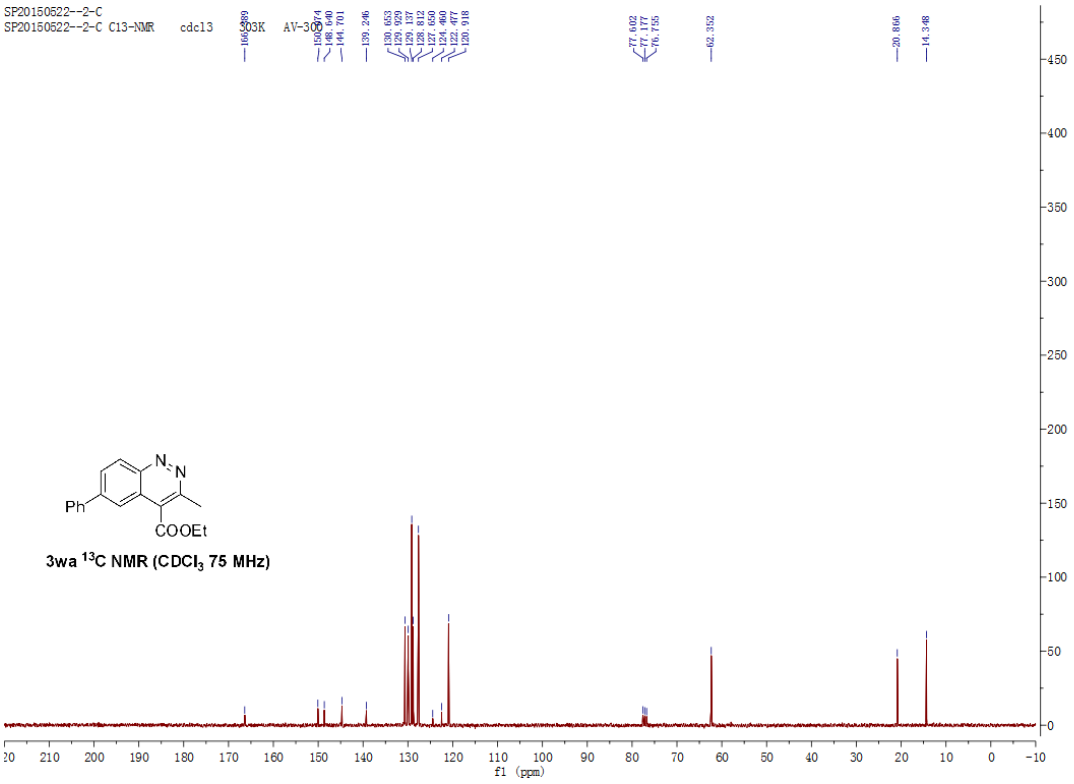
3va ^{1}H NMR ($CDCl_3$ 300 MHz)



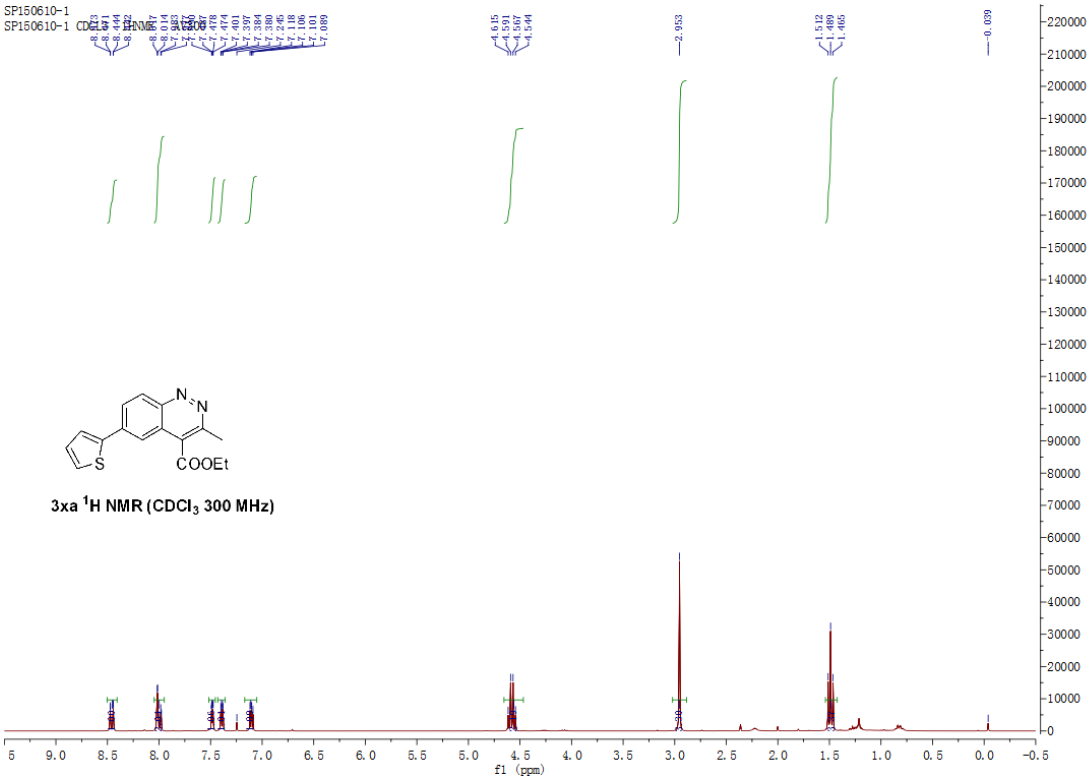
3va ^{13}C NMR ($CDCl_3$ 75 MHz)



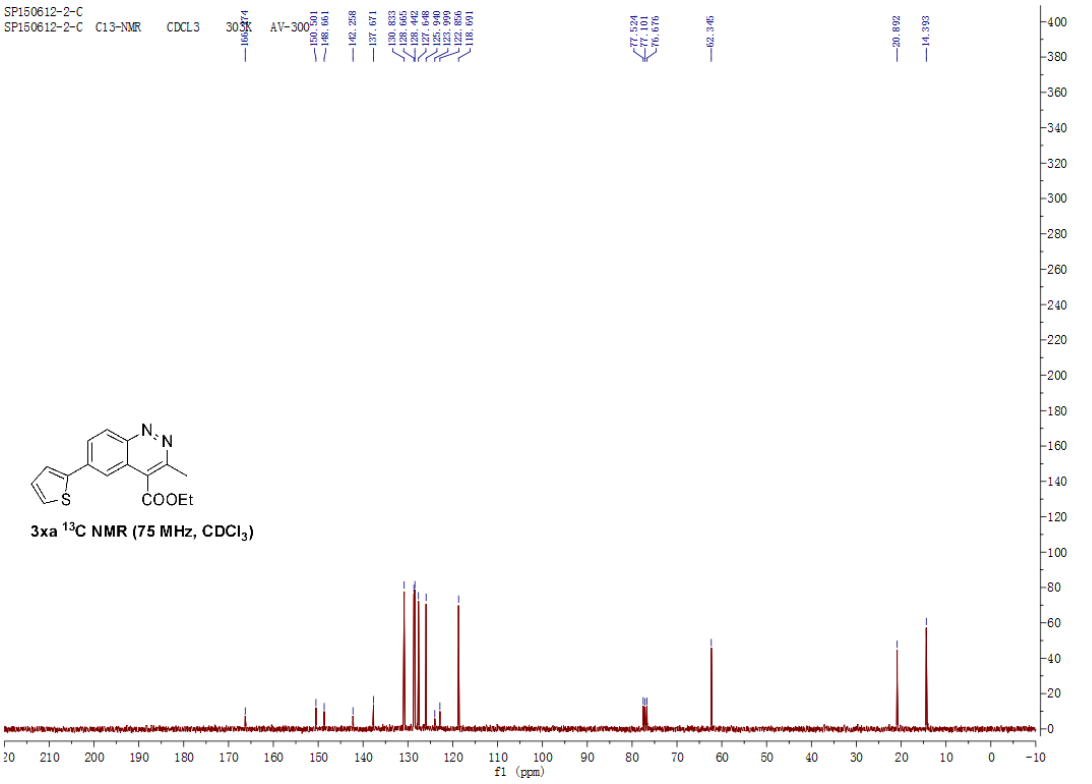
3wa ^{1}H NMR ($CDCl_3$ 300 MHz)



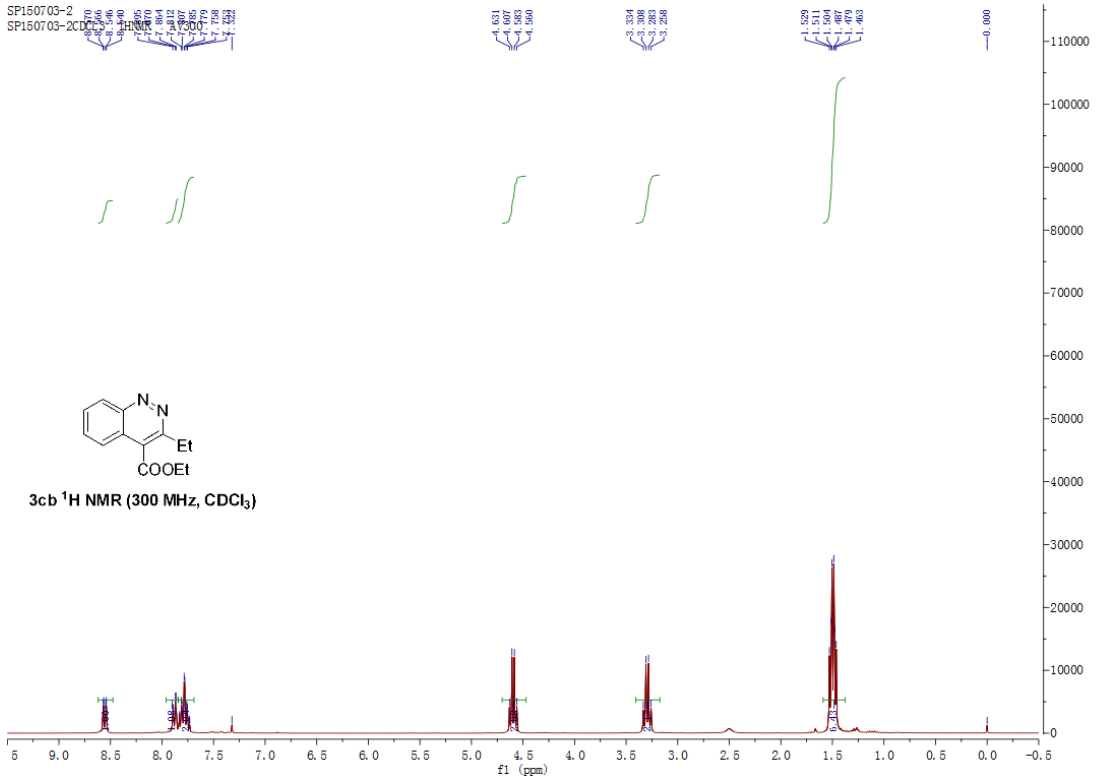
3wa ^{13}C NMR ($CDCl_3$ 75 MHz)



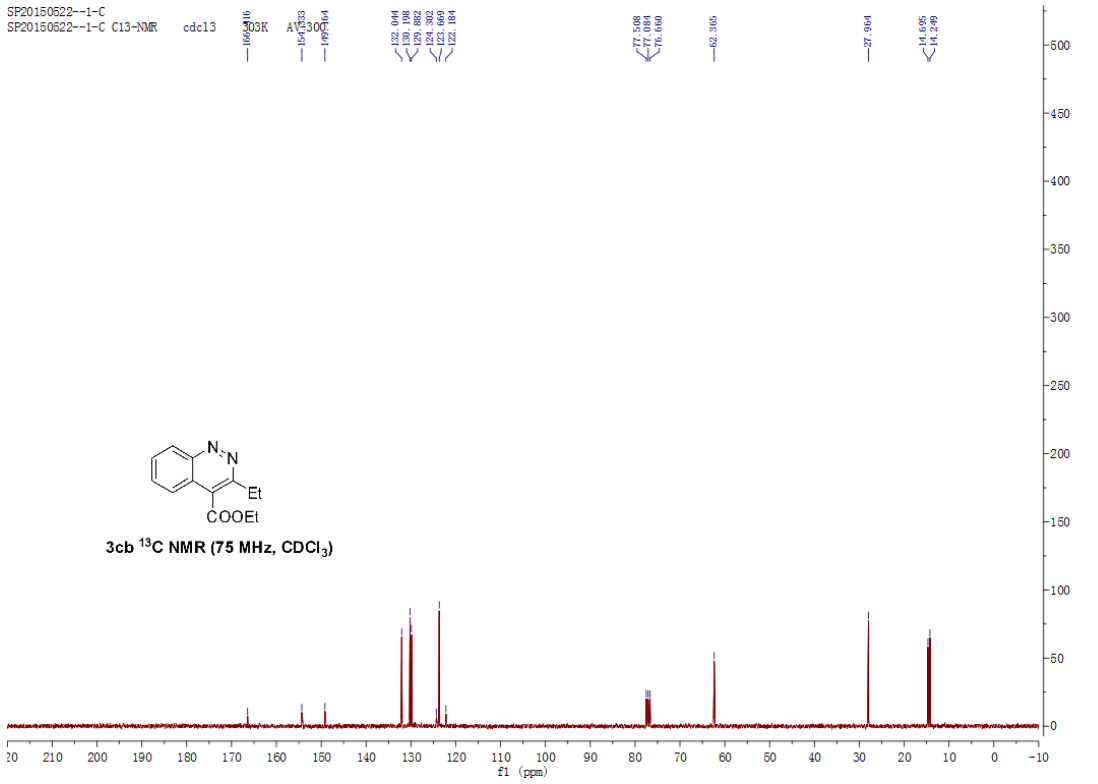
3xa ^{1}H NMR ($CDCl_3$ 300 MHz)



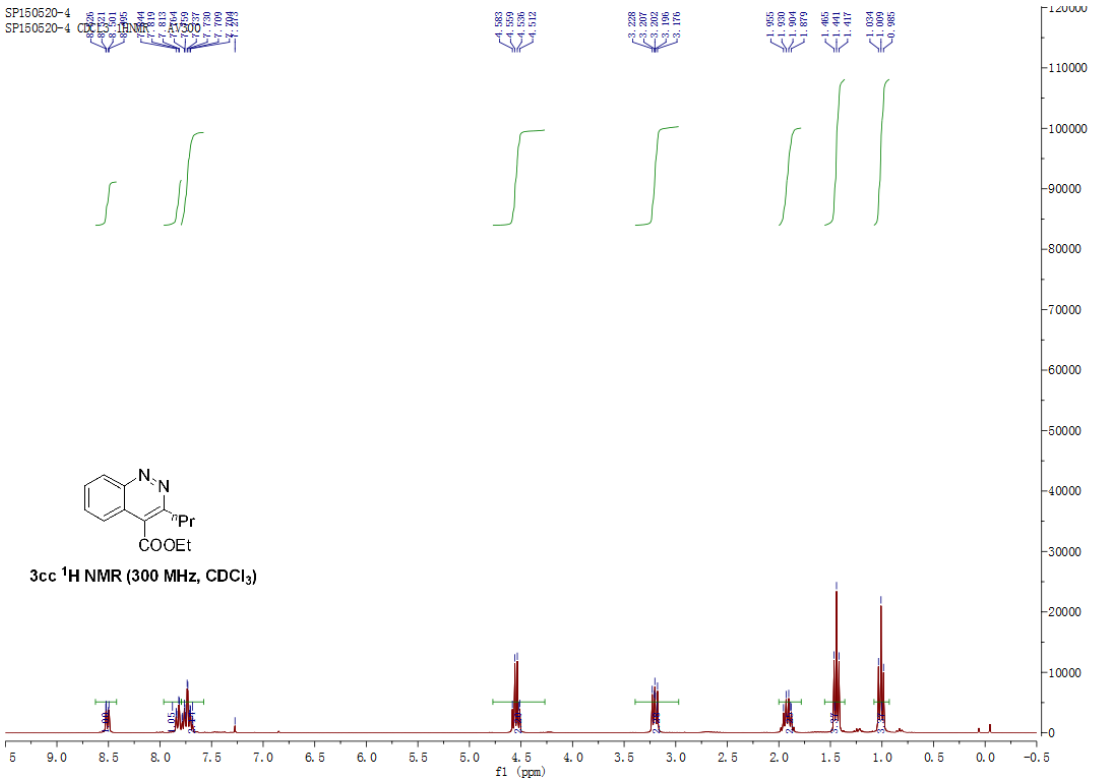
3xa ^{13}C NMR (75 MHz, $CDCl_3$)



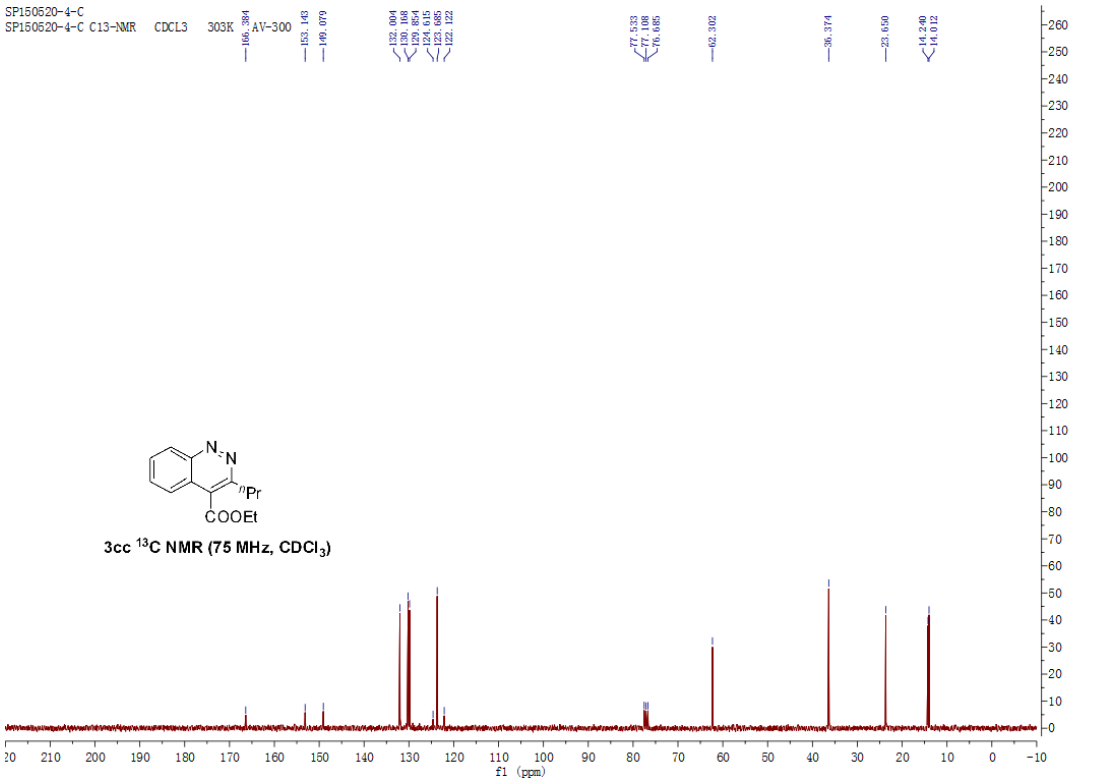
3cb ^{1}H NMR (300 MHz, $CDCl_3$)



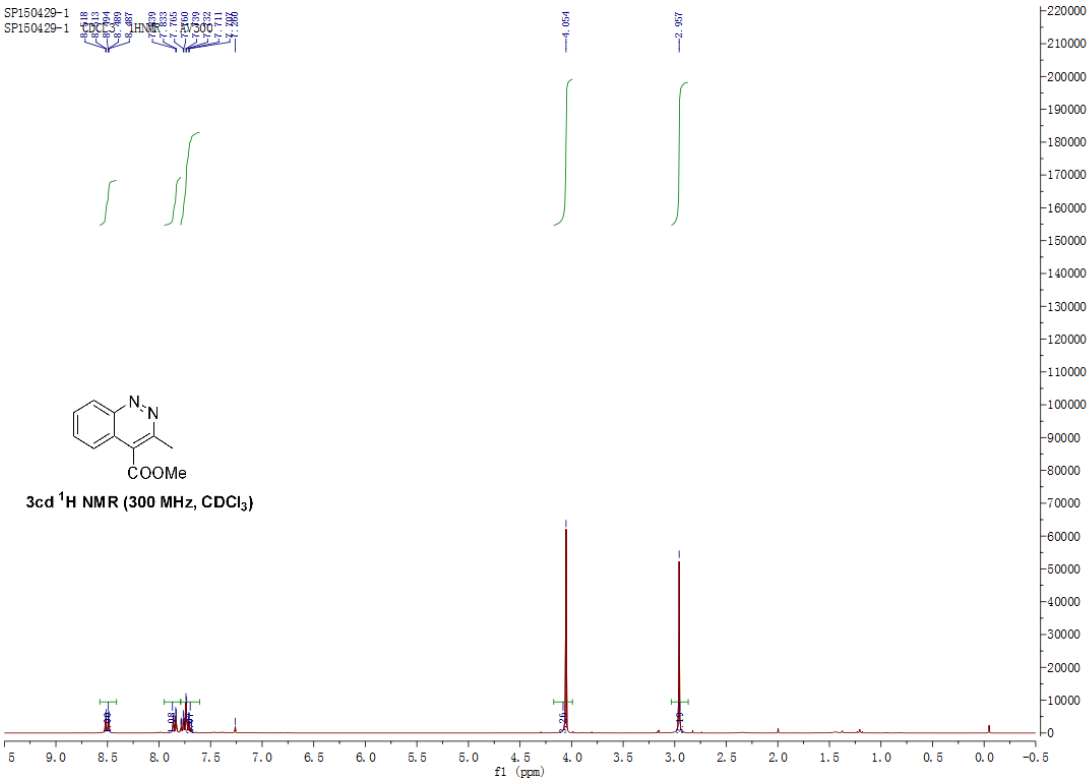
3cb ^{13}C NMR (75 MHz, $CDCl_3$)



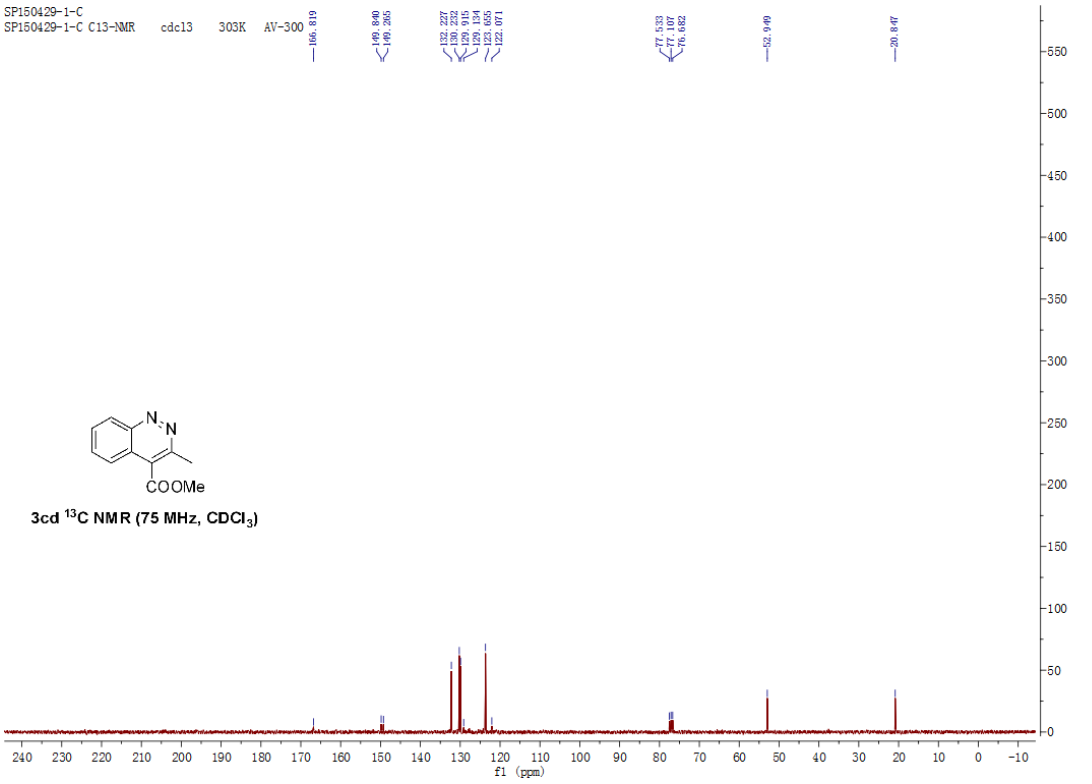
3cc ^{1}H NMR (300 MHz, $CDCl_3$)



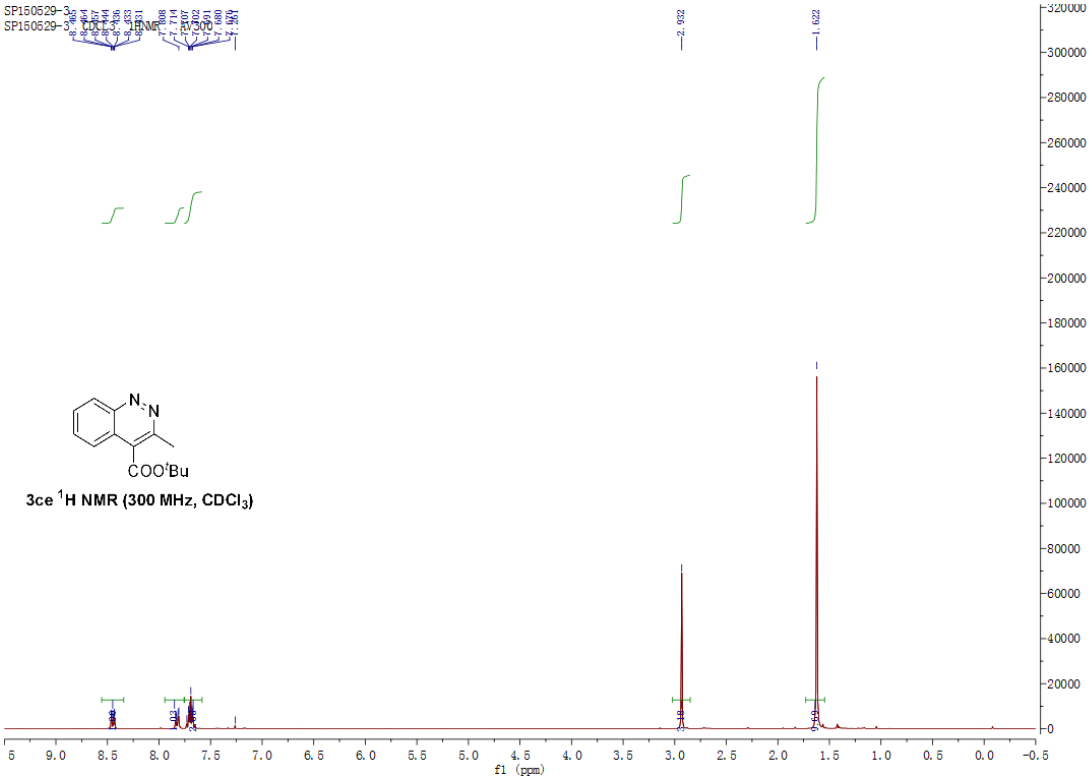
3cc ^{13}C NMR (75 MHz, $CDCl_3$)



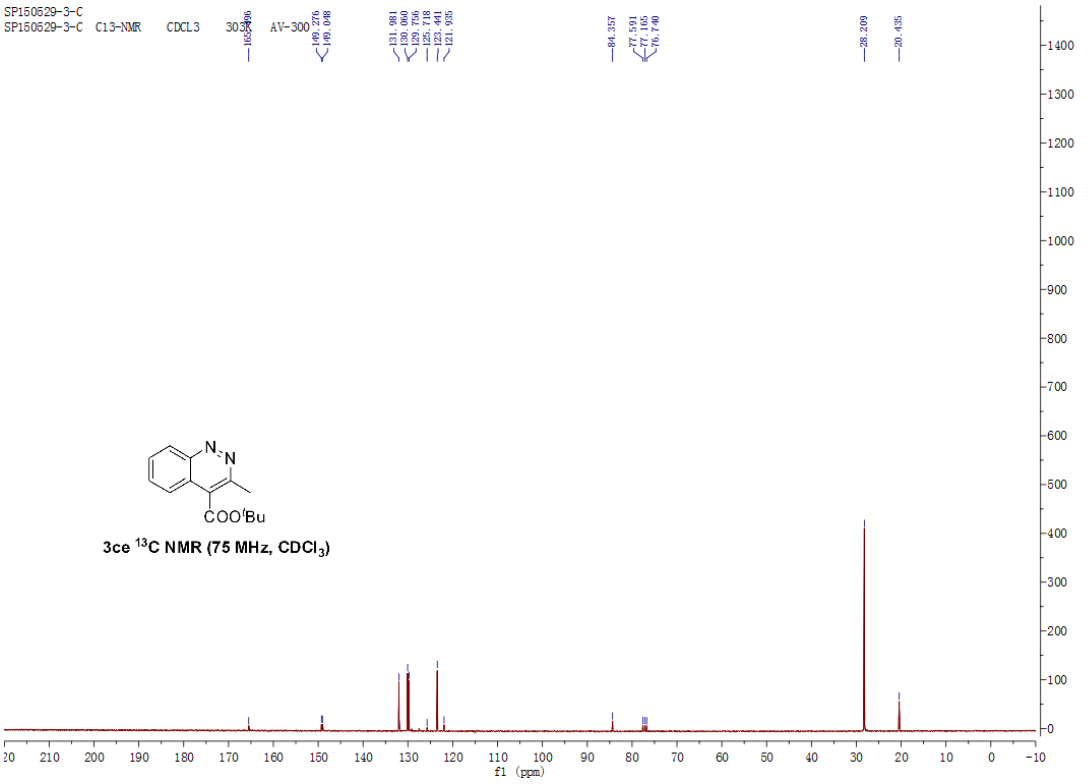
3cd ^{1}H NMR (300 MHz, $CDCl_3$)



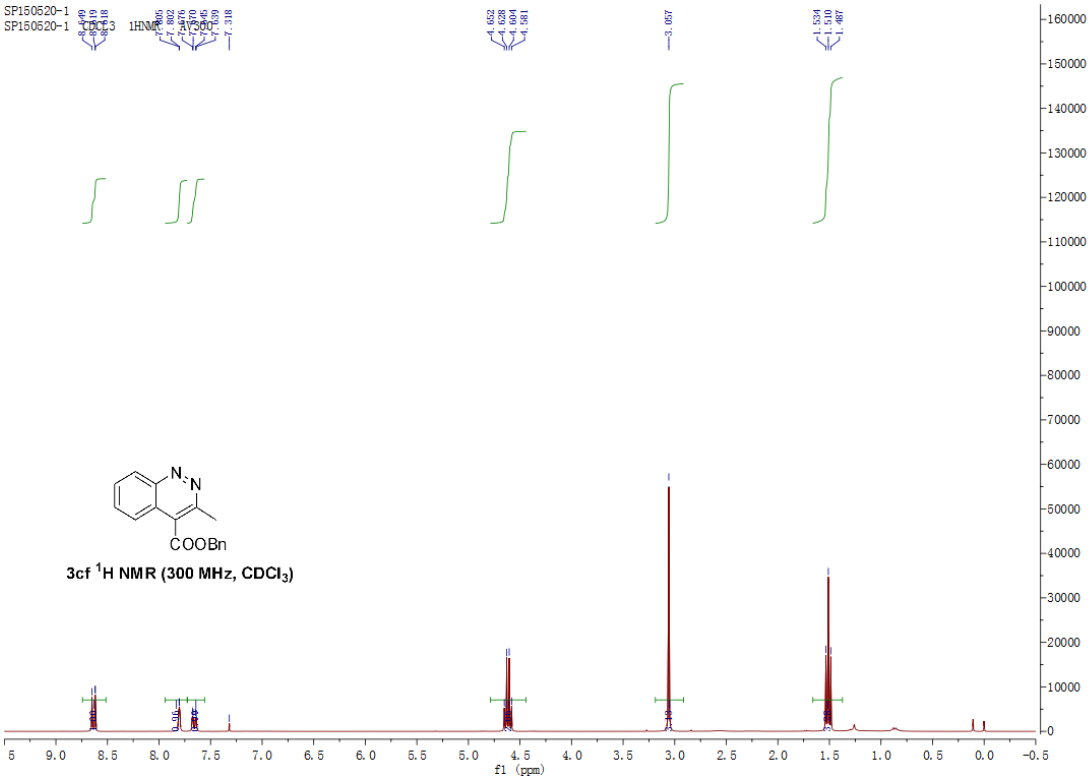
3cd ^{13}C NMR (75 MHz, $CDCl_3$)



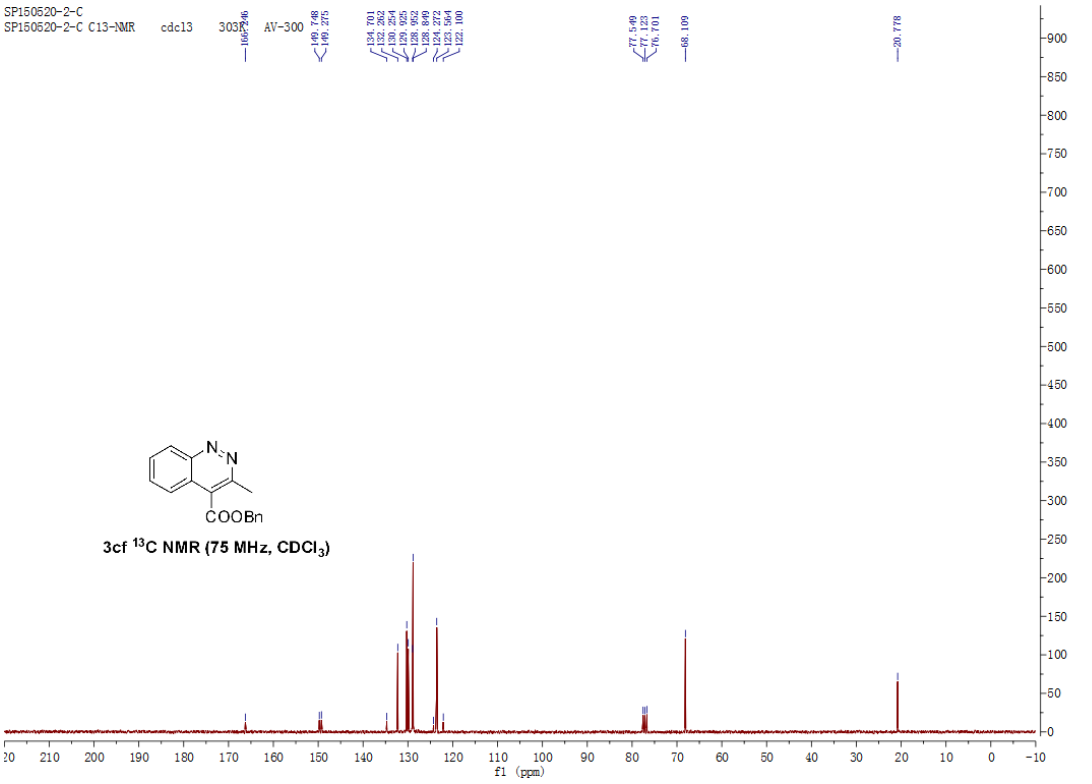
3ce ^{1}H NMR (300 MHz, $CDCl_3$)



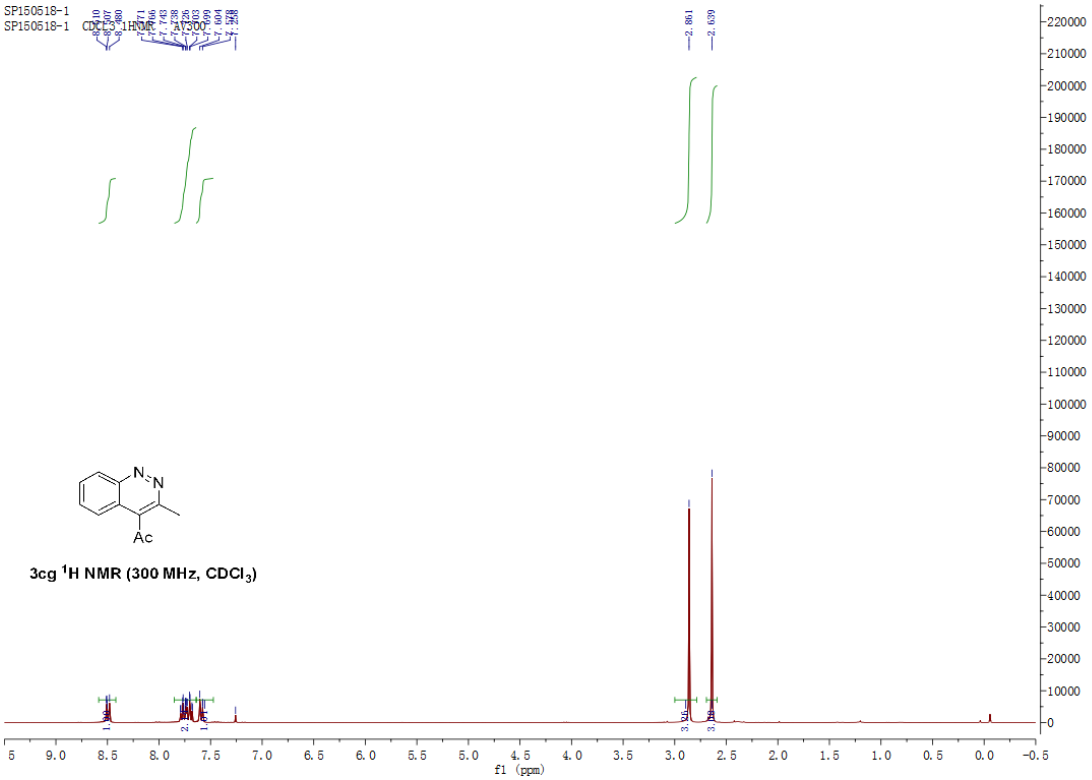
3ce ^{13}C NMR (75 MHz, $CDCl_3$)



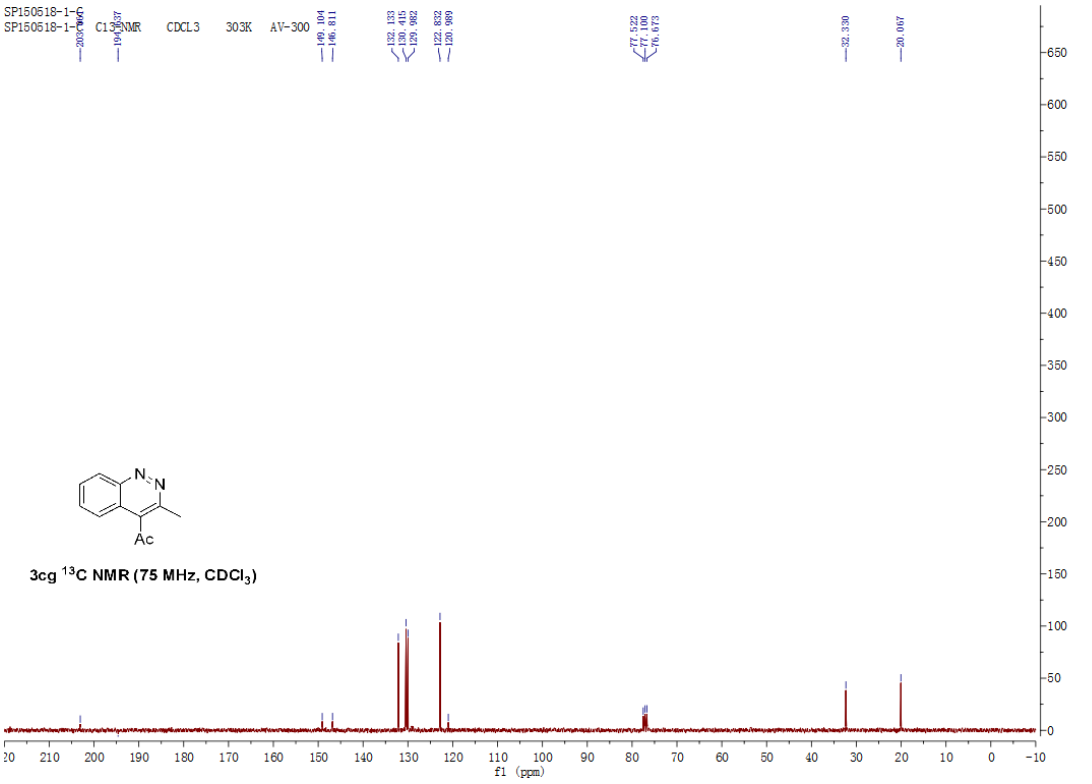
3cf ^{1}H NMR (300 MHz, $CDCl_3$)



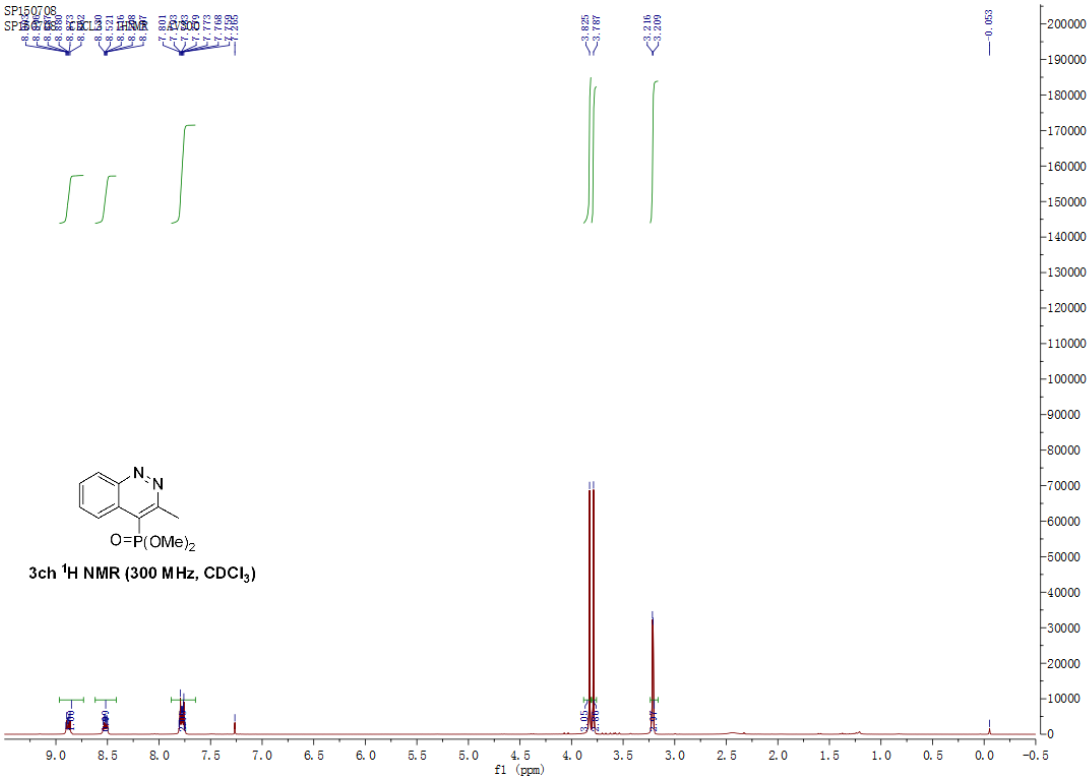
3cf ^{13}C NMR (75 MHz, $CDCl_3$)

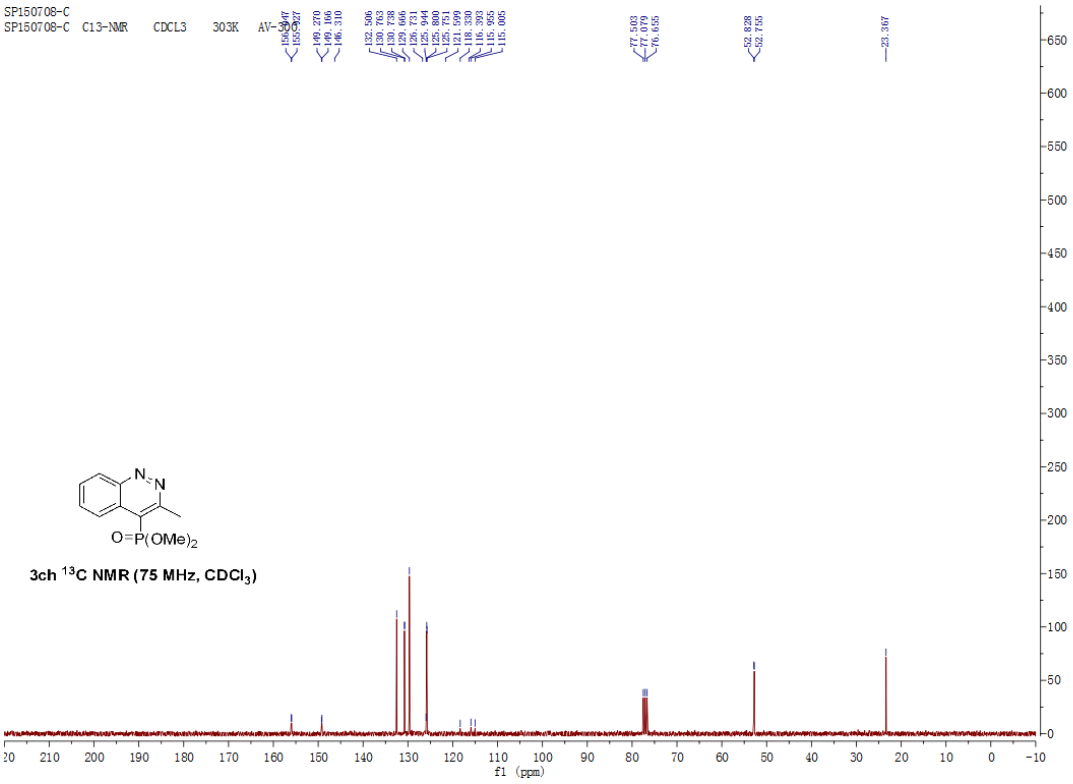


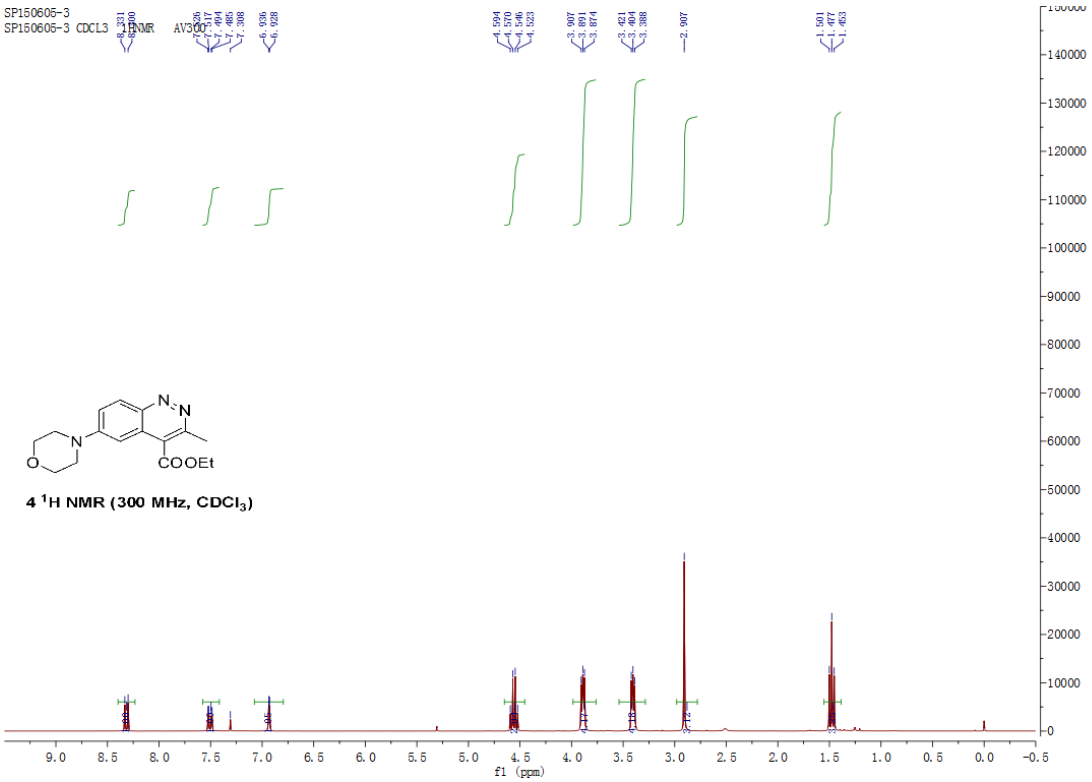
3cg ^{1}H NMR (300 MHz, $CDCl_3$)



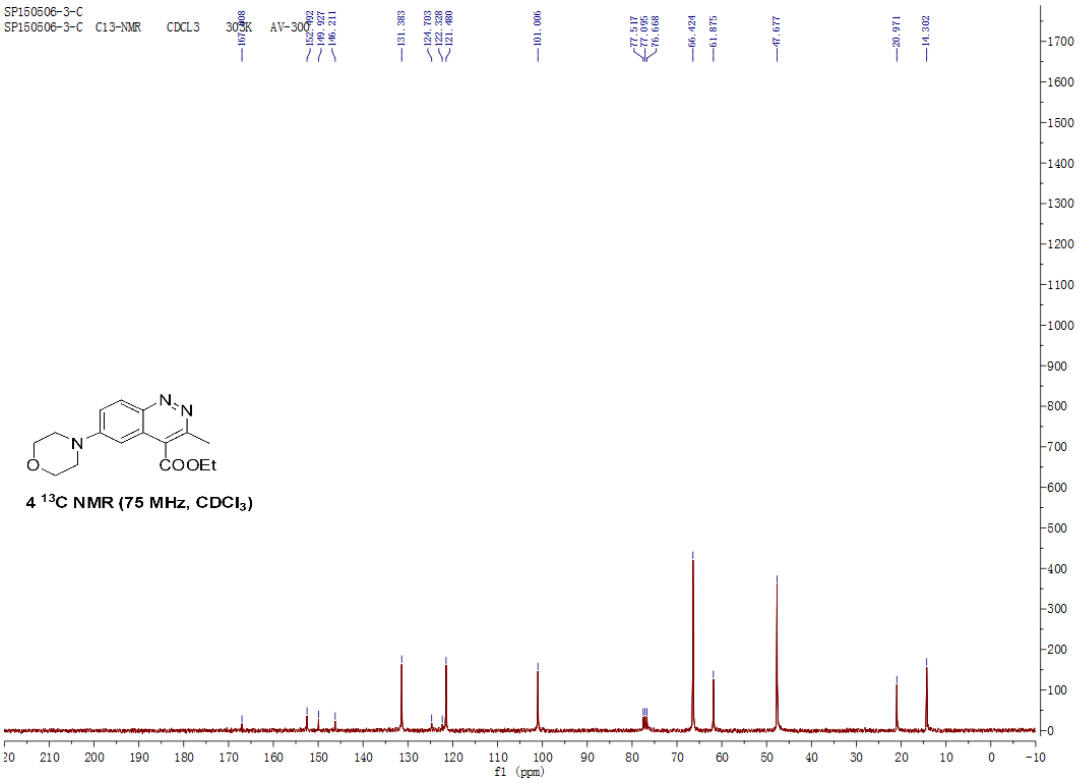
3cg ^{13}C NMR (75 MHz, $CDCl_3$)


O=P(OMe)2
3ch 1H NMR (300 MHz, CDCl3)
f1 (ppm)

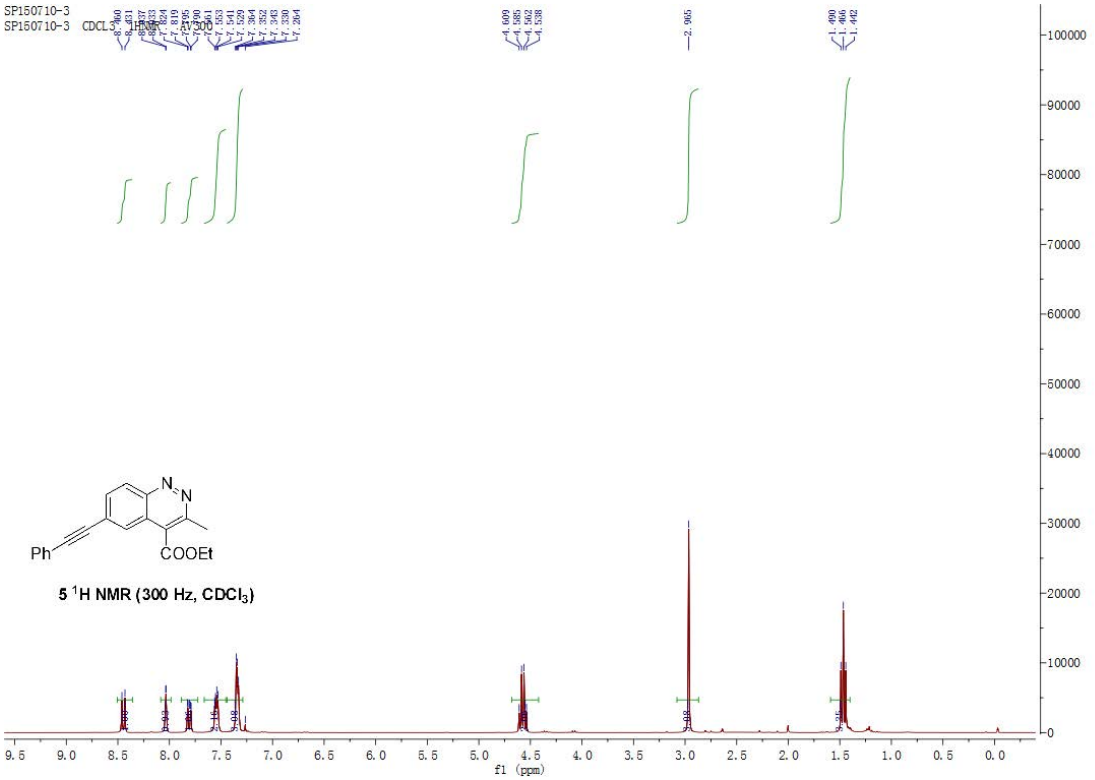

O=P(OMe)2
3ch 13C NMR (75 MHz, CDCl3)
f1 (ppm)



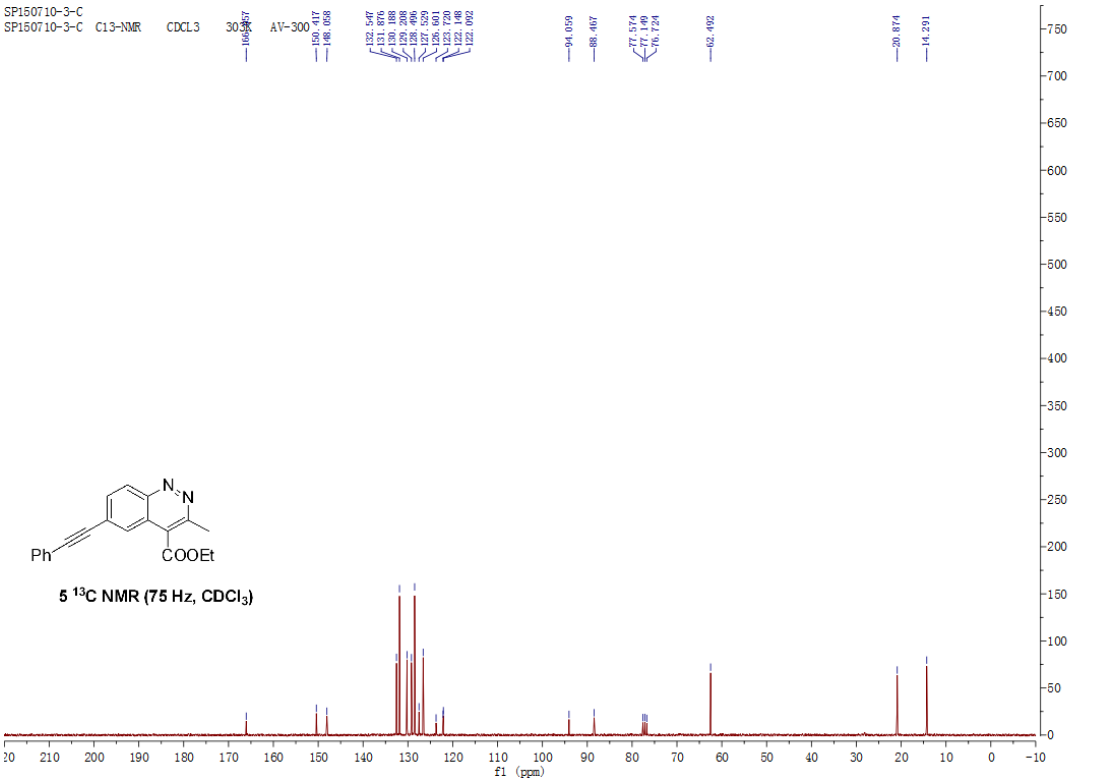
4 ^{1}H NMR (300 MHz, $CDCl_3$)



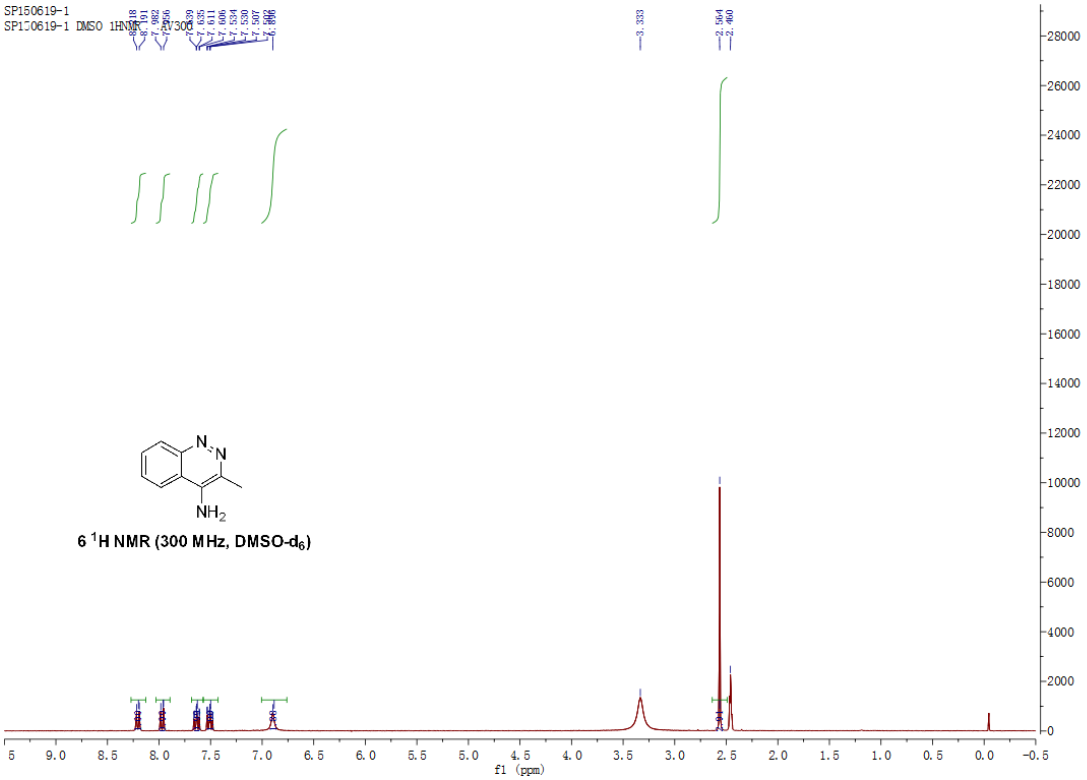
4 ^{13}C NMR (75 MHz, $CDCl_3$)



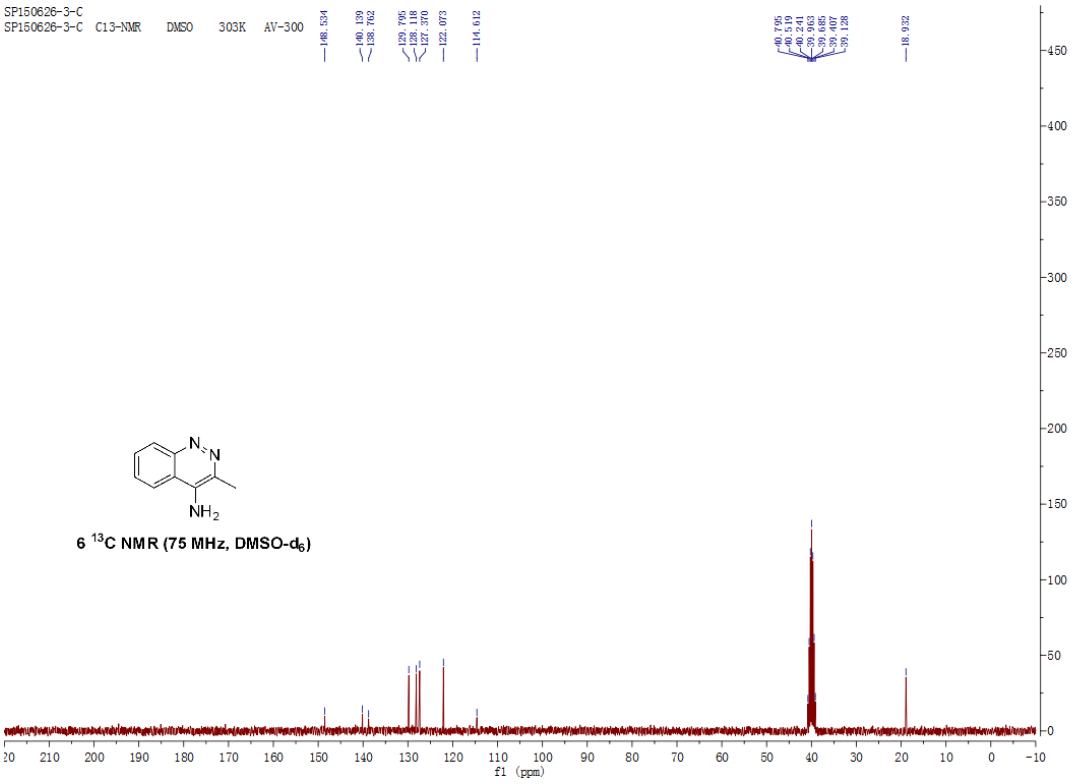
5 ^{1}H NMR (300 Hz, $CDCl_3$)



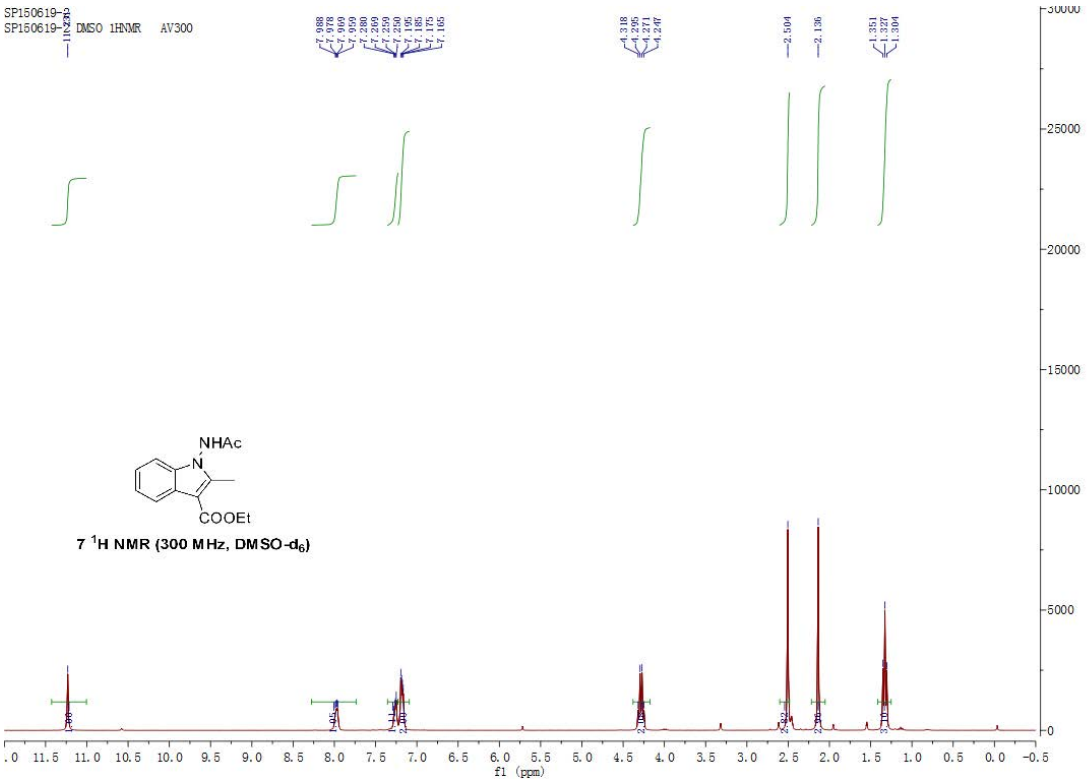
5 ^{13}C NMR (75 Hz, $CDCl_3$)



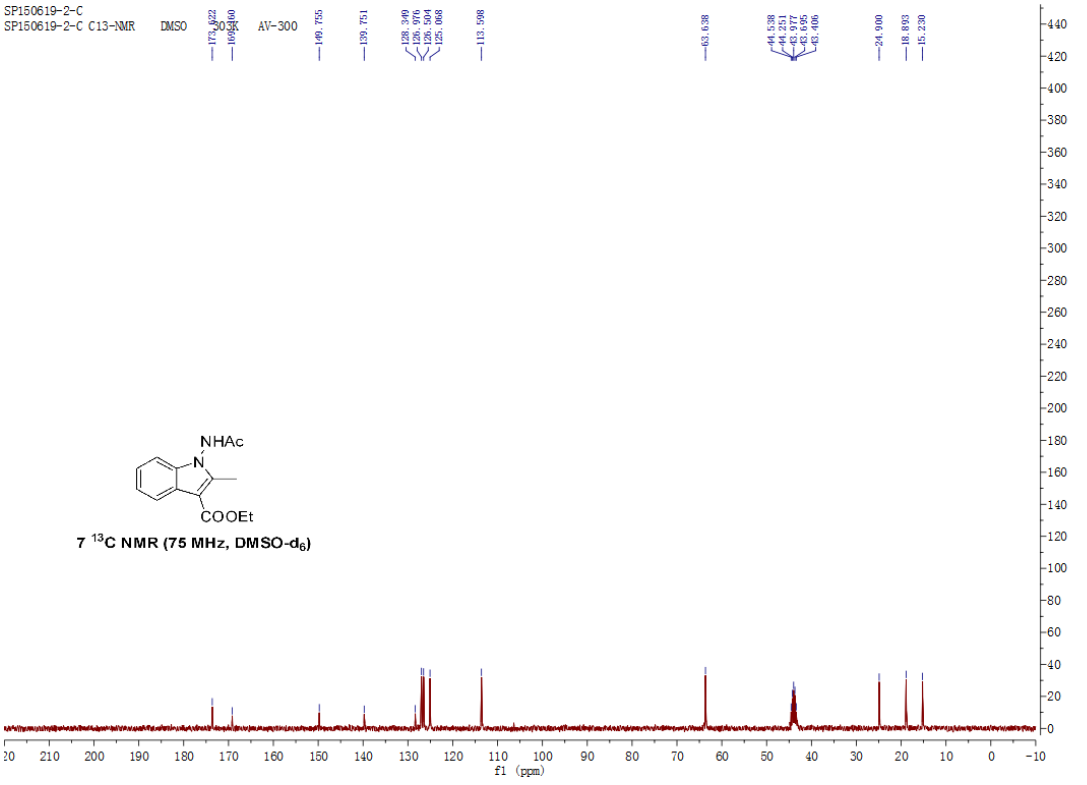
6 ^{1}H NMR (300 MHz, DMSO-d_6)



6 ^{13}C NMR (75 MHz, DMSO-d_6)



7 ^{1}H NMR (300 MHz, DMSO-d_6)



7 ^{13}C NMR (75 MHz, DMSO-d_6)