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3-Vinyl oxindole-chromone synthon as a skeletal reconstruction reactant for the synthesis of 2-hydroxy benzoyl pyridones

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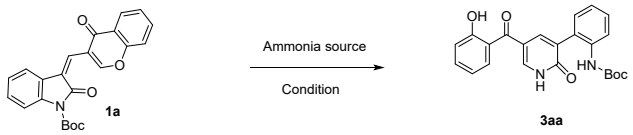
1. General information

Reactions were monitored by thin layer chromatography using UV light to visualize the course of reaction. Purification of reaction products was carried out by flash chromatography on silica gel or just by simple filtration and washing. ^{1}H and ^{13}CNMR spectra were obtained using a Bruker DPX-400 spectrometer. ^{1}H NMR chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm (δ) from tetramethylsilane (TMS) with the solvent resonance as the internal standard. Melting points were measured on an electrothermal digital melting point apparatus.

2. Table S1: optimization of reaction conditions for synthesis of compound 3aa



Entry [a]	Ammonia source	T (°C)	Time (h)	Yield [b] (%)
1[b]	NH_3 saturated THF	25	5	12
2[b]	NH_3 saturated toluene	25	5	<5
3[b]	NH_3 saturated CH_2Cl_2	25	5	<5
4[b]	NH_3 saturated EtOH	25	5	74
5[c]	$NH_3 \cdot H_2O$ (25%)	25	5	87
6[c]	$NH_3 \cdot H_2O$ (25%)	50	5	78
7[c]	$NH_3 \cdot H_2O$ (25%)	25	3	85
8[d]	NH_4Cl (2.0 eq)	25	5	-
9[d]	$(NH_4)_2CO_3$ (2.0 eq)	25	3	84
10[d]	NH_4HCO_3 (2.0 eq)	25	3	83
11[d]	NH_4OAc (2.0 eq)	25	3	85
12[d]	NH_4OAc (2.0 eq)	25	1	80
13[d]	NH_4OAc (2.0 eq)	50	5	77

[a] The reactions were carried out with **1a** (0.30 mmol) under specified reaction conditions. [b] The reactions were carried out in 1.5 mL of NH_3 saturated solvent. [c] The reactions were carried out in 1.5 mL of $NH_3 \cdot H_2O$ (25%). [d] The reactions were carried out in 1.5 mL of EtOH.

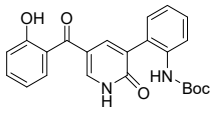
3. Synthesis of *N*-H 2-hydroxy benzoylpyridones 3 by reaction of ammonia

In a sealed tube equipped with a magnetic stirring bar, to 1.5 mL of $NH_3 \cdot H_2O$ (25%) was added 3-vinyl oxindole-chromone **1** (0.30 mmol). The reaction mixture was stirred at rt for 5 h. After completion of the reaction, as indicated by TLC, purification by flash column chromatography (hexane/EtOAc, 5/1, v/v) was carried out to furnish the *N*-H 2-hydroxy benzoylpyridones **3**.

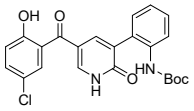
4. Synthesis of *N*-H 2-hydroxy benzoylpyridones 3 by reaction of NH_4OAc

In a sealed tube equipped with a magnetic stirring bar, to 1.5 mL of EtOH was added 3-vinyl oxindole-chromone **1** (0.30 mmol) and NH_4OAc (0.60 mmol). The reaction mixture was stirred at rt for 3 h. After completion of the reaction, as indicated by TLC, purification by flash column chromatography (hexane/EtOAc, 5/1, v/v) was carried out to furnish the *N*-H 2-hydroxy benzoylpyridones **3**.

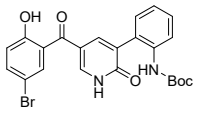
5. Characterization data of *N*-H 2-hydroxy benzoylpyridones 3



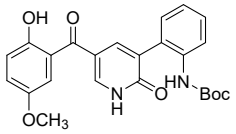
***tert*-butyl (2-(5-(2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3aa)**: Light yellow solid, m.p. 189.8-190.5 °C; 106.0 mg, yield 87% (103.5 mg, 85% for NH_4OAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.36 (s, 9H), 6.81-6.85 (m, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.03-7.07 (m, 1H), 7.14 (d, J = 7.6 Hz, 1H), 7.26-7.30 (m, 1H), 7.41-7.45 (m, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.58 (s, 1H), 7.65 (br s, 1H), 7.84 (s, 1H), 7.93 (s, 1H), 11.35 (br s, 1H), 13.14 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.3, 79.4, 117.6, 117.7, 118.2, 118.3, 123.1, 123.6, 127.4, 128.5, 130.0, 130.8, 135.5, 135.8, 138.3, 141.4, 152.8, 161.5, 162.7, 194.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{22}N_2NaO_5$ $[M+Na]^+$: 429.1421; Found: 429.1419.



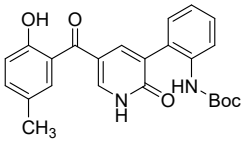
***tert*-butyl (2-(5-(5-chloro-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ab)**: Light yellow solid, m.p. 228.2-229.3 °C; 108.2 mg, yield 82% (110.9 mg, 84% for NH_4OAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.35 (s, 9H), 6.92 (d, J = 8.8 Hz, 1H), 7.03-7.07 (m, 1H), 7.13-7.15 (m, 1H), 7.23-7.27 (m, 1H), 7.34-7.37 (m, 1H), 7.45 (s, 1H), 7.48 (s, 1H), 7.63 (br s, 1H), 7.77 (s, 1H), 7.89 (s, 1H), 11.12 (br s, 1H), 12.94 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.3, 79.5, 117.6, 118.6, 119.3, 122.9, 123.7, 127.5, 128.5, 129.5, 129.9, 130.4, 135.2, 135.7, 138.5, 140.8, 152.8, 159.7, 162.5, 192.9; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{21}ClN_2NaO_5$ $[M+Na]^+$: 463.1031; Found: 463.1026.



***tert*-butyl (2-(5-(5-bromo-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ac)**: Light yellow solid, m.p. 200.1-201.3 °C; 106.0 mg, yield 73%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.36 (s, 9H), 6.90 (d, J = 9.2 Hz, 1H), 7.06-7.09 (m, 1H), 7.16-7.19 (m, 1H), 7.26-7.31 (m, 1H), 7.46 (s, 1H), 7.49-7.52 (m, 1H), 7.62 (s, 1H), 7.66 (br s, 1H), 7.82 (s, 1H), 7.91 (s, 1H), 11.16 (br s, 1H), 12.92 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 26.1, 78.3, 108.6, 116.4, 118.0, 118.5, 122.5, 128.7, 131.3, 134.6, 136.8, 137.2, 139.7, 151.6, 159.0, 161.4, 191.7; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{21}BrN_2NaO_5$ $[M+Na]^+$: 507.0526; Found: 507.0527.

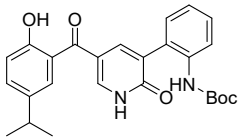


***tert*-butyl (2-(5-(2-hydroxy-5-methoxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ad)**: Light yellow solid, m.p. 201.3-202.5 °C; 113.8 mg, yield 87% (117.7 mg, 90% for NH_4OAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.34 (s, 9H), 3.63 (s, 3H), 6.89-6.92 (m, 2H), 7.01-7.04 (m, 2H), 7.12 (d, J = 6.4 Hz, 1H), 7.22-7.26 (m, 1H), 7.53 (s, 1H), 7.61 (br s, 1H), 7.79 (s, 1H), 7.91 (s, 1H), 10.74 (br s, 1H), 12.98 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 28.3, 56.0, 80.5, 115.1, 118.6, 119.2, 119.5, 123.5, 124.6, 128.6, 129.5, 130.9, 131.0, 136.8, 139.4, 142.2, 151.8, 153.8, 156.3, 163.5, 194.6; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{24}H_{24}N_2NaO_6$ $[M+Na]^+$: 459.1527; Found: 459.1531.

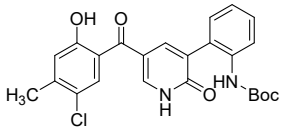


***tert*-butyl (2-(5-(2-hydroxy-5-methylbenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ae)**: Light yellow solid, m.p. 192.9-193.5 °C; 92.0 mg, yield 73% (103.3 mg, 82% for NH_4OAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.36 (s, 9H), 2.22 (s, 3H), 6.90 (d, J = 8.8 Hz, 1H), 7.05-7.09 (m, 1H), 7.15-7.18 (m, 1H), 7.24-7.31 (m, 3H), 7.55 (s, 1H), 7.67 (br s, 1H), 7.85 (s, 1H), 7.94 (s, 1H), 11.13 (br s, 1H), 13.16 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.7, 28.3, 80.4, 118.5, 118.6, 119.5, 124.6, 128.5, 129.5, 131.0, 131.2, 131.4, 136.9, 137.7, 139.1, 142.5,

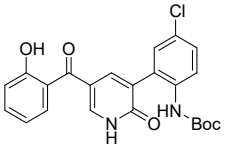
153.8, 160.5, 163.8, 195.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{24}H_{24}N_2NaO_5$ $[M+Na]^+$: 443.1577; Found: 443.1581.



***tert*-butyl (2-(5-(2-hydroxy-5-isopropylbenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3af)**: Light yellow solid, m.p. 165.8-166.3 °C; 112.9 mg, yield 84%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.12 (d, J = 7.2 Hz, 6H), 1.35 (s, 9H), 2.78-2.81 (m, 1H), 6.92 (d, J = 9.2 Hz, 1H), 7.02-7.06 (m, 1H), 7.14-7.17 (m, 1H), 7.24-7.28 (m, 1H), 7.31-7.34 (m, 2H), 7.56 (s, 1H), 7.64 (br s, 1H), 7.82 (d, J = 2.4 Hz, 1H), 7.93 (d, J = 2.4 Hz, 1H), 11.11 (br s, 1H), 13.06 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 23.0, 27.3, 32.2, 79.4, 117.5, 117.6, 118.5, 123.5, 128.0, 128.4, 129.9, 133.9, 135.9, 138.1, 138.5, 141.5, 152.7, 159.6, 162.6, 194.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{28}N_2NaO_5$ $[M+Na]^+$: 471.1890; Found: 471.1883.

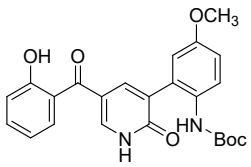


***tert*-butyl (2-(5-(5-chloro-2-hydroxy-4-methylbenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ag)**: Light yellow solid, m.p. 237.2-237.8 °C; 96.7 mg, yield 71% (110.3 mg, 81% for NH_4OAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.36 (s, 9H), 2.32 (s, 3H), 6.88 (s, 1H), 7.05-7.08 (m, 1H), 7.15-7.19 (m, 1H), 7.26-7.30 (m, 1H), 7.47 (s, 1H), 7.51 (s, 1H), 7.65 (br s, 1H), 7.81 (s, 1H), 7.91 (s, 1H), 11.23 (br s, 1H), 13.00 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.8, 27.3, 79.4, 116.6, 117.9, 119.8, 123.5, 123.6, 128.5, 129.9, 130.0, 130.4, 135.8, 138.0, 141.0, 144.9, 152.7, 159.9, 162.6, 192.7; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{24}H_{23}ClN_2NaO_5$ $[M+Na]^+$: 477.1188; Found: 477.1193.

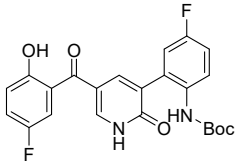


***tert*-butyl (4-chloro-2-(5-(2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ah)**: Light yellow solid, m.p. 151.2-151.9 °C; 101.6 mg, yield 77% (108.2 mg, 82% for

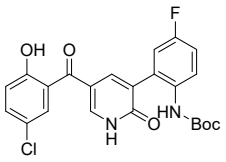
NH_4OAc); ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.36 (s, 9H), 6.84-6.88 (m, 1H), 7.00 (d, J = 8.0 Hz, 1H), 7.14 (d, J = 2.4 Hz, 1H), 7.24-7.26 (m, 1H), 7.43-7.51 (m, 3H), 7.62 (br s, 1H), 7.92-7.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 28.3, 80.8, 118.6, 118.9, 119.3, 119.4, 129.4, 129.7, 130.5, 131.7, 135.6, 136.7, 142.8, 153.6, 162.6, 163.5, 194.7; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{21}ClN_2NaO_5$ $[M+Na]^+$: 463.1031; Found: 463.1036.



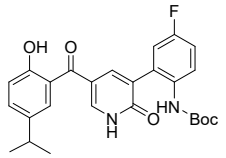
***tert*-butyl (2-(5-(2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-methoxyphenyl)carbamate (3ai)**: Light yellow solid, m.p. 208.2-209.7 °C; 94.2 mg, yield 72% (108.6 mg, 83% for NH_4OAc); ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.34 (s, 9H), 3.68 (s, 3H), 6.69 (d, J = 2.8 Hz, 1H), 6.81-6.86 (m, 2H), 6.98 (d, J = 8.0 Hz, 1H), 7.32 (br s, 1H), 7.40-7.45 (m, 2H), 7.49-7.52 (m, 1H), 7.85 (s, 1H), 7.93 (d, J = 2.8 Hz, 1H), 11.35 (br s, 1H), 13.15 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 28.4, 55.6, 80.2, 114.7, 116.0, 118.7, 119.1, 119.3, 129.7, 130.8, 131.8, 136.5, 139.5, 142.2, 156.8, 162.5, 163.5, 195.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{24}H_{24}N_2NaO_6$ $[M+Na]^+$: 459.1527; Found: 459.1531.



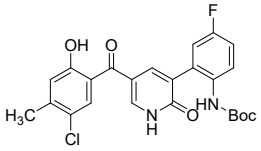
***tert*-butyl (4-fluoro-2-(5-(5-fluoro-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3aj)**: Light yellow solid, m.p. 245.7-246.8 °C; 119.3 mg, yield 90%; ^1H NMR (DMSO-d_6, 400 MHz) δ: 1.37 (s, 9H), 6.97-7.01 (m, 1H), 7.13-7.28 (m, 4H), 7.50-7.53 (m, 1H), 7.90 (s, 2H), 8.41 (br s, 1H), 10.14 (br s, 1H), 12.63 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 28.4, 79.4, 115.5 (d, J_{CF} = 22.1 Hz), 115.9 (d, J_{CF} = 24.4 Hz), 117.5 (d, J_{CF} = 20.5 Hz), 117.6, 118.3 (d, J_{CF} = 7.3 Hz), 119.4 (d, J_{CF} = 23.3 Hz), 126.4 (d, J_{CF} = 6.7 Hz), 128.5, 133.3, 139.7, 142.8, 151.9, 153.7, 156.8 (d, J_{CF} = 233.7 Hz), 158.9 (d, J_{CF} = 240.2 Hz), 161.9, 190.3; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{20}F_2N_2NaO_5$ $[M+Na]^+$: 465.1232; Found: 465.1230.



***tert*-butyl (2-(5-(5-chloro-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-fluorophenyl)carbamate (3ak)**: Light yellow solid, m.p. 223.4-224.3 °C; 98.9 mg, yield 72%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.35 (s, 9H), 6.89-7.02 (m, 3H), 7.37-7.40 (m, 2H), 7.47 (s, 1H), 7.56 (br s, 1H), 7.90-7.92 (m, 1H), 11.10 (br s, 1H), 12.99 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.3, 79.7, 115.2 (d, J_{CF} = 22.4 Hz), 116.2 (d, J_{CF} = 23.4 Hz), 117.5, 118.5, 119.4, 123.0, 129.4, 131.8, 135.2, 138.7, 141.0, 158.6 (d, J_{CF} = 237.7 Hz), 162.3, 192.7; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{20}ClFN_2NaO_5$ $[M+Na]^+$: 481.0937; Found: 481.0941.

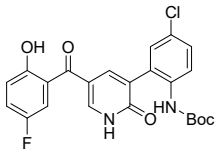


***tert*-butyl (4-fluoro-2-(5-(2-hydroxy-5-isopropylbenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3al)**: Light yellow solid, m.p. 240.5-241.4 °C; 106.2 mg, yield 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.13 (d, J = 7.2 Hz, 6H), 1.34 (s, 9H), 2.78-2.82 (m, 1H), 6.88-6.94 (m, 2H), 6.96-7.01 (m, 1H), 7.31-7.35 (m, 2H), 7.44 (s, 1H), 7.57 (br s, 1H), 7.93-7.94 (m, 2H), 11.06 (br s, 1H), 13.07 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 23.0, 27.2, 32.2, 79.5, 115.1 (d, J_{CF} = 22.3 Hz), 116.2 (d, J_{CF} = 23.3 Hz), 117.4, 117.7, 118.4, 127.9, 131.8, 131.9, 134.0, 138.5, 138.6, 141.7, 152.9, 158.0 (d, J_{CF} = 240.1 Hz), 159.6, 162.3, 193.8; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{27}FN_2NaO_5$ $[M+Na]^+$: 489.1796; Found: 489.1791.

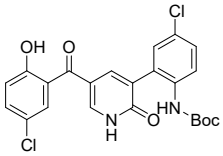


***tert*-butyl (2-(5-(5-chloro-2-hydroxy-4-methylbenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-fluorophenyl)carbamate (3am)**: Light yellow solid, m.p. 161.4-161.9 °C; 99.1 mg, yield 70% (113.3 mg, 80% for NH_4OAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.33 (s, 9H), 2.22 (s, 3H), 6.88 (d, J = 8.4 Hz, 2H), 6.96-7.01 (m, 1H), 7.24-7.27 (m, 1H), 7.43 (s, 1H), 7.57 (br s, 1H), 7.91-7.93 (m, 2H), 11.07 (br s, 1H), 13.13 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.6, 27.2, 79.6, 115.1 (d,

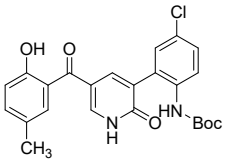
J_{CF} = 22.1 Hz), 116.2 (d, J_{CF} = 23.2 Hz), 117.4, 117.6, 118.4, 127.5, 130.2, 131.8, 136.7, 138.4, 141.6, 152.9, 158.7 (d, J_{CF} = 243.2 Hz), 159.6, 162.4, 193.7; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{24}H_{22}ClFN_2NaO_5$ $[M+Na]^+$: 495.1093; Found: 495.1094.



***tert*-butyl (4-chloro-2-(5-(5-fluoro-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3an)**: Light yellow solid, m.p. 250.2-251.0 °C; 115.4 mg, yield 84%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.35 (s, 9H), 6.94-6.97 (m, 1H), 7.09-7.12 (m, 1H), 7.19-7.24 (m, 1H), 7.34 (d, J = 2.4 Hz, 1H), 7.37-7.40 (m, 1H), 7.55 (d, J = 8.8 Hz, 1H), 7.84-7.87 (m, 2H), 8.47 (br s, 1H), 10.11 (br s, 1H), 12.61 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 28.4, 79.7, 115.9 (d, J_{CF} = 24.4 Hz), 117.5, 118.3 (d, J_{CF} = 7.2 Hz), 119.5 (d, J_{CF} = 23.2 Hz), 126.1, 126.3, 126.4, 128.4, 128.6, 130.7, 132.1, 136.1, 139.8, 142.9, 152.0, 153.4, 155.7 (d, J_{CF} = 235.6 Hz), 161.9, 190.3; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{20}ClFN_2NaO_5$ $[M+Na]^+$: 481.0937; Found: 481.0941.

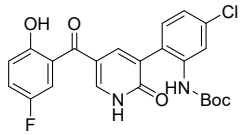


***tert*-butyl (4-chloro-2-(5-(5-chloro-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ao)**: Light yellow solid, m.p. 156.4-156.7 °C; 101.0 mg, yield 71%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.37 (s, 9H), 7.00 (d, J = 8.8 Hz, 1H), 7.27 (d, J = 2.4 Hz, 1H), 7.33 (d, J = 2.4 Hz, 1H), 7.38-7.41 (m, 2H), 7.56 (d, J = 8.8 Hz, 1H), 7.81 (d, J = 2.4 Hz, 1H), 7.92 (d, J = 2.8 Hz, 1H), 8.66 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 28.4, 79.6, 117.5, 118.9, 123.0, 127.7, 128.4, 129.1, 130.6, 132.1, 136.2, 139.6, 153.4, 154.7, 190.2; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{20}Cl_2N_2NaO_5$ $[M+Na]^+$: 497.0641; Found: 497.0646.

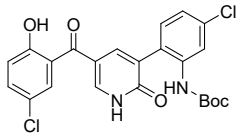


***tert*-butyl (4-chloro-2-(5-(2-hydroxy-5-methylbenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ap)**: Light yellow solid, m.p. 165.4-166.4 °C; 99.4 mg, yield 73%; ^{1}H NMR

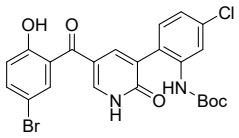
($CDCl_3$, 400 MHz) δ: 1.36 (s, 9H), 2.24 (s, 3H), 6.91 (d, J = 8.4 Hz, 1H), 7.16 (d, J= 2.4 Hz, 1H), 7.25-7.29 (m, 3H), 7.49 (s, 1H), 7.65 (br s, 1H), 7.94-7.96 (m, 2H), 11.08 (br s, 1H), 13.10 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.6, 27.3, 79.7, 117.3, 117.7, 118.5, 127.5, 128.4, 129.6, 130.2, 134.6, 136.8, 138.3, 141.8, 152.5, 159.5, 162.3, 193.7; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{24}H_{23}ClN_2NaO_5$ $[M+Na]^+$: 477.1188; Found: 477.1191.



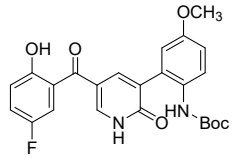
***tert*-butyl (5-chloro-2-(5-(5-fluoro-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3aq)**: Light yellow solid, m.p. 197.7-198.5 °C; 98.9 mg, yield 72%; ^1H NMR (DMSO-d_6, 400 MHz) δ: 1.39 (s, 9H), 6.95-6.98 (m, 1H), 7.12-7.15 (m, 1H), 7.21-7.25 (m, 2H), 7.31 (d, J = 8.4 Hz, 1H), 7.68 (s, 1H), 7.83 (d, J = 2.4 Hz, 1H), 7.87 (d, J = 2.4 Hz, 1H), 8.60 (br s, 1H), 10.13 (br s, 1H), 12.63 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 28.4, 80.0, 115.9 (d, J_{CF} = 23.2 Hz), 117.6, 118.3 (d, J_{CF} = 8.1 Hz), 119.4 (d, J_{CF} = 23.2 Hz), 123.2, 124.2, 126.5, 128.6, 130.1, 132.9, 133.2, 138.6, 139.9, 142.8, 151.9, 153.3, 155.6 (d, J_{CF} = 235.3 Hz), 162.0, 190.3; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{20}ClFN_2NaO_5$ $[M+Na]^+$: 481.0937; Found: 481.0941.



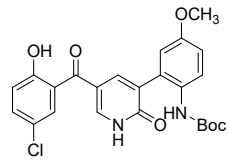
***tert*-butyl (5-chloro-2-(5-(5-chloro-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ar)**: Light yellow solid, m.p. 200.2-200.5 °C; 128.0 mg, yield 90%; ^1H NMR (DMSO-d_6, 400 MHz) δ: 1.46 (s, 9H), 7.04 (d, J = 8.8 Hz, 1H), 7.27-7.30 (m, 1H), 7.36-7.38 (m, 2H), 7.47-7.50 (m, 1H), 7.74 (s, 1H), 7.88 (d, J = 2.4 Hz, 1H), 7.93 (d, J = 2.4 Hz, 1H), 8.66 (br s, 1H), 10.47 (br s, 1H), 12.69 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 28.4, 80.0, 117.6, 118.8, 123.3, 124.2, 127.5, 128.6, 128.7, 129.2, 132.3, 132.9, 133.2, 138.5, 139.8, 142.8, 153.3, 154.4, 162.0, 190.1; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{20}Cl_2N_2NaO_5$ $[M+Na]^+$: 497.0641; Found: 497.0642.



***tert*-butyl (2-(5-(5-bromo-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)-5-chlorophenyl)carbamate (3as)**: Light yellow solid, m.p. 181.4-182.3 °C; 116.6 mg, yield 75%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.44 (s, 9H), 6.98 (d, J = 8.8 Hz, 1H), 7.25-7.28 (m, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 2.4 Hz, 1H), 7.57-7.60 (m, 1H), 7.73 (d, J = 1..6 Hz, 1H), 7.87 (d, J = 2.4 Hz, 1H), 7.92 (d, J = 2.8 Hz, 1H), 8.64 (br s, 1H), 10.48 (br s, 1H), 12.68 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 28.4, 80.0, 110.8, 117.6, 119.3, 123.2, 124.2, 128.0, 128.5, 128.7, 132.0, 132.9, 133.2, 135.2, 138.5, 139.8, 142.8, 153.2, 154.8, 162.0, 190.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{23}H_{20}BrClN_2NaO_5$ $[M+Na]^+$: 541.0136; Found: 541.0142.

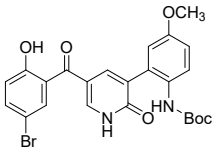


***tert*-butyl (2-(5-(5-fluoro-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-methoxyphenyl)carbamate (3at)**: Light yellow solid, m.p. 214.5-215.5 °C; 98.1 mg, yield 72%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.34 (s, 9H), 3.70 (s, 3H), 6.70 (d, J = 2.8 Hz, 1H), 6.82-6.85 (m, 1H), 6.94-6.98 (m, 1H), 7.15-7.22 (m, 3H), 7.47 (br s, 1H), 7.88 (s, 1H), 7.92 (d, J = 2.4 Hz, 1H), 10.99 (br s, 1H), 13.04 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 26.3, 53.6, 78.3, 112.9, 114.7 (d, J_{CF} = 23.4 Hz), 116.6 (d, J_{CF} = 22.4 Hz), 118.1, 121.9, 127.7, 137.5, 139.7, 153.6 (d, J_{CF} = 239.9 Hz), 154.9, 156.6, 161.5, 192.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{24}H_{23}FN_2NaO_6$ $[M+Na]^+$: 477.1432; Found: 477.1435.

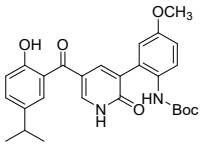


***tert*-butyl (2-(5-(5-chloro-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-methoxyphenyl)carbamate (3au)**: Light yellow solid, m.p. 183.2-184.4 °C; 118.4 mg, yield 84%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.36 (s, 9H), 3.77 (s, 3H), 6.87 (d, J = 3.2 Hz, 1H), 6.94-6.97 (m, 1H), 7.00 (d, J = 8.8 Hz, 1H), 7.32 (d, J = 2.4 Hz, 1H), 7.37-7.44 (m, 2H), 7.86-7.88 (m, 2H), 8.15

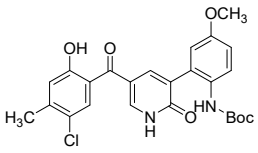
(br s, 1H), 10.42 (br s, 1H), 12.58 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 28.5, 55.8, 79.1, 114.4, 116.0, 117.5, 118.8, 123.4, 127.5, 129.2, 129.7, 129.9, 132.3, 139.5, 142.6, 153.9, 154.4, 156.5, 162.0, 190.1; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{24}H_{23}ClN_2NaO_6$ $[M+Na]^+$: 493.1137; Found: 493.1138.



***tert*-butyl (2-(5-(5-bromo-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-methoxyphenyl)carbamate (3av)**: Light yellow solid, m.p. 158.5-158.7 ^{o}C; 134.2 mg, yield 87%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.27 (s, 9H), 3.68 (s, 3H), 6.78 (d, J = 2.8 Hz, 1H), 6.85-6.88 (m, 2H), 7.28 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 2.4 Hz, 1H), 7.44-7.47 (m, 2H), 8.06 (br s, 1H), 10.36 (br s, 1H), 12.48 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 28.5, 55.8, 79.1, 110.8, 114.4, 116.0, 117.5, 119.3, 128.1, 129.7, 129.9, 132.0, 135.1, 139.5, 142.6, 153.9, 154.9, 156.5, 162.0, 190.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{24}H_{23}BrN_2NaO_6$ $[M+Na]^+$: 537.0632; Found: 537.0627.



***tert*-butyl (2-(5-(2-hydroxy-5-isopropylbenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-methoxyphenyl)carbamate (3aw)**: Light yellow solid, m.p. 154.8-155.5 ^{o}C; 100.4 mg, yield 70%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.13 (d, J = 7.2 Hz, 6H), 1.33 (s, 9H), 2.79-2.82 (m, 1H), 3.70 (s, 3H), 6.71 (d, J = 2.8 Hz, 1H), 6.81-6.84 (m, 1H), 6.93 (d, J = 7.2 Hz, 1H), 7.27-7.35 (m, 3H), 7.47 (br s, 1H), 7.86 (s, 1H), 7.94 (d, J = 2.4 Hz, 1H), 11.13 (br s, 1H), 13.07 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 22.3, 26.6, 31.4, 53.8, 78.3, 113.0, 114.3, 116.7, 116.9, 117.6, 127.3, 128.0, 129.2, 133.1, 137.4, 137.8, 140.5, 152.5, 155.0, 158.9, 161.7, 193.3; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{27}H_{30}N_2NaO_6$ $[M+Na]^+$: 501.1996; Found: 501.1992.



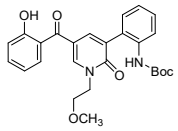
***tert*-butyl (2-(5-(5-chloro-2-hydroxy-4-methylbenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-**

methoxyphenyl)carbamate (3ax): Light yellow solid, m.p. 152.3-152.9 °C; 129.2 mg, yield 89%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.33 (s, 9H), 2.30 (s, 3H), 3.69 (s, 3H), 6.69 (d, J = 3.2 Hz, 1H), 6.79-8.02 (m, 1H), 6.87 (s, 1H), 7.27 (br s, 1H), 7.47-7.48 (m, 2H), 7.83 (d, J = 2.0 Hz, 1H), 7.89 (d, J = 2.4 Hz, 1H), 11.22 (br s, 1H), 13.02 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 19.8, 27.3, 54.5, 79.2, 113.9, 114.7, 116.7, 117.6, 119.7, 123.5, 128.7, 130.0, 130.1, 138.3, 140.8, 144.8, 155.8, 159.8, 162.4, 192.6; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{25}H_{25}ClN_2NaO_6$ $[M+Na]^+$: 507.1293; Found: 507.1297.

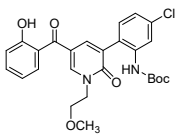
6. Synthesis of *N*-alkyl 2-hydroxy benzoylpyridones 3 by reaction of and primary amines 2

In a sealed tube equipped with a magnetic stirring bar, to 1.5 mL of EtOH was added 3-vinyl oxindole-chromone **1** (0.30 mmol) and primary amine **2** (0.60 mmol). The reaction mixture was stirred at rt for 5 h. After completion of the reaction, as indicated by TLC, purification by flash column chromatography (hexane/EtOAc, 5/1, v/v) was carried out to furnish the *N*-alkyl 2-hydroxy benzoylpyridones **3**.

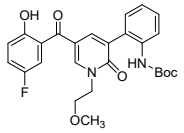
7. Characterization data of *N*-alkyl 2-hydroxy benzoylpyridones 3



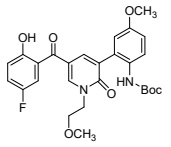
***tert*-butyl (2-(5-(2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)p-henyl)carbamate (3ba)**: Light yellow solid, m.p. 99.2-99.8 °C; 119.7 mg, yield 86%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.40 (s, 9H), 3.31 (s, 3H), 3.66-3.68 (m, 1H), 4.23-4.25 (m, 1H), 6.85-6.89 (m, 1H), 7.00 (d, J = 8.4 Hz, 1H), 7.04-7.08 (m, 1H), 7.14-7.16 (m, 1H), 7.29-7.33 (m, 1H), 7.42-7.47 (m, 1H), 7.59-7.62 (m, 2H), 7.71-7.74 (m, 1H), 7.86 (d, J = 2.4 Hz, 1H), 8.02 (d, J = 2.8 Hz, 1H), 11.45 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 28.4, 51.2, 59.1, 69.7, 79.9, 117.2, 118.7, 118.8, 119.0, 124.0, 129.0, 129.3, 131.0, 132.0, 136.4, 137.0, 140.7, 144.2, 153.8, 161.4, 162.7, 195.2; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{28}N_2NaO_6$ $[M+Na]^+$: 487.1840; Found: 487.1843.



***tert*-butyl (5-chloro-2-(5-(2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3bb)**: Light yellow solid, m.p. 99.0-99.8 °C; 134.5 mg, yield 90%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.41 (s, 9H), 3.32 (s, 3H), 3.66-3.68 (m, 1H), 4.24-4.26 (m, 1H), 6.85-6.89 (m, 1H), 6.99-7.08 (m, 3H), 7.43-7.47 (m, 1H), 7.58-7.60 (m, 1H), 7.66 (s, 1H), 7.83 (br s, 1H), 8.03 (d, J = 2.4 Hz, 1H), 11.41 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.3, 50.2, 58.1, 68.6, 79.4, 116.2, 117.7, 117.8, 118.0, 122.3, 123.1, 125.9, 128.9, 130.9, 134.1, 135.5, 137.2, 139.8, 143.4, 152.3, 160.2, 161.6, 194.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{27}ClN_2NaO_6$ $[M+Na]^+$: 521.1450; Found: 521.1456.

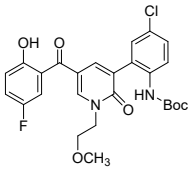


***tert*-butyl (2-(5-(5-fluoro-2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3bc)**: Light yellow solid, m.p. 93.8-94.4 °C; 131.6 mg, yield 91%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.39 (s, 9H), 3.35 (s, 3H), 3.64-3.67 (m, 1H), 4.22-4.25 (m, 1H), 6.94-6.97 (m, 1H), 7.05-7.08 (m, 1H), 7.15-7.21 (m, 2H), 7.29-7.35 (m, 2H), 7.51 (br s, 1H), 7.70-7.72 (m, 1H), 7.86 (d, J = 2.4 Hz, 1H), 8.02 (d, J = 2.4 Hz, 1H), 11.13 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 28.4, 50.9, 59.0, 79.9, 116.4, 117.1 (d, J_{CF} = 24.4 Hz), 118.4, 120.0, 120.1, 123.7 (d, J_{CF} = 23.3 Hz), 124.4, 129.3, 131.0, 131.5, 137.0, 140.2, 144.5, 153.6, 154.8 (d, J_{CF} = 238.8 Hz), 158.7, 161.3, 194.1; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{27}FN_2NaO_6$ $[M+Na]^+$: 505.1745; Found: 505.1748.

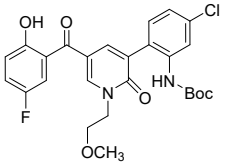


***tert*-butyl (2-(5-(5-fluoro-2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-methoxyphenyl)carbamate (3bd)**: Light yellow solid, m.p. 100.2-101.1 °C; 115.2 mg, yield 75%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.37 (s, 9H), 3.36 (s, 3H), 3.66-3.68 (m, 2H), 3.73 (s, 3H), 4.24-4.26 (m, 2H), 6.71 (d, J = 3.2 Hz, 1H), 6.86-6.89 (m, 1H), 6.96-6.99 (m, 1H), 7.17-7.22 (m, 2H), 7.33-7.36 (m, 1H), 7.54 (br s, 1H), 7.88 (d, J = 2.8 Hz, 1H), 8.03 (d, J = 2.8 Hz, 1H), 11.15 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 28.4, 50.9, 55.6, 59.1, 69.8, 79.7, 114.7, 116.0,

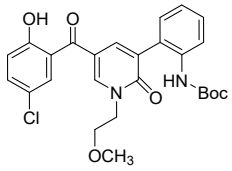
116.3, 117.0 (d, J_{CF} = 24.4 Hz), 118.4, 120.0 (d, J_{CF} = 7.3 Hz), 123.7 (d, J_{CF} = 23.4 Hz), 129.9, 131.4, 140.0, 144.6, 154.2, 154.9 (d, J_{CF} = 224.5 Hz), 156.6, 158.7, 161.1, 194.1; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{27}H_{29}FN_2NaO_7$ $[M+Na]^+$: 535.1851; Found: 535.1855.



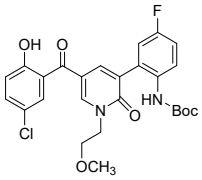
***tert*-butyl (4-chloro-2-(5-(5-fluoro-2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3be)**: Light yellow solid, m.p. 103.6-104.7 °C; 114.6 mg, yield 74%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.40 (s, 9H), 3.37 (s, 3H), 3.66-3.68 (m, 2H), 4.26-4.28 (m, 2H), 6.98-7.01 (m, 1H), 7.17-7.24 (m, 2H), 7.27-7.30 (m, 1H), 7.32-7.35 (m, 1H), 7.44 (br s, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.88 (d, J = 2.4 Hz, 1H), 8.06 (d, J = 2.8 Hz, 1H), 11.13 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.3, 49.9, 58.1, 68.7, 79.3, 115.3, 115.9 (d, J_{CF} = 24.1 Hz), 117.3, 119.1 (d, J_{CF} = 7.3 Hz), 122.9 (d, J_{CF} = 23.3 Hz), 124.1, 128.2, 129.3, 129.6, 134.7, 139.5, 143.8, 152.5, 153.9 (d, J_{CF} = 238.7 Hz), 157.8, 160.0, 192.9; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{26}ClFN_2NaO_6$ $[M+Na]^+$: 539.1356; Found: 539.1353.



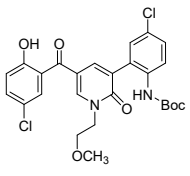
***tert*-butyl (5-chloro-2-(5-(5-fluoro-2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3bf)**: Light yellow solid, m.p. 135.7-136.6 °C; 134.7 mg, yield 87%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.41 (s, 9H), 3.37 (s, 3H), 3.66-3.68 (m, 2H), 4.25-4.27 (m, 2H), 6.96-7.00 (m, 1H), 7.03-7.10 (m, 2H), 7.18-7.23 (m, 1H), 7.32-7.35 (m, 1H), 7.58 (br s, 1H), 7.85 (d, J = 2.8 Hz, 1H), 8.05 (d, J = 2.8 Hz, 1H), 11.12 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.3, 49.9, 58.0, 68.7, 79.4, 115.4, 115.9 (d, J_{CF} = 24.2 Hz), 117.3, 119.1 (d, J_{CF} = 8.3 Hz), 122.4, 122.8 (d, J_{CF} = 23.3 Hz), 123.2, 125.8, 129.5, 130.9, 134.3, 137.1, 139.4, 143.7, 152.2, 153.8 (d, J_{CF} = 238.8 Hz), 157.8, 160.2, 193.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{26}ClFN_2NaO_6$ $[M+Na]^+$: 539.1356; Found: 539.1357.



***tert*-butyl (2-(5-(5-chloro-2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3bg)**: Light yellow solid, m.p. 103.5-104.4 °C; 115.0 mg, yield 77%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.40 (s, 9H), 3.39 (s, 3H), 3.68-3.70 (m, 1H), 4.26-4.28 (m, 1H), 6.98 (d, J = 9.2 Hz, 1H), 7.08-7.12 (m, 1H), 7.18-7.20 (m, 1H), 7.32-7.36 (m, 1H), 7.40-7.43 (m, 1H), 7.50 (br s, 1H), 7.63 (d, J = 2.4 Hz, 1H), 7.73-7.74 (m, 1H), 7.89 (d, J = 2.4 Hz, 1H), 8.01 (d, J = 2.8 Hz, 1H), 11.32 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.4, 50.2, 58.3, 68.7, 78.9, 115.4, 118.5, 119.4, 122.8, 123.4, 128.4, 129.8, 130.0, 130.7, 135.1, 136.0, 139.2, 143.4, 152.8, 160.1, 160.3, 193.1; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{27}ClN_2NaO_6$ $[M+Na]^+$: 521.1450; Found: 521.1456.

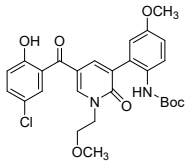


***tert*-butyl (2-(5-(5-chloro-2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-fluorophenyl)carbamate (3bh)**: Light yellow solid, m.p. 154.5-155.3 °C; 139.3 mg, yield 90%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.38 (s, 9H), 3.38 (s, 3H), 3.66-3.68 (m, 2H), 4.24-4.26 (m, 2H), 6.89-6.93 (m, 1H), 6.97 (d, J = 9.2 Hz, 1H), 7.00-7.05 (m, 1H), 7.35 (br s, 1H), 7.39-7.42 (m, 1H), 7.60-7.64 (m, 2H), 7.87 (d, J = 2.8 Hz, 1H), 8.10 (d, J = 2.4 Hz, 1H), 11.27 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.3, 50.2, 58.2, 68.6, 79.0, 114.9 (d, J_{CF} = 21.5 Hz), 115.3, 116.3 (d, J_{CF} = 23.4 Hz), 118.4, 119.4, 122.8, 129.5, 129.8, 132.0, 135.2, 139.5, 143.8, 152.8, 158.8 (d, J_{CF} = 243.4 Hz), 160.0, 192.8; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{26}ClFN_2NaO_6$ $[M+Na]^+$: 539.1356; Found: 539.1352.

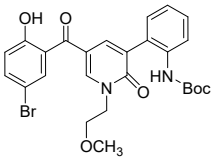


***tert*-butyl (4-chloro-2-(5-(5-chloro-2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dih-**

ydropyridin-3-yl)phenyl)carbamate (3bi): Light yellow solid, m.p. 96.7-97.5 °C; 126.1 mg, yield 79%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.39 (s, 9H), 3.38 (s, 3H), 3.66-3.68 (m, 2H), 4.24-4.26 (m, 2H), 6.97 (d, J = 8.8 Hz, 1H), 7.17-7.19 (m, 1H), 7.27-7.29 (m, 1H), 7.39-7.42 (m, 1H), 7.44 (br s, 1H), 7.61 (d, J = 2.4 Hz, 1H), 7.69 (d, J = 7.6 Hz, 1H), 7.88 (d, J = 2.4 Hz, 1H), 8.02 (d, J = 2.4 Hz, 1H), 11.27 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.3, 50.2, 58.2, 68.6, 79.2, 115.4, 118.4, 119.4, 122.8, 128.2, 128.3, 129.3, 129.6, 129.8, 134.7, 135.2, 139.6, 143.8, 152.4, 160.0, 160.1, 192.8; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{26}Cl_2N_2NaO_6$ $[M+Na]^+$: 555.1060; Found: 555.1065.

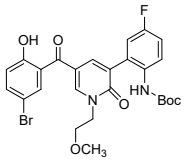


***tert*-butyl (2-(5-(5-chloro-2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-methoxyphenyl)carbamate (3bj)**: Light yellow solid, m.p. 107.1-108.1 °C; 120.4 mg, yield 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.37 (s, 9H), 3.39 (s, 3H), 3.67-3..69 (m, 2H), 3.74 (s, 3H), 4.25-4.27 (m, 2H), 6.73 (d, J = 2.8 Hz, 1H), 6.87-6.90 (m, 1H), 6.97 (d, J = 8.8 Hz, 1H), 7.19 (s, 1H), 7.40-7.43 (m, 1H), 7.54 (br s, 1H), 7.62 (d, J = 2.8 Hz, 1H), 7.88 (d, J = 2.8 Hz, 1H), 8.00 (d, J = 2.4 Hz, 1H), 11.31 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.4, 50.2, 54.6, 58.2, 68.7, 78.7, 113.8, 114.9, 115.3, 118.5, 119.4, 122.8, 128.9, 129.8, 130.5, 135.1, 139.1, 143.5, 153.1, 155.6, 160.1, 193.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{27}H_{29}ClN_2NaO_7$ $[M+Na]^+$: 551.1556; Found: 551.1554.

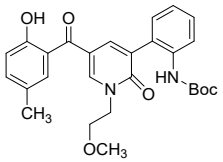


***tert*-butyl (2-(5-(5-bromo-2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3bk)**: Light yellow solid, m.p. 114.9-115.5 °C; 126.8 mg, yield 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.40 (s, 9H), 3.39 (s, 3H), 3.67-3.69 (m, 1H), 4.24-4.26 (m, 1H), 6.91 (d, J = 8.8 Hz, 1H), 7.07-7.11 (m, 1H), 7.17-7.20 (m, 1H), 7.31-7.35 (m, 1H), 7.50-7.55 (m, 2H), 7.72-7.76 (m, 2H), 7.88 (d, J = 2.8 Hz, 1H), 7.99 (d, J = 2.8 Hz, 1H), 11.31 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.4, 50.3, 58.3, 68.6, 78.9, 109.7, 115.4, 119.2, 119.7, 123.4, 128.4,

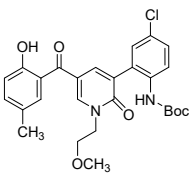
130.0, 130.7, 132.8, 136.0, 137.9, 139.2, 143.4, 152.7, 160.3, 160.5, 192.9; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{27}BrN_2NaO_6$ $[M+Na]^+$: 565.0945; Found: 565.0948.



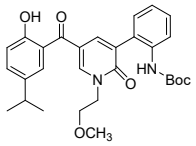
***tert*-butyl (2-(5-(5-bromo-2-hydroxybenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-fluorophenyl)carbamate (3bl)**: Light yellow solid, m.p. 149.3-150.2 °C; 122.6 mg, yield 73%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.39 (s, 9H), 3.40 (s, 3H), 3.67-3.69 (m, 1H), 4.25-4.27 (m, 1H), 6.91-6.94 (m, 2H), 7.01-7.06 (m, 1H), 7.35 (br s, 1H), 7.53-7.56 (m, 1H), 7.64 (br s, 1H), 7.75 (d, J = 2.4 Hz, 1H), 7.88 (d, J = 2.8 Hz, 1H), 8.01 (d, J = 2.4 Hz, 1H), 11.29 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 28.4, 51.4, 59.4, 69.6, 80.1, 110.7, 116.0 (d, J_{CF} = 21.4 Hz), 116.4, 117.3 (d, J_{CF} = 23.5 Hz), 120.1, 120.8, 130.6, 133.0, 133.7, 139.0, 140.5, 144.8, 153.8, 159.5 (d, J_{CF} = 230.4 Hz), 161.0, 161.5, 193.8; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{26}BrFN_2NaO_6$ $[M+Na]^+$: 583.0850; Found: 583.0854.



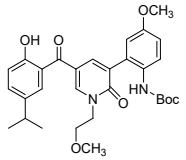
***tert*-butyl (2-(5-(2-hydroxy-5-methylbenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3bm)**: Light yellow solid, m.p. 143.6-143.9 °C; 117.6 mg, yield 82%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.40 (s, 9H), 2.25 (s, 3H), 3.32 (s, 3H), 3.67-3.69 (m, 1H), 4.21-4.24 (m, 1H), 6.90 (d, J = 8.8 Hz, 1H), 7.05-7.08 (m, 1H), 7.15-7.18 (m, 1H), 7.25-7.33 (m, 2H), 7.40 (s, 1H), 7.60 (br s, 1H), 7.72-7.74 (m, 1H), 7.87 (d, J = 2.4 Hz, 1H), 7.99 (d, J = 2.4 Hz, 1H), 11.23 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.6, 27.4, 58.1, 68.7, 78.8, 116.3, 117.5, 123.3, 127.2, 128.2, 130.0, 130.1, 130.6, 136.0, 136.3, 139.7, 143.1, 152.7, 159.5, 160.3, 194.1; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{27}H_{30}N_2NaO_6$ $[M+Na]^+$: 501.1996; Found: 501.1997.



***tert*-butyl (4-chloro-2-(5-(2-hydroxy-5-methylbenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3bn)**: Light yellow solid, m.p. 95.4-95.7 °C; 116.7 mg, yield 76%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.40 (s, 9H), 2.27 (s, 3H), 3.33 (s, 3H), 3.67-3.70 (m, 2H), 4.24-4.26 (m, 2H), 6.92 (d, J = 8.4 Hz, 1H), 7.17 (d, J = 2.4 Hz, 1H), 7.27-7.30 (m, 2H), 7.39 (s, 1H), 7.54 (br s, 1H), 7.70 (d, J = 6.8 Hz, 1H), 7.88 (d, J = 2.4 Hz, 1H), 8.02 (d, J = 2.4 Hz, 1H), 11.21 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.6, 27.3, 50.5, 58.2, 68.6, 79.2, 116.3, 117.4, 117.6, 127.2, 128.1, 129.6, 130.5, 134.8, 136.5, 143.5, 152.5, 159.6, 160.1, 193.9; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{27}H_{29}ClN_2NaO_6$ $[M+Na]^+$: 535.1606; Found: 535.1608.

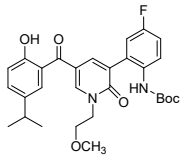


***tert*-butyl (2-(5-(2-hydroxy-5-isopropylbenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3bo)**: Light yellow solid, m.p. 92.8-93.4 °C; 132.1 mg, yield 87%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18 (d, J = 7.2 Hz, 6H), 1.39 (s, 9H), 2.79-2.86 (m, 1H), 3.30 (s, 3H), 3.67-3.70 (m, 1H), 4.19-4.22 (m, 1H), 6.92 (d, J = 8.8 Hz, 1H), 7.04-7.08 (m, 1H), 7.17-7.19 (m, 1H), 7.28-7.35 (m, 2H), 7.44 (d, J = 2.4 Hz, 1H), 7.58 (br s, 1H), 7.72 (d, J = 7.2 Hz, 1H), 7.89 (d, J = 2.8 Hz, 1H), 7.99 (d, J = 7.2 Hz, 1H), 11.20 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 23.0, 27.3, 32.3, 50.8, 58.1, 68.6, 78.8, 116.4, 117.5, 123.3, 128.2, 129.9, 130.1, 133.7, 136.0, 138.4, 139.8, 143.1, 152.7, 159.6, 160.4, 194.1; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{29}H_{34}N_2NaO_6$ $[M+Na]^+$: 529.2309; Found: 529.2314.

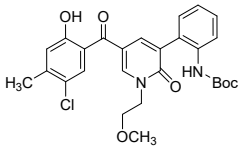


***tert*-butyl (2-(5-(2-hydroxy-5-isopropylbenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-methoxyphenyl)carbamate (3bp)**: Light yellow solid, m.p. 140.2-141.0 °C; 128.6 mg, yield 80%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18 (d, J = 7.2 Hz, 6H), 1.37 (s, 9H), 2.81-2.85 (m, 1H), 3.31 (s, 3H), 3.70-3.72 (m, 2H), 3.73 (s, 3H), 4.21-4.23 (m, 2H), 6.74 (d, J = 3.2 Hz, 1H), 6.86-6.89 (m, 1H), 6.95 (d, J = 8.8 Hz, 1H), 7.28-7.36 (m, 2H), 7.44 (d, J = 2.4 Hz, 1H), 7.55 (br s, 1H), 7.91 (d, J = 2.4 Hz, 1H), 7.98 (d, J = 2.4 Hz, 1H), 11.21 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100

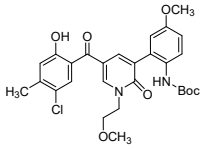
MHz) δ: 24.1, 28.4, 33.4, 51.9, 55.6, 59.1, 69.6, 79.6, 114.6, 116.0, 117.3, 118.5, 118.6, 129.2, 130.0, 131.1, 134.7, 139.4, 140.6, 144.2, 154.2, 156.6, 160.7, 161.2, 195.1; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{30}H_{36}N_2NaO_7$ $[M+Na]^+$: 559.2415; Found: 559.2411.



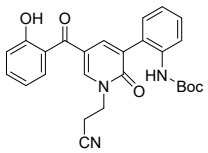
***tert*-butyl (4-fluoro-2-(5-(2-hydroxy-5-isopropylbenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3bq)**: Light yellow solid, m.p. 150.8-151.1 °C; 122.6 mg, yield 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.18 (d, J = 6.8 Hz, 6H), 1.38 (s, 9H), 2.81-2.84 (m, 1H), 3.30 (s, 3H), 3.68-3.70 (m, 2H), 4.21-4.23 (m, 2H), 6.91-6.95 (m, 2H), 6.98-7.03 (m, 1H), 7.33-7.36 (m, 1H), 7.41-7.43 (m, 2H), 7.64 (br s, 1H), 7.89 (d, J = 2.4 Hz, 1H), 8.01 (d, J = 2.4 Hz, 1H), 11.17 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 24.0, 28.4, 33.4, 51.9, 59.1, 69.5, 80.0, 115.8 (d, J_{CF} = 22.2 Hz), 117.3 (d, J_{CF} = 22.4 Hz), 118.4, 118.6, 129.1, 133.1, 134.8, 139.5, 141.1, 144.5, 153.8, 159.5 (d, J_{CF} = 242.1 Hz), 160.7, 161.1, 194.9; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{29}H_{33}FN_2NaO_6$ $[M+Na]^+$: 547.2215; Found: 547.2219.



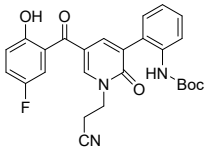
***tert*-butyl (2-(5-(5-chloro-2-hydroxy-4-methylbenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3br)**: Light yellow solid, m.p. 96.9-97.9 °C; 122.9 mg, yield 80%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.40 (s, 9H), 2.34 (s, 3H), 3.39 (s, 3H), 3.67-3.69 (m, 2H), 4.24-4.26 (m, 2H), 6.90 (s, 1H), 7.066-7.10 (m, 1H), 7.17-7.19 (m, 1H), 7.30-7.35 (m, 1H), 7.53 (br s, 1H), 7.62 (s, 1H), 7.72-7.74 (m, 1H), 7.87 (d, J = 2.4 Hz, 1H), 7.99 (d, J = 2.4 Hz, 1H), 11.36 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 19.8, 27.4, 50.2, 58.2, 68.7, 78.9, 115.6, 116.7, 119.8, 123.4, 128.3, 130.0, 130.3, 130.6, 136.0, 139.3, 143.1, 144.6, 152.7, 160.1, 160.3, 192.8; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{27}H_{29}ClN_2NaO_6$ $[M+Na]^+$: 535.1606; Found: 535.1603.



***tert*-butyl (2-(5-(5-chloro-2-hydroxy-4-methylbenzoyl)-1-(2-methoxyethyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-methoxyphenyl)carbamate (3bs)**: Light yellow solid, m.p. 94.7-95.5 °C; 149.6 mg, yield 92%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.37 (s, 9H), 2.34 (s, 3H), 3.38 (s, 3H), 3.66-3.69 (m, 2H), 3.73 (s, 3H), 4.23-4.25 (m, 2H), 6.73 (d, J = 2.8 Hz, 1H), 6.86-6.90 (m, 2H), 7.25 (br s, 1H), 7.54 (br s, 1H), 7.61 (s, 1H), 7.88 (d, J = 2.4 Hz, 1H), 7.98 (d, J = 2.4 Hz, 1H), 11.35 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.9, 28.4, 51.2, 55.6, 59.3, 69.7, 79.6, 114.8, 115.9, 116.6, 117.8, 120.8, 124.4, 130.0, 131.3, 131.4, 140.2, 144.2, 145.7, 154.1, 156.6, 161.1, 193.8; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{28}H_{31}ClN_2NaO_7$ $[M+Na]^+$: 565.1712; Found: 565.1715.

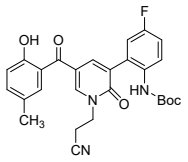


***tert*-butyl (2-(1-(2-cyanoethyl)-5-(2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ca)**: Light yellow solid, m.p. 95.4-96.6 °C; 119.8 mg, yield 87%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.37 (s, 9H), 3.00-3.04 (m, 2H), 4.36-4.40 (m, 2H), 6.93-6.97 (m, 1H), 7.00 (d, J = 8.0 Hz, 1H), 7.15-7.19 (m, 1H), 7.29-7.31 (m, 1H), 7.33-7.37 (m, 1H), 7.41 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 2.8 Hz, 1H), 8.30 (br s, 1H), 8.46 (d, J = 2.4 Hz, 1H), 10.33 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 17.1, 28.5, 46.4, 79.3, 117.3, 117.8, 118.7, 119.7, 124.6, 124.8, 128.9, 129.0, 130.5, 130.7, 131.2, 133.5, 137.0, 139.6, 145.2, 153.6, 156.8, 160.9, 192.3; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{25}N_3NaO_5$ $[M+Na]^+$: 482.1686; Found: 482.1690.

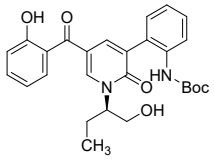


***tert*-butyl (2-(1-(2-cyanoethyl)-5-(5-fluoro-2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3cb)**: Light yellow solid, m.p. 86.6-87.7 °C; 115.9 mg, yield 81%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.37 (s, 9H), 2.99-3.02 (m, 2H), 4.36-4.39 (m, 2H), 6.97-7.00 (m, 1H), 7.14-7.19 (m, 2H), 7.23-7.30 (m, 2H), 7.33-7.37 (m, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 2.4 Hz, 1H), 8.29 (s, 1H), 8.47 (s, 1H), 10.15 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 17.1, 28.5, 46.3, 79.3, 115.9 (d, J_{CF} = 28.4 Hz), 117.5, 118.4 (d, J_{CF} = 8.1 Hz), 118.6, 119.6 (d, J_{CF}

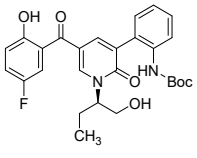
= 23.4 Hz), 124.6, 124.8, 126.0 (d, J_{CF} = 7.4 Hz), 128.9, 129.1, 130.4, 131.2, 137.0, 139.2, 145.6, 152.4, 153.6, 155.6 (d, J_{CF} = 234.5 Hz), 161.0, 190.6; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{24}FN_3NaO_5$ $[M+Na]^+$: 500.1592; Found: 500.1592.



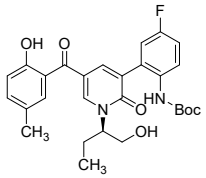
***tert*-butyl (2-(1-(2-cyanoethyl)-5-(2-hydroxy-5-methylbenzoyl)-2-oxo-1,2-dihydropyridin-3-yl)-4-fluorophenyl)carbamate (3cc)**: Light yellow solid, m.p. 82.9-82.9 °C; 135.5 mg, yield 92%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.35 (s, 9H), 2.25 (s, 3H), 3.01-3.04 (m, 2H), 4.36-4.39 (m, 2H), 6.90 (d, J = 8.0 Hz, 1H), 7.17-7.25 (m, 4H), 7.44-7.47 (m, 1H), 7.80 (d, J = 2.4 Hz, 1H), 8.36 (br s, 1H), 8.46 (d, J = 2.0 Hz, 1H), 10.13 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 17.1, 20.3, 28.4, 46.4, 79.3, 115.5 (d, J_{CF} = 21.3 Hz), 117.3, 117.6 (d, J_{CF} = 9.4 Hz), 118.7, 124.2, 127.7, 128.4, 130.7, 133.3, 134.4, 139.6, 145.4, 153.8, 154.9, 159.4 (d, J_{CF} = 240.1 Hz), 160.6, 192.3; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{27}H_{26}FN_3NaO_5$ $[M+Na]^+$: 514.1749; Found: 514.1752.



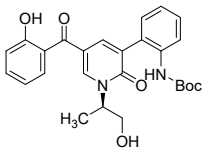
***tert*-butyl (*R*)-(2-(5-(2-hydroxybenzoyl)-1-(1-hydroxybutan-2-yl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3da)**: Light yellow solid, m.p. 88.7-89.9 °C; 124.8 mg, yield 87%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.83-0.87 (m, 3H), 1.35 (s, 9H), 1.73-1.81 (m, 2H), 3.11 (s, 1H), 3.76 (d, J = 4.0 Hz, 2H), 4.98 (s, 1H), 6.81-6.84 (m, 1H), 6.96 (d, J = 8.0 Hz, 1H), 7.02-7.06 (m, 1H), 7.11-7.13 (m, 1H), 7.25-7.29 (m, 1H), 7.39-7.43 (m, 1H), 7.46 (br s, 1H), 7.52-7.55 (m, 1H), 7.63 (d, J = 6.4 Hz, 1H), 7.79 (d, J = 2.4 Hz, 1H), 8.08 (d, J = 2.4 Hz, 1H), 11.40 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 9.5, 22.2, 27.3, 59.4, 62.0, 79.0, 116.7, 117.7, 117.8, 118.1, 123.1, 123.6, 128.2, 128.5, 129.4, 129.8, 130.9, 135.3, 135.7, 138.9, 139.9, 152.8, 161.1, 161.5, 194.3; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{27}H_{30}N_2NaO_6$ $[M+Na]^+$: 501.1996; Found: 501.1995.



***tert*-butyl (*R*)-(2-(5-(5-fluoro-2-hydroxybenzoyl)-1-(1-hydroxybutan-2-yl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3db)**: Light yellow solid, m.p. 94.9-95.3 °C; 116.1 mg, yield 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.86-0..90 (m, 3H), 1.36 (s, 9H), 1.81-1.86 (m, 2H), 2.75 (s, 1H), 3.84 (s, 2H), 5.02 (s, 1H), 6.94-6.98 (m, 1H), 7.05-7.09 (m, 1H), 7.15-7.20 (m, 2H), 7.27-7.32 (m, 2H), 7.38 (s, 1H), 7.65 (d, J = 6.0 Hz, 1H), 7.81 (d, J = 2.4 Hz, 1H), 8.12 (d, J = 2.0 Hz, 1H), 11.11 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 9.5, 22.2, 27.3, 59.4, 62.1, 79.0, 115.8 (d, J_{CF} = 24.3 Hz), 116.1, 117.4, 119.0 (d, J_{CF} = 8.2 Hz), 122.7 (d, J_{CF} = 24.5 Hz), 123.2, 123.6, 128.3, 129.8, 129.9, 135.7, 138.4, 140.2, 152.8, 153.7 (d, J_{CF} = 238.8 Hz), 157.6, 161.0, 193.2; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{27}H_{29}FN_2NaO_6$ $[M+Na]^+$: 519.1902; Found: 519.1908.

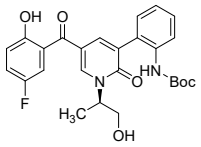


***tert*-butyl (*R*)-(4-fluoro-2-(5-(2-hydroxy-5-methylbenzoyl)-1-(1-hydroxybutan-2-yl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3dc)**: Light yellow solid, m.p. 97.6-98.5 °C; 110.2 mg, yield 72%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.86-0.90 (m, 3H), 1.33 (s, 9H), 1.77-1.84 (m, 2H), 2.20 (s, 3H), 2.86 (s, 1H), 3.82 (d, J = 4.4 Hz, 2H), 5.02 (s, 1H), 6.86-6.89 (m, 2H), 6.95-7.00 (m, 1H), 7.23-7.34 (m, 3H), 7.56 (s, 1H), 7.82 (d, J = 2.4 Hz, 1H), 8.08 (s, 1H), 11.17 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 9.5, 19.4, 22.2, 27.3, 59.5, 62.1, 79.1, 114.7 (d, J_{CF} = 22.4 Hz), 116.1 (d, J_{CF} = 23.1 Hz), 116.6, 117.4 (d, J_{CF} = 8.3 Hz), 127.3, 128.5, 130.6, 131.8, 136.4, 139.1, 152.9, 158.7 (d, J_{CF} = 242.1 Hz), 159.4, 160.7, 194.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{28}H_{31}FN_2NaO_6$ $[M+Na]^+$: 533.2058; Found: 533.2056.

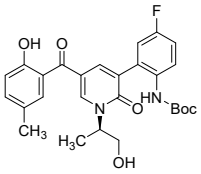


***tert*-butyl (*R*)-(2-(5-(2-hydroxybenzoyl)-1-(1-hydroxypropan-2-yl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ea)**: Light yellow solid, m.p. 95.9-96.7 °C; 103.0 mg, yield 74%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.37 (s, 9H), 1.41 (d, J = 7.2 Hz, 3H), 2.88 (br s, 1H), 3.72-3.76 (m, 1H), 3.80-3.84 (m, 1H), 5.16-5.21 (m, 1H), 6.83-6..87 (m, 1H), 6.99 (d, J = 8.0 Hz, 1H), 7.03-

7.07 (m, 1H), 7.11-7.13 (m, 1H), 7.27-7.31 (m, 1H), 7.41-7.47 (m, 2H), 7.55-7.57 (m, 1H), 7.66 (br s, 1H), 7.81 (d, J = 2.4 Hz, 1H), 8.11 (d, J = 2.4 Hz, 1H), 11.42 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 15.9, 28.3, 55.1, 64.3, 80.2, 117.8, 118.7, 119.2, 124.5, 129.3, 130.5, 130.9, 131.9, 136.4, 136.8, 140.0, 140.5, 153.9, 161.8, 162.6, 195.4; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{28}N_2NaO_6$ $[M+Na]^+$: 487.1840; Found: 487.1841.



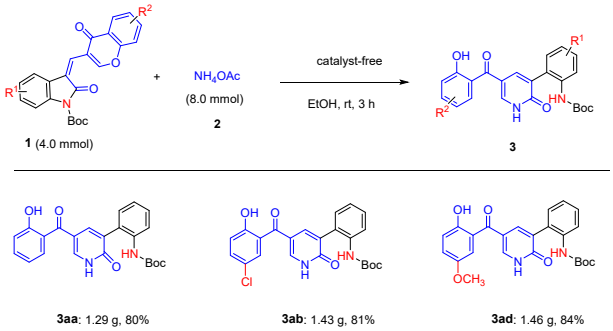
***tert*-butyl (*R*)-(2-(5-(5-fluoro-2-hydroxybenzoyl)-1-(1-hydroxypropan-2-yl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3eb)**: Light yellow solid, m.p. 97.8-98.9 °C; 104.1 mg, yield 72%; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.37 (s, 9H), 1.44 (d, J = 6.8 Hz, 3H), 2.70 (br s, 1H), 3.76-3.80 (m, 1H), 3.84-3.87 (m, 1H), 5.22 (br s, 1H), 6.95-6.98 (m, 1H), 7.06-7.09 (m, 1H), 7.13-7.20 (m, 2H), 7.27-7.33 (m, 2H), 7.39 (br s, 1H), 7.67 (br s, 1H), 7.81 (d, J = 2.0 Hz, 1H), 8.14 (d, J = 2.4 Hz, 1H), 11.11 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 16.3, 28.4, 54.5, 62.9, 79.3, 115.9 (d, J_{CF} = 24.1 Hz), 116.8, 118.4 (d, J_{CF} = 8.2 Hz), 119.5 (d, J_{CF} = 23.1 Hz), 124.7, 126.2 (d, J_{CF} = 6.3 Hz), 128.6, 128.8, 131.0, 131.2, 137.0, 138.5, 142.9, 152.1, 153.6, 155.7 (d, J_{CF} = 235.3 Hz), 161.1, 190.6; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{26}H_{27}FN_2NaO_6$ $[M+Na]^+$: 505.1745; Found: 505.1742.



***tert*-butyl (*R*)-(4-fluoro-2-(5-(2-hydroxy-5-methylbenzoyl)-1-(1-hydroxypropan-2-yl)-2-oxo-1,2-dihydropyridin-3-yl)phenyl)carbamate (3ec)**: Light yellow solid, m.p. 89.7-90.5 °C; 129.5 mg, yield 87%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.35 (s, 9H), 1.40 (d, J = 7.2 Hz, 3H), 2.21 (s, 3H), 2.88 (br s, 1H), 3.73-3.76 (m, 1H), 3.81-3..85 (m, 1H), 5.21 (s, 1H), 6.84-6.90 (m, 2H), 6.96-7.01 (m, 1H), 7.24-7.31 (m, 1H),7.32 (br s, 1H), 7.35 (s, 1H), 7.57 (br s, 1H), 7.81 (d, J = 2.4 Hz, 1H), 8.12 (d, J = 2.0 Hz, 1H), 11.17 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 15.9, 20.5, 28.3, 54.7, 64.2, 80.3, 115.8 (d, J_{CF} = 22.4 Hz), 117.3 (d, J_{CF} = 23.3 Hz), 117.6, 118.4 (d, J_{CF} =

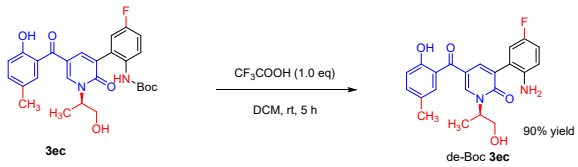
9.1 Hz), 128.4, 131.6, 132.9, 137.5, 140.1, 141.0, 154.0, 159.8 (d, J_{CF} = 243.2 Hz), 160.4, 161.4, 195.0; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{27}H_{29}FN_2NaO_6$ $[M+Na]^+$: 519.1902; Found: 519.1906.

8. Gram scale synthesis of the products 3aa, 3ab and 3ad



In a sealed tube equipped with a magnetic stirring bar, to 1.5 mL of EtOH was added 3-vinyl oxindole-chromone **1** (4.0 mmol) and NH_4OAc (8.0 mmol). The reaction mixture was stirred at rt for 3 h. After completion of the reaction, as indicated by TLC, purification by flash column chromatography (hexane/EtOAc, 5/1, v/v) was carried out to furnish the *N*-H 2-hydroxy benzoylpyridones **3** (**3aa**: 1.29 g, 80%; **3ab**: 1.43 g, 81%; **3ad**: 1.46 g, 84%).

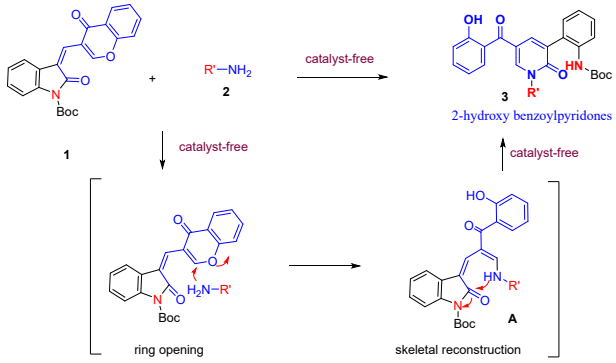
9. Transformation of compound 3ec into de-Boc 3ec



A mixture of compound **3ec** (0.30 mmol) and CF_3COOH (1.0 eq, 0.30 mmol) in 2.0 mL of DCM was stirred at reflux for 5 h. After completion of the reaction, as indicated by TLC, the mixture was purified by flash chromatography to afford the corresponding product de-Boc **3ec** (106.9 mg, 90% yield).

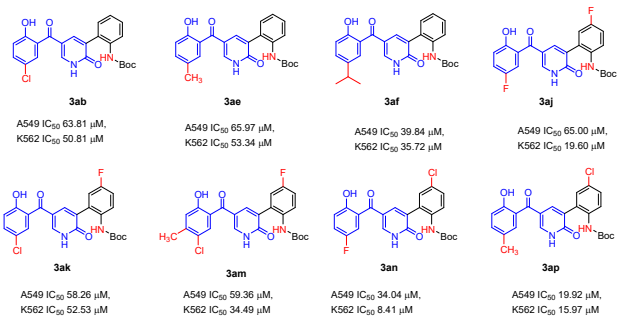
de-Boc **3ec**: ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.26 (d, J = 6.8 Hz, 3H), 2.17 (s, 3H), 3.57 (s, 2H), 4.63 (br s, 2H), 4.96-5.00 (m, 1H), 5.07 (br s, 1H), 6.64-6.68 (m, 1H), 6.77-6.88 (m, 3H), 7.12-7.16 (m, 2H), 7.63 (s, 1H), 8.18 (s, 1H), 10.19 (br s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 16.4, 20.3, 53.9, 63.0, 115.5 (d, J_{CF} = 21.5 Hz), 116.1, 116.8 (d, J_{CF} = 18.3 Hz), 117.0, 119.1, 123.5, 123.6, 124.7, 128.2, 128.3, 130.7, 134.0, 138.7, 142.3, 143.6, 153.6, 154.3, 157.6 (d, J_{CF} = 246.4 Hz), 158.6, 160.6, 192.4; HRMS (ESI-TOF) *m/z*: Calcd. for $C_{22}H_{21}FN_2NaO_4$ $[M+H]^+$: 419.1378; Found: 419.1374.

10. A proposed mechanism for the formation of 3

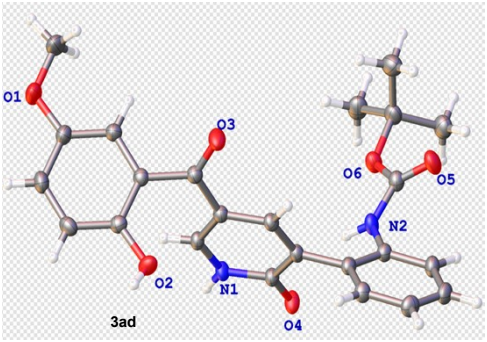


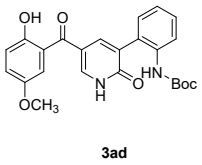
11. Evaluation of cytotoxicity toward cancer cell lines

Two human cancer cell lines, K562 and A549 were purchased from Chinese Academy of Sciences. All the cells were cultured in RPMI-1640 medium (GIBICO, USA), supplemented with 10% fetal bovine serum (Hyclone, USA) and Penicillin-Streptomycin (respectively 100 U/mL) in 5% CO_2 at 37°C. The cytotoxicity assay was performed according to the MTT (3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide) method in 96-well microplates. Briefly, 5000 cells were seeded into each well of 96-well cell culture plates and allowed to grow for 24 h before drug addition. The K562 tumor cell line was exposed to test compounds **3** at the concentrations of 10, 20, 40, 80, and 100 μmol·L^{-1} in triplicates for 48 h, comparable to cisplatin (Aladdin, China). Then the MTT reagent was added to reaction with the cancer cells for 4 hours. At least, measure the OD value at 490 wavelengths. IC_{50} of all the compounds were calculated by IBM SPSS Statistics (version 19).



12. X-ray crystal data for compounds 3ad and 3au



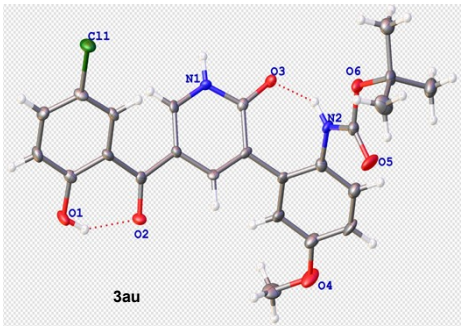


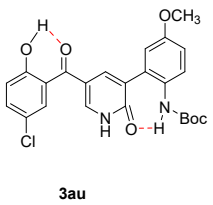
3ad

Table S2 Crystal data and structure refinement for 3ad

Identification code	**3ad**
Empirical formula	$C_{24}H_{24}N_2O_6$
Formula weight	436.45
Temperature/K	149.99(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å, b/Å, c/Å	9.3858(3), 25.0398(5), 9.6706(2)
α/°, β/°, γ/°,	90, 109.796(3), 90.
Volume/Å^3	2138.46(10)
Z	4
ρ_{calc}g/cm^3	1.356
μ/mm^{-1}	0.812
F(000)	920.0
Radiation	Cu Kα (λ = 1.54184)
Crystal size/mm^3	0.14 × 0.13 × 0.12
2Θ range for data collection/°	7.06 to 148.57
Index ranges	$-9 \le h \le 11$, $-29 \le k \le 30$, $-12 \le l \le 9$
Reflections collected	8412
Independent reflections	4239 [R_{int} = 0.0203, R_{sigma} = 0.0259]
Data/restraints/parameters	4239/0/294
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0390, wR_2 = 0.0997
Final R indexes [all data]	R_1 = 0.0430, wR_2 = 0.1025
Largest diff. peak/hole / e Å^{-3}	0.23/-0.24

Crystal Data for $C_{24}H_{24}N_2O_6$ (M =436.45 g/mol): monoclinic, space group $P2_1/n$ (no. 14), a = 9.3858(3) Å, b = 25.0398(5) Å, c = 9.6706(2) Å, β = 109.796(3)°, V = 2138.46(10) Å^3, Z = 4, T = 149.99(10) K, μ(Cu Kα) = 0.812 mm^{-1}, *Dcalc* = 1.356 g/cm^3, 8412 reflections measured (7.06° ≤ 2Θ ≤ 148.57°), 4239 unique (R_{int} = 0.0203, R_{sigma} = 0.0259) which were used in all calculations. The final R_1 was 0.0390 (I > 2σ(I)) and wR_2 was 0.1025 (all data).





3au

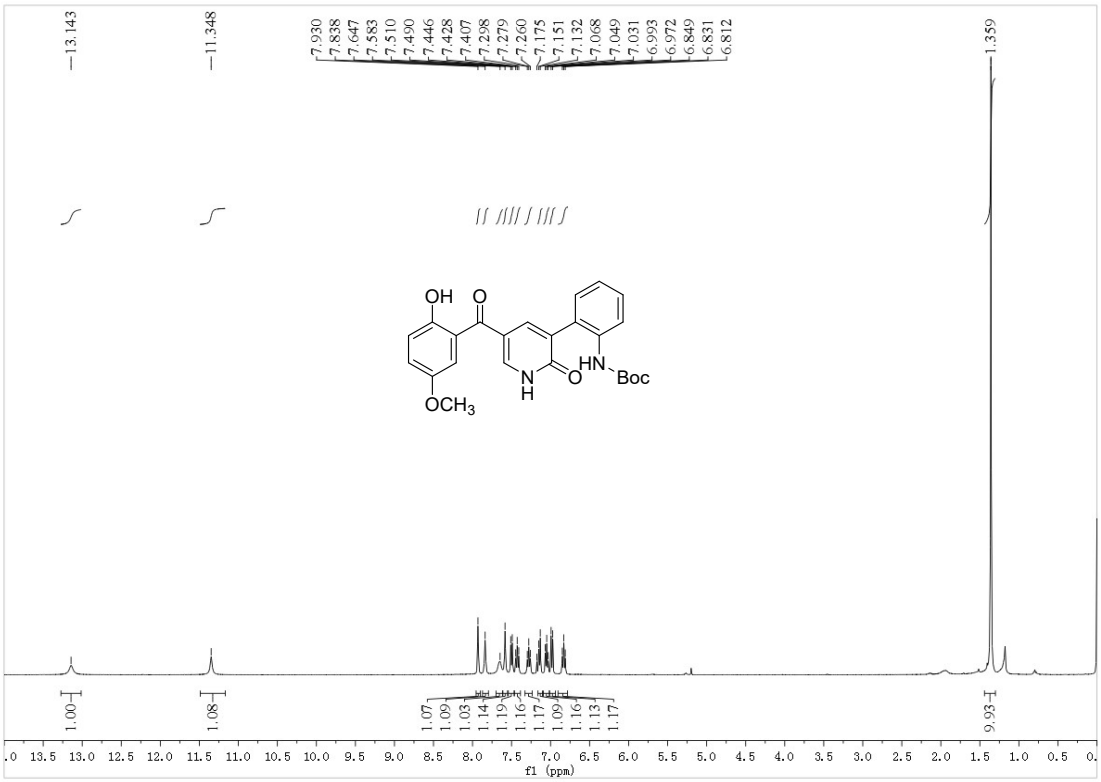
Table S3 Crystal data and structure refinement for 3au

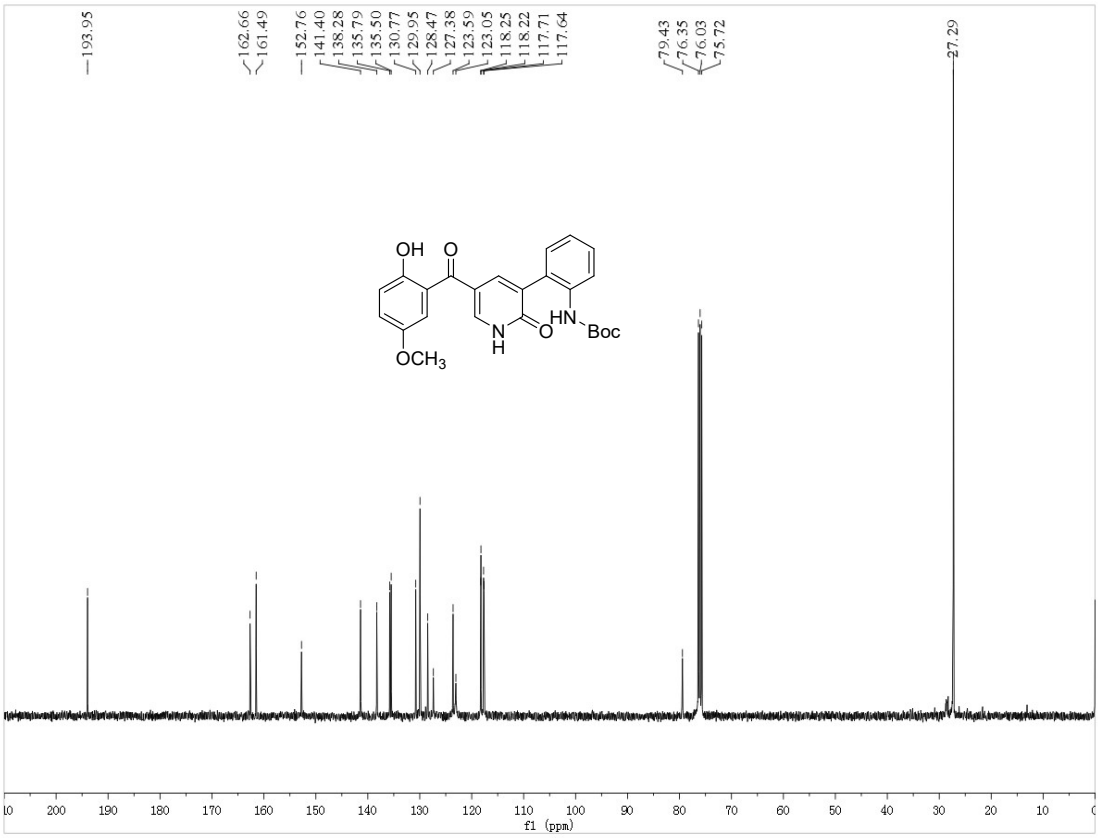
Identification code	**3au**
Empirical formula	$C_{24}H_{23}ClN_2O_6$
Formula weight	470.89
Temperature/K	149.99(10)
Crystal system	triclinic
Space group	P-1
a/Å, b/Å, c/Å	7.0463(4), 10.8325(7), 15.8212(15)
α/°, β/°, γ/°,	92.200(7), 101.856(7), 108.128(6).
Volume/Å^3	1116.38(15)
Z	2
ρ_{calc}g/cm^3	1.401
μ/mm^{-1}	0.215
F(000)	492.0
Radiation	Mo Kα (λ = 0.71073)
Crystal size/mm^3	0.14 × 0.13 × 0.09
2Θ range for data collection/°	3.98 to 49.994
Index ranges	-8 ≤ h ≤ 8, -12 ≤ k ≤ 12, -8 ≤ l ≤ 18
Reflections collected	3934
Independent reflections	3934 [R_{int} = 0.0362, R_{sigma} = 0.1305]
Data/restraints/parameters	3934/0/304
Goodness-of-fit on F^2	1.042
Final R indexes [I>=2σ (I)]	R_1 = 0.0883, wR_2 = 0.2324
Final R indexes [all data]	R_1 = 0.1090, wR_2 = 0.2447
Largest diff. peak/hole / e Å^{-3}	0.47/-0.84

Crystal Data for $C_{24}H_{23}ClN_2O_6$ (M =470.89 g/mol): triclinic, space group P-1 (no. 2), a = 7.0463(4) Å, b = 10.8325(7) Å, c = 15.8212(15) Å, α = 92.200(7)°, β = 101.856(7)°, γ = 108.128(6)°, V = 1116.38(15) Å^3, Z = 2, T = 149.99(10) K, μ(Mo Kα) = 0.215 mm^{-1}, *Dcalc* = 1.401 g/cm^3, 3934 reflections measured (3.98° ≤ 2Θ ≤ 49.994°), 3934 unique (R_{int} = 0.0362, R_{sigma} = 0.1305) which were used in all calculations. The final R_1 was 0.0883 (I > 2σ(I)) and wR_2 was 0.2447 (all data).

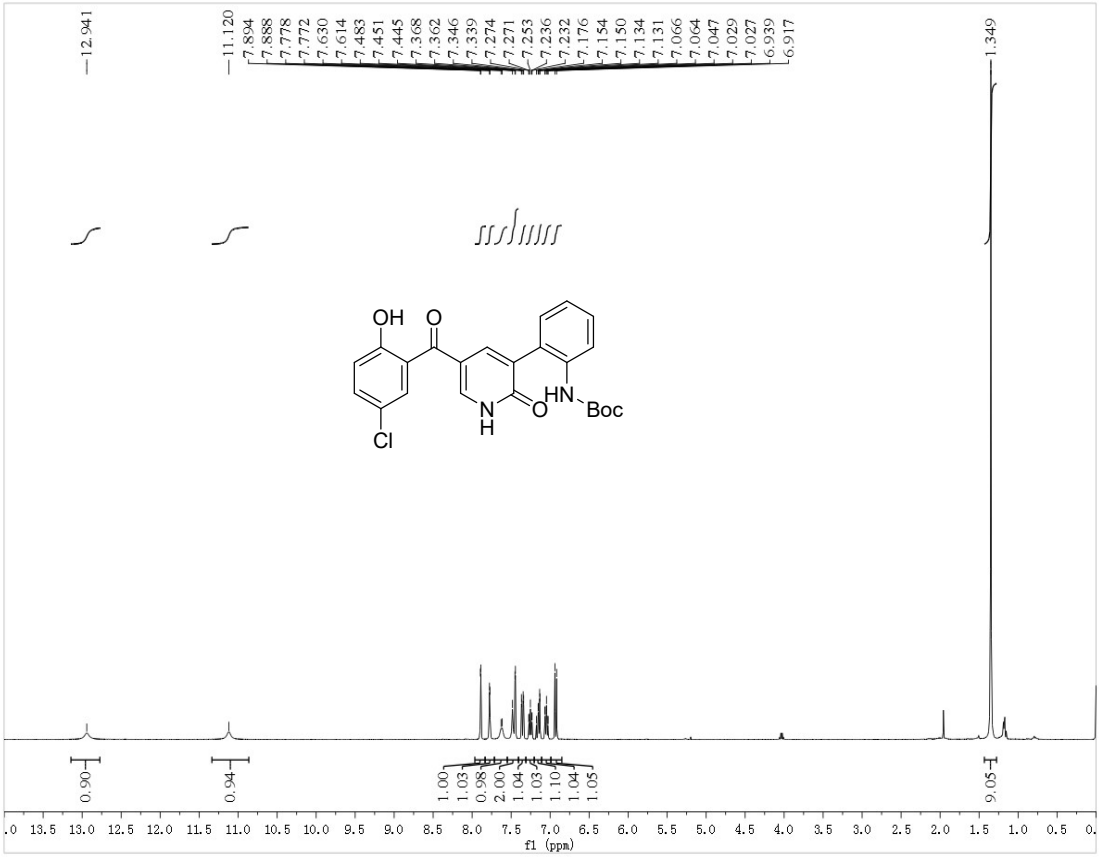
13. The copies of 1H NMR and 13C NMR spectra for compounds 3

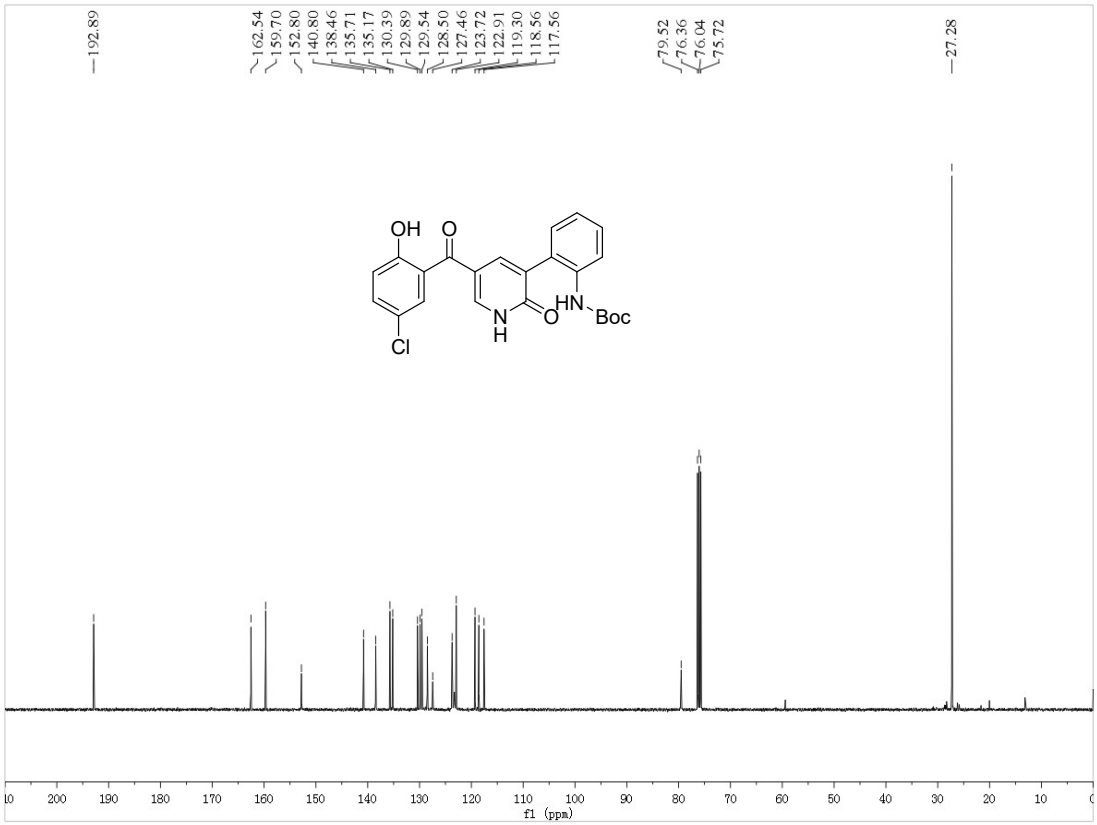
^{1}H and ^{13}C NMR of 3aa



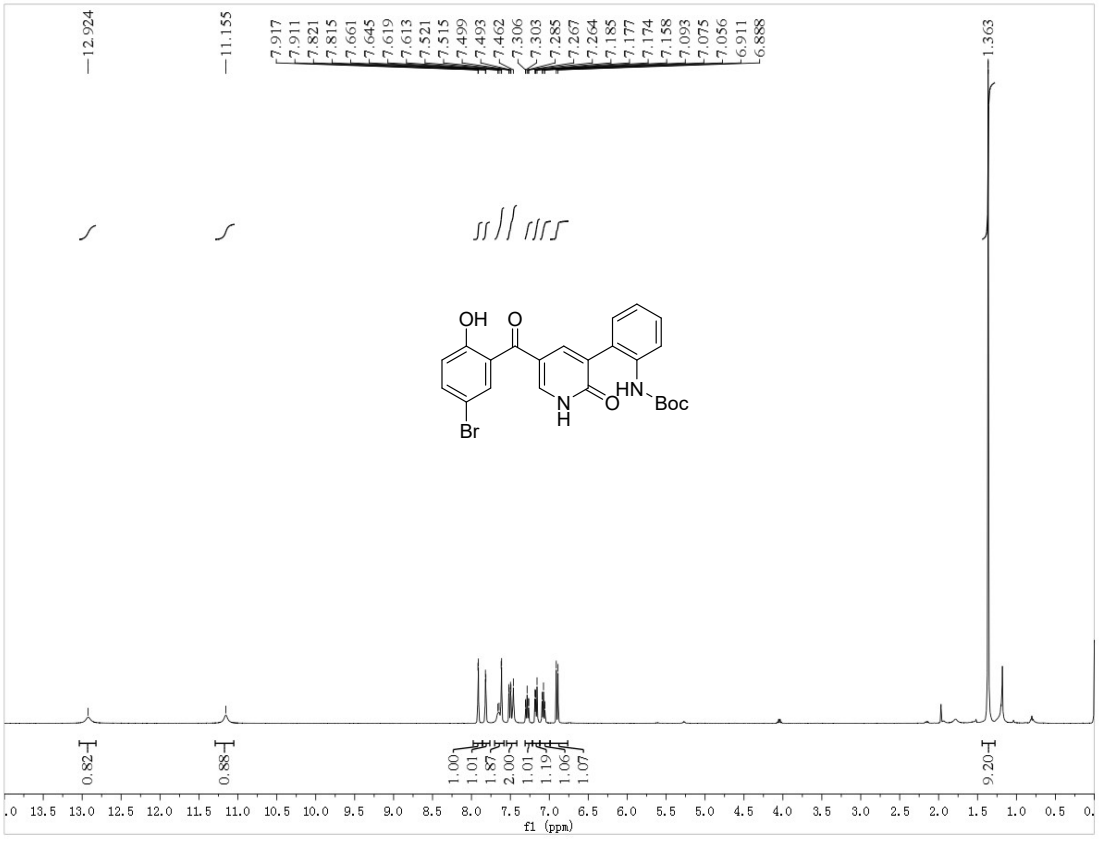


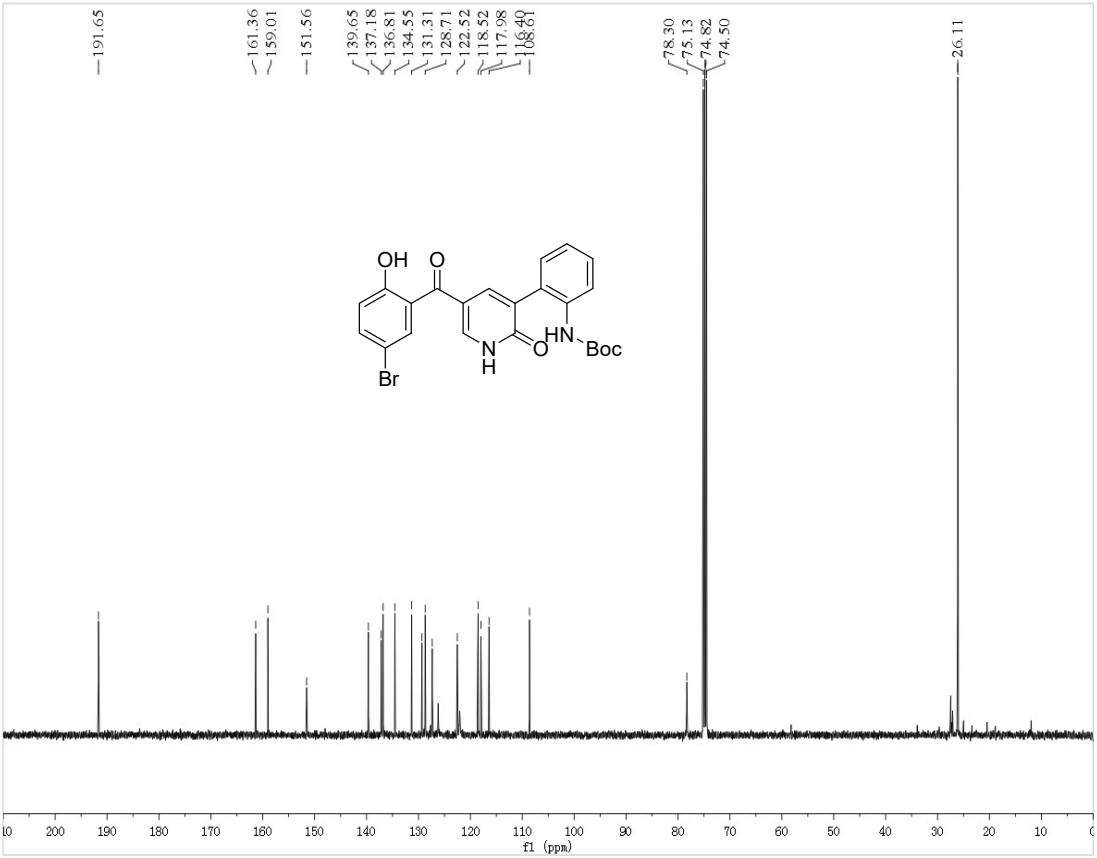
^{1}H and ^{13}C NMR of 3ab



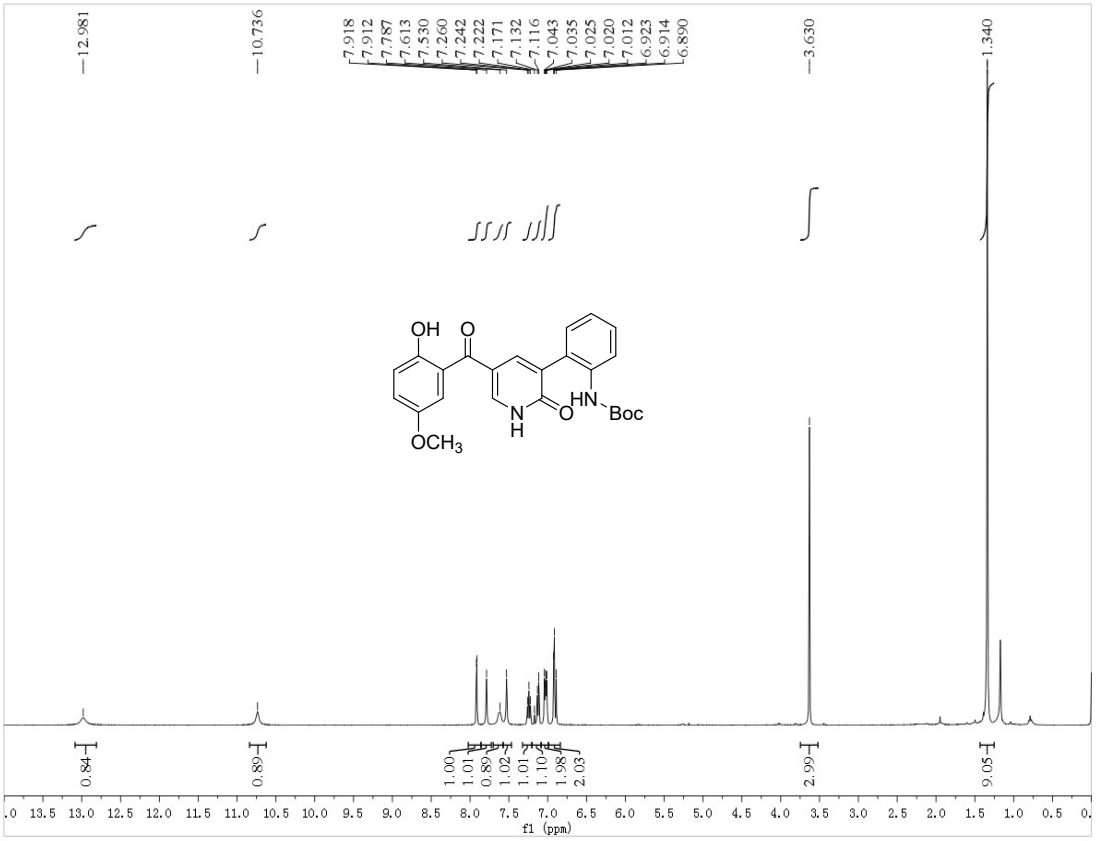


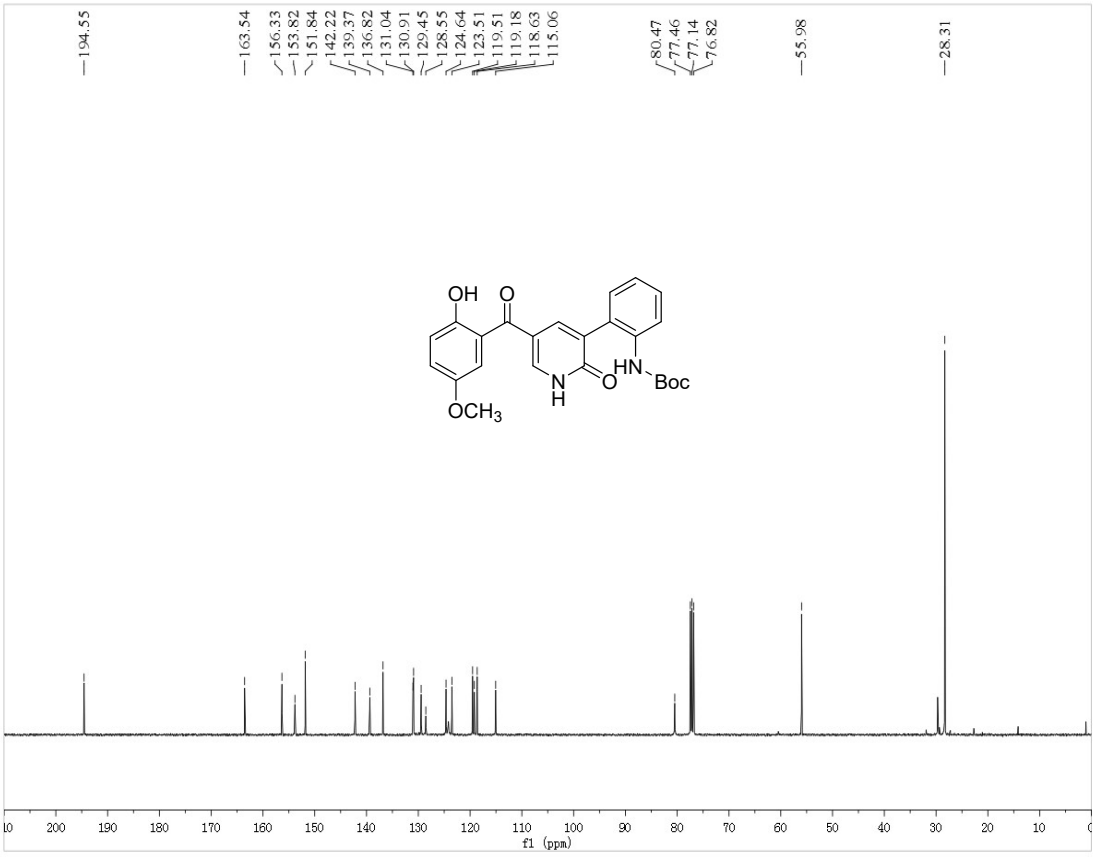
^{1}H and ^{13}C NMR of 3ac



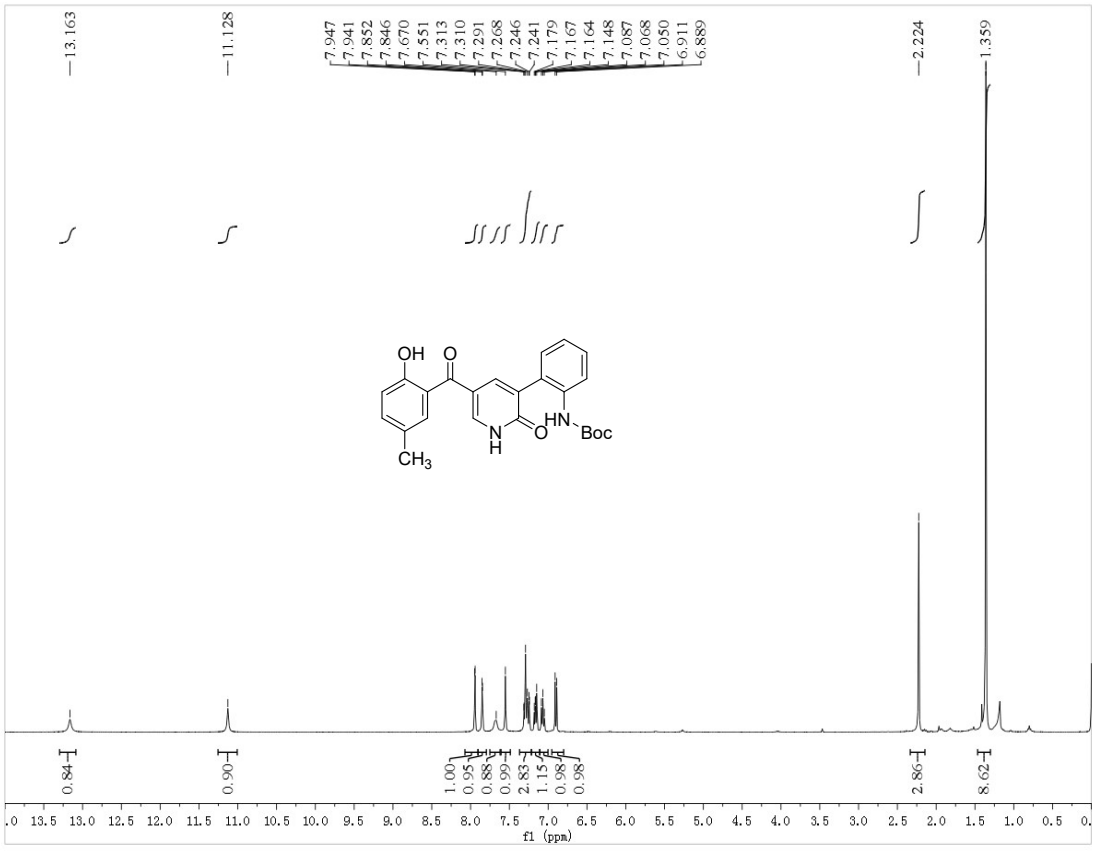


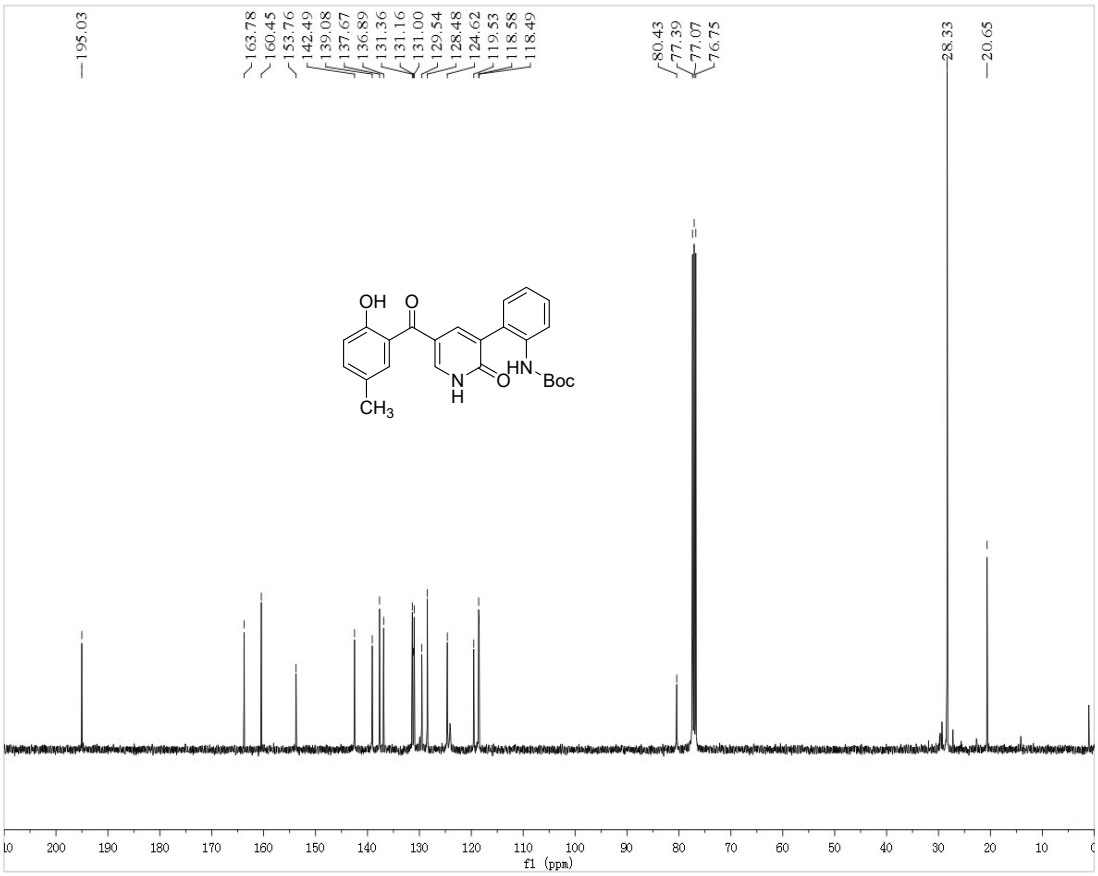
^{1}H and ^{13}C NMR of 3ad



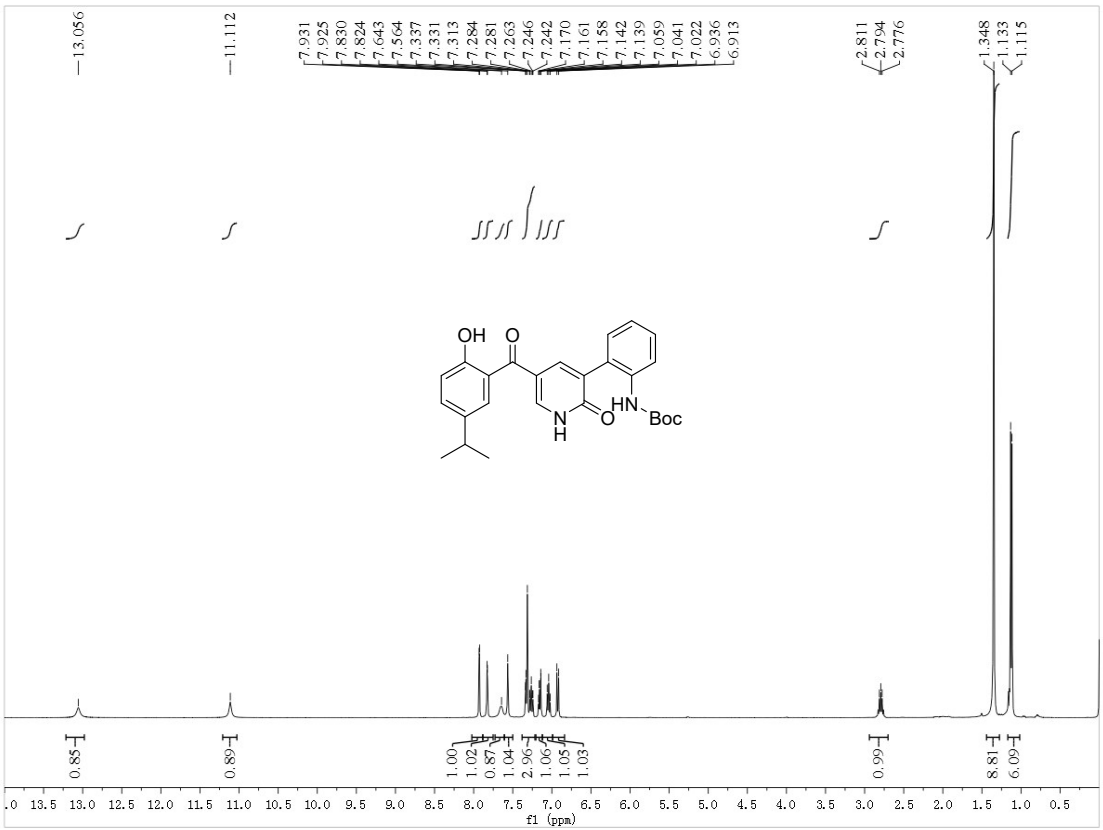


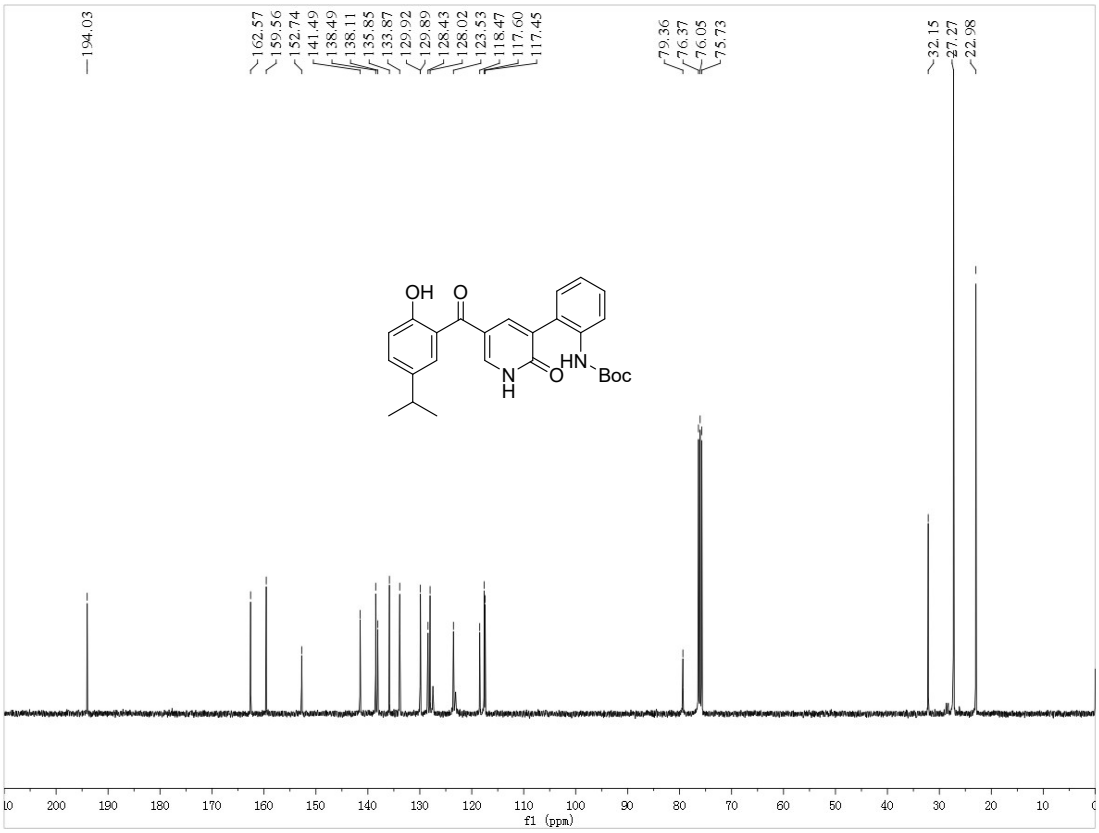
^{1}H and ^{13}C NMR of 3ae



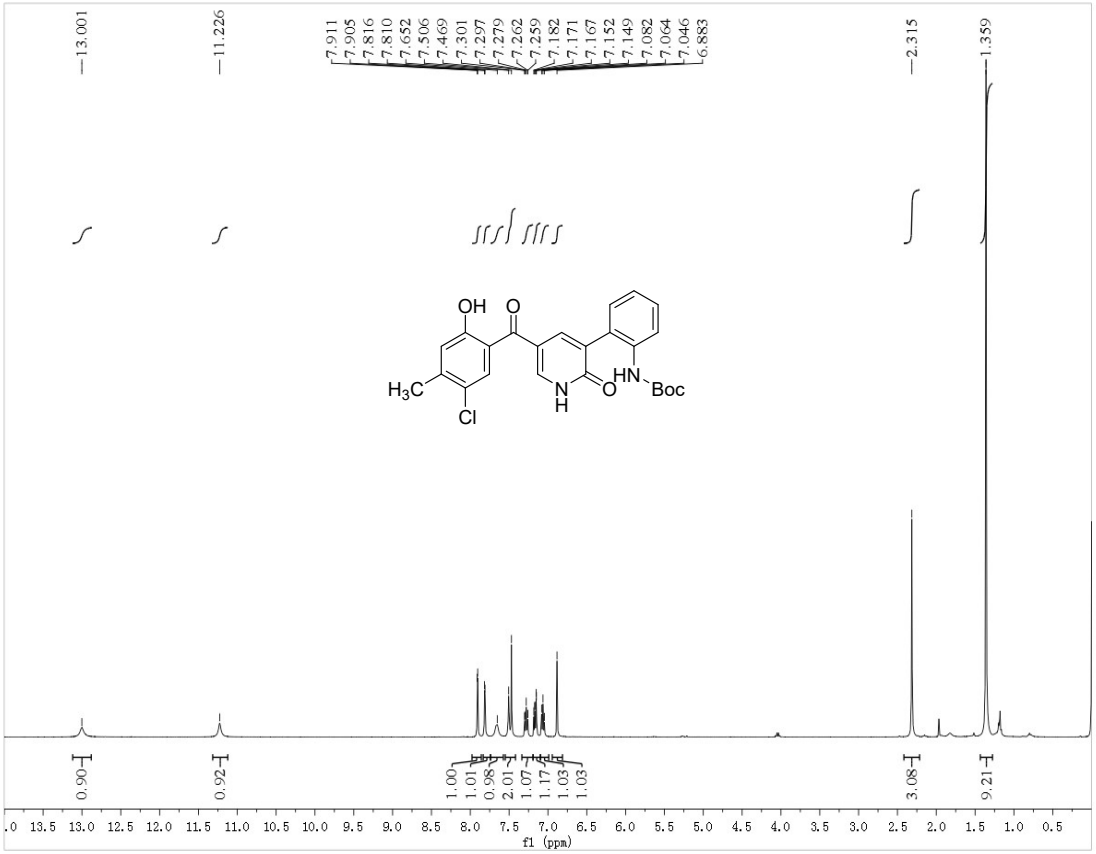


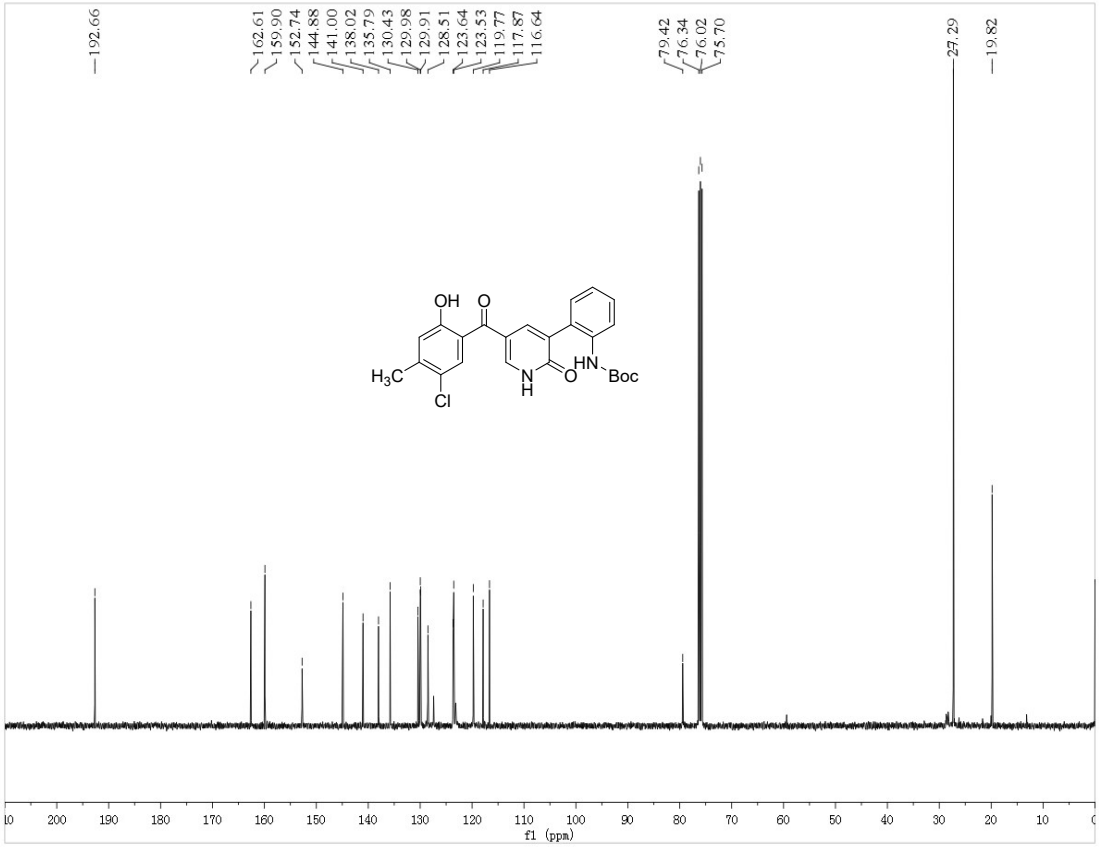
^{1}H and ^{13}C NMR of 3af



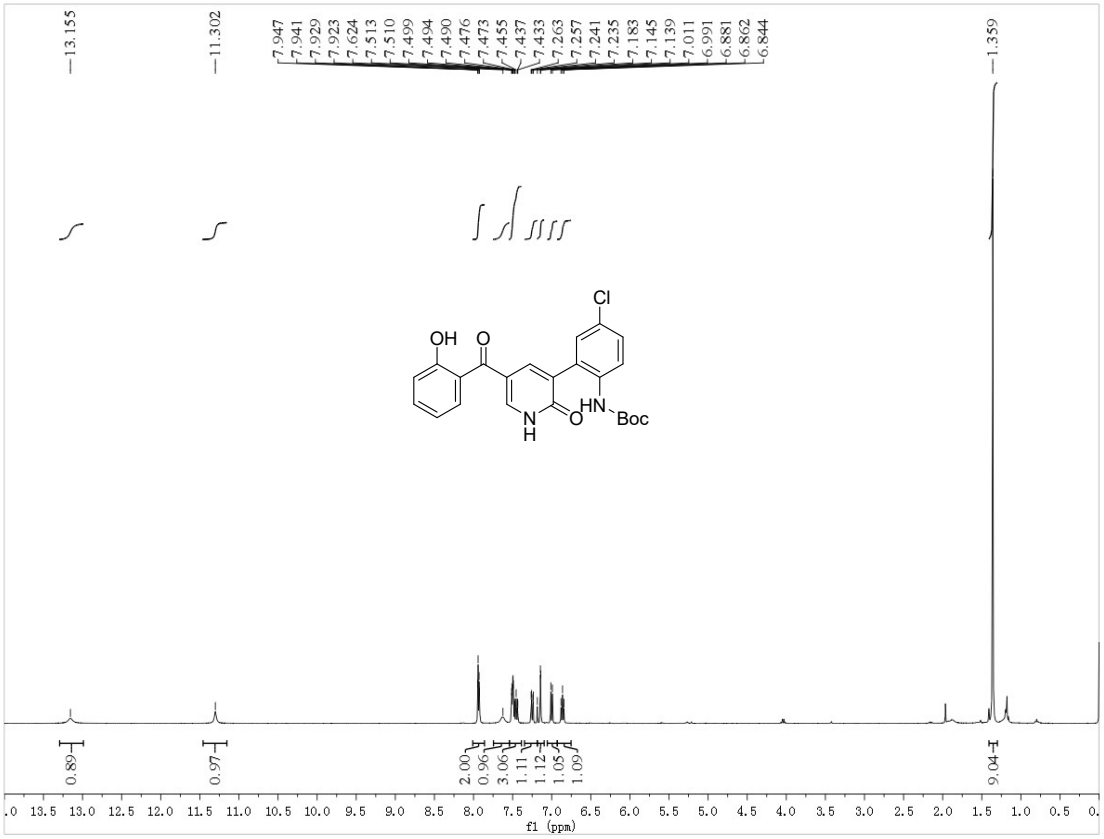


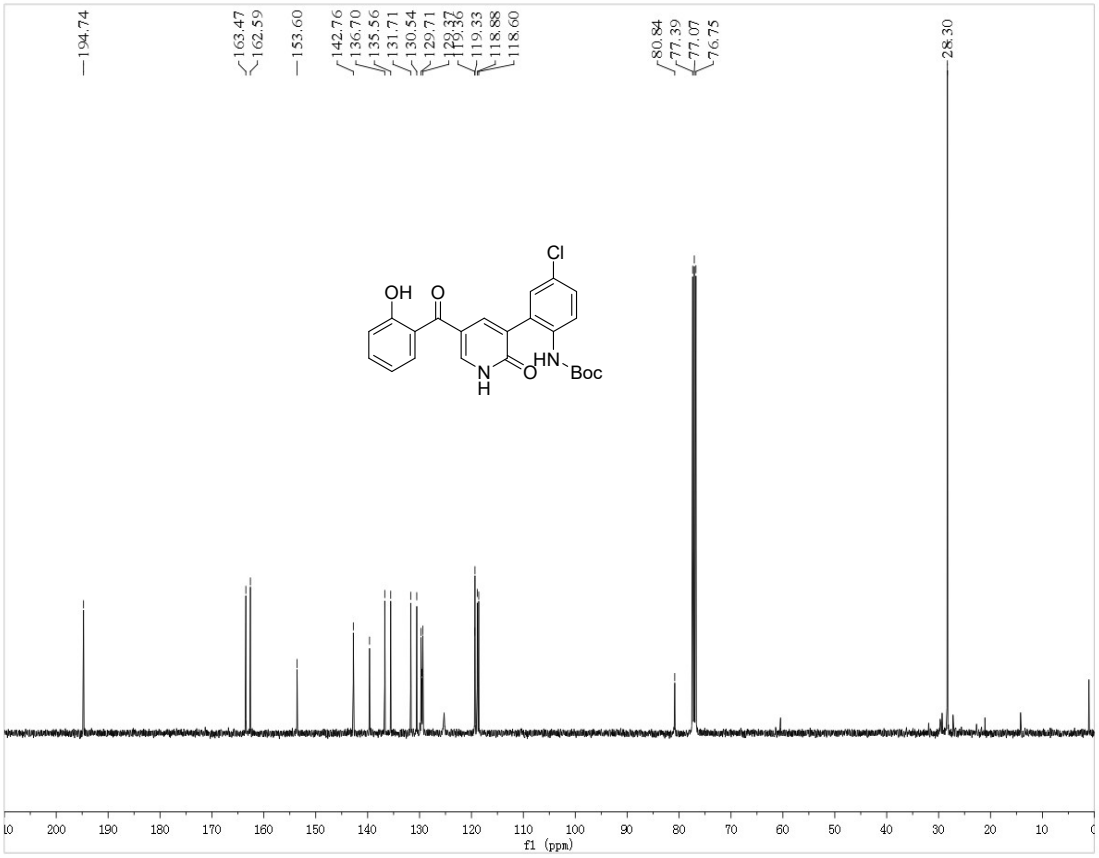
^{1}H and ^{13}C NMR of 3ag



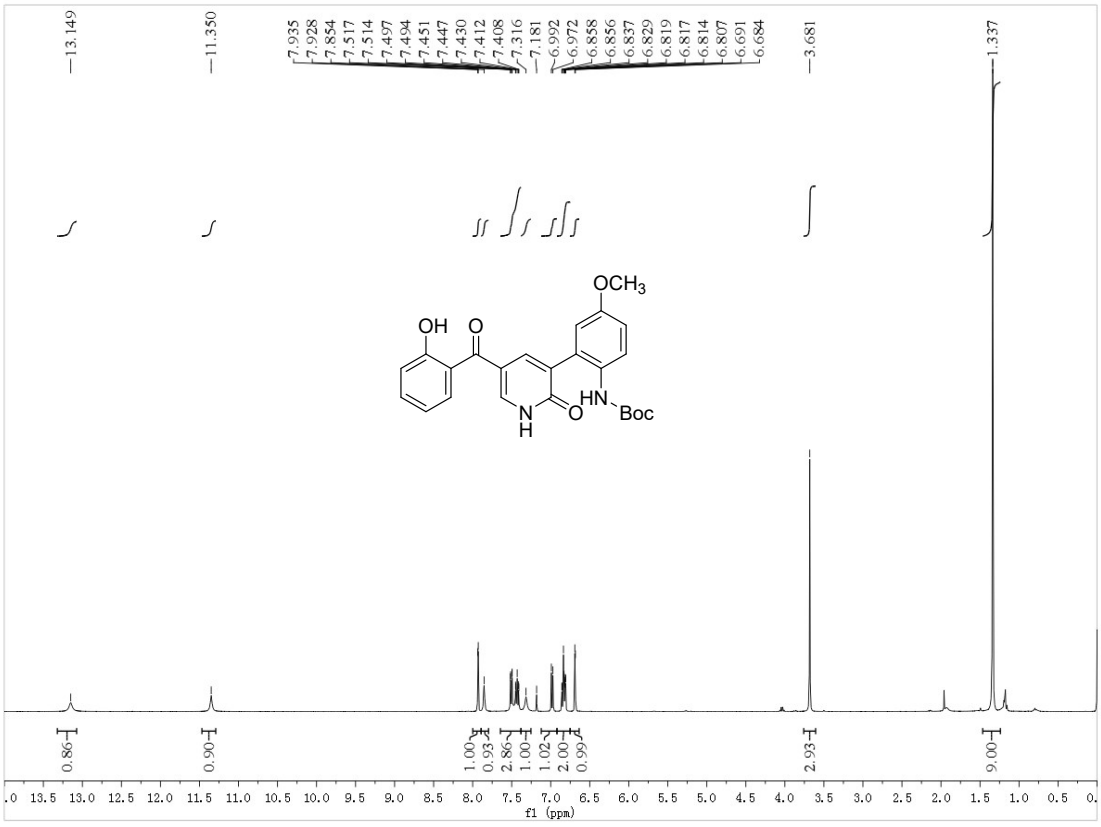


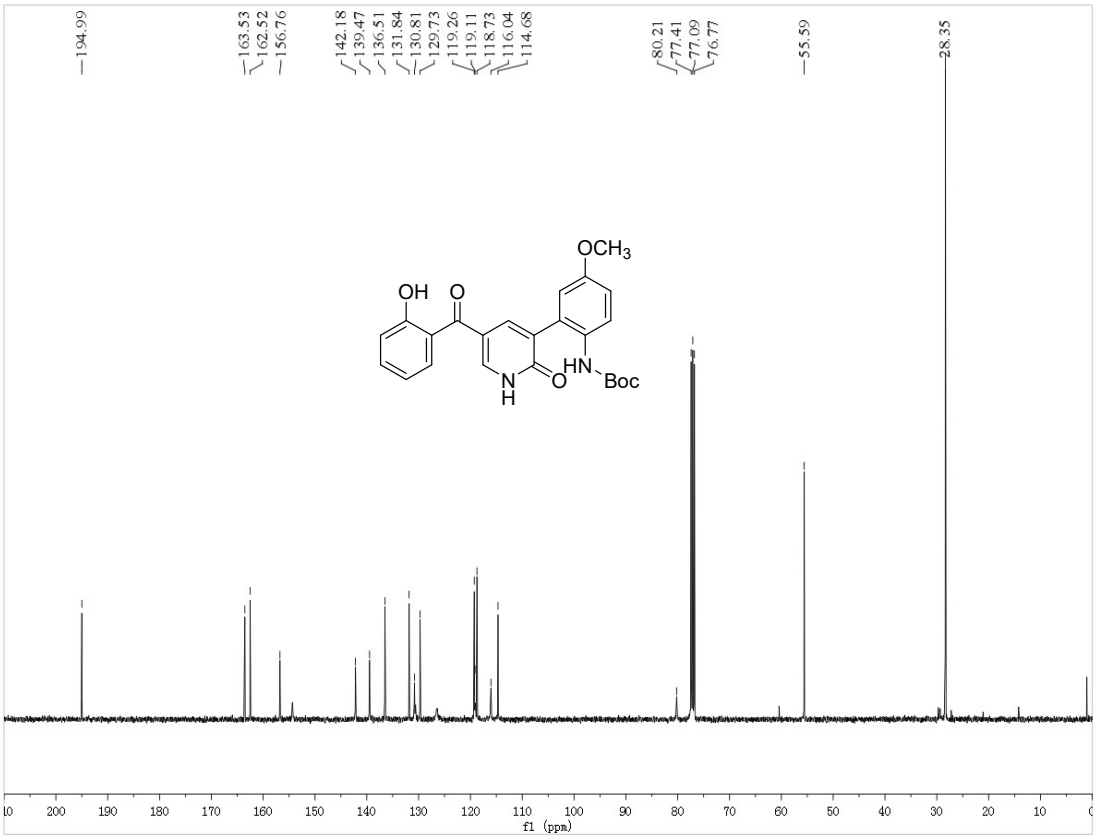
^{1}H and ^{13}C NMR of 3ah



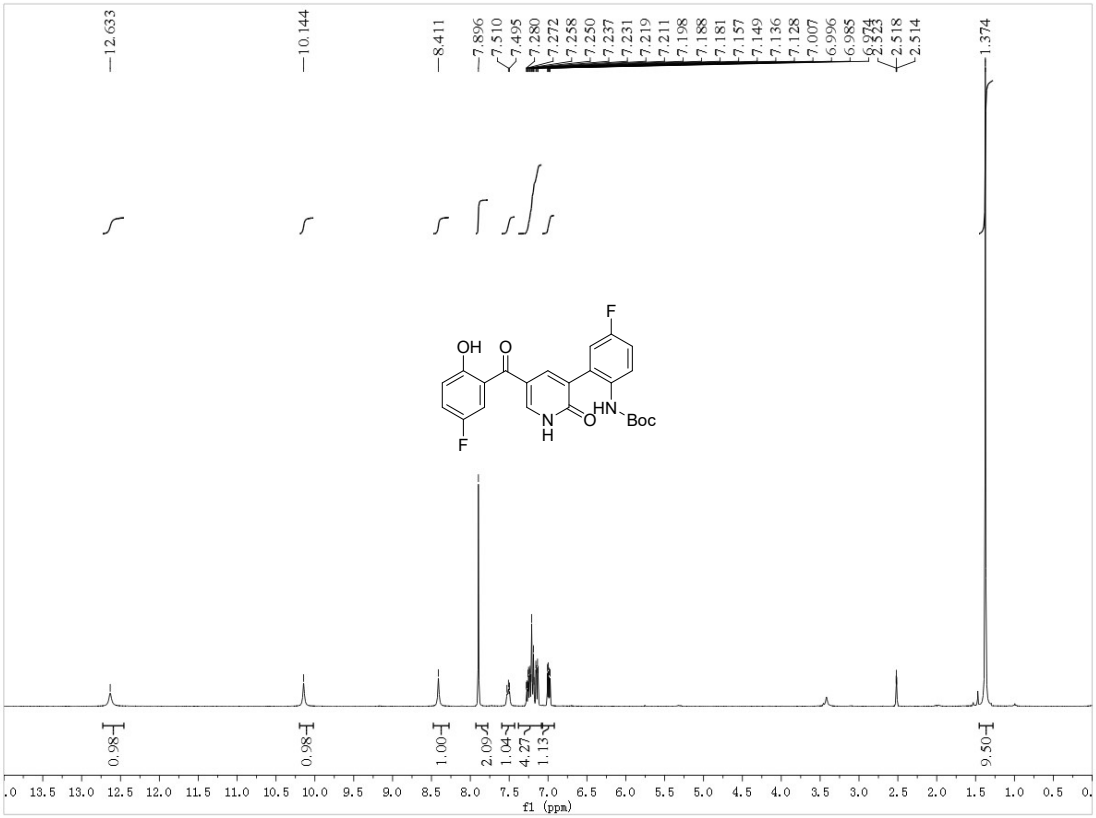


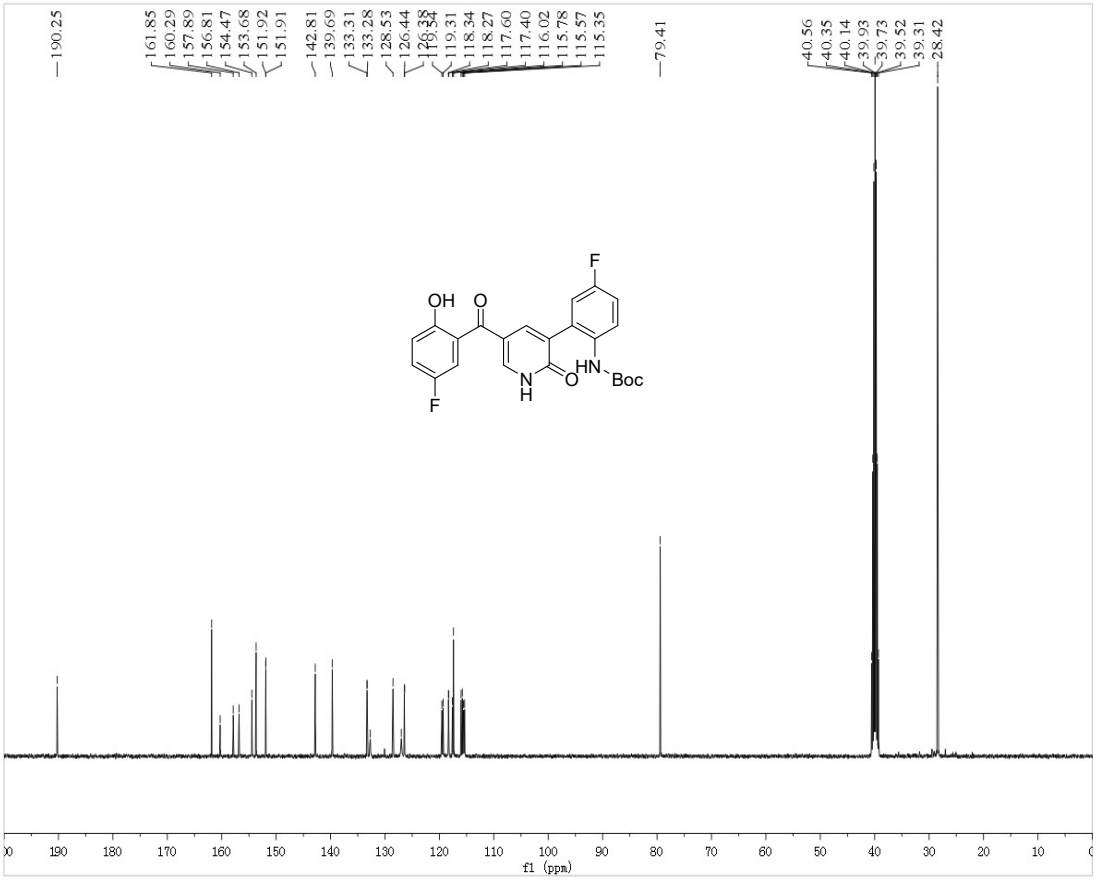
^{1}H and ^{13}C NMR of 3ai



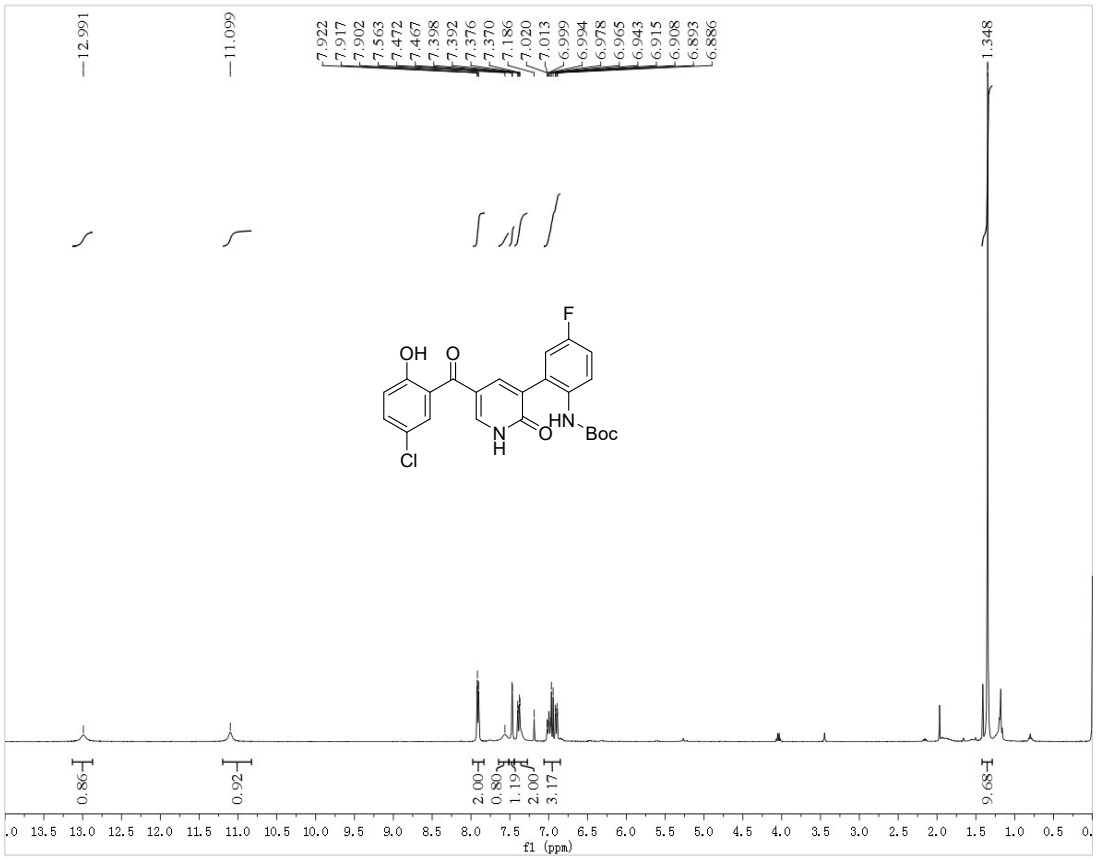


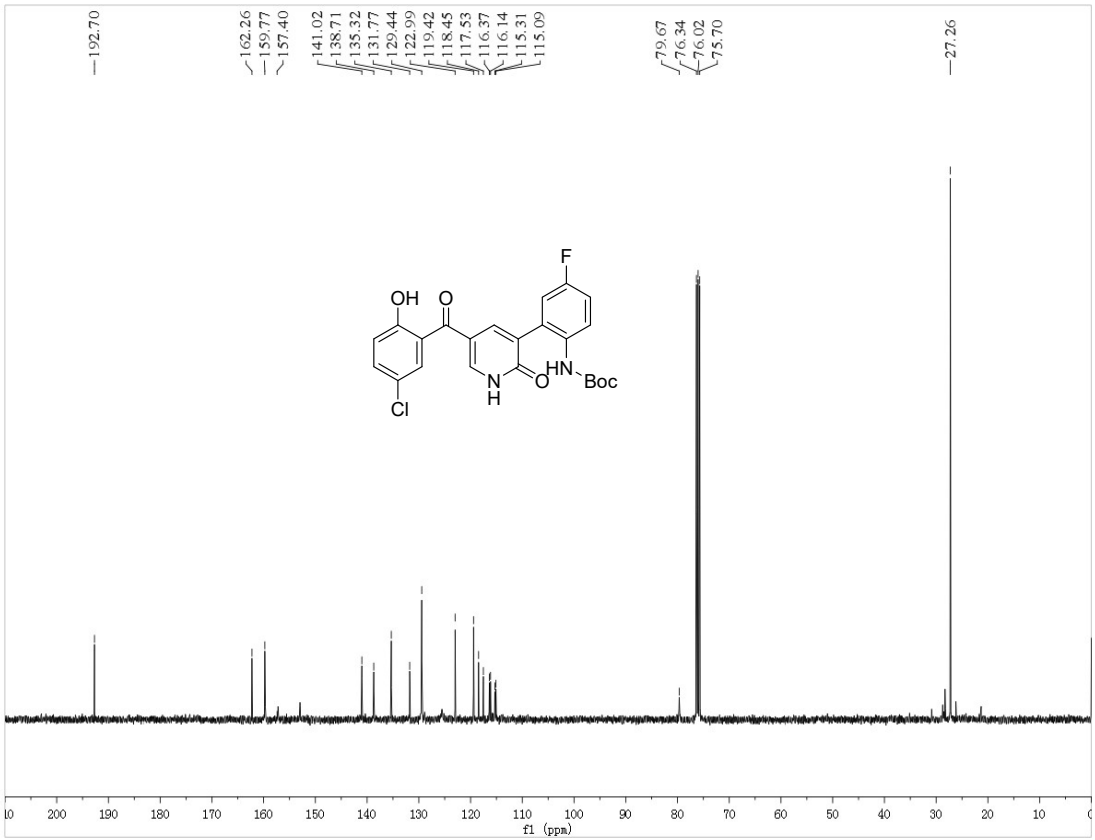
^{1}H and ^{13}C NMR of 3aj



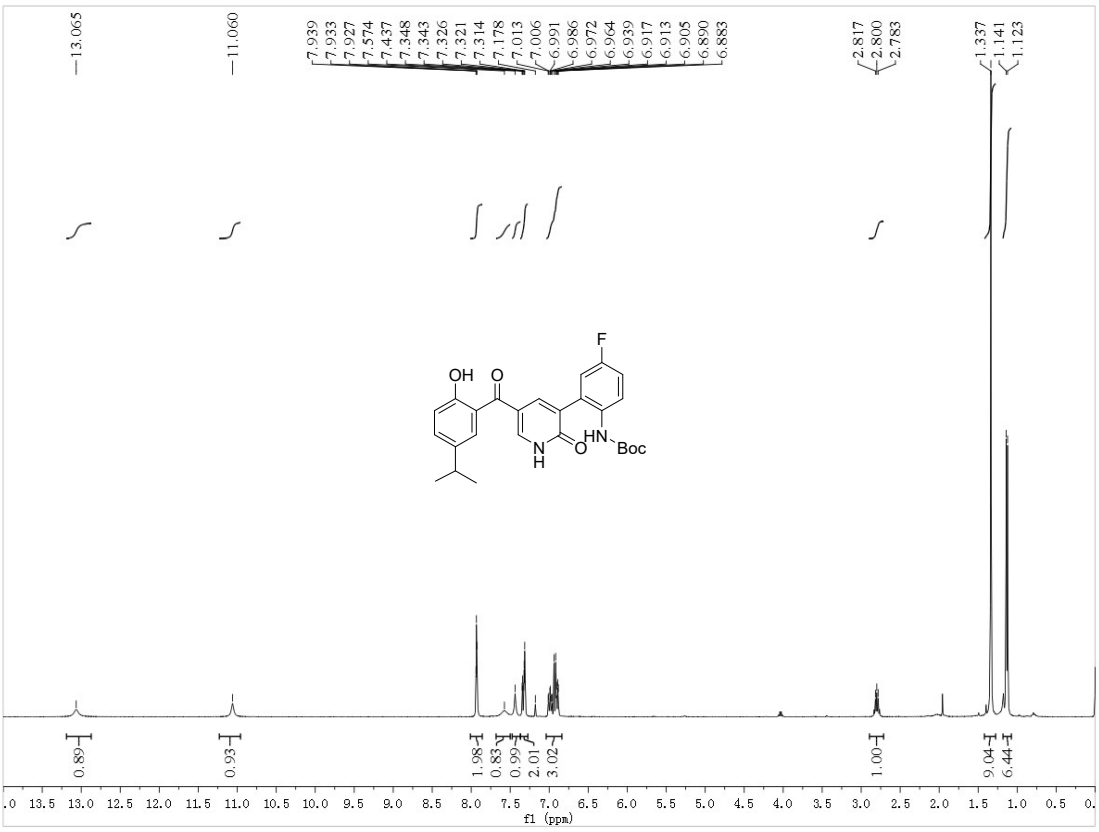


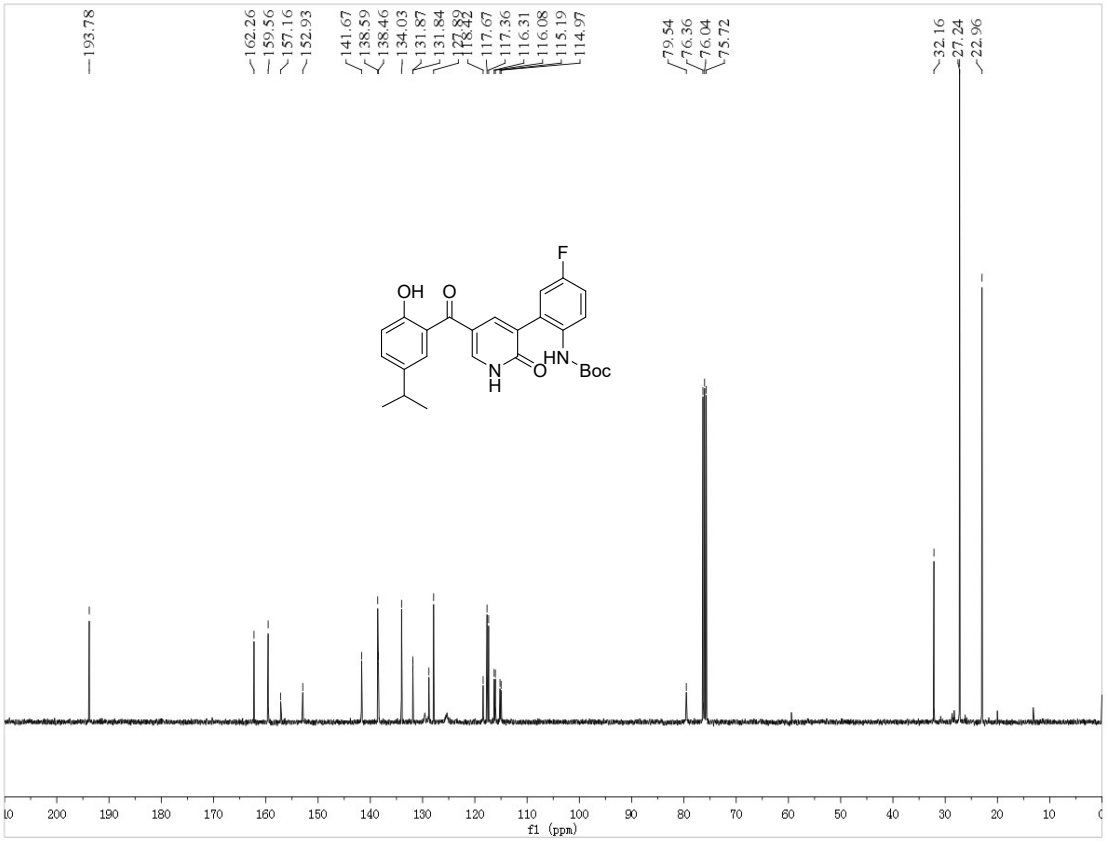
^{1}H and ^{13}C NMR of 3ak



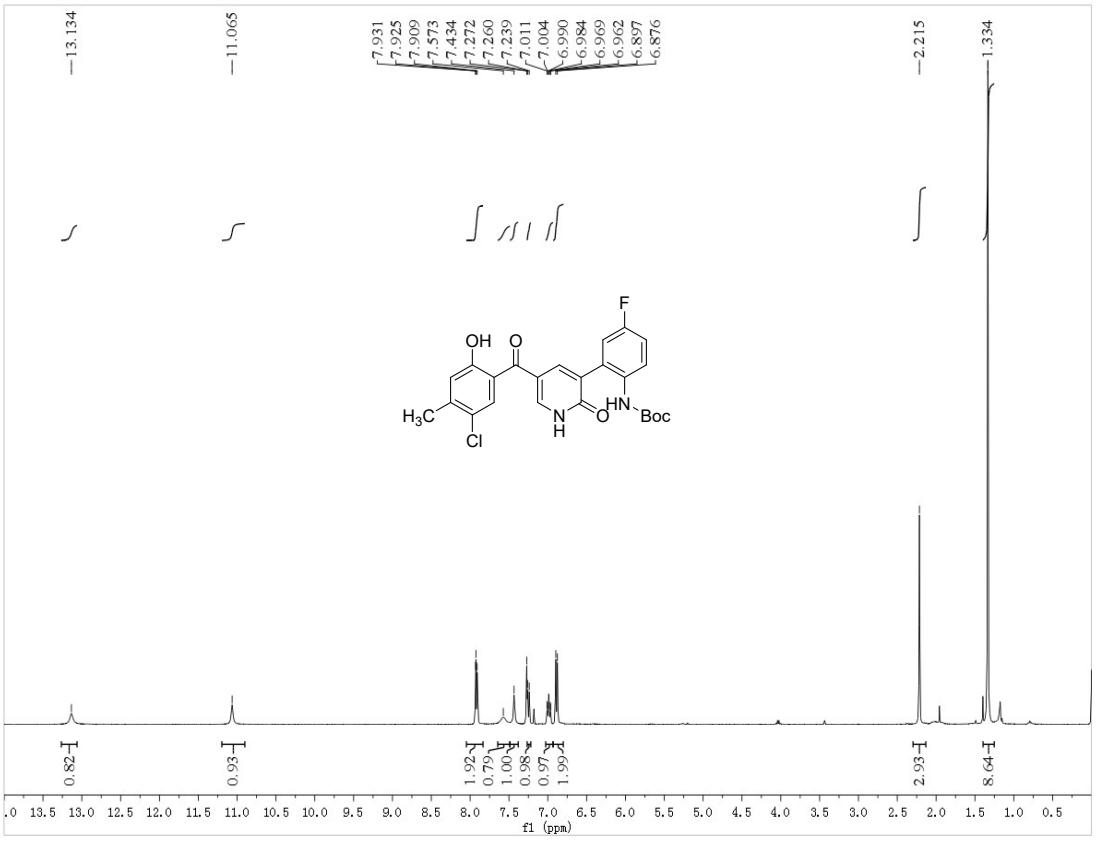


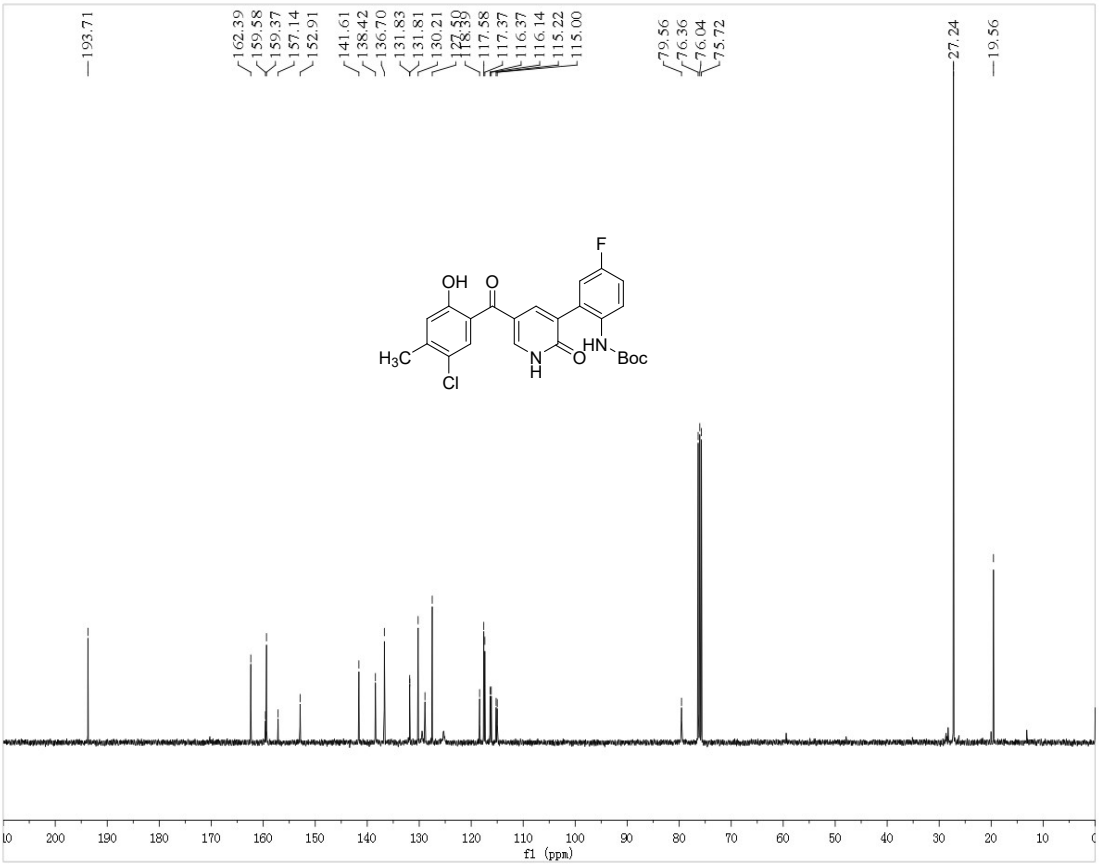
^{1}H and ^{13}C NMR of 3al



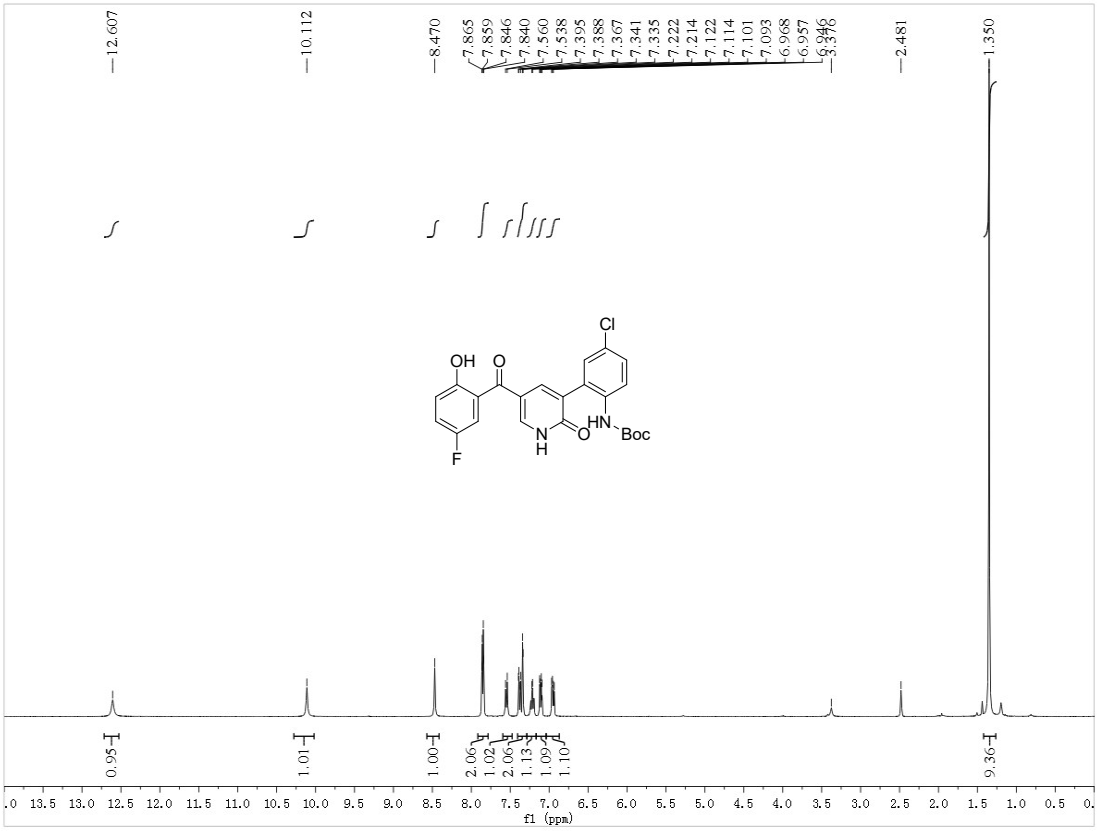


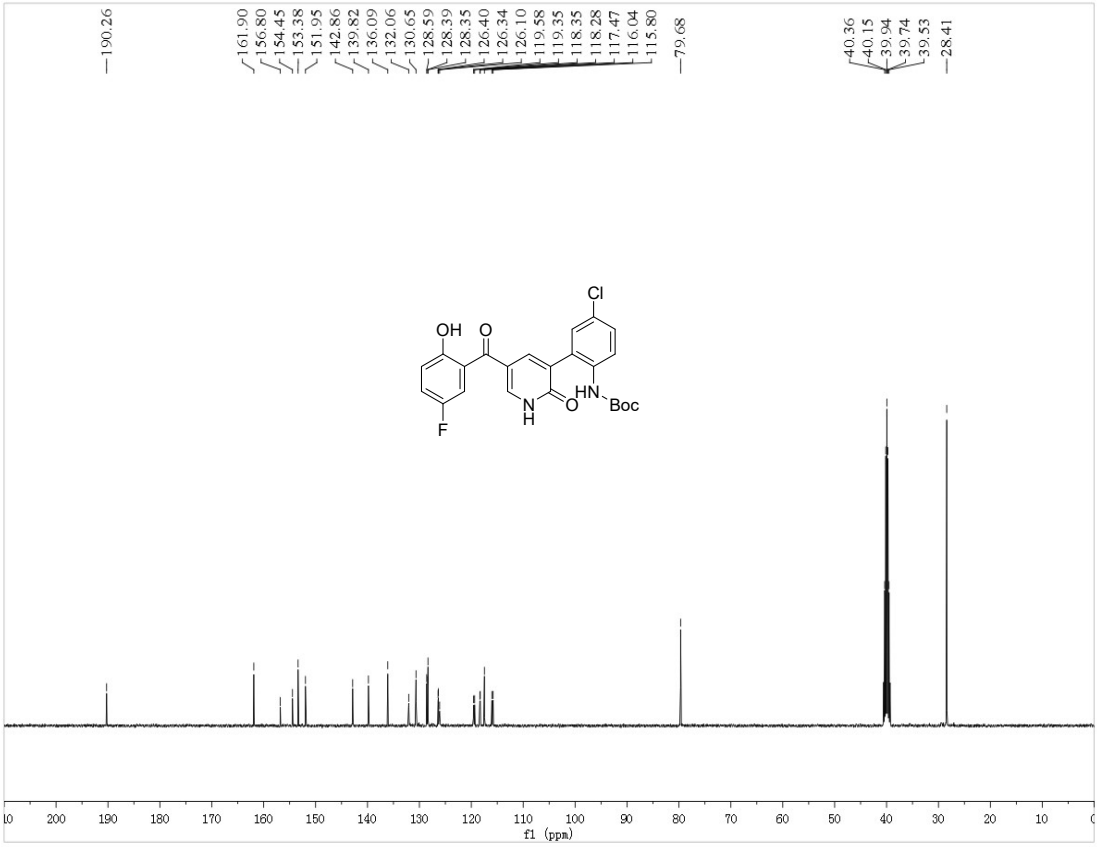
^{1}H and ^{13}C NMR of 3am



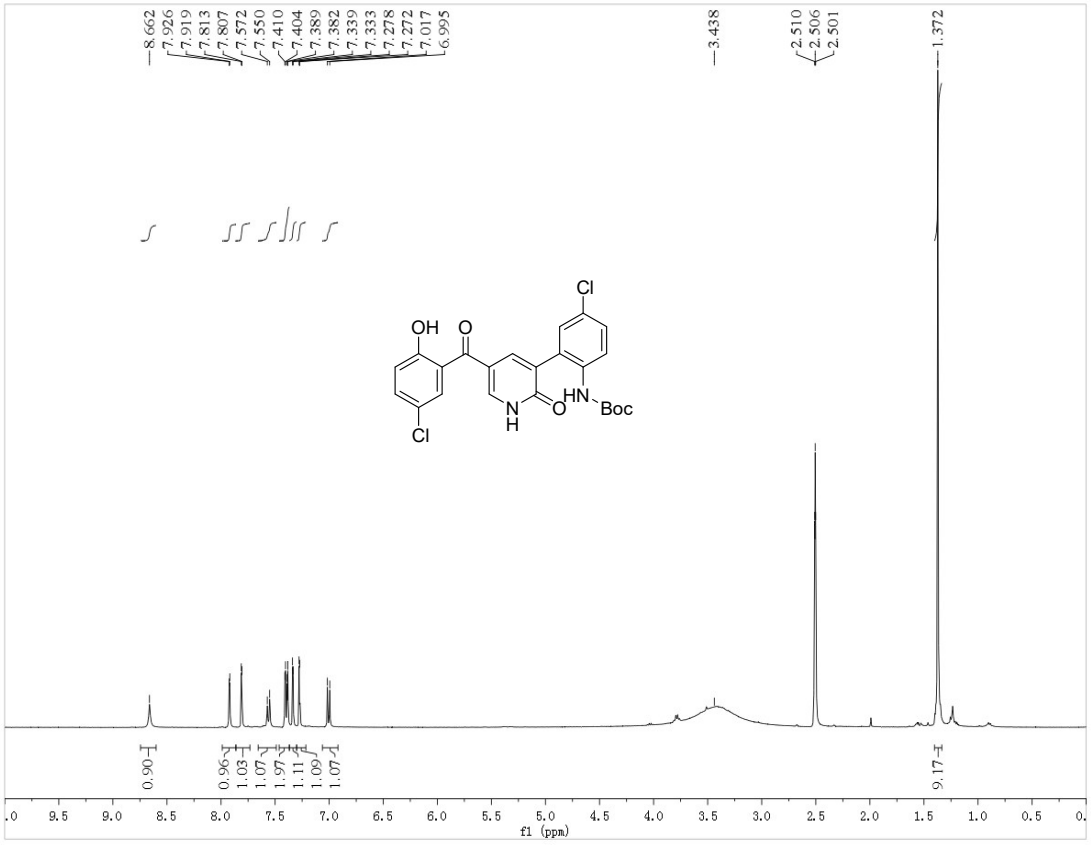


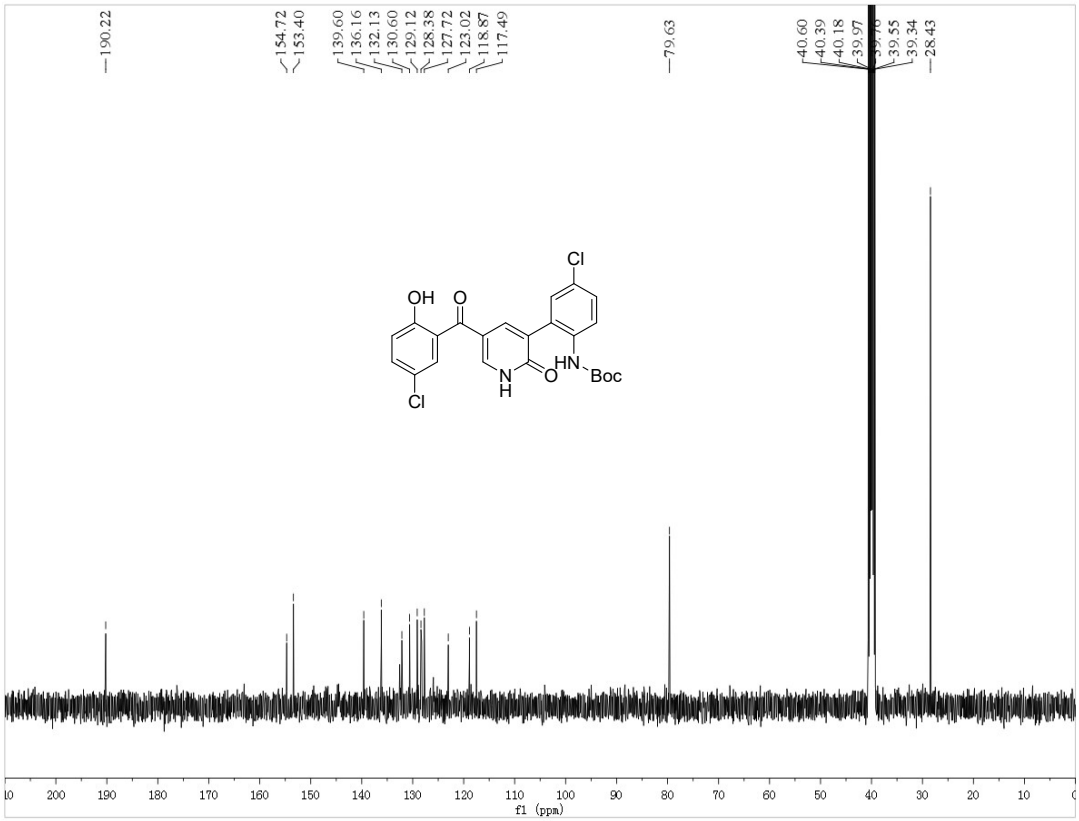
^{1}H and ^{13}C NMR of 3an



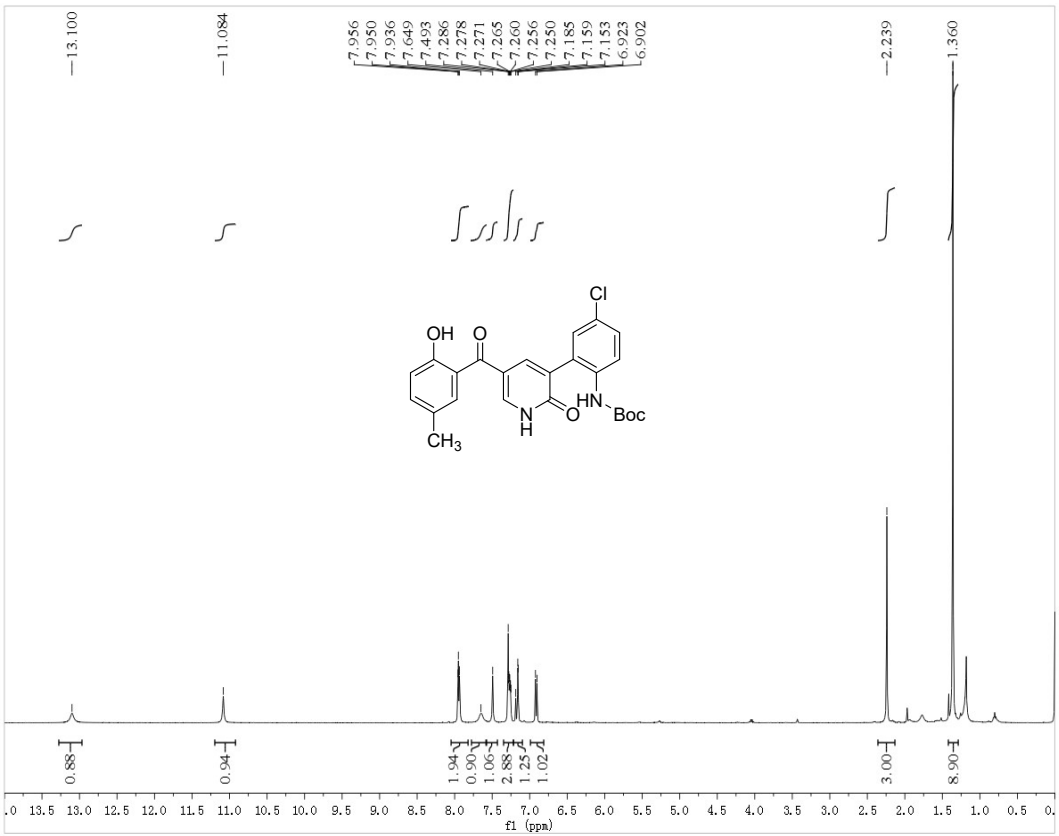


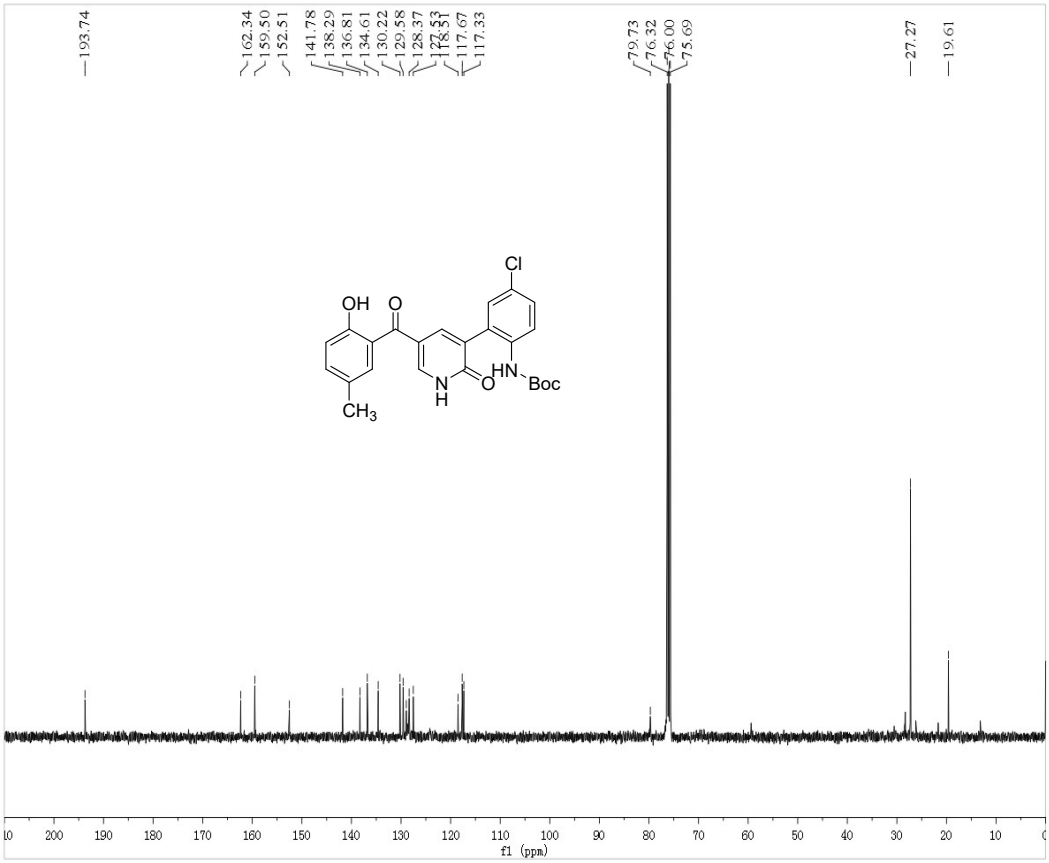
^{1}H and ^{13}C NMR of 3ao



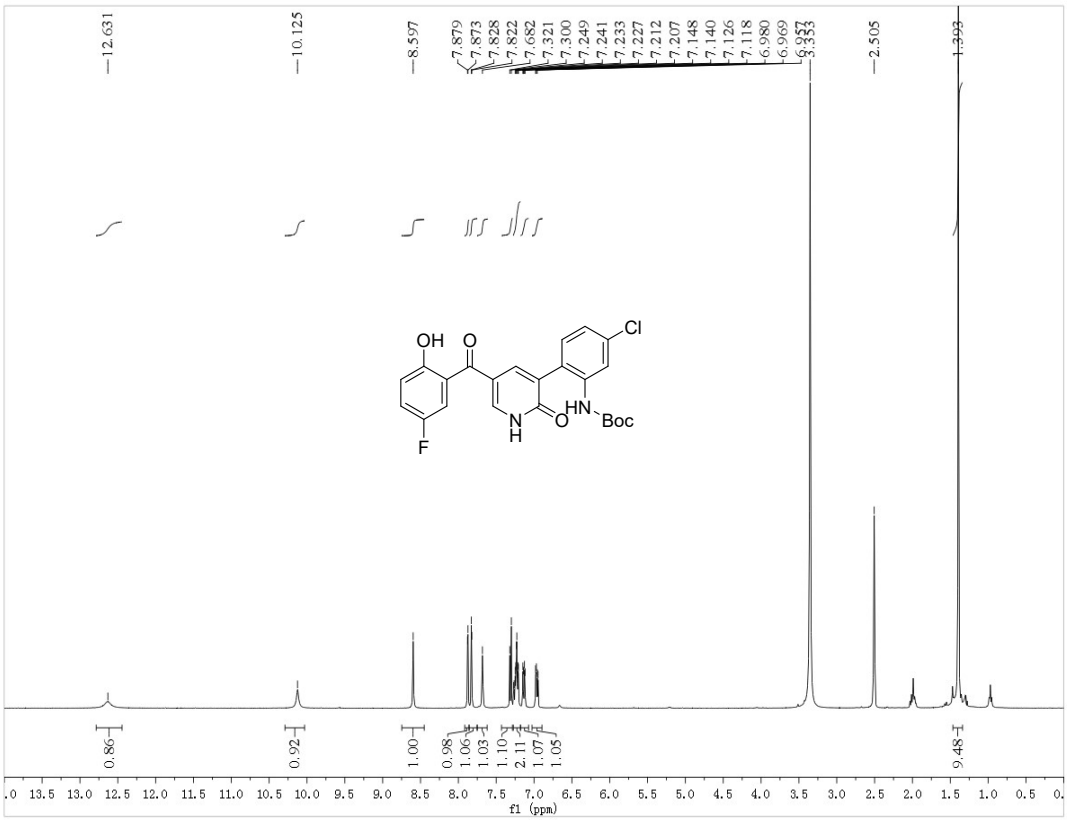


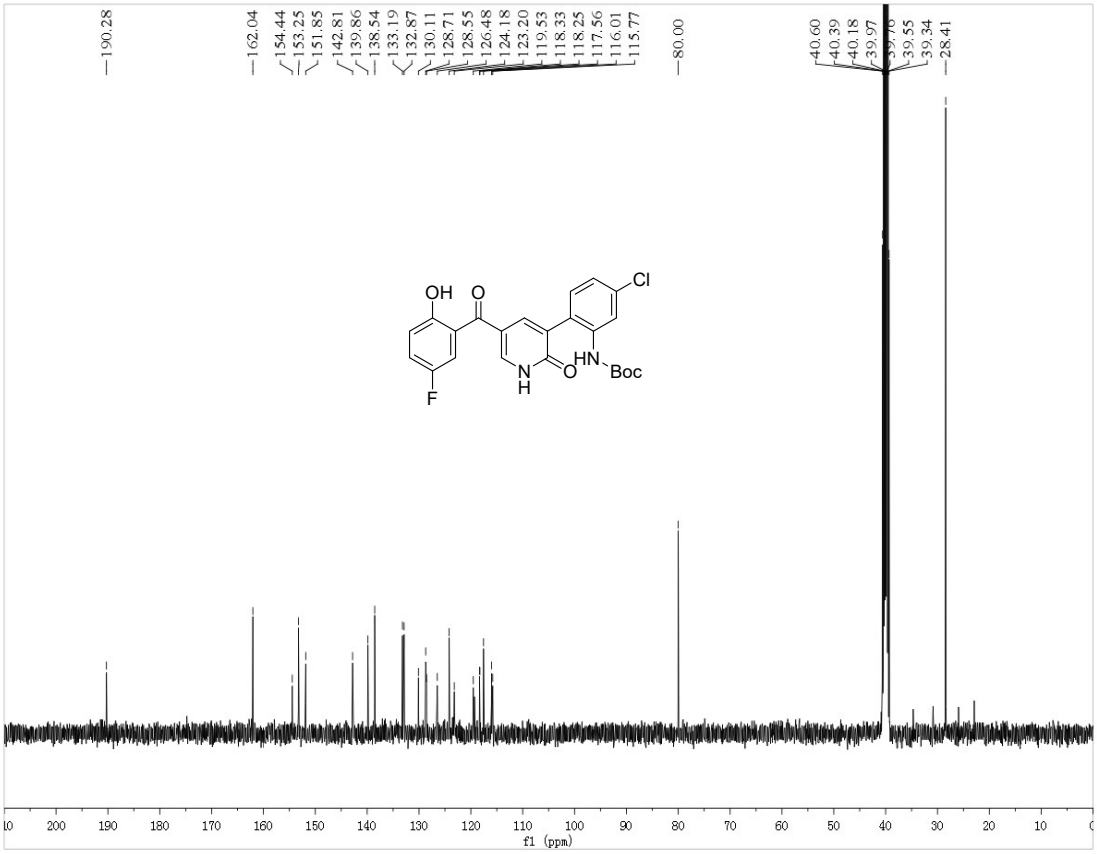
^{1}H and ^{13}C NMR of 3ap



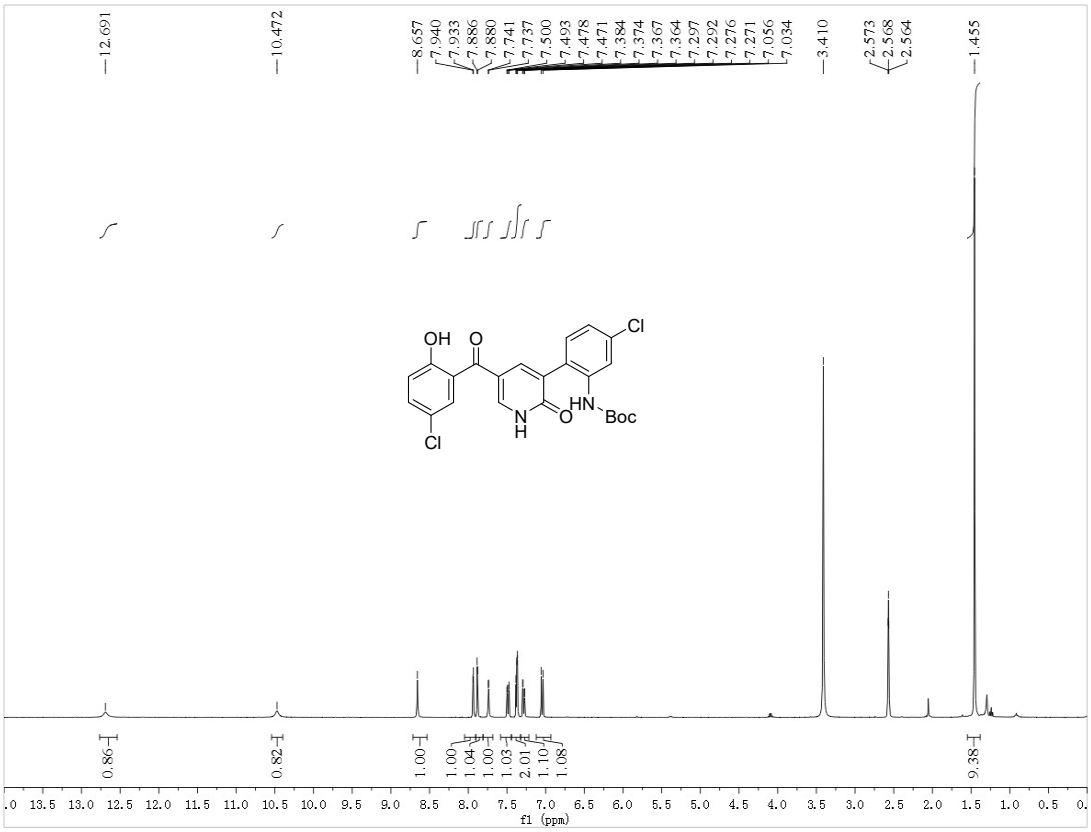


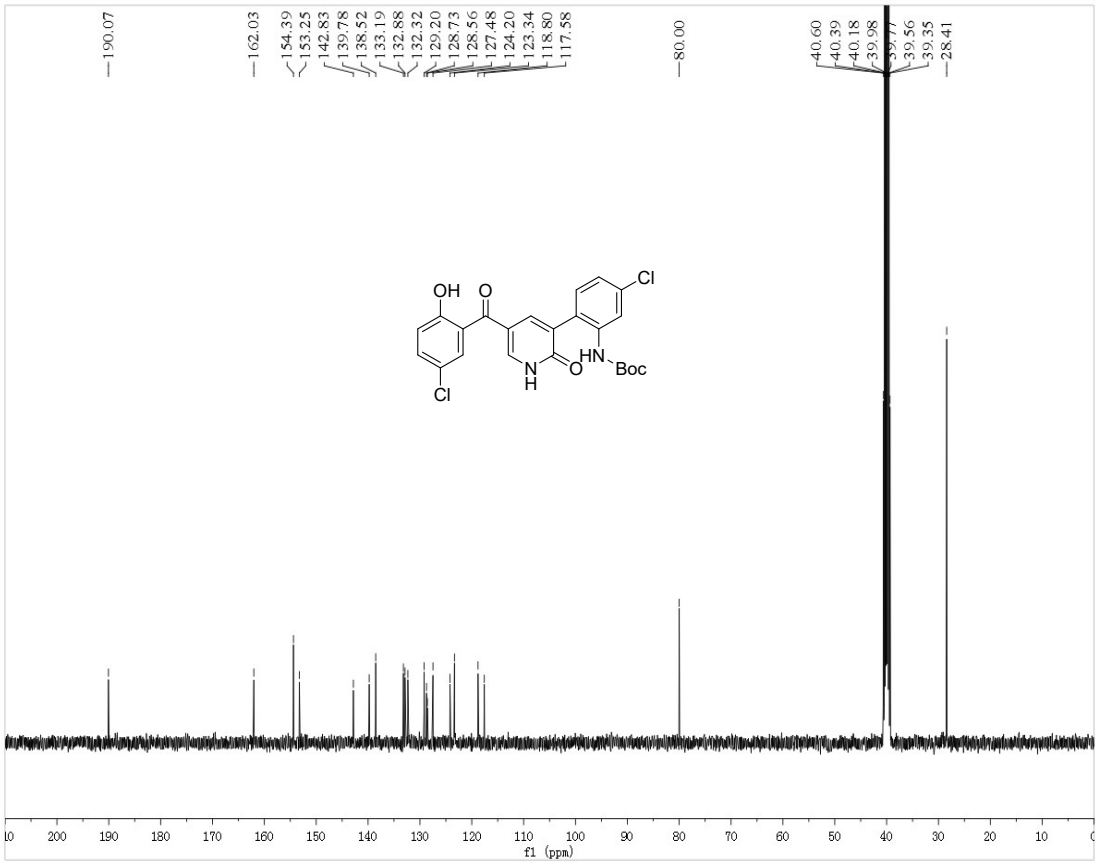
^{1}H and ^{13}C NMR of 3aq



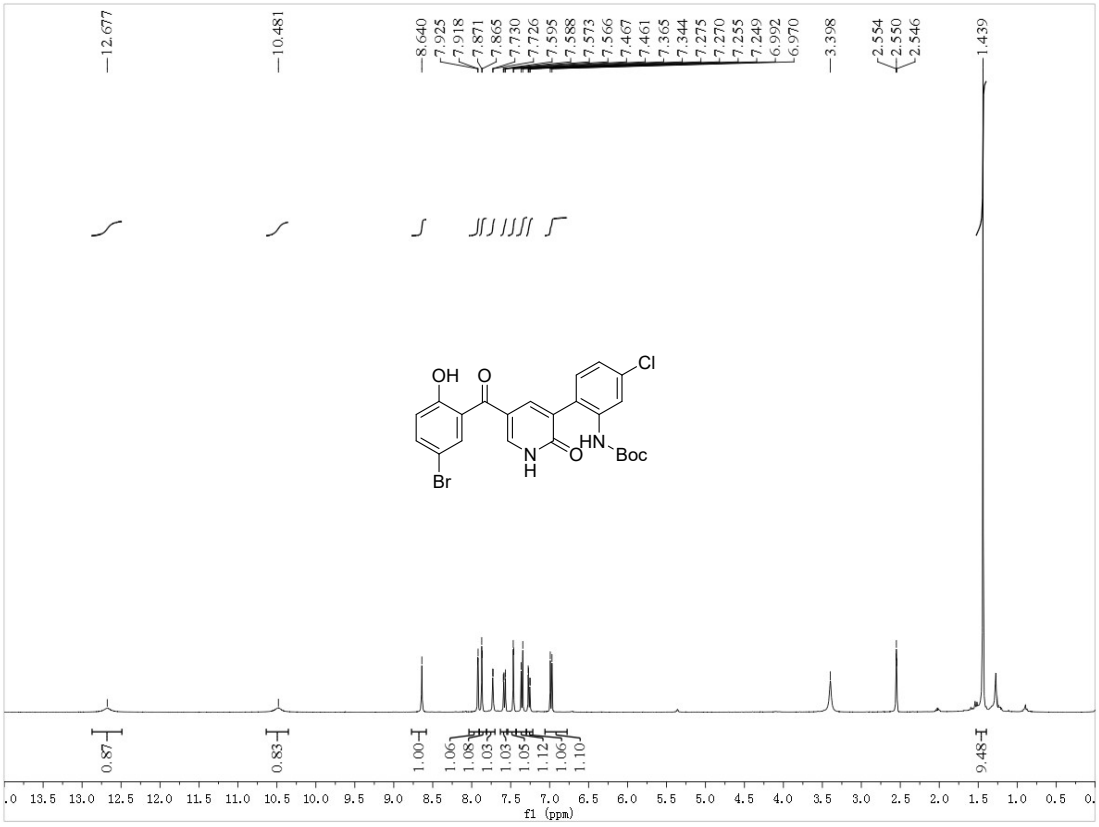


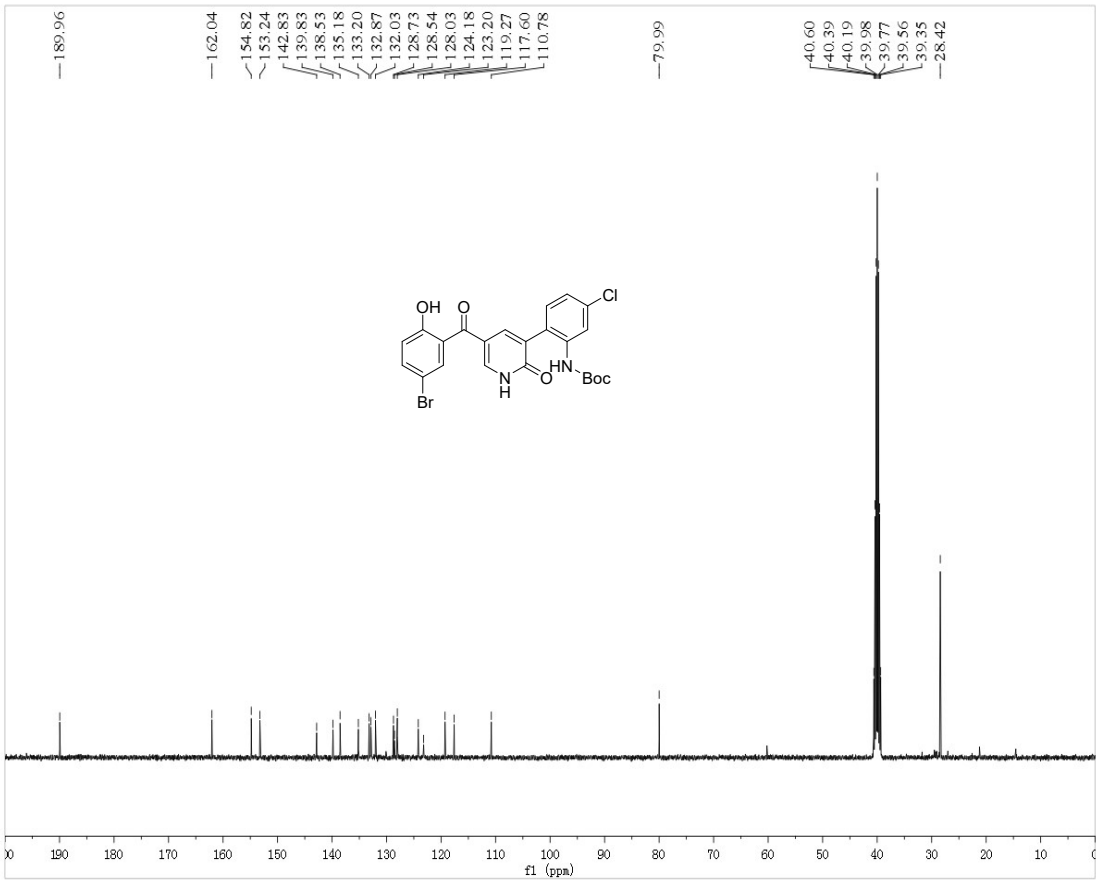
^{1}H and ^{13}C NMR of 3ar



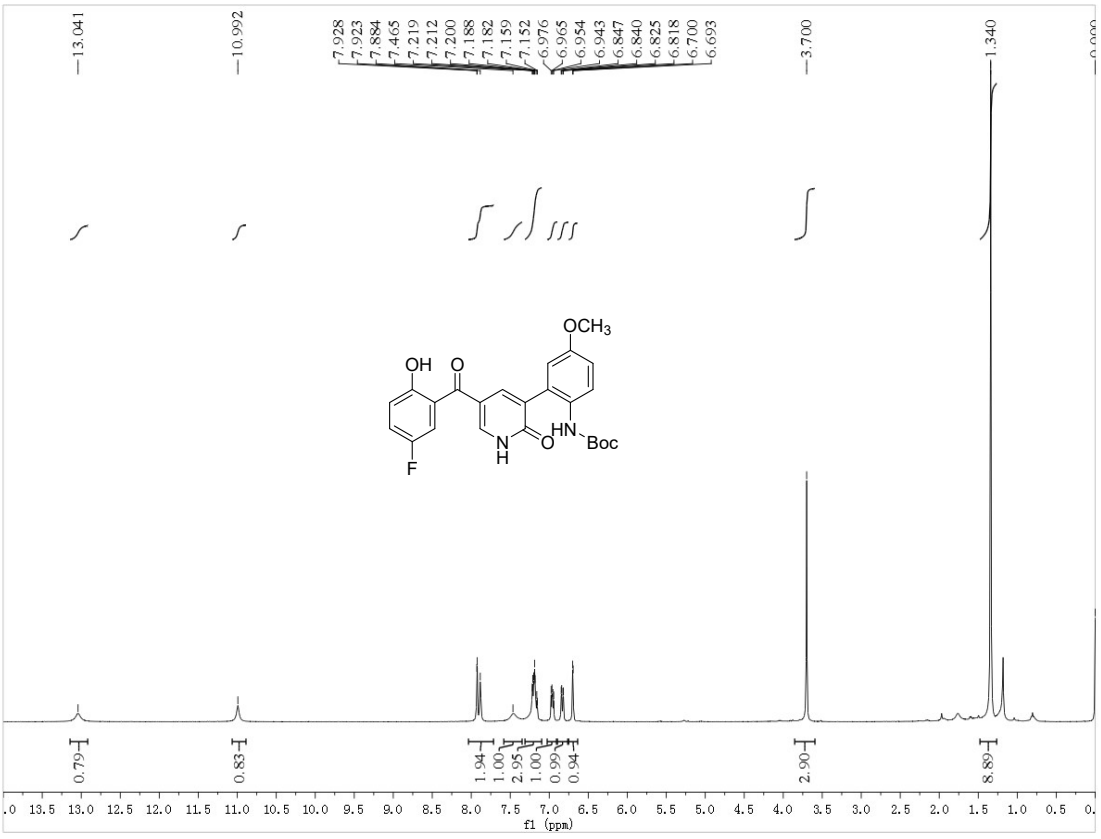


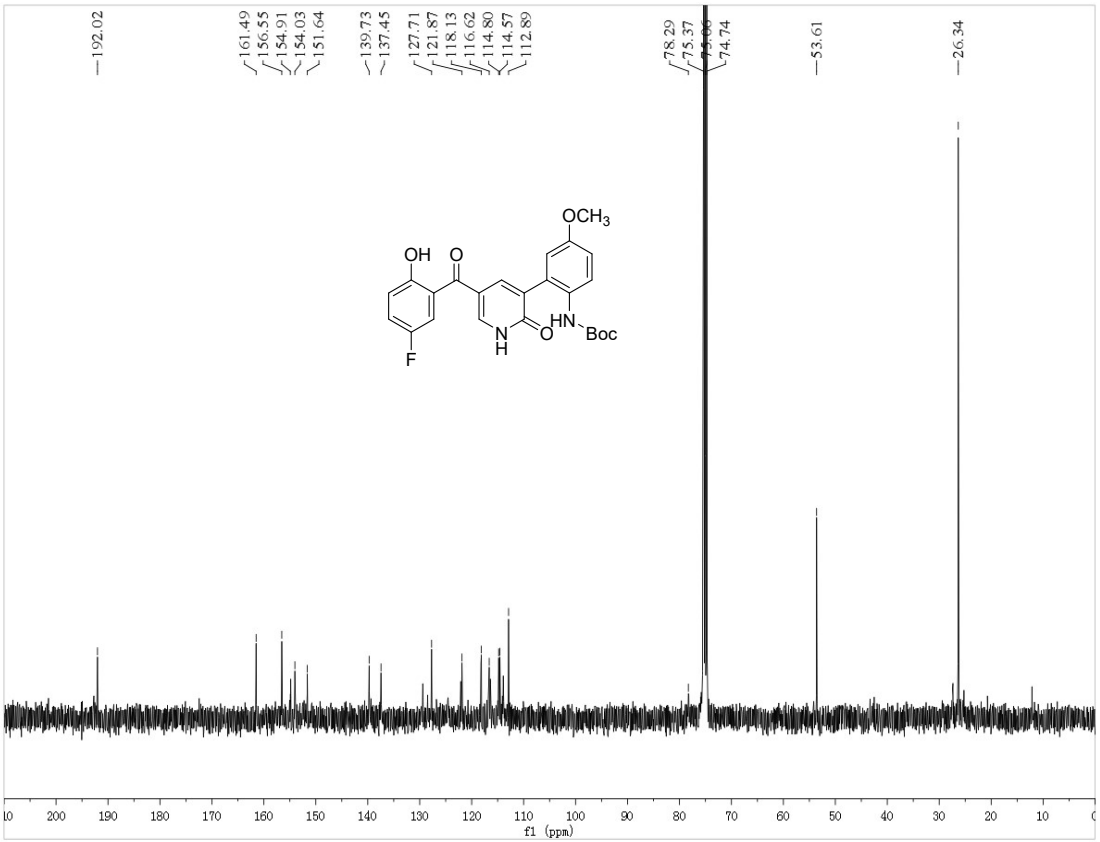
^{1}H and ^{13}C NMR of 3as



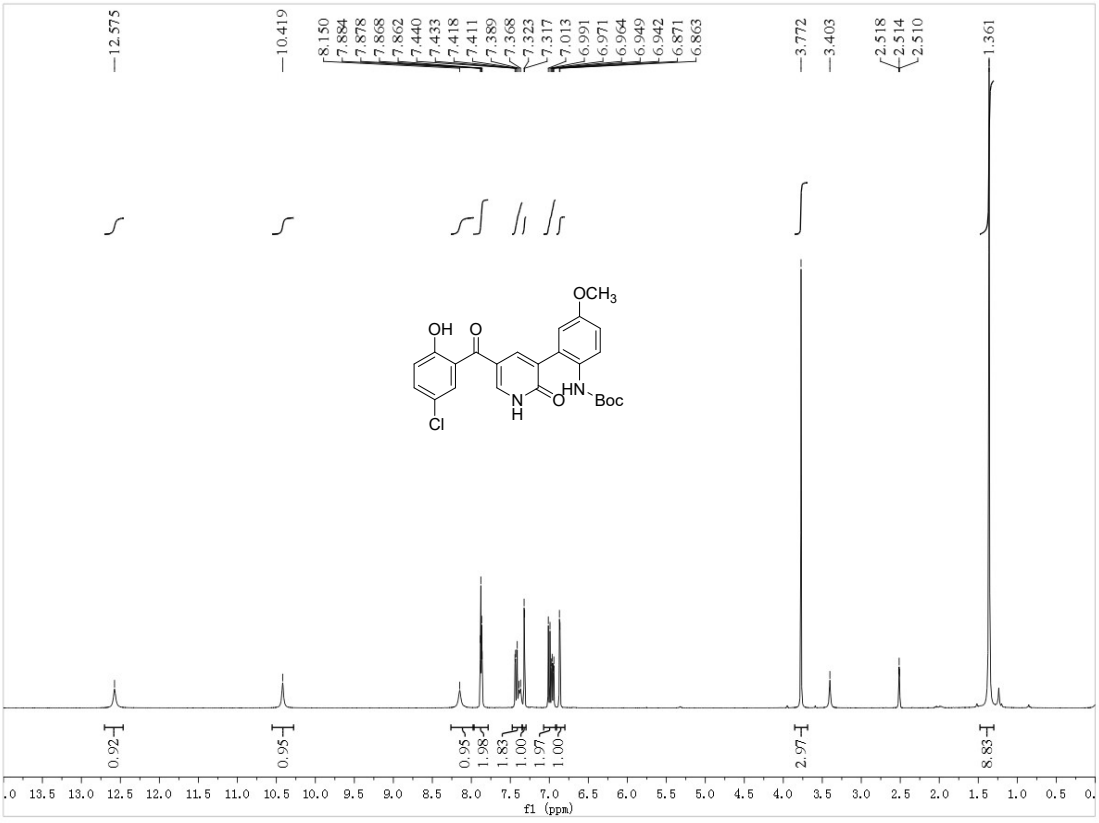


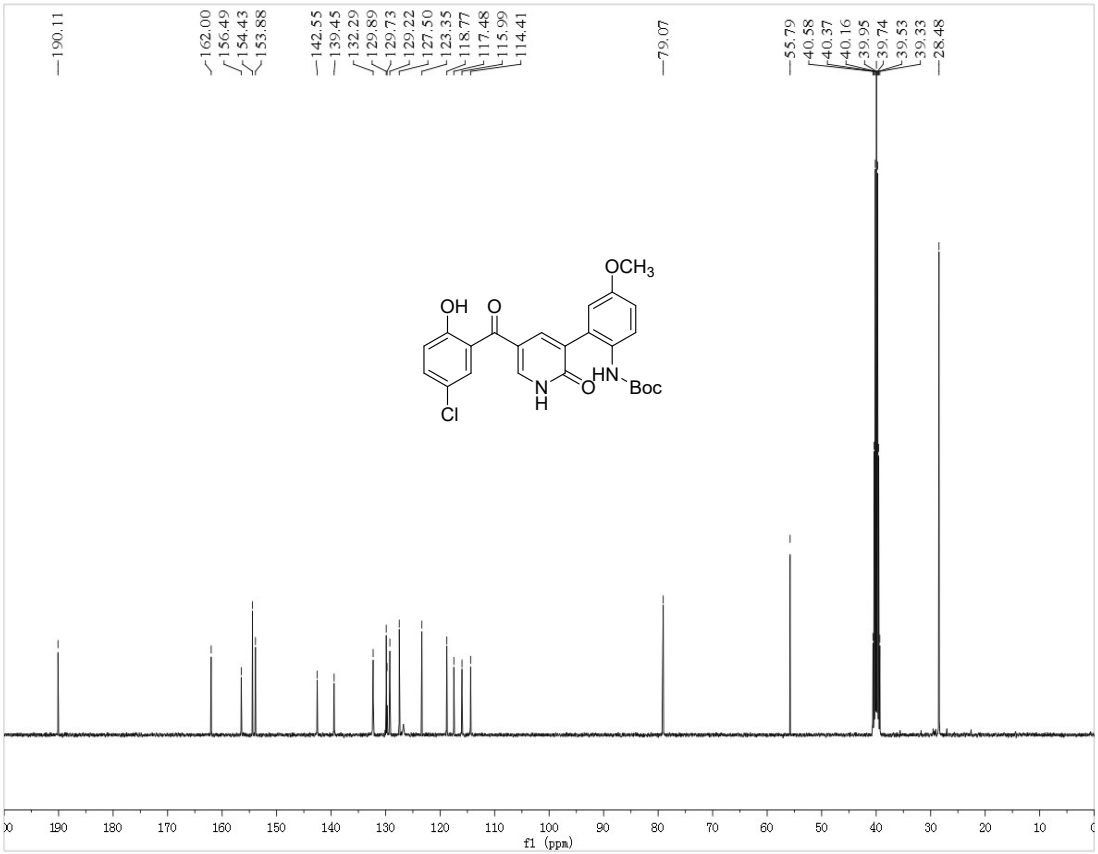
^{1}H and ^{13}C NMR of 3at



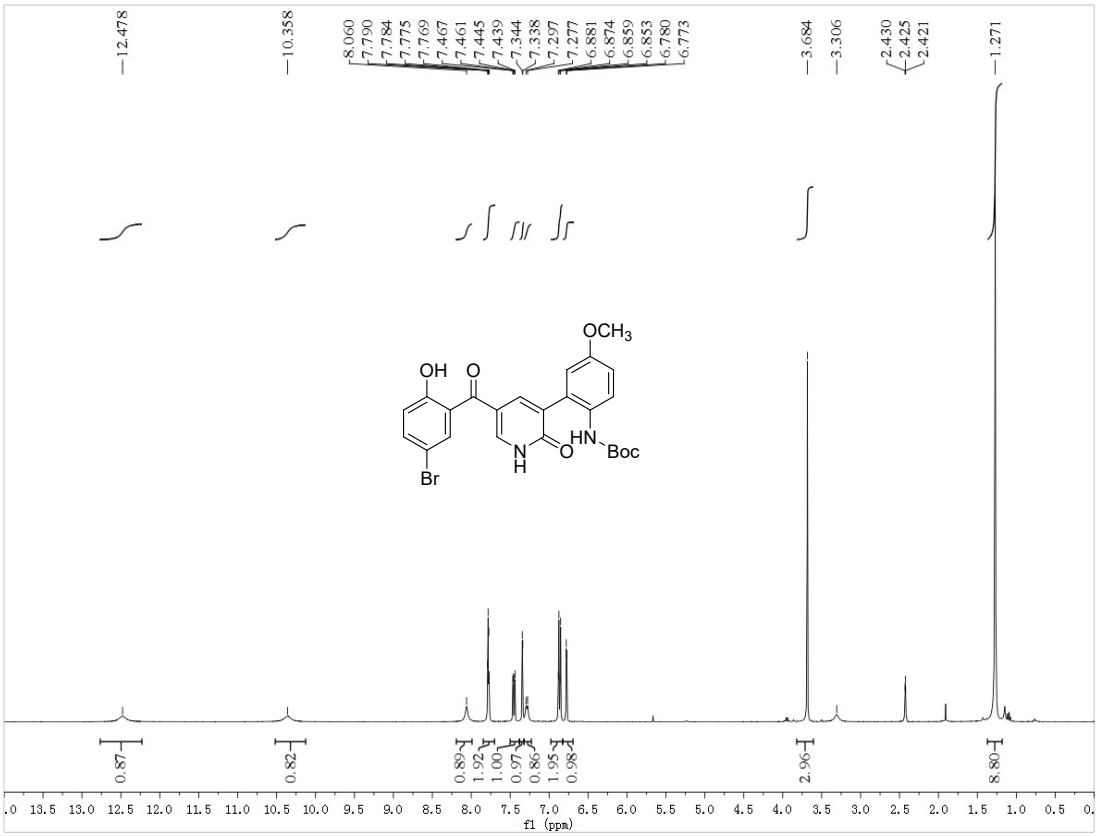


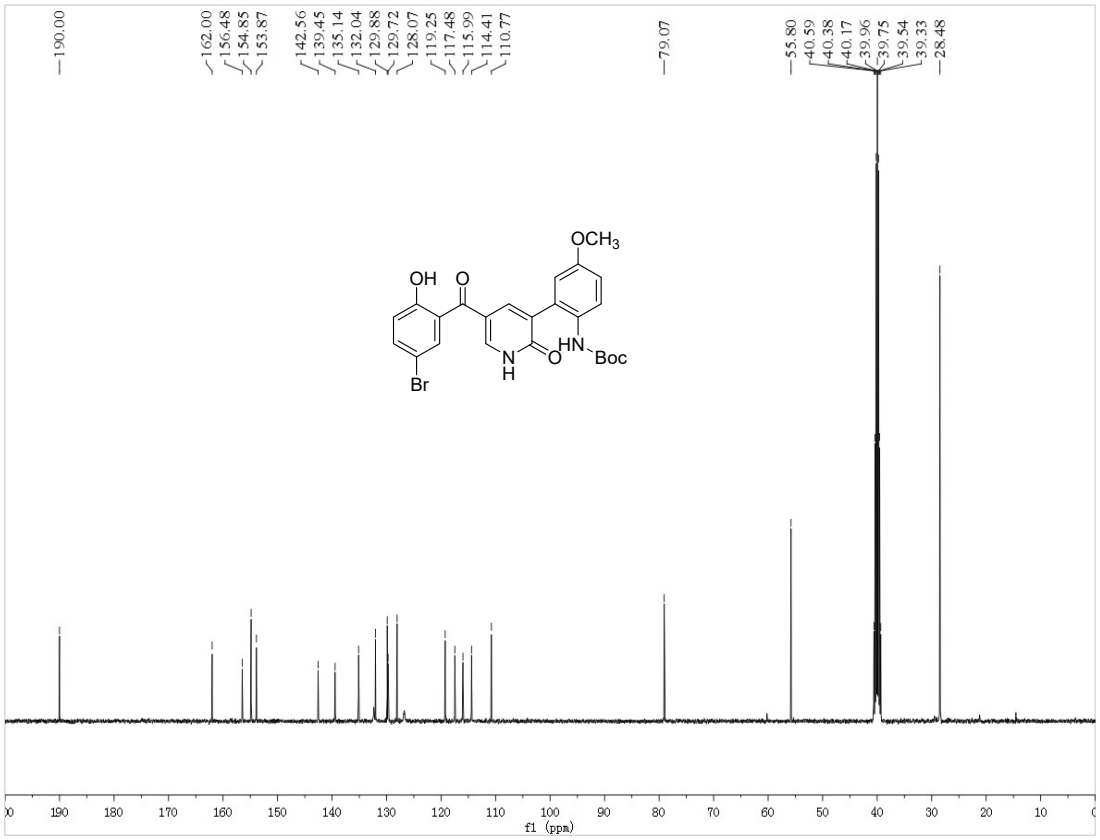
^{1}H and ^{13}C NMR of 3au



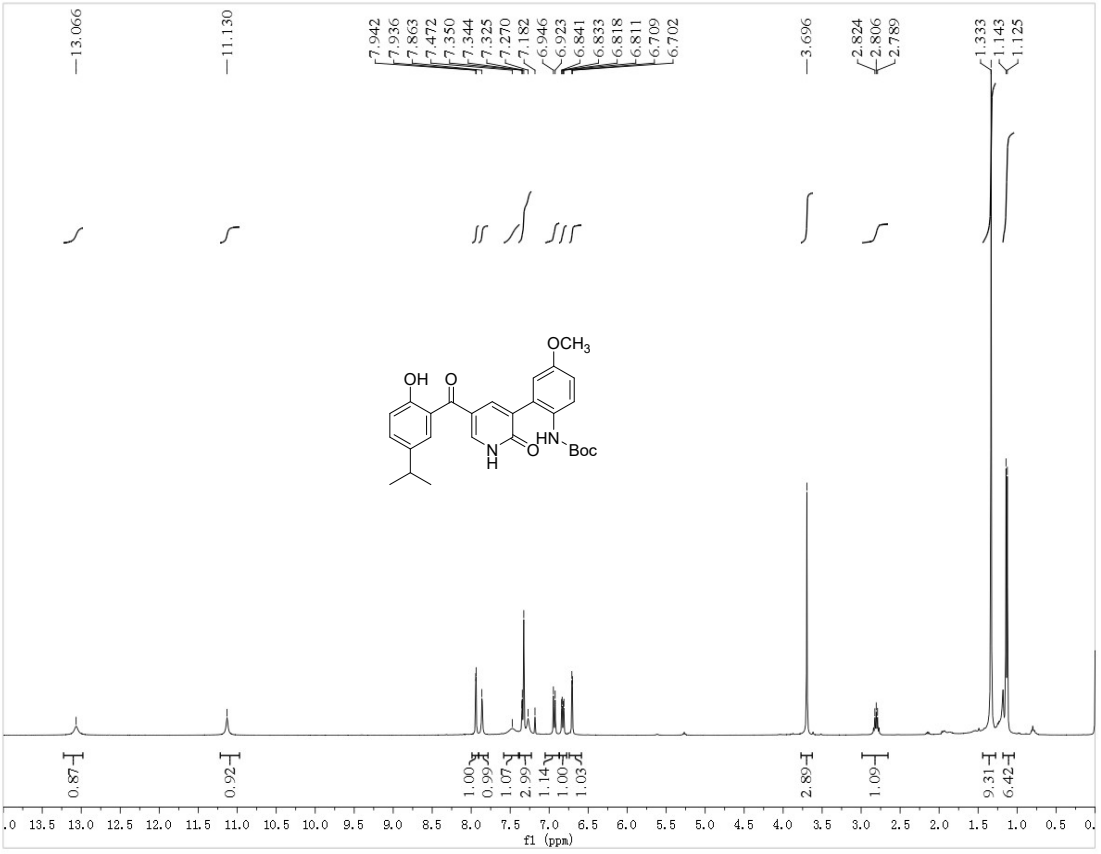


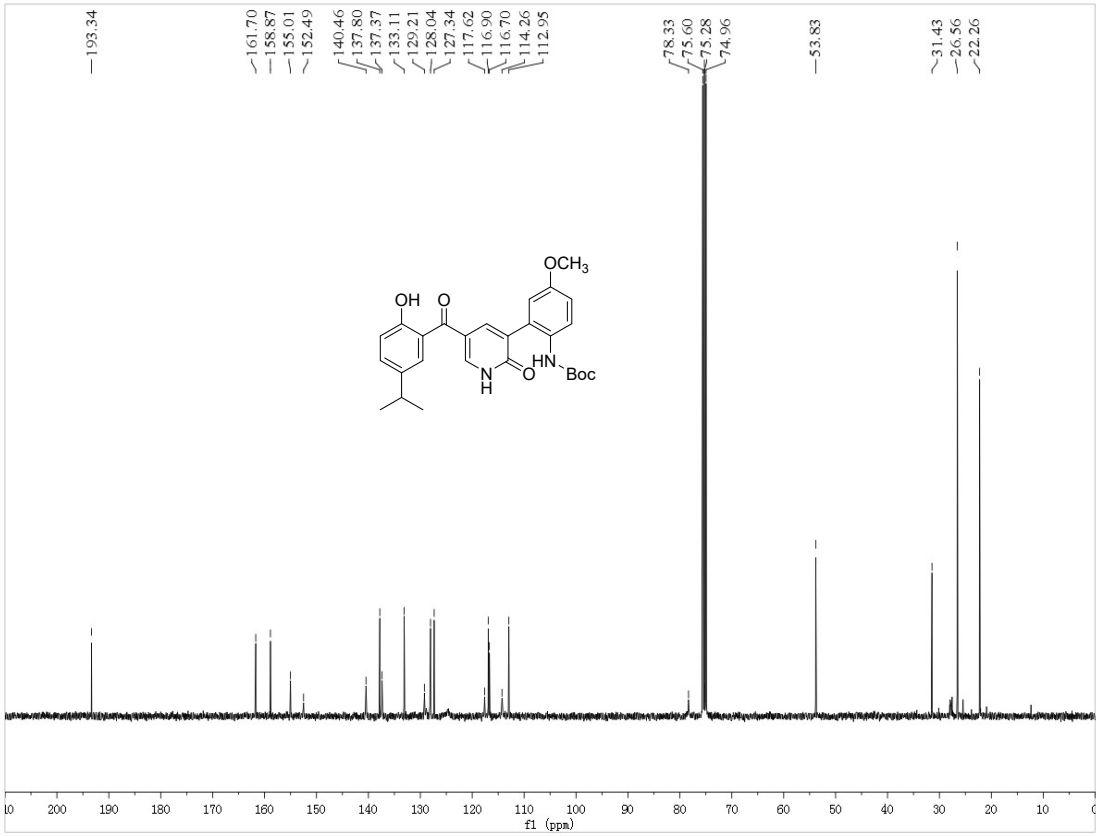
^{1}H and ^{13}C NMR of 3av



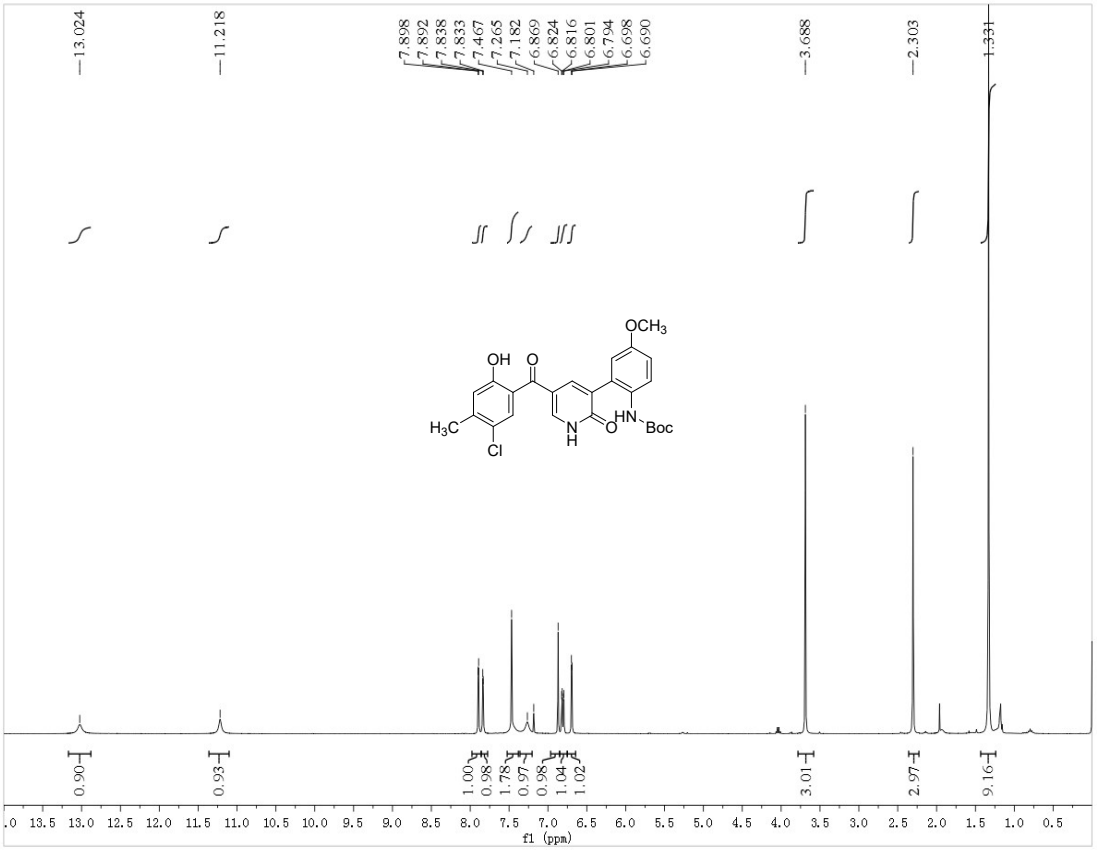


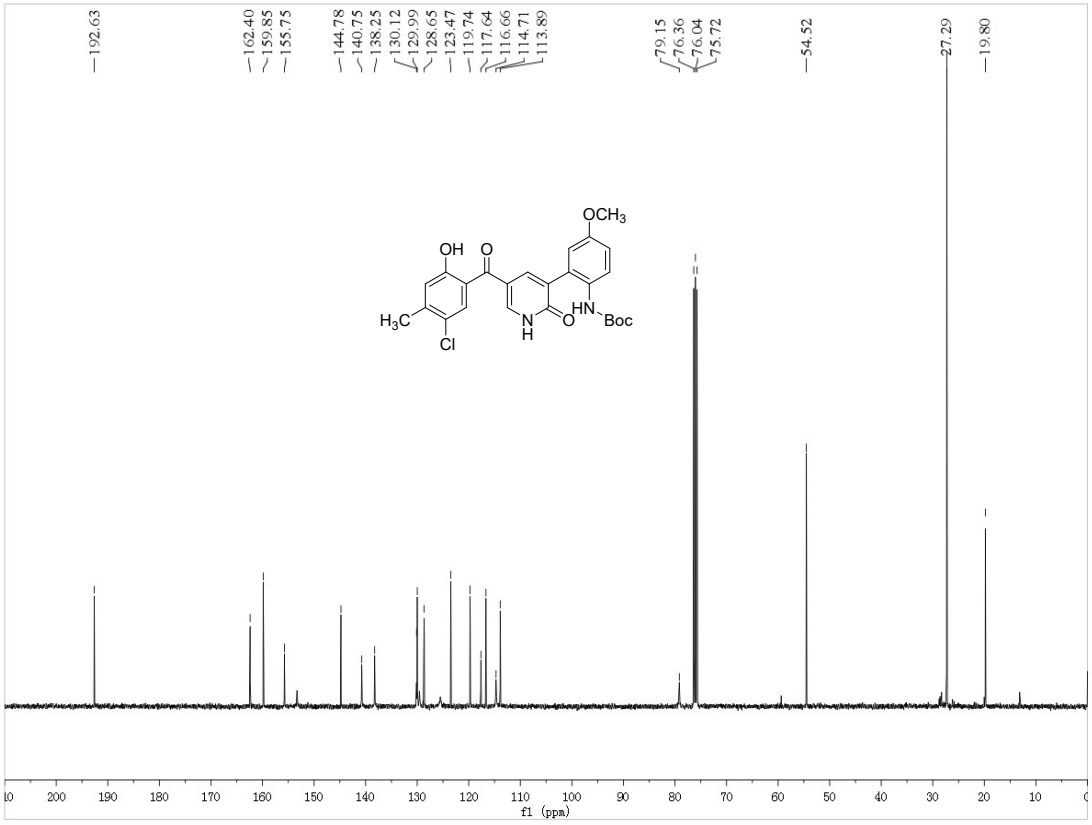
^{1}H and ^{13}C NMR of 3aw



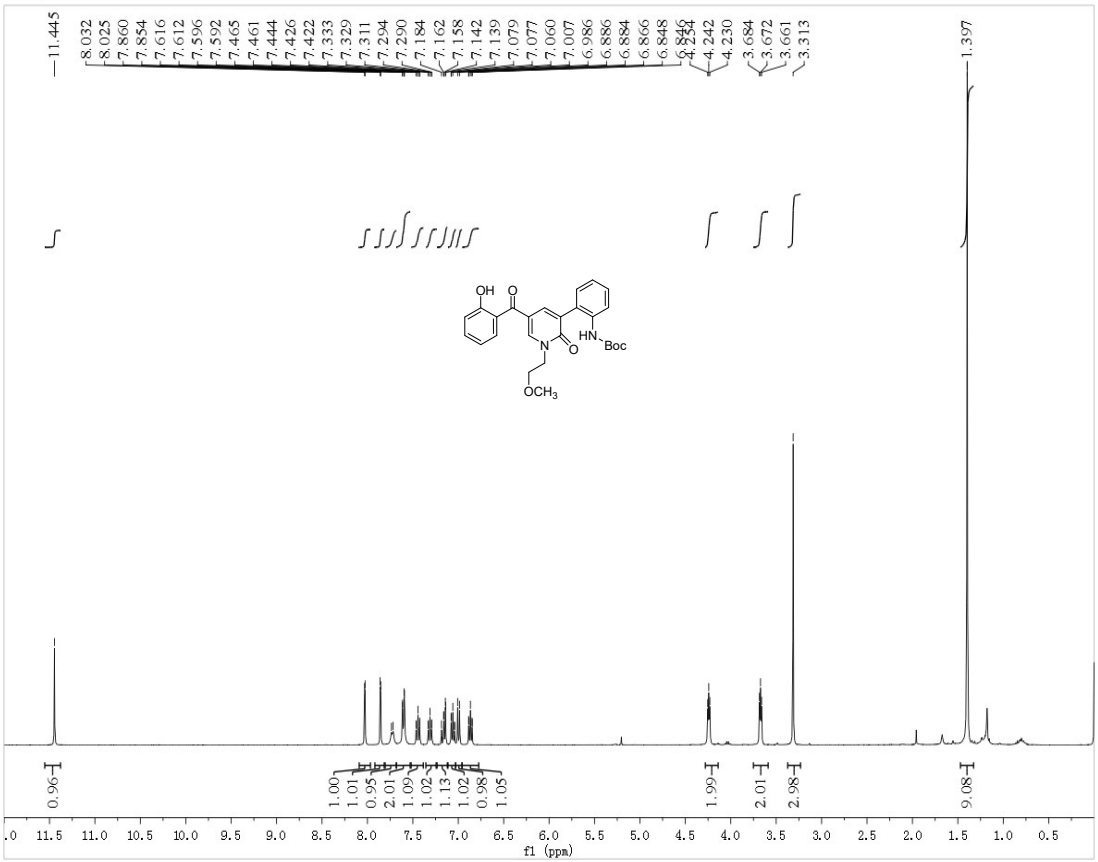


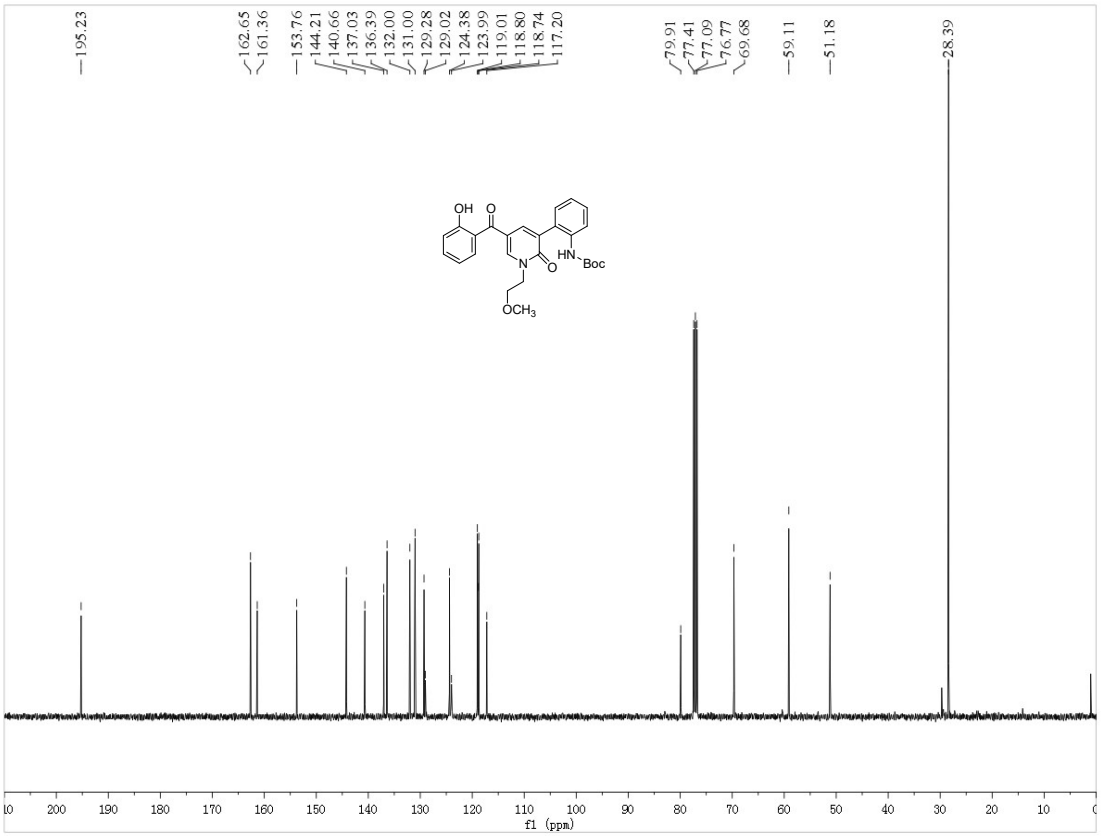
^{1}H and ^{13}C NMR of 3ax



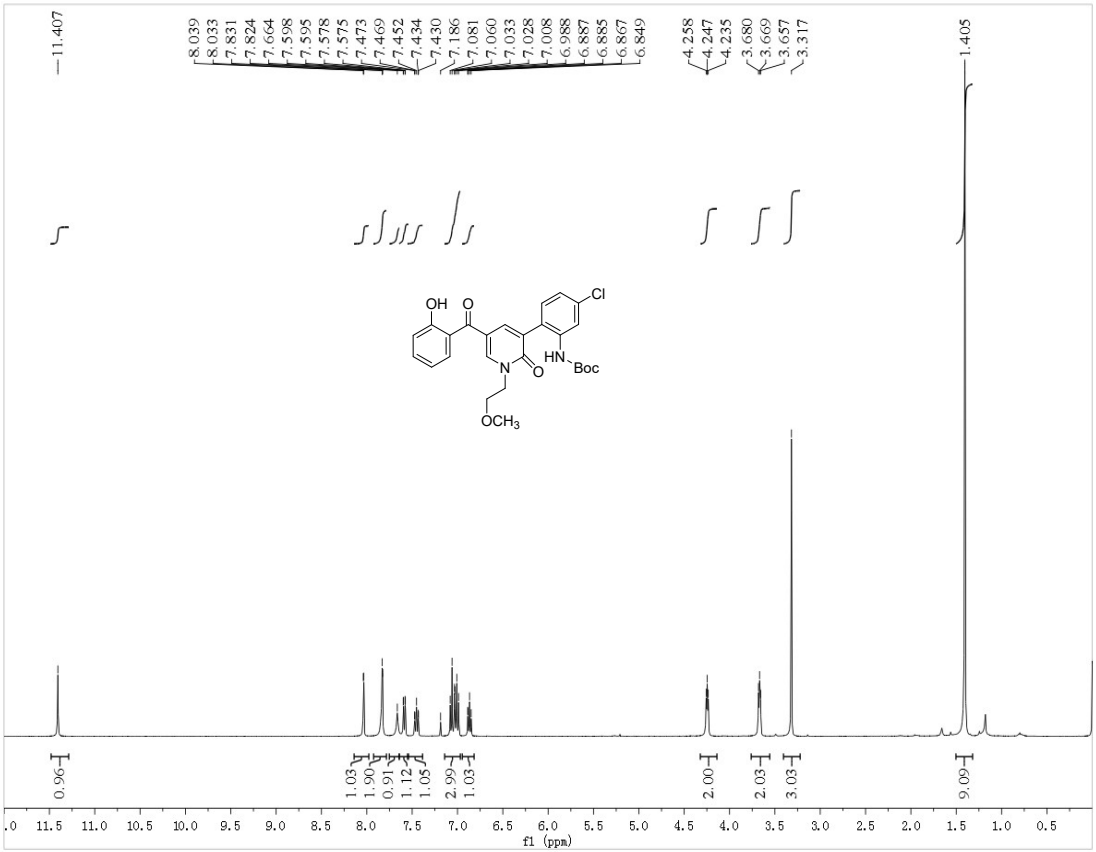


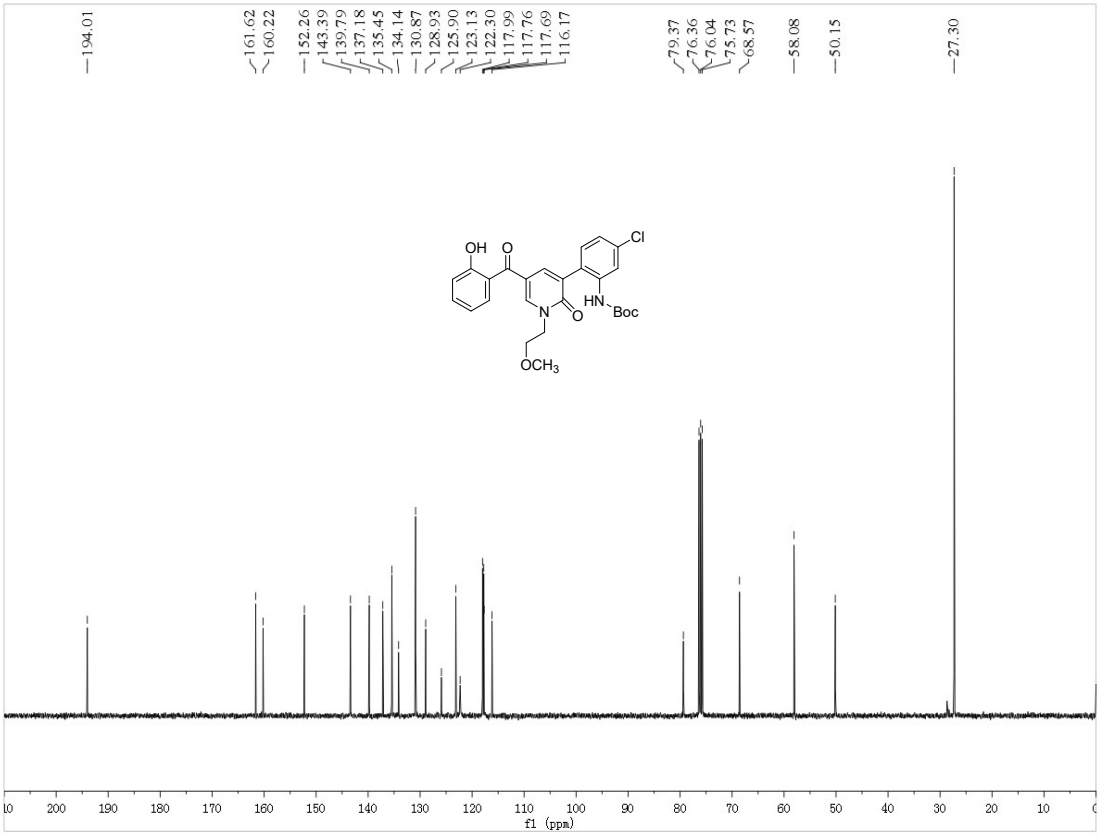
^{1}H and ^{13}C NMR of 3ba



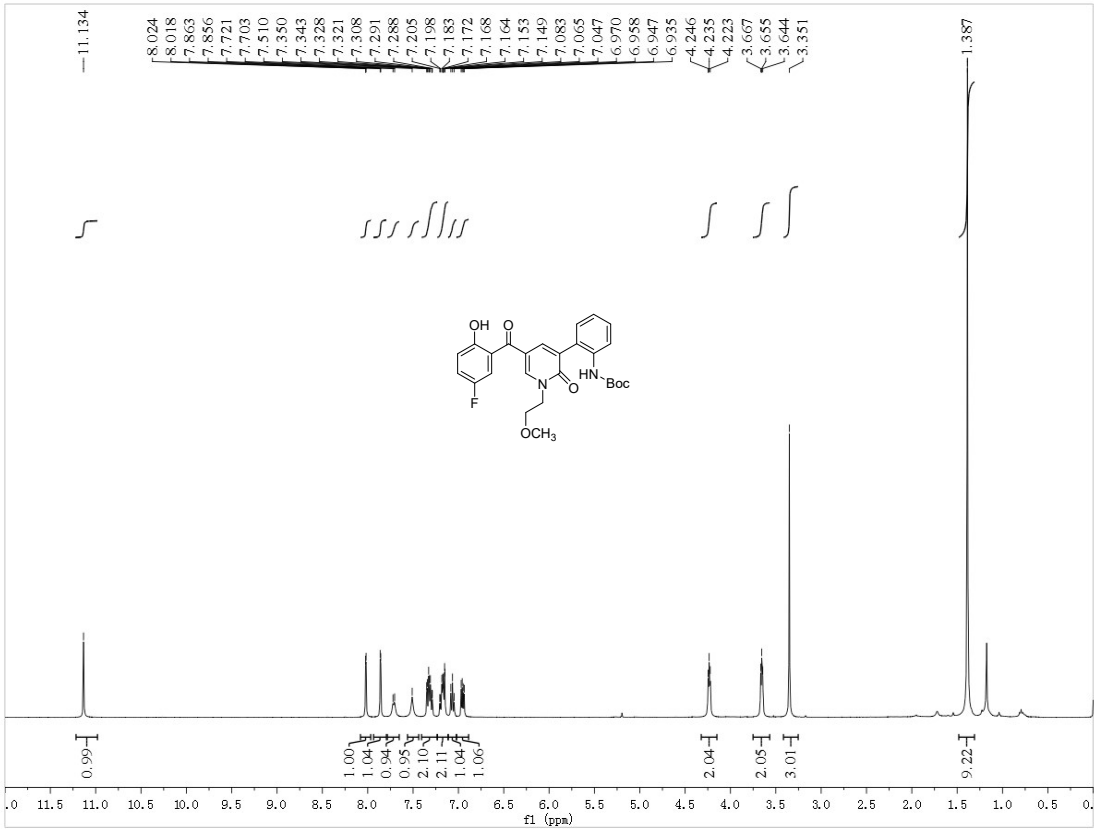


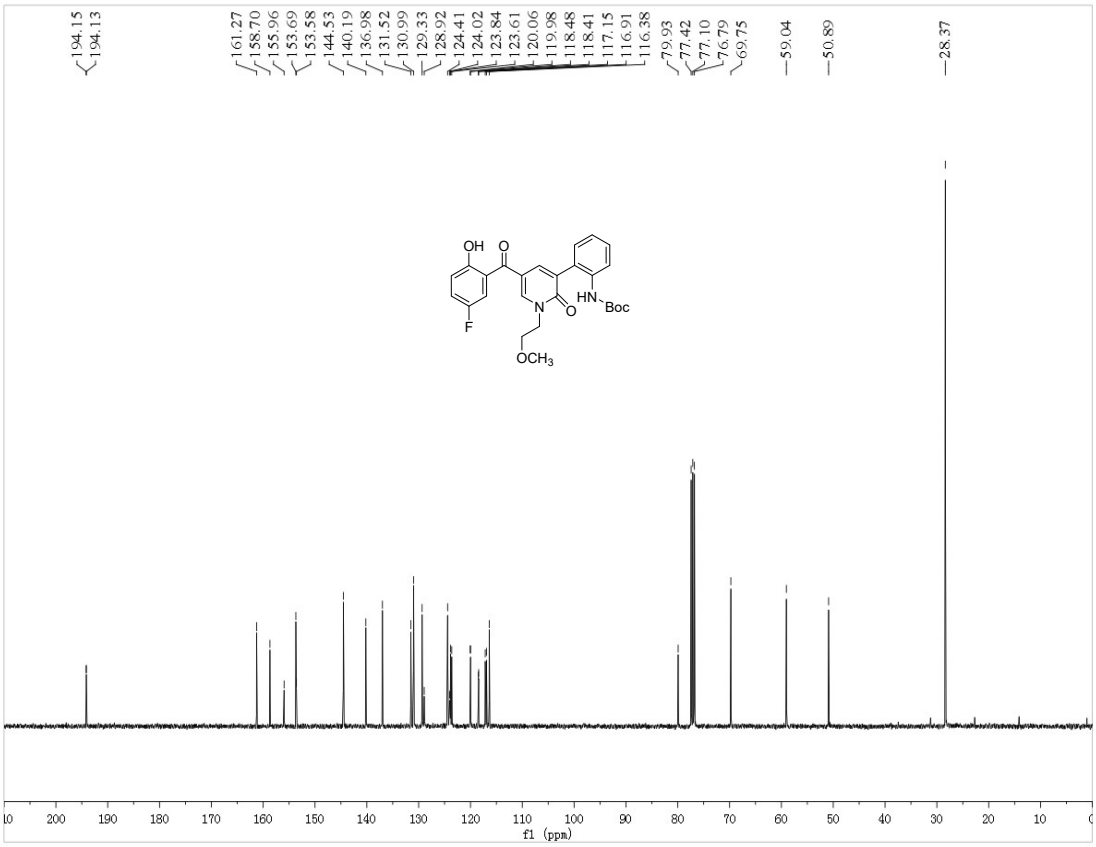
^{1}H and ^{13}C NMR of 3bb



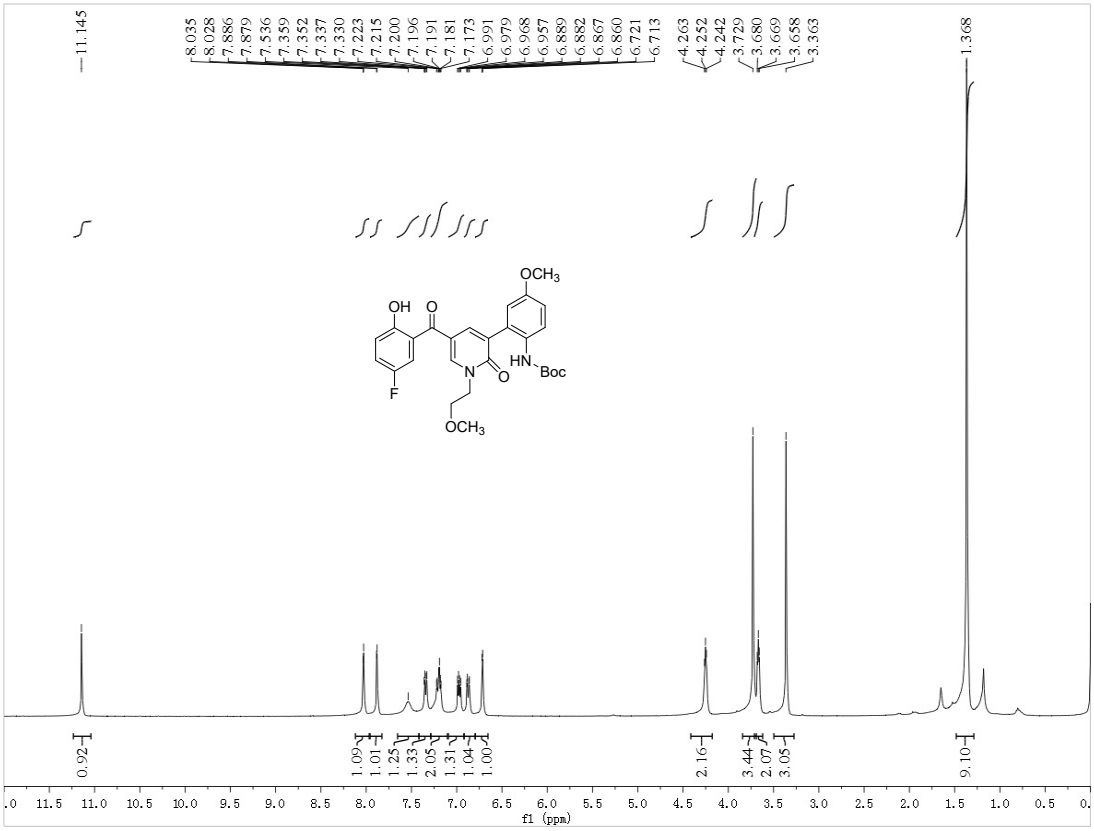


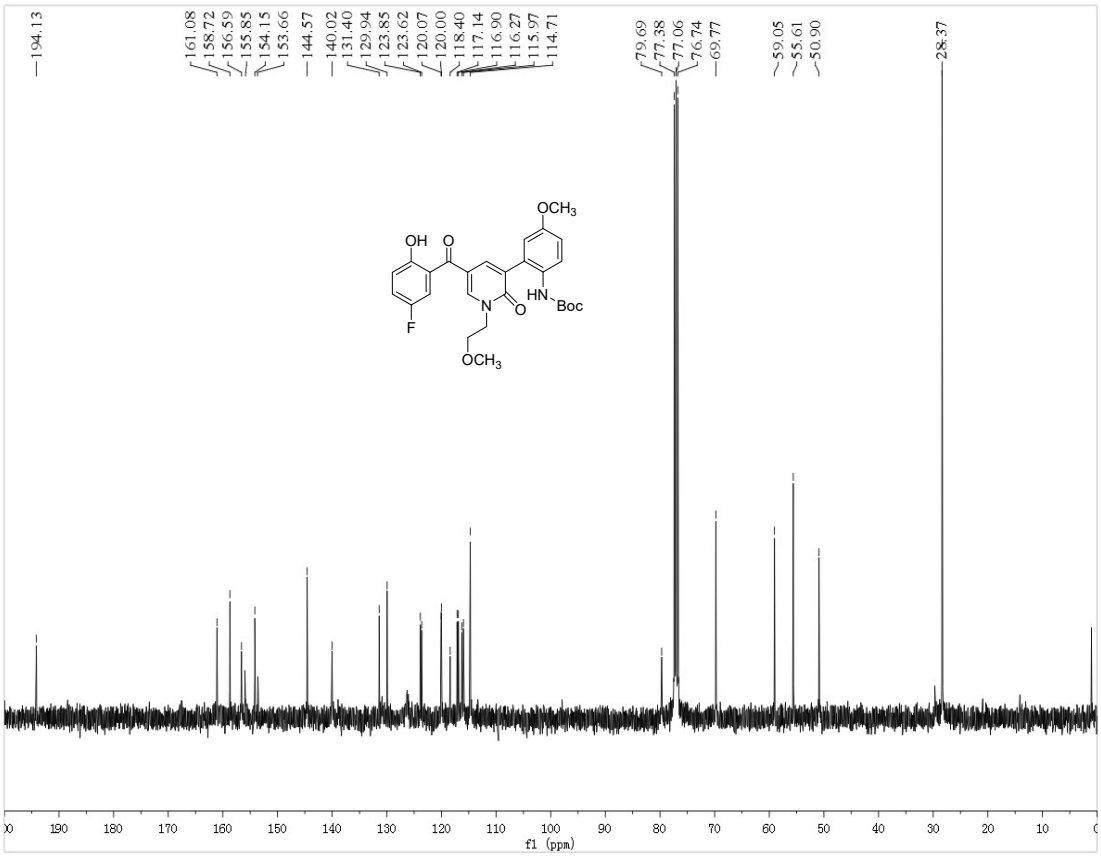
^{1}H and ^{13}C NMR of 3bc



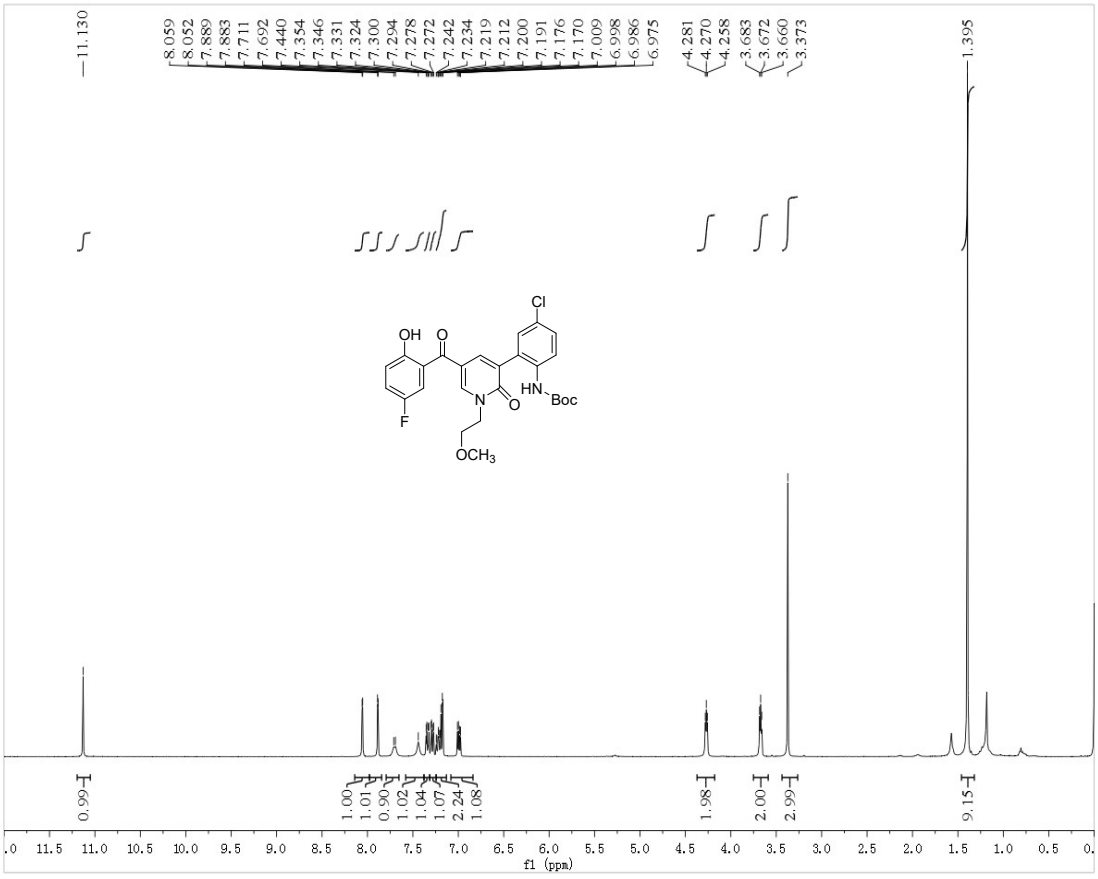


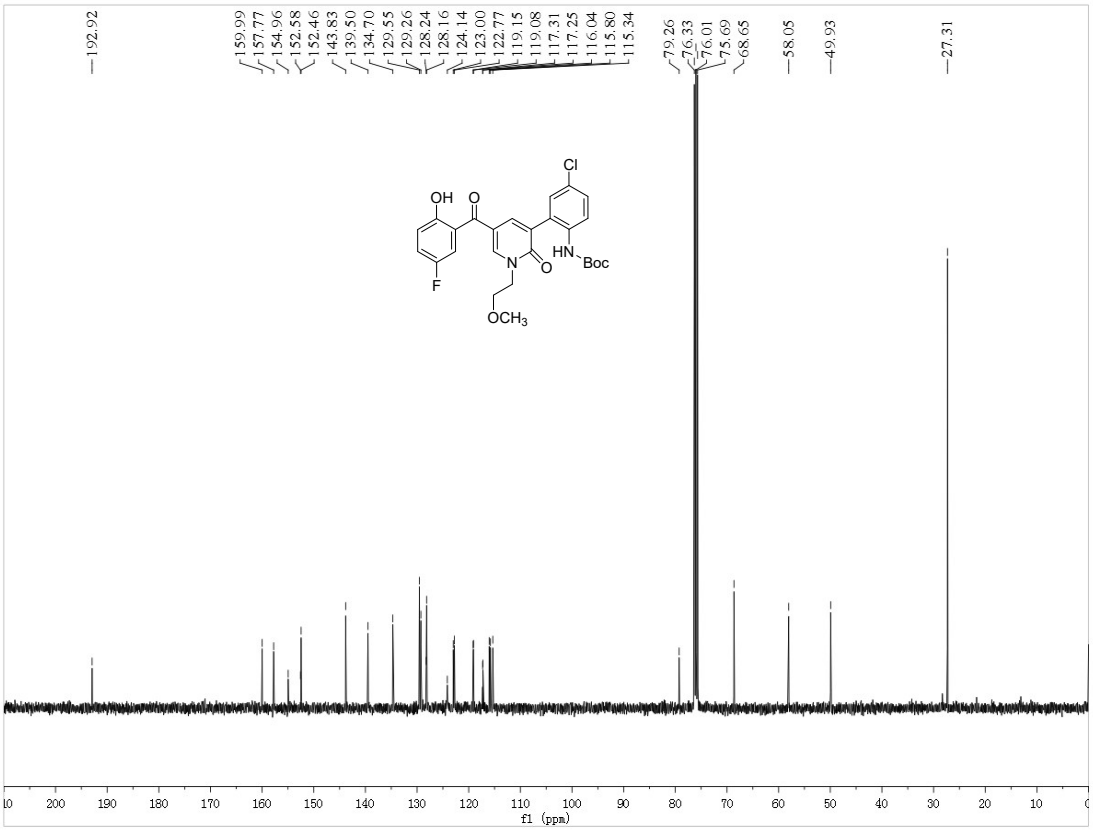
^{1}H and ^{13}C NMR of 3bd



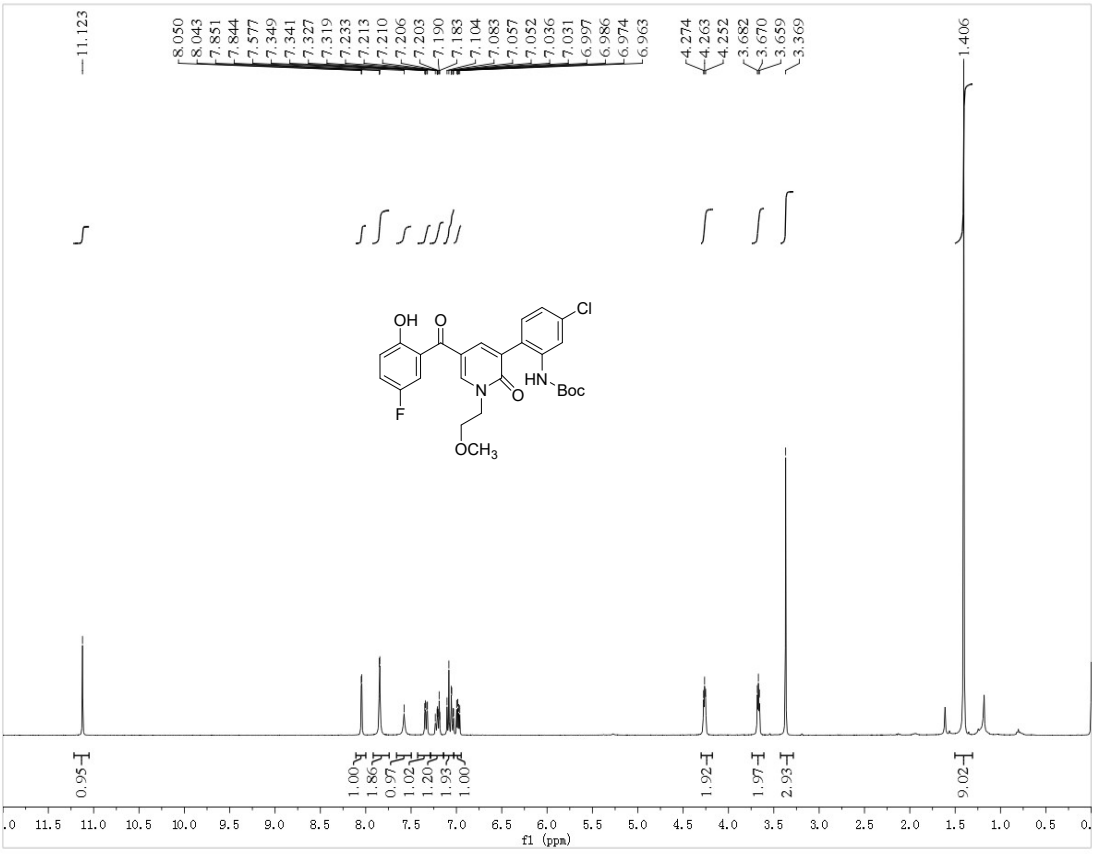


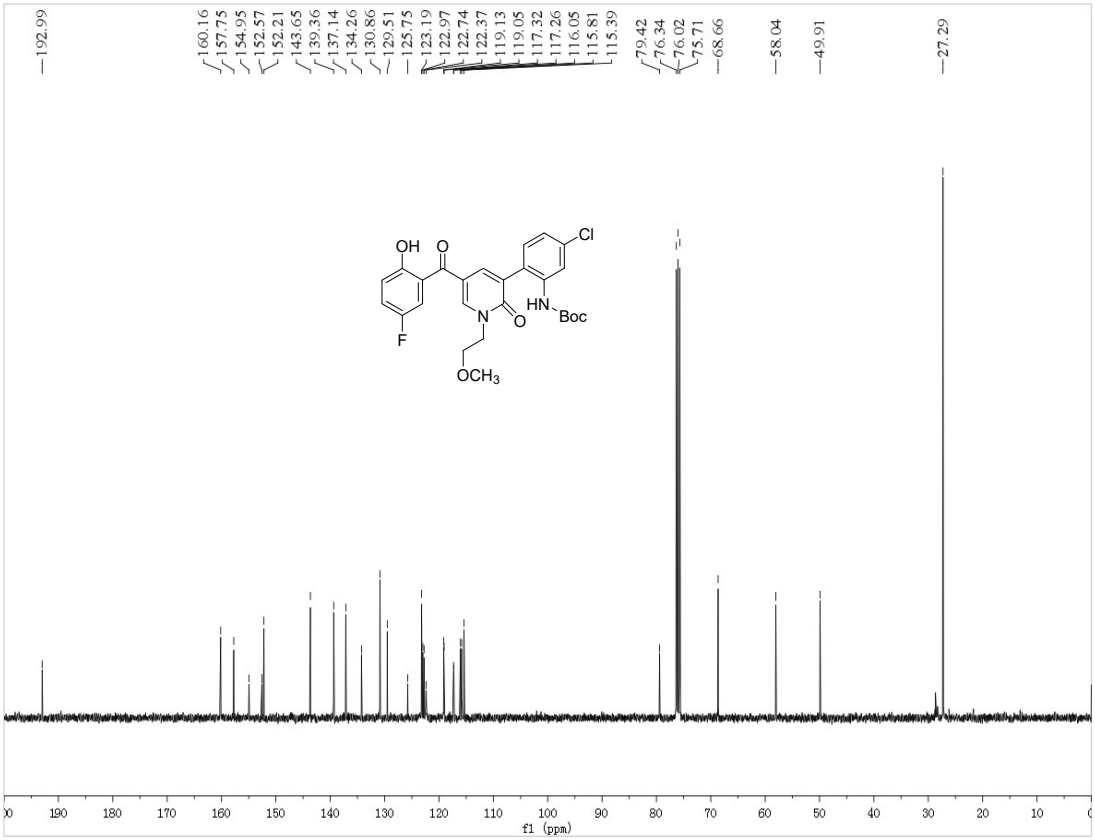
^{1}H and ^{13}C NMR of 3be



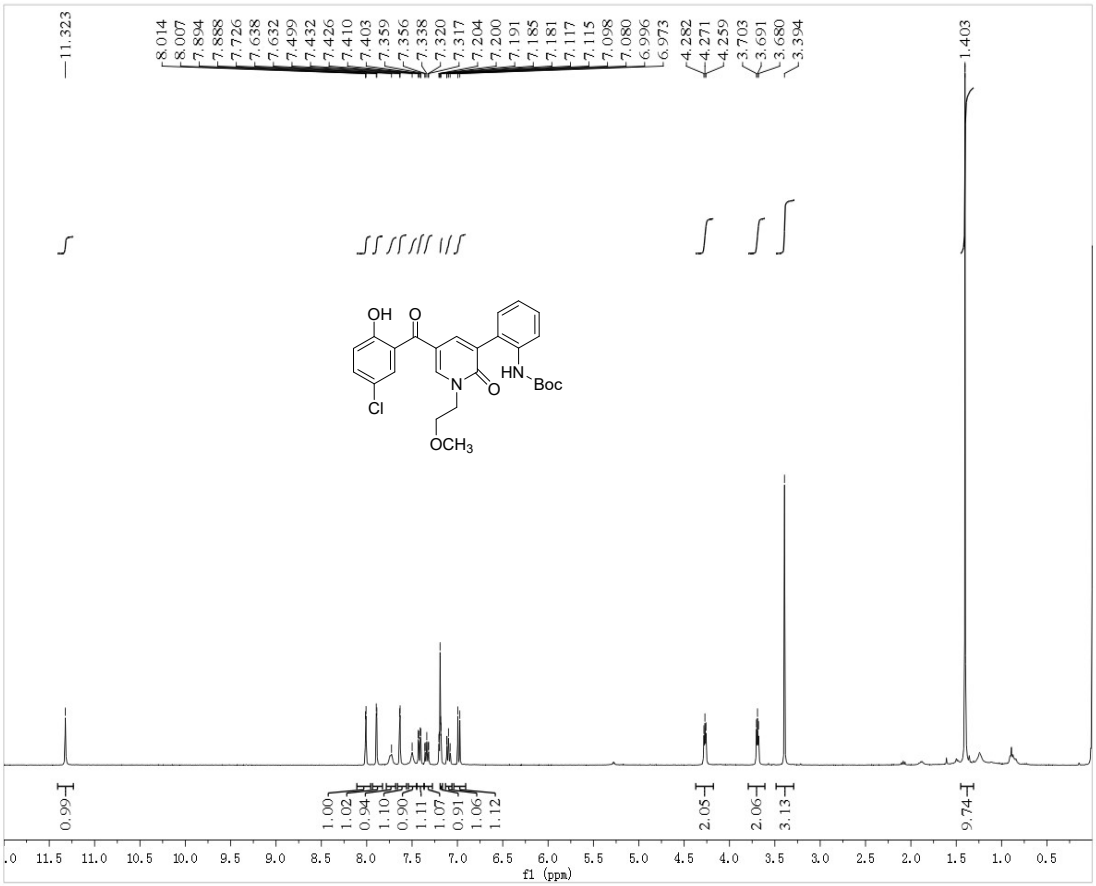


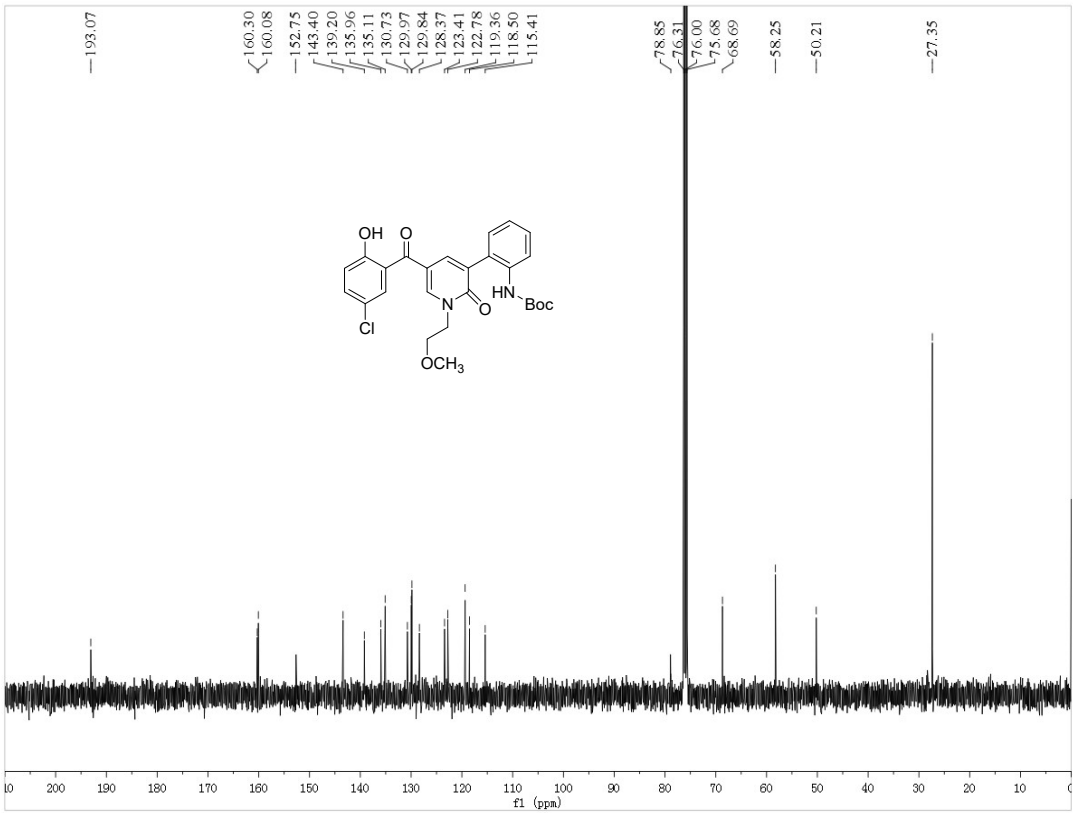
^{1}H and ^{13}C NMR of 3bf



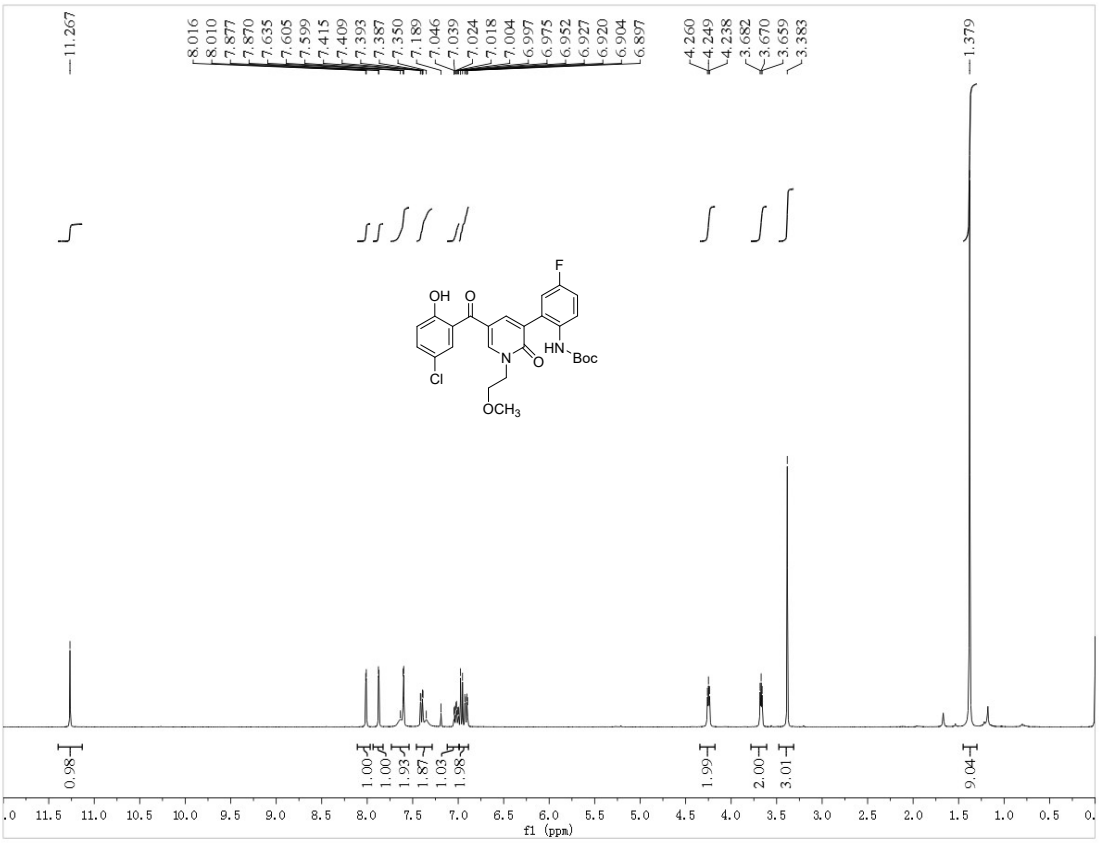


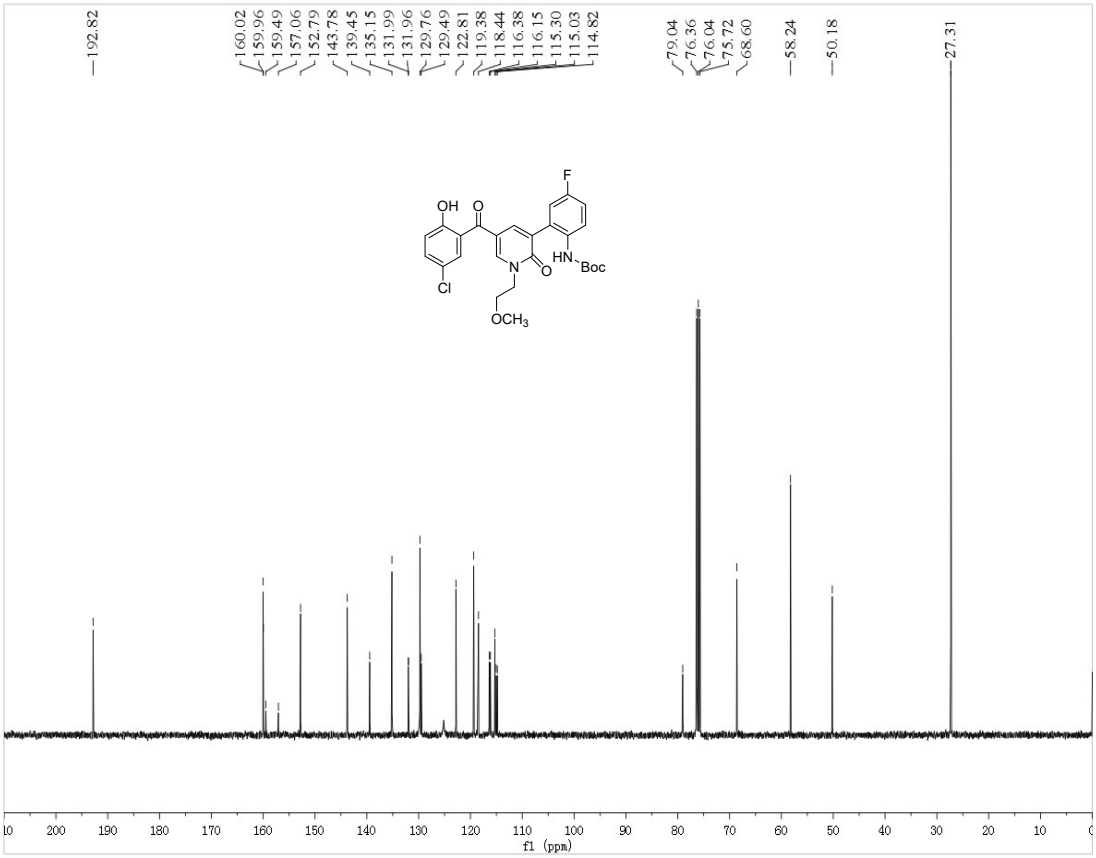
^{1}H and ^{13}C NMR of 3bg



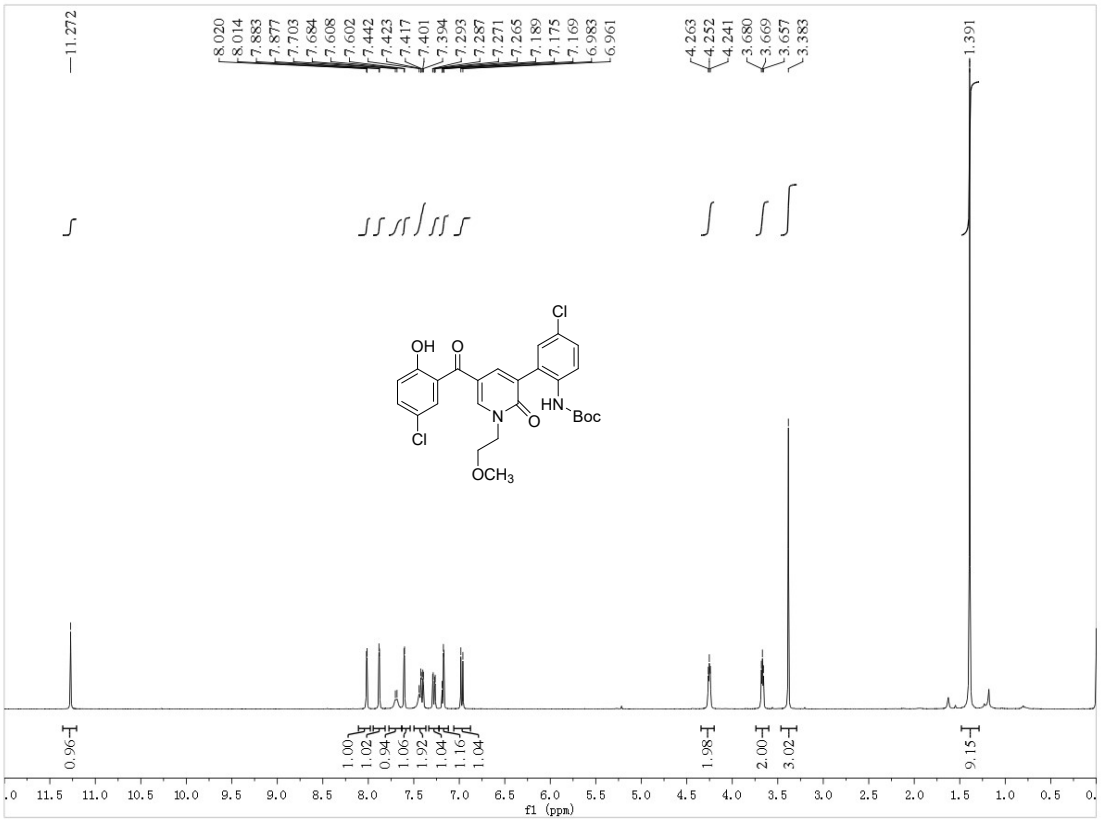


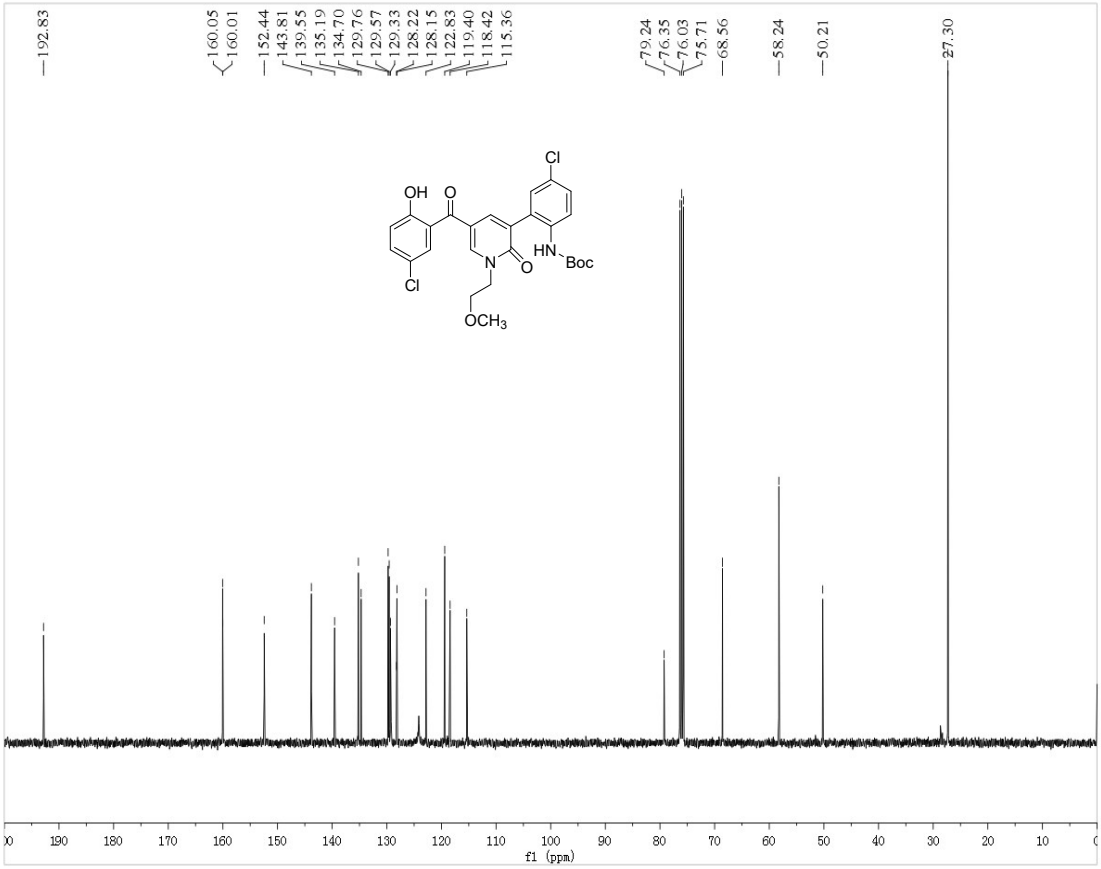
^{1}H and ^{13}C NMR of 3bh



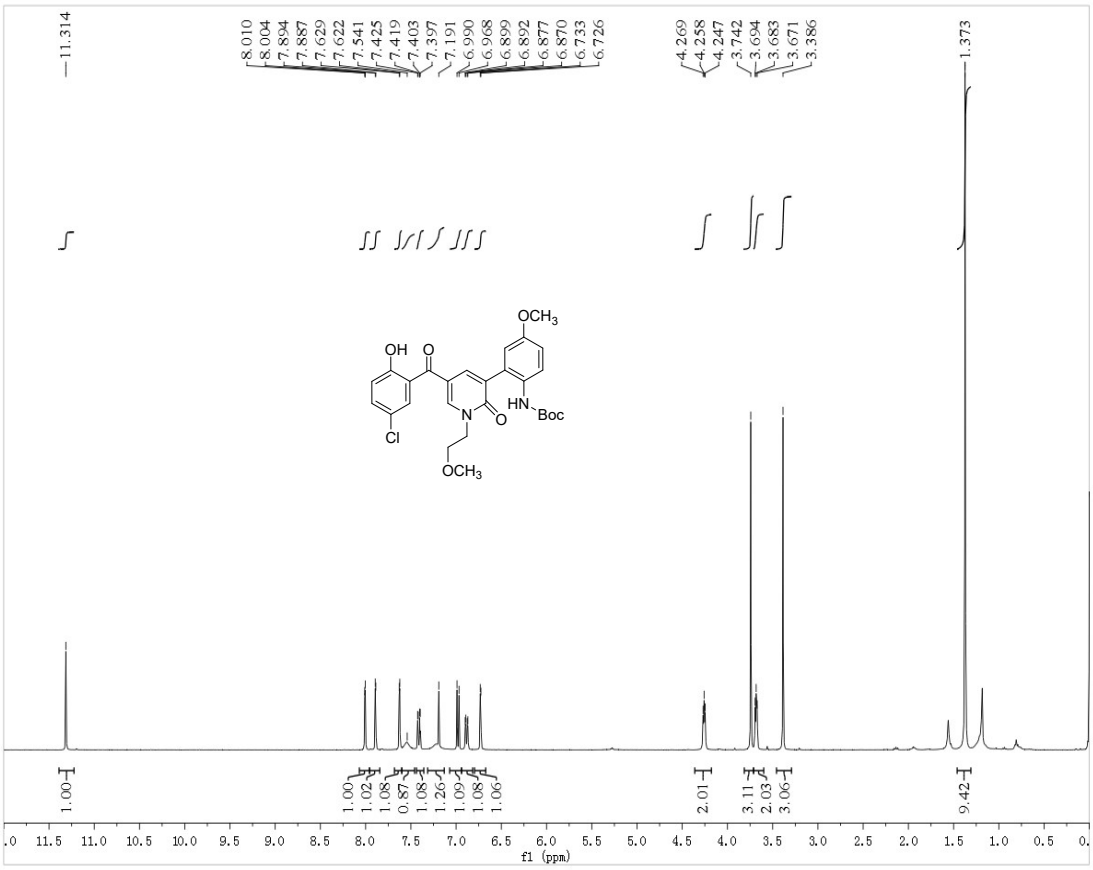


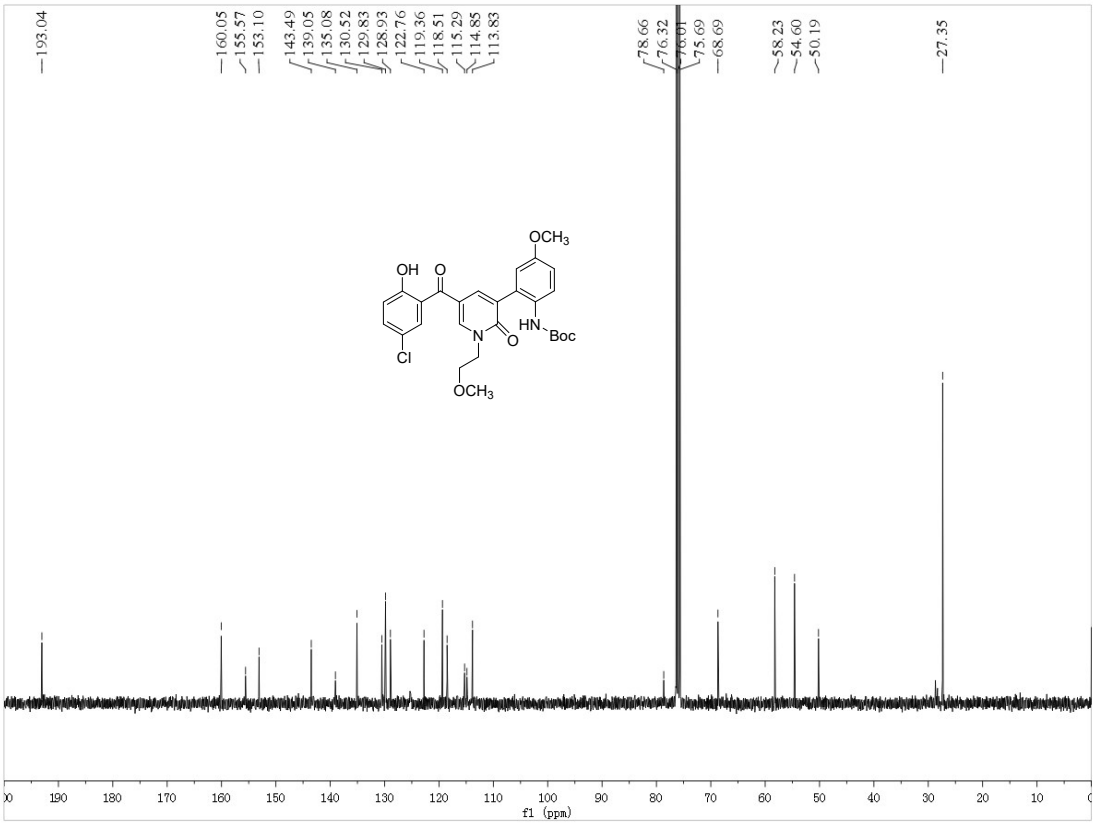
^{1}H and ^{13}C NMR of 3bi



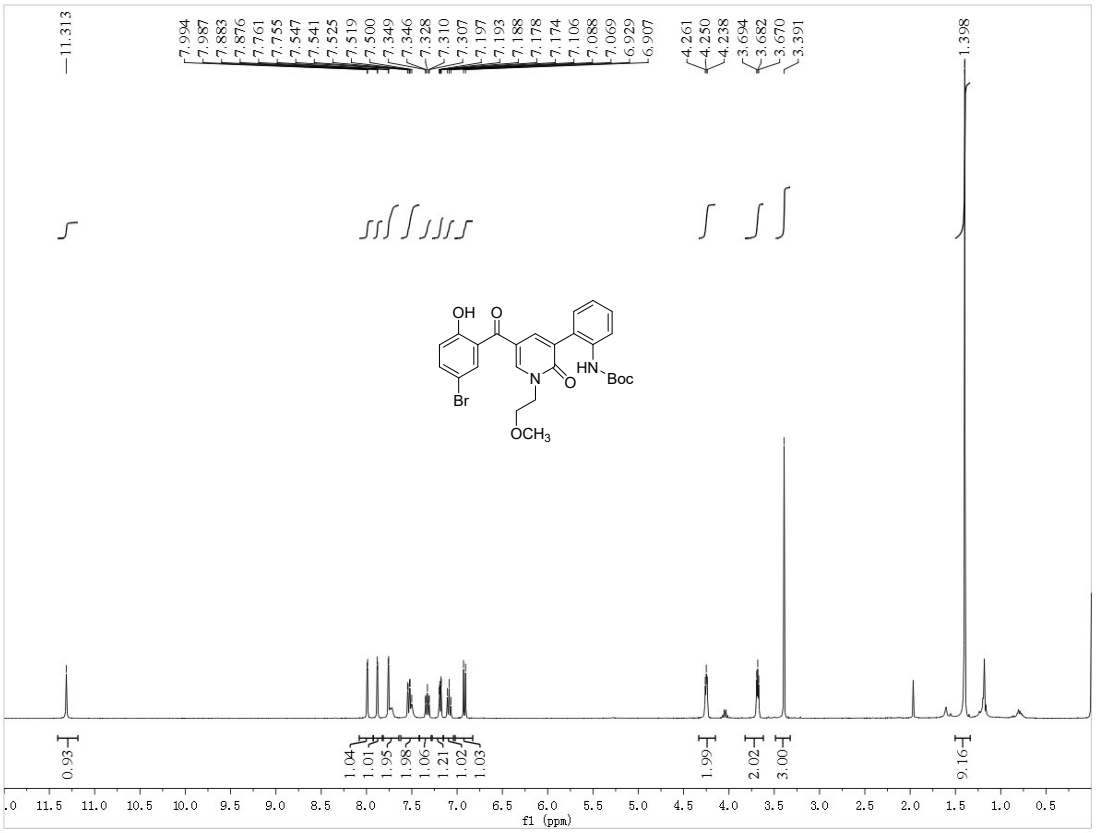


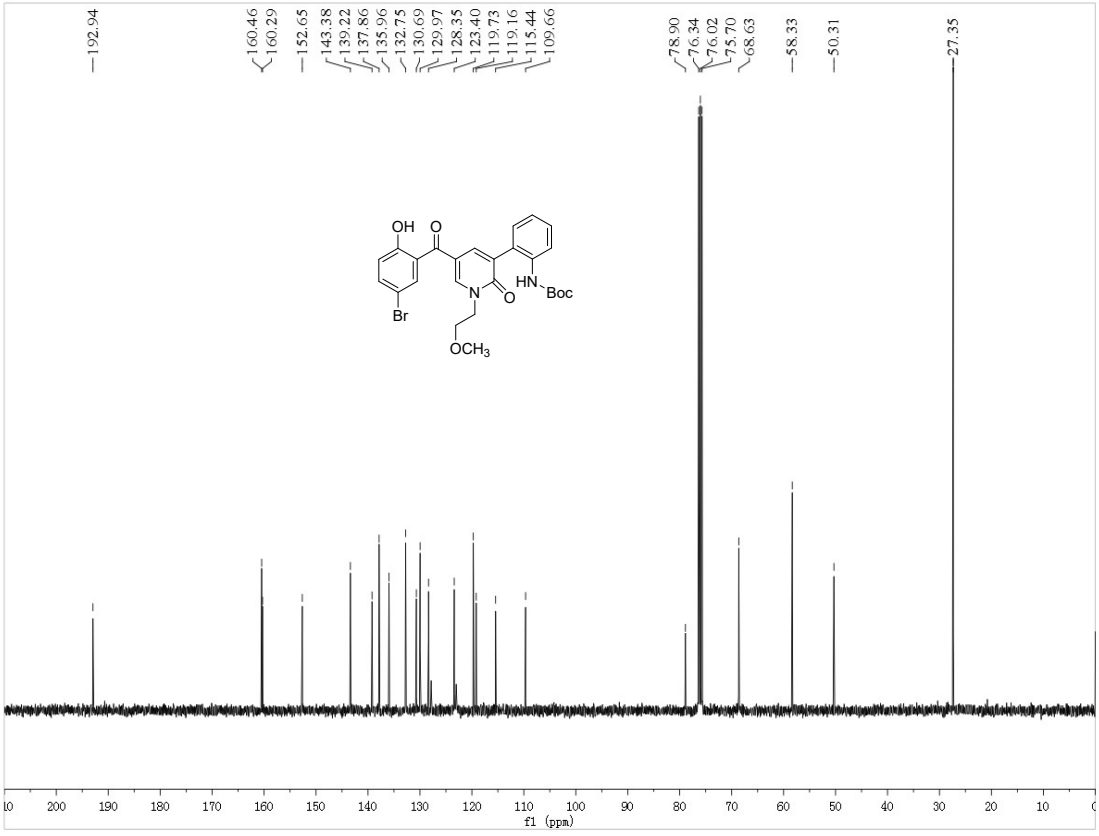
^{1}H and ^{13}C NMR of 3bj



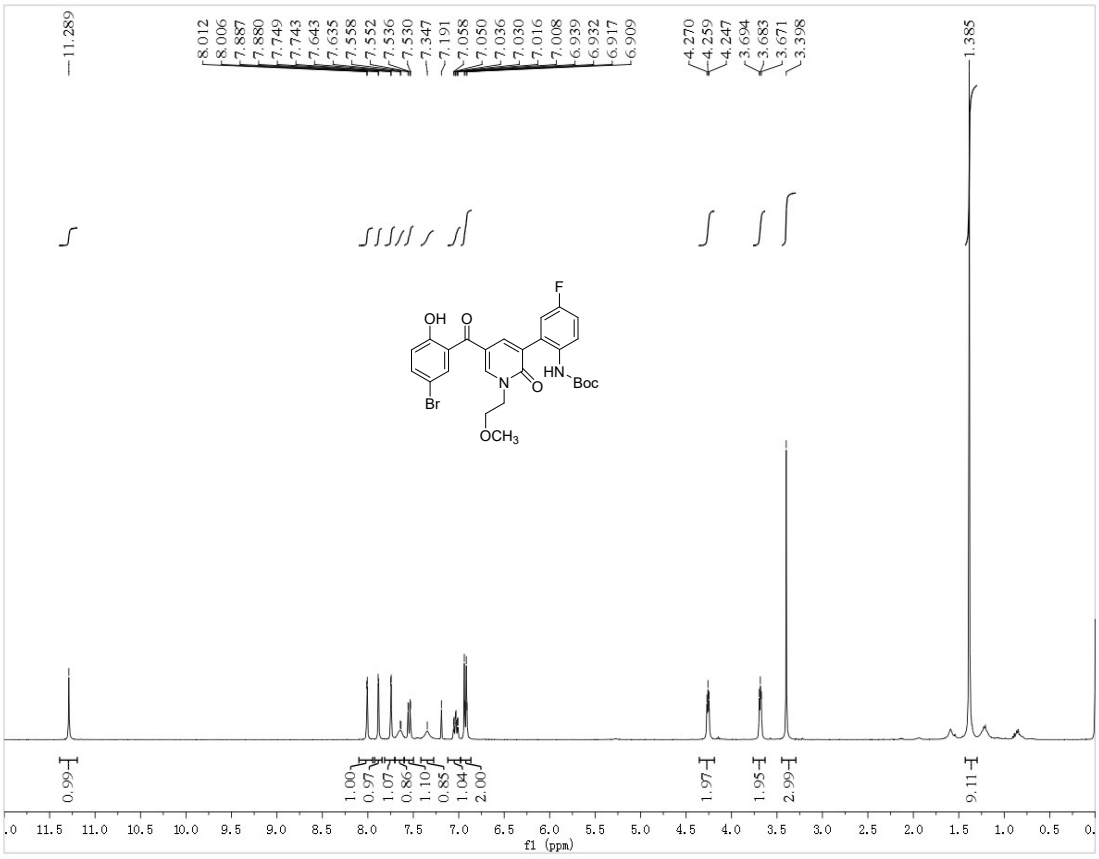


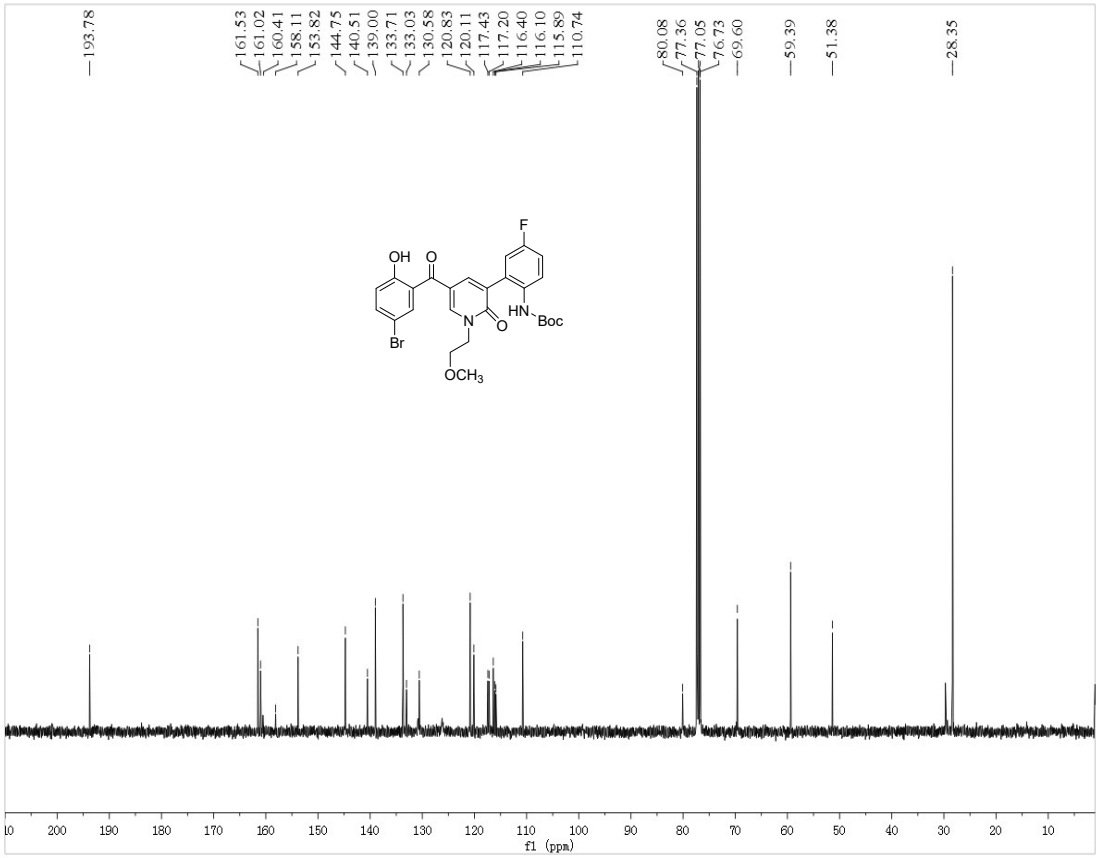
^{1}H and ^{13}C NMR of 3bk



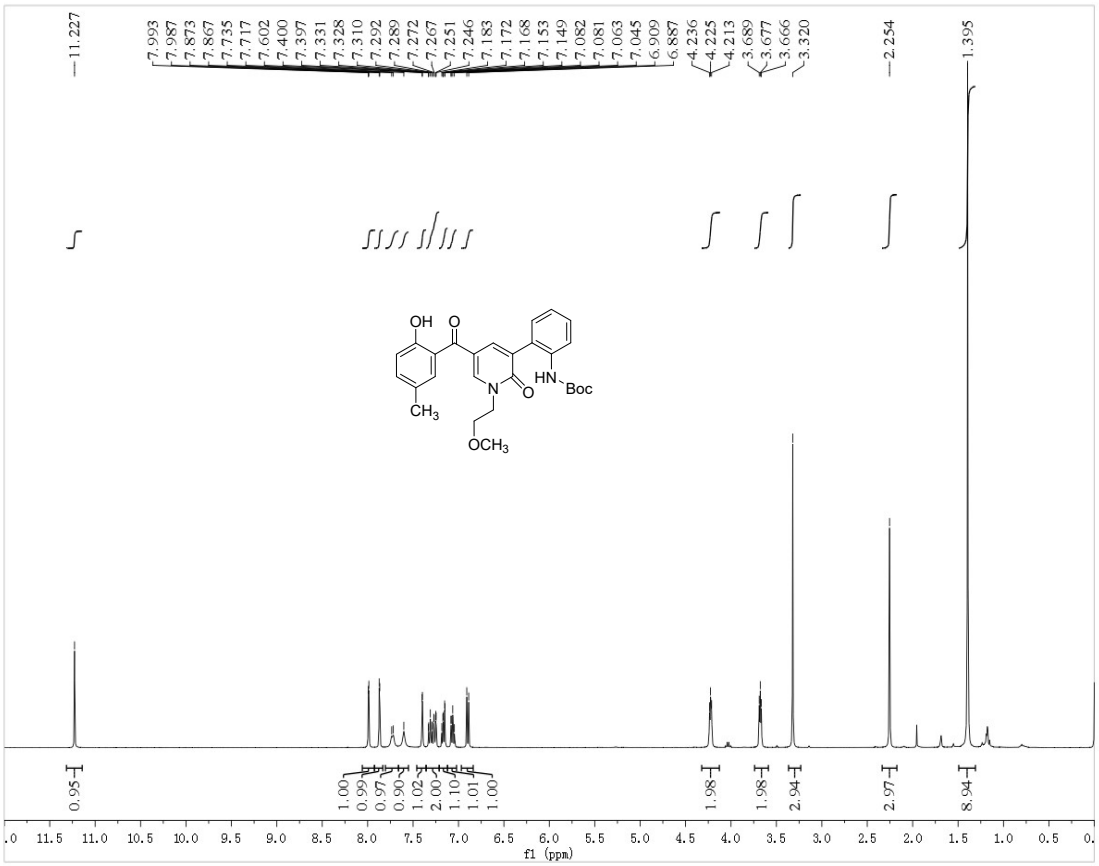


^{1}H and ^{13}C NMR of 3bl





^{1}H and ^{13}C NMR of 3bm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7.987
7.873
7.867
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7.397
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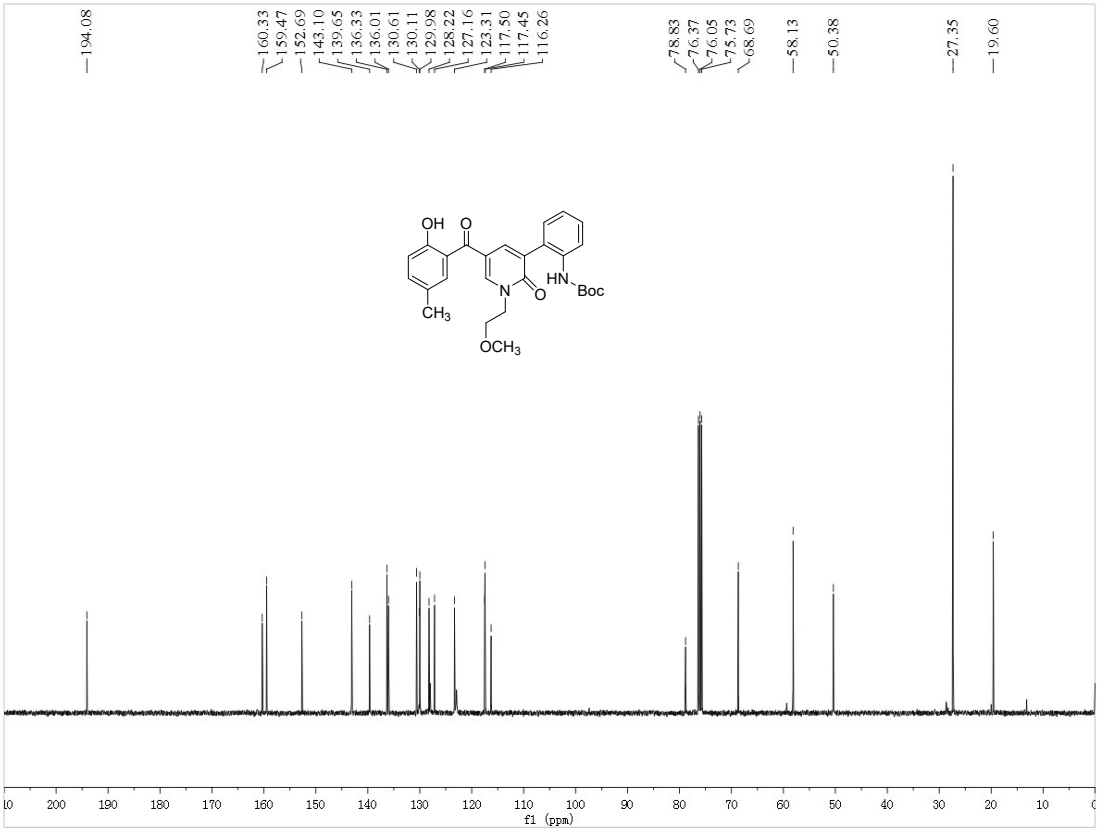
7.310
7.292
7.289
7.272
7.267
7.251
7.246
7.183
7.172
7.168
7.153
7.149
7.082
7.081
7.063
7.045
6.909
6.887
4.236
4.225
4.213
3.689
3.677
3.666
3.320
2.254
1.395
OH
O
HN
Boc
N
O
CH3
OCH3
0.95
1.00
0.99
0.97
0.90
1.02
2.00
1.10
1.01
1.00
1.98
1.98
2.94
2.97
8.94
f1 (ppm)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159.47
152.69
143.10
139.65
136.33
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130.11
129.98
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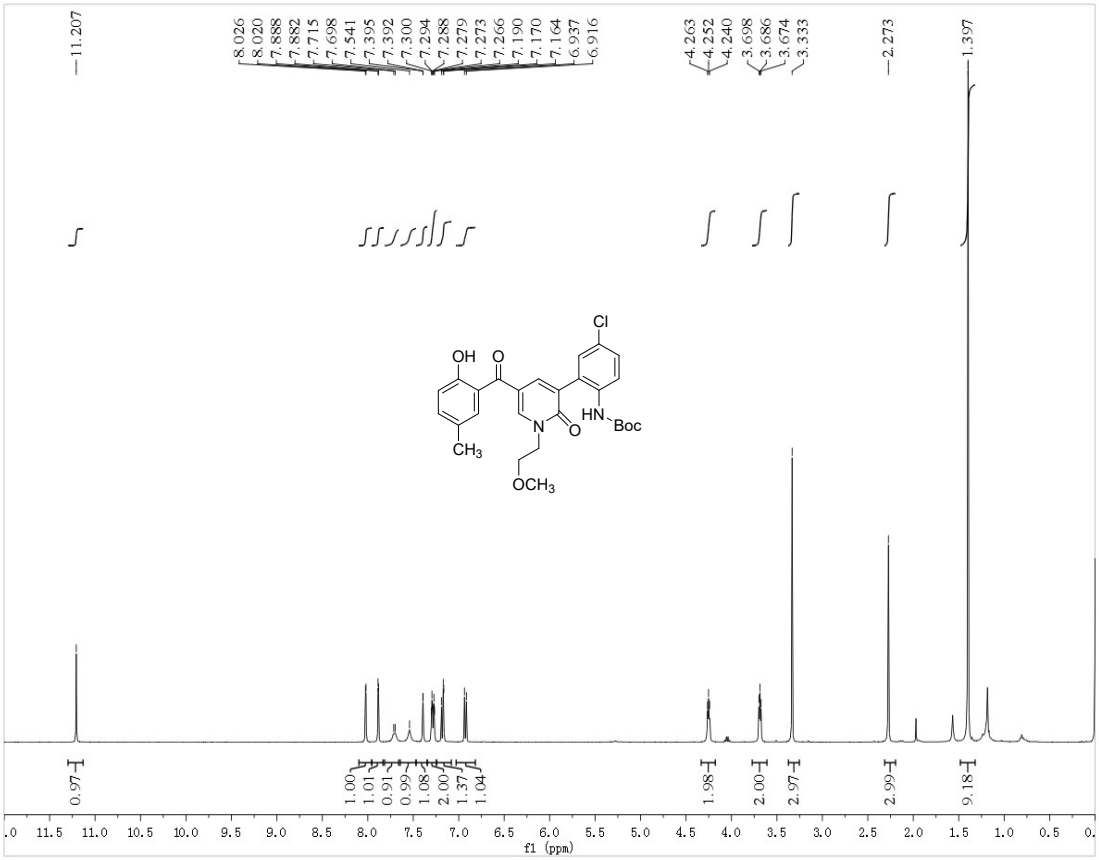
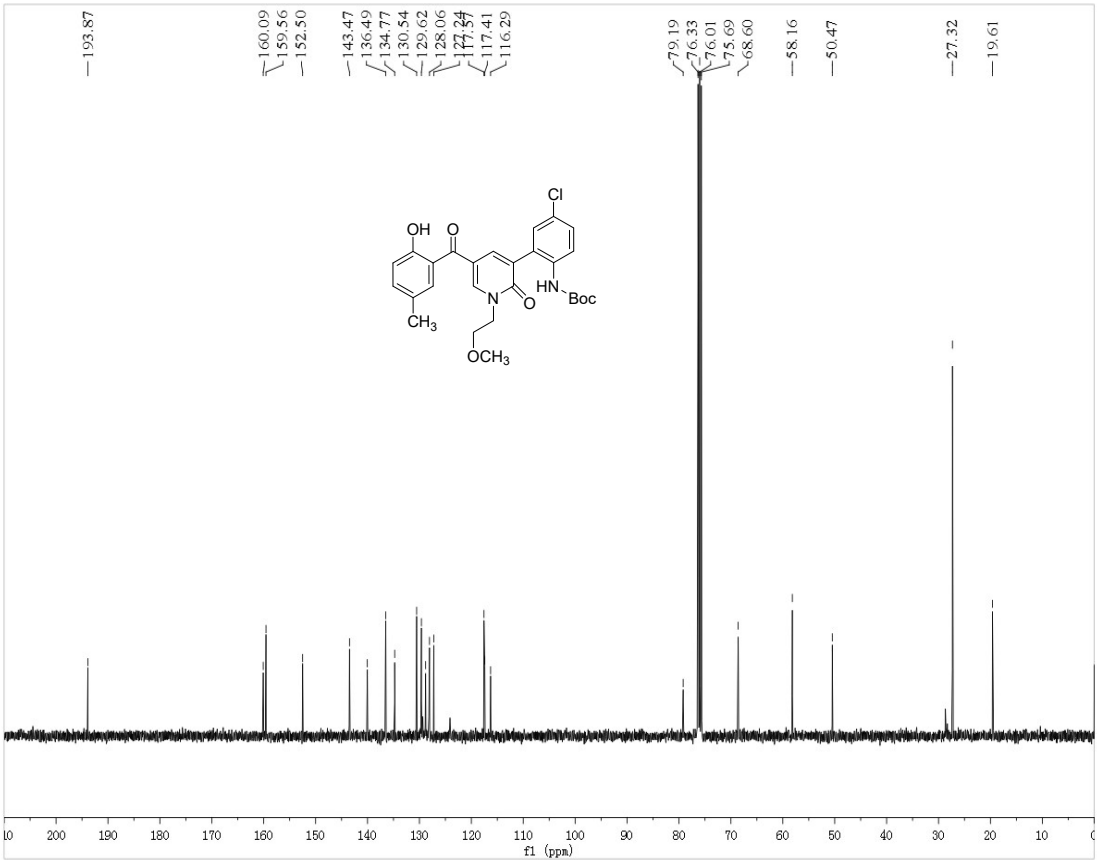
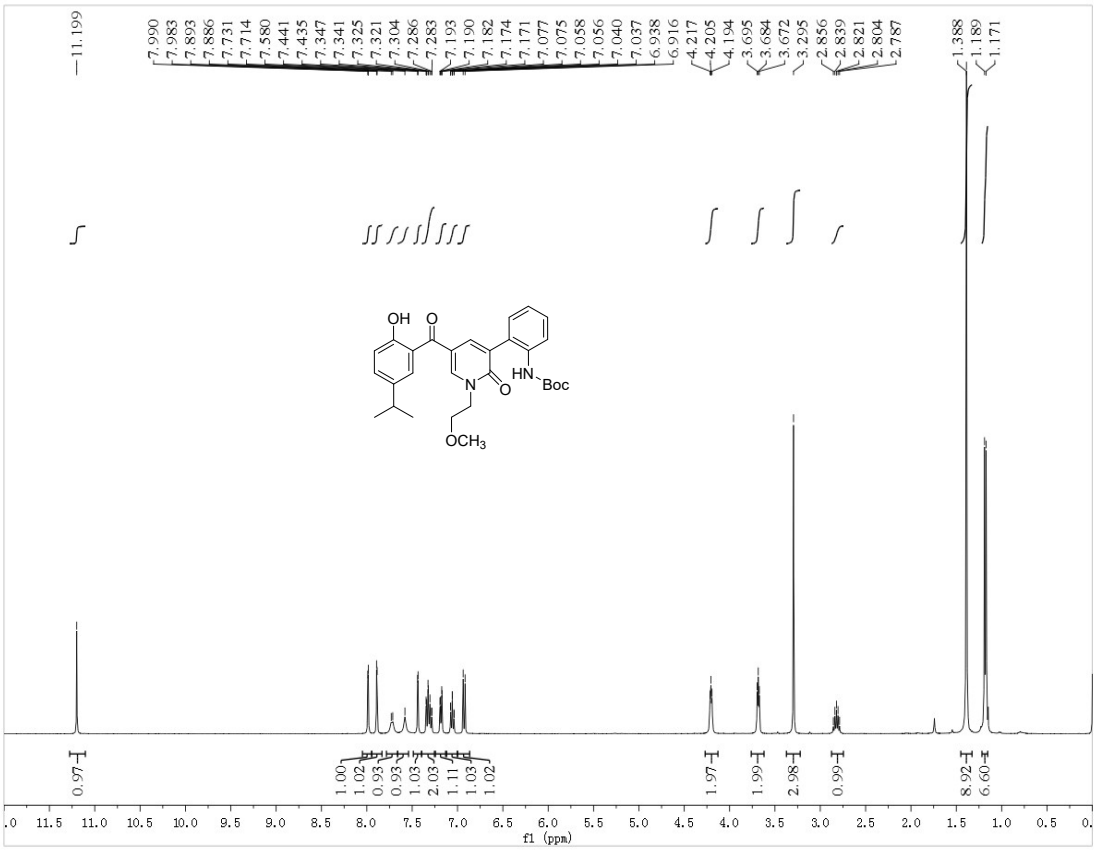
127.16
123.31
117.50
117.45
116.26
78.83
76.37
76.05
75.73
68.69
58.13
50.38
27.35
19.60
OH
O
HN
Boc
N
O
CH3
OCH3
f1 (ppm)

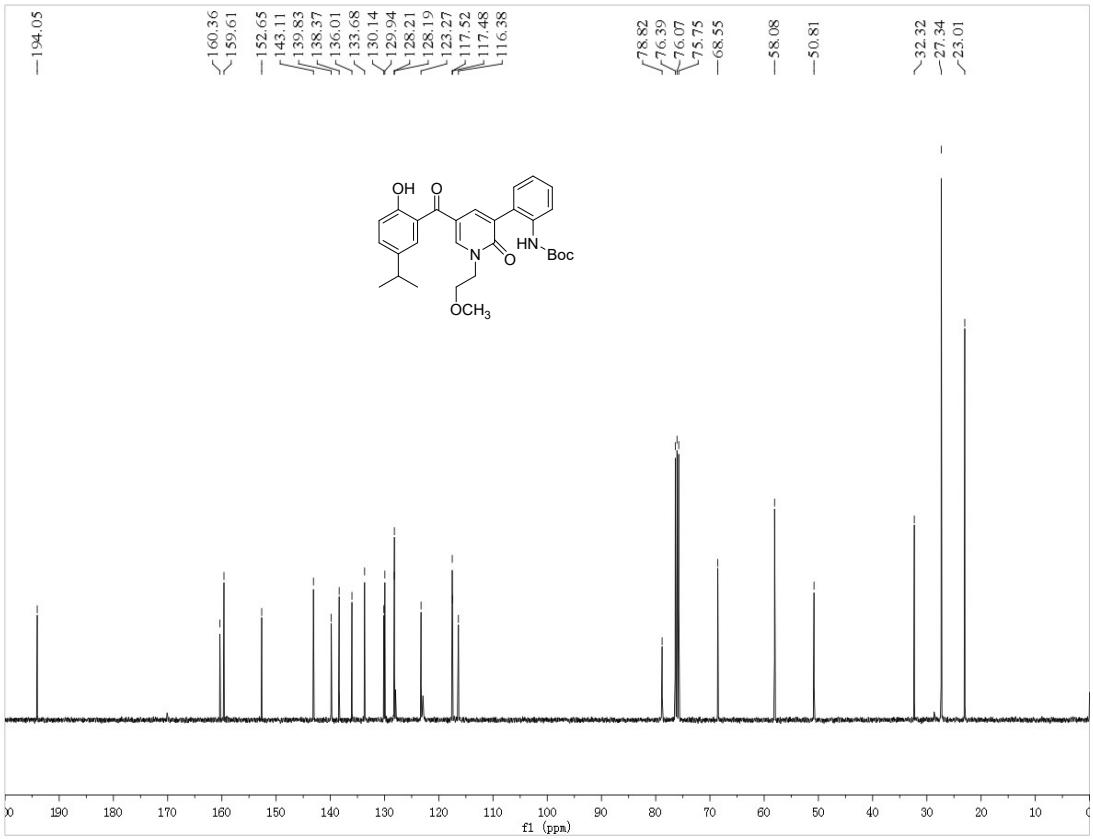
^{1}H and ^{13}C NMR of 3bn



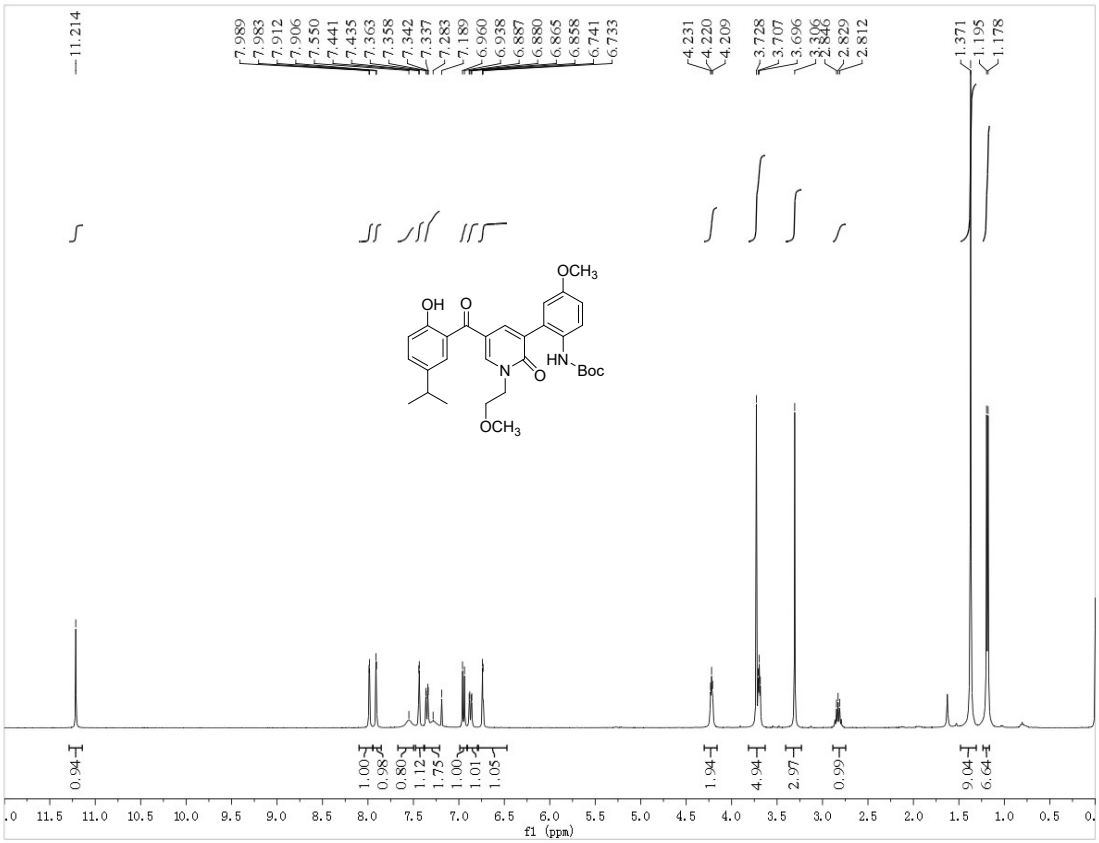


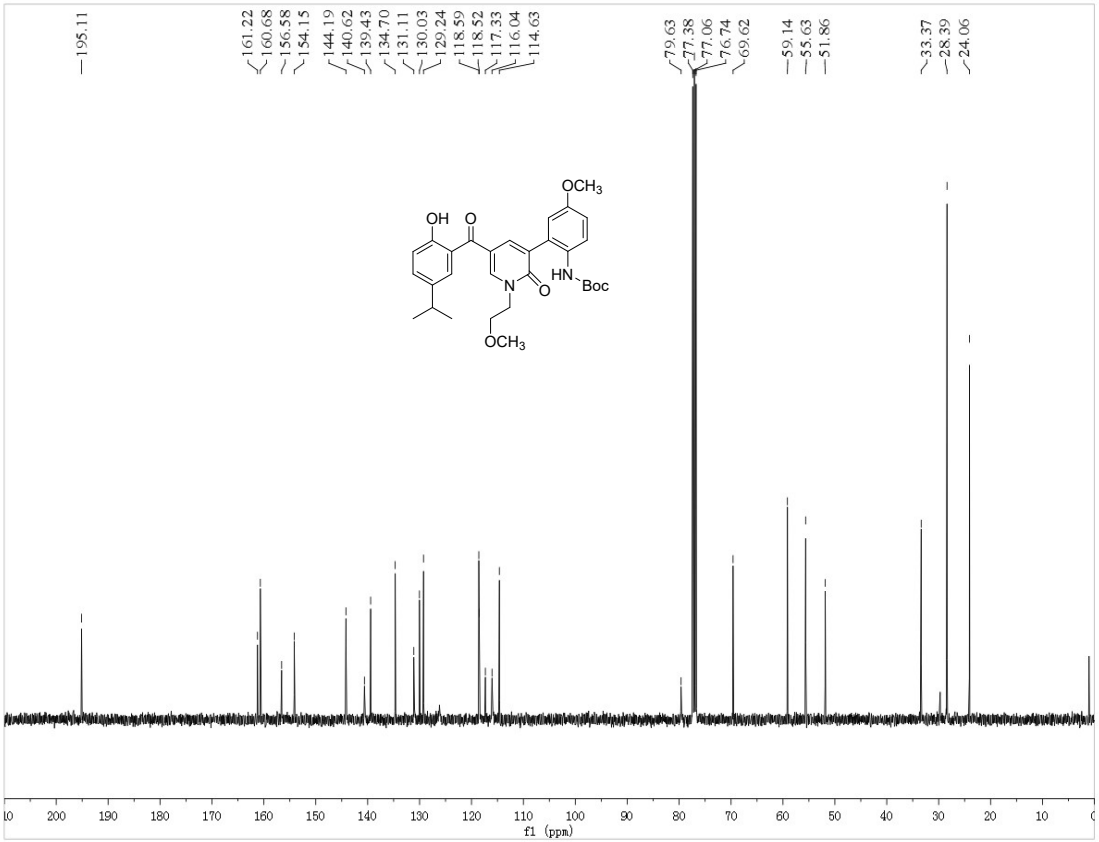
^{1}H and ^{13}C NMR of 3bo



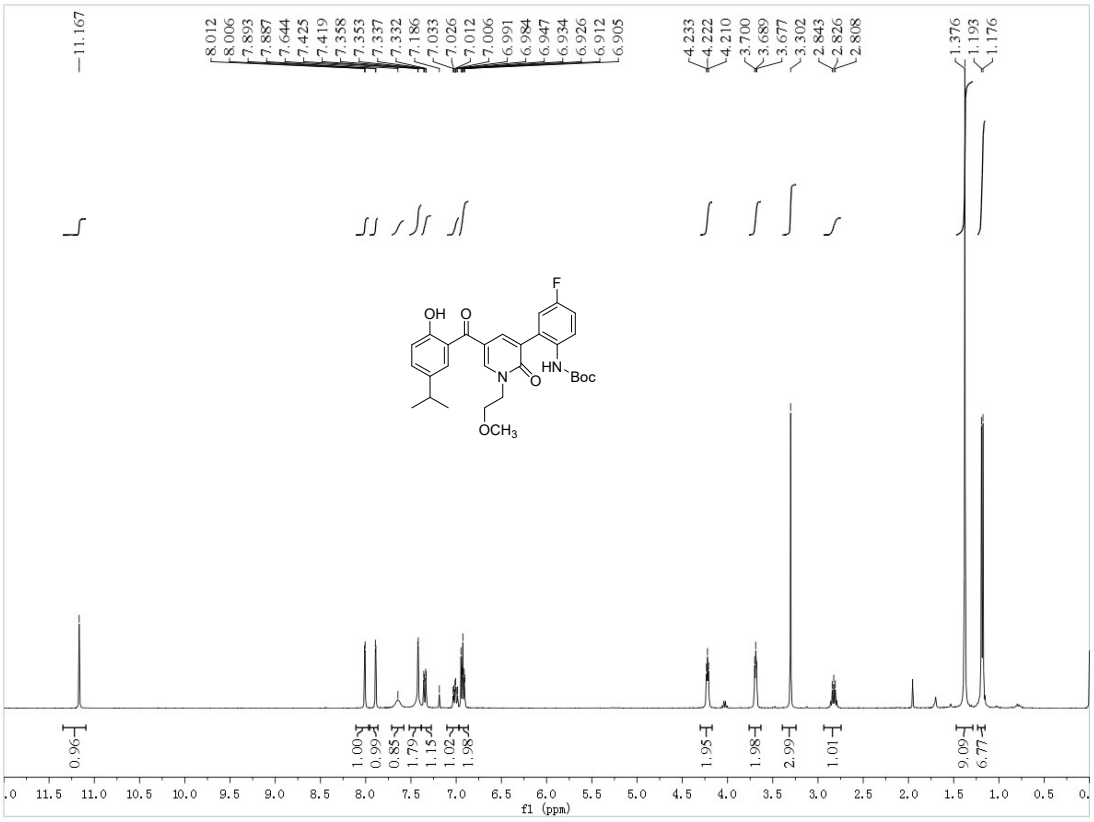


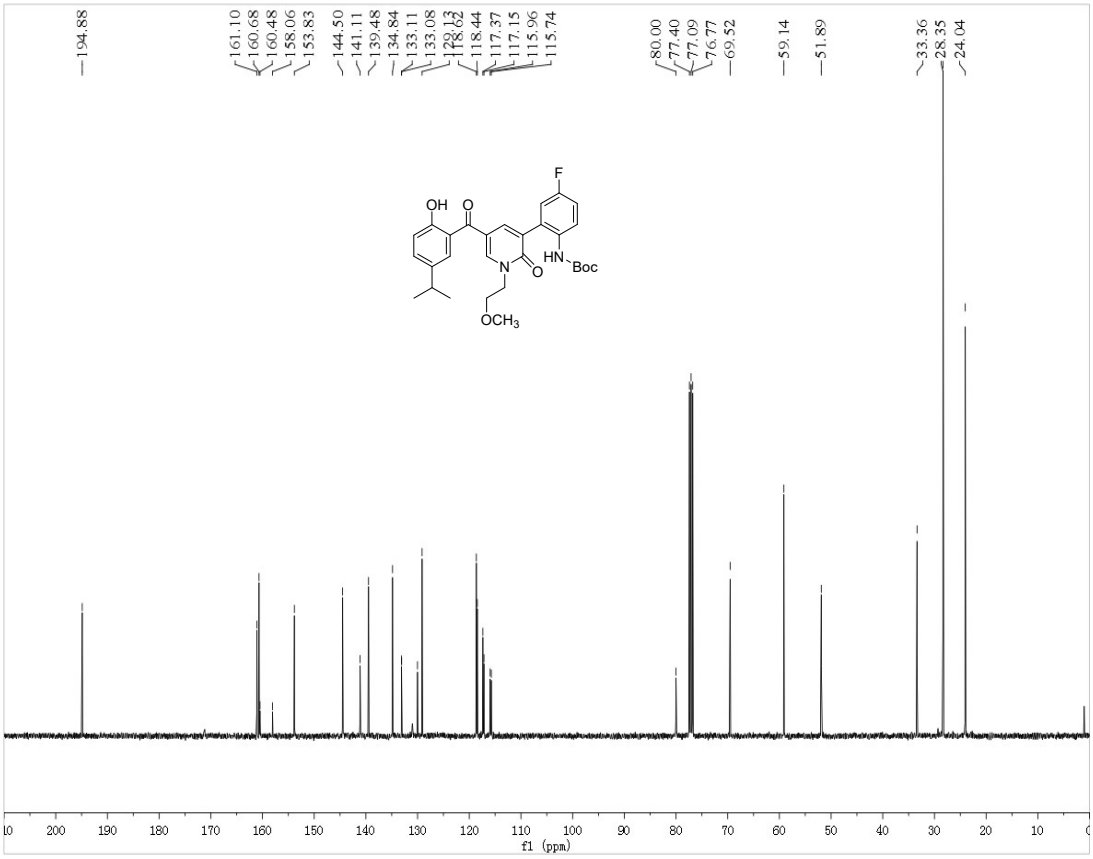
^{1}H and ^{13}C NMR of 3bp



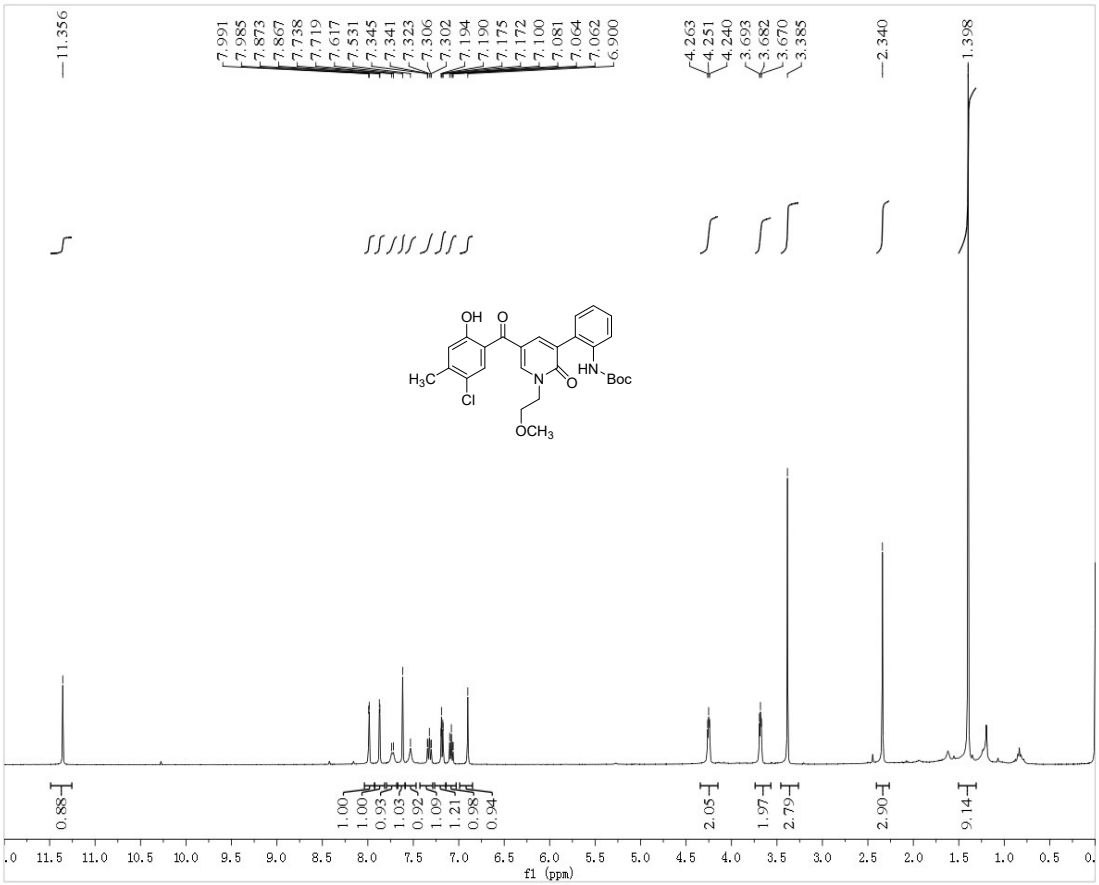


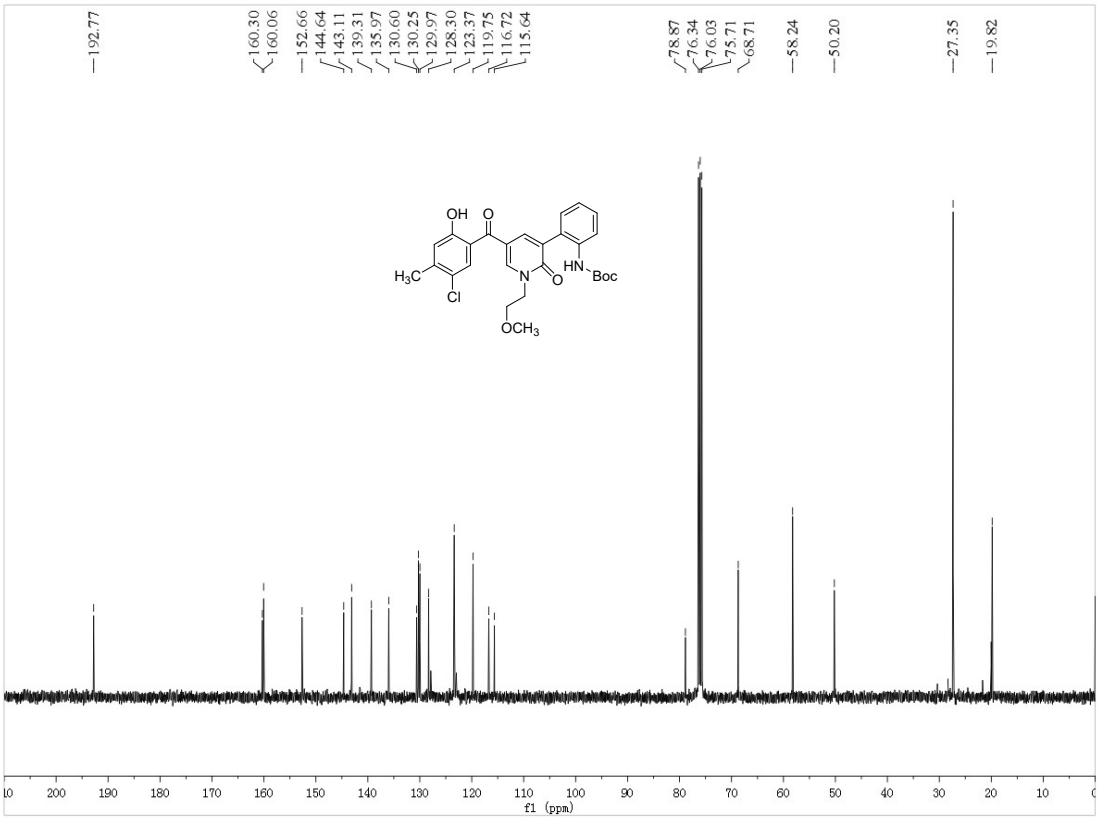
^{1}H and ^{13}C NMR of 3bq



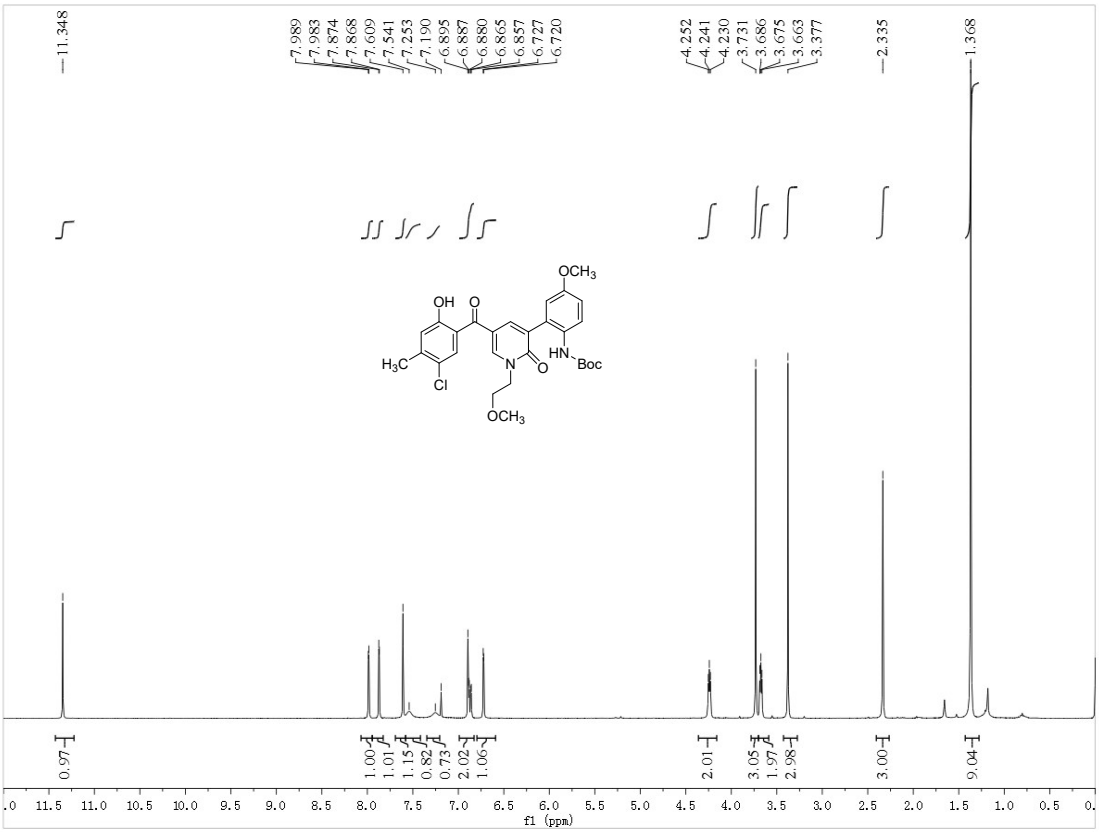


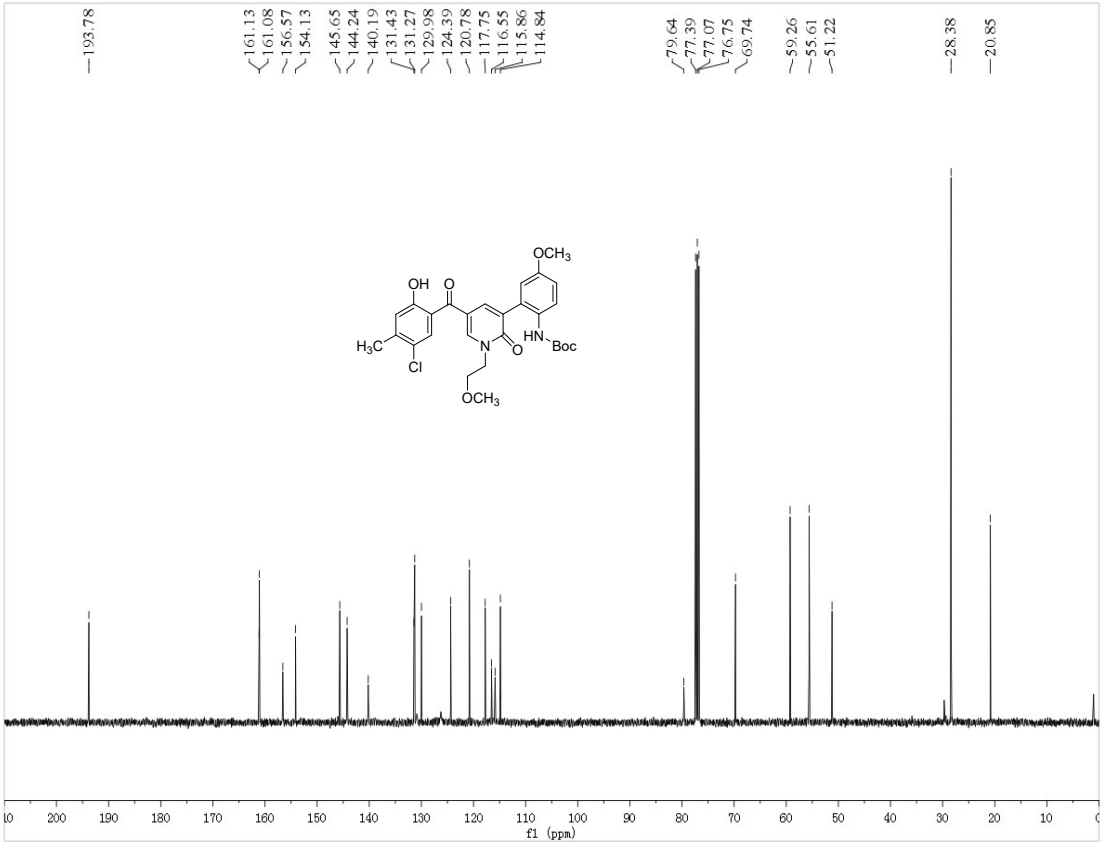
^{1}H and ^{13}C NMR of 3br



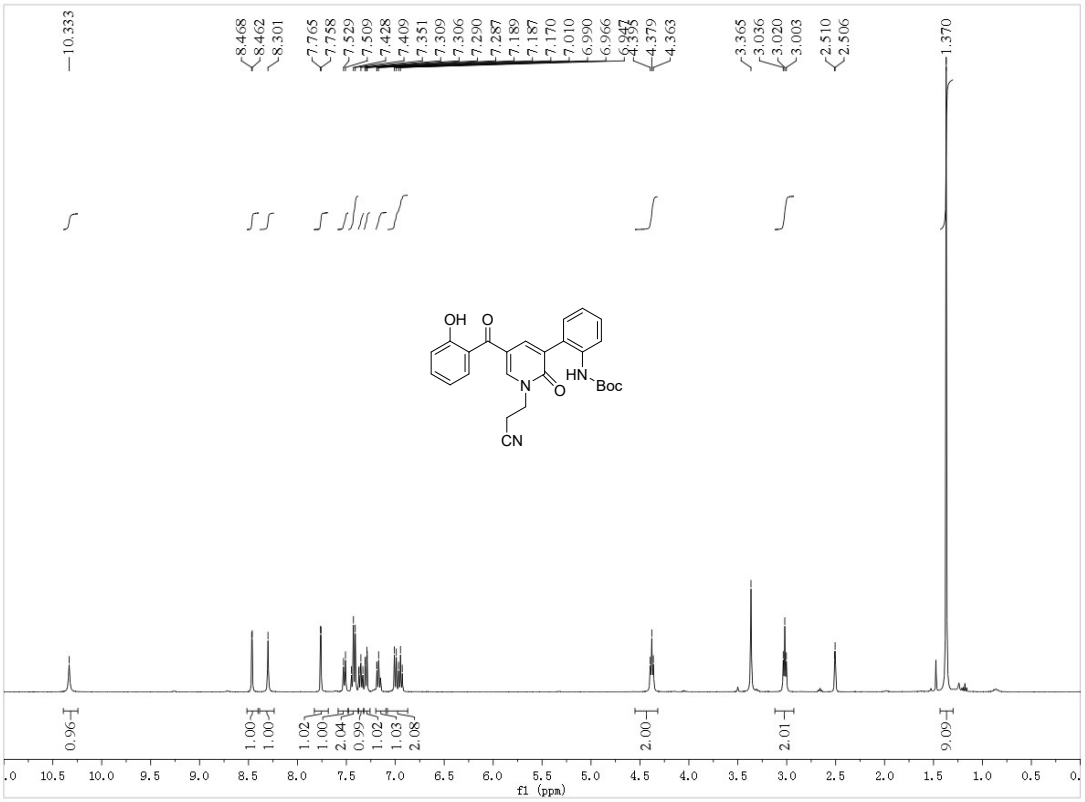


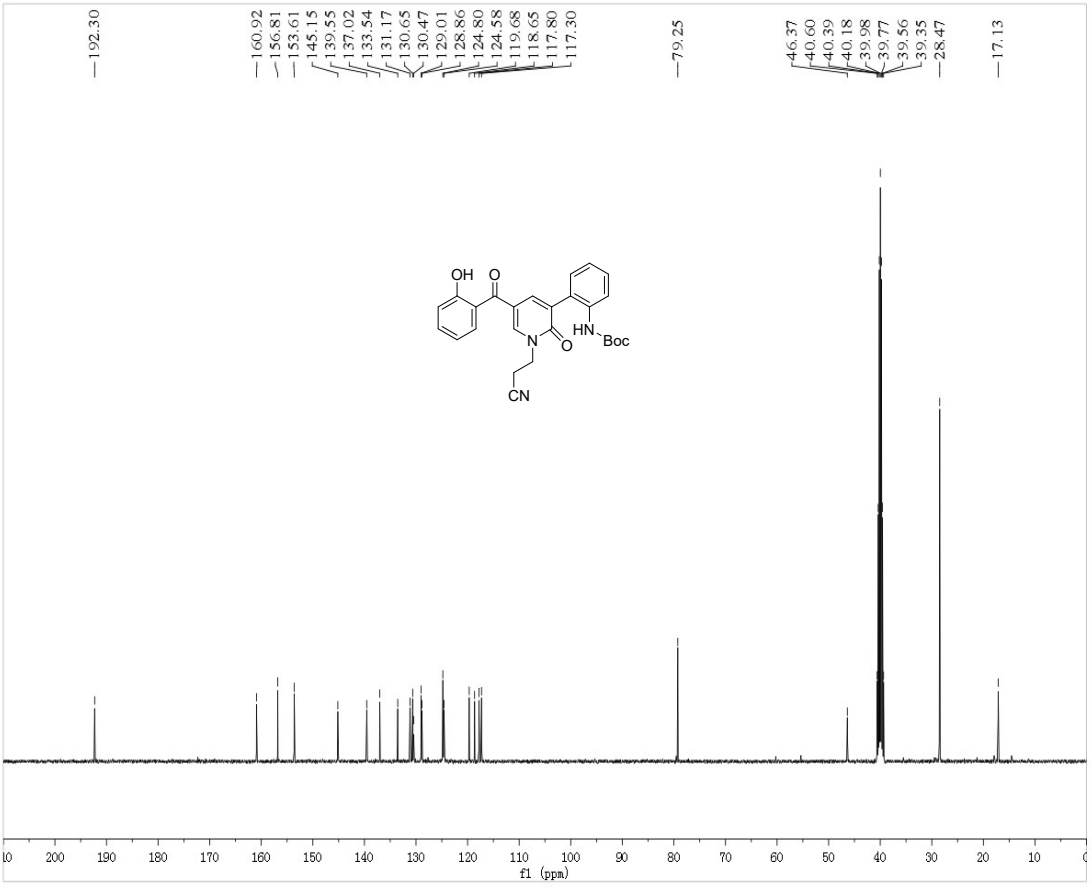
^{1}H and ^{13}C NMR of 3bs



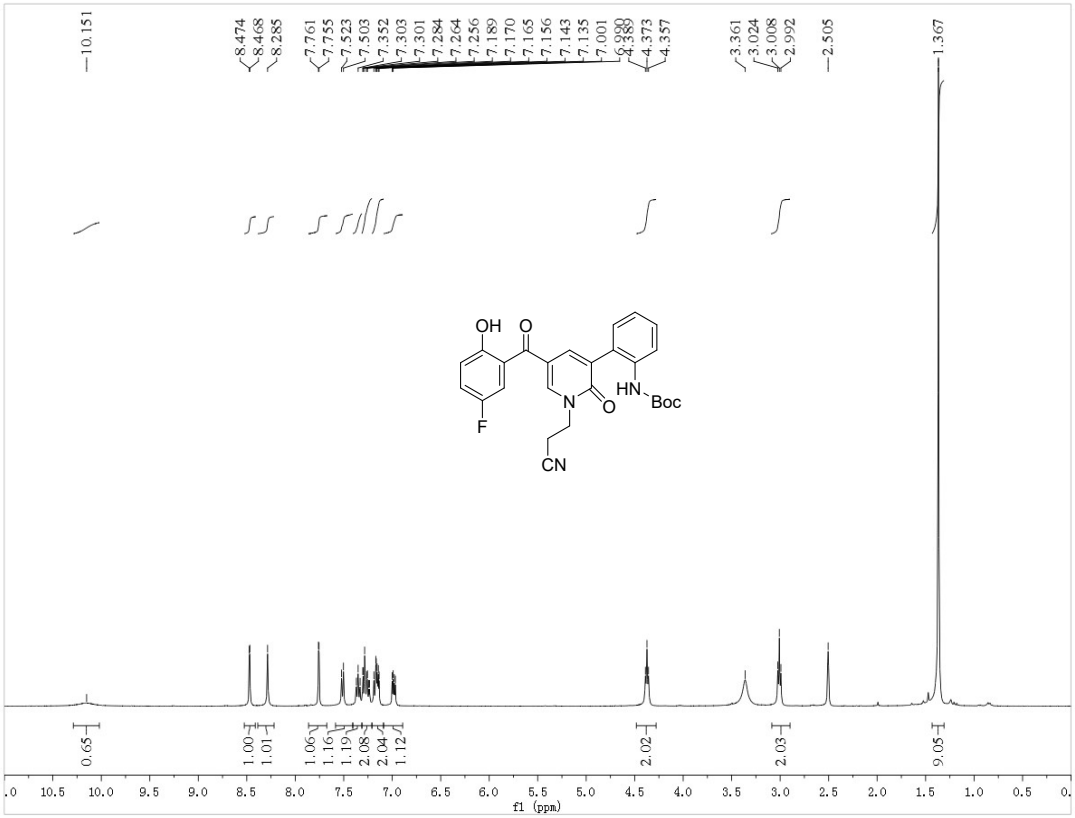


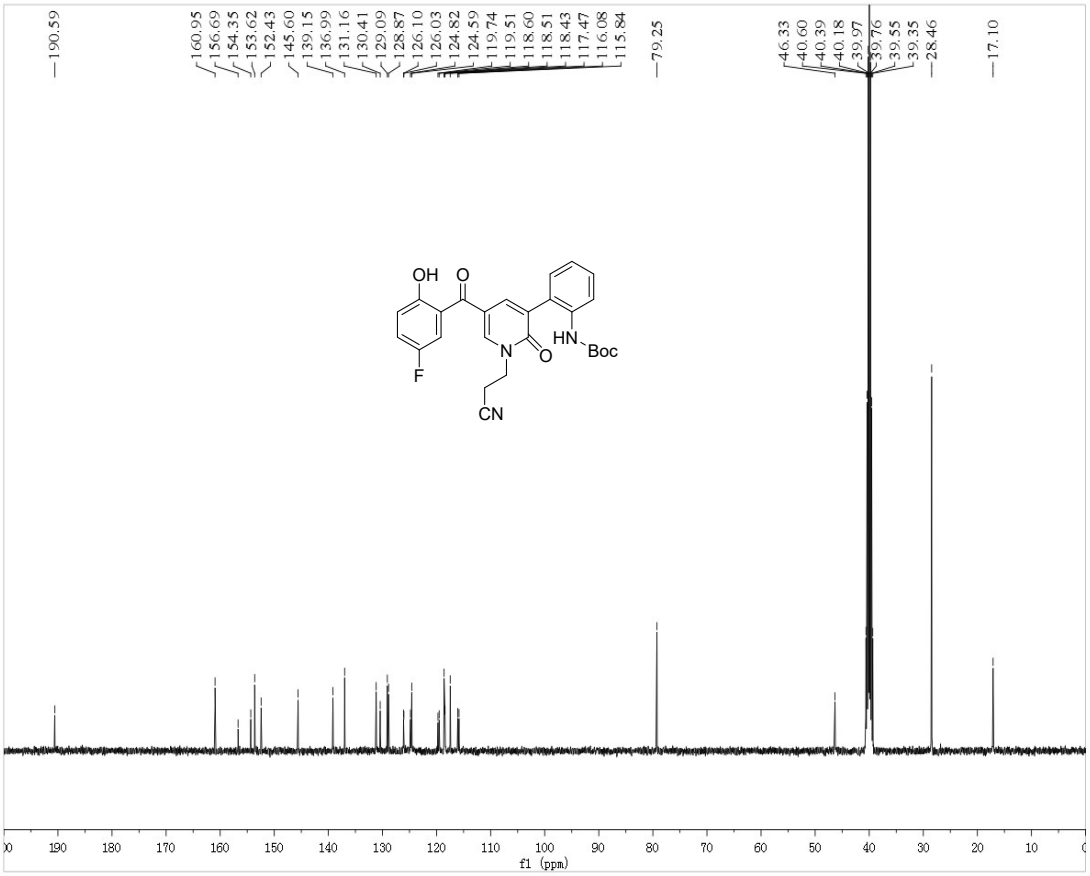
^{1}H and ^{13}C NMR of 3ca



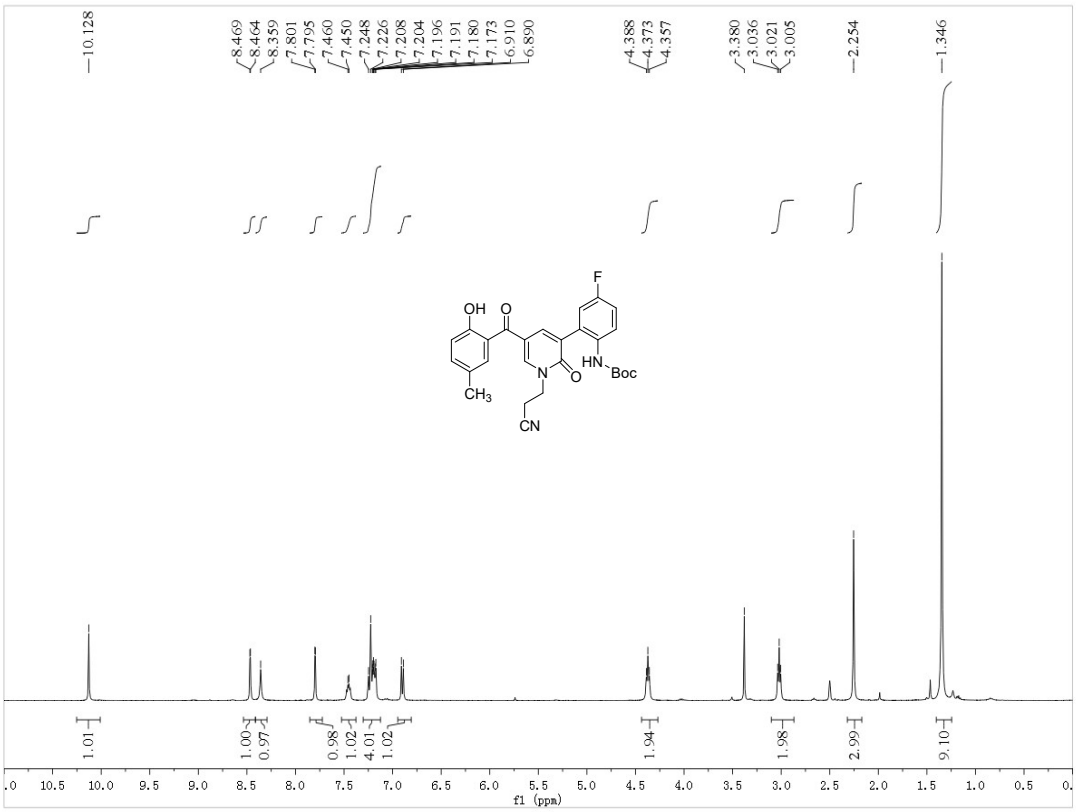


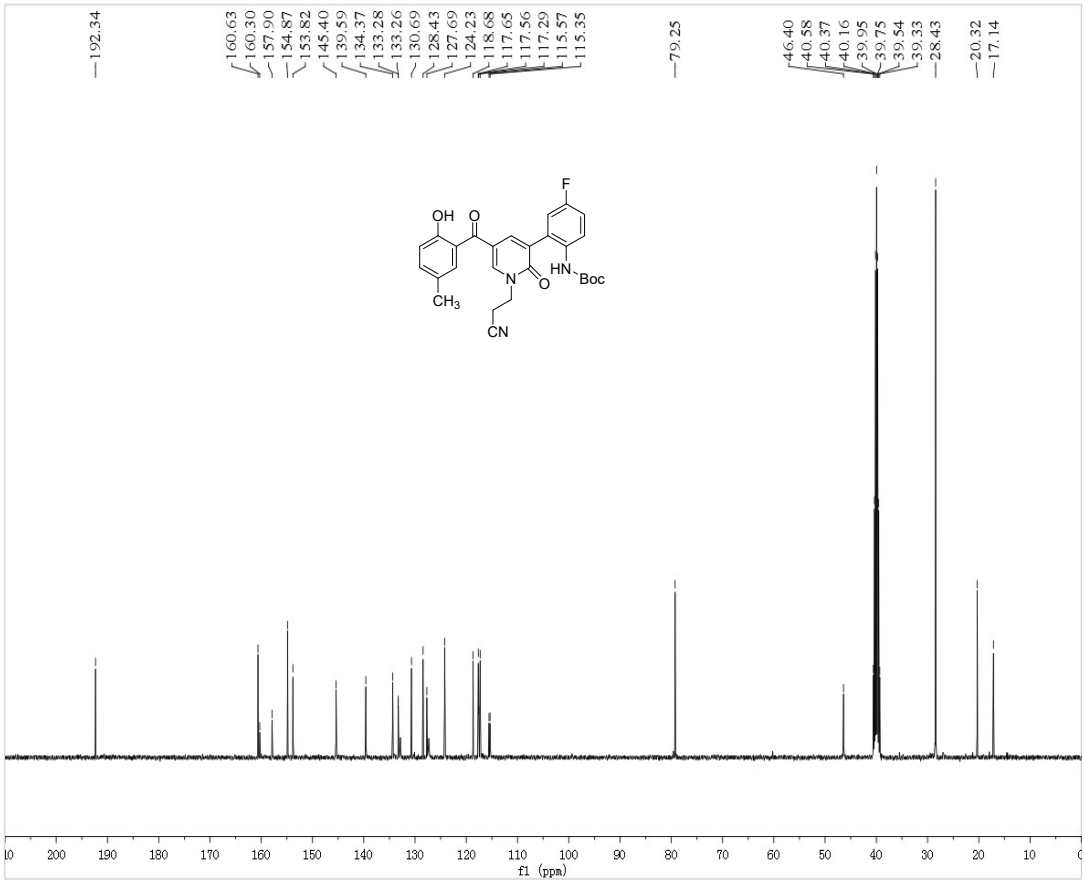
^{1}H and ^{13}C NMR of 3cb



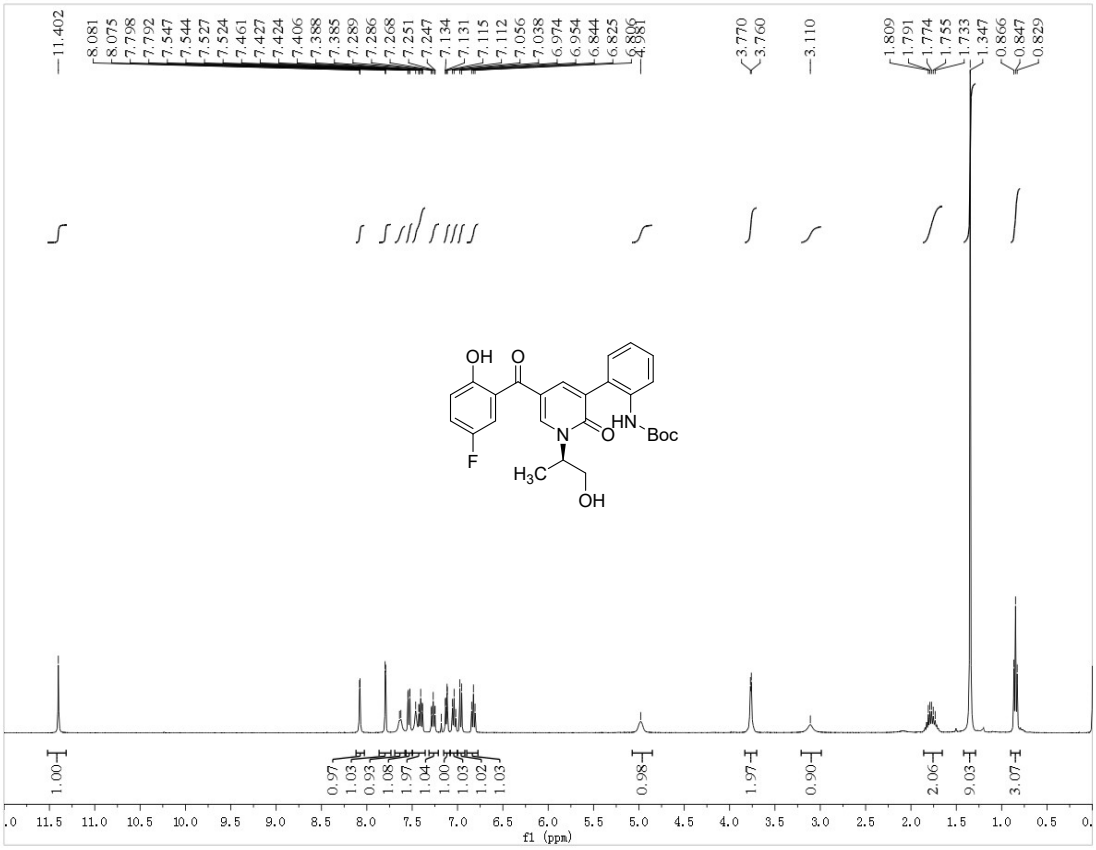


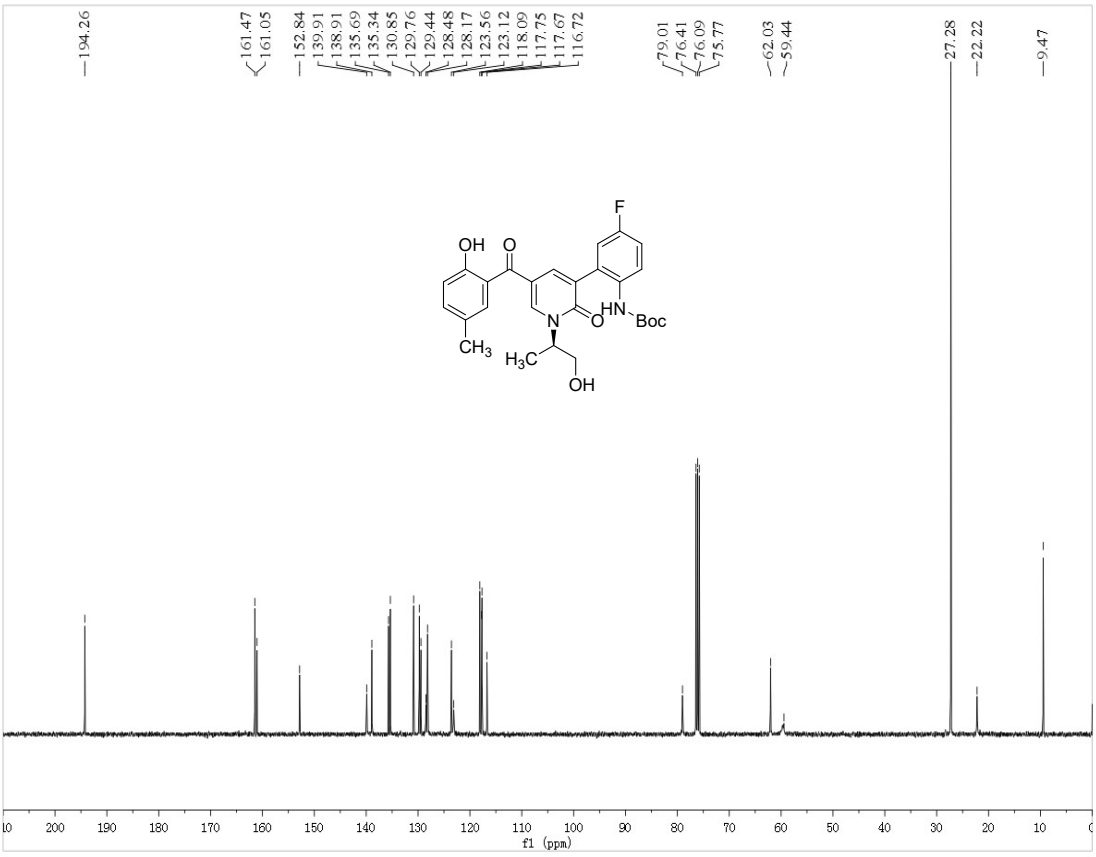
^{1}H and ^{13}C NMR of 3cc



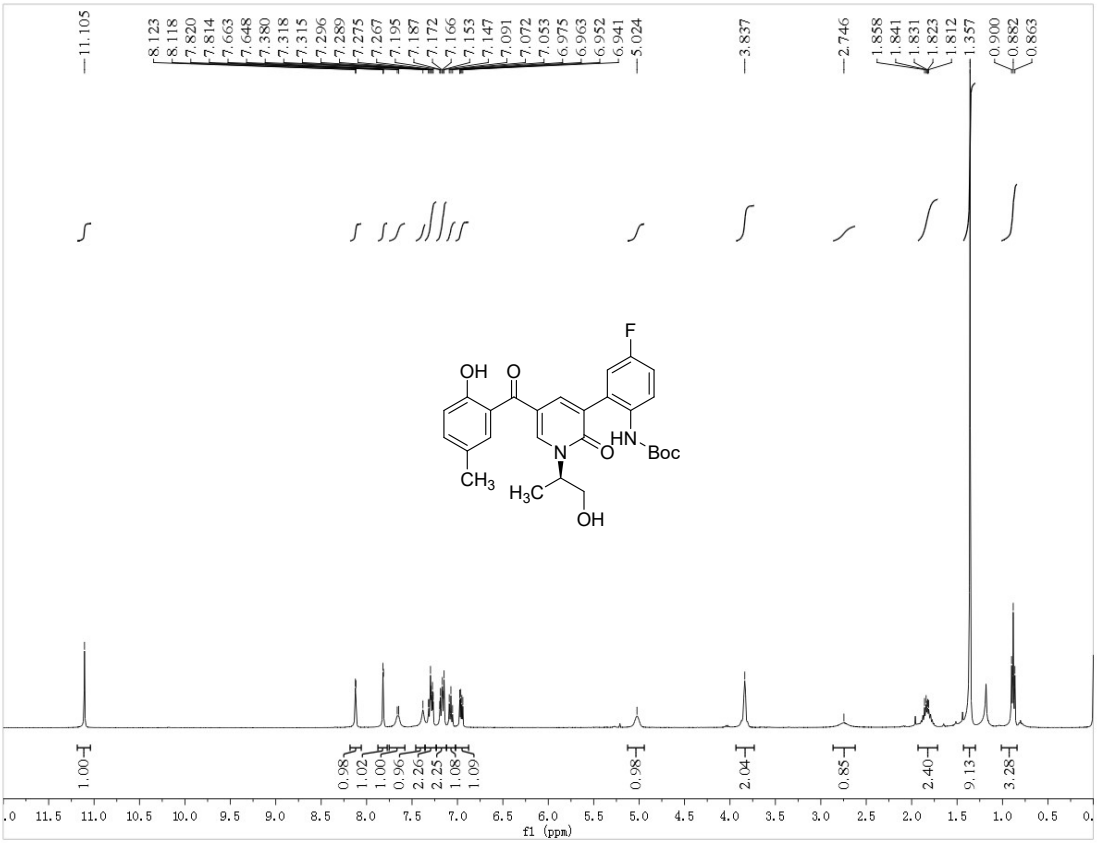


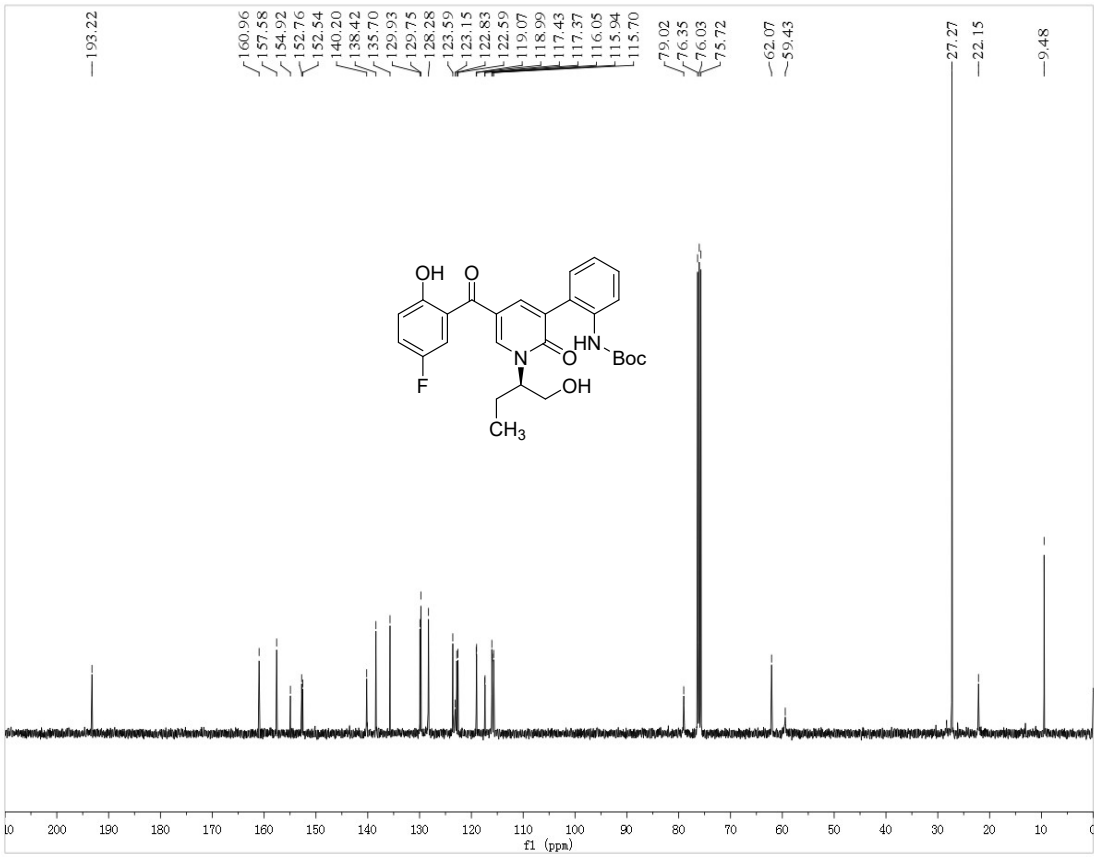
^{1}H and ^{13}C NMR of 3da



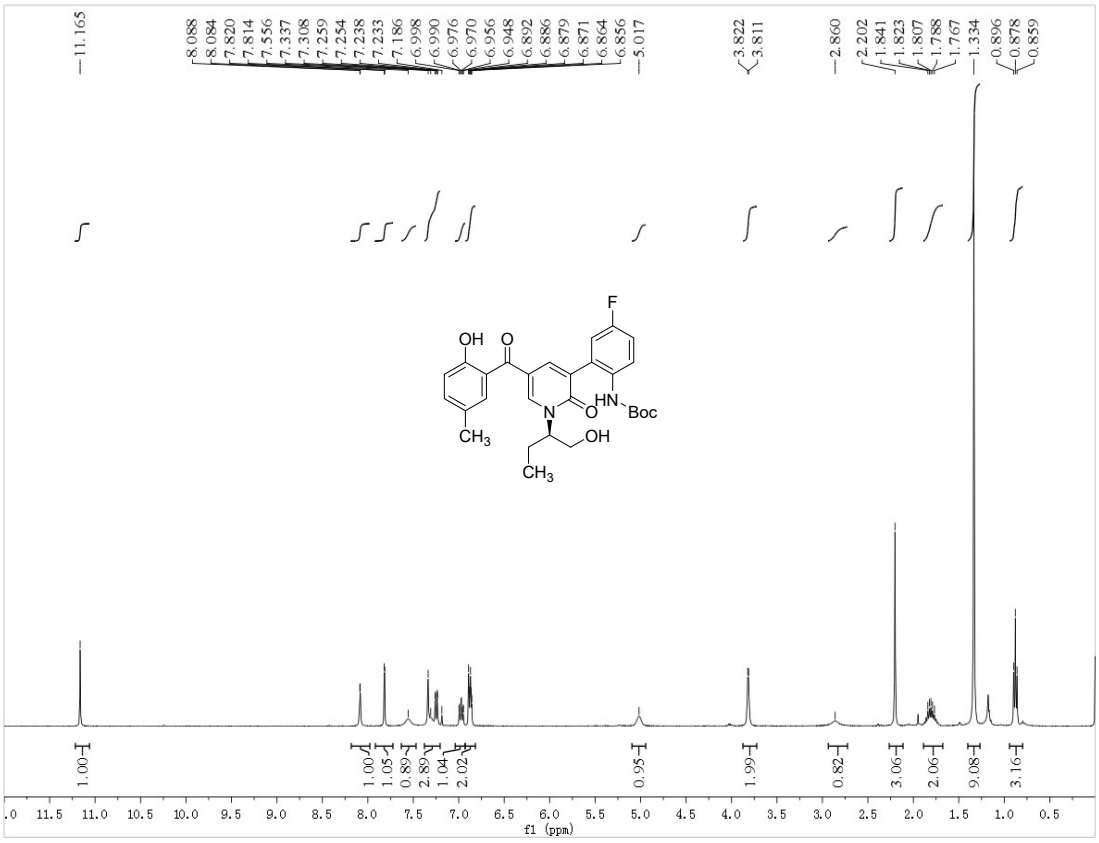


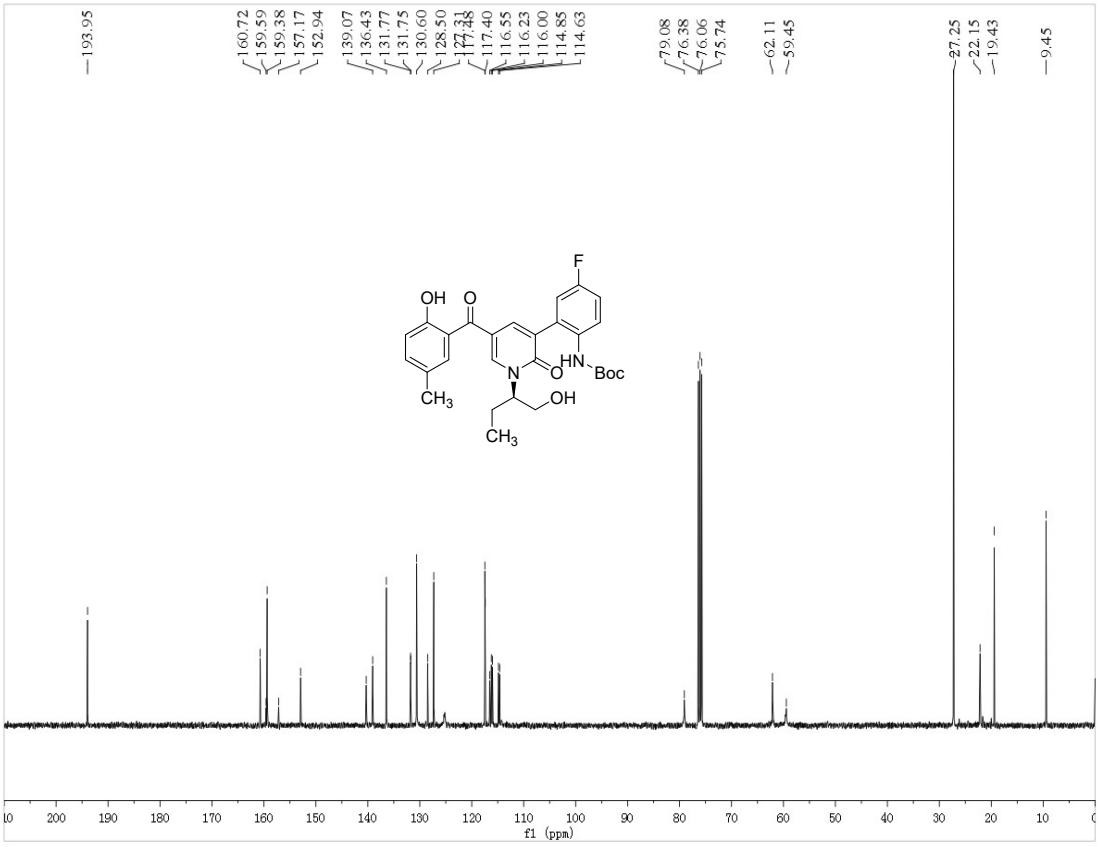
^{1}H and ^{13}C NMR of 3db



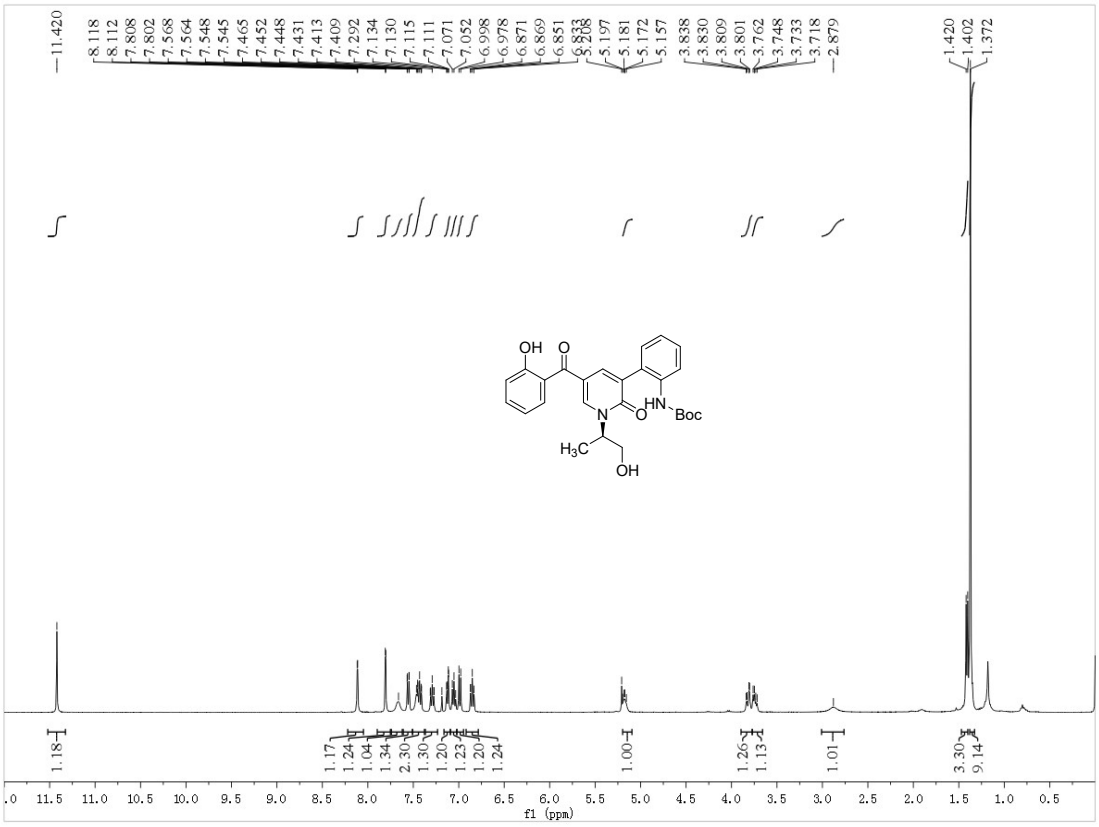


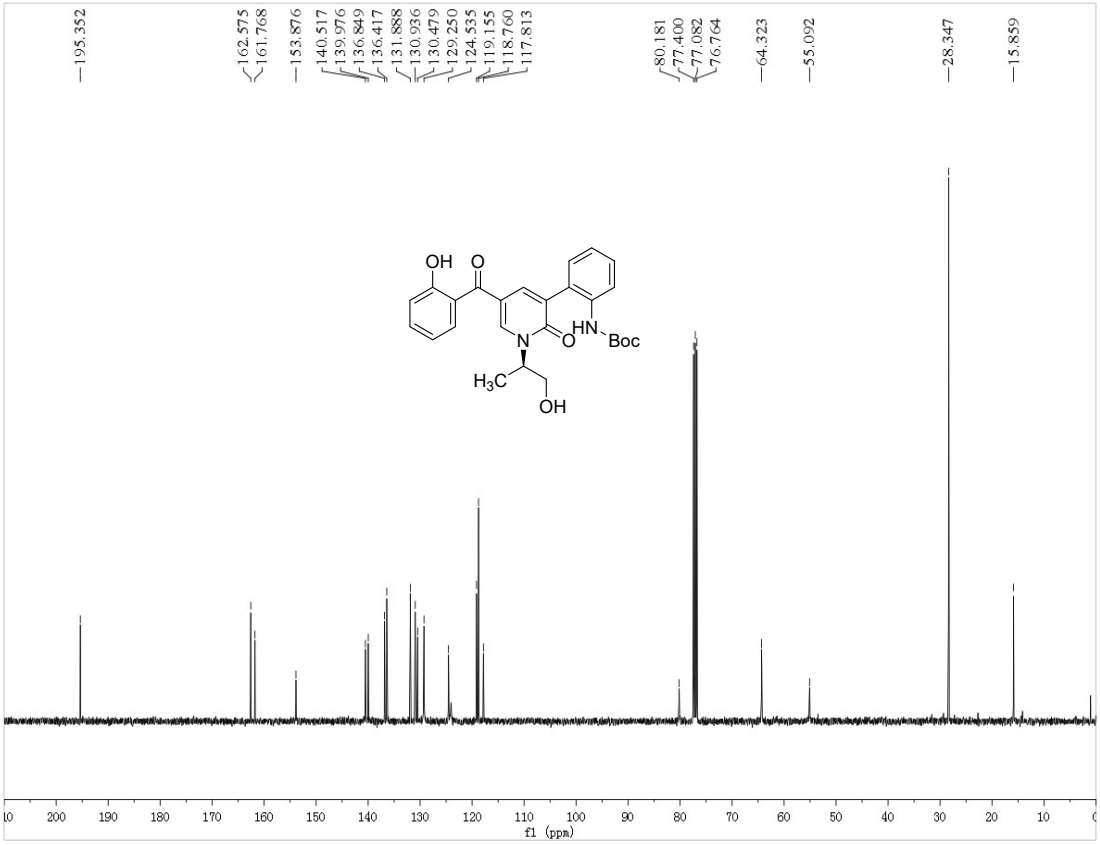
^{1}H and ^{13}C NMR of 3dc



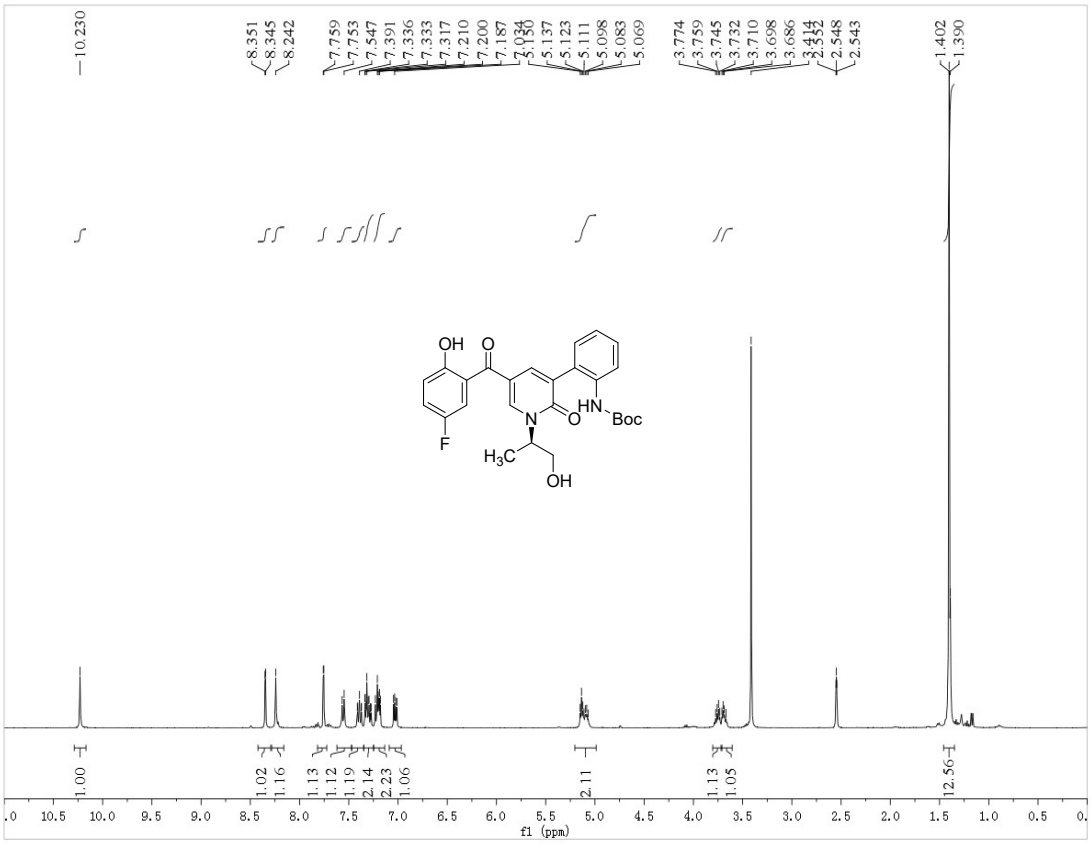


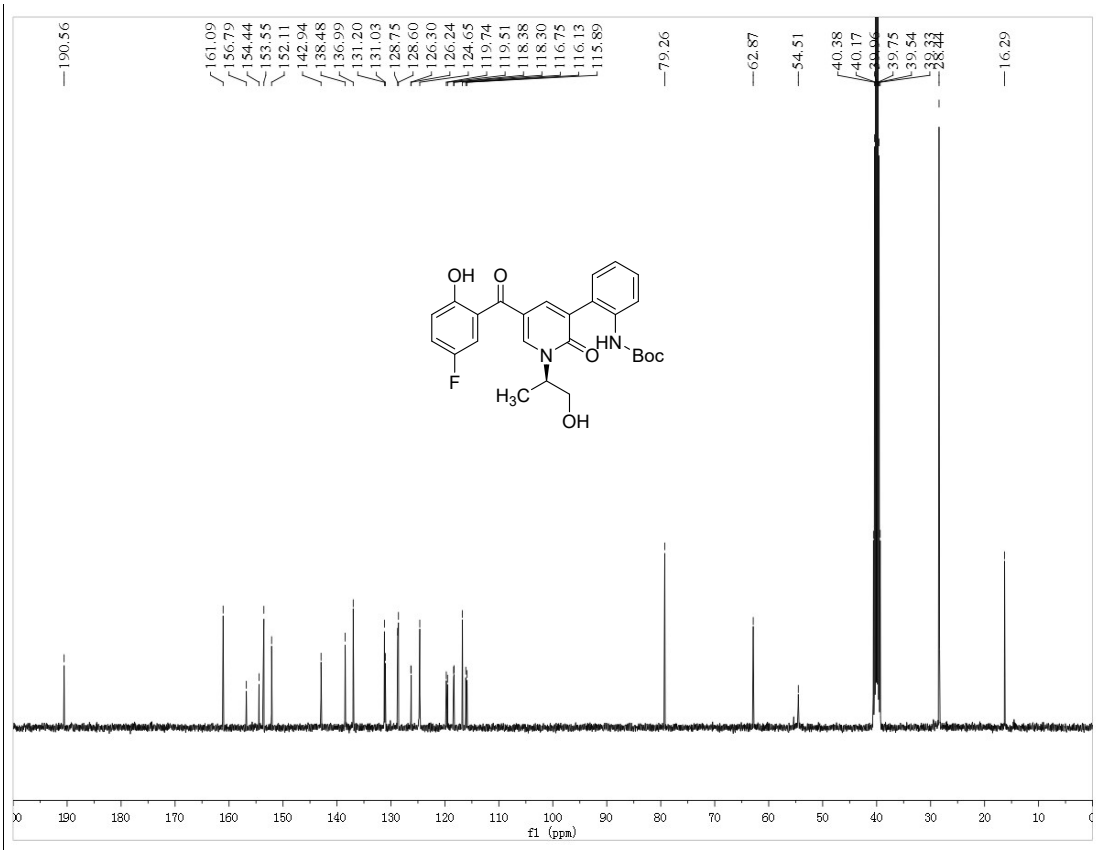
^{1}H and ^{13}C NMR of 3ea



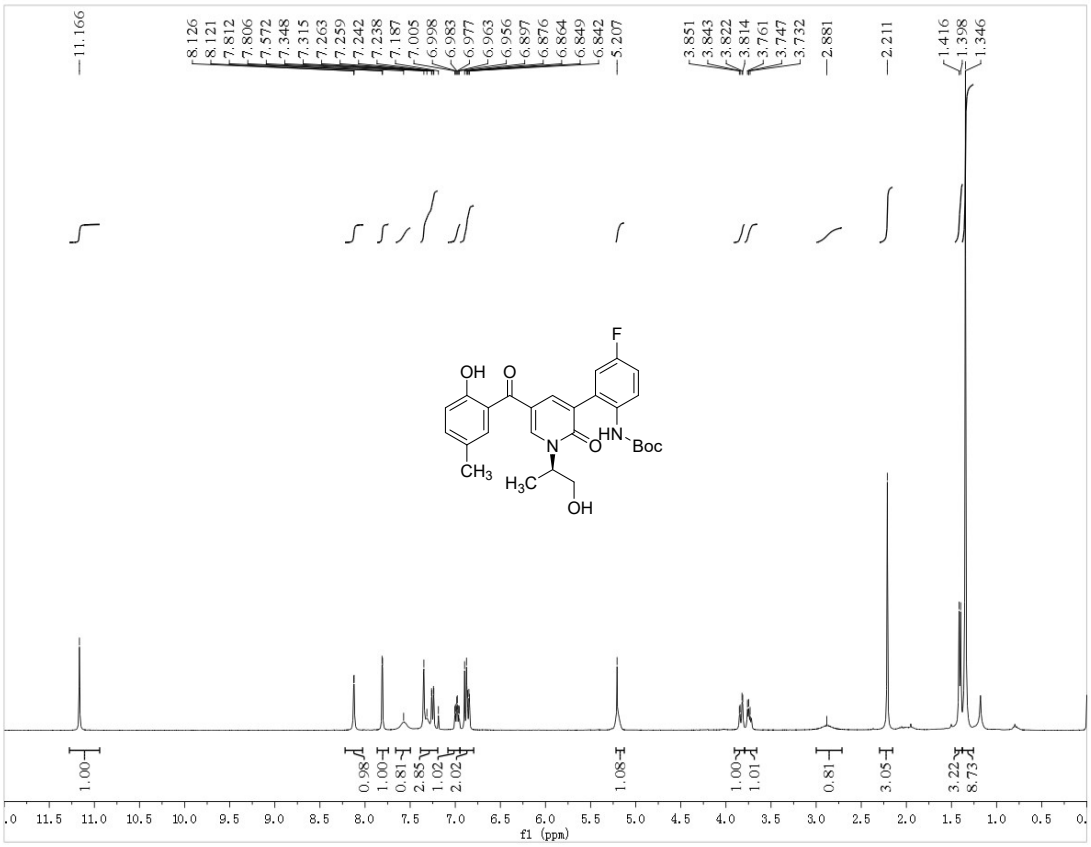


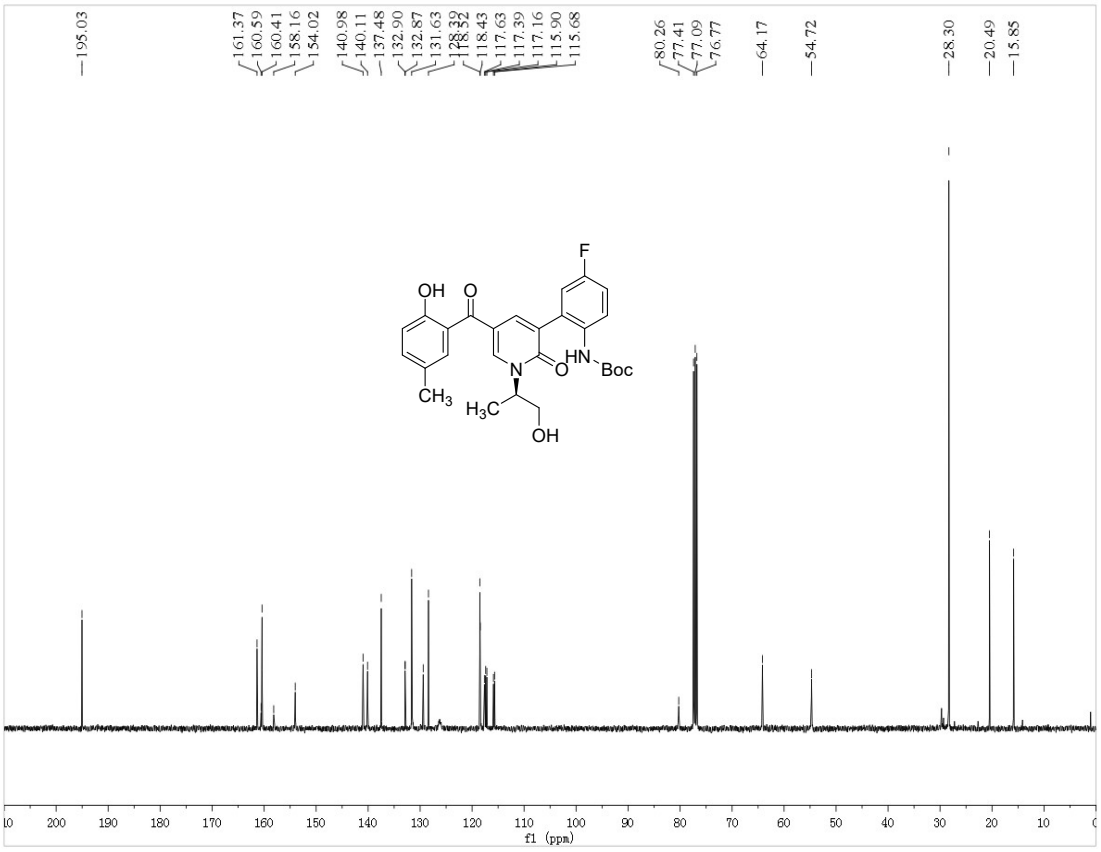
^{1}H and ^{13}C NMR of 3eb





^{1}H and ^{13}C NMR of 3ec





^{1}H and ^{13}C NMR of de-Boc 3ec