Supporting Information

Claisen rearrangement enabled efficiently access to biaryl phenols

Ke Yu, Tongxiang Cao*, Shifa Zhu*

Key Lab of Functional Molecular Engineering of Guangdong Province, School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou 510640, China.
E-mail: caotx@scut.edu.cn
E-mail: zhusf@scut.edu.cn

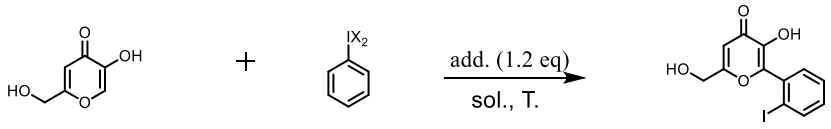
Table of Contents

1 General information

All reagents were purchased from commercial suppliers (such as Energy Chemical, MACKLIN, J&K Scientific) and used without further purification or prepared as described in the literature. All reactions were carried out under an inert atmosphere of dry N_2 in Schlenk tube, solvents were purified by standard method. ^{1}H, ^{13}C, ^{19}F NMR spectra were recorded on a Bruker AVANCE 400 and Bruker AVANCE 500, ^{1}H NMR and ^{13}C NMR chemical shifts were determined relative to internal standard TMS at δ 0.0 or DMSO δ 2.5 and ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as external standard. Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad. Mass spectra (HRMS) were obtained using Agilent UHD Accurate Mass Q-TOF LC/MS (ESI) mass spectrometer. Melting points were determined using a hot stage apparatus. All reagents were used as received from commercial sources, unless specified otherwise, or prepared as described in the literature.

2 optimization of reaction conditions

Table 1 Optimization of the reaction conditions[a]



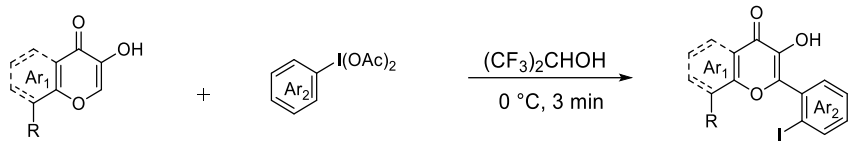
1a **2a** **3a**

Entry	Sol.	T. (°C)	2a, equiv	X	Additive	3a[b] (%)
1	THF	rt	1.5	OAc	–	trace
2	CH_2Cl_2	rt	1.5	OAc	–	trace
3	CH_3CN	rt	1.5	OAc	–	18
4	CH_2Cl_2:CH_3CN (1:1)	rt	1.5	OAc	–	15
5	$(CH_3)_2CHOH$	rt	1.5	OAc	–	trace
6	CH_3COOH	rt	1.5	OAc	–	20
7	CF_3CH_2OH	rt	1.5	OAc	–	16
8	$(CF_3)_2CHOH$	rt	1.5	OAc	–	66
9	$(CF_3)_2CHOH$	rt	1.3	OAc	–	68
10	$(CF_3)_2CHOH$	rt	1.2	OAc	–	70
11	$(CF_3)_2CHOH$	rt	1.2	$OCOCF_3$	–	66
12	$(CF_3)_2CHOH$	rt	1.2	OBz	–	Mess
13	$(CF_3)_2CHOH$	0	1.2	OAc	–	76
14	$(CF_3)_2CHOH$	0	1.2	OAc	BF_3•Et_2O	74
15	$(CF_3)_2CHOH$	0	1.2	OAc	Tf_2O	72

[a] Unless otherwise noted, the reaction was performed under N_2 with 1a (0.2 mmol), 2a and additive (0.24 mmol) in 1.5 mL of solvent at 0 °C. [b] NMR yields.

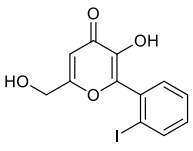
3 Experimental procedures

3.1 General procedure for the synthesis of products 3



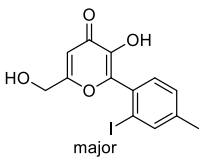
A 10 mL Schlenk flask was evacuated and refilled with nitrogen three times. **2** (0.24 mmol) and $(CF_3)_2CHOH$ (1 mL) were then added to the flask. After cooling to 0 ºC, **1** (0.2 mmol) was dissolved in 1 mL $(CF_3)_2CHOH$ and added to the mixture. The mixture was stirred at 0 ºC for 3 min. Then the mixture was treated with saturated aqueous $NaHCO_3$ solution and extracted with DCM. The organic layer was dried over Na_2SO_4 and concentrated. The obtained residue was purified by silica gel column chromatography to afford the title compound **3**.

Compound 3a: 3-hydroxy-6-(hydroxymethyl)-2-(2-iodophenyl)-4H-pyran-4-one



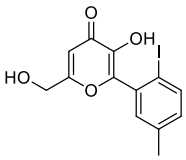
Yield: 74%, 52 mg, pale yellow solid, m. p. 163-165 ℃, Rf= 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.20 (s, 1H), 8.00 (d, J = 7.9 Hz, 1H), 7.64 – 7.40 (m, 2H), 7.24 (td, J = 7.2, 2.5 Hz, 1H), 6.45 (s, 1H), 5.76 (s, 1H), 4.35 (s, 2H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.39, 168.00, 148.30, 142.19, 139.20, 135.64, 131.65, 131.55, 128.24, 109.12, 98.69, 59.60; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_9IO_4$ 366.9438; Found 366.9439.

Compound 3b: 3-hydroxy-6-(hydroxymethyl)-2-(2-iodo-4-methylphenyl)-4H-pyran-4-one (Major)



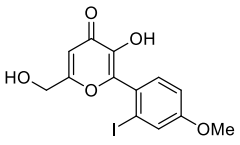
Total yield: 68%, 48 mg, brown solid, m. p. 165-166 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); Major:**^{1}H NMR** (500 MHz, DMSO-*d6*) δ 9.22 (s, 1H), 7.80 (d, J = 7.83, 1H), 7.40 – 7.34 (m, 1H), 7.15 (t, J = 7.74, 1H), 6.47 (s, 1H), 5.79 (s, 1H), 4.36 (s, 2H), 2.22 (s, 3H); Minor: **^{1}H NMR** (500 MHz,DMSO-*d6*) δ 9.15 (s, 1H), 7.85 (d, J = 1.51, 1H), 7.39 – 7.35 (m, 1H), 7.32 (dd, J = 7.98, 1.63, 1H), 6.45 (s, 1H), 5.79 (s, 1H), 4.36 (s, 2H), 2.33 (s, 3H); **^{13}C NMR** (126 MHz, DMSO-*d*6) δ 174.74 (minor), 174.67 (major), 168.62 (major), 168.33 (minor), 148.70, 142.79, 142.59, 142.16, 139.92, 139.84, 136.72, 135.56, 133.16, 132.17, 131.55, 130.23, 129.27, 109.66 (major), 109.41(minor), 100.81 (major), 98.92(minor), 59.97 (major), 59.95(minor), 20.75(minor), 20.47 (major); $[M+Na]^+$ Calcd for $C_{13}H_{11}IO_4$ 380.9594; Found 380.9594.

Compound 3c: 3-hydroxy-6-(hydroxymethyl)-2-(2-iodo-5-methylphenyl)-4H-pyran-4-one



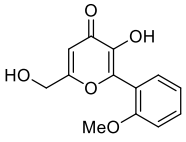
Yield: 18%, 13 mg, pale yellow solid, m. p. 200-202 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (500 MHz,DMSO-*d*6) δ 9.18 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.32 (s, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.44 (s, 1H), 5.76 (t, *J* = 6.1 Hz, 1H), 4.34 (d, *J* = 5.9 Hz, 2H), 2.30 (s, 3H); **^{13}C NMR** (126 MHz, DMSO-*d*6) δ 174.28, 167.90, 148.31, 142.06, 138.87, 137.91, 135.44, 132.41, 132.02, 108.98, 94.58, 59.48, 20.33; **HRMS** (ESI–TOF) m/z: [M+Na] $^{+}$ Calcd for $C_{13}H_{11}IO_4$ 380.9594; Found 380.9595.

Compound 3d: 3-hydroxy-6-(hydroxymethyl)-2-(2-iodo-4-methoxyphenyl)-4H-pyran-4-one



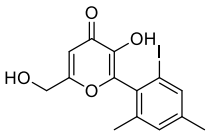
Yield: 70%, 52 mg, pale yellow solid, m. p. 168-170 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (400 MHz, DMSO- *d*6) δ 9.06 (s, 1H), 7.58 – 7.48 (m, 1H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.15 – 6.94 (m, 1H), 6.42 (s, 1H), 5.75 (t, *J* = 6.2 Hz, 1H), 4.34 (s, *J* = 4.9 Hz, 2H), 3.81 (s, 3H); **^{13}C NMR** (101 MHz, DMSO- *d*6) δ 174.28, 167.82, 160.40, 148.20, 142.21, 132.16, 127.89, 124.12, 114.08, 108.91, 99.16, 59.52, 55.73; **HRMS** (ESI–TOF) m/z: [M+Na] $^{+}$ Calcd for $C_{13}H_{11}IO_5$ 396.9543; Found 396.9547.

Compound 3e: 3-hydroxy-6-(hydroxymethyl)-2-(2-methoxyphenyl)-4H-pyran-4-one



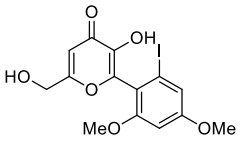
Yield: 43 %, 21mg, brown solid, m. p. 140-142 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.82 (s, 1H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.39 (s, 1H), 5.69 (t, *J* = 6.1 Hz, 1H), 4.31 (d, *J* = 5.9 Hz, 2H), 3.78 (s, 3H); **^{13}C NMR** (126 MHz, DMSO-*d*6) δ 174.04, 167.84, 157.05, 145.43, 142.57, 131.61, 130.97, 120.12, 119.41, 111.97, 108.71, 59.64, 55.75; **HRMS** (ESI–TOF) m/z: [M+Na] $^{+}$ Calcd for $C_{13}H_{12}IO_5$ 271.0577; Found 271.0583.

Compound 3f: 3-hydroxy-6-(hydroxymethyl)-2-(2-iodo-4,6-dimethylphenyl)-4H-pyran-4-one



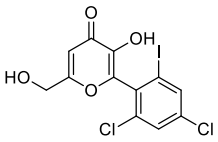
Yield: 78%, 58 mg, pale yellow solid, m. p. 228-230 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 9.12 (s, 1H), 7.63 (d, *J* = 1.5 Hz, 1H), 7.17 (d, *J* = 1.6 Hz, 1H), 6.44 (s,1H), 5.76 (t, *J* = 6.2 Hz, 1H), 4.33 (dd, *J* = 6.0, 2.1 Hz, 2H), 2.27 (s, 3H), 2.16 (s, 3H); **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 174.25, 168.17, 148.31, 142.49, 141.71, 139.03, 136.61, 132.34, 130.55, 109.18, 100.26, 59.58, 20.24, 20.00; **HRMS** (ESI–TOF) m/z: [M+Na] $^{+}$ Calcd for $C_{14}H_{13}IO_4$ 394.9751; Found 394.9752.

Compound 3g: 3-hydroxy-6-(hydroxymethyl)-2-(2-iodo-4,6-dimethylphenyl)-4H-pyran-4-one



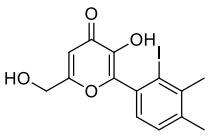
Yield: 81 %, 65 mg, pale yellow solid, m. p. 202-204 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.89 (s, 1H), 7.10 (d, J = 2.2 Hz, 1H), 6.70 (d, J = 2.2 Hz,1H), 6.41 (s, 1H), 5.76 (t, J = 6.2 Hz, 1H), 4.32 (d, J = 6.1 Hz, 2H), 3.82 (s, 3H), 3.73 (s, 3H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 174.70, 168.51, 162.70, 159.26, 147.11, 143.72, 117.82, 115.66, 109.43, 101.93, 99.33, 60.01, 56.60, 56.29; **HRMS** (ESI–TOF) m/z: [M+Na] $^{+}$ Calcd for $[C_{14}H_{13}IO_6]^{+}$ 426.9649; Found 426.9653.

Compound 3h: 2-(2,4-dichloro-6-iodophenyl)-3-hydroxy-6-(hydroxymethyl)-4H-pyran-4-one



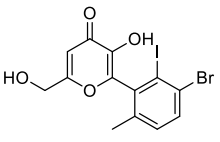
Yield: 66%, 54 mg, pale yellow solid, m. p. 234-236 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (500 MHz, DMSO-*d*6) δ 9.52 (s, 1H), 8.10 (d, J = 1.9 Hz, 1H), 7.87 (d, J = 2.0 Hz, 1H), 6.47 (s, 1H), 5.78 (t, J = 6.2 Hz, 1H), 4.35 (d, J = 6.1 Hz, 2H); **^{13}C NMR** (126 MHz, DMSO-*d*6) δ 174.08, 168.33, 145.74, 142.95, 136.97, 136.36, 134.31, 133.45, 129.03, 109.47, 102.20, 59.47; **HRMS** (ESI–TOF) m/z: [M+H] $^{+}$ Calcd for $C_{12}H_7Cl_2IO_4$ 412.8839; Found 412.8840.

Compound 3i: 3-hydroxy-6-(hydroxymethyl)-2-(2-iodo-3,4-dimethylphenyl)-4H-pyran-4-one



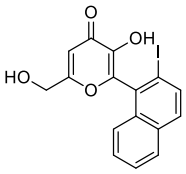
Yield: 62%, 46 mg, pale yellow solid, m. p. 181-183 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (500 MHz,DMSO-*d*6) δ 9.02 (s, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.16 (d, J = 7.6 Hz, 1H), 6.44 (s, 1H), 5.76 (t, J = 6.1 Hz, 1H), 4.34 (d, J = 5.2 Hz, 2H), 2.45 (s, 3H), 2.38 (s, 3H); **^{13}C NMR** (126 MHz, DMSO-*d*6) δ 174.71, 167.96, 150.21, 142.10, 140.58, 139.26, 134.68, 129.83, 128.68, 109.25, 106.84, 59.72, 25.81, 21.79; **HRMS** (ESI–TOF) m/z: [M+H] $^{+}$ Calcd for $C_{14}H_{13}IO_4$ 372.9932; Found 372.9933.

Compound 3j: 2-(3-bromo-2-iodo-6-methylphenyl)-3-hydroxy-6-(hydroxymethyl)-4H-pyran-4-one



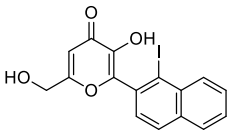
Yield: 49%, 43 mg, brown solid, m. p. 232-235 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.32 (s, 1 H), 7.74 (d, J = 8.14, 1H), 7.32 (d, J = 8.21, 1H), 6.46 (s, 1H), 5.79 (t, J = 6.14, 1H), 4.35 (d, J = 5.20, 2H), 2.17 (s, 3H).; **^{13}C NMR** (126 MHz, DMSO-*d*6) δ 174.32, 168.20, 148.83, 142.08, 138.17, 138.09, 133.72, 131.59, 127.27, 109.43, 108.07, 59.55, 19.66; **HRMS** (ESI–TOF) m/z: [M+H] $^{+}$ Calcd for $C_{13}H_{10}B_rIO_4$ 436.8880; Found 436.8883.

Compound 3k: 3-hydroxy-6-(hydroxymethyl)-2-(2-iodonaphthalen-1-yl)-4H-pyran-4-one



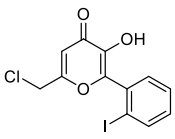
Yield: 69%, 57 mg, brown solid, m. p. 221-223 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (500 MHz, DMSO-*d*6) δ 9.26 (s, 1H), 8.03 (d, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 8.7 Hz, 1H), 7.65 – 7.53 (m, 3H), 6.55 (s, 1H), 5.78 (t, *J* = 6.1 Hz, 1H), 4.36 (d, *J* = 6.0 Hz, 2H); **^{13}C NMR** (126 MHz, DMSO-*d*6) δ 174.66, 168.94, 147.64, 143.75, 135.57, 133.66, 132.58, 132.41, 132.01, 128.89, 128.54, 127.36, 125.57, 109.88, 100.37, 60.02; **HRMS** (ESI–TOF) m/z: [M+Na] $^{+}$ Calcd for $C_{16}H_{11}IO_4$ 416.9594; Found 416.9597.

Compound 3l: 3-hydroxy-6-(hydroxymethyl)-2-(1-iodonaphthalen-2-yl)-4H-pyran-4-one



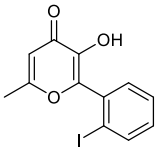
Yield: 42%, 33 mg, brown solid, m. p. 208-210 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:2); **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 9.27 (s, 1 H), 8.23 (d, *J* = 8.26, 1H,), 8.09 (d, *J* = 8.32, 1H), 8.02 (d, *J* = 8.01, 1H), 7.77 – 7.66 (m, 2H), 7.56 (d, *J* = 8.39, 1H), 6.50 (s, 1H), 5.79 (t, 1H), 4.38 (d, *J* = 4.61, 2H); **^{13}C NMR** (126 MHz, DMSO-*d*6) δ 174.83, 168.43, 149.97, 142.66, 135.85, 134.59, 133.99, 132.91, 129.35, 129.21, 129.12, 128.45, 128.08, 109.65, 105.78, 60.00.; **HRMS** (ESI–TOF) m/z: [M+Na] $^{+}$ Calcd for $C_{16}H_{11}IO_4$ 416.9594; Found 416.9596.

Compound 3m: 6-(chloromethyl)-3-hydroxy-2-(2-iodophenyl)-4H-pyran-4-one



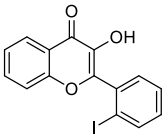
Yield: 84%, 61 mg, pale yellow solid, m. p. 158-160 ℃, Rf = 0.3 (petroleum ether/EtOAc= 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.8 Hz, 1H), 7.48 (dd, *J* = 19.5, 7.4 Hz, 2H), 7.16 (t, *J* = 7.6 Hz, 1H), 6.64 (s, 1H), 4.40 (s, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.53, 162.38, 148.46, 142.43, 139.97, 134.58, 131.78, 131.49, 128.18, 111.72, 97.05, 41.11; **HRMS** (ESI–TOF) m/z: [M+H] $^{+}$ Calcd for $C_{12}H_8ClIO_3$ 362.9280; Found 362.9281.

Compound 3n: 3-hydroxy-2-(2-iodophenyl)-6-methyl-4H-pyran-4-one



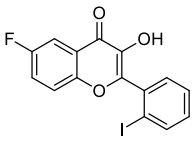
Yield: 60%, 39 mg, pale yellow solid, m. p. 223-225 ℃, Rf = 0.3 (petroleum ether/EtOAc= 1:1); **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 9.11 (s, 1H), 8.00 (d, *J* = 7.9 Hz, 1H), 7.60 – 7.43 (m, 2H), 7.24 (td, *J* = 7.4, 6.7, 2.3 Hz, 1H), 6.36 (s, 1H), 2.30 (s, 3H); **^{13}C NMR** (126 MHz, DMSO-*d*6) δ = 174.72, 165.40, 148.84, 142.26, 139.61, 136.08, 131.98, 131.89, 128.63, 111.87, 99.01, 19.74; **HRMS** (ESI–TOF) m/z: [M+Na] $^{+}$ Calcd for $C_{12}H_9IO_3$ 350.9488; Found 350.9492.

Compound 3o: 3-hydroxy-2-(2-iodophenyl)-4H-chromen-4-one



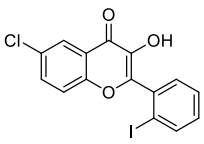
Yield: 79%, 57 mg, brown solid, m. p. 158-160 ℃, Rf = 0.4 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 – 8.26 (m, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.76 – 7.66 (m, 1H), 7.62 – 7.39 (m, 4H), 7.20 (td, *J* = 7.8, 1.7 Hz, 1H), 6.73 (s, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.44, 155.53, 147.90, 139.77, 138.13, 135.34, 133.58, 131.38, 131.15, 127.87, 125.39, 124.47, 121.23, 118.29, 96.65; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{15}H_9IO_3$ 386.9488; Found 386.9491.

Compound 3p**:** 6-fluoro-3-hydroxy-2-(2-iodophenyl)-4H-chromen-4-one



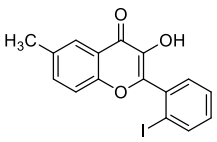
Yield: 80%, 61 mg, pale yellow solid, m. p. 171-173 ℃, Rf = 0.3 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.0 Hz, 1H), 7.92 (dd, *J* = 8.2, 3.1 Hz, 1H), 7.62 – 7.40 (m, 4H), 7.21 (t, *J* = 7.7 Hz, 1H), 6.87 (s, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.83, 158.93 (d, *J* 246.78), 150.12 (d, *J* 338.51), 139.78, 137.90, 135.06, 131.52, 131.14, 127.90, 122.21 (d, *J* 7.95), 122.21 (d, *J* 25.70), 120.51, 120.43, 109.85 (d, *J* = 23.87), 96.57; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -114.3; HRMS (ESI–TOF) m/z: [M+Na] + Calcd for $C_{15}H_9FIO_3$ 404.9394; Found 404.9397.

Compound 3q: 6-chloro-3-hydroxy-2-(2-iodophenyl)-4H-chromen-4-one



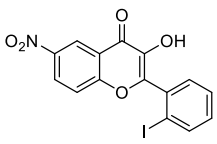
Yield: 75%, 60 mg, pale yellow solid, m. p. 194-196 ℃, Rf = 0.3 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 9.50 (s, 1H), 8.10 (d, *J* = 2.6 Hz, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 7.83 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.74 (d, *J* = 9.0 Hz, 1H), 7.63 – 7.52 (m, 2H), 7.29 (td, *J* = 7.6, 1.9 Hz, 1H); **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 171.88, 153.15, 149.94, 138.86, 138.70, 135.61, 133.52, 131.60, 131.23, 129.07, 127.97, 123.58, 123.03, 120.77, 98.22; **HRMS** (ESI–TOF) m/z: $[M+H]^+$ Calcd for $C_{15}H_8ClIO_3$ 398.9280; Found 398.9285.

Compound 3r: 3-hydroxy-2-(2-iodophenyl)-6-methyl-4H-chromen-4-one



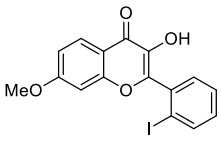
Yield: 63%, 48 mg, pale yellow solid, m. p. 181-183 ℃, Rf = 0.3 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.59 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.54 – 7.42 (m,3H), 7.19 (td, *J* = 7.7, 1.7 Hz, 1H), 6.70 (s, 1H), 2.49 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ173.36, 153.93, 147.73, 139.77, 138.04, 135.45, 135.09, 134.49, 131.34, 131.14, 127.86, 124.47, 120.91, 118.06, 96.68, 20.75; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{11}IO_3$ 400.9645; Found 400.4648.

Compound 3s: 3-hydroxy-2-(2-iodophenyl)-6-nitro-4H-chromen-4-one



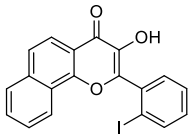
Yield: 60%, 49 mg, pale yellow solid, m. p. 205-207 ℃, Rf = 0.2 (petroleum ether/EtOAc= 1:1); **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 8.88 (d, J = 2.8 Hz, 1H), 8.56 (d, J = 9.2 Hz, 1H), 8.06 (d, J = 7.9 Hz, 1H), 7.94 (d, J = 9.2 Hz, 1H), 7.69 – 7.53 (m, 2H), 7.32 (t, J = 7.5 Hz, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 172.52, 157.55, 150.45, 143.90, 139.31, 139.14, 135.45, 132.01, 131.52, 128.25, 127.83, 121.98, 121.40, 120.72, 98.41; **HRMS** (ESI–TOF) m/z: [M+H] $^{+}$ Calcd for $C_{15}H_8INO_5$ 409.9520; Found 409.9522.

Compound 3t: 3-hydroxy-2-(2-iodophenyl)-7-methoxy-4H-chromen-4-one



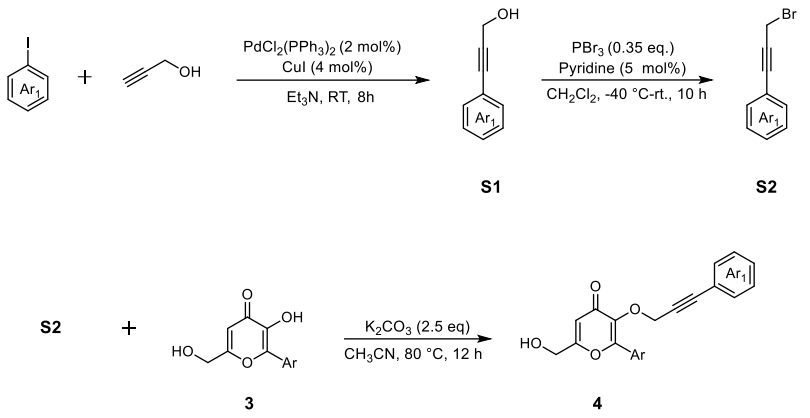
Yield: 67%, 48 mg, pale yellow solid, m. p. 177-179 ℃, Rf = 0.3 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.18 (d, J = 8.9 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 7.02 (d, J = 8.8 Hz, 1H), 6.91 (s, 1H), 6.58 (s, 1H), 3.91 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.93, 164.40, 157.75, 147.19, 139.98, 137.97, 135.65, 131.54, 131.36, 128.14, 126.89, 115.30, 115.14, 99.97, 97.02, 55.90; **HRMS** (ESI–TOF) m/z: [M+Na] $^{+}$ Calcd for $C_{16}H_{11}IO_4$ 416.9594; Found 416.9594.

Compound 3u: 3-hydroxy-2-(2-iodophenyl)-4H-benzo[h]chromen-4-one



Yield: 70%, 58mg, pale yellow solid, m. p. 203-205 ℃, Rf = 0.2 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.66 (d, J = 8.1 Hz, 1H), 8.23 (d, J = 8.8 Hz, 1H), 8.13 – 8.06 (m, 1H), 7.96 (d, J = 7.9 Hz, 1H), 7.81 (d, J = 8.7 Hz, 1H), 7.76 – 7.65 (m, 3H), 7.61 – 7.52 (m, 1H), 7.30 – 7.20 (m, 1H), 6.92 (s, 1H) ; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.76, 153.96, 147.54, 140.62, 140.06, 136.17, 135.96, 132.18, 132.10, 130.07, 128.61, 128.58, 127.76, 125.60, 124.69, 123.36, 120.91, 118.06, 97.30; **HRMS** (ESI–TOF) m/z: [M+Na] $^{+}$ Calcd for $C_{19}H_{11}IO_3$ 436.9845; Found 436.9646.

3.2 General procedre for the synthesis of substrate 4

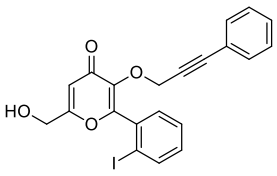


To a stirred solution of substituted aryl iodide (5 mmol, 1.0 equiv.) in triethylamine (50 mL) under nitrogen were sequentially added $Pd(PPh_3)_2Cl_2$ (0.1 mmol, 2 mol%) and CuI (0.2 mmol, 4 mol%) at room temperature. The mixture was allowed to stir for 10 minutes. Then propargyl alcohol (6 mmol, 1.2 equiv.) was added. The mixture was allowed to stir 8 hours. After completion, water was added and the solution was extracted with CH_2Cl_2. The organic phase was dried with anhydrous Na_2SO_4 and concentrated under vacuo. The product **S1** was obtained by column chromatography on silica gel using petroleum ether/ethyl acetate.

To a stirred solution of **S1**(4 mmol, 1.0 equiv.) in Diethylether (30 mL) under nitrogen were sequentially added pyridine (0.2 mmol, 5 mol%) at −40 °C. Phosphorus tribromide (1.4 mmol, 0.35 equiv.) was added over a period of 10 minutes from a dropping funnel, and the mixture was stirred for 30 minutes resulting in an orange solution and a white solid suspension. The temperature was allowed to increase to room temperature. After completion, saturated aqueous sodium chloride solution was added to the reaction solution, and the organic layer was extracted with a separating funnel. The organic layer was extracted from the aqueous layer three times with 20 mL of ethyl acetate , and the organic layer was washed twice with 20 mL of water, twice with 20 mL of saturated aqueous sodium hydrogen carbonate solution, and once with 20 mL of a saturated aqueous sodium chloride solution. The organic phase was dried with anhydrous Na_2SO_4 and concentrated under vacuo. The product **S2** was obtained by column chromatography on silica gel using petroleum ether/ethyl acetate.[1]

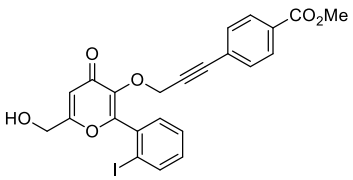
To a solution of **3** (1 mmol, 1 equiv.) and K_2CO_3 (2.5 mmol, 2.5 equiv.) in CH_3CN (20 mL) was added **S2** (1.5 mmol, 1.5 equiv.) at room temperature. The reaction mixture was stirred at 80 ºC (oil bath) for 12 hours. After completion, the reaction was cooled down to room temperature, diluted with EtOAc and filtered through silica gel to remove the solid. The crude product was concentrated under vacuo. The product **4** was obtained by column chromatography on silica gel using petroleum ether/ethyl acetate.

Compound 4a



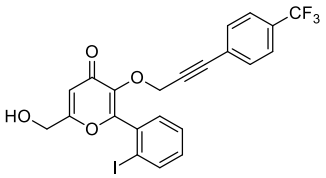
Pale yellow solid, m. p. 93-95 ℃, Rf = 0.3 (petroleum ether/EtOAc= 3:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.9 Hz, 1H), 7.50 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.30 – 7.21 (m, 5H), 7.10 (td, *J* = 7.7, 1.7 Hz, 1H), 6.71 (s, 1H), 5.02 (s, 2H), 4.56 (s, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.14, 168.27, 159.01, 142.20, 139.53, 135.03, 131.90, 131.75, 131.61, 128.67, 128.22, 127.78, 122.26, 112.53, 97.20, 87.84, 84.12, 60.56, 59.86; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{15}IO_4$ 480.9907; Found 480.9914.

Compound 4b



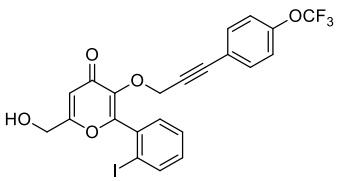
Pale yellow solid, m. p. 138-140 ℃, Rf = 0.2 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.34 (dd, *J* = 19.2, 7.8 Hz, 3H), 7.10 (t, *J* = 7.8 Hz, 1H), 6.69 (s, 1H), 5.01 (s, 2H), 4.56 (s, 2H), 3.87 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.21, 168.40, 166.79, 159.17, 142.47, 139.88, 135.25, 132.11, 132.01, 131.94, 130.08, 129.61, 128.09, 127.28, 112.90, 97.39, 87.43, 87.10, 60.89, 59.97, 52.60; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{17}IO_6$ 538.9962; Found 538.9967.

Compound 4c



Pale yellow solid, m. p. 140-142 ℃, Rf = 0.3 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.01, 1.13, 1H), 7.51 (d, *J* = 8.18, 2H), 7.48 (dd, *J* = 7.68, 1.72, 1H), 7.38 (td, *J* = 7.58, 1.20, 3H), 7.13 (td, *J* = 7.73, 1.76, 1H), 6.71 (s, 1H), 5.03 (s, 2H), 4.58 (s, 2H), 4.50 (s, 1H); **^{13}C NMR** (101MHz, $CDCl_3$) 177.02, 168.21, 158.95, 142.22, 139.64, 134.97, 132.17, 131.73, 130.33 (q, *J* = 32.69), 127.85, 126.11, 126.10, 125.15 (q, *J* = 3.73), 122.47, 112.62, 97.09, 86.58, 86.28, 60.62, 59.68; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.8; **HRMS** (ESI–TOF) m/z: $C_{22}H_{14}F_3IO_4$ 548.9781; Found 548.9787.

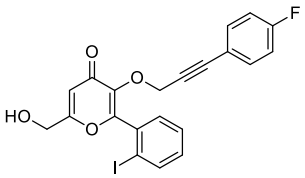
Compound 4d



Pale yellow solid, m. p. 132-135 ℃, Rf = 0.3 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.01, 1H), 7.48 (d, *J* = 7.58, 1H), 7.37 (t, *J* = 7.55, 1H), 7.32 (d, *J* = 8.64, 2H), 7.12 (dt, *J* = 13.05, 4.84, 3H), 6.70 (s, 1H), 5.00 (s, 2H), 4.57 (s, 3H); **^{13}C NMR** (101MHz, $CDCl_3$) δ 177.07, 168.21, 158.96, 149.16, 149.14, 142.22, 139.62, 135.02, 133.51, 131.75, 131.67, 127.82, 121.06, 120.67, 120.34 (q, *J*

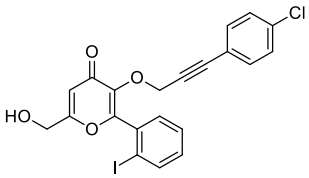
257.88), 112.61, 97.11, 86.31, 85.01, 76.79, 60.62, 59.75; **^{19}F NMR**(471 MHz, $CDCl_3$) δ -57.77; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $[M+Na]^+$ Calcd for $C_{22}H_{14}F_3IO_5$ 564.9730; Found 564.9731.

Compound 4e



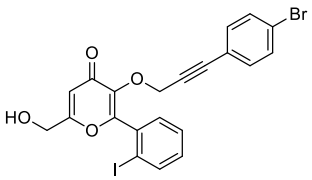
Pale yellow solid, m. p. 130-132 ℃, Rf = 0.3 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.51 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.35 – 7.26 (m, 2H), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H), 6.98 (t, *J* = 8.7 Hz, 2H), 6.70 (s, 1H), 5.04 (s, 2H), 4.59 (s, 2H), 4.04 (s, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.97, 167.71, 162.69 (d, *J* = 249.97), 158.86, 142.25, 139.61, 135.07, 133.97, 133.88, 131.79, 131.63, 127.80, 118.43 (d, *J* = 3.56), 115.64, 115.42, 112.74, 97.11, 86.73, 83.87, 60.74, 59.77; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.16; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{14}FIO_4$ 498.9813; Found 49839813.

Compound 4f



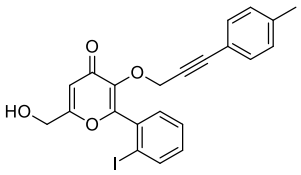
Pale yellow solid, m. p. 132-134 ℃, Rf = 0.2 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.9 Hz, 1H), 7.49 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.22 (m, 4H), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H), 6.72 (s, 1H), 5.02 (s, 2H), 4.59 (d, *J* = 5.5 Hz, 2H), 4.46 (d, *J* = 24.2 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.06, 168.13, 158.97, 142.20, 139.62, 134.99, 134.73, 133.21, 131.78, 131.69, 128.59, 127.83, 120.79, 112.61, 97.15, 86.64, 85.11, 60.65, 59.77; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{14}ClIO_4$ 514.9517; Found 514.9520.

Compound 4g



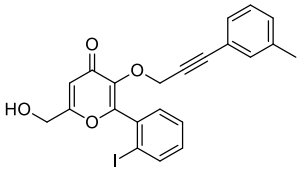
Pale yellow solid, m. p. 145-147 ℃, Rf = 0.2 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.9 Hz, 1H), 7.50 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.42 (dq, *J* = 7.7, 1.7, 1.0 Hz, 3H), 7.20 – 7.13 (m, 3H), 6.69 (s, 1H), 5.04 (s, 2H), 4.59 (d, *J* = 5.8 Hz, 2H), 3.78 (t, *J* = 6.9 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.86, 167.51, 158.80, 142.24, 139.62, 135.04, 131.78, 131.66, 131.51, 127.82, 122.99, 121.30, 112.80, 97.11, 86.67, 85.34, 60.79, 59.72. **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{14}BrIO_4$ 558.9012; Found 558.9012.

Compound 4h



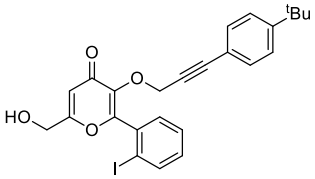
Pale yellow solid, m. p. 132-134 ℃, Rf = 0.2 (petroleum ether/EtOAc= 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.0, 1.2 Hz,1H), 7.54 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.39 (td, *J* = 7.6, 1.2 Hz, 1H), 7.26 – 7.21 (m, 2H), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 2H), 6.68 (s, 1H), 5.08 (s, 2H), 4.58 (s, 2H), 2.35 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.91, 167.26, 158.80, 142.29, 139.57, 138.82, 135.17, 131.85, 131.57, 128.99, 127.79, 119.30, 112.86, 97.17, 88.03, 83.50, 60.85, 59.85, 21.52; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{17}IO_4$ 495.0064; Found 495.0068.

Compound 4i



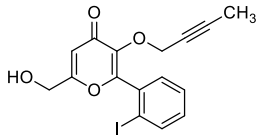
Pale yellow solid, m. p. 111-113 ℃, Rf = 0.2 (petroleum ether/EtOAc= 3:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.53 (dd, *J* = 7.7, 1.7 Hz,1H), 7.37 (td, *J* = 7.6, 1.2 Hz, 1H), 7.27 (q, *J* = 7.8, 6.9 Hz, 4H), 7.12 (td, *J* = 7.7, 1.7 Hz, 1H), 6.69 (s, 1H), 5.04 (s, 2H), 4.56 (s, 2H), 1.29 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.20, 168.25, 159.05, 142.23, 139.59, 137.90, 135.08, 132.55, 131.84, 131.63, 129.59, 129.00, 128.16, 127.82, 122.09, 112.57, 97.23, 88.06, 83.77, 60.62, 59.90, 21.26; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{17}IO_4$ 495.0064; Found 495.0062.

Compound 4j



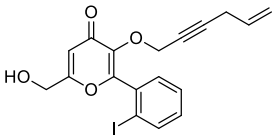
Pale yellow solid, m. p. 141-143 ℃, Rf = 0.3 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.53 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.37 (td, *J* = 7.6, 1.2 Hz, 1H), 7.27 (q, *J* = 7.8, 6.9 Hz, 4H), 7.12 (td, *J* = 7.7, 1.7 Hz, 1H), 6.69 (s, 1H), 5.04 (s, 2H), 4.56 (s, 2H), 1.29 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.17, 167.99, 158.98, 152.01, 142.30, 139.61, 135.20, 131.86, 131.73, 131.64, 127.85, 125.29, 119.34, 112.70, 97.27, 88.13, 83.52, 60.74, 59.97, 34.85, 31.23; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{23}IO_4$ 537.0533; Found 537.0533.

Compound 4k



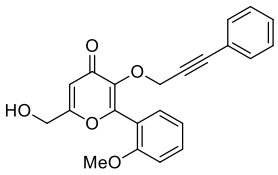
Pale yellow solid, m. p. 80-82 ℃, Rf = 0.4 (petroleum ether/EtOAc= 3:1);**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.46 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.41 (td, *J* = 7.5, 1.2 Hz, 1H), 7.13 (td, *J* = 7.7, 1.8 Hz, 1H), 6.64 (s, 1H), 4.70 (q, *J* = 2.4 Hz, 2H), 4.55 (s, 2H), 1.71 (t, *J* = 2.4 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.21, 168.15, 158.87, 142.18, 139.57, 135.12, 131.85, 131.60, 127.78, 112.52, 97.03, 84.55, 74.12, 60.58, 59.77, 4.08; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{13}IO_4$ 418.9751; Found 418.9756.

Compound 4l



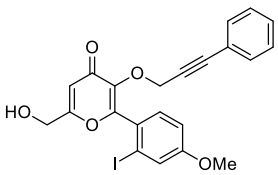
Yellow viscous liquid, Rf = 0.4 (petroleum ether/EtOAc= 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.48 (dd, *J* = 7.7, 1.8 Hz,1H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.14 (td, *J* = 7.7, 1.8 Hz, 1H), 6.65 (s, 1H), 5.67 (ddt, *J* = 12.9, 10.3, 5.2 Hz, 1H), 5.14 (dq, *J* = 17.0, 1.8 Hz, 1H), 5.02 (dq, *J* = 10.0, 1.7 Hz, 1H), 4.81 (t, *J* = 2.2 Hz, 2H), 4.55 (s, 2H), 2.89 (dt, *J* = 5.5, 2.0 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.52, 168.34, 159.17, 142.55, 139.97, 135.45, 132.28, 132.22, 131.97, 128.18, 116.76, 112.94, 97.42, 85.76, 61.00, 60.02, 23.72. **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{15}IO_4$ 444.9907; Found 444.9912.

Compound 4m



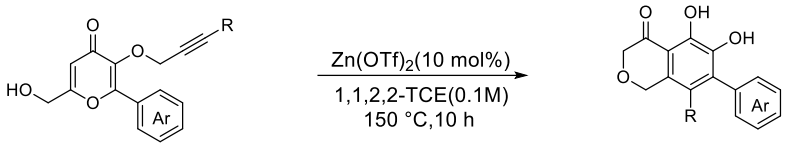
Yellow viscous liquid, Rf = 0.3 (petroleum ether/EtOAc= 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 2H), 7.19 (d, *J* = 5.9 Hz, 5H), 6.91 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.55 (s, 1H), 5.88 (s, 1H), 4.96 (s, 2H), 4.44 (s, 2H), 3.62 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.90, 167.46, 157.37, 156.91, 142.82, 131.97, 131.82, 131.40, 128.49, 128.18, 122.50, 120.20, 119.15, 112.40, 111.30, 87.28, 84.33, 74.18, 60.98, 59.75, 55.59. **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{18}IO_5$ 385.1046; Found 385.1049.

Compound 4n



Yellow viscous liquid, Rf = 0.2 (petroleum ether/EtOAc= 3:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.6 Hz,1 H), 7.40 (d, *J* = 2.5 Hz, 1H), 7.36 – 7.26 (m, 5H), 6.90 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.68 (s, 1H), 5.04 (s, 2H), 4.58 (s, 2H), 3.80 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.44, 168.51, 161.17, 159.39, 142.69, 132.77, 132.21, 128.92, 128.49, 127.57, 125.23, 122.63, 113.97, 112.72, 97.84, 87.99, 84.52, 60.88, 60.19, 55.87; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{17}IO_5$ 511.0013; Found 511.0010.

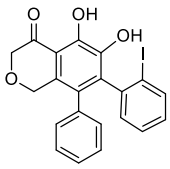
3.3 General procedure for the synthesis of products 5



4 **5**

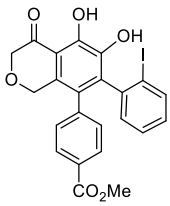
A dry reaction tube was charged with **4** (0.1 mmol) and $Zn(OTf)_2$ (10 mol%), followed by the addition of 1,1,2,2-TCE (0.1 M). The reaction mixture was stirred at 150 °C for 10 h. After completion, the reaction was cooled down to room temperature and diluted with EtOAc and filtered through silica gel to remove the solids. The crude product was concentrated under vacuo. The product **5** was obtained by column chromatography on silica gel using petroleum ether/ethyl acetate.

Compound 5a: 5,6-dihydroxy-7-(2-iodophenyl)-8-phenylisochroman-4-one



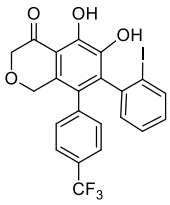
Yield: 56%, 23mg, brown solid, m. p. 183-185 ℃, Rf= 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** δ 11.81 (s, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 9.7 Hz,5H), 7.01 (d, *J* = 7.2 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.88 (t, *J* = 7.7 Hz, 1H), 5.76 (s, 1H), 4.66 – 4.51 (m,2H), 4.41 (q, *J* = 3.0 Hz,2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.73, 148.16, 140.92, 140.56, 138.66, 137.19, 136.33, 130.80, 130.38, 129.96, 129.49, 129.15, 129.05, 128.18, 127.72, 127.61, 127.40, 113.66, 100.09, 72.23, 66.86; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{15}IO_4$ 480.9907; Found 480.9909.

Compound 5b: methyl 4-(5,6-dihydroxy-7-(2-iodophenyl)-4-oxoisochroman-8-yl)benzoate



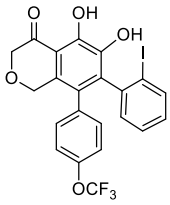
Yield: 51%, 25mg, brown solid, m. p. 201-203 ℃, Rf = 0.3 (petroleum ether/EtOAc=5:1); **^{1}H NMR** δ 11.85 (s, 1H), 7.93 – 7.83 (m, 2H), 7.77 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.19 (td, *J* = 7.5, 1.2 Hz, 1H), 7.12 – 7.08 (m, 1H), 6.96 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.89 (td, *J* = 7.7, 1.7 Hz, 1H), 5.76 (s, 1H), 4.64 – 4.50 (m, 2H), 4.41 (q, *J* = 2.7 Hz, 2H), 3.89 (s, 3H).; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.58, 166.74, 148.54, 141.30, 141.13, 140.12, 138.81, 136.74, 130.70, 130.12, 130.09, 129.76, 129.45, 129.32, 129.18, 129.03, 128.05, 127.77, 113.69, 99.91, 72.22, 66.66, 52.18; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{17}IO_6$ 538.9962; Found 538.9965

Compound 5c: 5,6-dihydroxy-7-(2-iodophenyl)-8-phenylisochroman-4-one



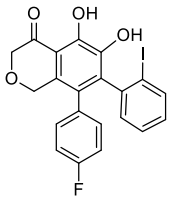
Yield: 48%, 25mg, brown solid, m. p. 191-193 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.84 (s, 1H), 7.76 (d, *J* = 7.88, 1H), 7.45 (t, *J* = 6.51, 2H), 7.31 (d, *J* = 7.44, 1H), 7.22 – 7.16 (m, 1H), 7.12 (d, *J* = 7.49, 1H), 6.96 – 6.85 (m, 2H), 5.80 (s, 1H), 4.60 – 4.48 (q, 2H), 4.39 (q, *J* = 2.77, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.56, 148.63, 141.19, 140.21, 140.02, 138.87, 136.79, 130.64, 130.40, 130.19, 130.06, 129.75, 129.41, 127.84, 127.58, 125.31, 125.16 (d, *J* = 3.78), 124.74 (d, *J* = 3.78), 113.70, 99.88, 72.22, 66.64; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.61; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{14}F_3IO_4$ 548.9781; Found 548.9784.

Compound 5d: 5,6-dihydroxy-7-(2-iodophenyl)-8-phenylisochroman-4-one



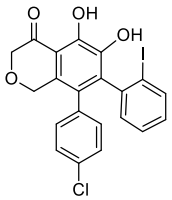
Yield: 47%, 25mg, brown solid, m. p. 190-192 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.82 (s, 1H), 7.76 (d, *J* = 7.93, 1H), 7.19 (dt, *J* = 10.40, 5.72, 2H), 7.02 (t, *J* = 5.75, 3H), 6.96 – 6.82 (m, 2H), 5.83 (s, 1H), 4.62 – 4.50 (q, 2H), 4.39 (q, *J* = 2.91, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.58, 148.49, 148.40, 141.11, 140.22, 138.80, 137.08, 134.98, 131.25 (d, *J* = 31.21), 130.67, 130.34, 129.25, 127.75, 127.62, 120.28 (d, *J* = 44.19), 113.67, 99.93, 77.38, 77.06, 76.75, 72.21, 66.7; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -57.85; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{14}F_3IO_5$ 564.9730; Found 564.9728.

Compound 5e: 8-(4-fluorophenyl)-5,6-dihydroxy-7-(2-iodophenyl)isochroman-4-one



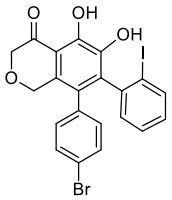
Yield: 46%, 22mg, yellow solid, m. p. 195-197 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.80 (s, 1H), 7.76 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.23 – 7.10 (m, 2H), 6.99 – 6.81 (m, 5H), 5.80 (s, 1H), 4.55 (q, *J* = 3.2 Hz, 2H), 4.38 (q, *J* = 2.7 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) 200.71, 161.92 (d, *J* = 247.1 Hz), 148.40, 141.09, 140.48, 138.85, 137.32, 132.21 (d, *J* = 3.5 Hz), 131.57 (d, *J* = 8.1 Hz), 131.26 (d, *J* = 8.1 Hz), 130.78, 130.58, 129.28, 128.09, 127.83, 115.13 (d, *J* = 41.5 Hz), 114.92 (d, *J* = 41.6 Hz), 113.73, 100.03, 72.29, 66.85; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -114.27; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{14}FIO_4$ 498.9813; Found 498.9813.

Compound 5f: 8-(4-chlorophenyl)-5,6-dihydroxy-7-(2-iodophenyl)isochroman-4-one



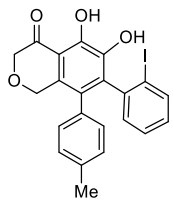
Yield: 52%, 26mg, brown solid, m. p. 195-197 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ11.81 (s, 1H), 7.76 (d, *J* = 7.71, 1H), 7.24 – 7.05 (m, 4 H), 6.91 (dtd, *J* = 11.08, 7.62, 1.68, 3H), 5.84 (s, 1H), 4.54 (q, *J* = 2.31, 2H), 4.38 (q, *J* = 2.31, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.61, 148.40, 141.07, 140.25, 138.81, 137.02, 134.78, 133.44, 131.29, 130.94, 130.67, 130.33, 129.31, 128.47, 128.05, 127.82, 127.78, 113.66, 99.93, 72.20, 66.72; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{14}ClIO_4$ 514.9517; Found 514.9521.

Compound 5g: 8-(4-bromophenyl)-5,6-dihydroxy-7-(2-iodophenyl)isochroman-4-one



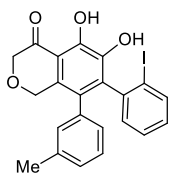
Yield: 45%, 24mg, brown solid, m. p. 200-202 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.73 (s, 1H), 7.23 (ddd, *J* = 8.1, 5.7, 2.1 Hz, 2H), 7.13 (td, *J* = 7.5, 1.1 Hz, 1H), 6.97 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.88 – 6.75 (m, 3H), 5.69 (s, 1H), 4.46 (q, *J* = 1.6 Hz, 2H), 4.30 (q, *J* = 2.2 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.68, 148.50, 141.17, 140.31, 138.93, 137.01, 135.37, 131.70, 131.50, 131.35, 131.08, 130.75, 130.38, 129.41, 127.91, 127.86, 121.80, 113.77, 100.00, 72.30, 66.81; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{14}BrIO_4$ 558.9012; Found 558.9011.

Compound 5h: 5,6-dihydroxy-7-(2-iodophenyl)-8-(p-tolyl)isochroman-4-one



Yield: 39%, 18mg, yellow solid, m. p. 193-195 ℃, R_f = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.79 (s, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.08 – 6.95 (m, 3H), 6.92 – 6.84 (m, 2H), 5.74 (s, 1H), 4.65 – 4.52 (m, 2H), 4.40 (q, *J* = 2.9 Hz, 2H), 2.27 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.76, 147.98, 140.84, 140.67, 138.65, 137.29, 136.95, 133.24, 130.77, 130.56, 129.77, 129.31, 129.19, 129.00, 128.87, 128.42, 127.62, 113.64, 100.04, 72.22, 66.92, 21.18; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{17}IO_4$ 495.0064; Found 495.0064.

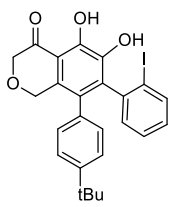
Compound 5i: 5,6-dihydroxy-7-(2-iodophenyl)-8-(m-tolyl)isochroman-4-one



Yield: 64%, 30mg, brown solid, m. p. 178-180 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.80 (s, 1H), 7.78 (dt, *J* = 8.0, 1.4 Hz, 1H), 7.19 (tdd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 7.08 (dt, *J* = 11.1, 7.5 Hz, 1H), 7.03 – 6.95 (m, 3H), 6.88 (tt, *J* = 7.6, 1.8 Hz, 1H), 6.84 – 6.78 (m, 1H), 5.84 (s, 1H), 4.81 – 4.49 (m, 2H), 4.41 (q, *J* = 2.1 Hz, 2H), 2.25 (d, *J* = 18.9 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.79, 140.89, 140.64, 138.62, 137.68, 137.25, 136.19, 130.77,

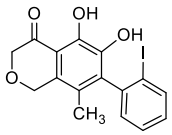
130.64, 130.32, 130.24, 129.31, 129.03, 128.02, 127.57, 126.95, 126.59, 113.64, 100.09, 72.22, 66.92, 21.35; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{17}IO_4$ 495.0064; Found 495.0062.

Compound 5j: 8-(4-(tert-butyl)phenyl)-5,6-dihydroxy-7-(2-iodophenyl)isochroman-4-one



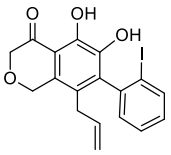
Yield: 47%, 24mg, brown solid, m. p. 200-202 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.78 (s, 1H), 7.78 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.23 – 7.12 (m, 3H), 7.05 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.92 (dt, *J* = 7.8, 2.3 Hz, 2H), 6.87 (td, *J* = 7.7, 1.7 Hz, 1H), 5.84 (s, 1H), 4.59 (q, *J* = 15.2 Hz, 2H), 4.40 (q, *J* = 4.1 Hz, 2H), 1.25 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.79, 150.14, 148.02, 140.85, 140.70, 138.58, 137.41, 133.21, 130.79, 130.56, 129.55, 129.24, 129.07, 128.88, 127.53, 124.95, 124.47, 113.64, 100.14, 72.24, 66.97, 34.44, 31.22; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{23}IO_4$ 537.0533; Found 537.0529.

Compound 5k: 5,6-dihydroxy-7-(2-iodophenyl)-8-methylisochroman-4-one



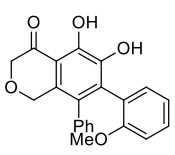
Yield: 50%, 20mg, light yellow solid, m. p. 183-185 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.62 (s, 1H), 8.00 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.48 (td, *J* = 7.5, 1.2 Hz, 1H), 7.23 – 7.04 (m, 2H), 5.64 (s, 1H), 5.00 – 4.75 (m, 2H), 4.40 (s, 2H), 1.82 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.36, 146.92, 141.18, 140.78, 139.25, 138.24, 129.98, 129.72, 129.56, 128.52, 122.21, 113.70, 99.32, 71.81, 66.11, 14.62; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{13}IO_4$ 418.9751; Found 418.9756.

Compound 5l: 8-allyl-5,6-dihydroxy-7-(2-iodophenyl)isochroman-4-one



Yield: 30%, 13mg, brown solid, m. p. 138-140 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.61 (s, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.13 – 6.92 (m, 2H), 5.63 – 5.51 (m, 2H), 4.97 – 4.65 (m, 4H), 4.31 (s, 2H), 2.99 (dd, *J* = 16.5, 5.8 Hz, 1H), 2.80 (dd, *J* = 16.5, 5.5 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 200.65, 147.50, 141.12, 140.69, 139.25, 138.28, 134.97, 131.11, 130.11, 129.79, 128.29, 123.82, 116.14, 114.01, 99.74, 72.11, 65.96, 33.22; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{15}IO_4$ 444.9907; Found 444.9912.

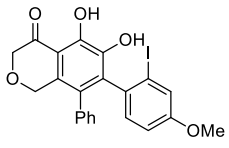
Compound 5m: 5,6-dihydroxy-7-(2-methoxyphenyl)-8-phenylisochroman-4-one



Yield: 54%, 19mg, brown solid, m. p. 163-165 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.80 (s, 1H), 7.23 – 7.12 (m, 4H), 7.01 (t, *J* = 7.0 Hz, 2H), 6.92 (d, *J* = 4.9 Hz, 1H), 6.86 (t, *J* = 7.4 Hz, 1H), 6.75 (d, *J* = 8.3 Hz, 1H), 5.61 (s, 1H), 4.60 (s, 2H),

4.38 (s, 2H), 3.62 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 200.67, 156.36, 148.35, 141.31, 137.14, 132.66, 131.31, 130.17, 129.88, 129.80, 129.61, 129.54, 127.57, 127.51, 127.02, 123.76, 120.23, 113.32, 110.68, 72.23, 66.99, 55.27; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{18}IO_5$ 385.1046; Found 385.1038.

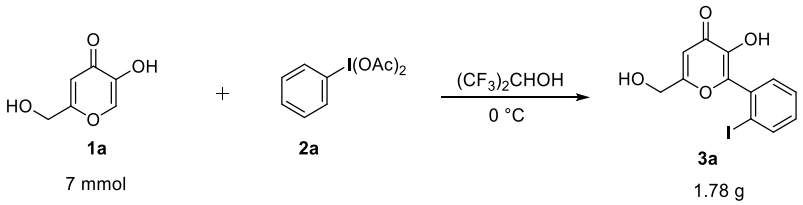
Compound 5n: 5,6-dihydroxy-7-(2-iodo-4-methoxyphenyl)-8-phenylisochroman-4-one



Yield: 58%, 28mg, brown solid, m. p. 128-130 ℃, Rf = 0.4 (petroleum ether/EtOAc=5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.80 (s, 1H), 7.31 (d, *J* = 2.5 Hz, 1H), 7.25 – 7.14 (m, 4H), 7.03 – 6.99 (m, 1H), 6.84 (d, *J* = 8.5 Hz, 1H), 6.74 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.80 (s, 1H), 4.65 – 4.51 (q, 2H), 4.39 (q, *J* = 2.8 Hz, 2H), 3.72 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.71, 158.81, 148.12, 141.25, 136.97, 136.55, 132.61, 131.07, 130.27, 129.92, 129.61, 129.54, 128.21, 127.75, 127.32, 123.66, 114.08, 113.59, 100.06, 72.21, 66.88, 55.35; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{17}IO_5$ 511.0013; Found 511.0019.

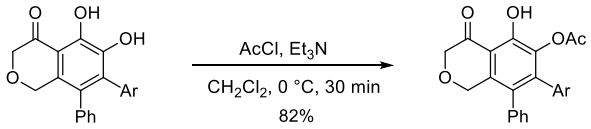
4 Gram-Scale synthesis and product derivatization

4.1 Gram-scale synthesis of 3a



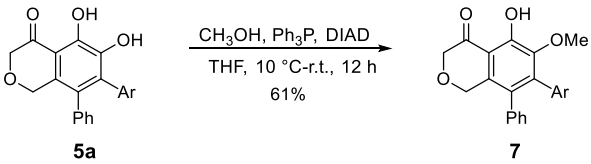
A 100 mL Schlenk flask was evacuated and refilled with nitrogen three times. $PhI(OAc)_2$, **2a** (2.70 g, 8.4 mmol) and $(CF_3)_2CHOH$ (30 mL) were then added to the flask. After cooling to 0 ºC, kojic acid (994 mg, 7 mmol) was dissolved in 10 mL $(CF_3)_2CHOH$ and added dropwise to the mixture within 1 minute. The mixture was stirred at -0 ºC for 3 min. The mixture was treated with saturated aqueous $NaHCO_3$ solution and extracted with DCM. The organic layer was dried over Na_2SO_4 and concentrated. The obtained residue was purified by silica gel column chromatography to afford the title compound **3a** (1.78 g, 74%).

4.2 Procedure for preparation of 6



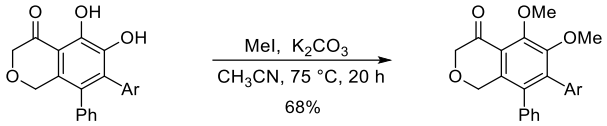
Acetyl chloride (3.4 μL, 0.1 mmol) and triethylamine (17 μL, 0.12 mmol) were added to a solution of **5a** (46 mg, 0.1 mmol) in anhydrous CH_2Cl_2 (1 mL) at 0 °C, then the reaction mixture was stirred at room temperature for 2 hours. After the reaction mixture was poured into ice-cold aq satd NaCl, the whole was extracted with EtOAc. The EtOAc extract was washed with 5% HCl, aq satd $NaHCO_3$, and aq satd NaCl successively, then dried over Na_2SO_4. Removal of the solvent from the EtOAc extract under reduced pressure gave a residue, which was purified by column chromatography (ethyl acetate/petroleum ether = 1:3) to give **6** (41 mg, 82%).[2]

4.3 Procedure for preparation of 7



To a flask was added **5a** (46 mg, 0.1mmol), ethanol (4.5 μL, 0.11 mmol), triphenylphosphine (27mg,1.1 eq), and THF(1mL), then diisopropyl azodicarboxylate (21 mg, 0.1 mmol) was added dropwise to the stirring mixture over the course of 2 min at 10 °C. Then the reaction mixture was stirred at room temperature for 12h. Evaporated the solvent, the residue was purified by flash chromatography(ethyl acetate/petroleum ether = 1:3) to give **7** (29 mg, 82%).

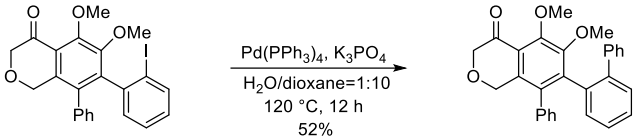
4.4 Procedure for preparation of 8



5a **8**

To the stirring solution of **5a** (1.6 g, 1.0 eq) and K_2CO_3 (4.54g, 5.0 eq) in acetonitrile (20 mL) was added methyl iodide (2.78 g, 3.0 eq) and then stirred at 75 °C for 20 hours. After cooled to room temperature, the mixture was filtrated through a short pad of silica gel. The solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1:3) to give **8** (1.13 g, 68% yield).

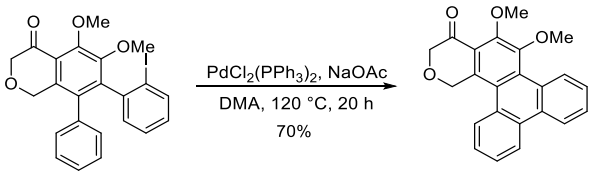
4.5 Procedure for preparation of 9



6 **9**

A mixture of **8** (49 mg, 0.1 mmol), phenylboronic acid (19 mg, 0.15 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) and K_3PO_4 (24 mg, 0.11 mmol) in H_2O (0.1 mL) and dioxane (1 mL) was stirred at 100 °C for 12 h in a sealed tube. After cooled to rt, the mixture was treated with saturated aqueous $NaHCO_3$ solution, extracted with DCM, dried over Na_2SO_4. And then evaporated under reduced pressure to give residue. Purification by column chromatography on silica (ethyl acetate/petroleum ether = 1:5) to give **9** (23 mg, 52% yield).

4.6 Procedure for preparation of 10

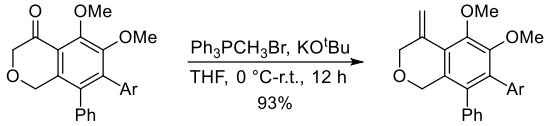


8 **10**

Charge a 25 mL Schlenk tube with **8** (49 mg, 0.1 mmol), $PdCl_2(PPh_3)_2$ (8 mg, 0.01 mmol) and CH_3COONa (27 mg, 0.2 mmol) under a nitrogen atmosphere, followed by addition of DMA (1 ml). Heat the resulting solution

at 120 °C for 20 hours. Cool the reaction mixture to rt. Add HCl solution (10 ml, 1 M) to the reaction mixture.Extract the resulting mixture with dichloromethane. The combined organic layers were dried with Na_2SO_4. And then evaporated under reduced pressure to give residue. Purification by column chromatography on silica (ethyl acetate/petroleum ether = 1:10) to give **10** (35 mg, 70% yield).[3]

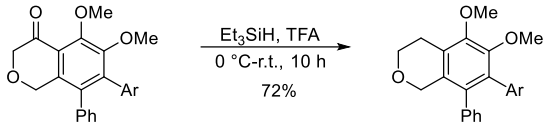
4.7 Procedure for preparation of 11



8 **11**

Methyltriphenylphosphonium bromide (54 mg, 0.15 mmol) was dissolved in THF (1 mL) under a N_2 atmosphere. The solution was cooled to 0 °C, and then potassium tert-butoxide (17 mg, 0.15 mmol) was added. Following stirring for 30 minutes, **8** (49 mg, 0.1 mmol) was added, and then warming to room temperature and stirring for 12 hours. After the reaction was completed , queous NH_4Cl was added to the solution, and organic products were extracted with ethyl acetate. The organic layer was washed with water and brine. The combined organic layers were dried with Na_2SO_4, and then evaporated under reduced pressure to give residue. Purification by column chromatography on silica (ethyl acetate/petroleum ether = 1:20) to give **11** (43 mg, 93% yield).

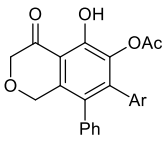
4.8 Procedure for preparation of 12



8 **12**

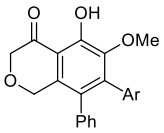
Add triethylsilane (56 μL, 0.35 mmol) slowly to a solution of **8** (49 mg, 0.1 mmol) in TFA (1.5 mL) at 0 °C. And then stir the reaction mixture at room temperature for 10 hours. After the reaction was completed, remove the volatiles in vacuo. Dissolve the residue in EtOAc (5 mL) and Wash the residue with $NaHCO_3$ and 1N HCl. Extract the resulting mixture with dichloromethane.The combined organic layers were dried with Na_2SO_4, and then evaporated under reduced pressure to give residue. Purification by column chromatography on silica (ethyl acetate/petroleum ether = 1:20) to give **12** (35 mg, 72% yield).[4]

Compound 6: 6-hydroxy-7-(2-iodophenyl)-4-oxo-8-phenylisochroman-5-yl acetate



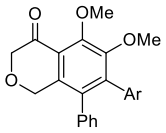
Yield: 82%, 41mg, pale yellow solid, m. p. 173-175 ℃, Rf = 0.2 (petroleum ether/EtOAc= 10:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.83 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.18 (dddd, *J* = 19.0, 15.0, 6.8, 2.5 Hz, 5H), 6.97 – 6.90 (m, 2H), 6.85 (td, *J* = 7.7, 1.7 Hz, 1H), 4.59 (d, *J* = 2.6 Hz, 2H), 4.44 – 4.25 (m, 2H), 1.98 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.60, 168.86, 153.73, 145.59, 140.47, 138.93, 138.07, 136.07, 135.80, 130.95, 130.43, 129.93, 129.58, 129.41, 128.61, 128.31, 128.07, 127.76, 115.39, 99.31, 72.53, 67.45, 20.48; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{17}IO_5$ 523.0010; Found 523.0013.

Compound 7: 6-hydroxy-7-(2-iodophenyl)-5-methoxy-8-phenylisochroman-4-one



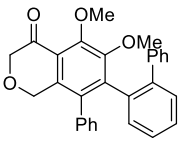
Yield: 61%, 29 mg, pale yellow solid, m. p. 143-145 ℃, Rf = 0.2 (petroleum ether/EtOAc= 10:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 11.93 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.19 – 7.12 (m, 4H), 6.97 (dd, *J* = 7.7, 1.7 Hz,1H), 6.91 (dt, *J* = 6.3, 2.1 Hz, 1H), 6.84 (t, *J* = 7.7 Hz, 1H), 4.61 – 4.50 (m, 2H), 4.38 (d, *J* = 3.1 Hz, 2H), 3.78 (3, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 200.58, 154.71, 145.31, 144.22, 141.35, 138.51, 136.13, 134.48, 130.45, 130.01, 129.62, 128.98, 128.76, 128.04, 127.69, 127.37, 127.21, 115.00, 99.66, 72.23, 67.04, 60.65; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{17}IO_4$ 495.0065; Found 495.0064.

Compound 8: 7-(2-iodophenyl)-5,6-dimethoxy-8-phenylisochroman-4-one



Yield: 68%, 565 mg, pale yellow solid, m. p. 165-167 ℃, Rf = 0.3 (petroleum ether/EtOAc= 10:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.85, 1H), 7.25 – 7.09 (m, 2H), 6.97 (d, *J* = 6.56, 2H), 6.85 (t, *J* = 7.34, 1H), 4.51 (s, 3H), 4.32 (s, 2H), 4.01 (s, 3H), 3.74 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 193.23, 153.02, 150.29, 144.12, 141.40, 138.50, 136.69, 136.32, 134.07, 130.50, 129.70, 129.19, 128.75, 128.16, 127.76, 127.53, 127.24, 124.08, 100.07, 73.97, 67.50, 61.44, 61.10; **HRMS** (ESI–TOF) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{19}IO_4$ 509.0225, Found 509.0220.

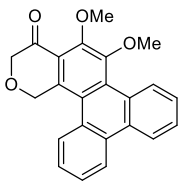
Compound 9: 7-([1,1'-biphenyl]-2-yl)-5,6-dimethoxy-8-phenylisochroman-4-one



Yield: 52 %, 23 mg, pale yellow solid, m. p. 173-175 ℃, Rf = 0.2 (petroleum ether/EtOAc= 10:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 – 7.15 (m, 7H), 7.14 – 7.09 (m, 2H), 7.04 (td, *J* = 7.2, 6.8, 2.0 Hz, 1H), 7.00 – 6.95 (m, 2H), 6.82 (dt, *J* = 7.7, 1.8 Hz, 1H), 6.20 (d, *J* = 7.8 Hz, 1H), 4.39 (d, *J* = 15.1 Hz, 1H), 4.34 – 4.27 (m, 2H), 4.21 (d, *J* = 17.3 Hz, 1H), 3.96 (s, 3H), 3.78 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.42, 152.74, 151.17, 142.22, 140.85, 140.79, 136.30, 136.18, 134.64, 134.06, 131.03,

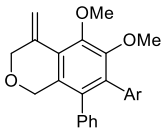
129.83, 129.60, 129.18, 127.92, 127.63, 127.54, 127.10, 126.76, 126.15, 123.55, 73.88, 67.48, 61.20, 60.90; **HRMS** (ESI–TOF) m/z: [M+Na] $^+$ Calcd for $C_{29}H_{24}O_4$ 459.1541; Found 459.1567.

Compound 10: 5,6-dimethoxy-8H-phenanthro[9,10-h]isochromen-7(10H)-one



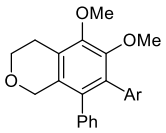
Yield: 70%, 35 mg, white solid, m. p. 143-145 ℃, Rf = 0.2 (petroleum ether/EtOAc= 10:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.54 (d, *J* = 8.3 Hz, 1H), 8.55 (t, *J* = 7.1 Hz,2H), 7.71 – 7.59 (m, 4H), 7.54 (t, *J* = 7.5 Hz,1H), 5.35 (s, 2H), 4.44 (s, 2H), 4.10 (s, 3H), 3.95 (s, 3H); **^{13}C NMR** (126 MHz, CDCl3) δ 194.60, 151.69, 151.47, 136.27, 131.29, 131.20, 129.68, 128.82, 128.72, 128.68, 128.67, 128.55, 127.86, 127.79, 127.59, 126.36, 123.82, 123.67, 123.02, 74.34, 69.75, 62.03, 60.86; **HRMS** (ESI–TOF) m/z: [M+H] $^+$ Calcd for $C_{23}H_{18}O_4$ 359.1278; Found 359.1281.

Compound 11: 7-(2-iodophenyl)-5,6-dimethoxy-4-methylene-8-phenylisochromane



Yield: 93%, 43 mg, pale yellow solid, m. p. 145-147 ℃, Rf = 0.4 (petroleum ether/EtOAc= 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.21 – 7.08 (m, 5H), 6.99 (dt, *J* = 7.4, 2.1 Hz, 2H), 6.80 (td, *J* = 7.7, 1.7 Hz, 1H), 6.35 (s, 1H), 5.35 (q, *J* = 1.4 Hz, 1H), 4.42 (s, 2H), 4.38 (d, *J* = 4.2 Hz, 2H), 3.93 (s,3H), 3.70 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.37, 149.53, 142.13, 138.34, 138.15, 137.26, 135.67, 133.88, 131.06, 130.00, 129.75, 129.11, 128.32, 128.01, 127.57, 127.09, 127.02, 125.64, 114.55, 101.36, 72.38, 68.54, 60.72, 59.50; **HRMS** (ESI–TOF) m/z: [M+Na] $^+$ Calcd for $C_{23}H_{21}IO_3$ 507.0426; Found 507.0427.

Compound 12: 7-(2-iodophenyl)-5,6-dimethoxy-8-phenylisochromane



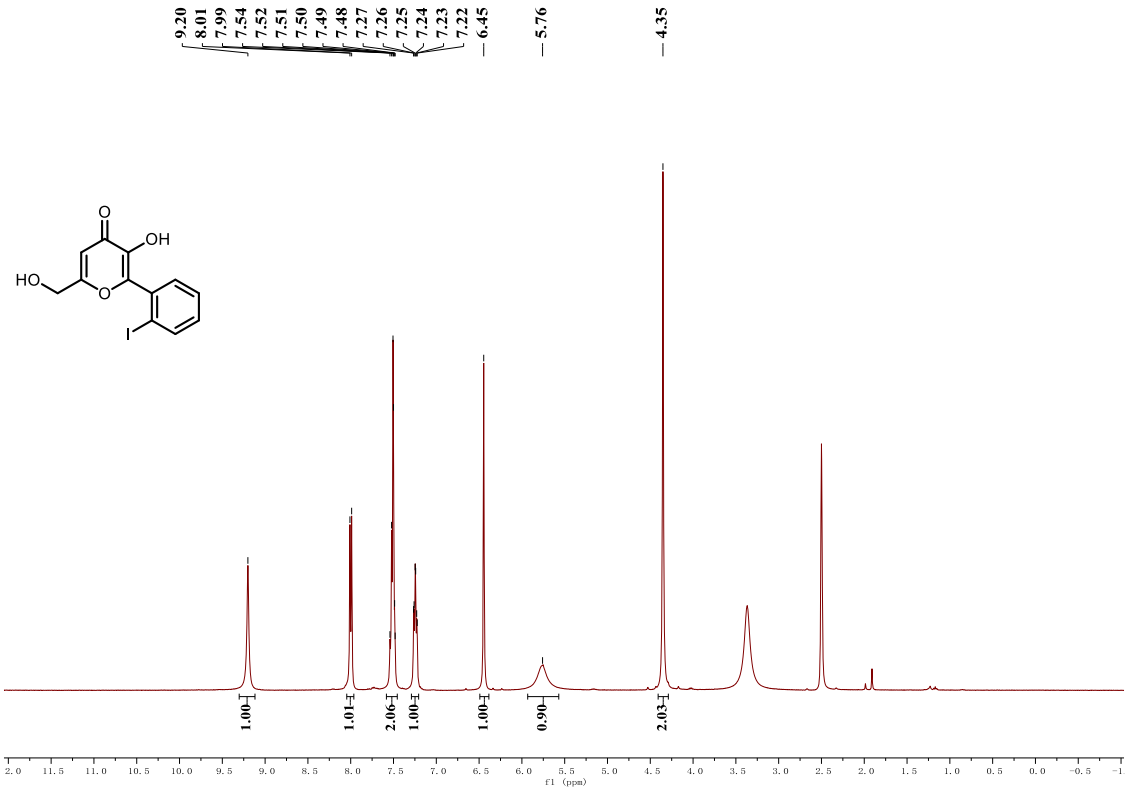
Yield: 72%, 35 mg, pale yellow solid, m. p. 150-152 ℃, Rf = 0.4 (petroleum ether/EtOAc= 20:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.9 Hz, 1H), 7.25 – 7.10 (m, 5H), 7.01 (ddd, *J* = 9.0, 7.0, 2.1 Hz, 2H), 6.82 (td, *J* = 7.6, 1.8 Hz, 1H), 4.38 (s,2H), 4.06 – 3.97 (m, 2H), 3.97 (s,3H), 3.70 (s, 3H), 2.97 (t, *J* = 5.8 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.69, 148.13, 142.39, 138.30, 137.28, 136.48, 133.78, 131.29, 129.76, 129.26, 129.17, 128.20, 128.00, 127.91, 127.48, 127.07, 126.86, 101.83, 67.37, 64.88, 60.55, 60.13, 23.52; **HRMS** (ESI–TOF) m/z: [M+Na] $^+$ Calcd for $C_{23}H_{21}IO_3$ 495.0395; Found 495.0427.

5 References

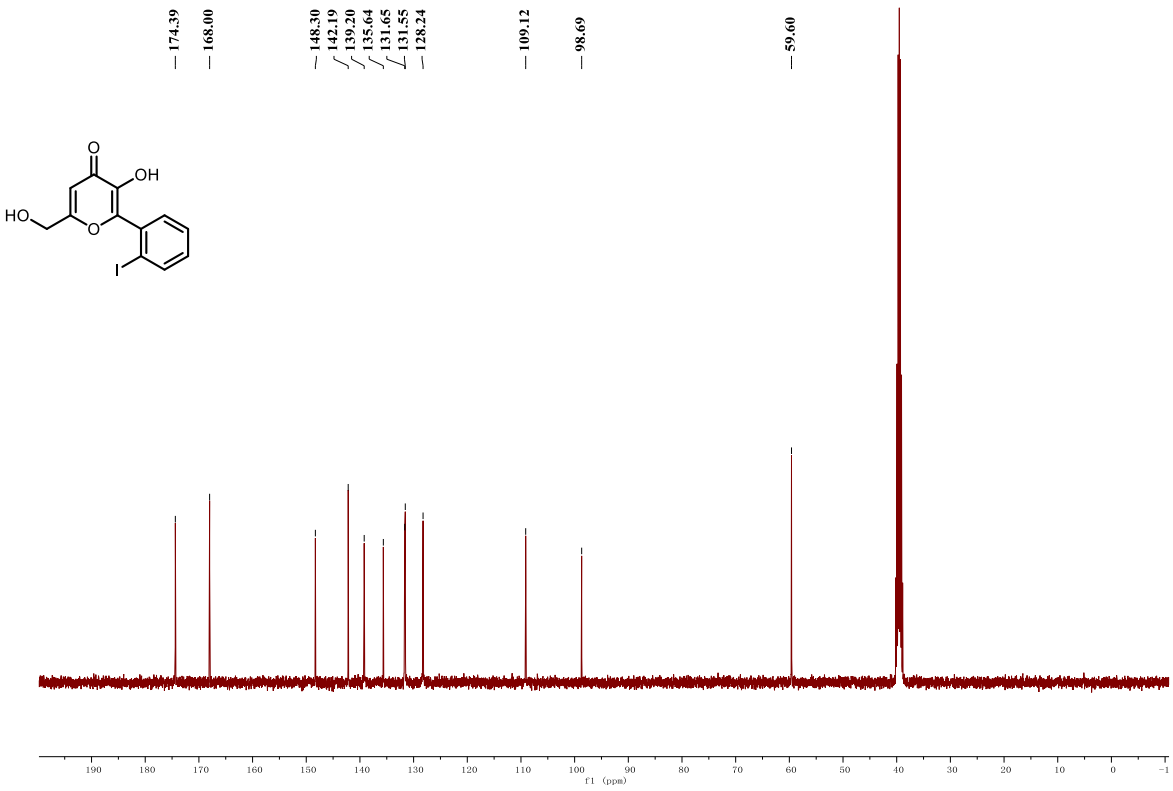
1. T. Morimoto, J. Jia, Y. Yamaguchi, H. Tanimoto and K. Kakiuchi, *Asian J. Org. Chem.*, 2020, **9**, 1778-1782.
2. S. Tamura, K. Yoshihira, T. Kawano and N. Murakami, *Bioorg. Med. Chem. Lett.*, 2018, **28**, 3342-3345.
3. C.-I. W. Chia-Wen Li, Hsin-Yi Liao, Rupsha Chaudhuri, and Rai-Shung Liu, *J. Org. Chem.*, 2007, **92**, 9203-9207.
4. S. J. D. Charles T. West, Dale A. Kooistra, and Michael P. Doyle, *J. Org. Chem.*, 1973, **38**, 15.

6. Copies of NMR spectra

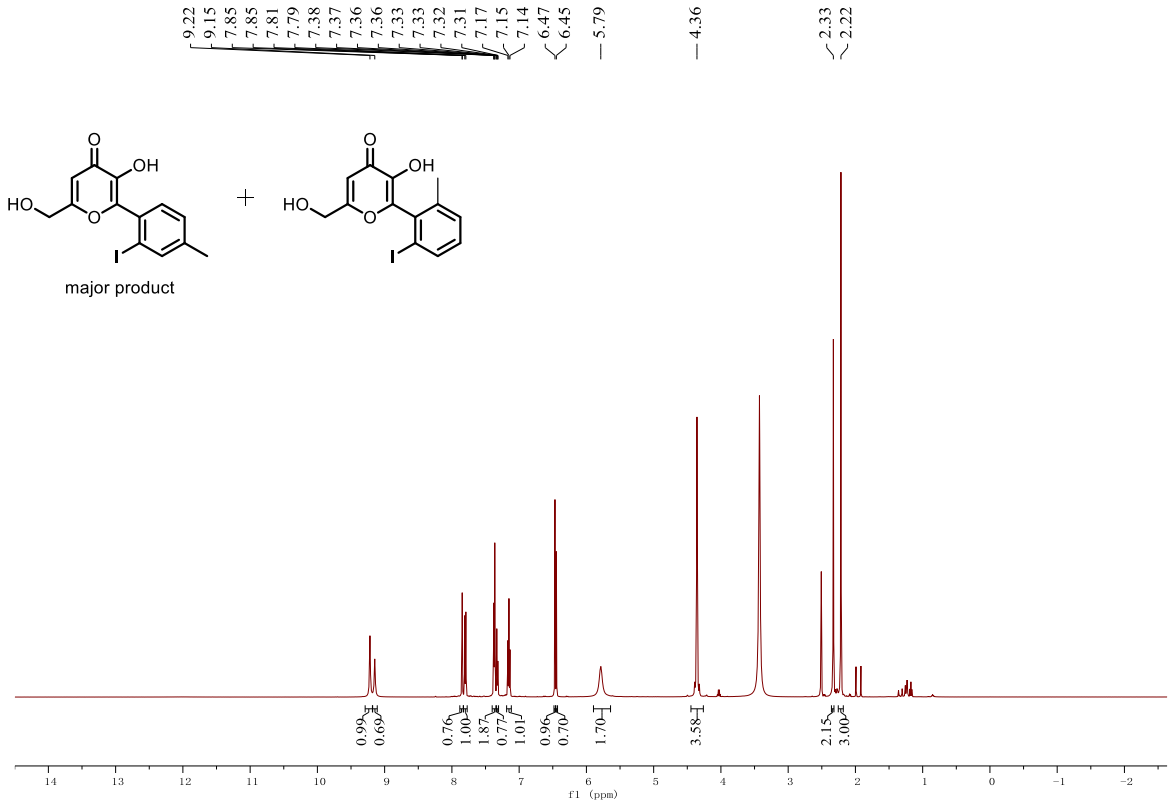
^{1}H NMR (400 MHz, DMSO-d_6) of **3a**



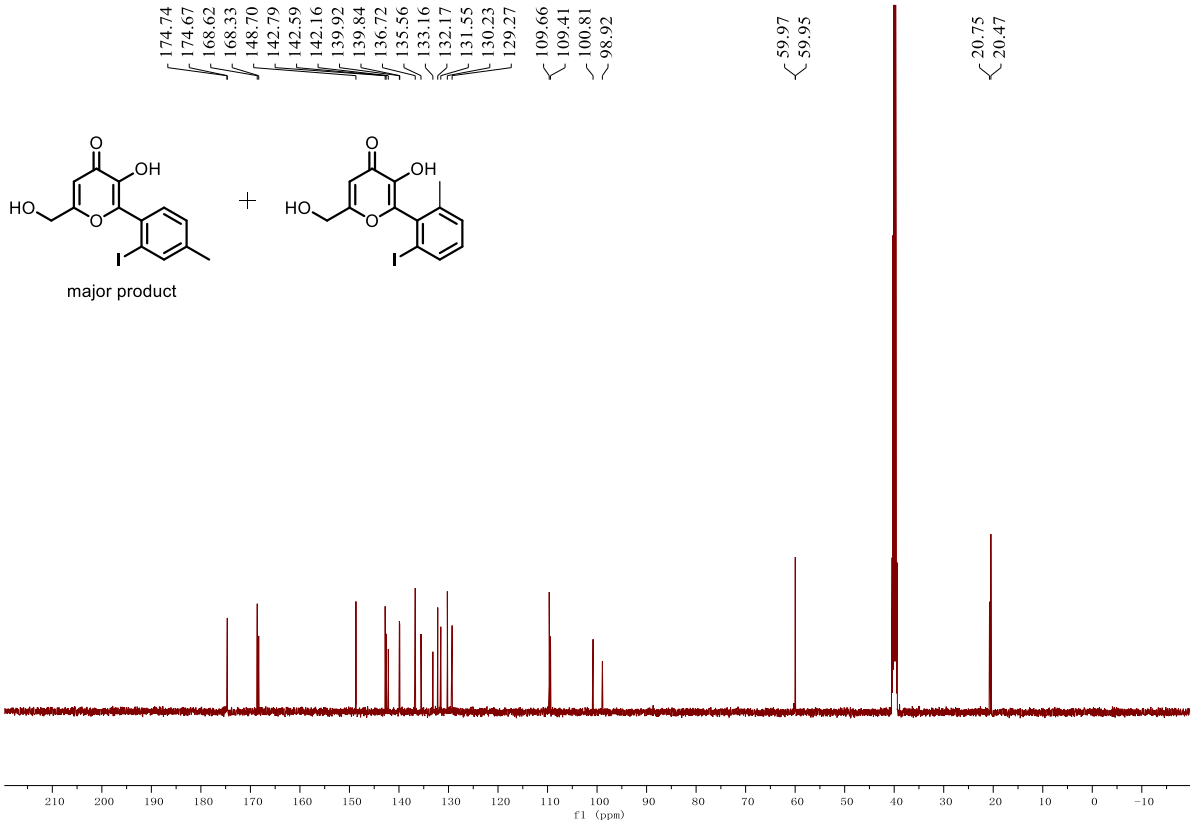
^{13}C NMR (101 MHz, DMSO-d_6) of **3a**



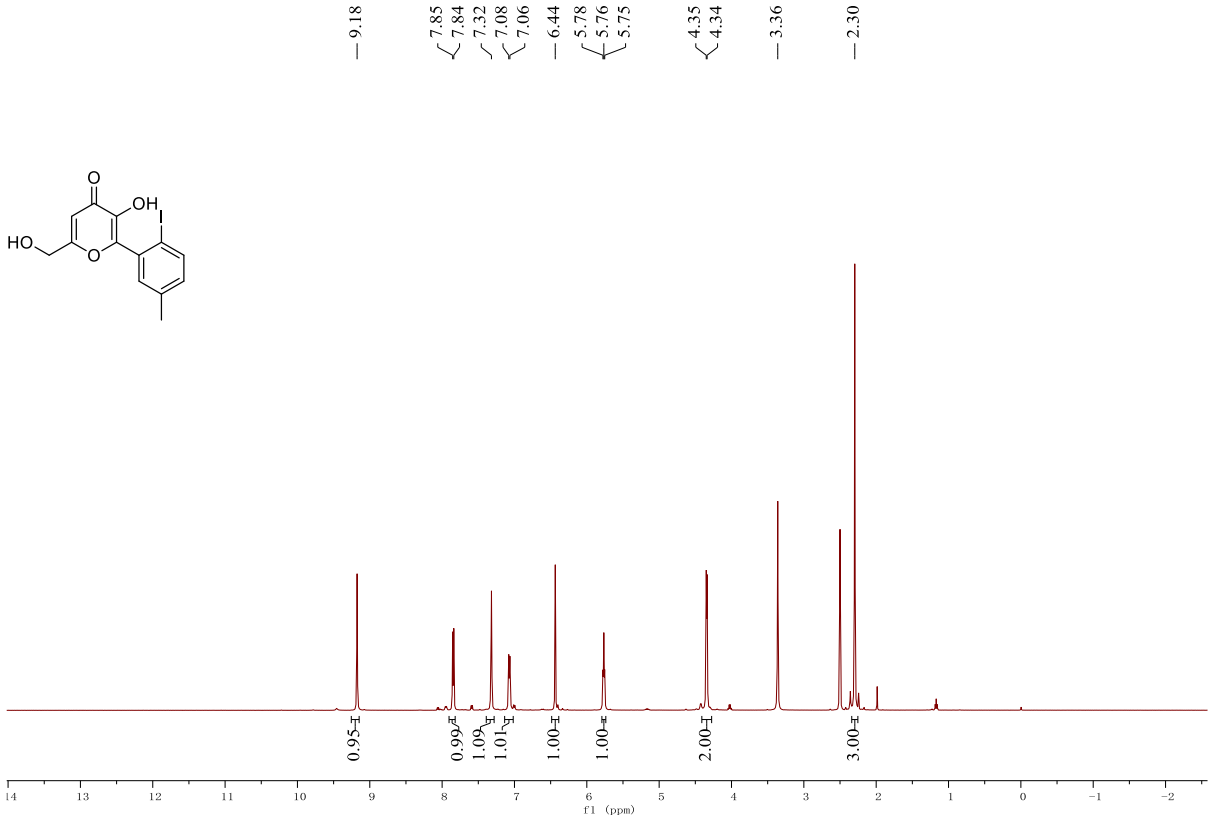
^{1}H NMR (500 MHz, DMSO-d_6) of **3b**



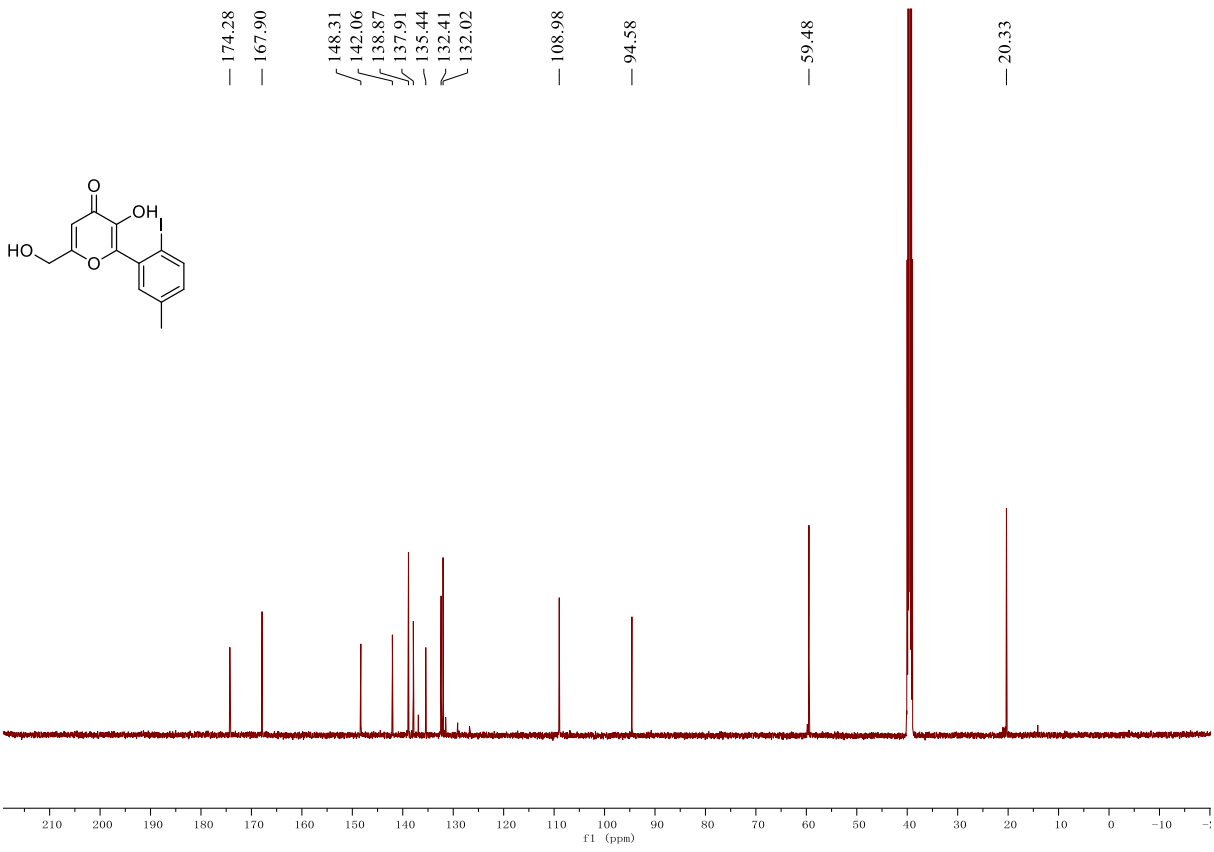
^{13}C NMR (126 MHz, DMSO-d_6) of **3b**



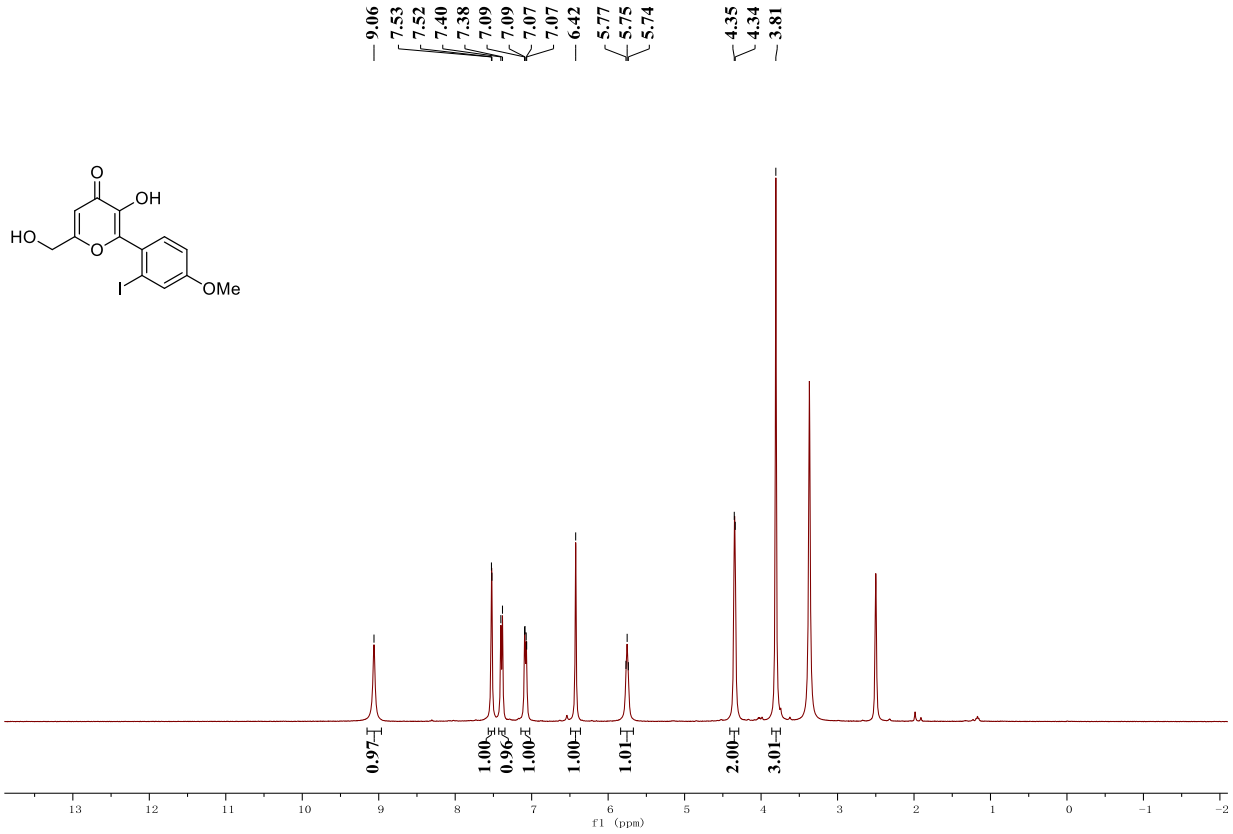
^{1}H NMR (500 MHz, DMSO-d_6) of **3c**



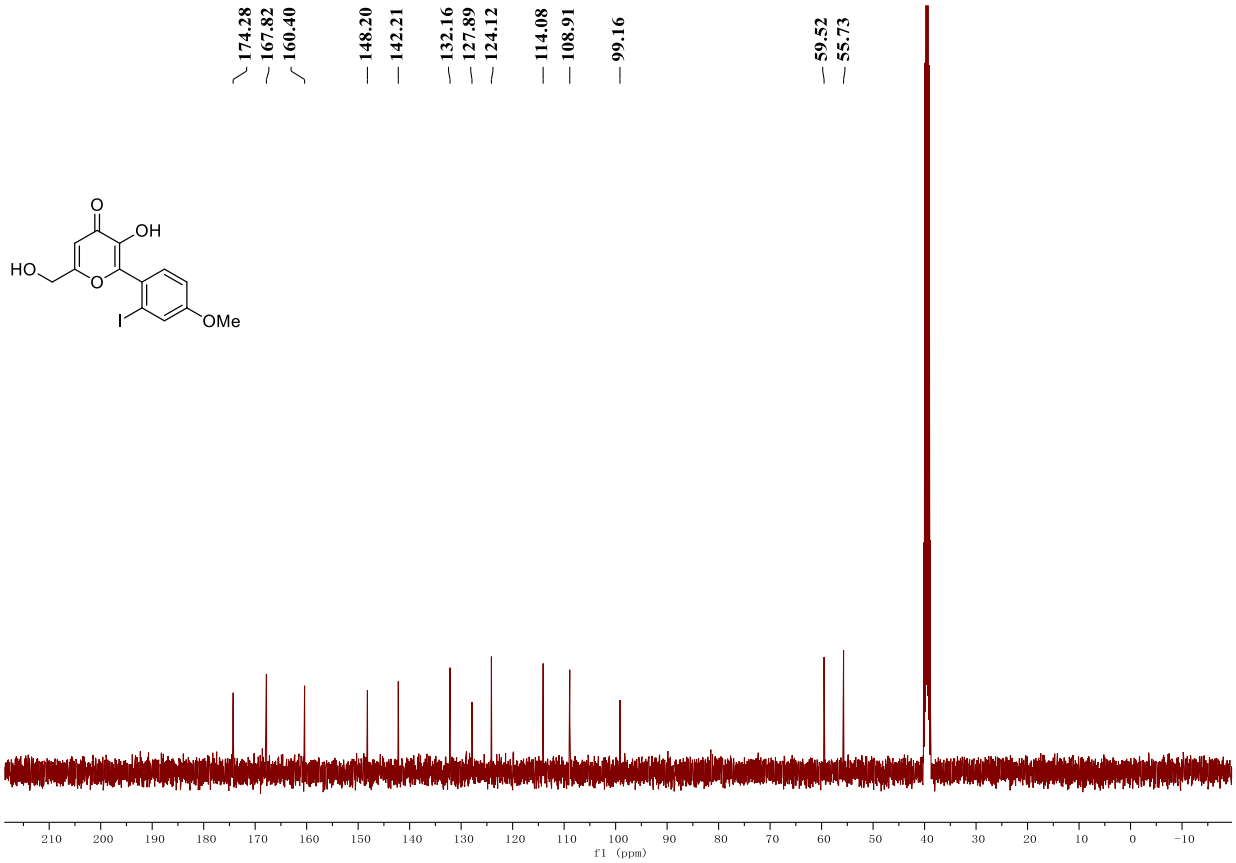
^{13}C NMR (126 MHz, DMSO-d_6) of **3c**



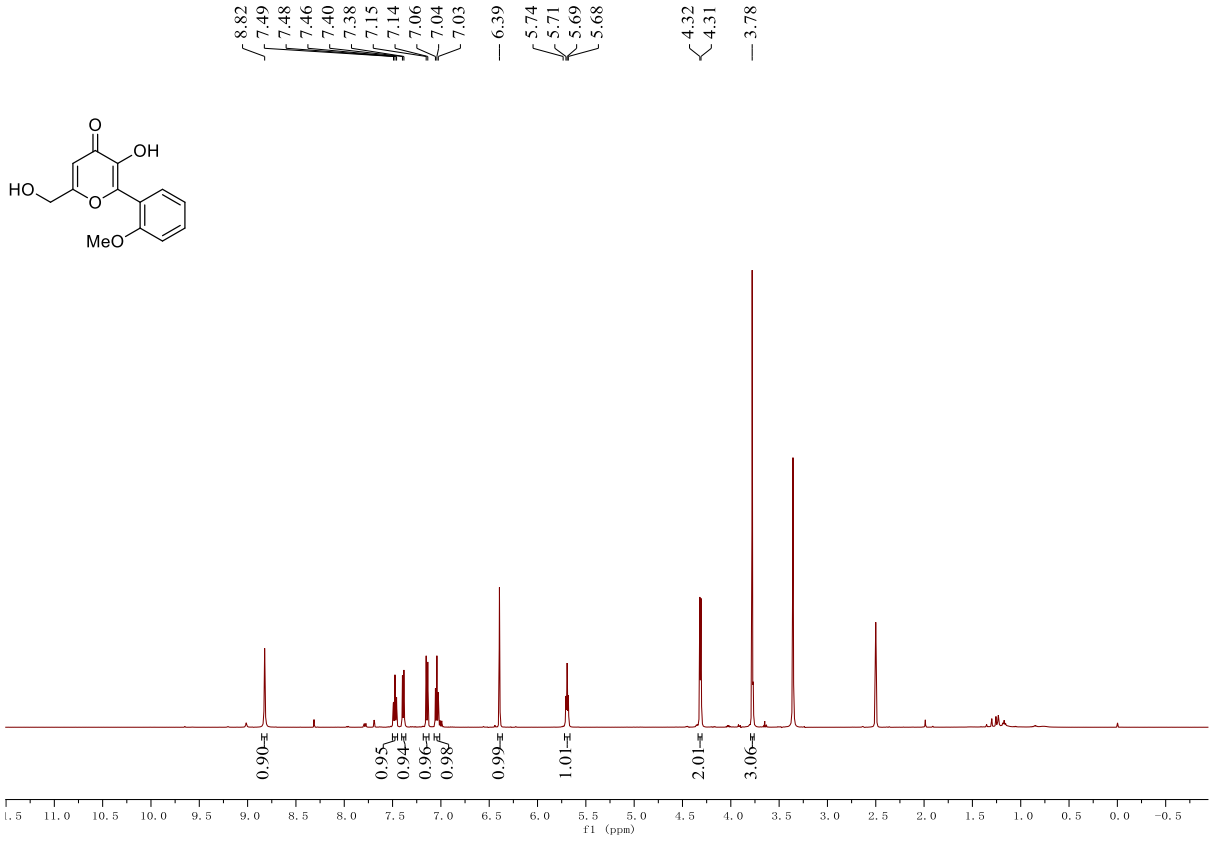
^{1}H NMR (400 MHz, DMSO-d_6) of **3d**



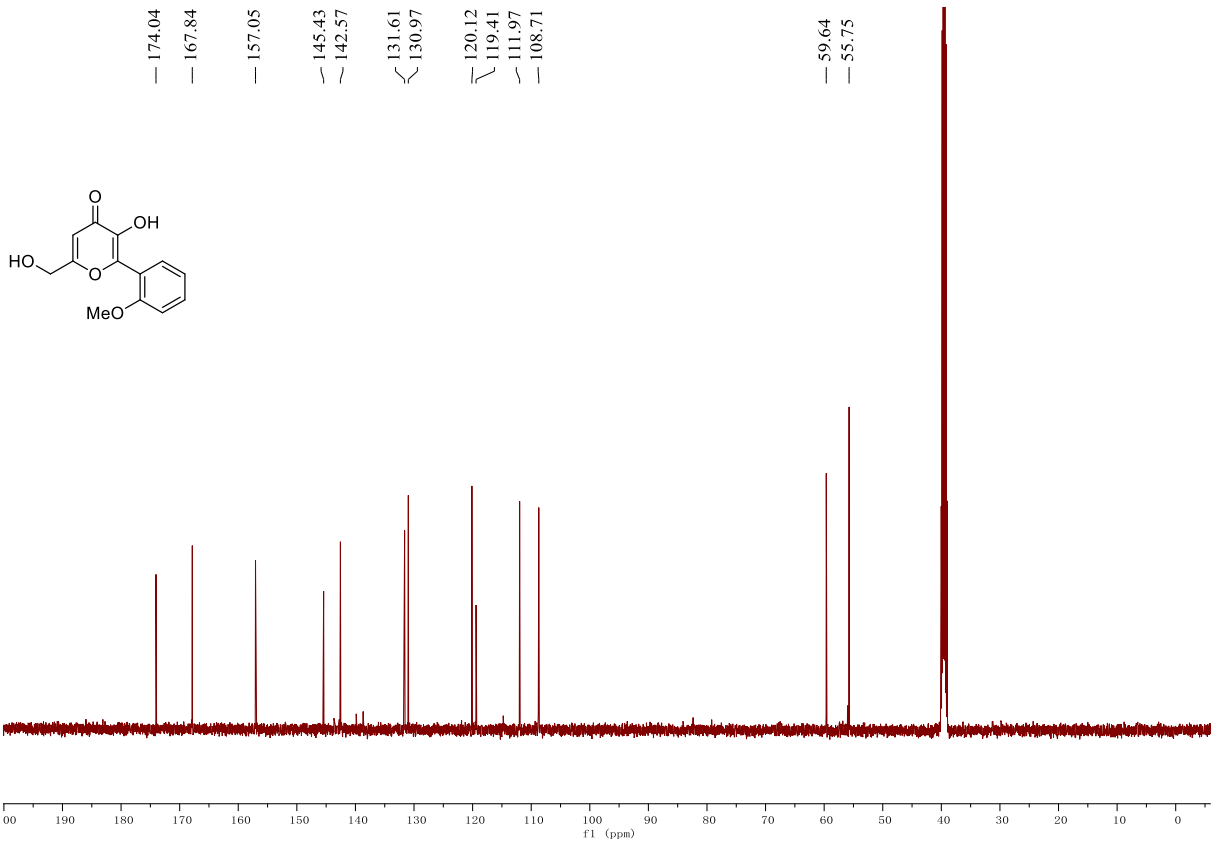
^{13}C NMR (101 MHz, DMSO-d_6) of **3d**



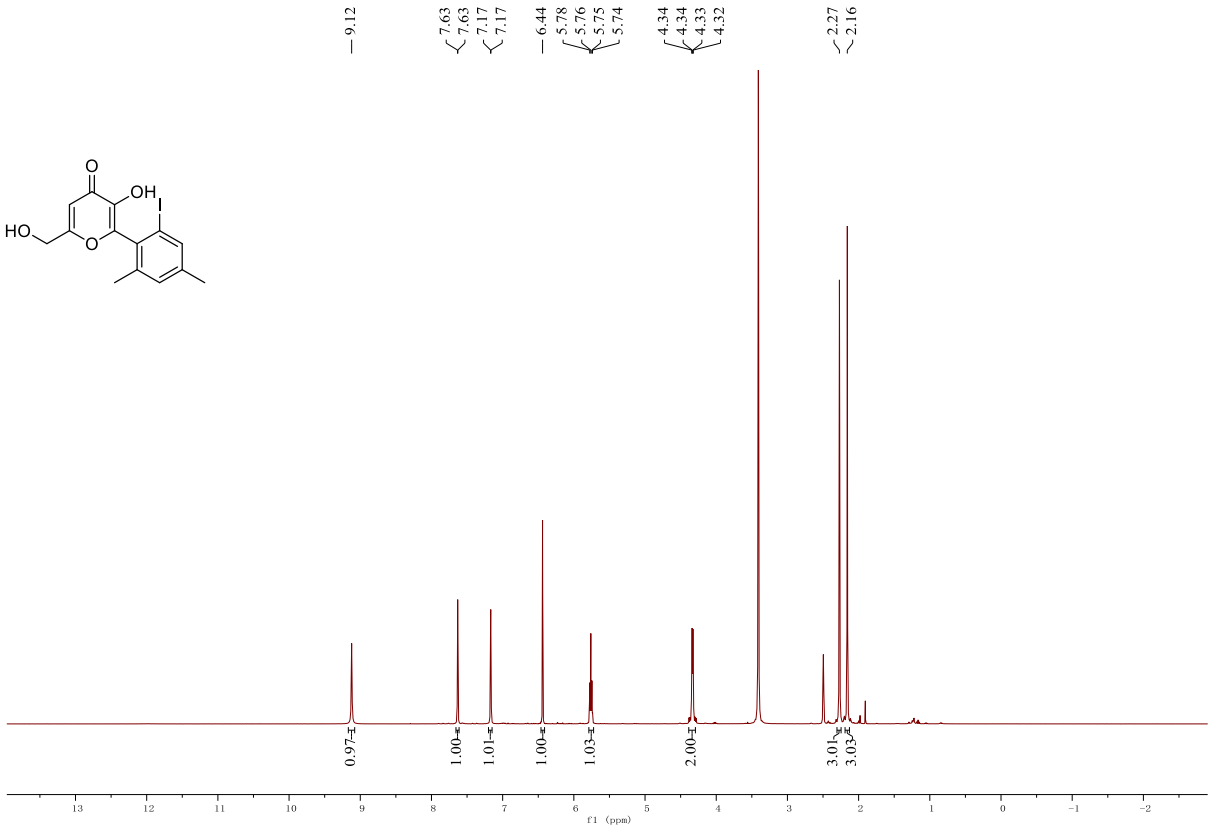
^{1}H NMR (500 MHz, DMSO-d_6) of **3e**



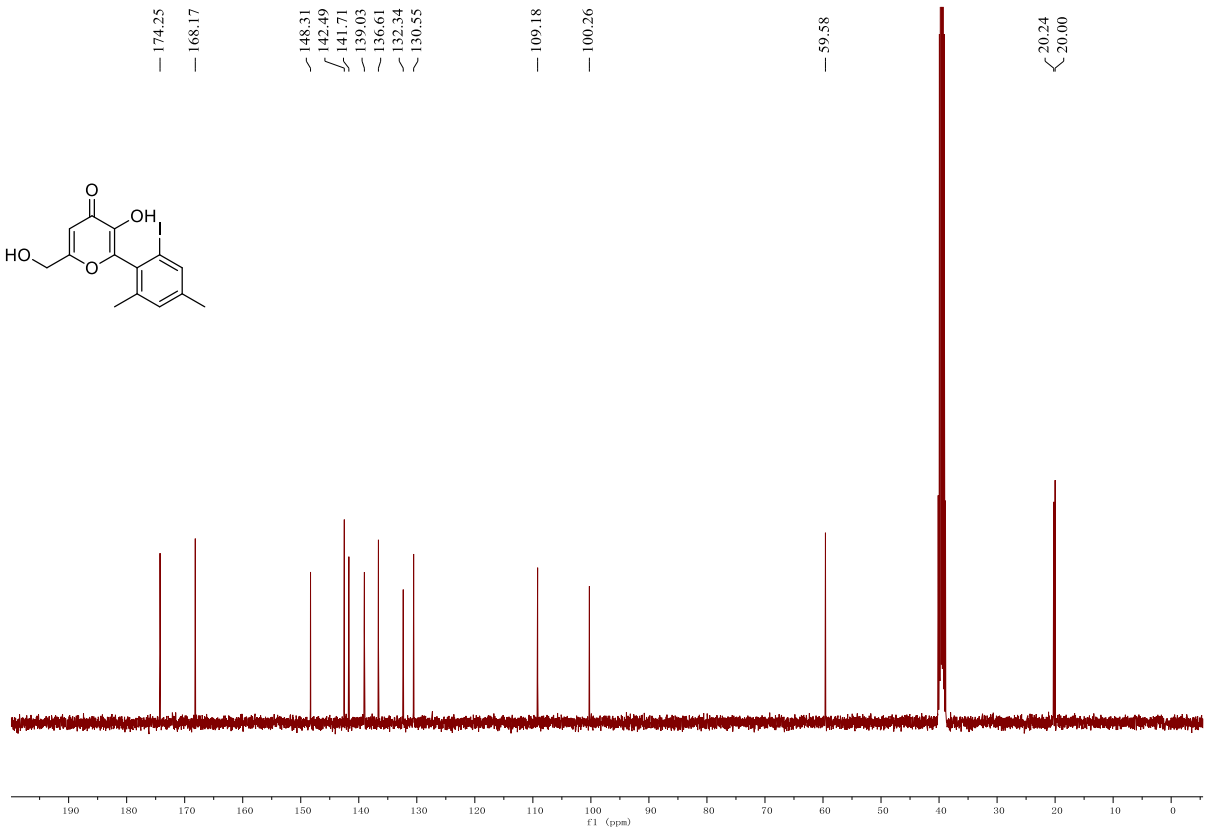
^{13}C NMR (126 MHz, DMSO-d_6) of **3e**



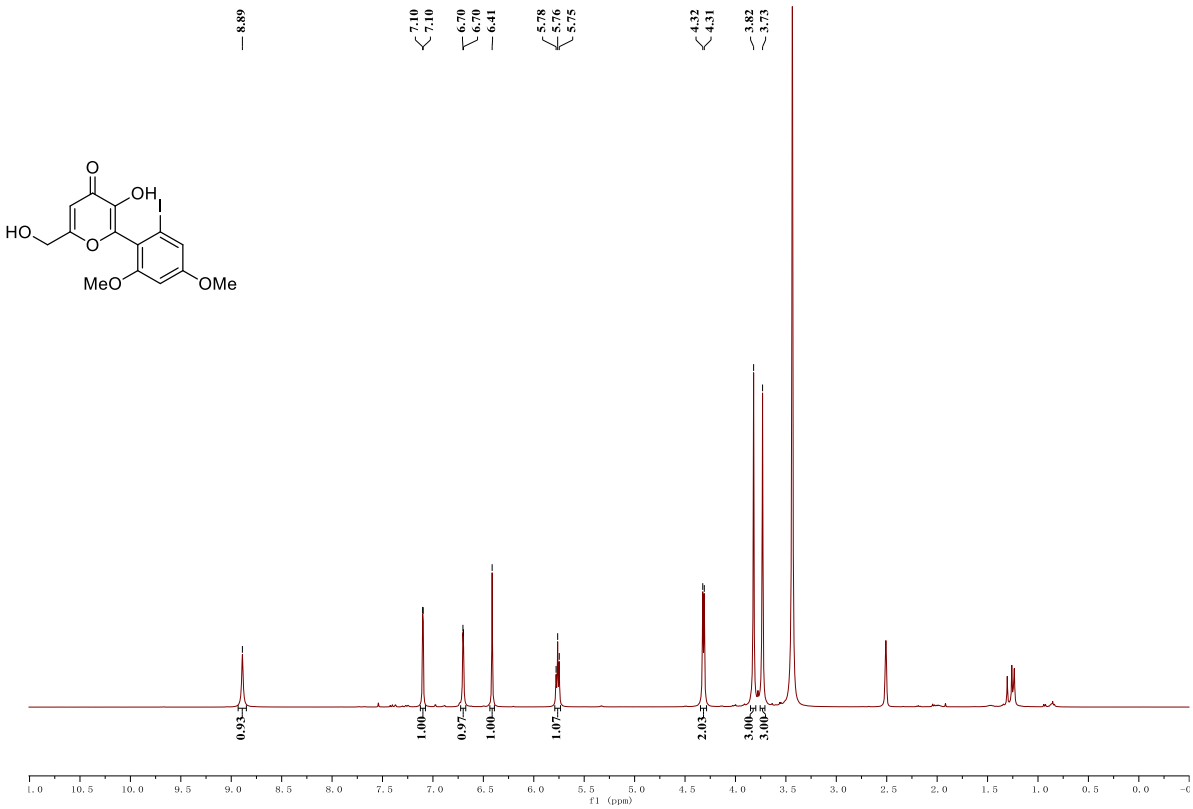
^{1}H NMR (400 MHz, DMSO-d_6) of **3f**



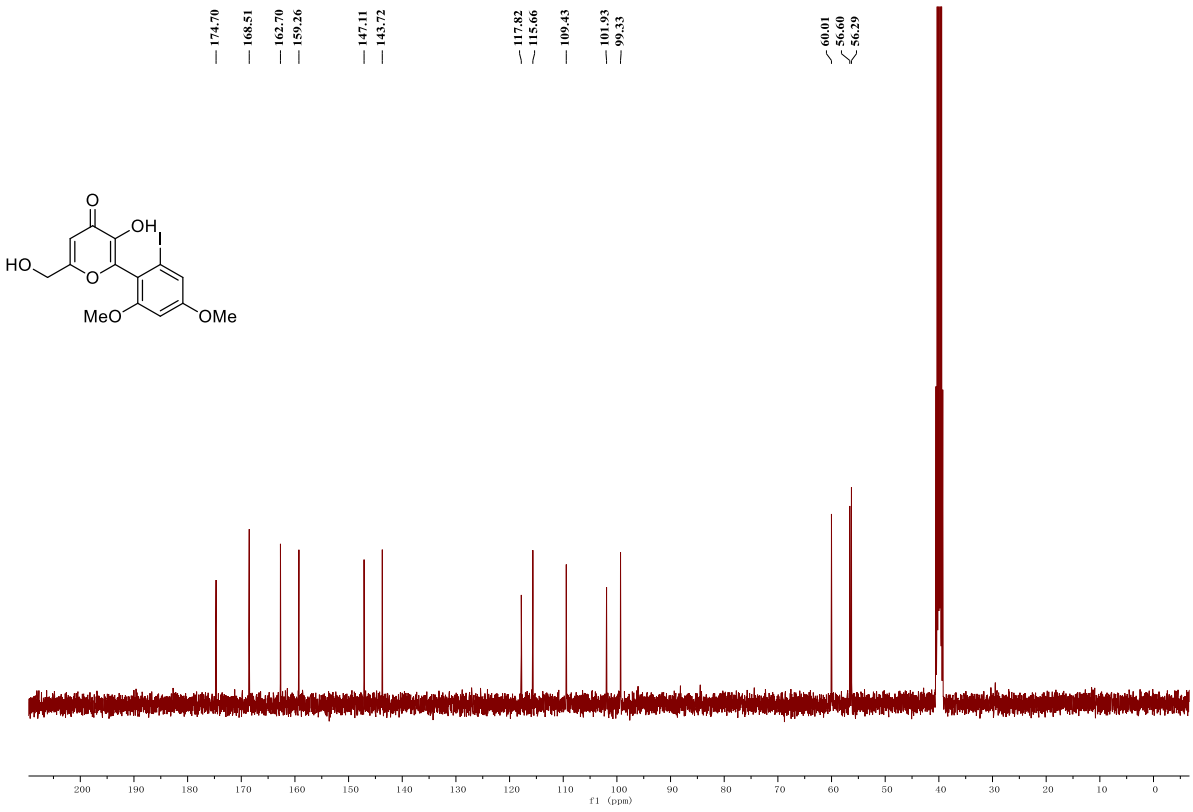
^{13}C NMR (101 MHz, DMSO-d_6) of **3f**



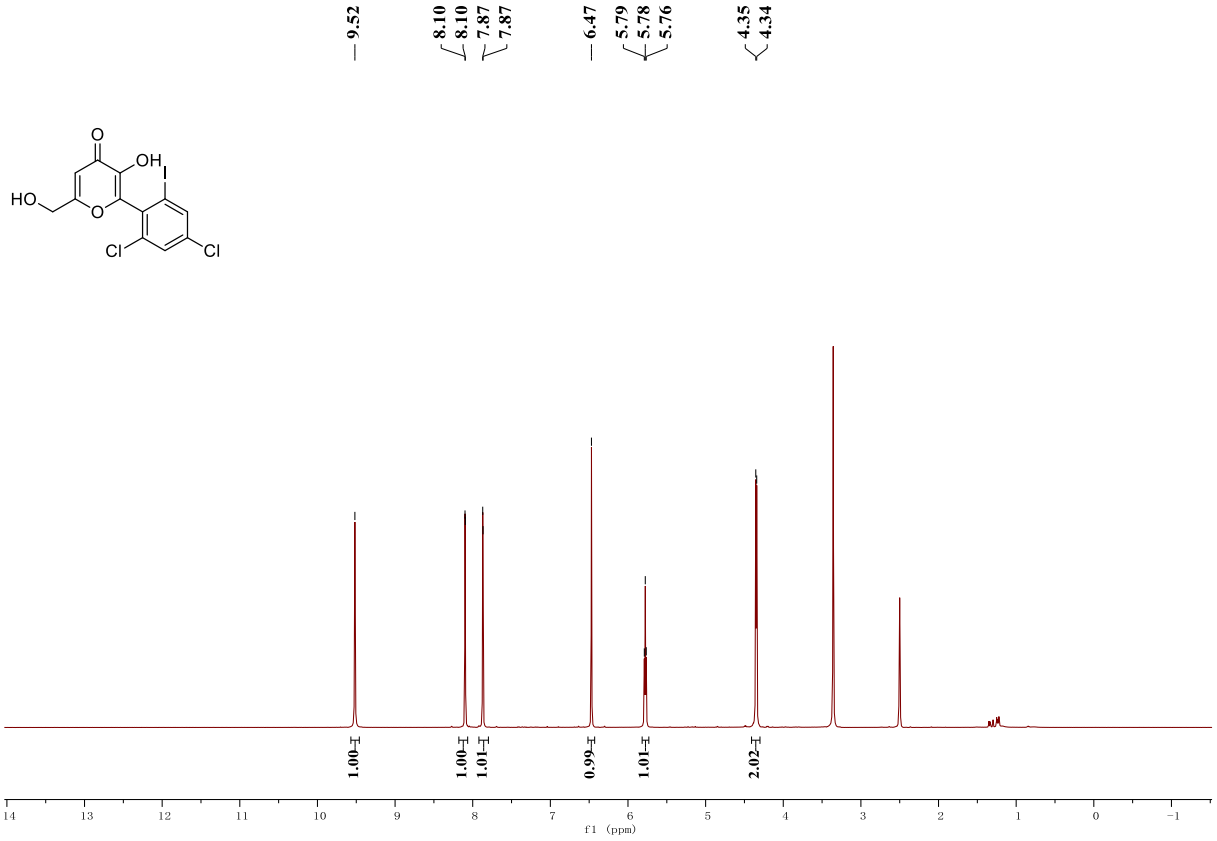
[1]H NMR (400 MHz, DMSO-d_6) of **3g**



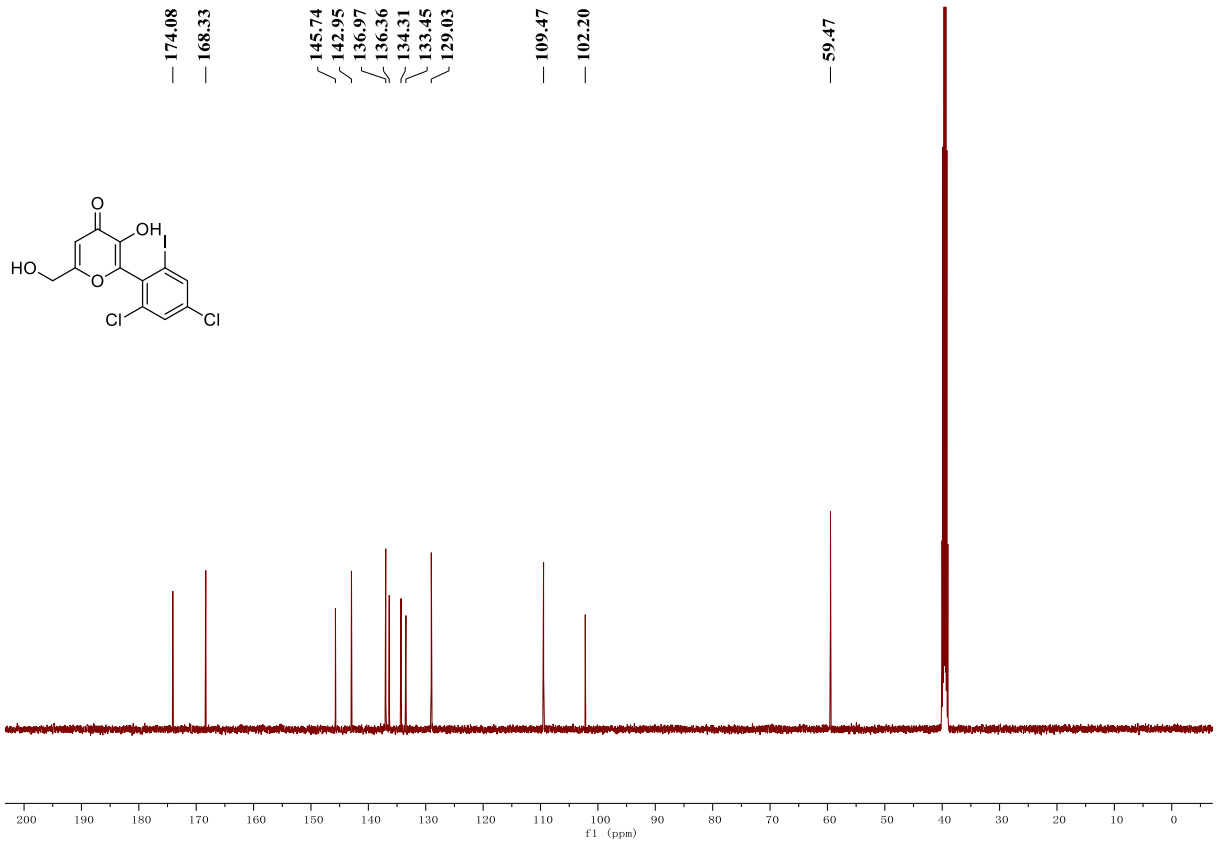
[13]C NMR (101 MHz, DMSO-d_6) of **3g**



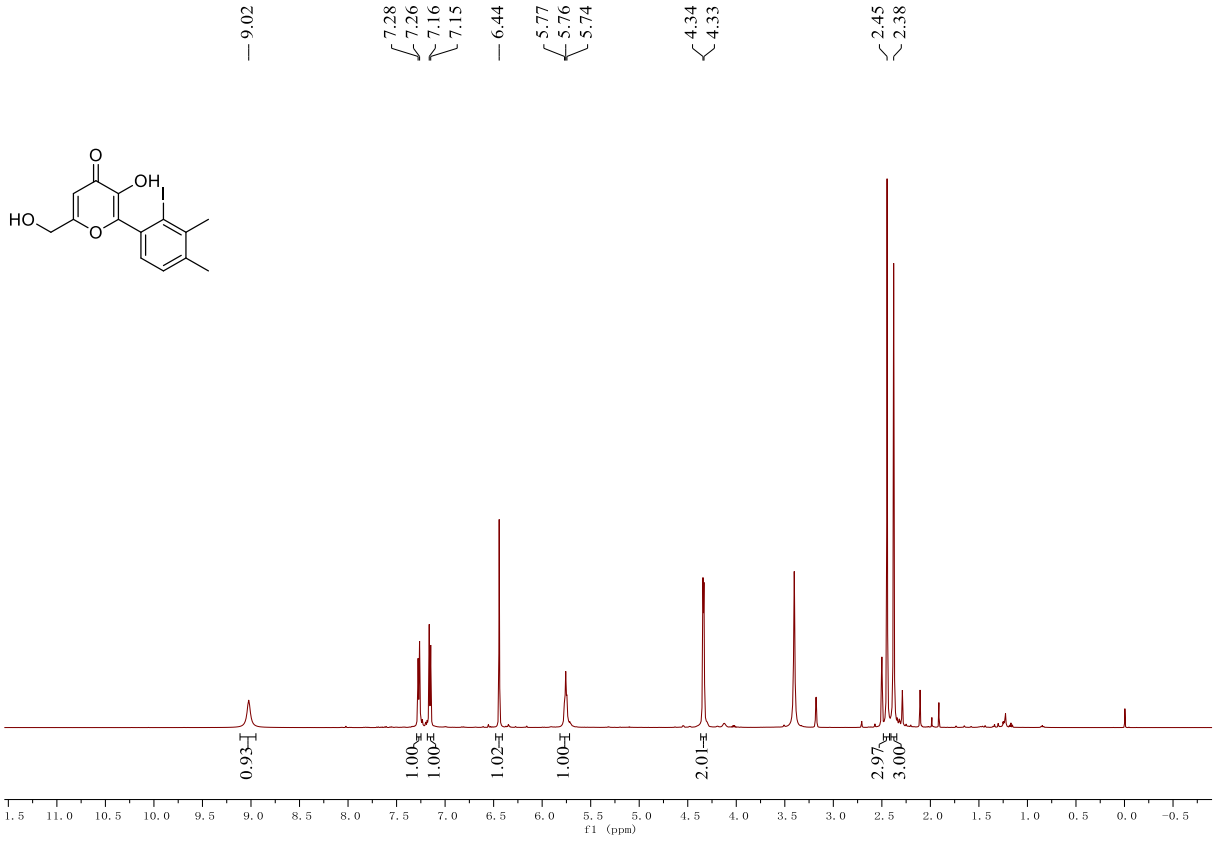
^{1}H NMR (500 MHz, DMSO-d_6) of **3h**



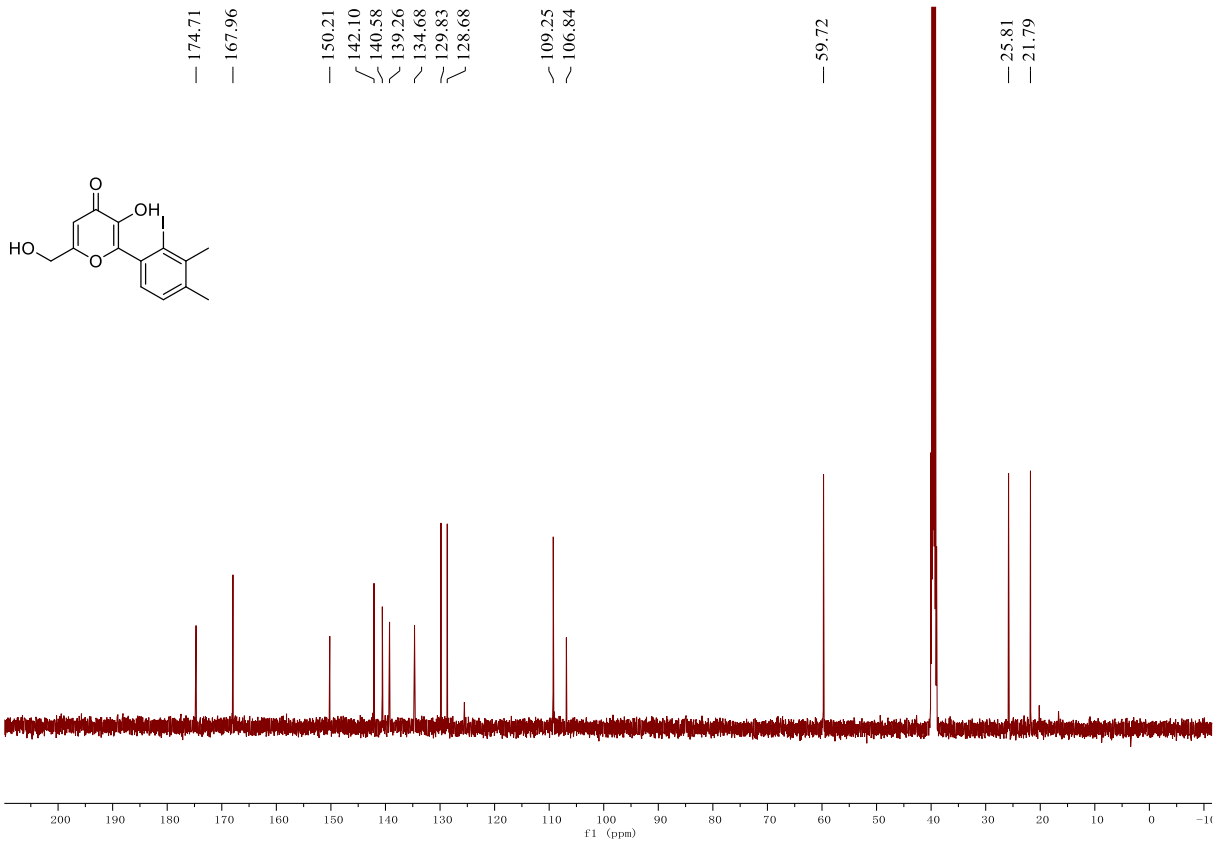
^{13}C NMR (126 MHz, DMSO-d_6) of **3h**



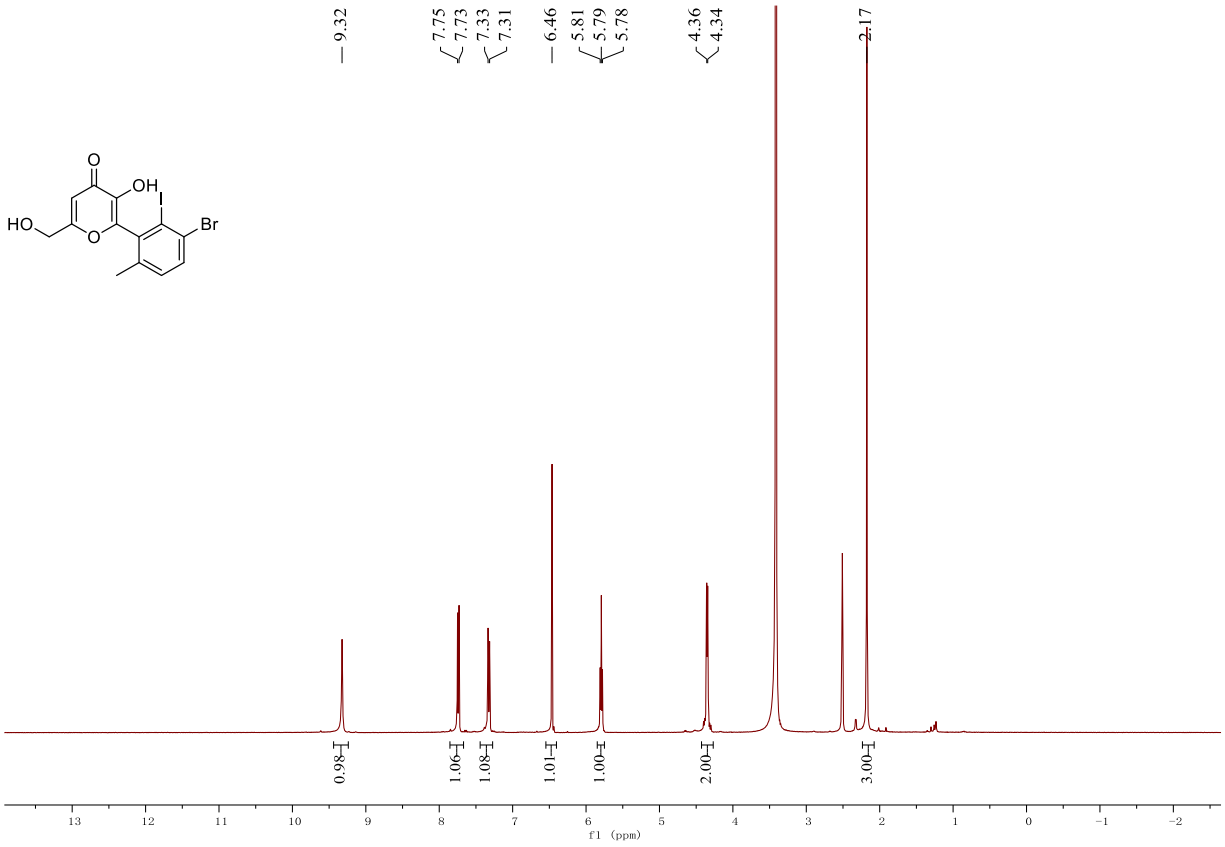
^{1}H NMR (500 MHz, DMSO-d_6) of **3i**



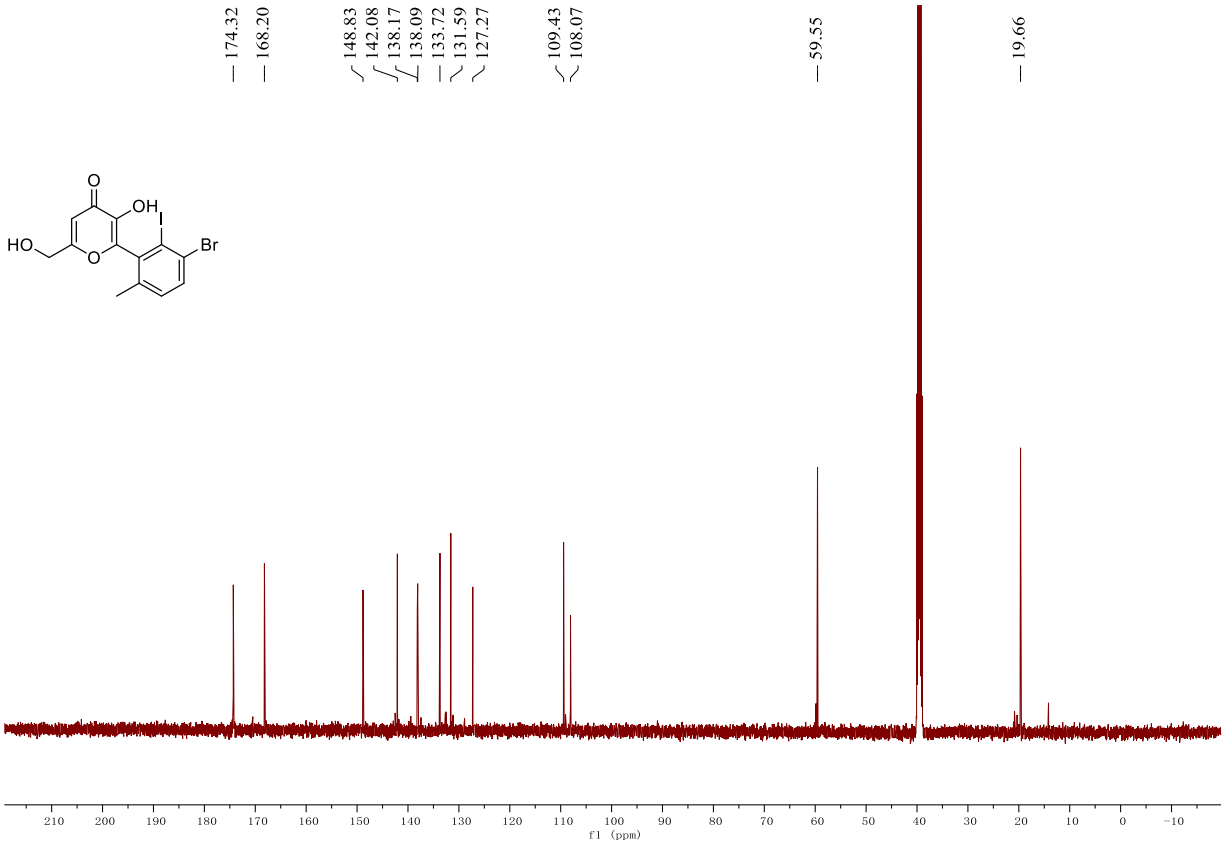
^{13}C NMR (126 MHz, DMSO-d_6) of **3i**



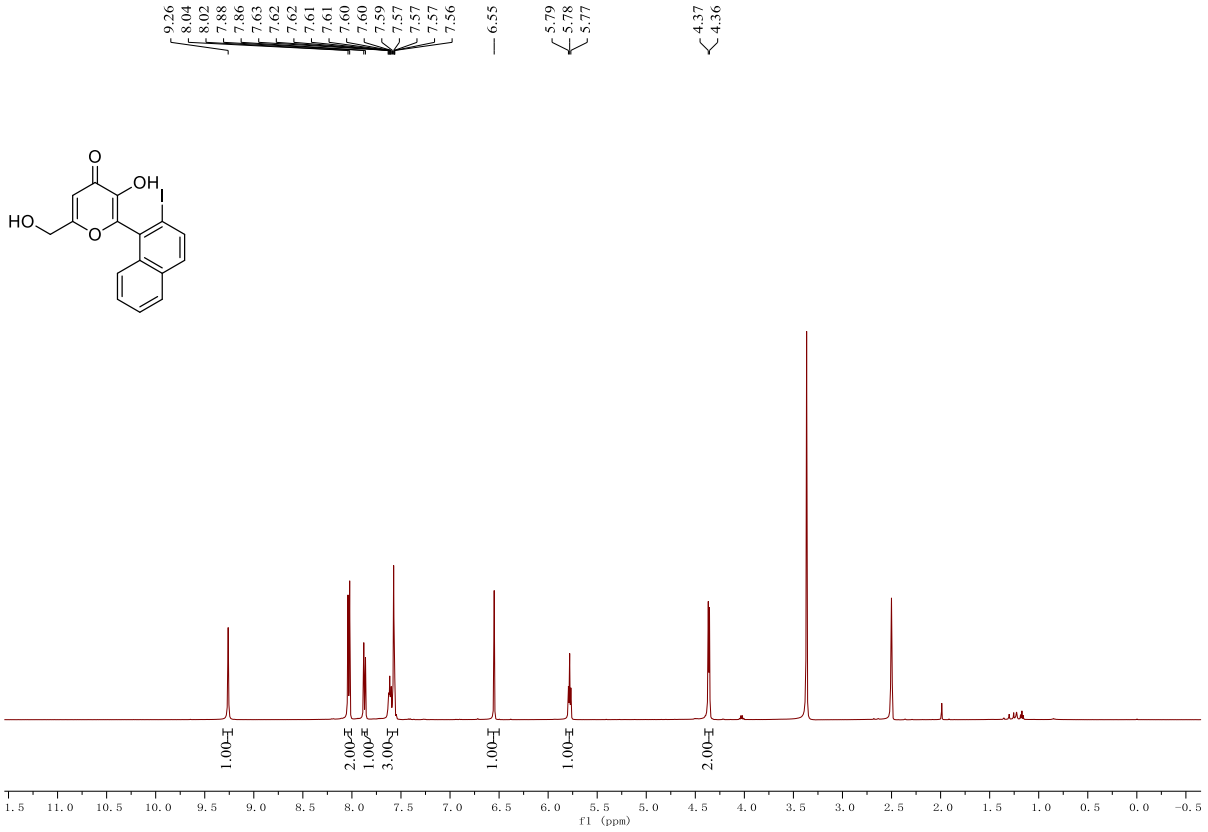
^{1}H NMR (500 MHz, DMSO-d_6) of **3j**



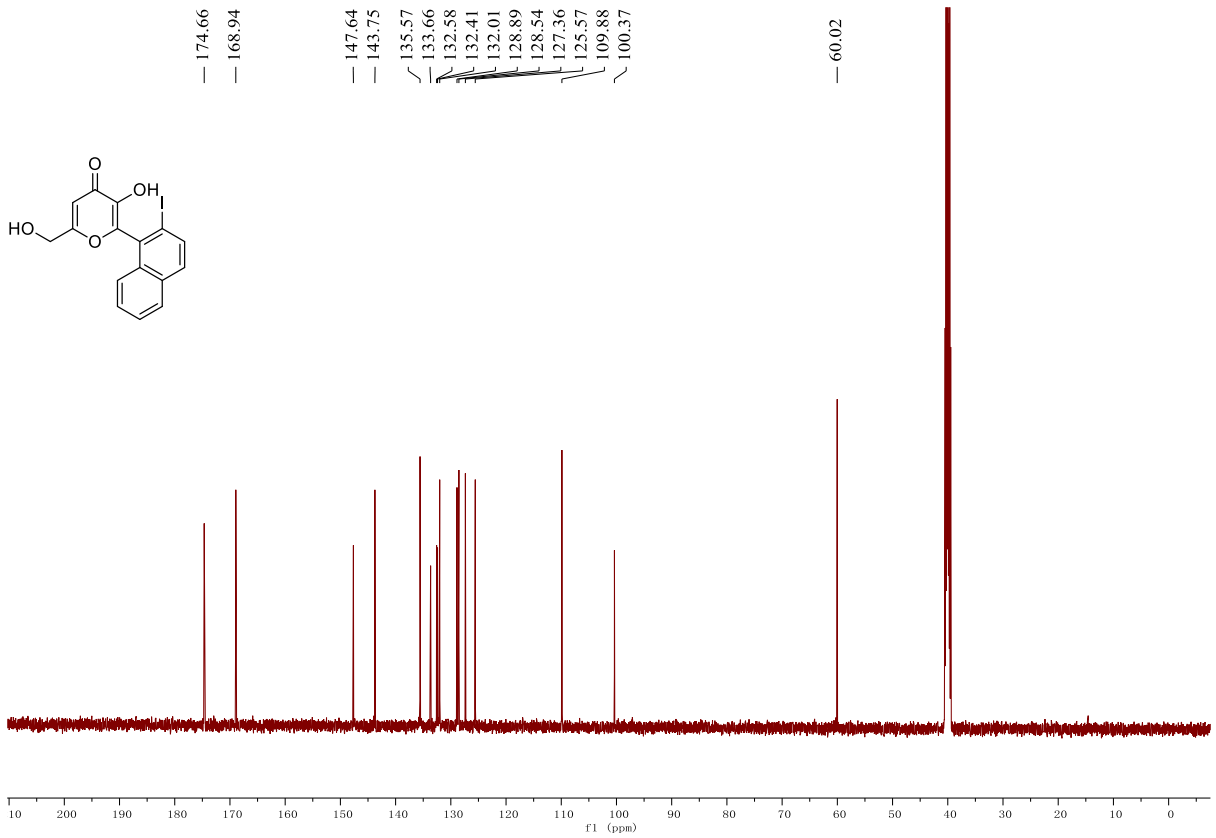
^{13}C NMR (126 MHz, DMSO-d_6) of **3j**



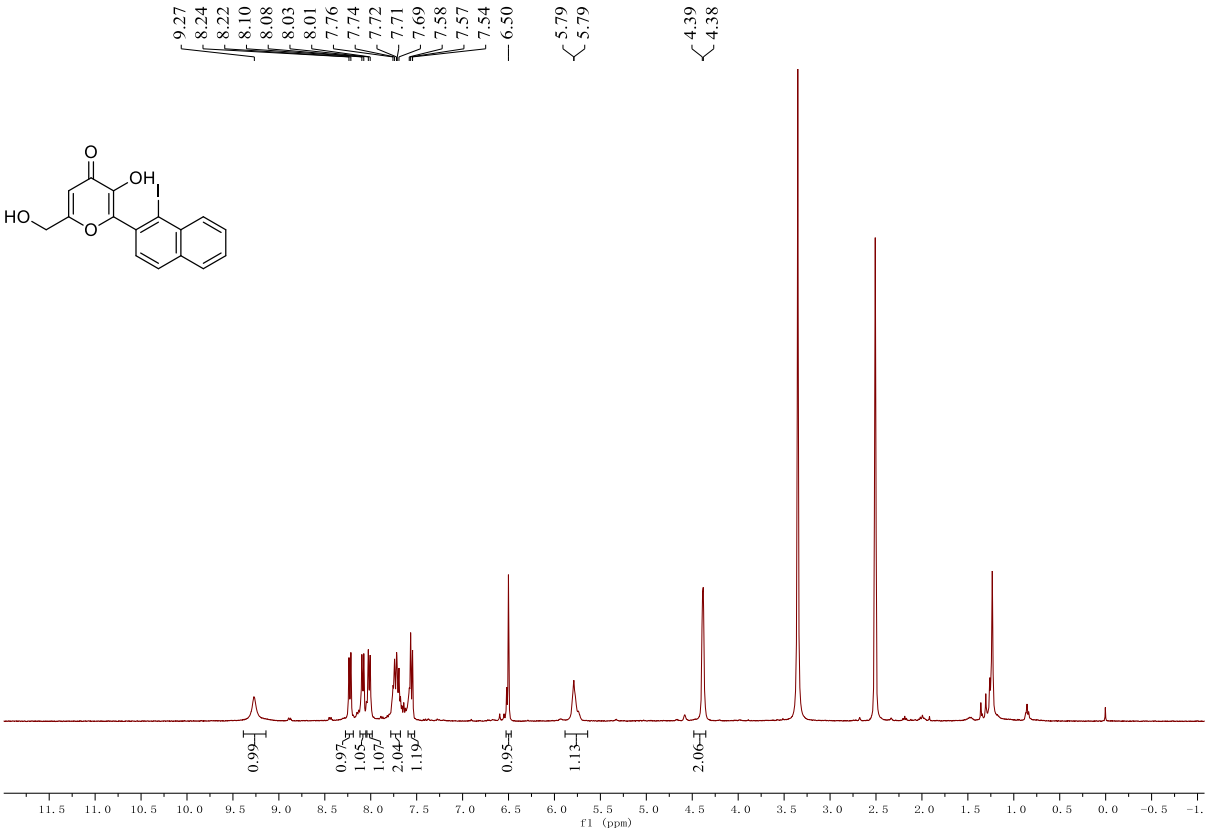
^{1}H NMR (500 MHz, DMSO-d_6) of **3k**



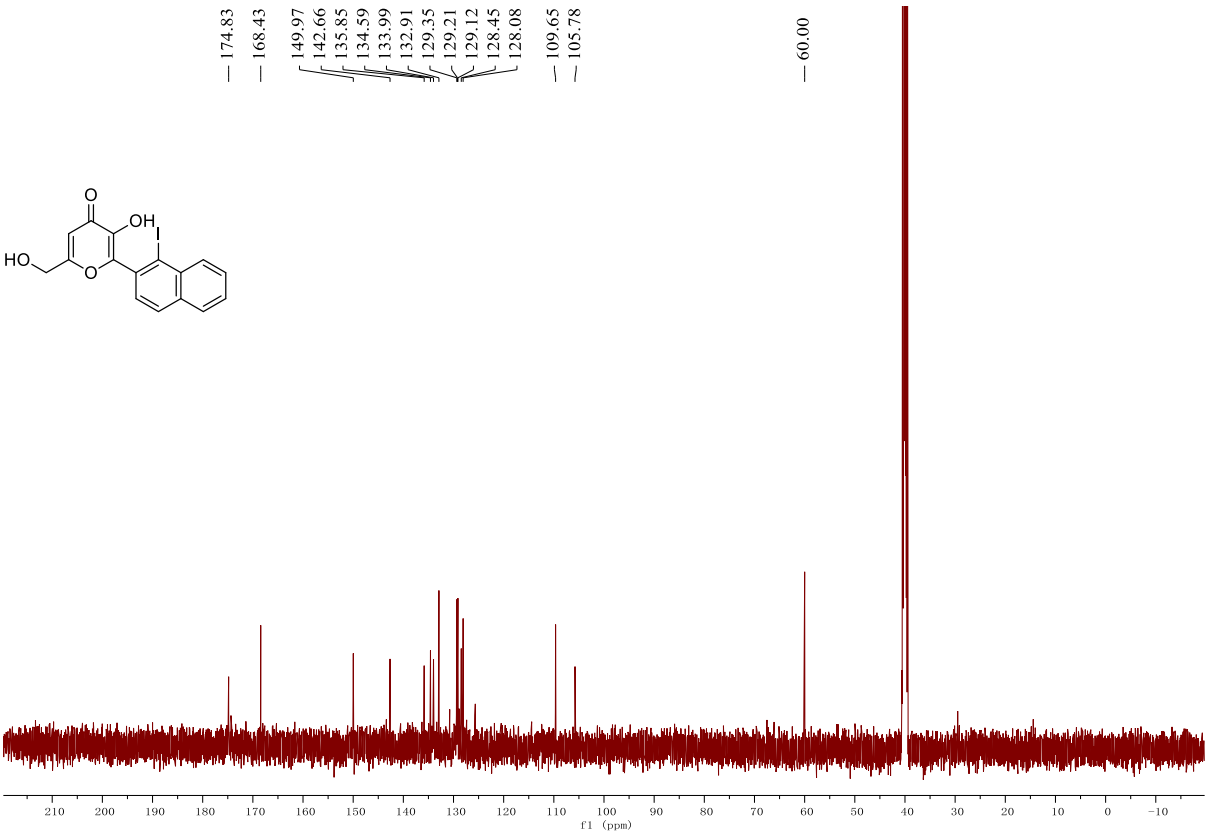
^{13}C NMR (126 MHz, DMSO-d_6) of **3k**



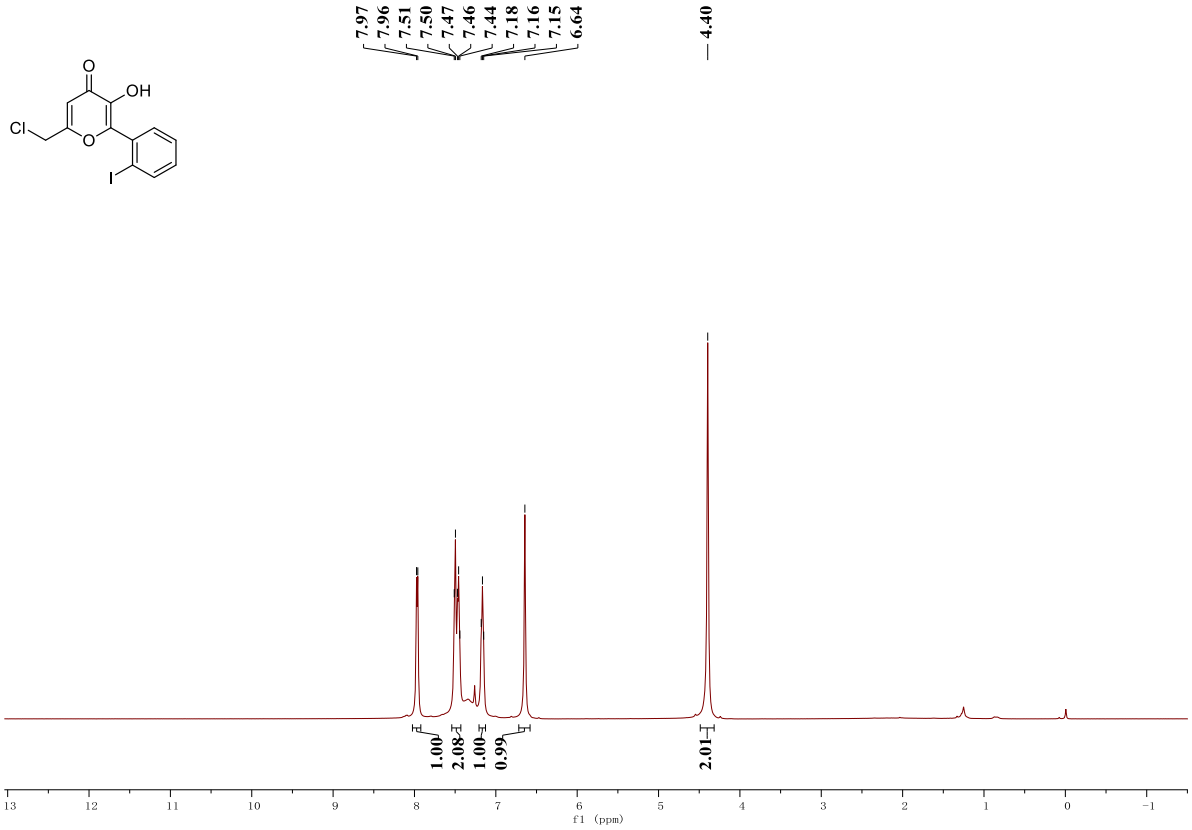
^{1}H NMR (400 MHz, DMSO-d_6) of **3l**



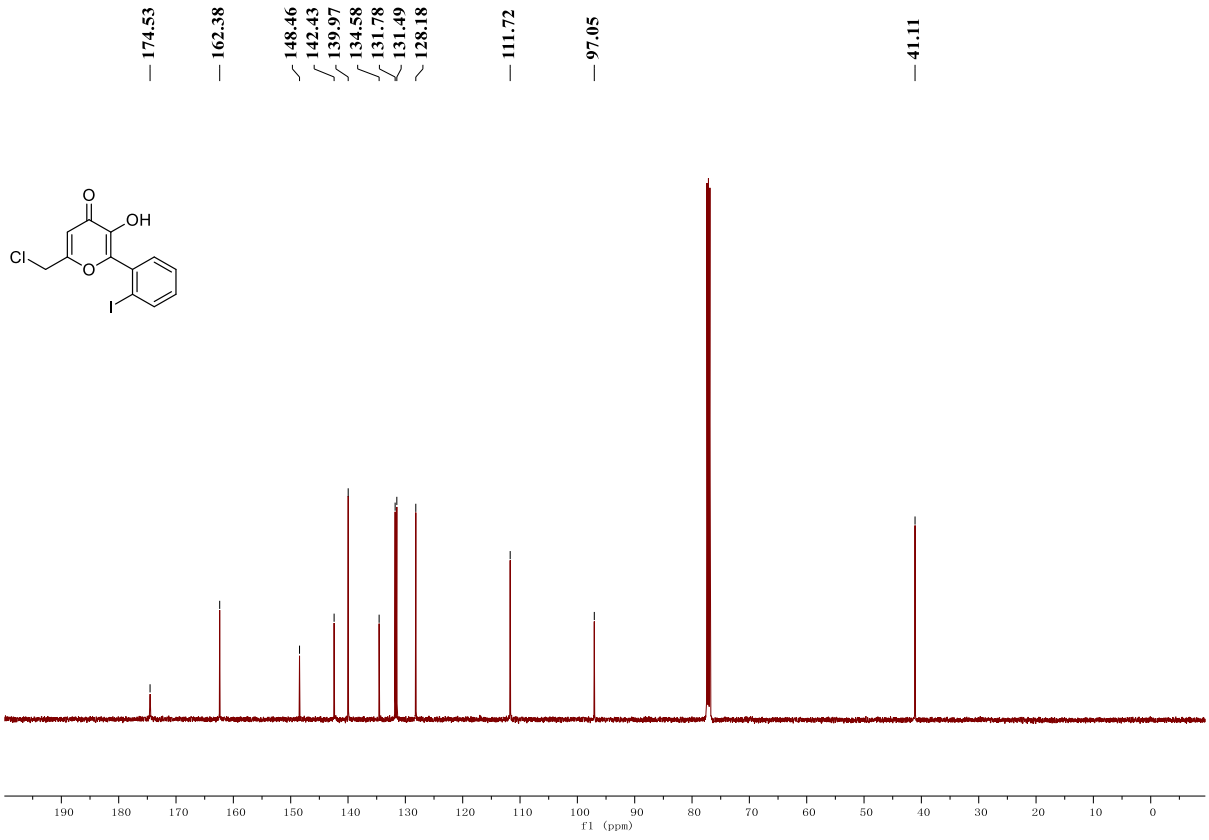
^{13}C NMR (126 MHz, DMSO-d_6) of **3l**



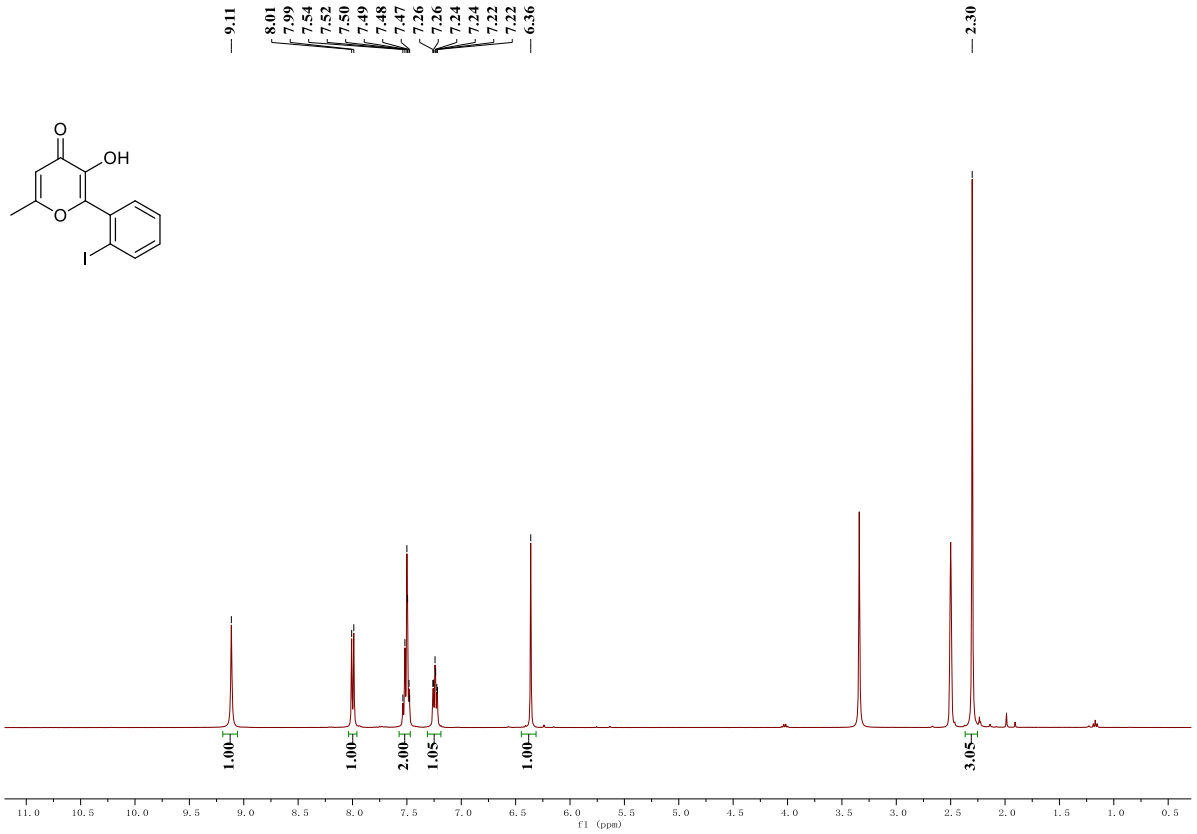
^{1}H NMR (500 MHz,$CDCl_3$) of **3m**



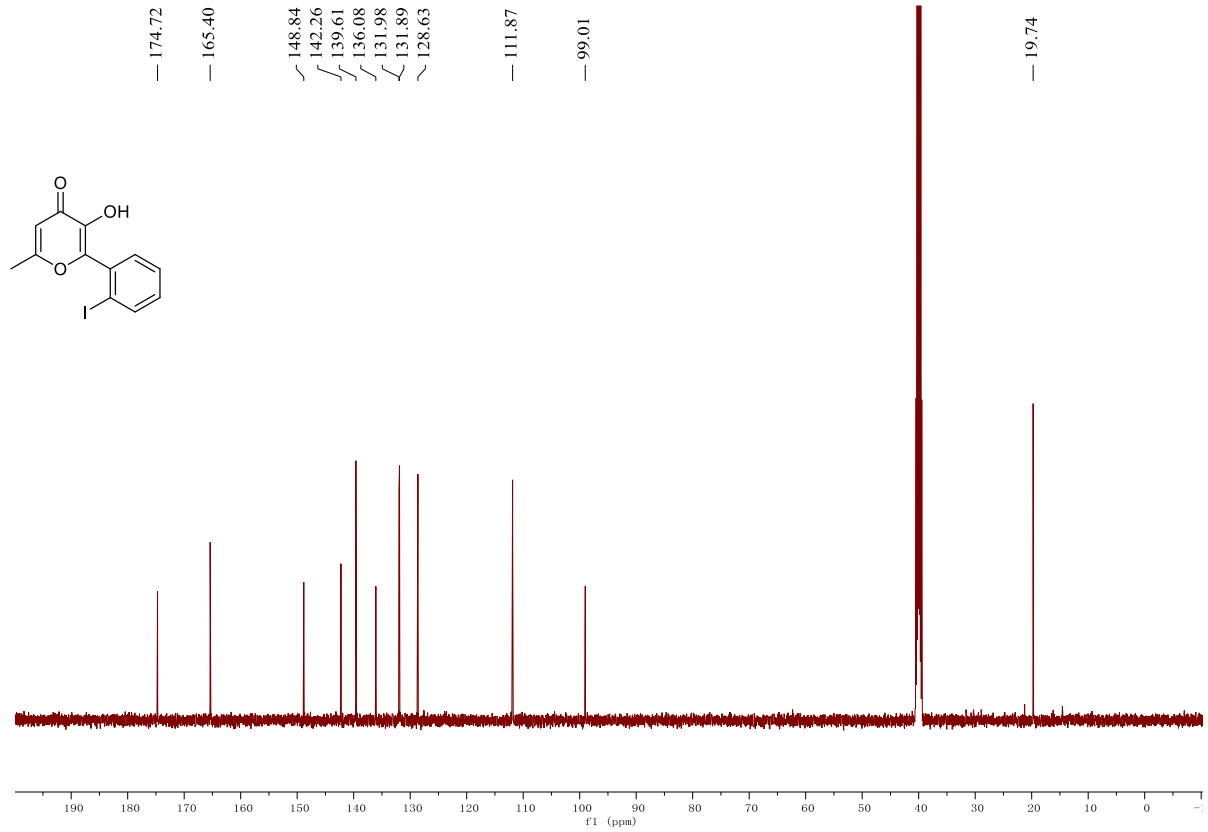
^{13}C NMR (126 MHz, $CDCl_3$) of **3m**



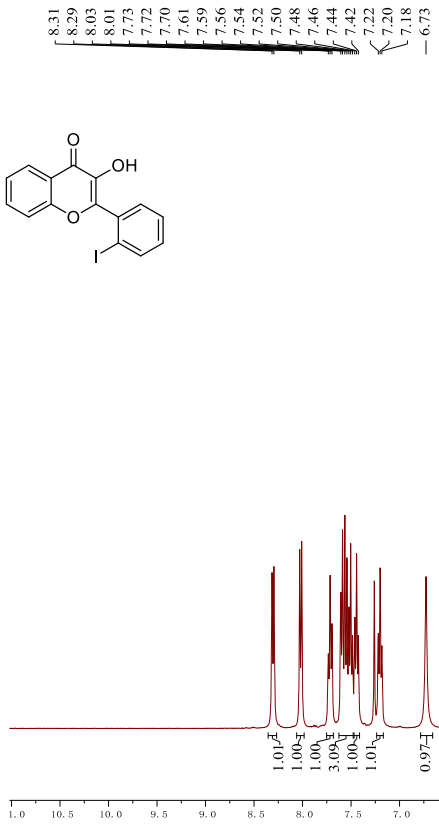
[1]H NMR (400 MHz, DMSO-d_6) of **3n**



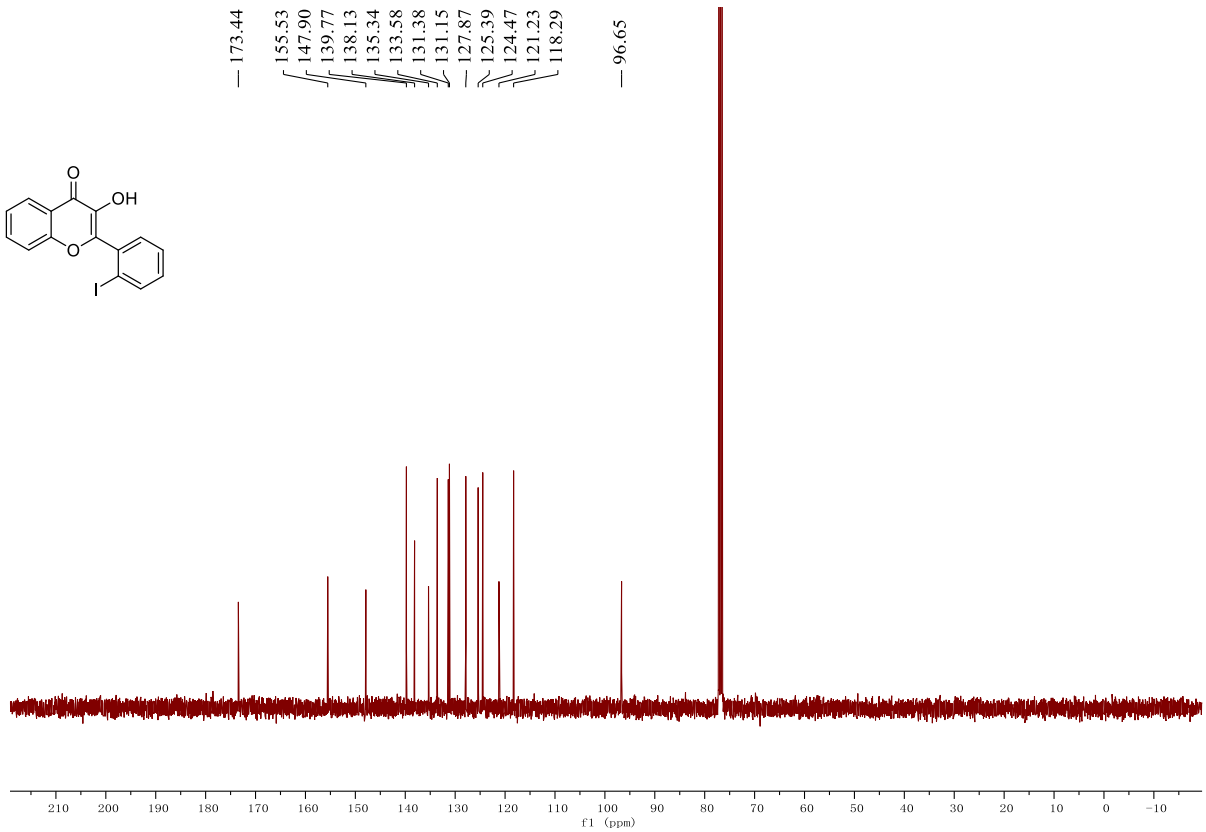
[13]C NMR (101 MHz, DMSO-d_6) of **3n**



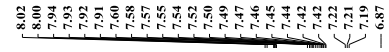
^{1}H NMR (400 MHz,$CDCl_3$) of **3o**

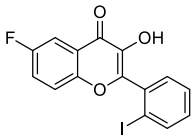


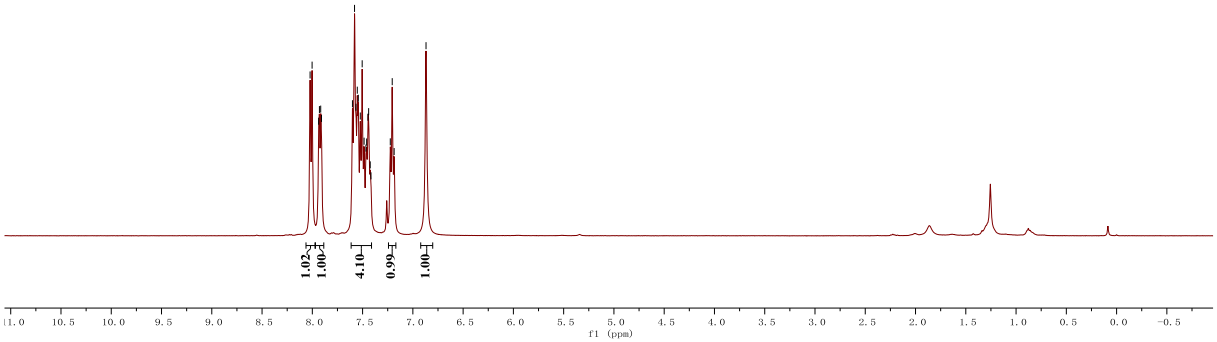
^{13}C NMR (101 MHz, $CDCl_3$) of **3o**



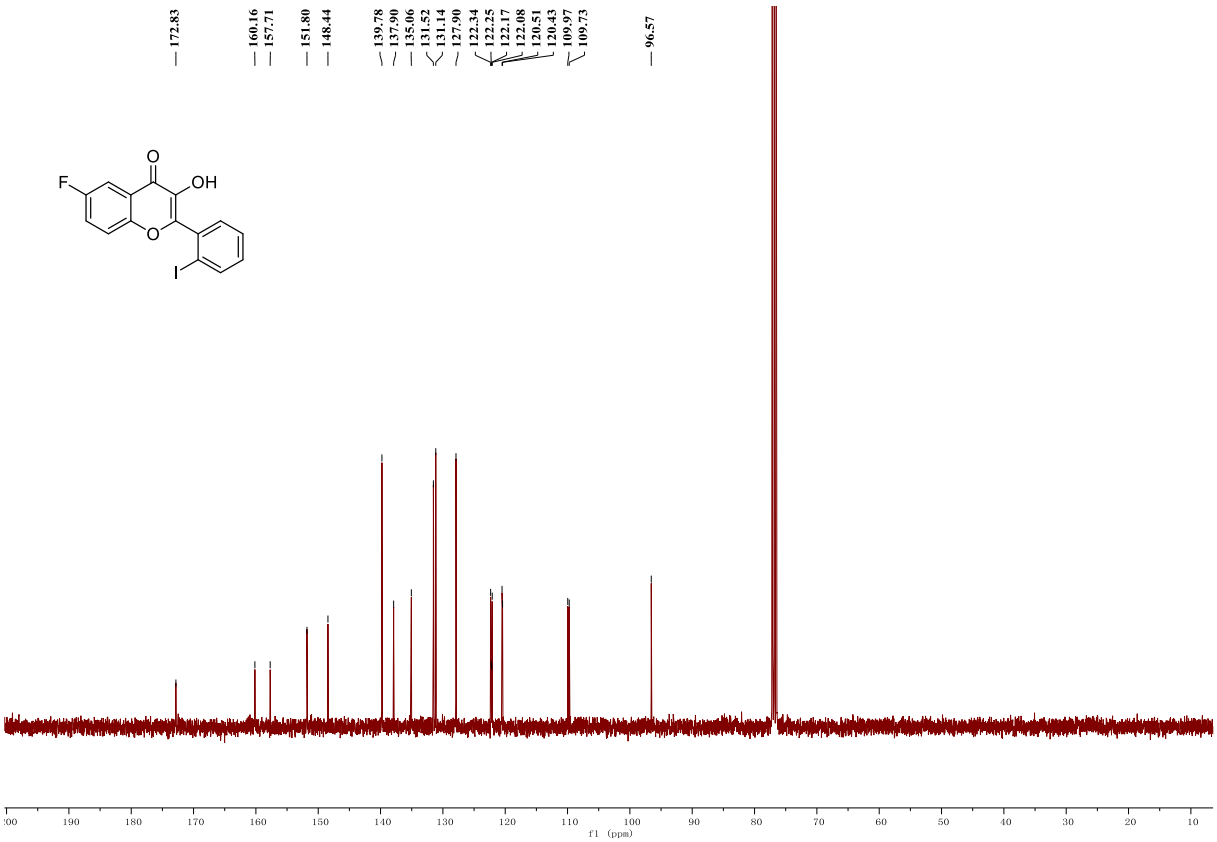
^{1}H NMR (400 MHz,$CDCl_3$) of **3p**



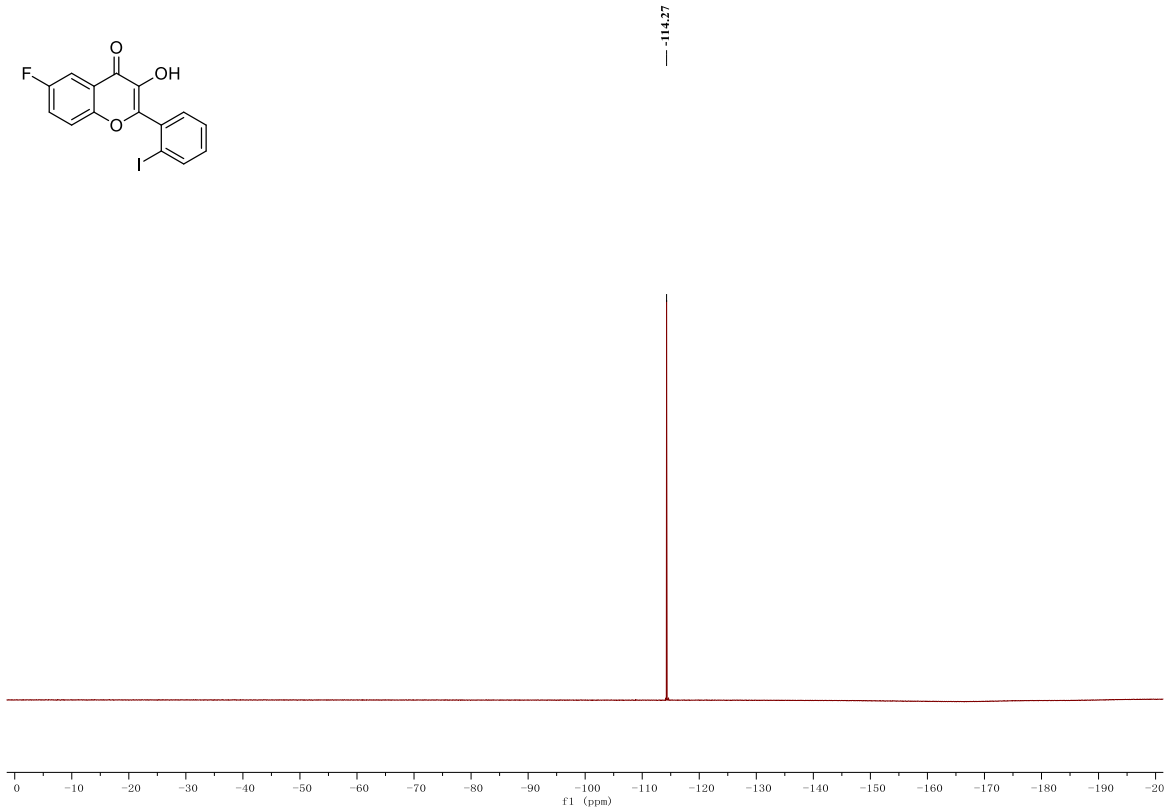




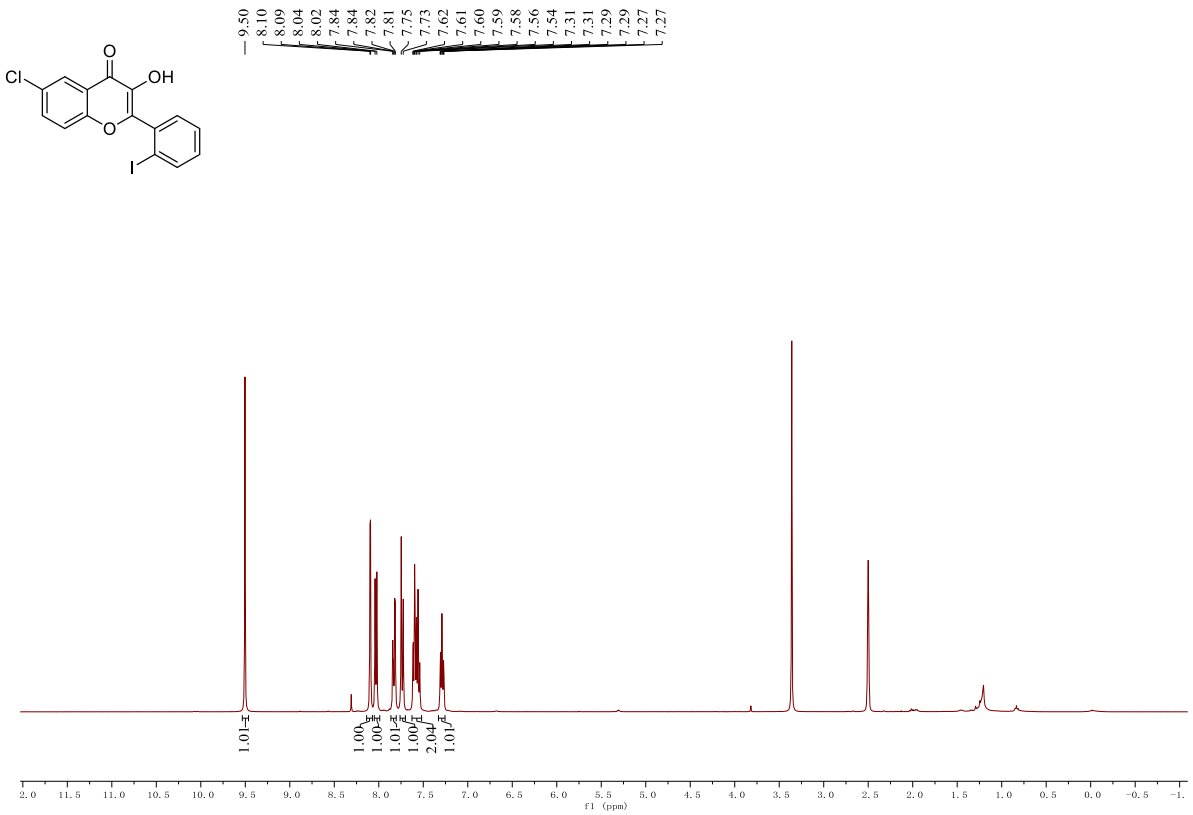
^{13}C NMR (101 MHz, $CDCl_3$) of **3p**



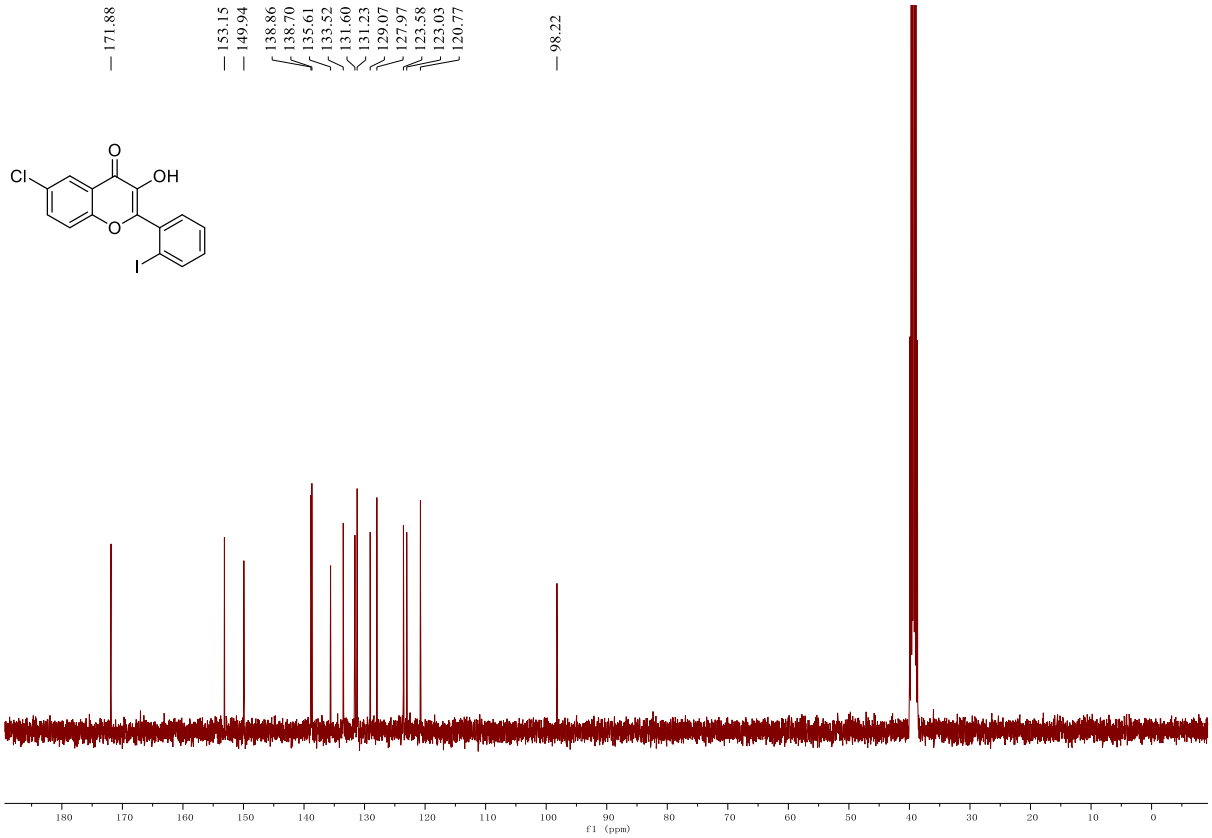
^{19}F NMR (471 MHz, $CDCl_3$) of **3p**



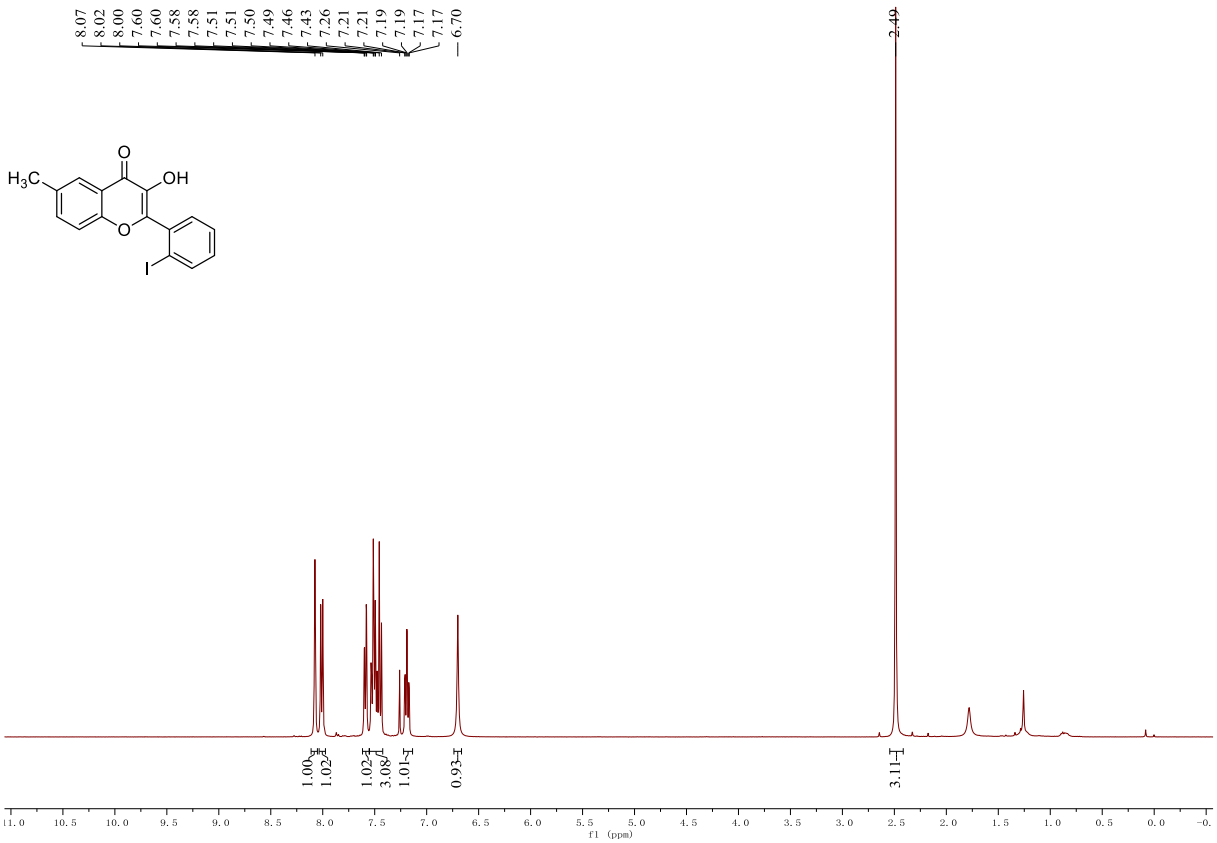
^{1}HNMR (400 MHz, DMSO-d_6) of **3q**



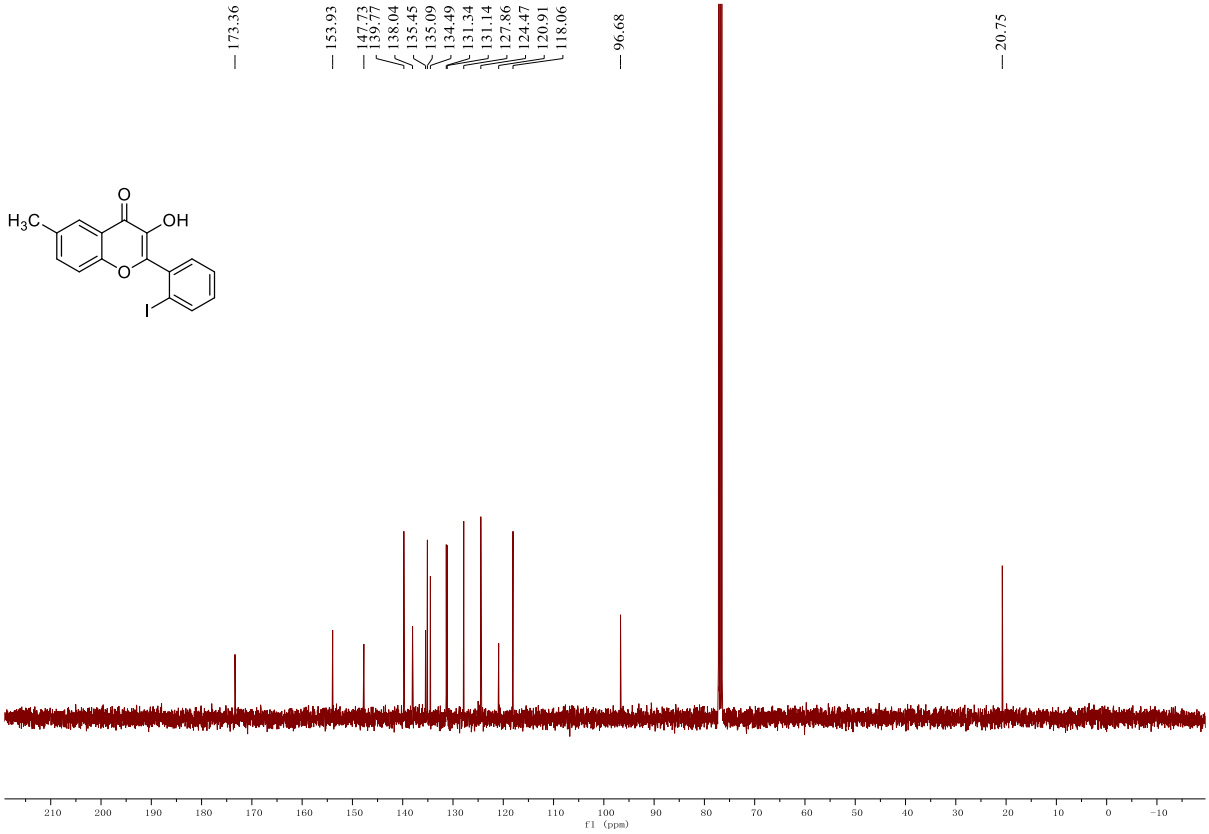
^{13}C NMR (101 MHz, DMSO-d_6) of **3q**



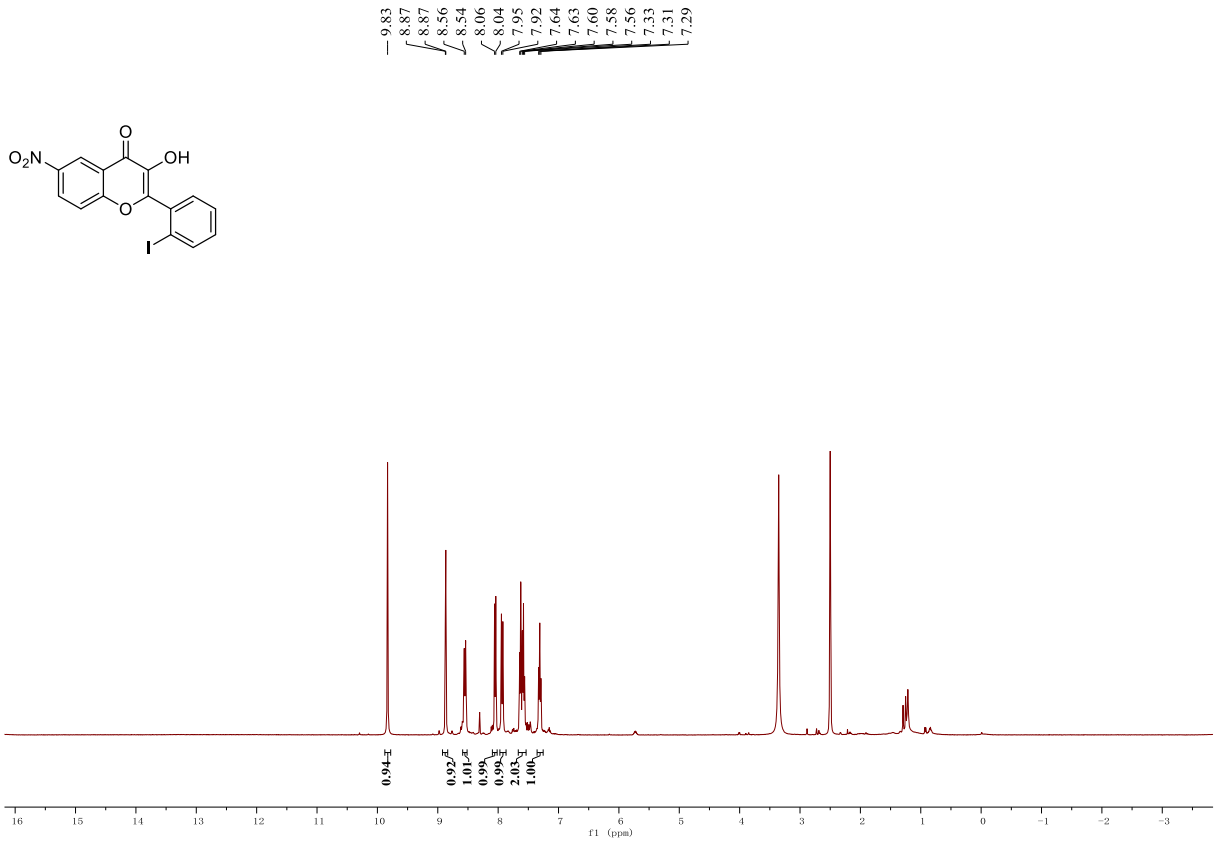
^{1}H NMR (400 MHz,$CDCl_3$) of **3r**



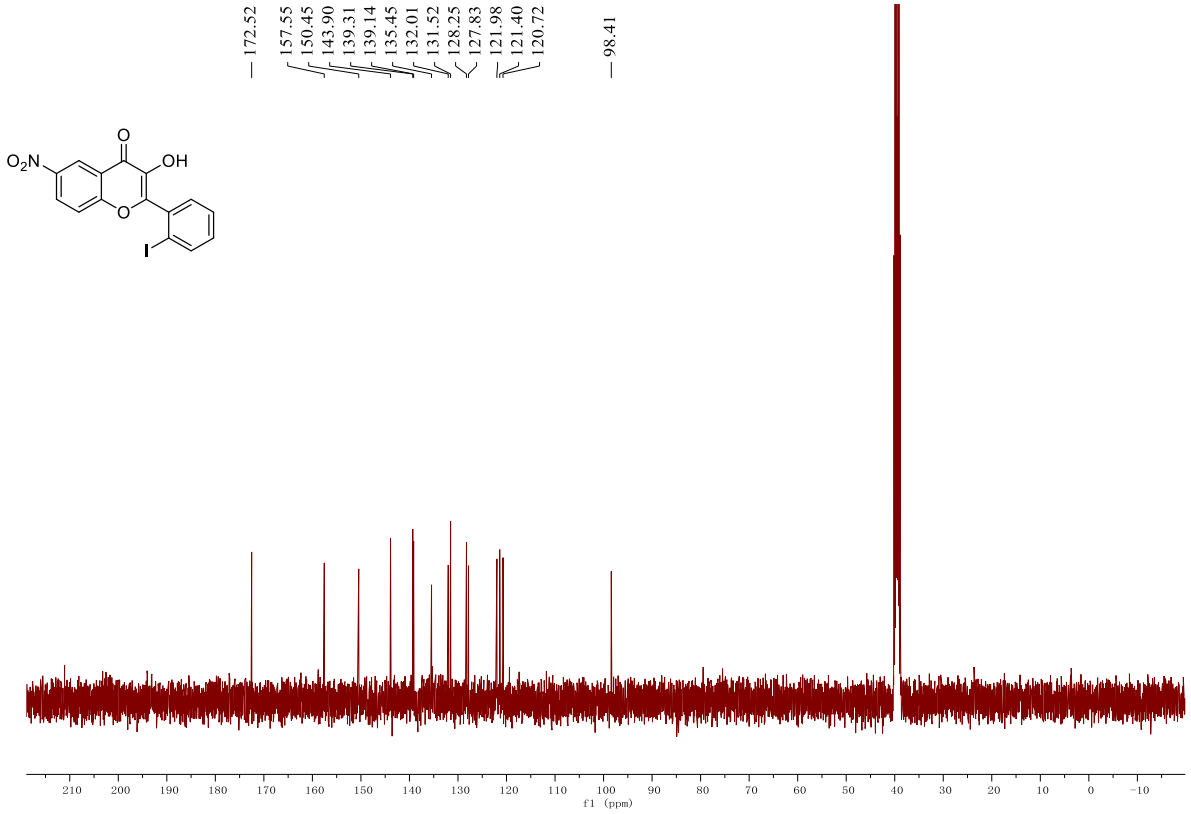
^{13}C NMR (101 MHz, $CDCl_3$) of **3r**



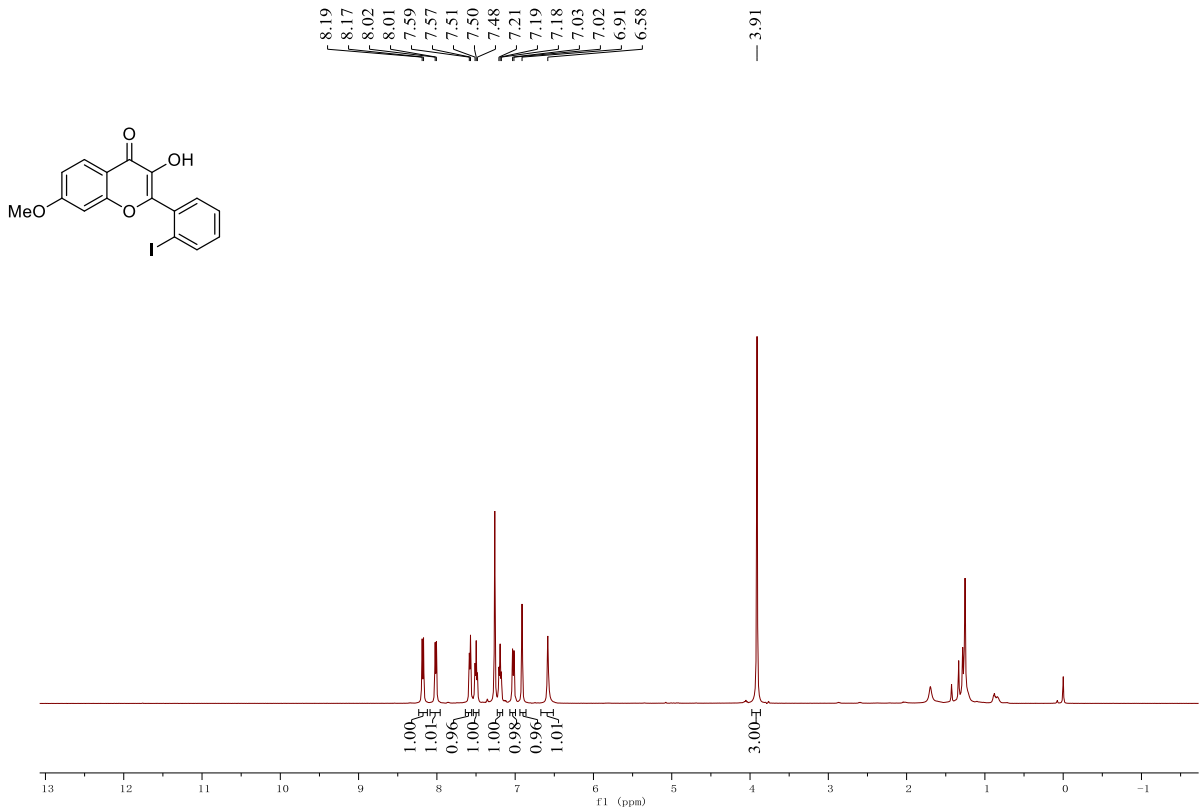
^{1}H NMR (400 MHz, DMSO-d_6) of **3s**



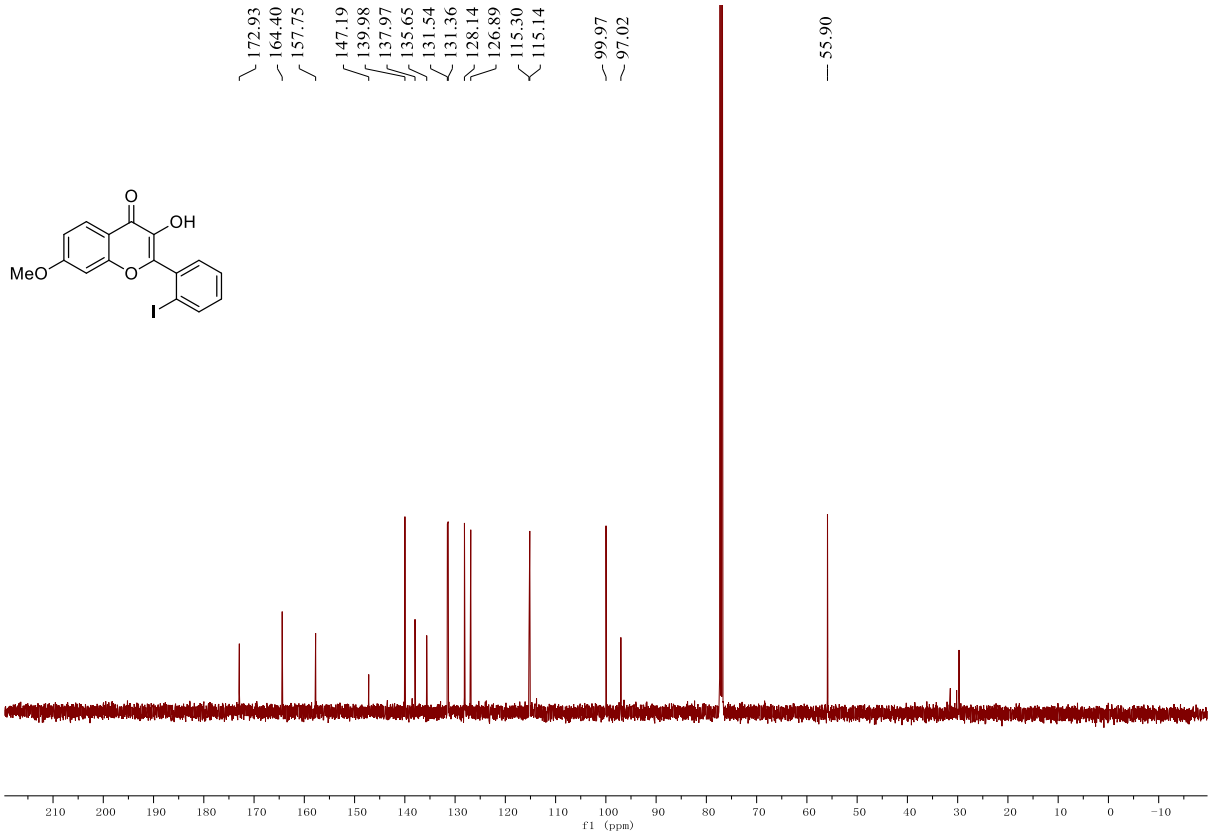
^{13}C NMR (101 MHz, DMSO-d_6) of **3s**



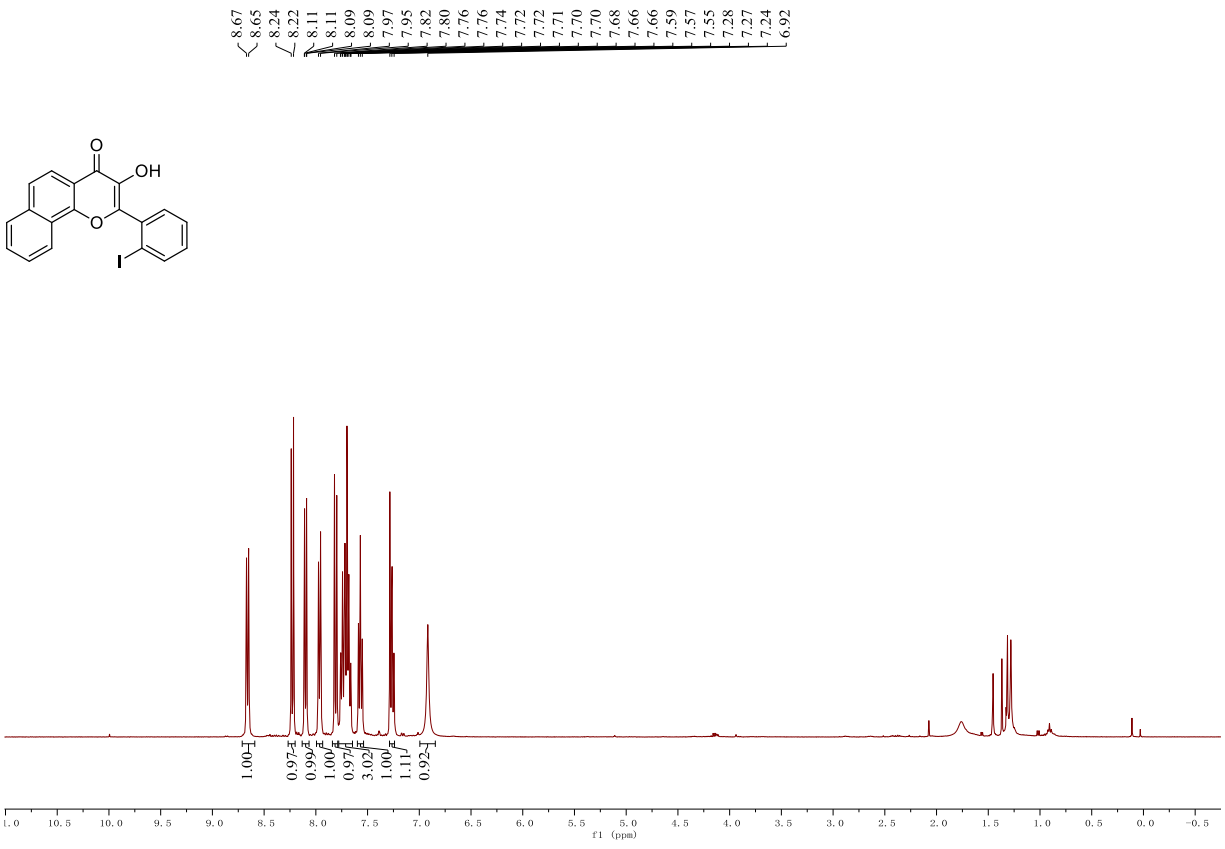
^{1}H NMR (500 MHz, $CDCl_3$) of **3t**



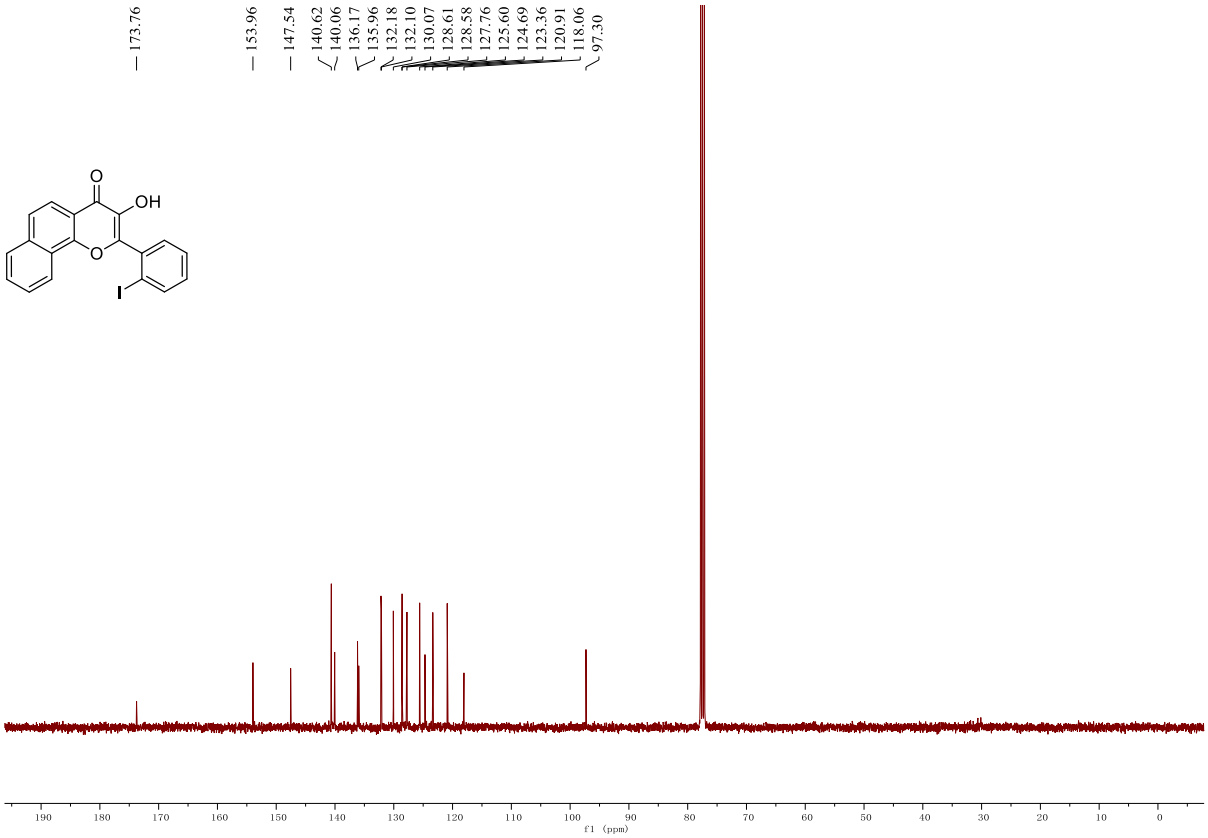
^{13}C NMR (126 MHz, $CDCl_3$) of **3t**



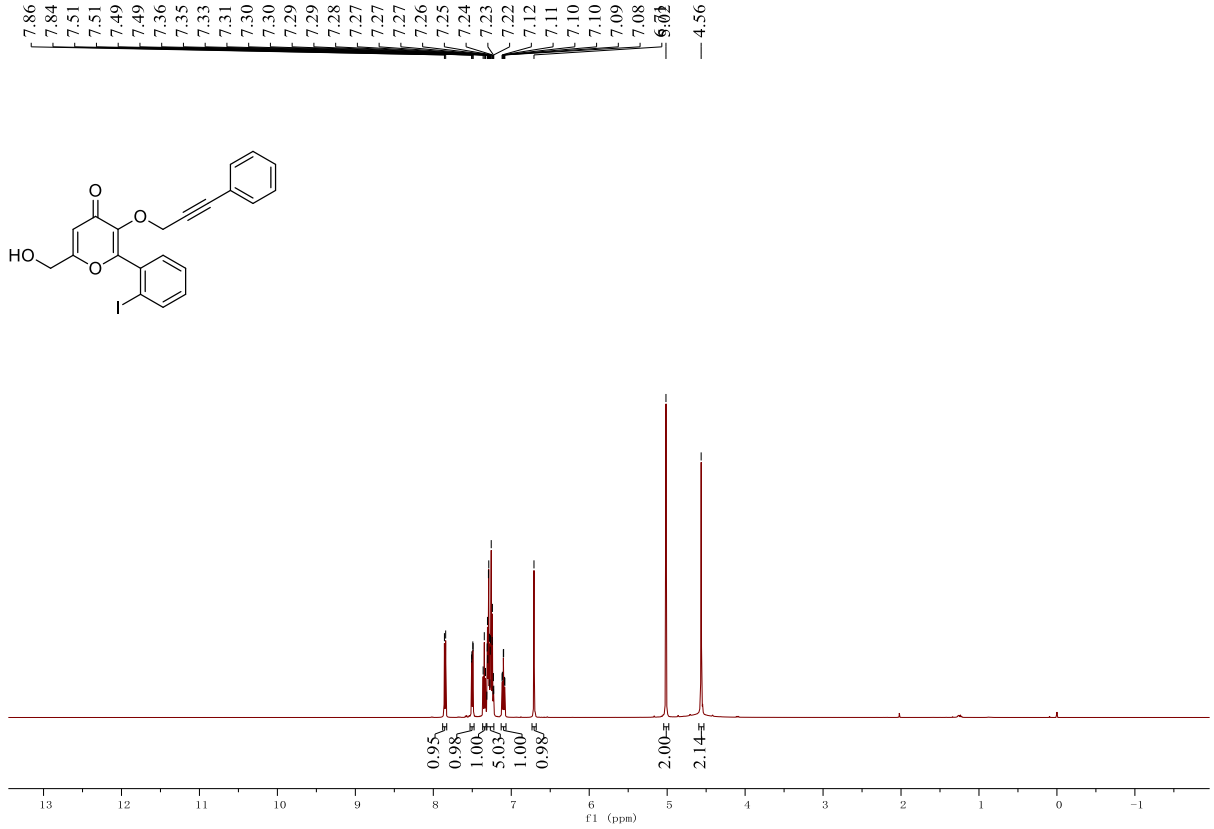
^{1}H NMR (400 MHz, $CDCl_3$) of **3u**



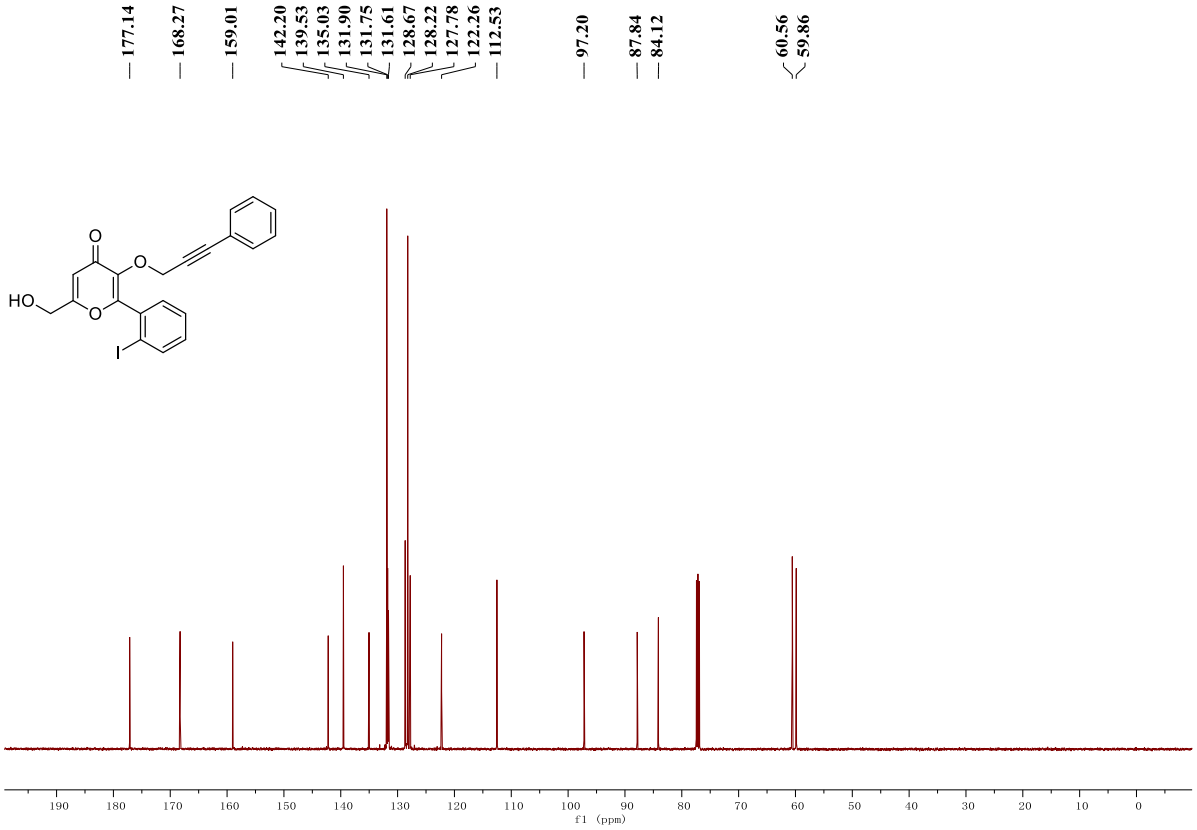
^{13}C NMR (101 MHz, $CDCl_3$) of **3u**



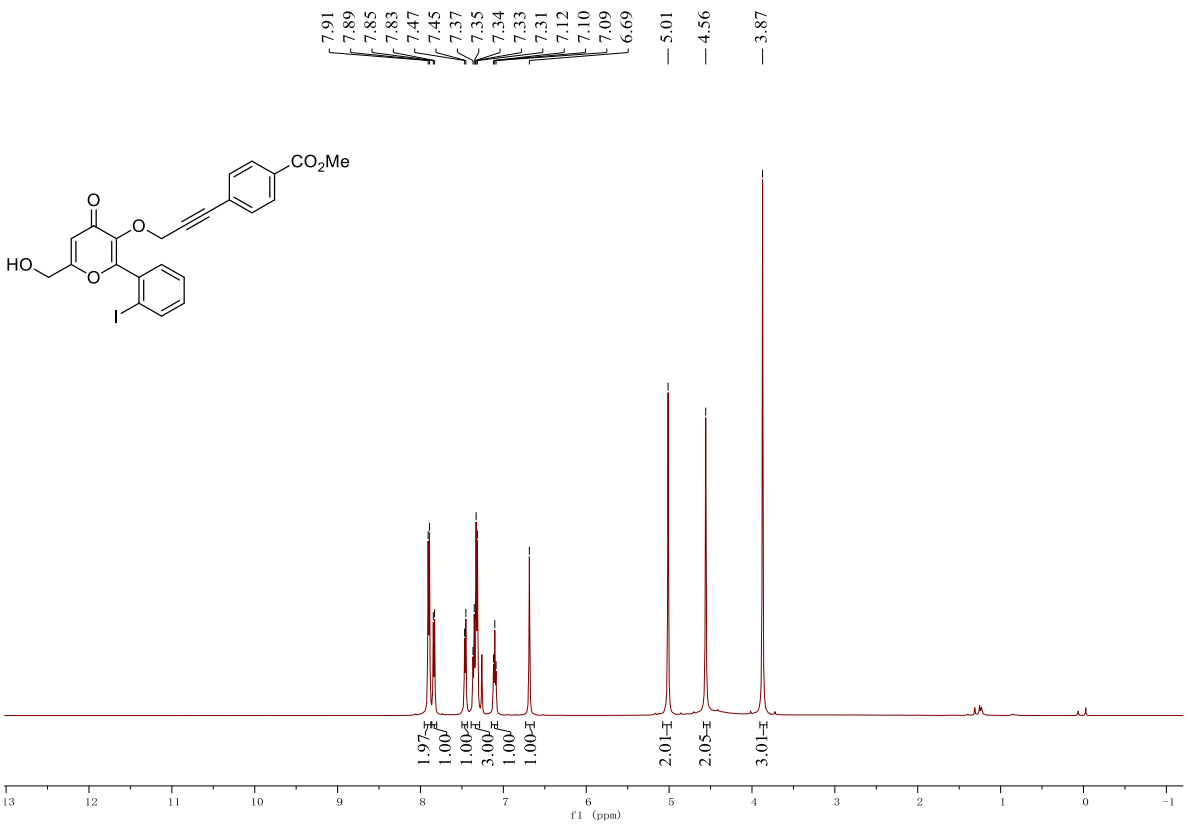
^{1}H NMR (500 MHz, $CDCl_3$) of **4a**



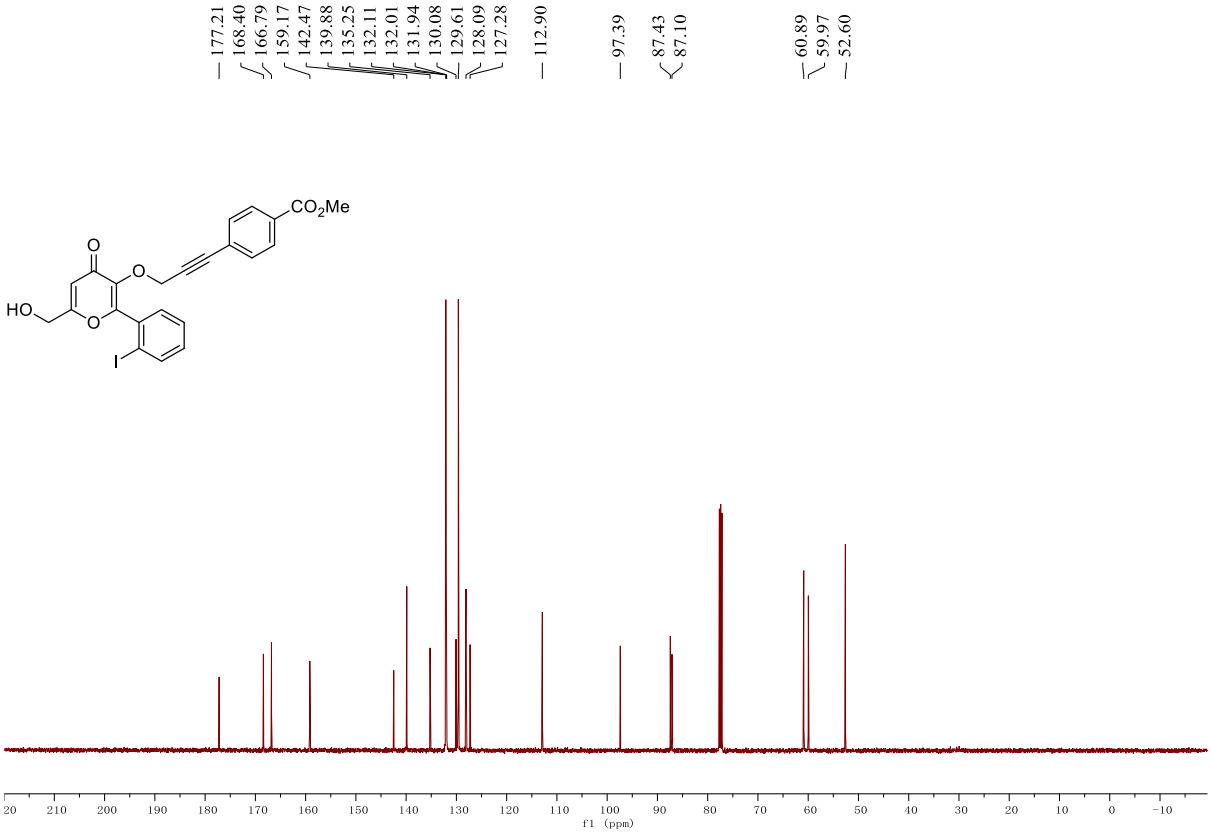
^{13}C NMR (126 MHz, $CDCl_3$) of **4a**



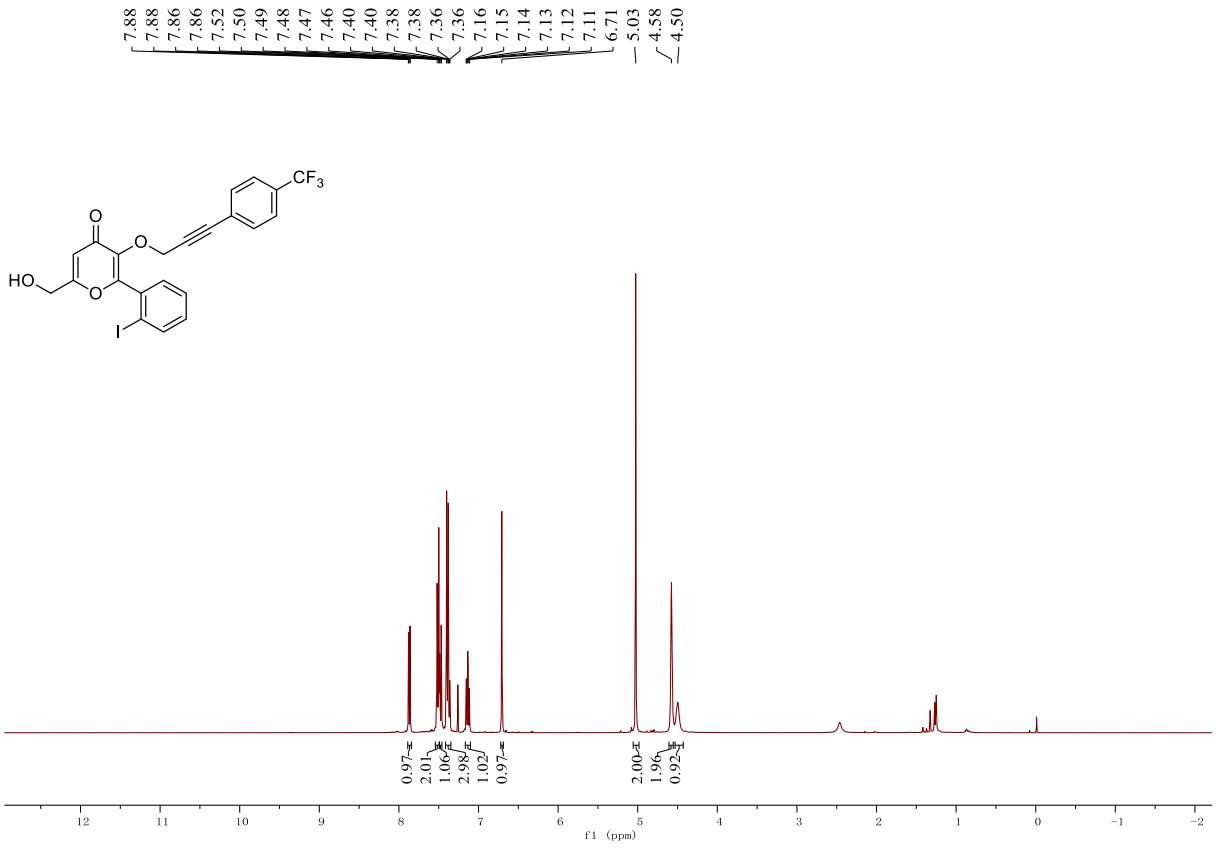
^{1}H NMR (500 MHz, $CDCl_3$) of **4b**



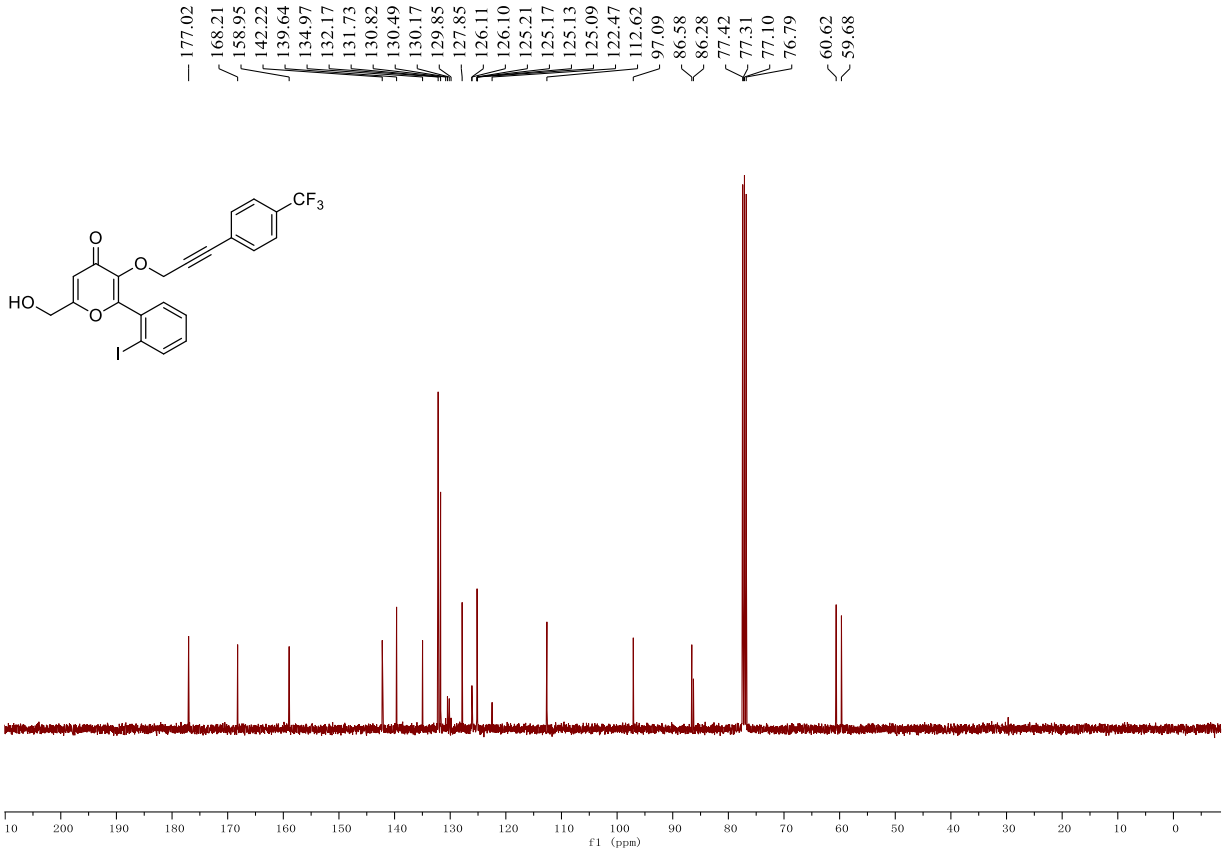
^{13}C NMR (126 MHz, $CDCl_3$) of **4b**



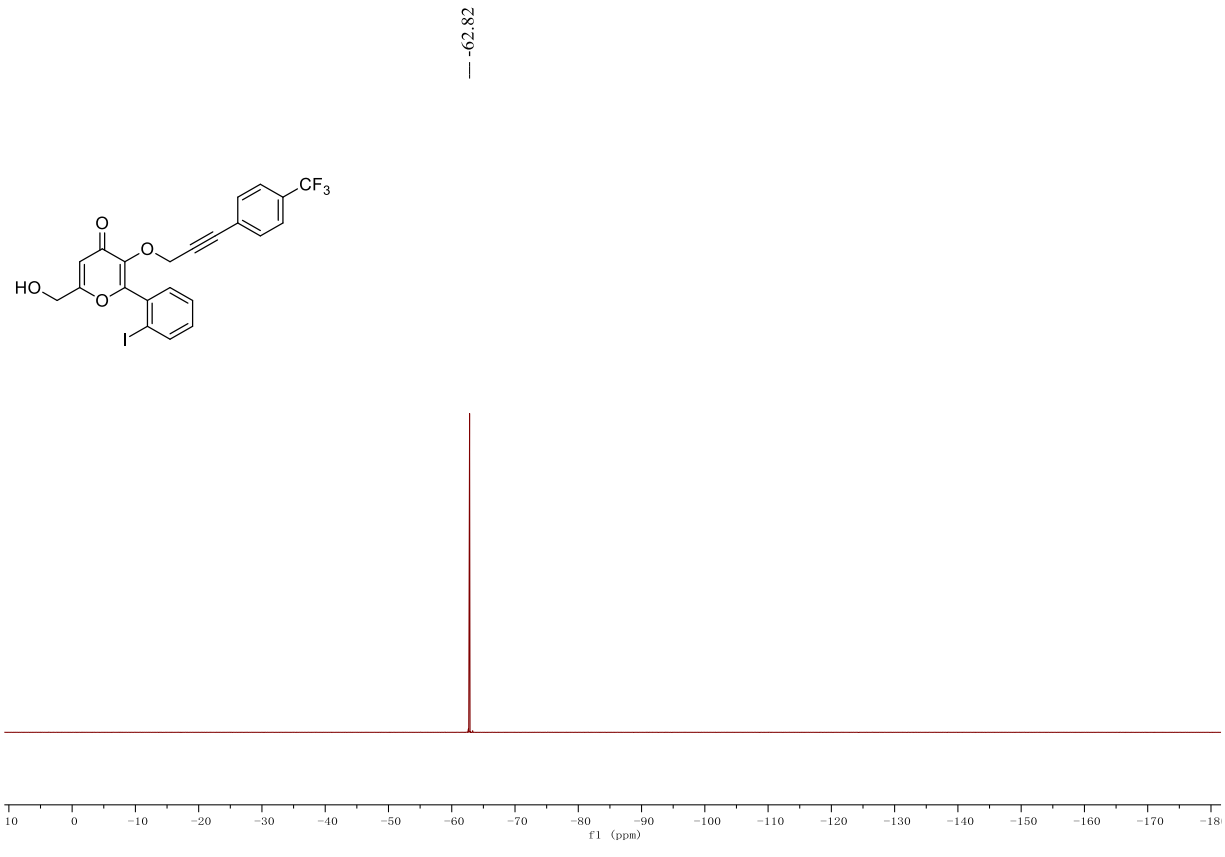
^{1}H NMR (400 MHz, $CDCl_3$) of **4c**



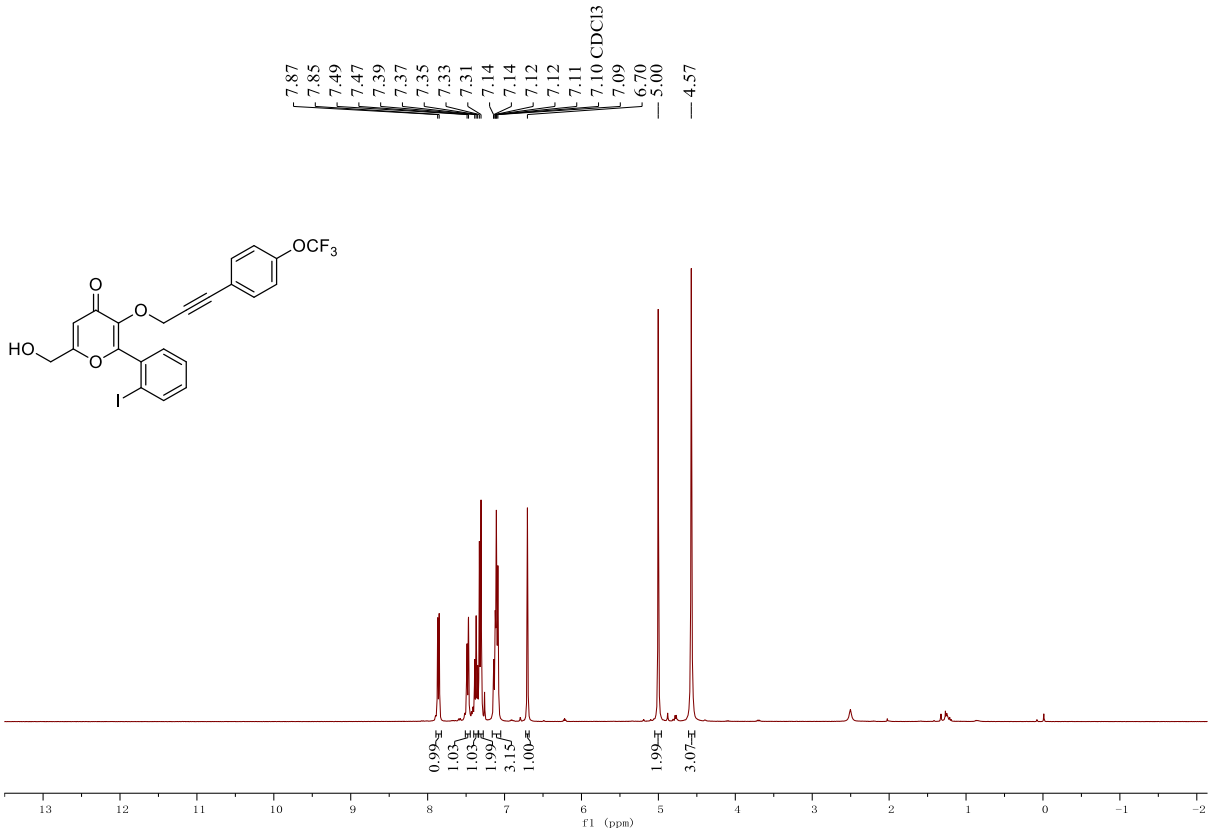
^{13}C NMR (101 MHz, $CDCl_3$) of **4c**



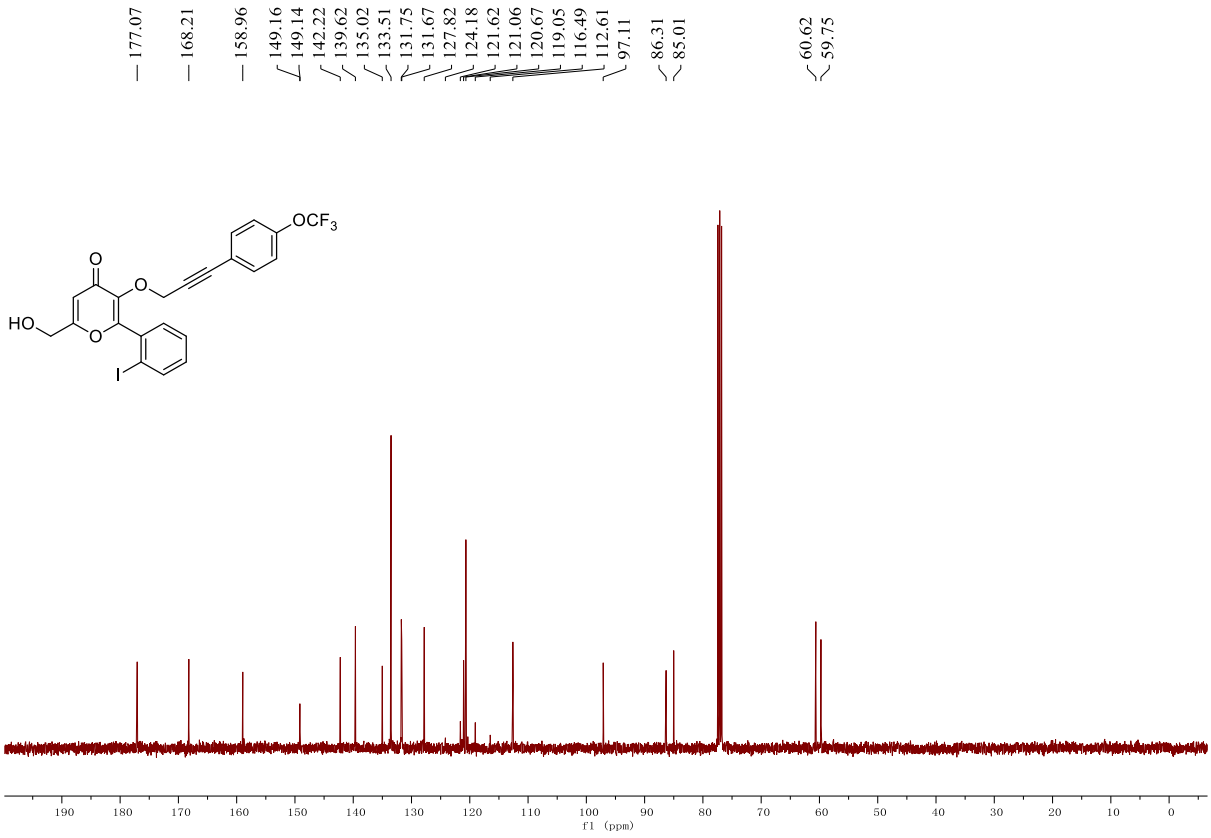
^{19}F NMR (376 MHz, $CDCl_3$) of **5c**



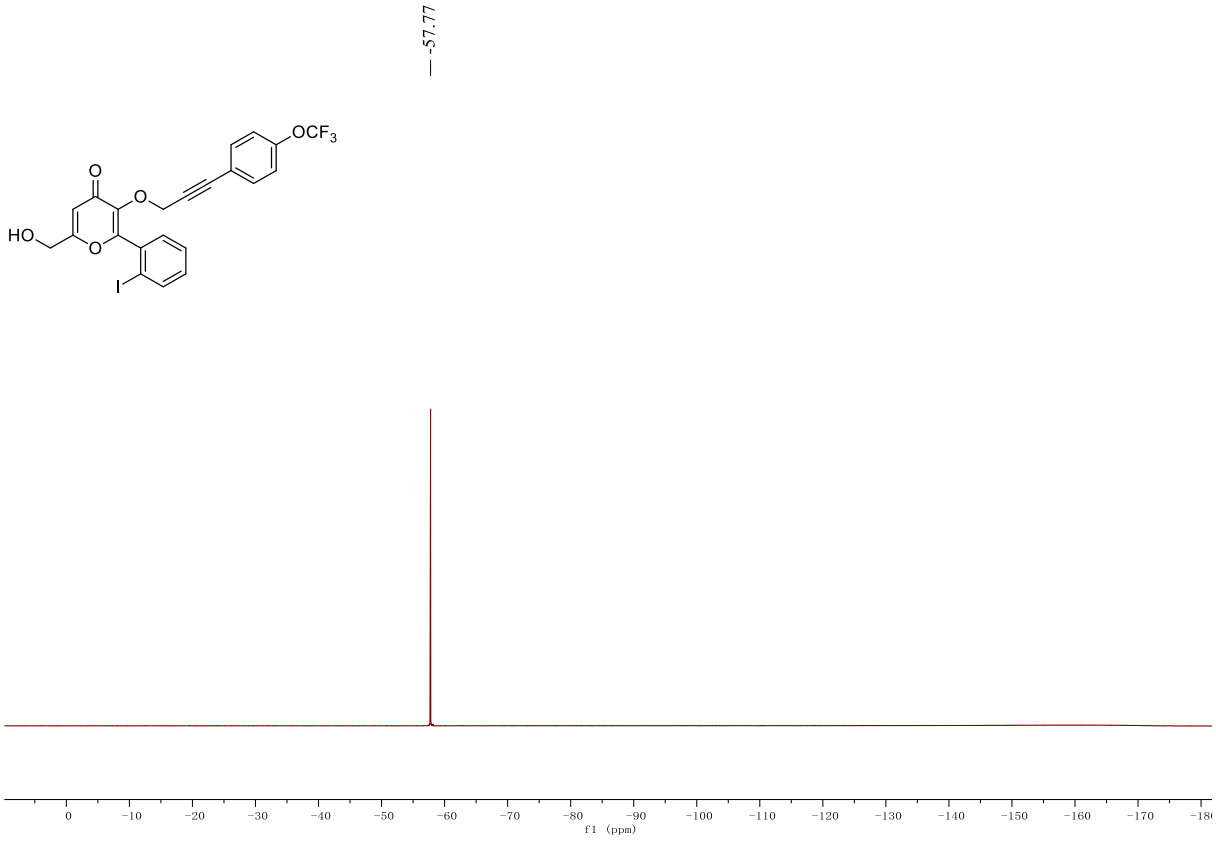
^{1}H NMR (400 MHz, $CDCl_3$) of **4d**



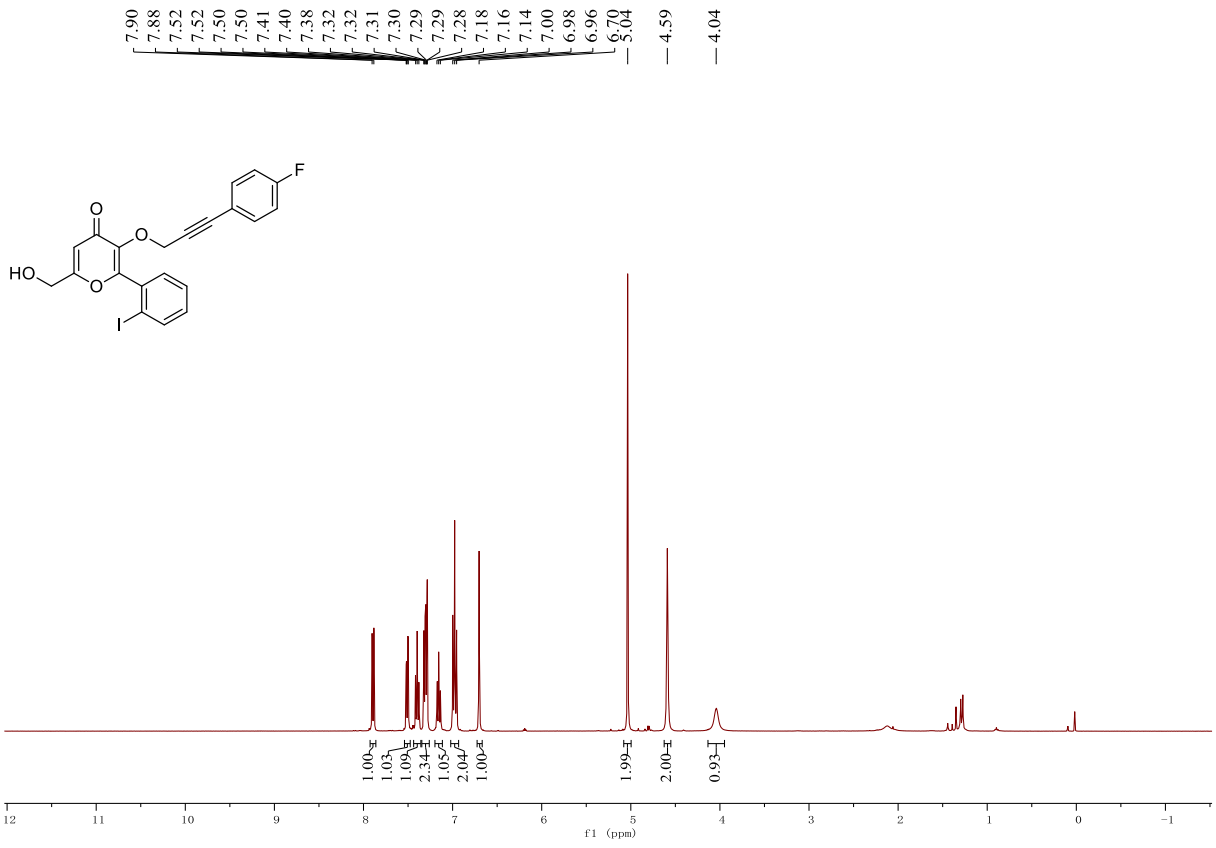
^{13}C NMR (101 MHz, $CDCl_3$) of **4d**



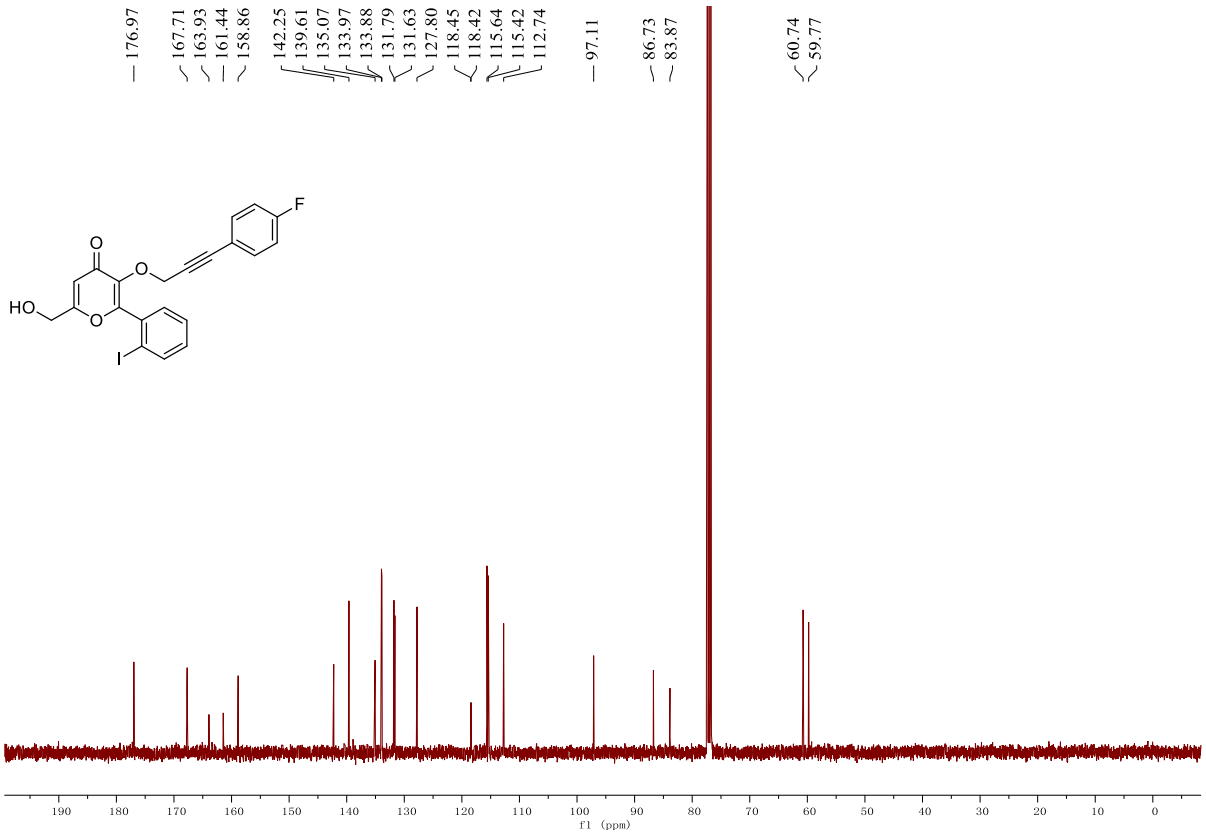
^{19}F NMR (471 MHz, $CDCl_3$) of **5d**



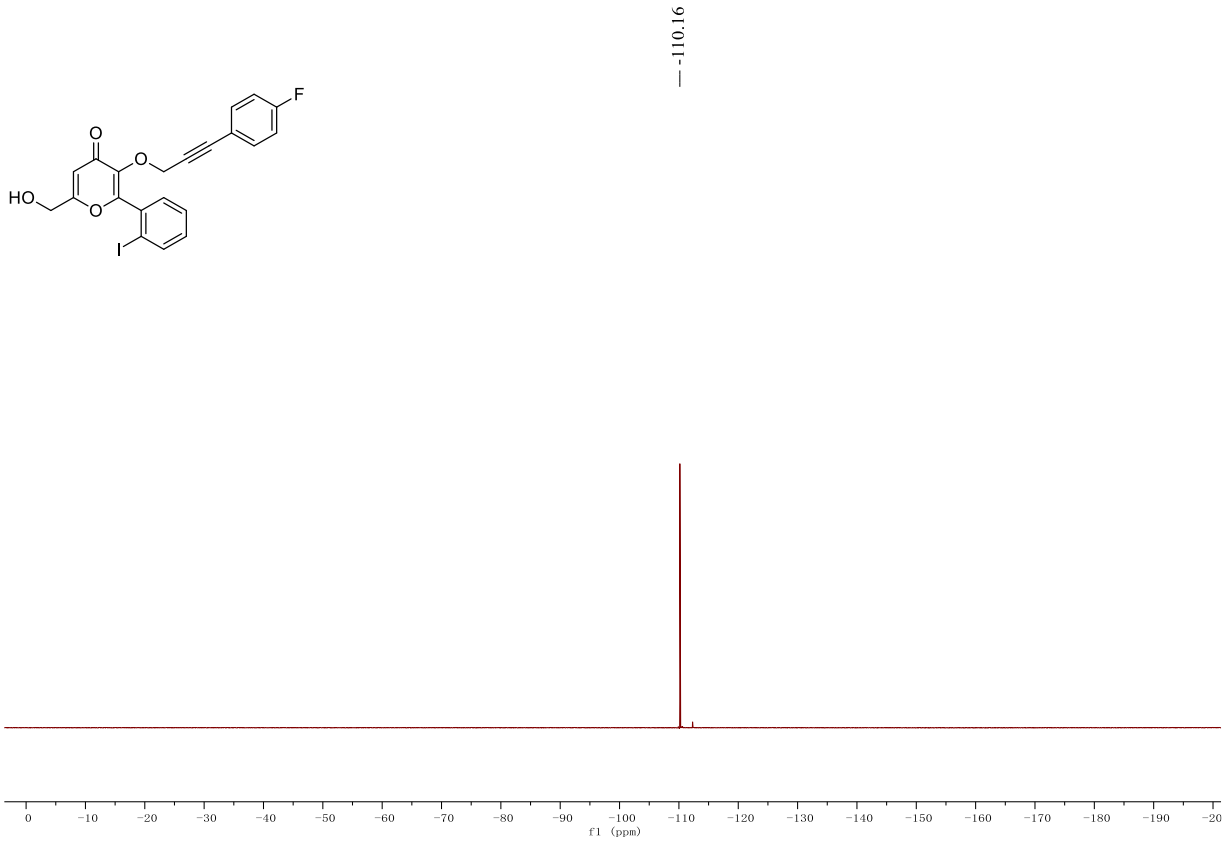
^{1}H NMR (400 MHz, $CDCl_3$) of **4e**



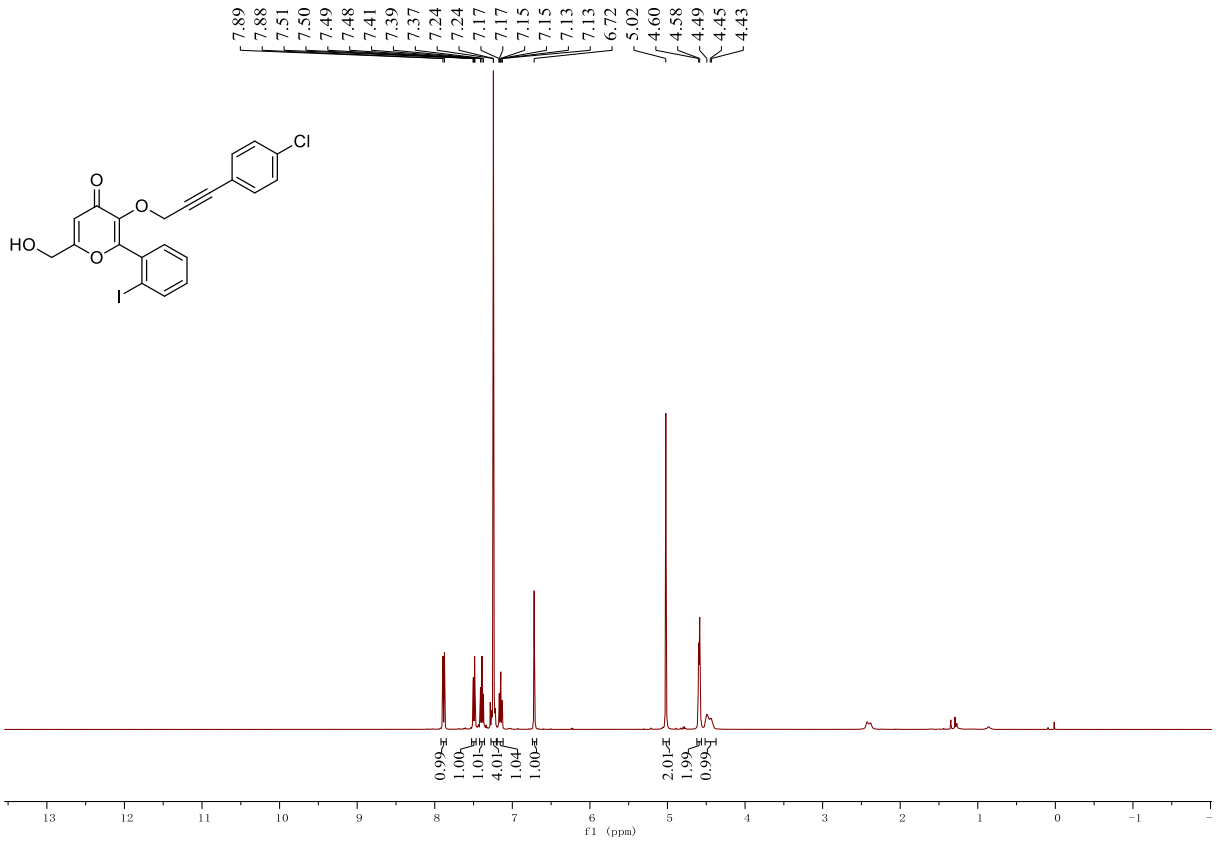
^{13}C NMR (101 MHz, $CDCl_3$) of **4e**



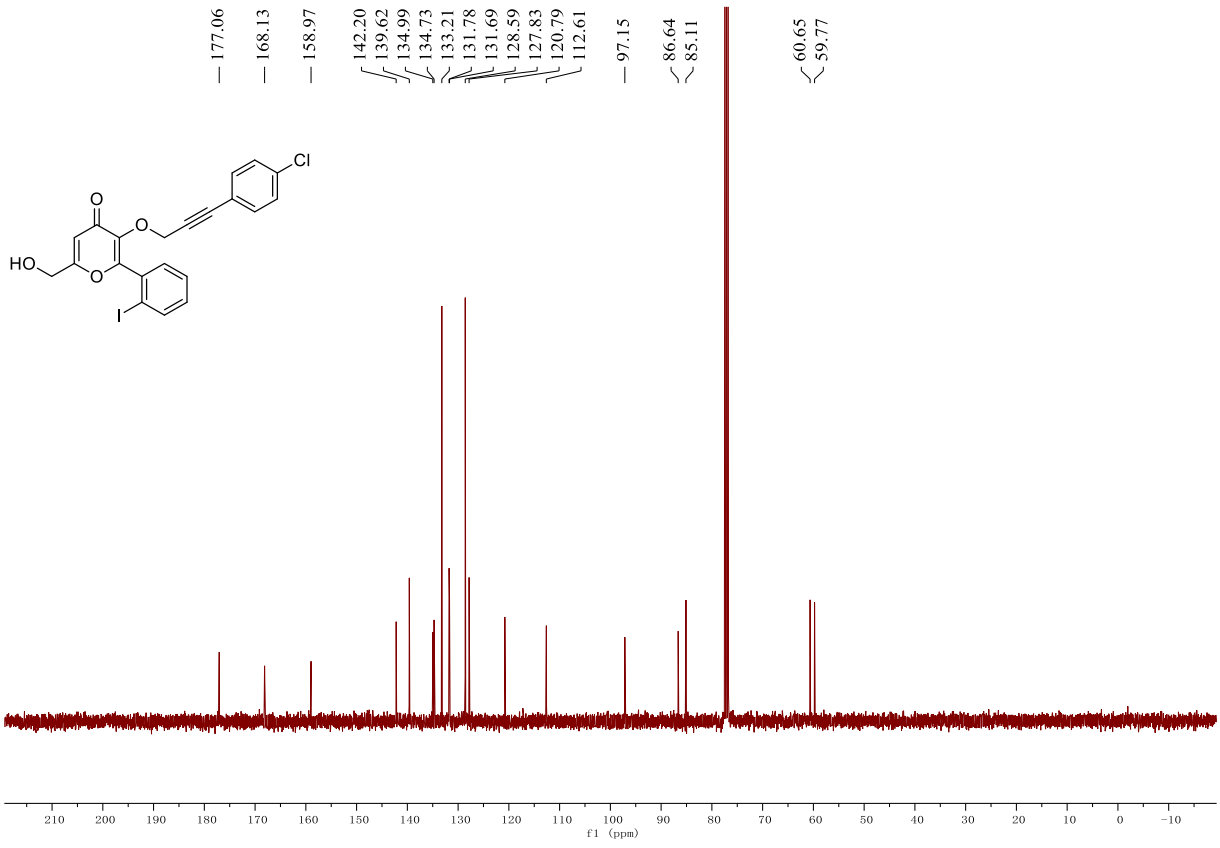
^{19}F NMR (376MHz, $CDCl_3$) of **5e**



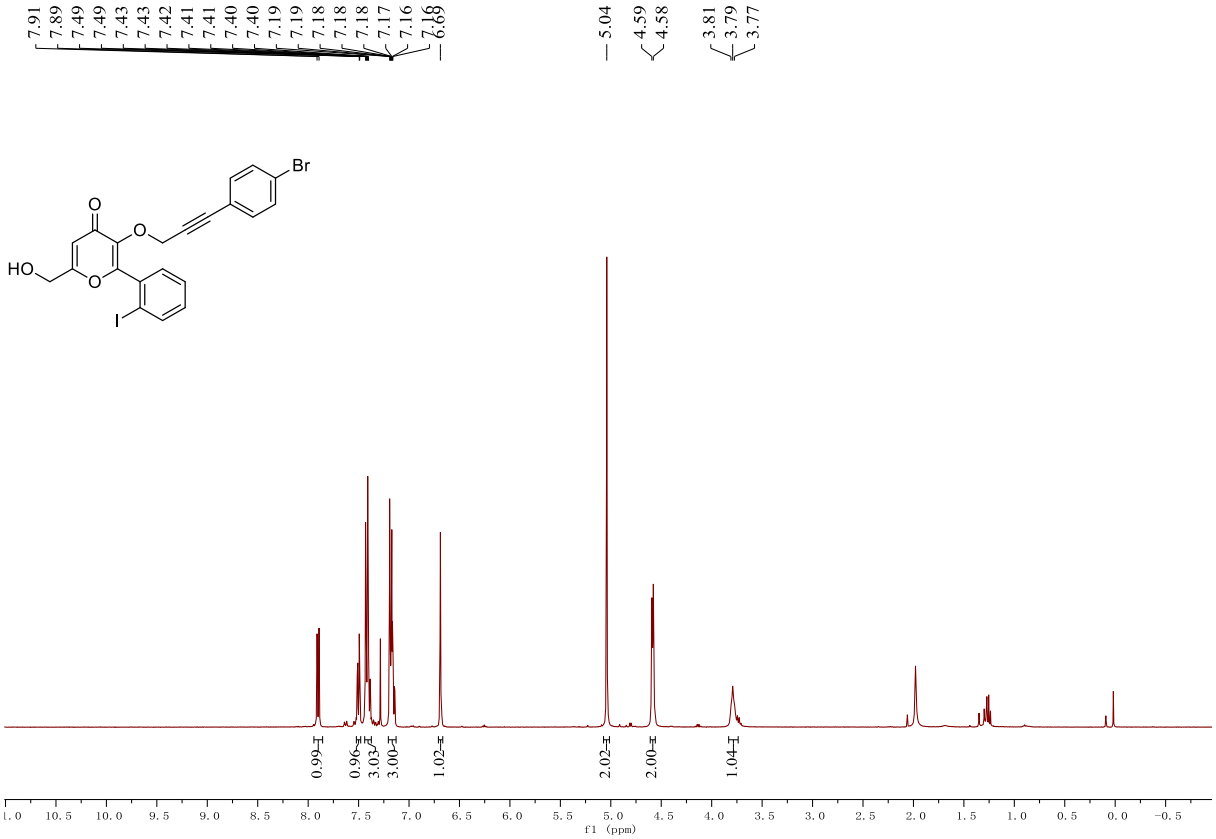
^{1}H NMR (500 MHz, $CDCl_3$) of **4f**



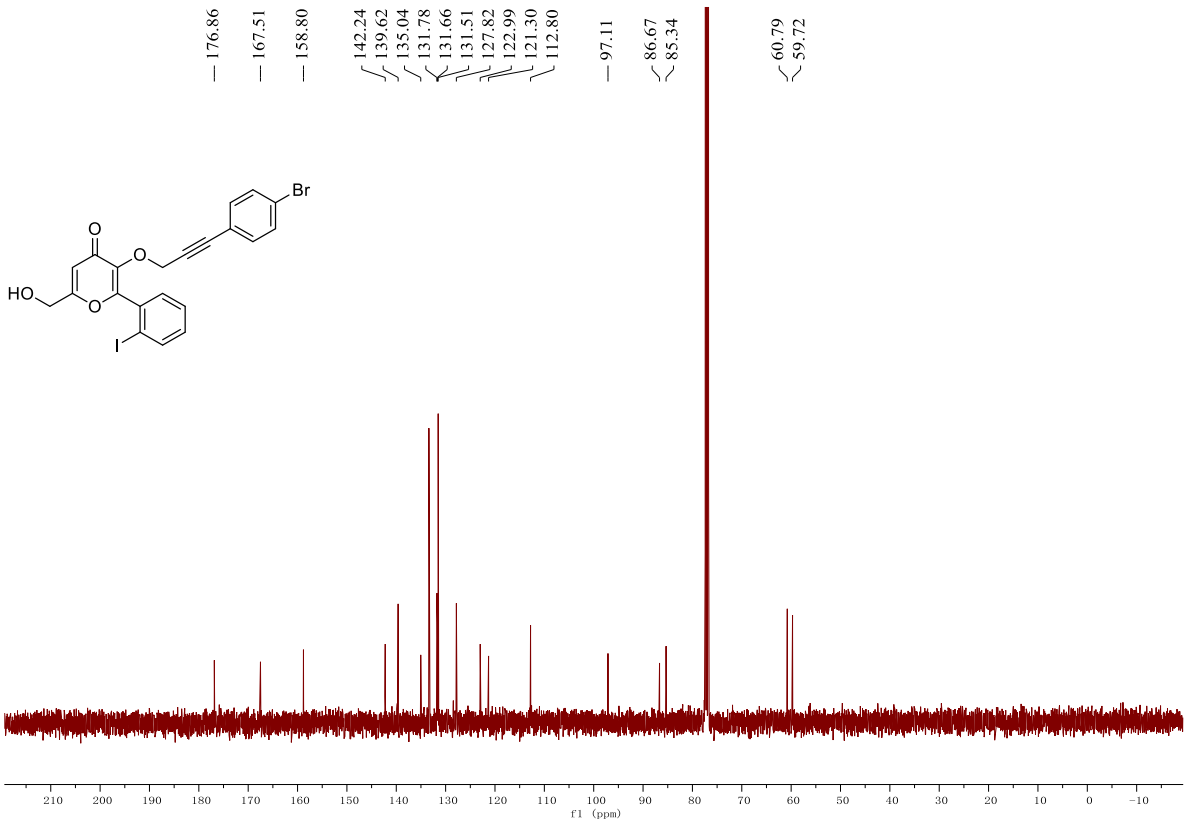
^{13}C NMR (101 MHz, $CDCl_3$) of **4f**



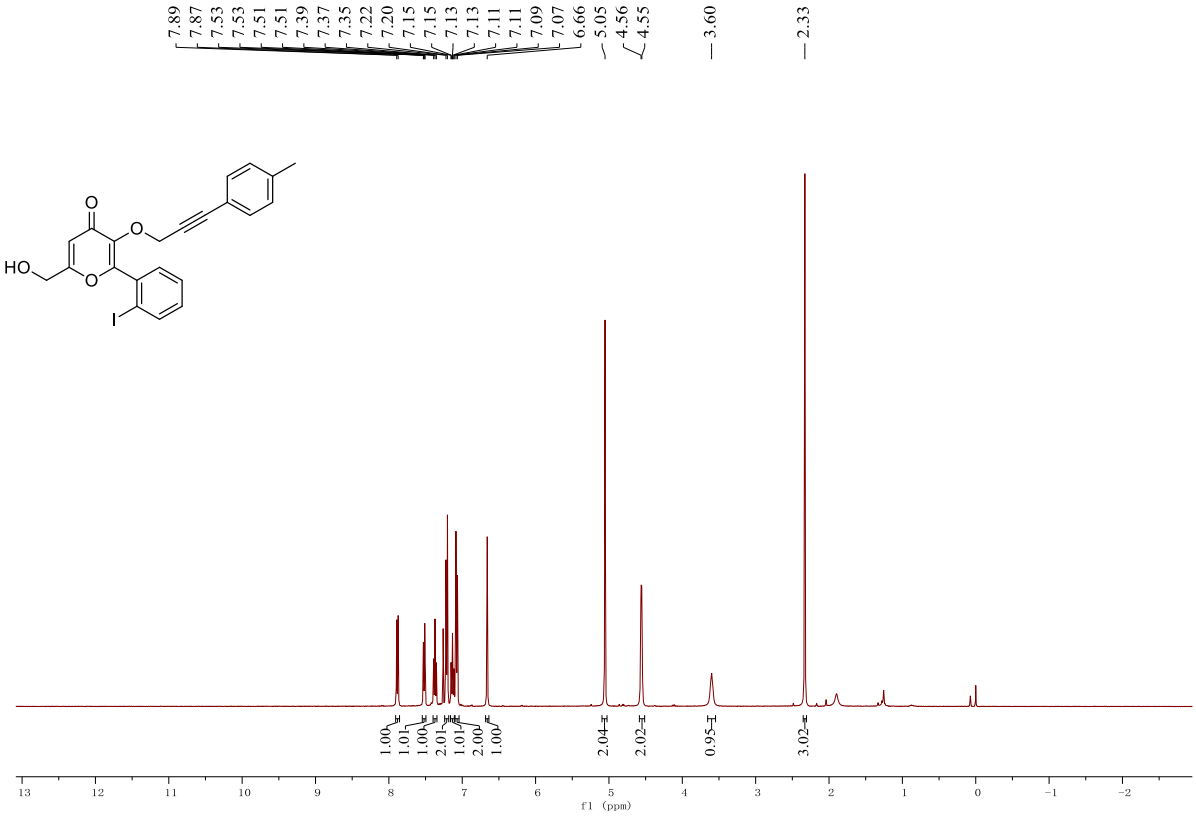
^{1}H NMR (400 MHz, $CDCl_3$) of **4g**



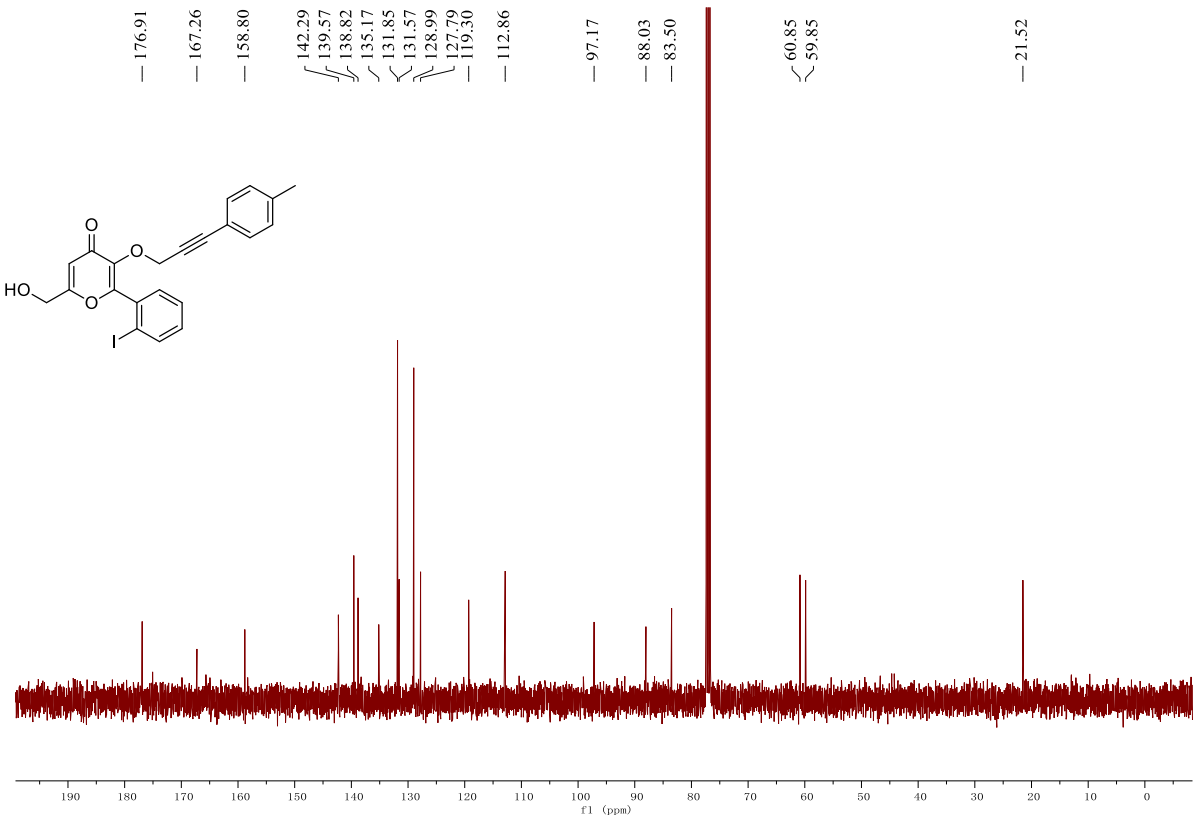
^{13}C NMR (101 MHz, $CDCl_3$) of **4g**



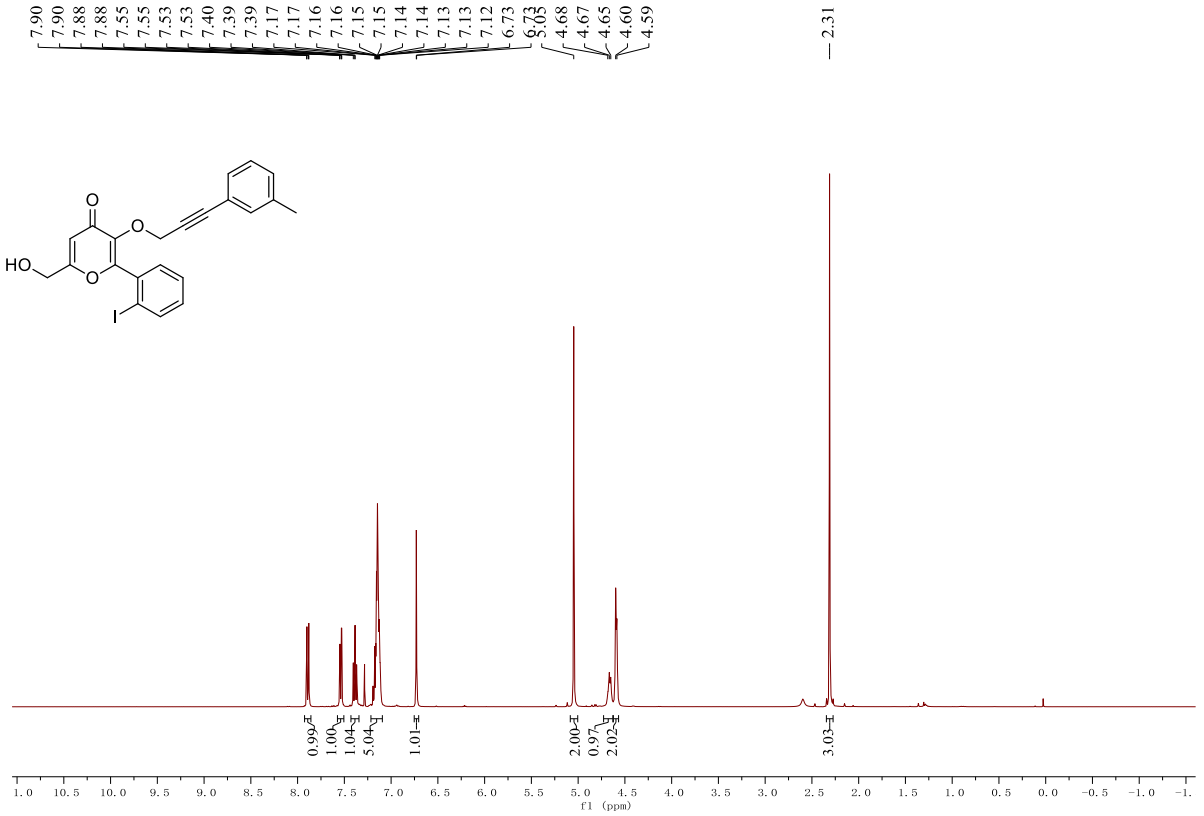
^{1}H NMR (400 MHz, $CDCl_3$) of **4h**



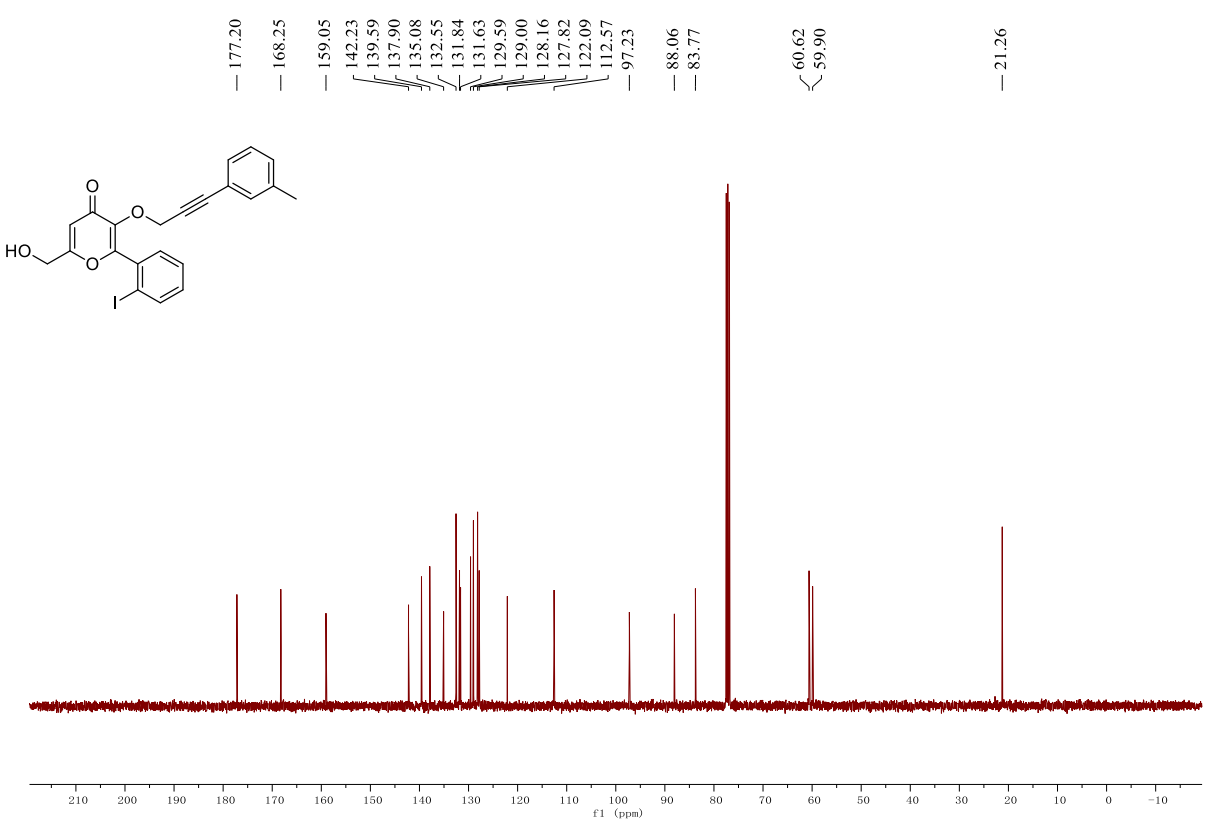
^{13}C NMR (101 MHz, $CDCl_3$) of **4h**



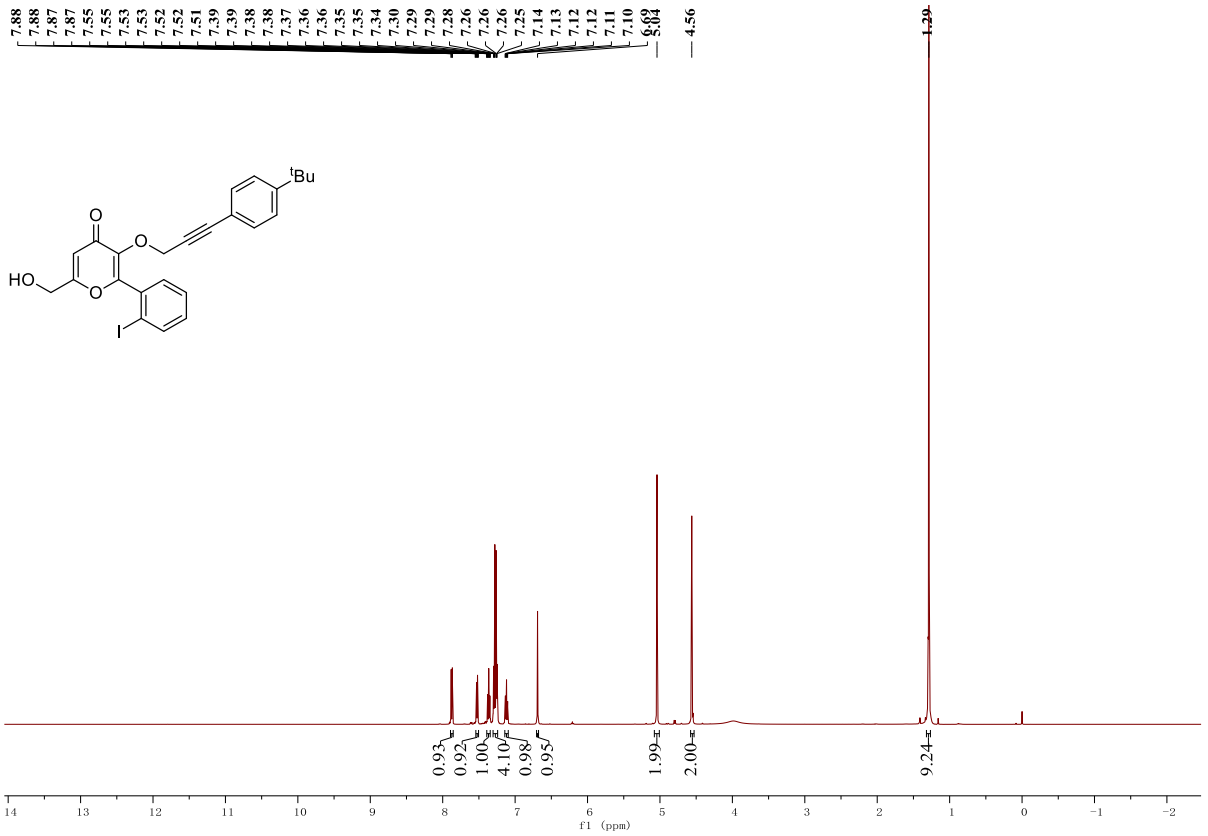
^{1}H NMR (400 MHz, $CDCl_3$) of **4i**



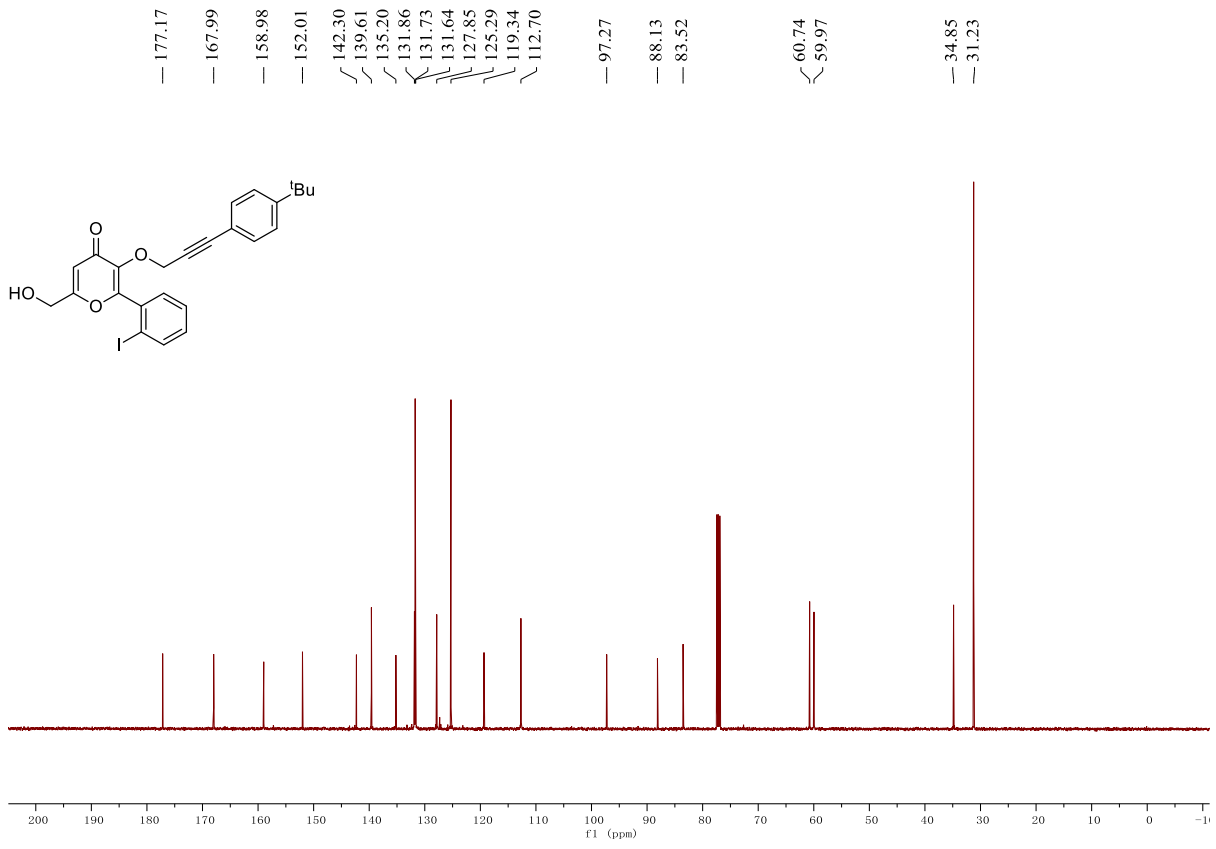
^{13}C NMR (101 MHz, $CDCl_3$) of **4i**



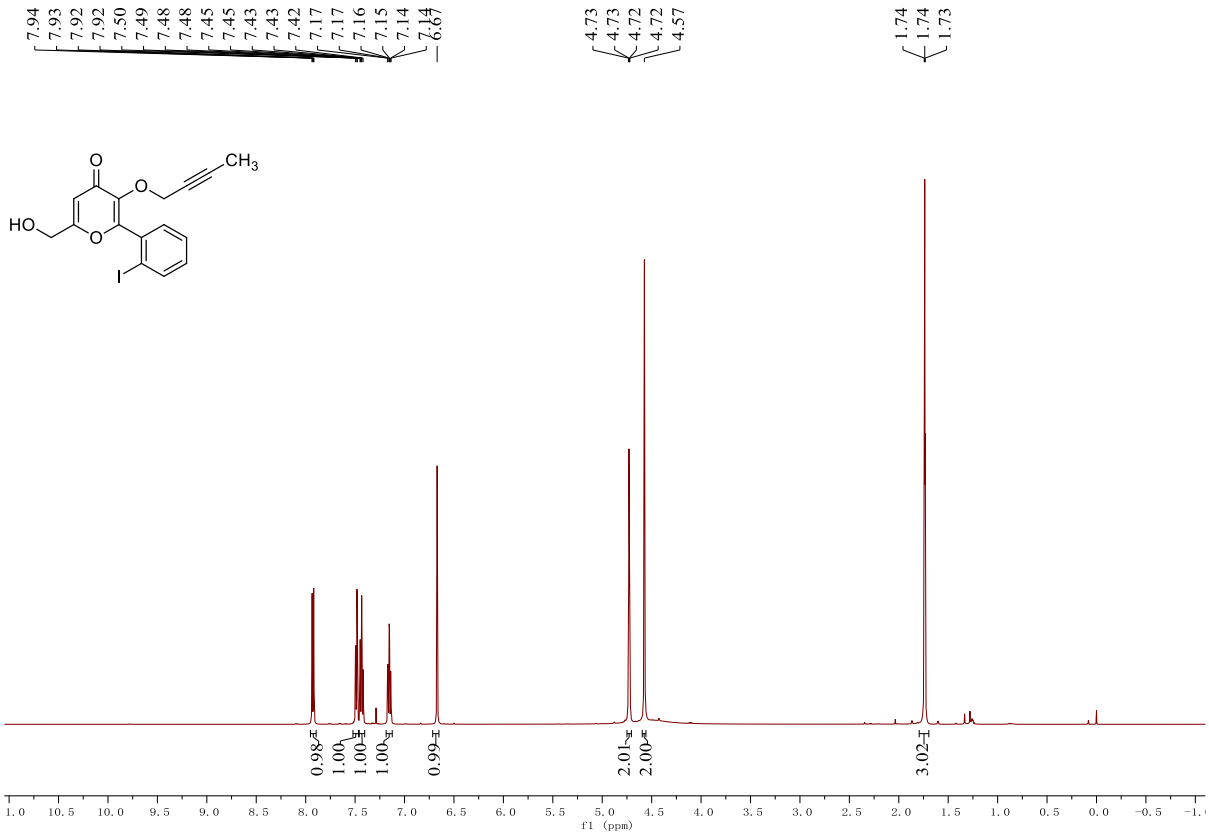
^{1}H NMR (500 MHz, $CDCl_3$) of **4j**



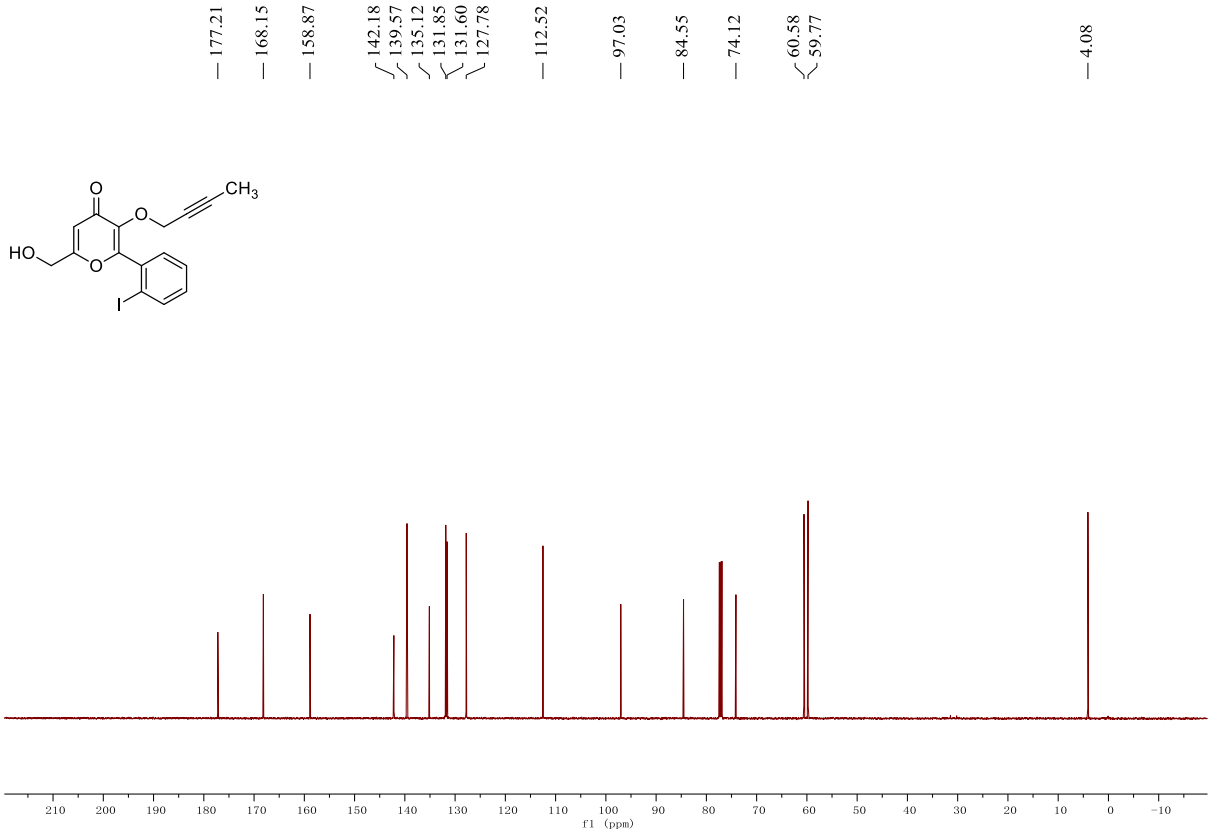
^{13}C NMR (126 MHz, $CDCl_3$) of **4j**



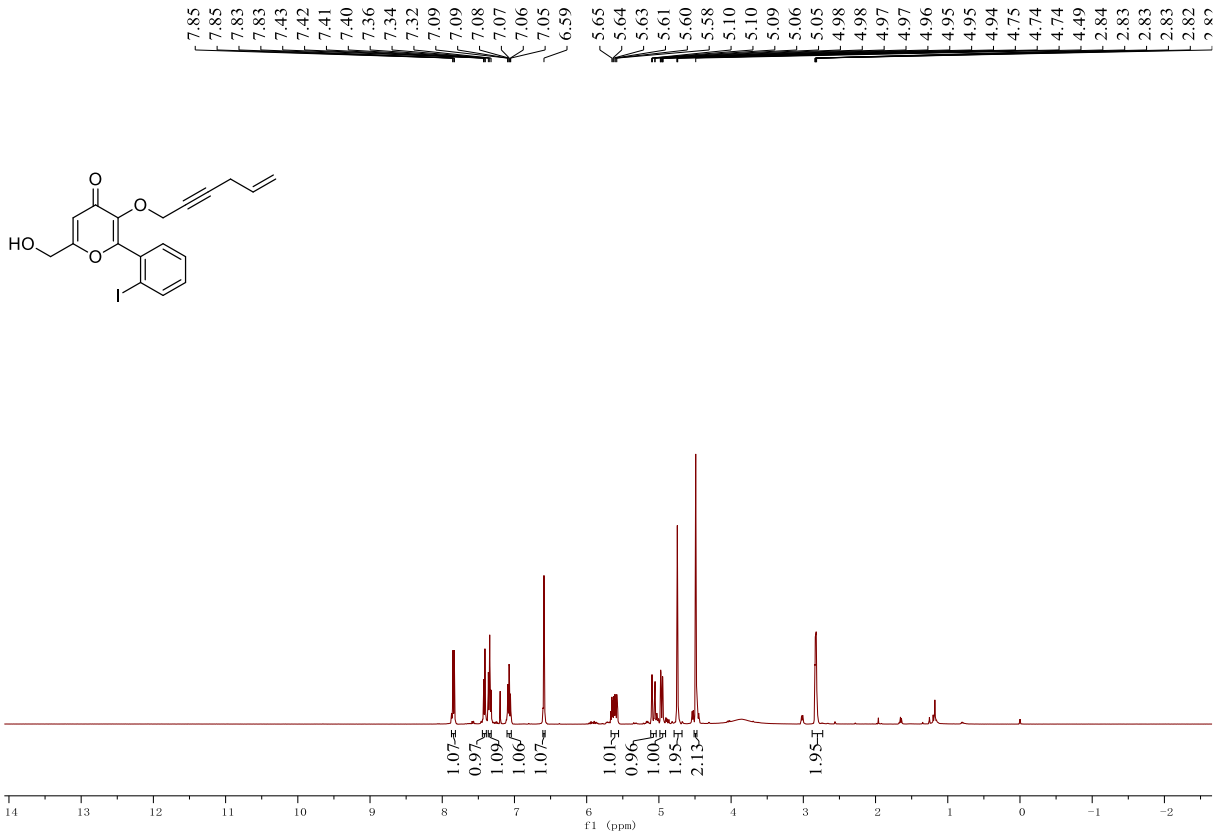
^{1}H NMR (500 MHz, $CDCl_3$) of **4k**



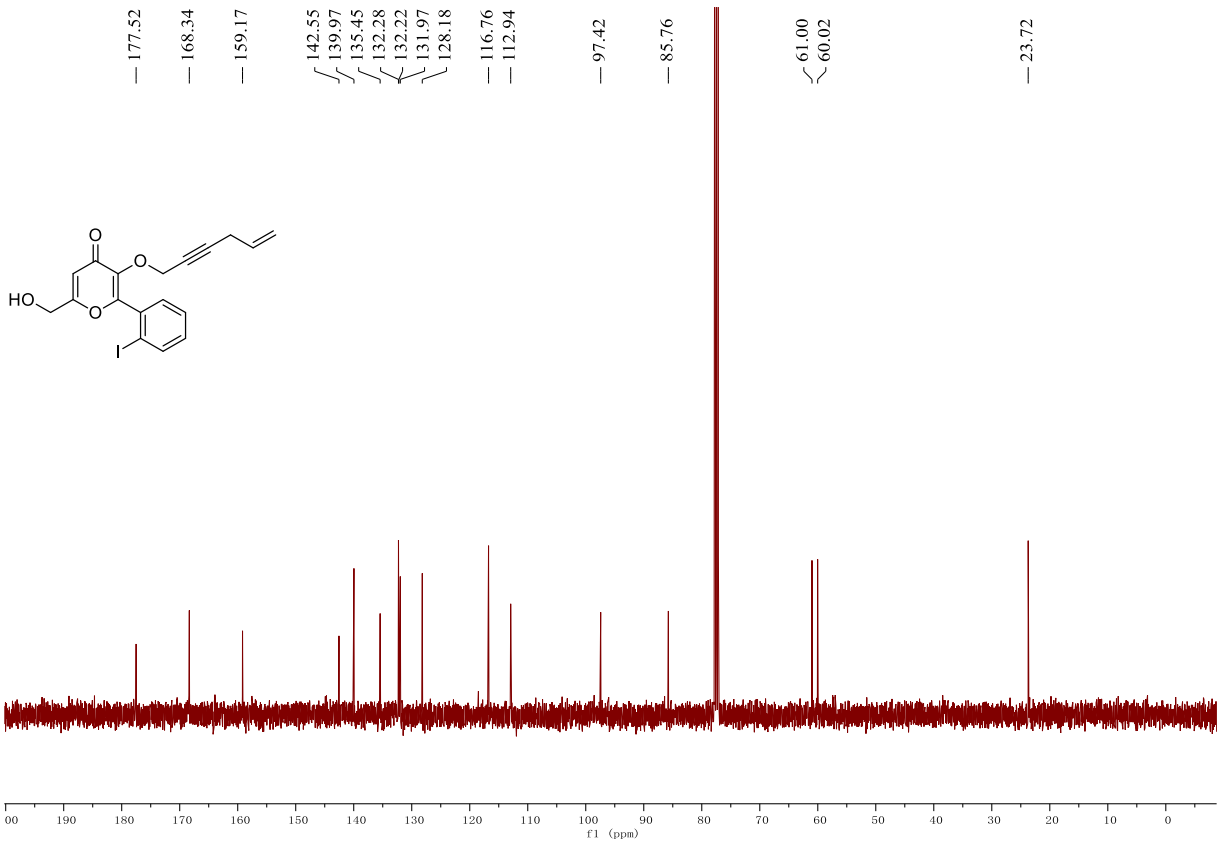
^{13}C NMR (126 MHz, $CDCl_3$) of **4k**



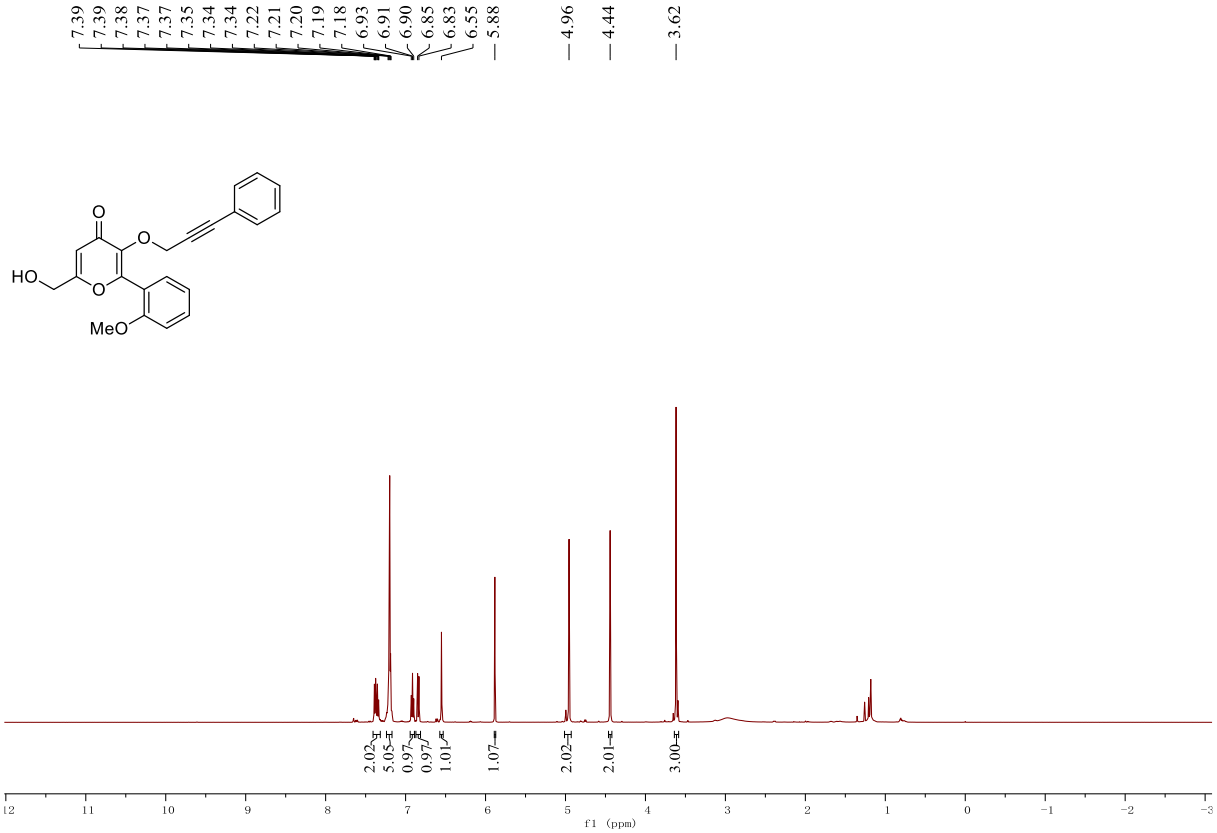
^{1}H NMR (400 MHz, $CDCl_3$) of **4l**



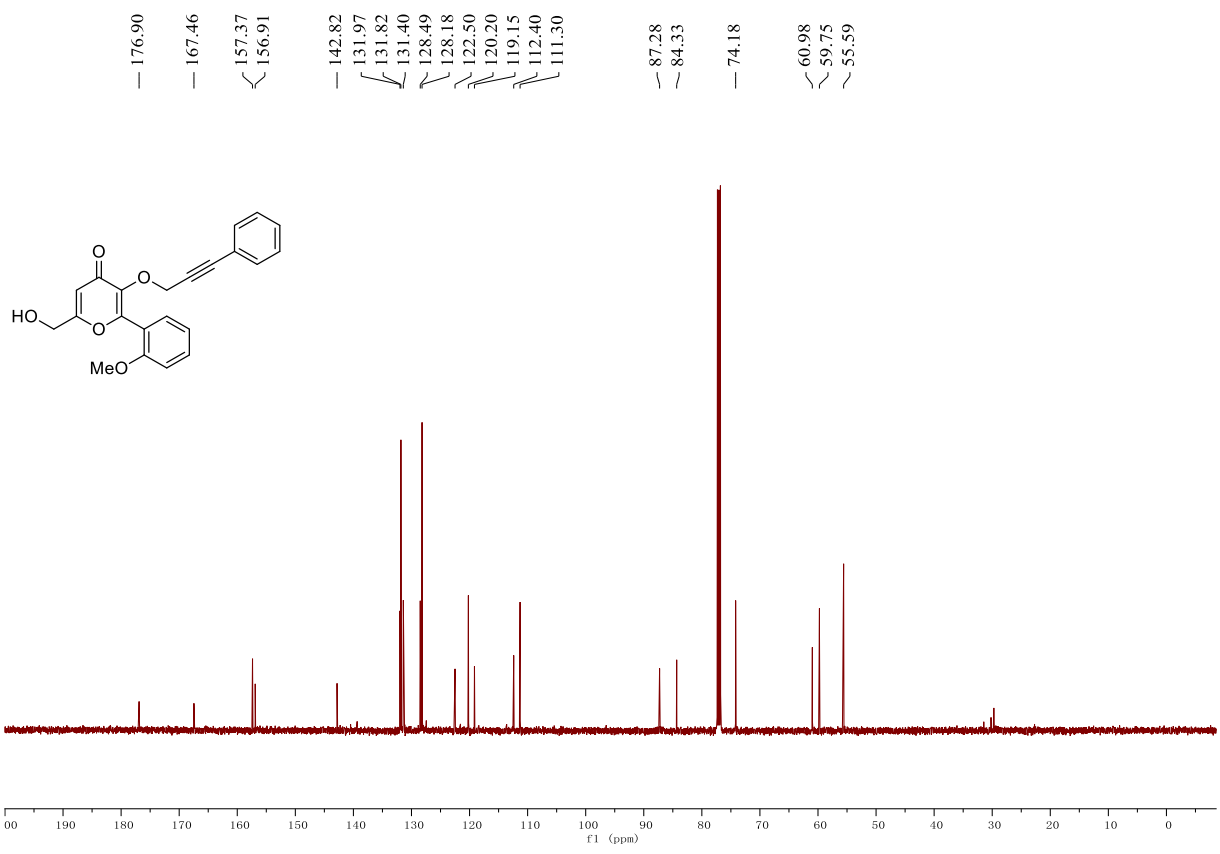
^{13}C NMR (101 MHz, $CDCl_3$) of **4l**



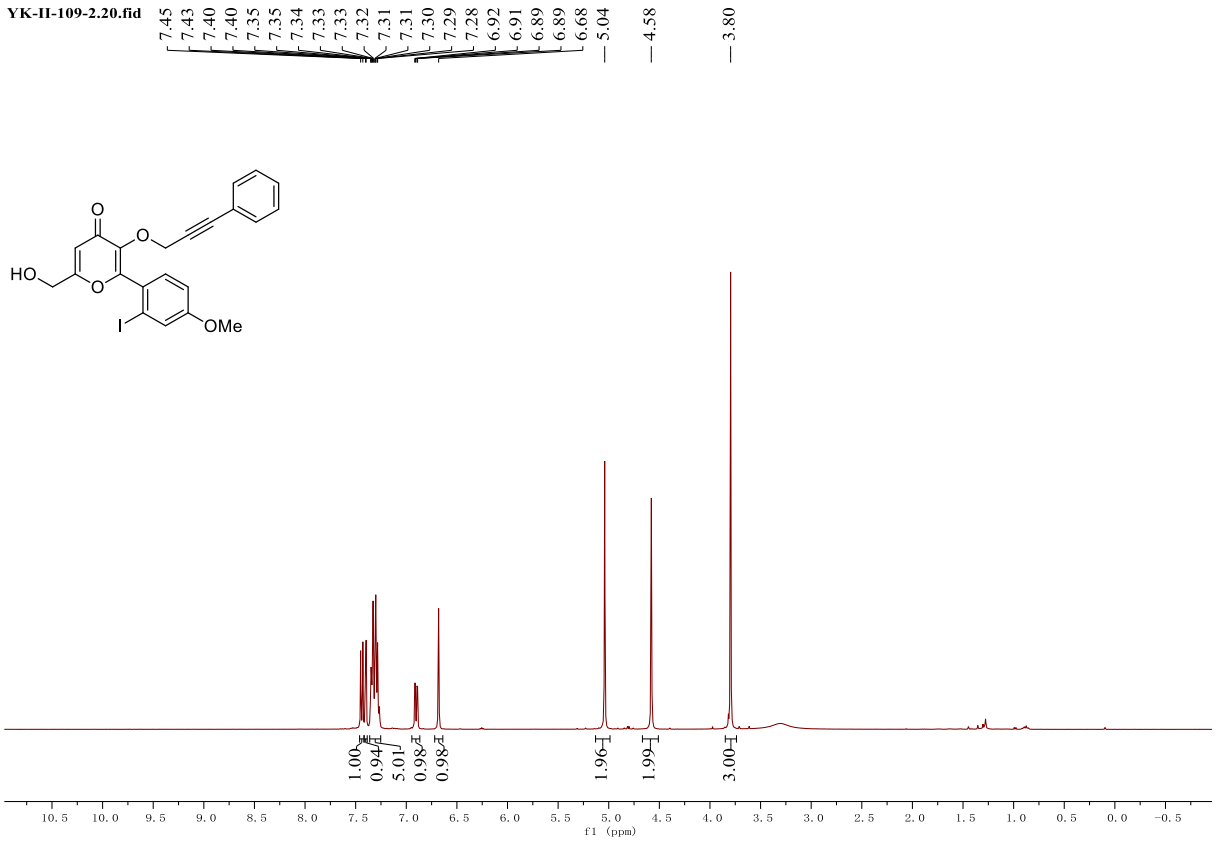
^{1}H NMR (500 MHz, $CDCl_3$) of **4m**



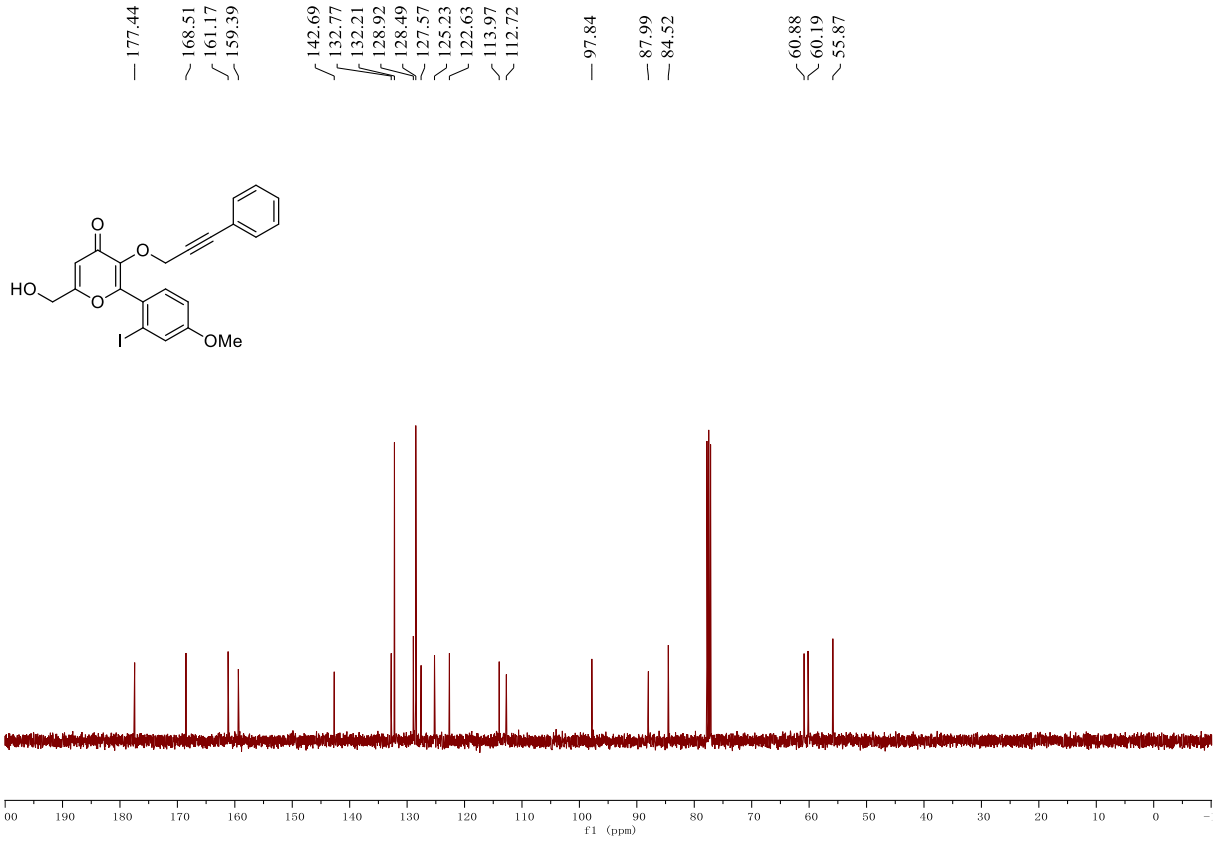
^{13}C NMR (126 MHz, $CDCl_3$) of **4m**



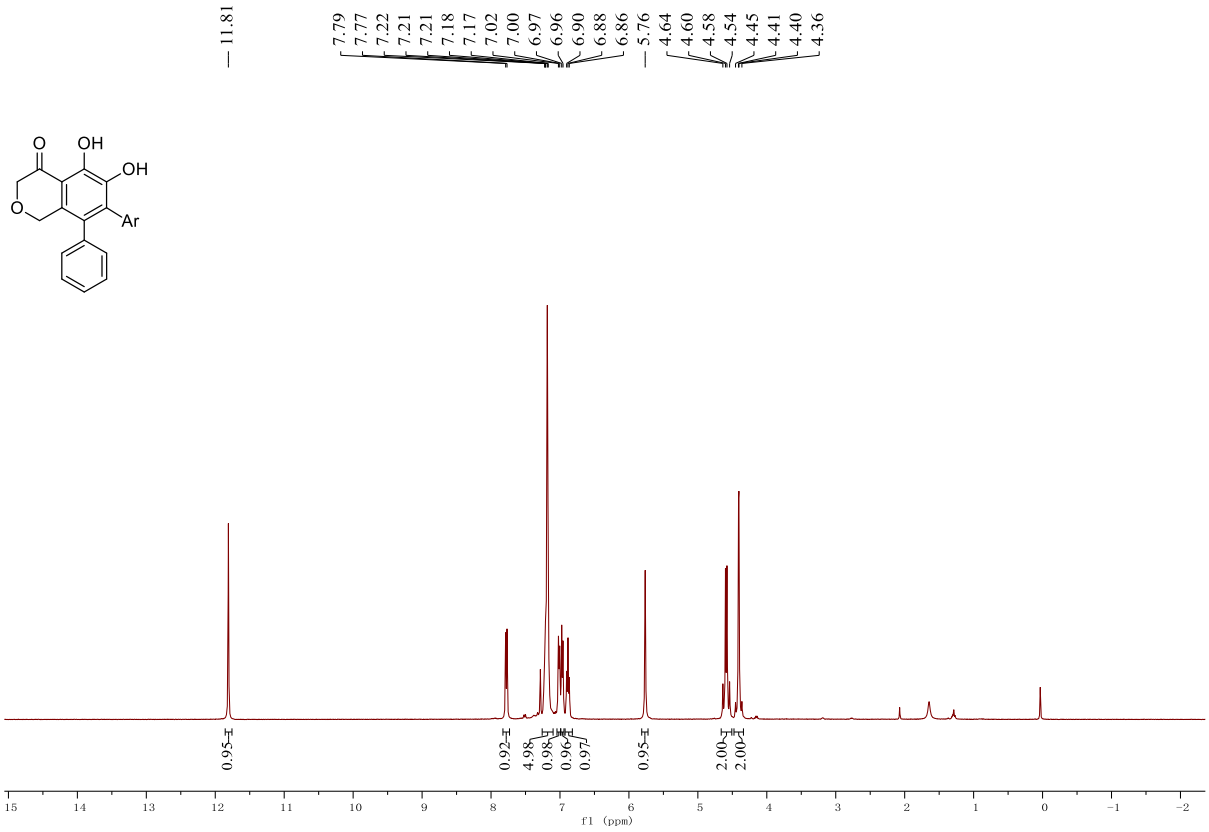
^{1}H NMR (400 MHz, $CDCl_3$) of **4n**



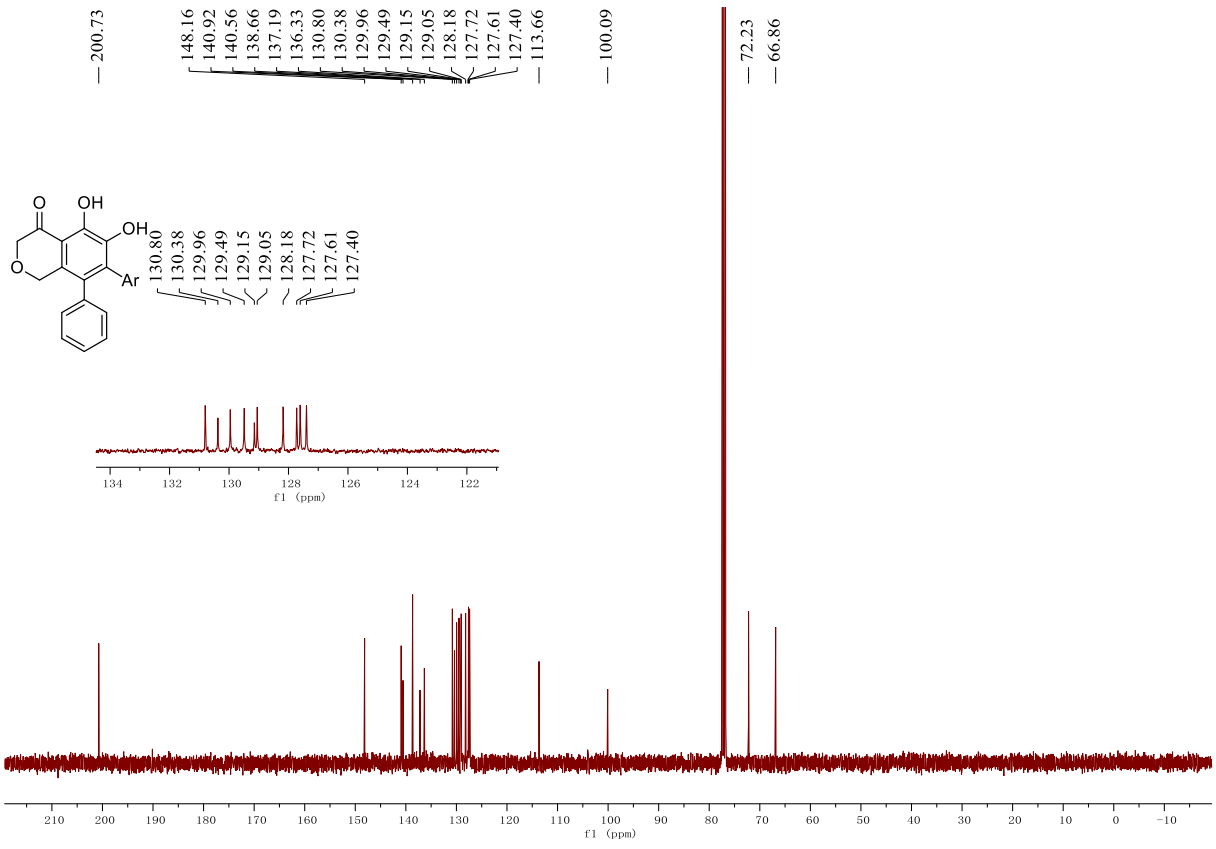
^{13}C NMR (101 MHz, $CDCl_3$) of **4n**



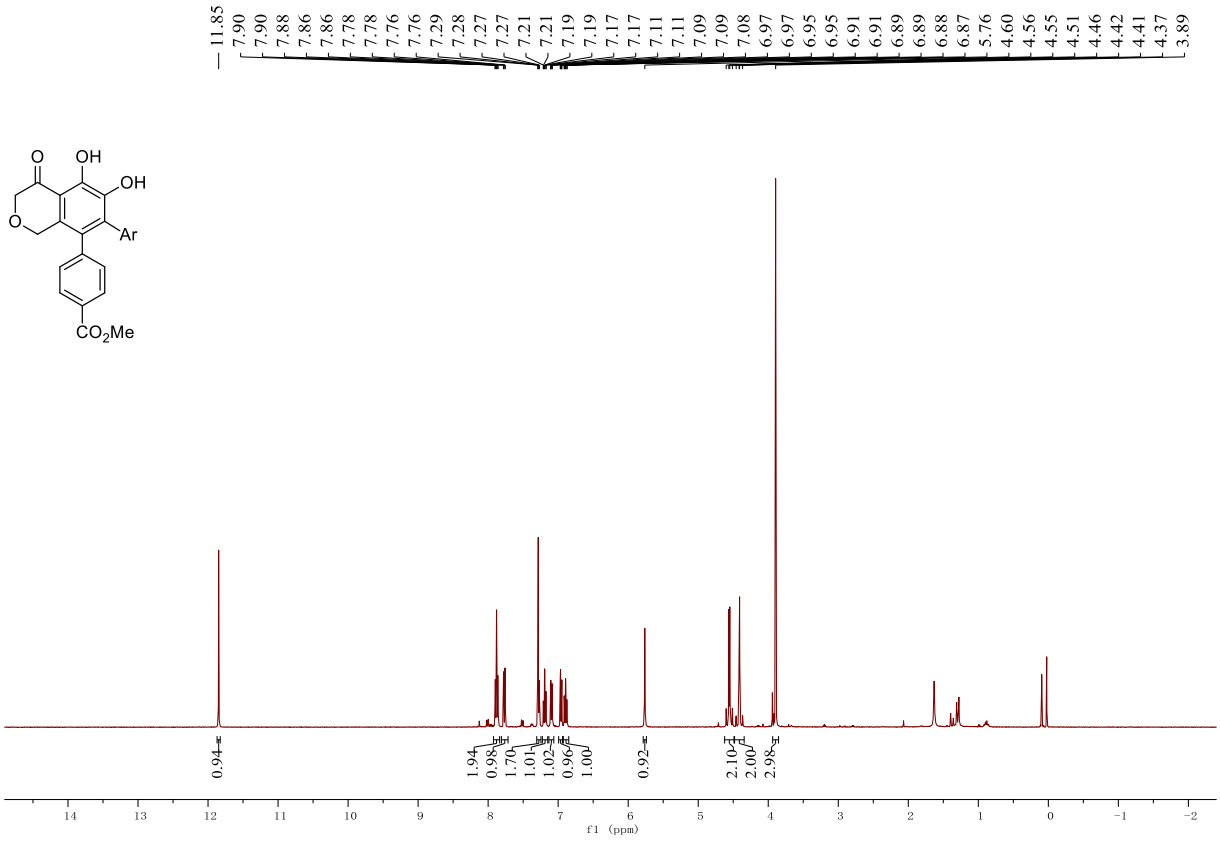
^{1}H NMR (400 MHz, $CDCl_3$) of **4a**



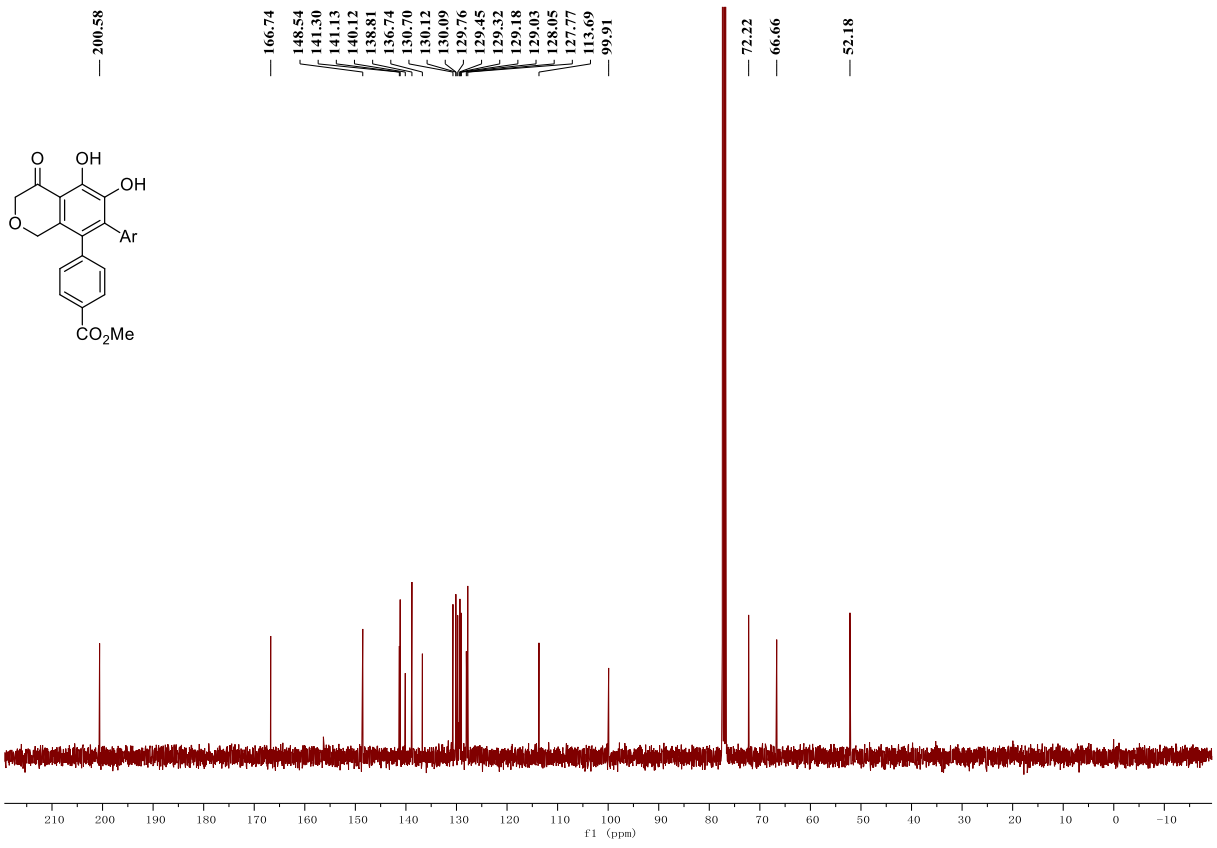
^{13}C NMR (101 MHz, $CDCl_3$) of **4a**



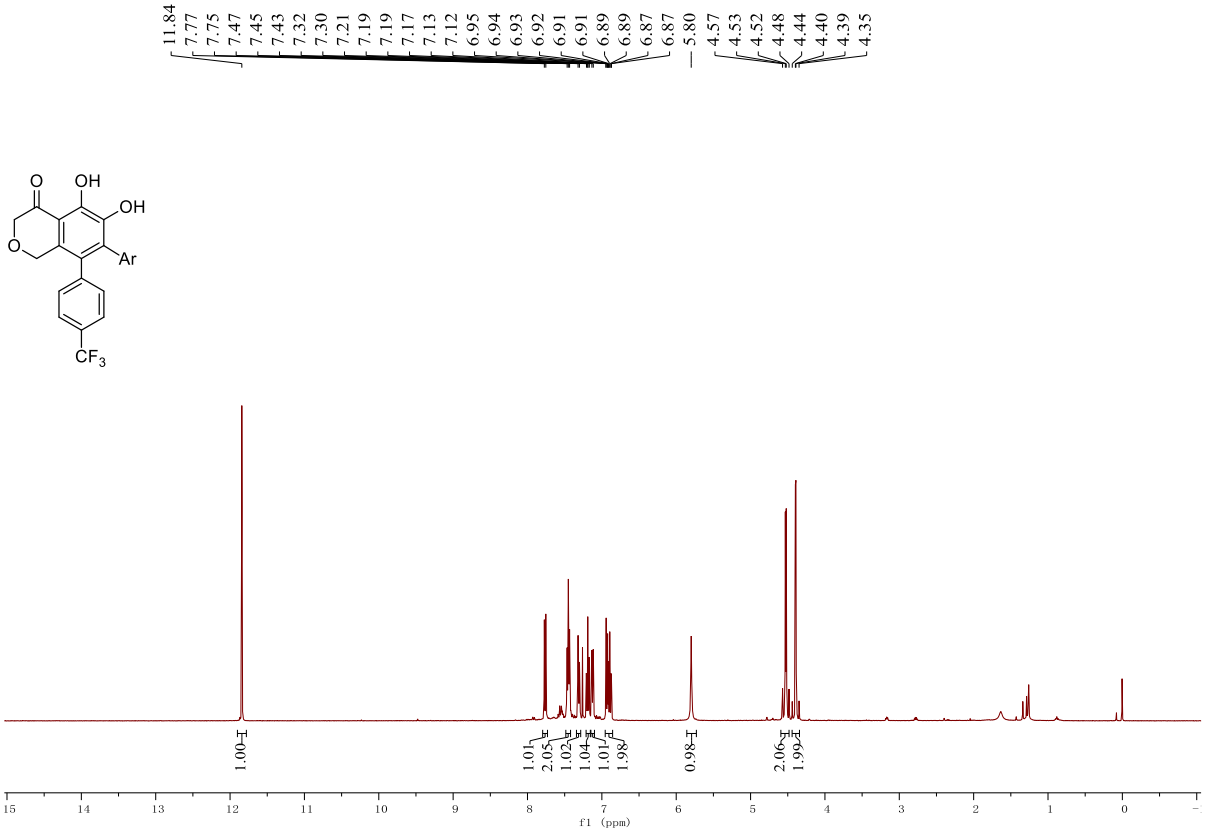
^{1}H NMR (400 MHz, $CDCl_3$) of **4b**



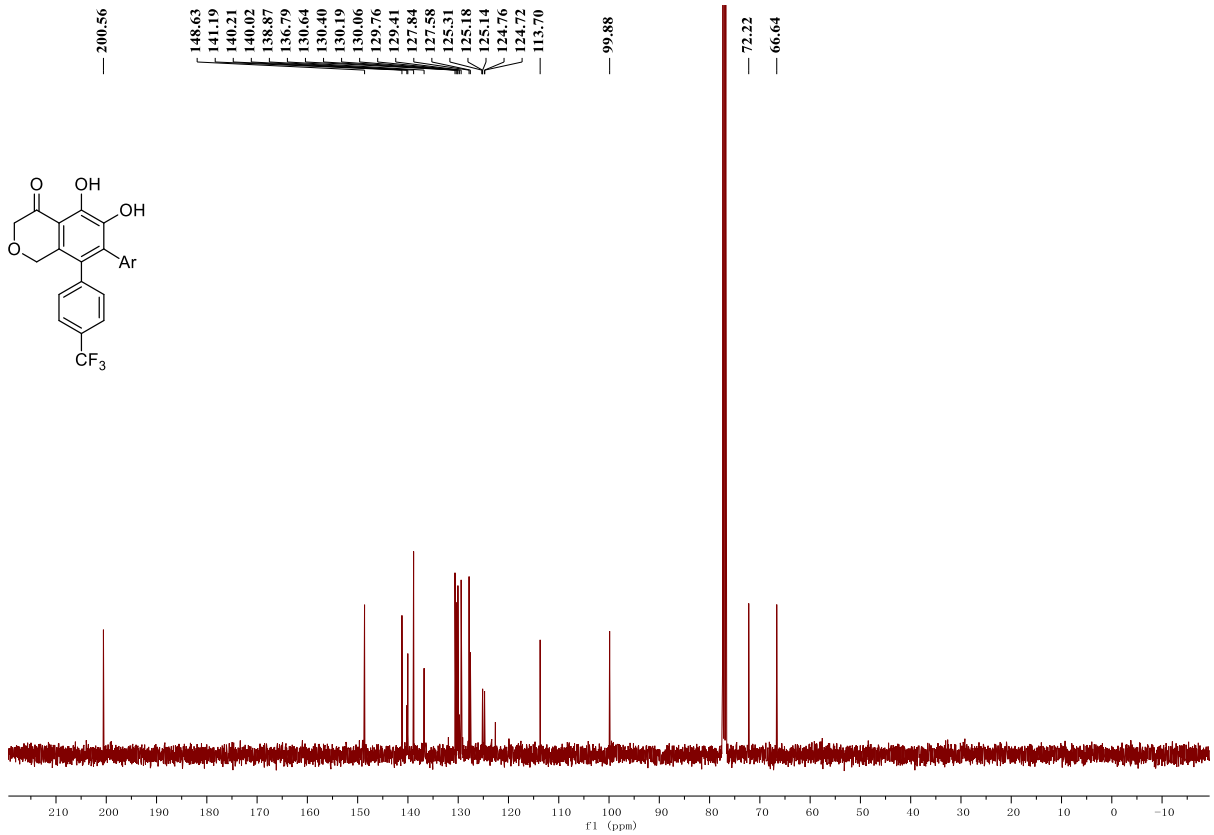
^{13}C NMR (101 MHz, $CDCl_3$) of **4b**



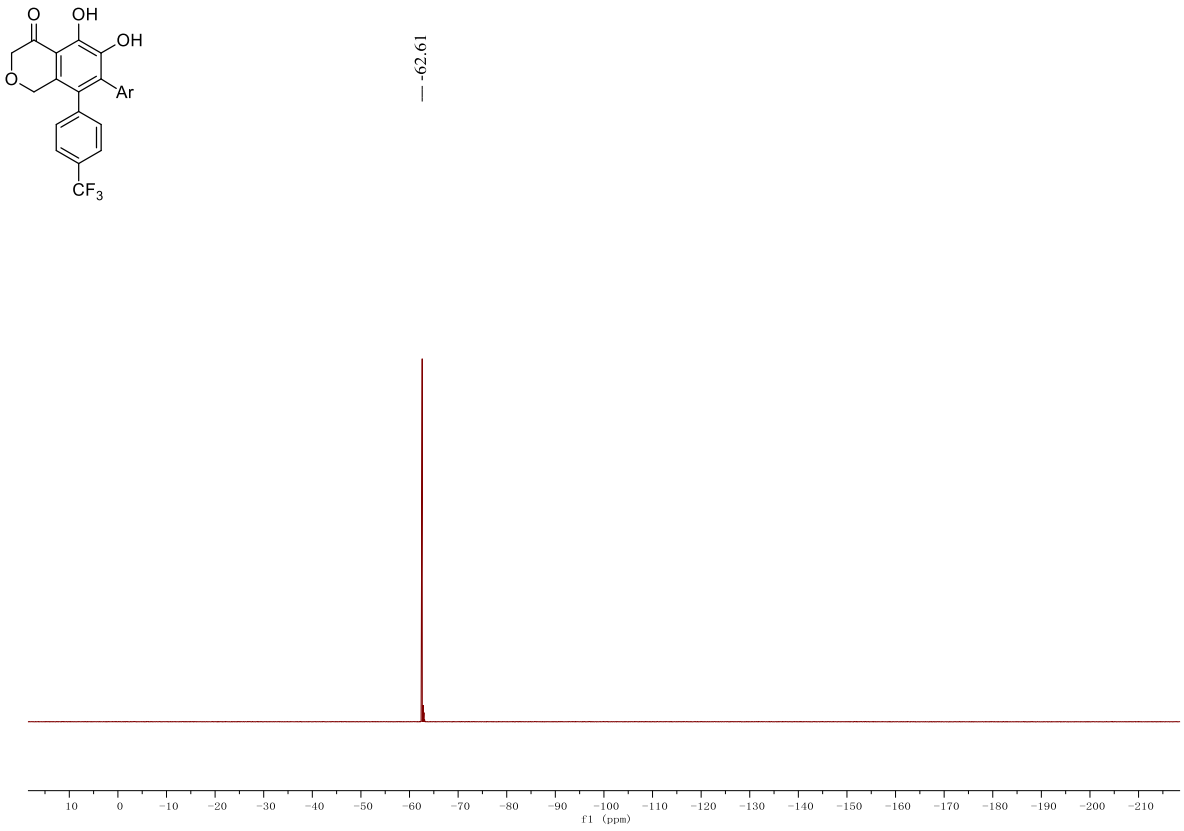
^{1}H NMR (400 MHz, $CDCl_3$) of **4c**



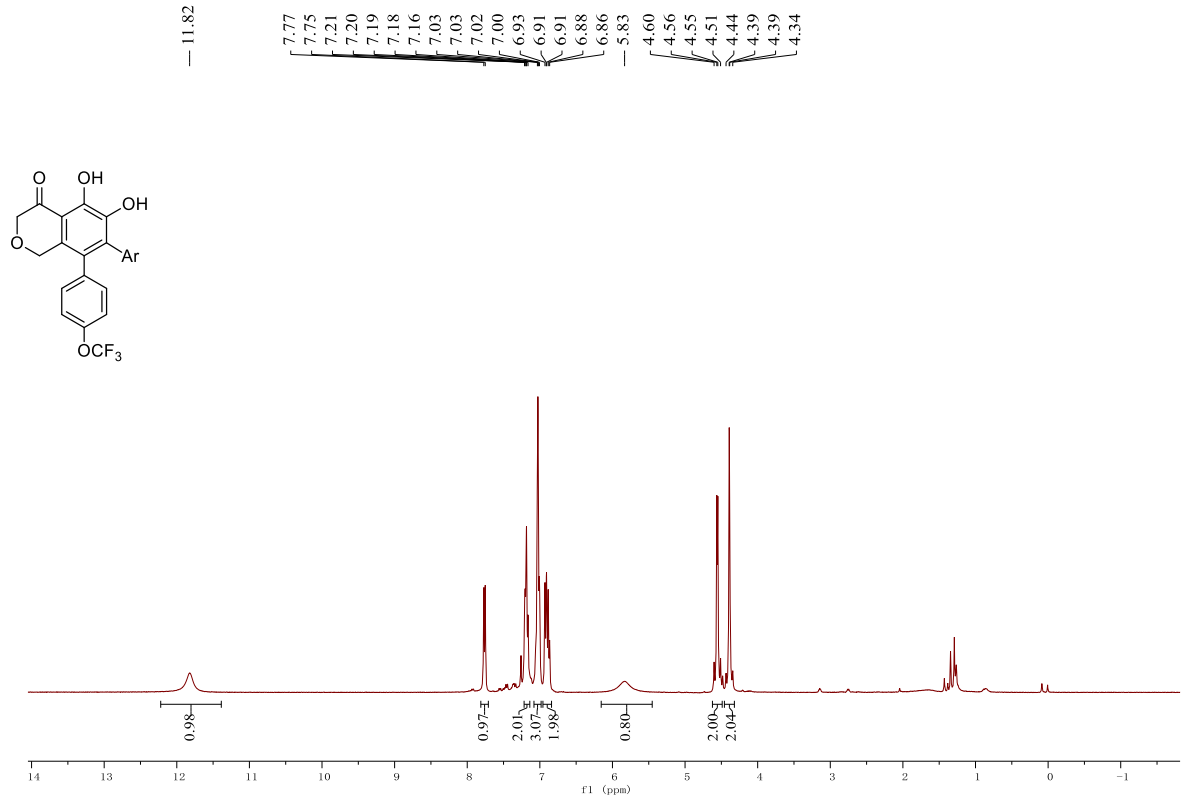
^{13}C NMR (101 MHz, $CDCl_3$) of **4c**



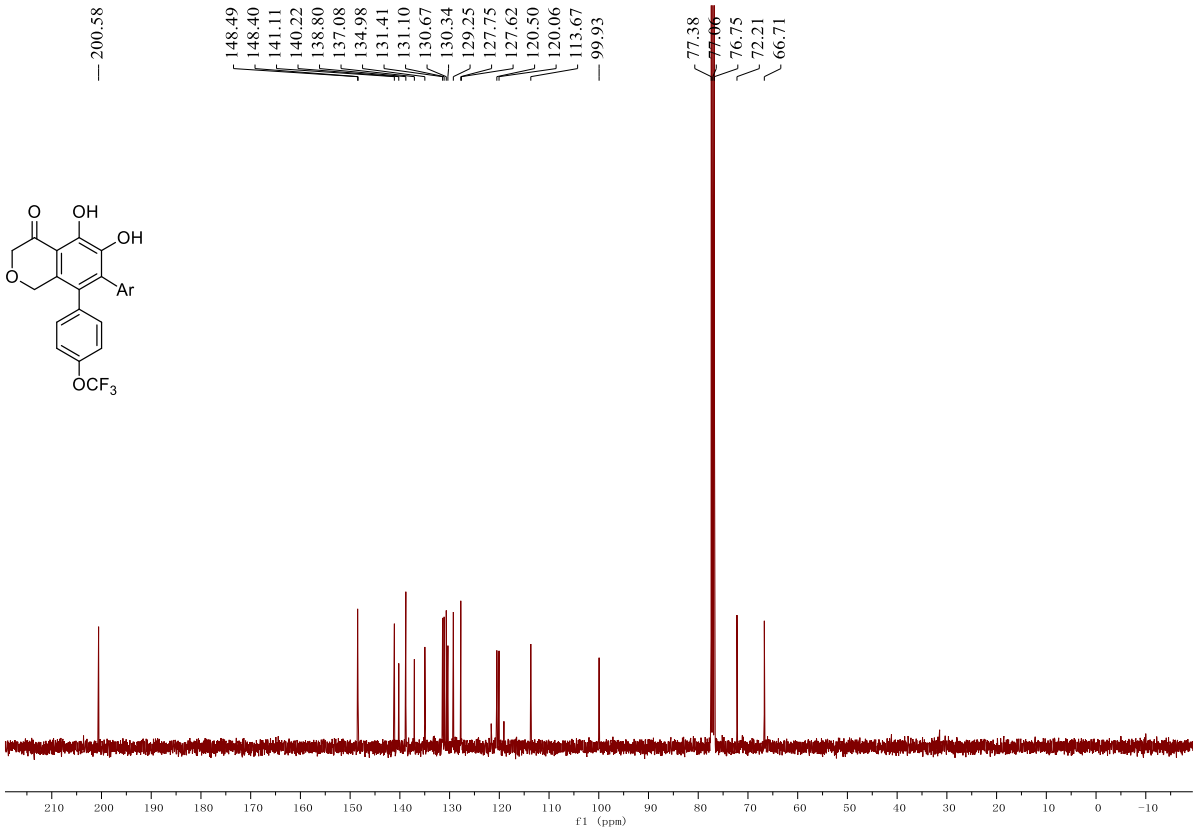
^{19}F NMR (376MHz, $CDCl_3$) of **5c**



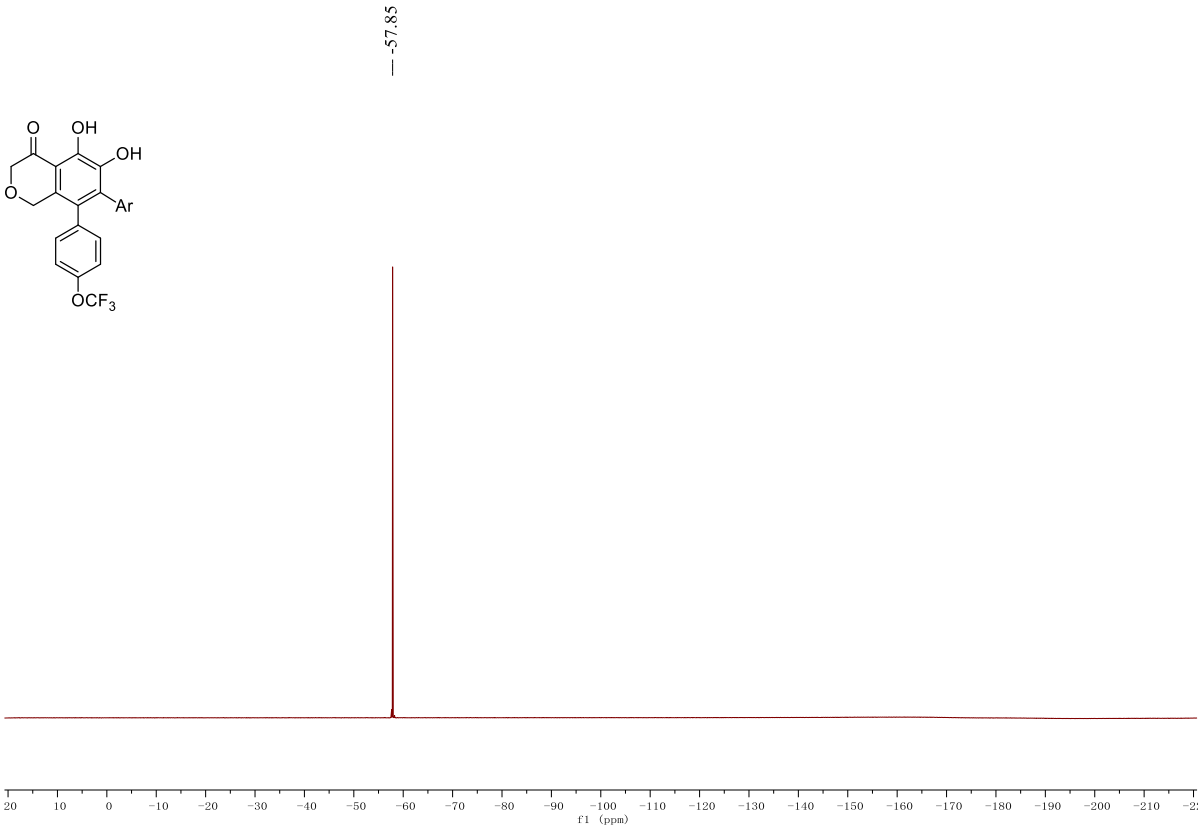
^{1}H NMR (400 MHz, $CDCl_3$) of **4d**



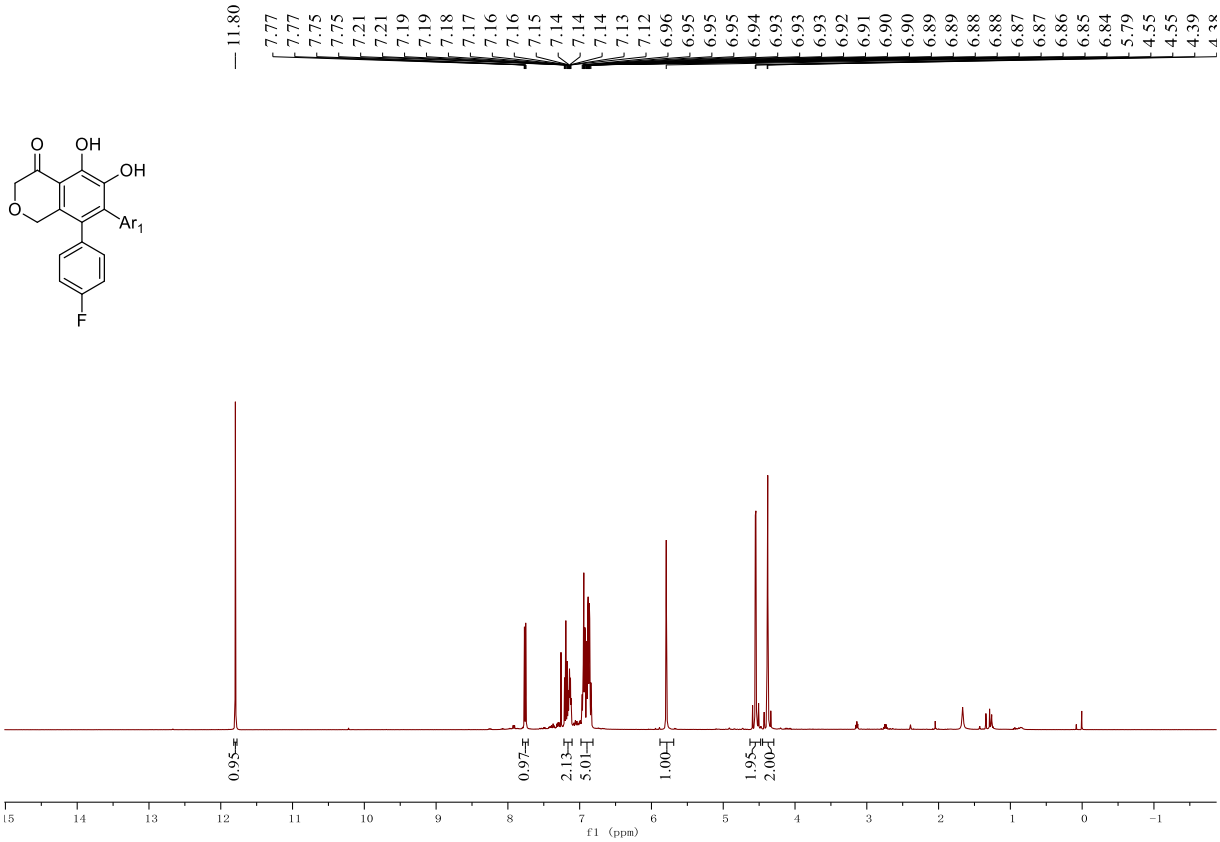
^{13}C NMR (101 MHz, $CDCl_3$) of **4d**



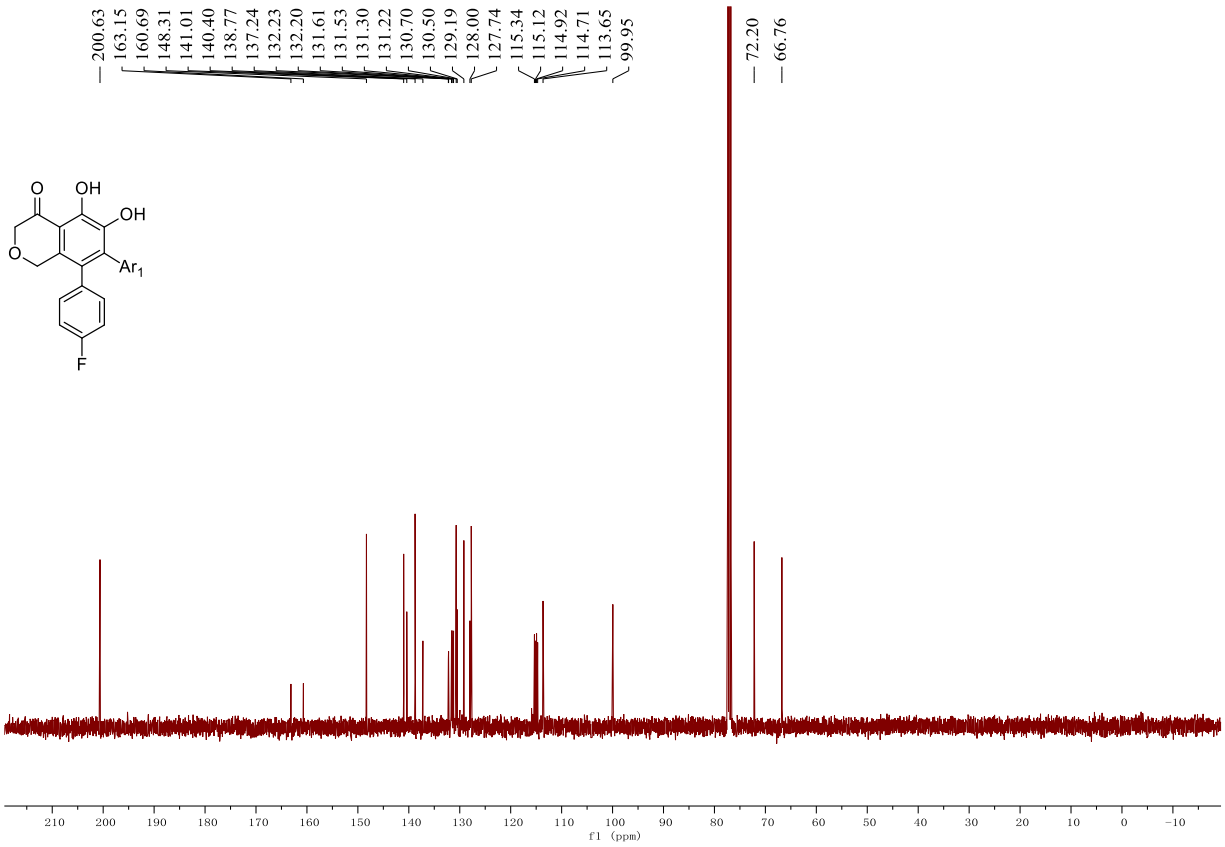
^{19}F NMR (376MHz, $CDCl_3$) of **5d**



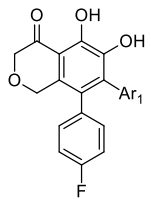
^{1}H NMR (400 MHz, $CDCl_3$) of **5e**



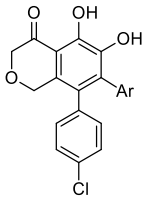
^{13}C NMR (101 MHz, $CDCl_3$) of **5e**



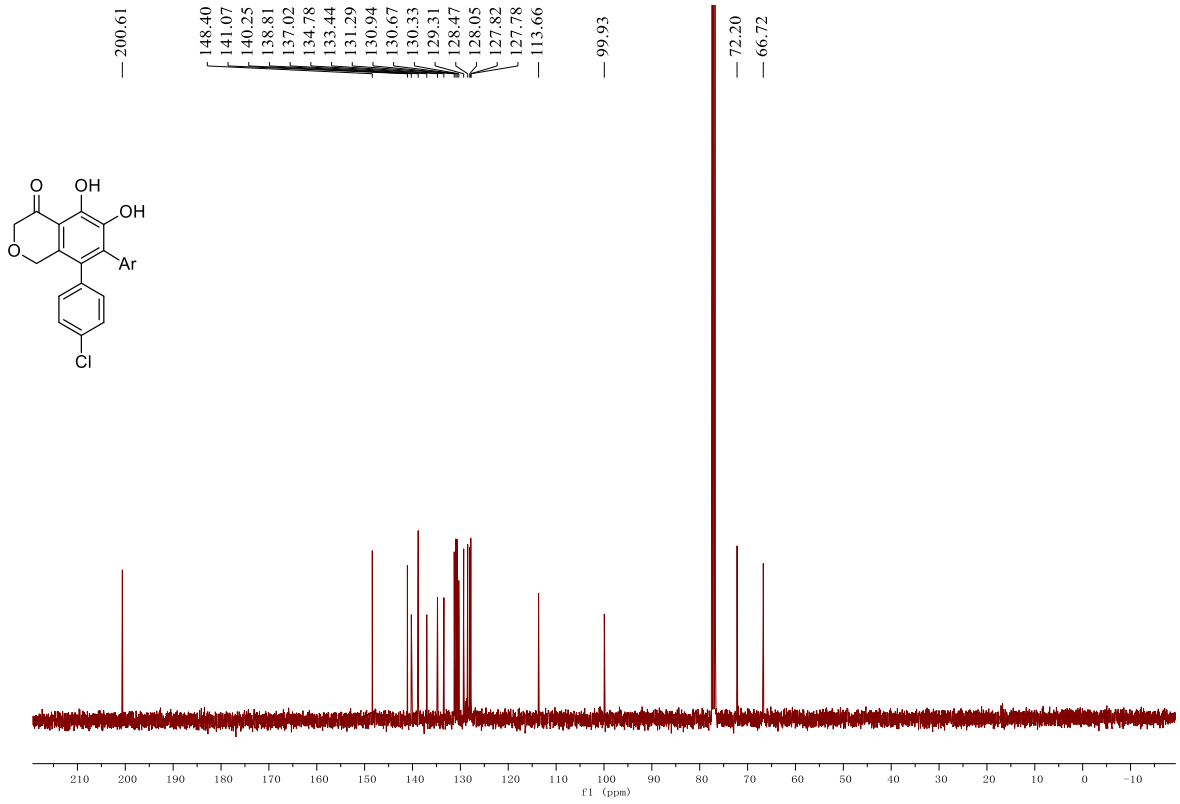
^{19}F NMR (471 MHz, $CDCl_3$) of **5e**



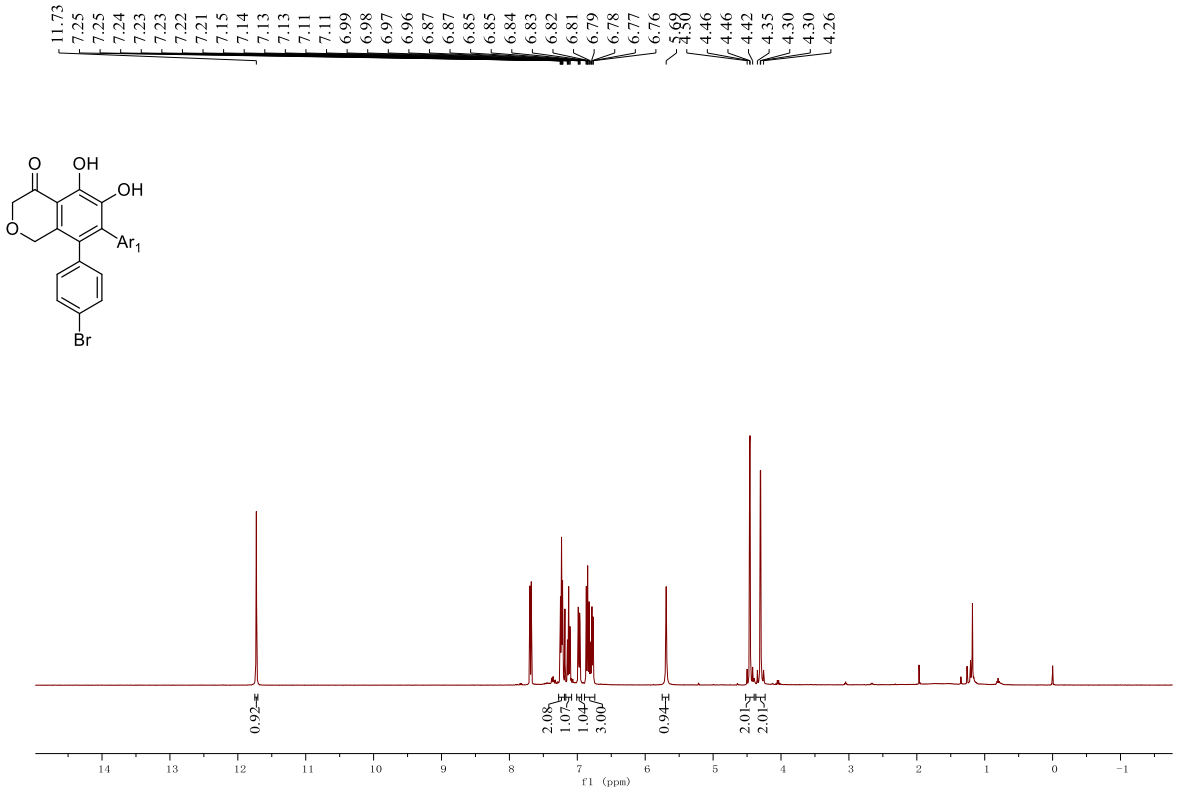
^{1}H NMR (400 MHz, $CDCl_3$) of **5f**



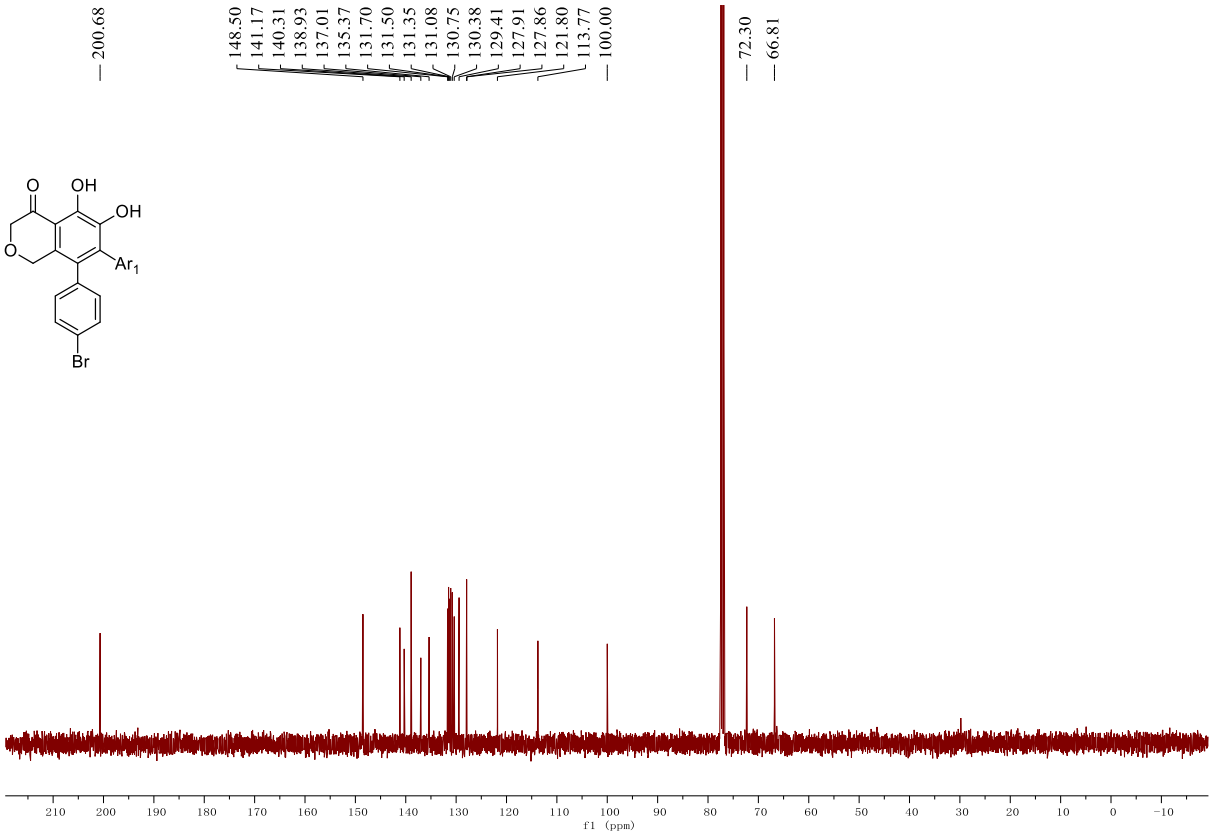
^{13}C NMR (101 MHz, $CDCl_3$) of **5f**



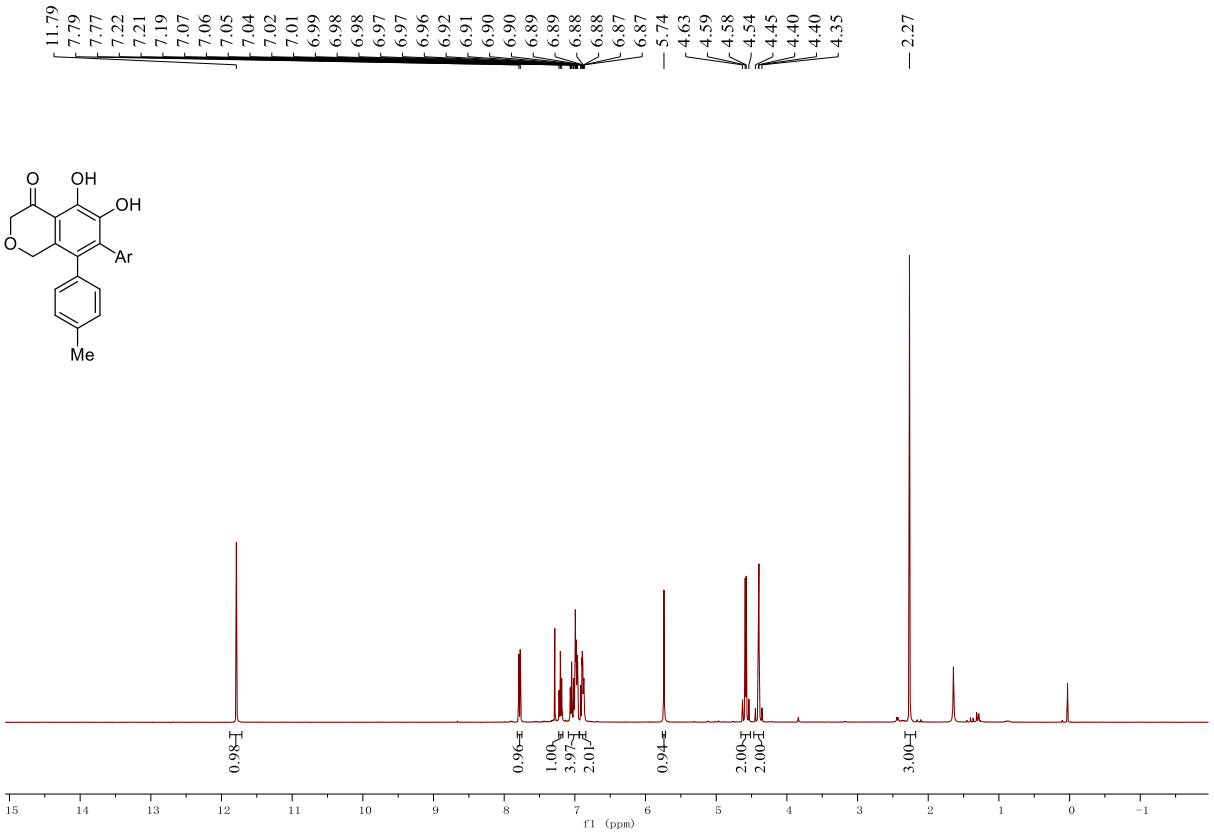
^{1}H NMR (400 MHz, $CDCl_3$) of **5g**



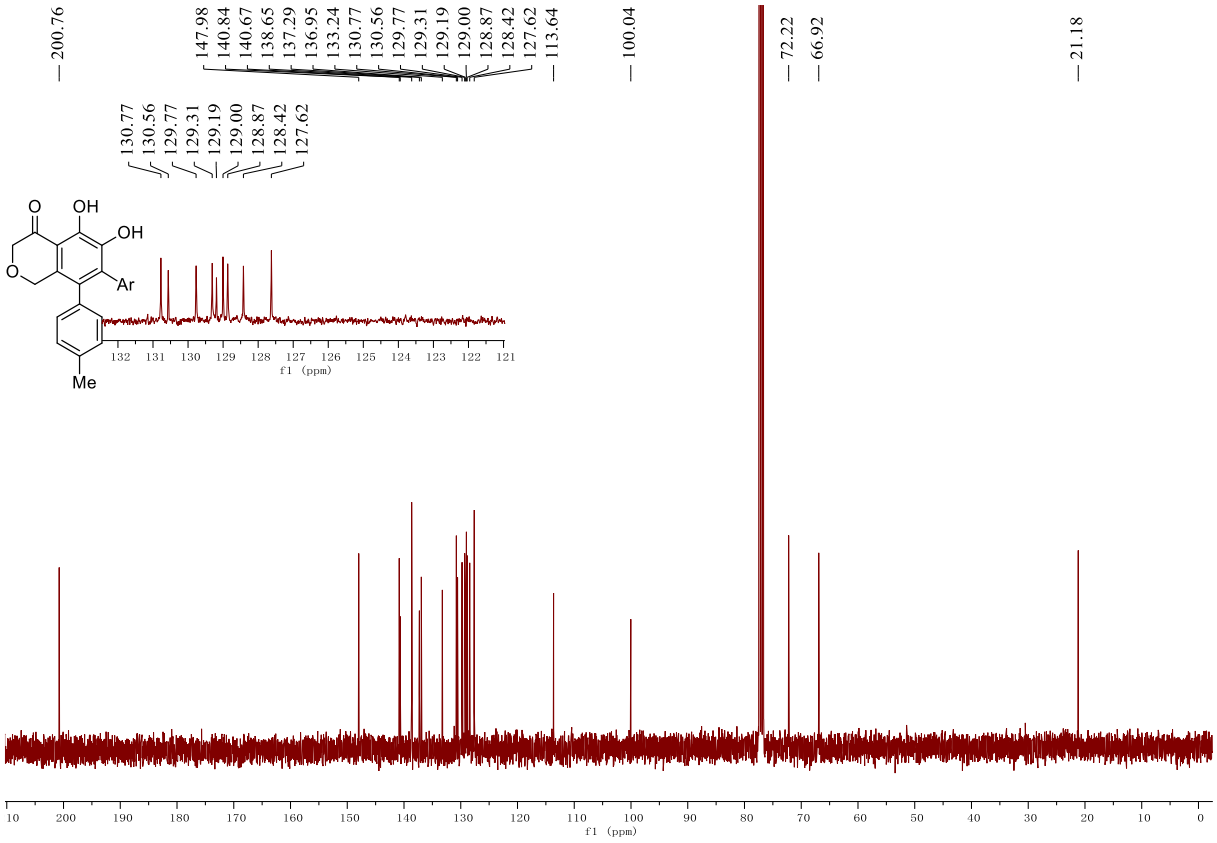
^{13}C NMR (101 MHz, $CDCl_3$) of **5g**



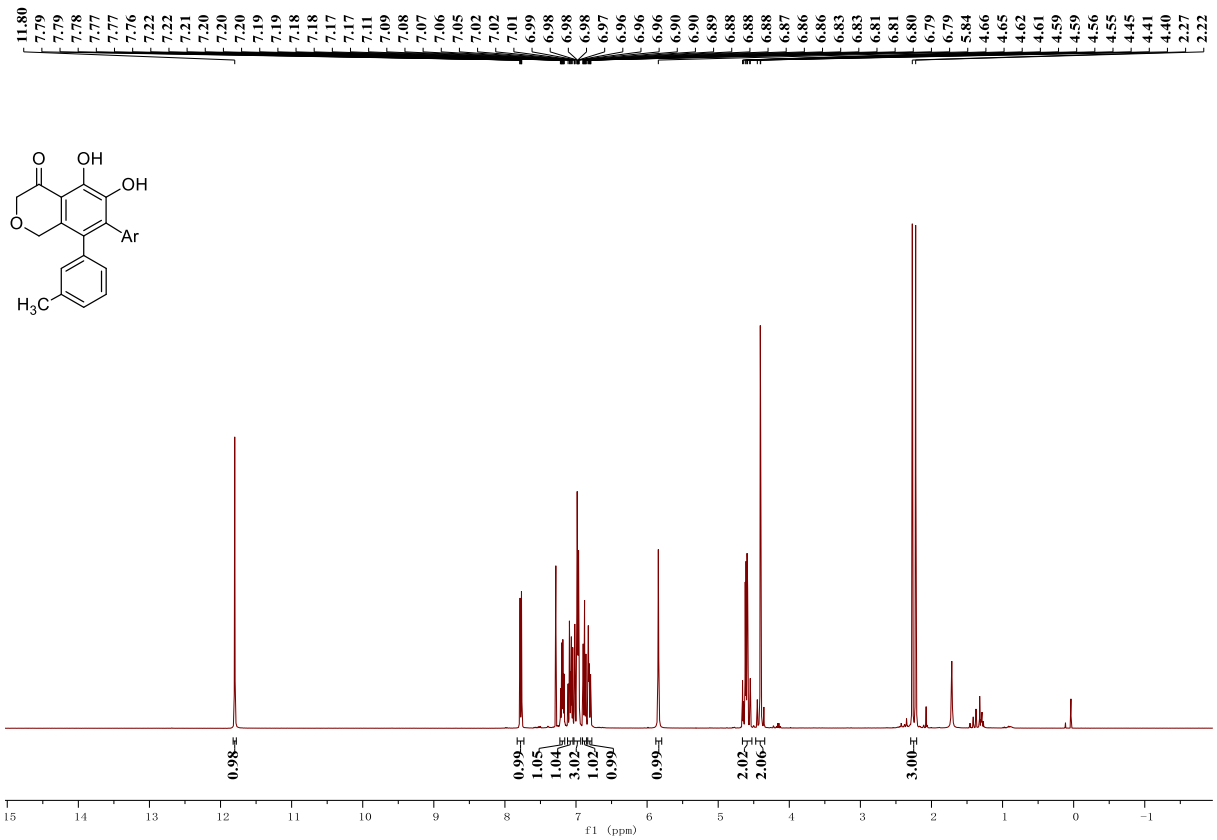
^{1}H NMR (400 MHz, $CDCl_3$) of **5h**



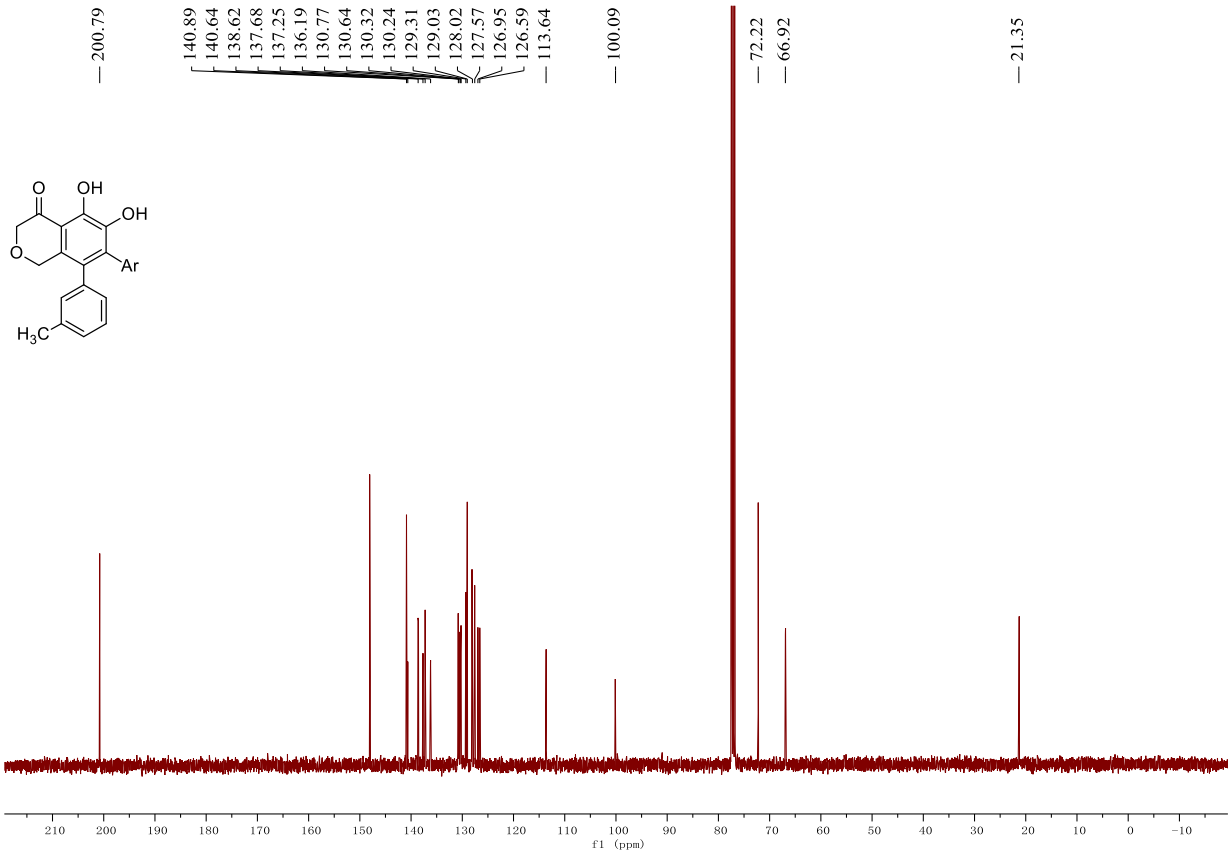
^{13}C NMR (101 MHz, $CDCl_3$) of **5h**



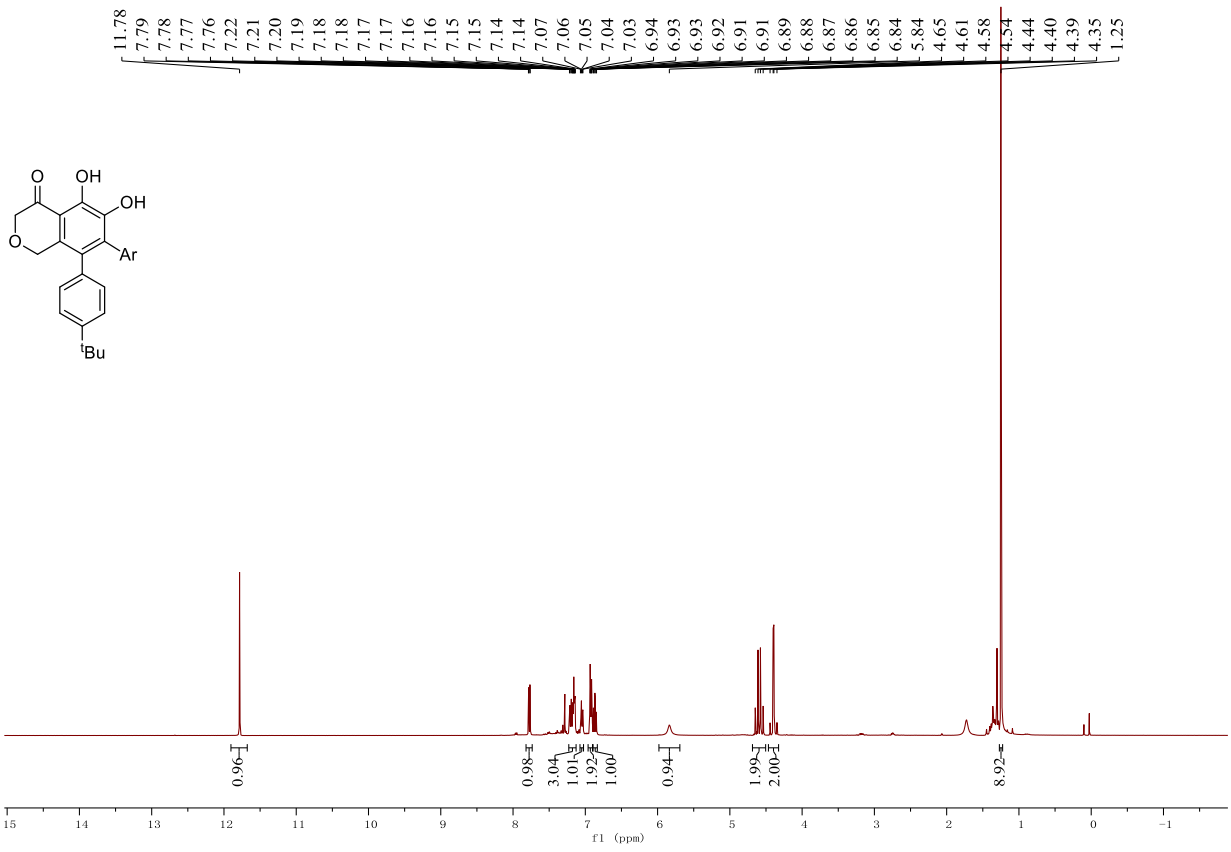
^{1}H NMR (400 MHz, $CDCl_3$) of **5i**



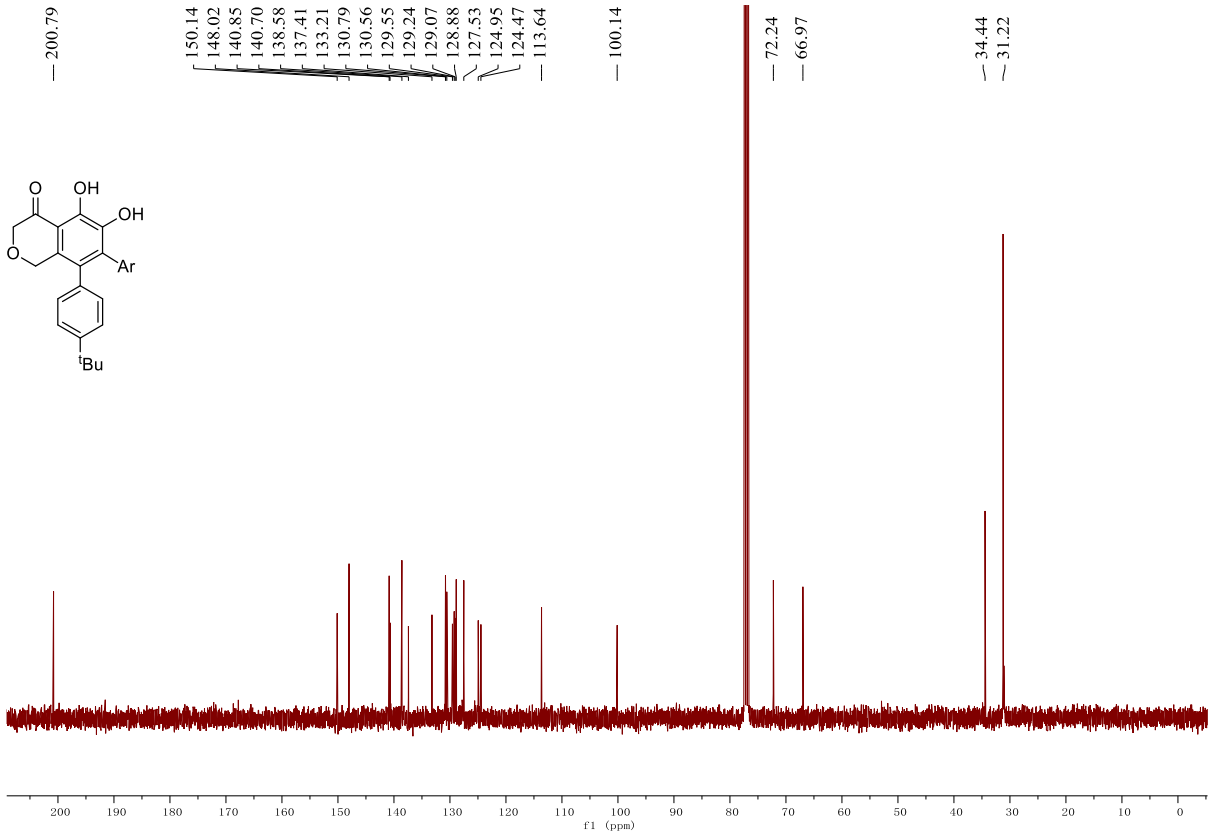
^{13}C NMR (101 MHz, $CDCl_3$) of **5i**



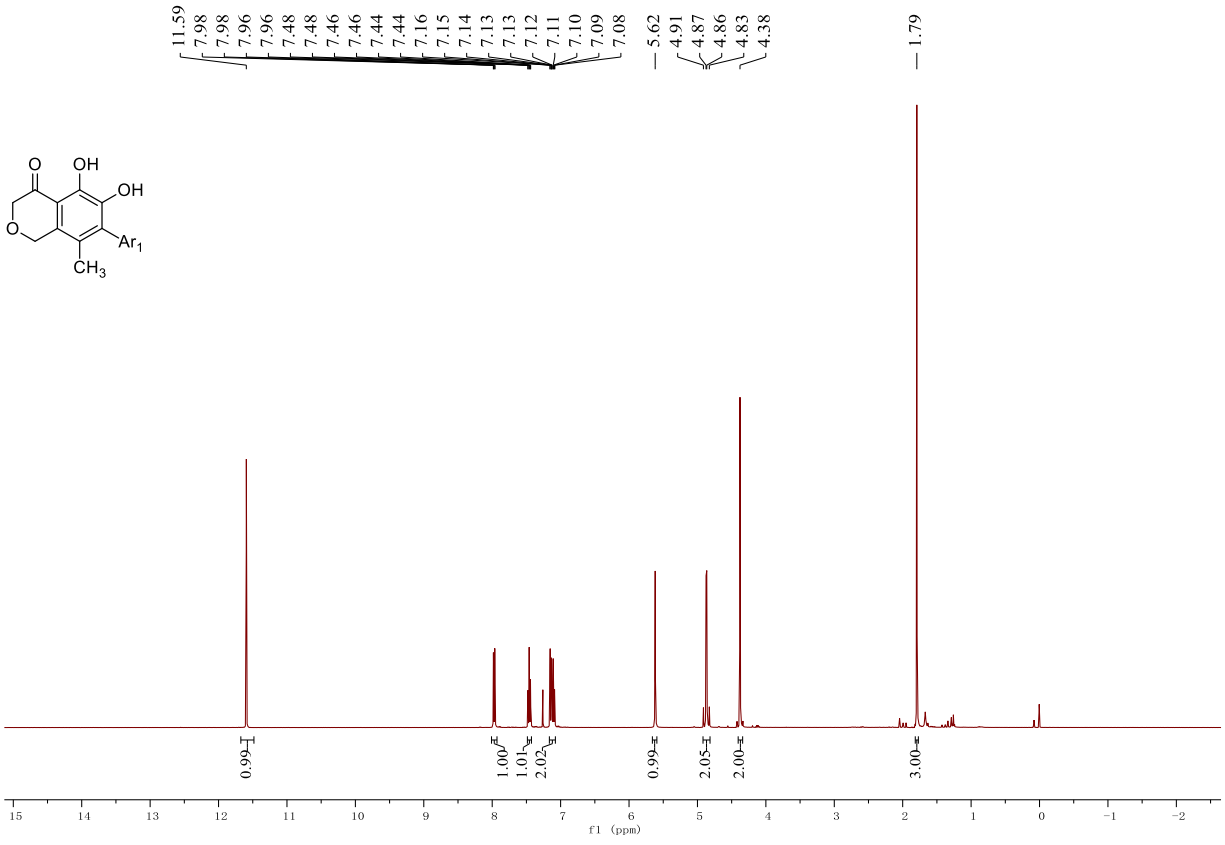
^{1}H NMR (400 MHz, $CDCl_3$) of **5j**



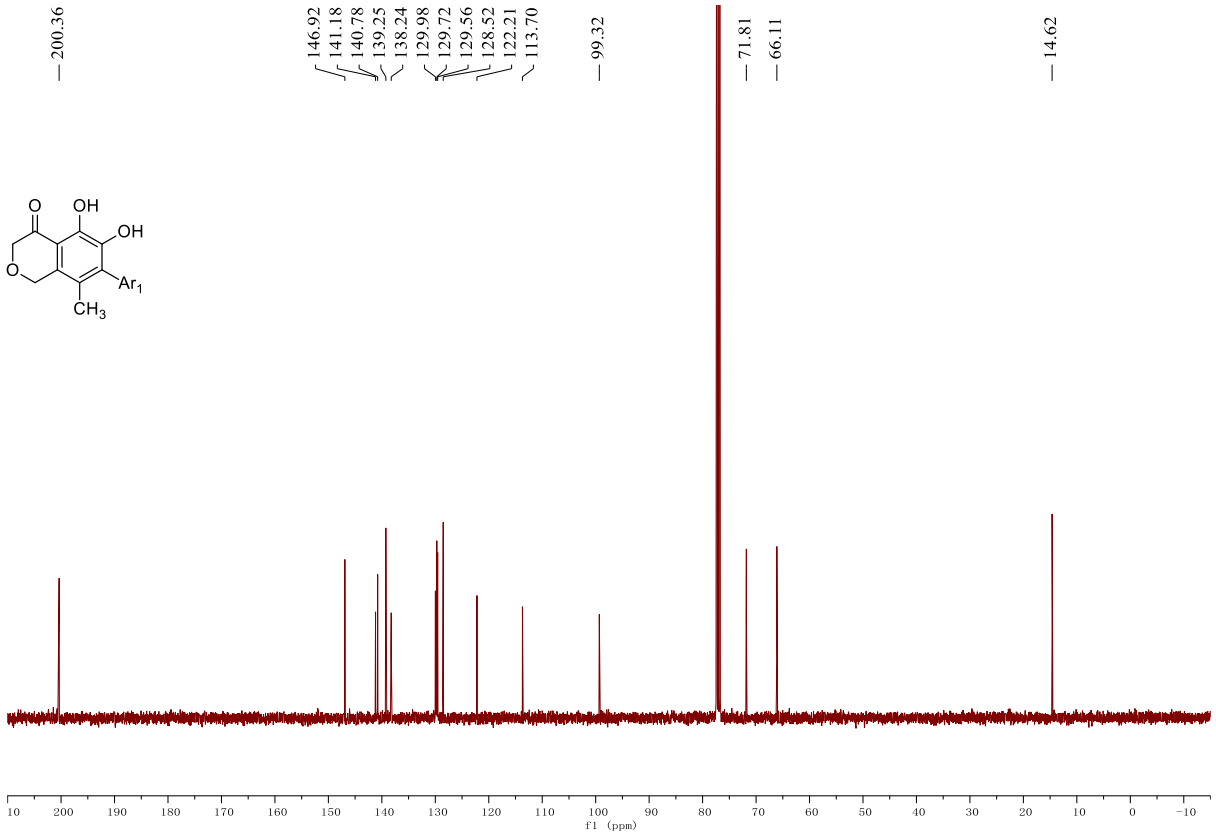
^{13}C NMR (101 MHz, $CDCl_3$) of **5j**



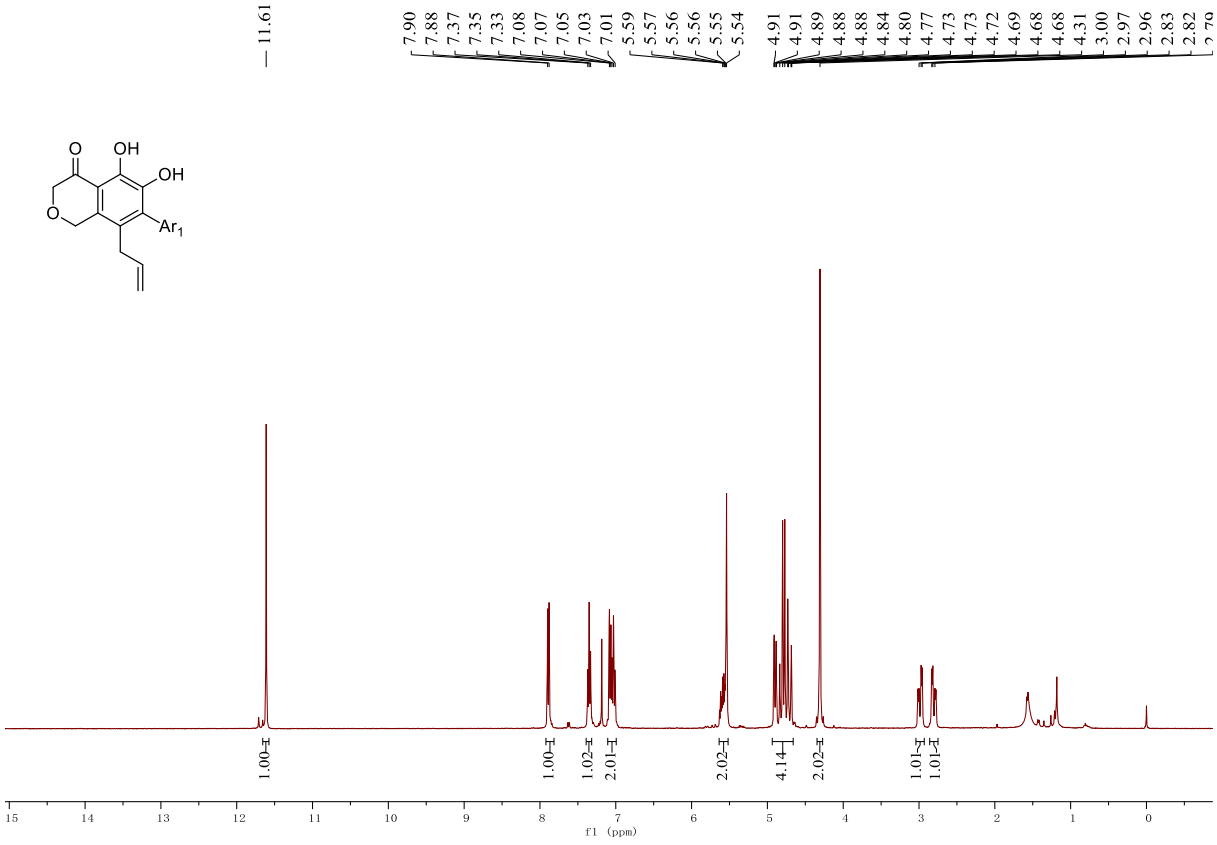
^{1}H NMR (400 MHz, $CDCl_3$) of **5k**



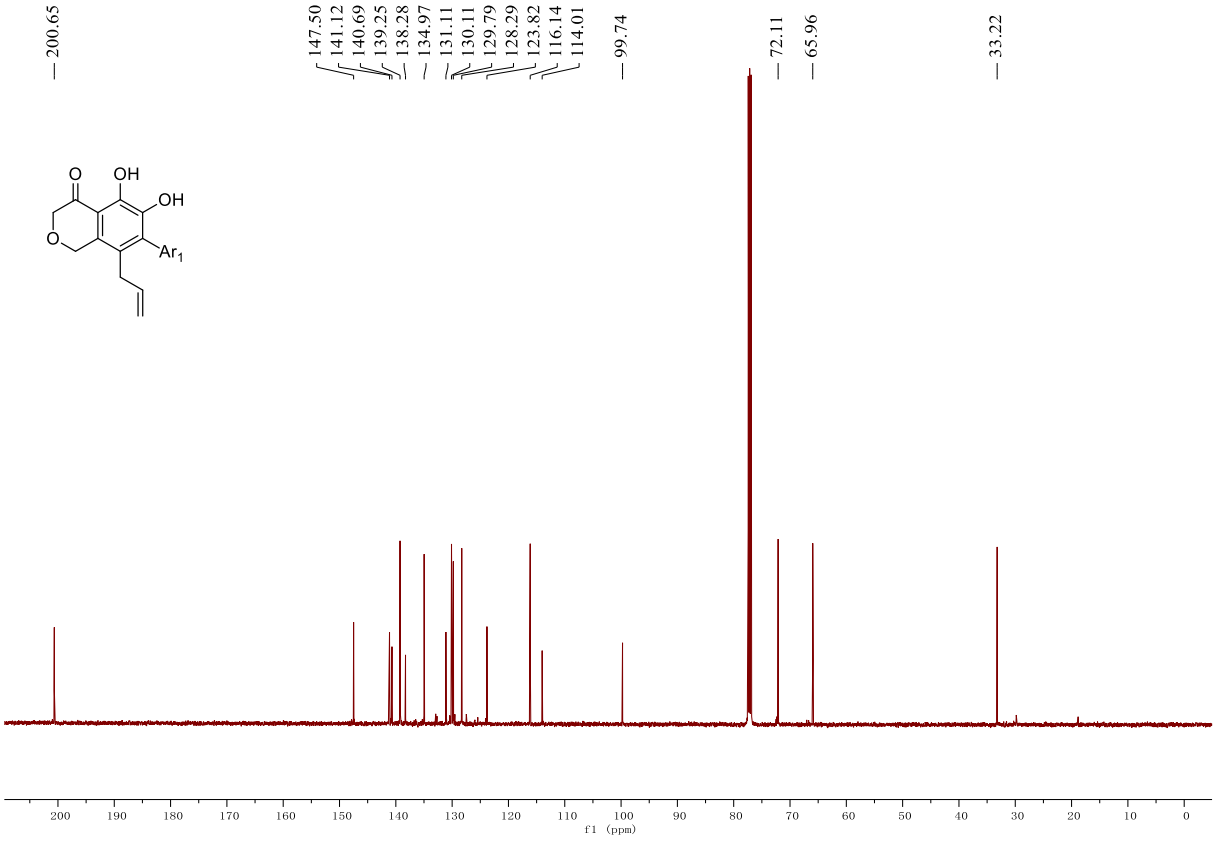
^{13}C NMR (101 MHz, $CDCl_3$) of **5k**



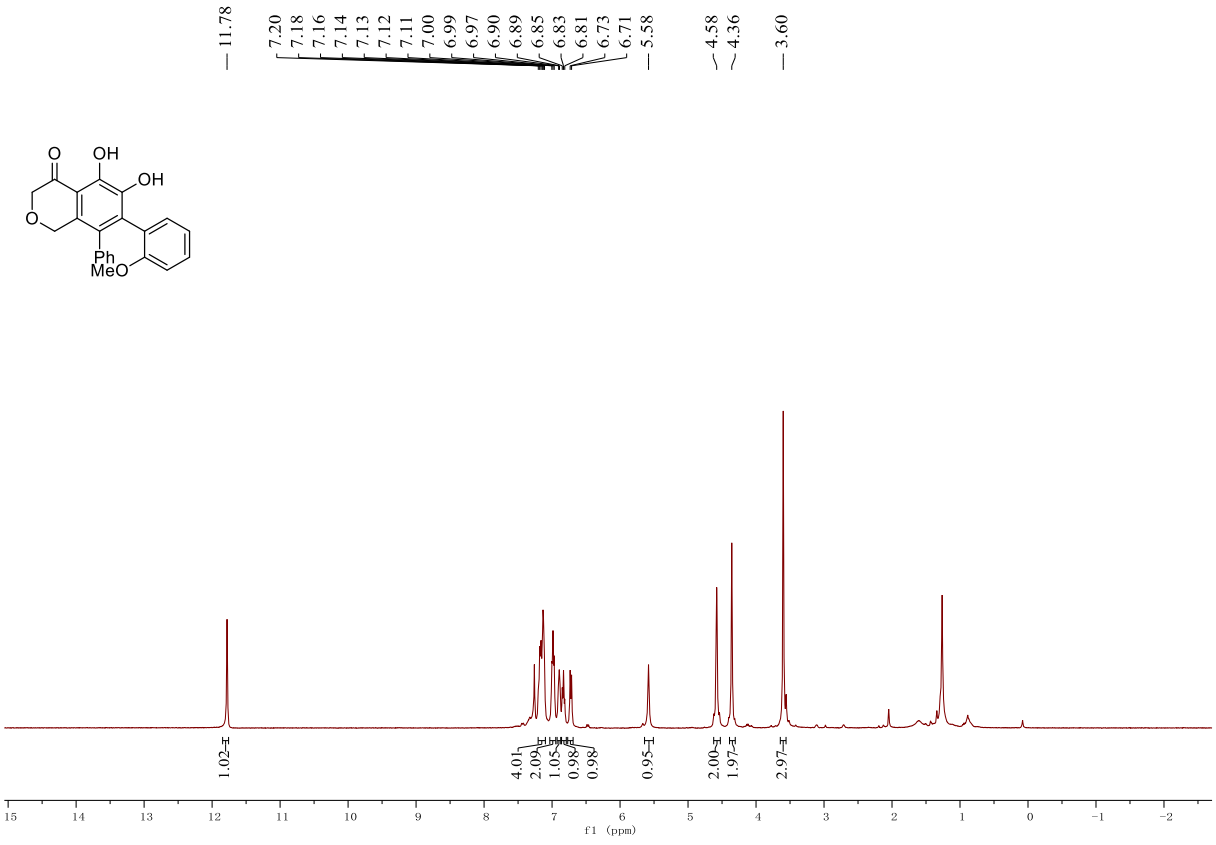
^{1}H NMR (400 MHz, $CDCl_3$) of **5l**



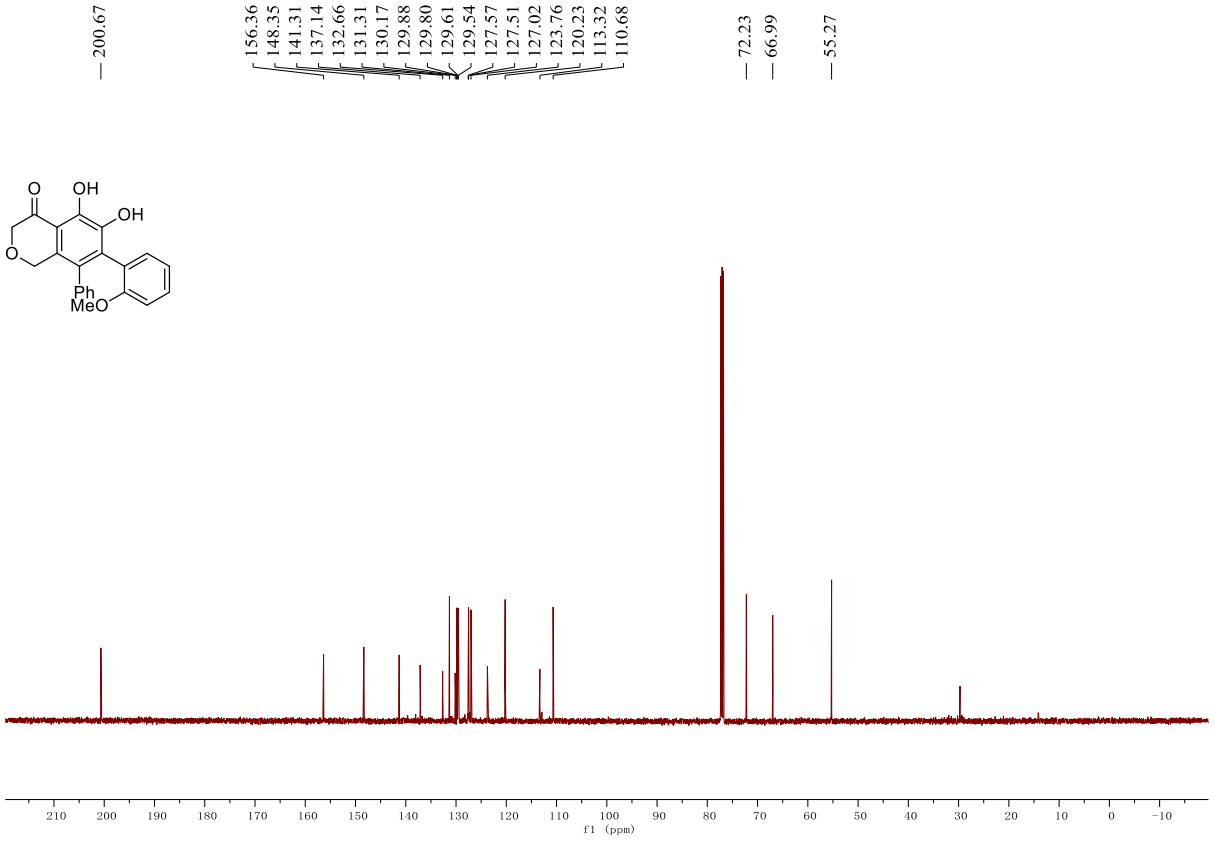
^{13}C NMR (126 MHz, $CDCl_3$) of **5l**



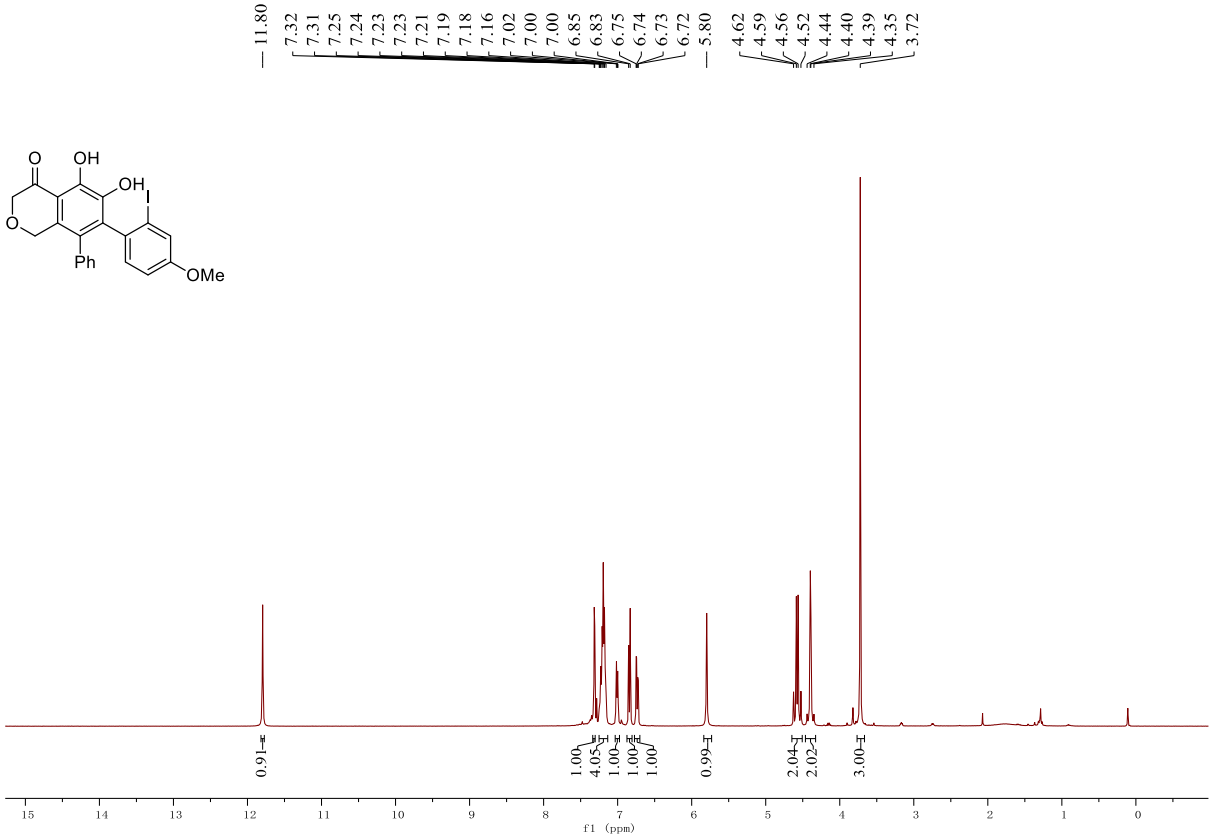
^{1}H NMR (500 MHz, $CDCl_3$) of **5m**



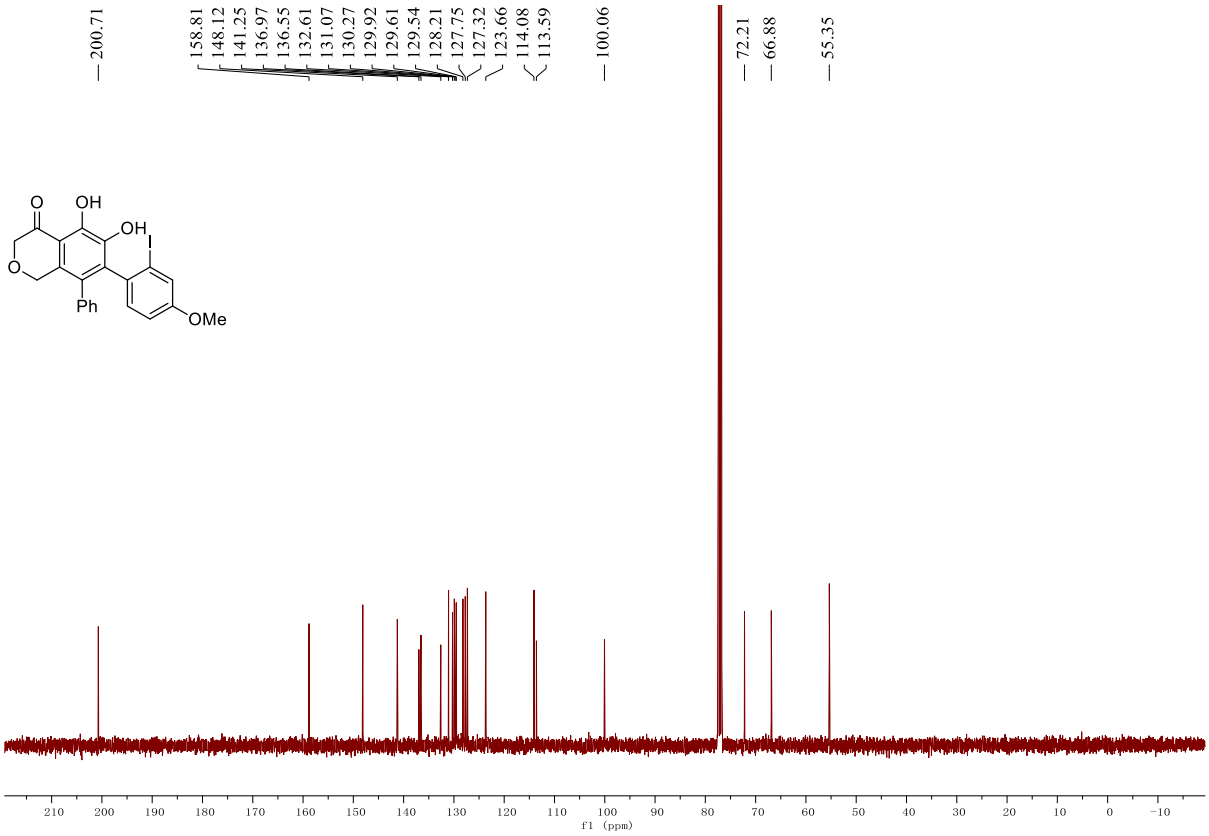
^{13}C NMR (126 MHz, $CDCl_3$) of **5m**



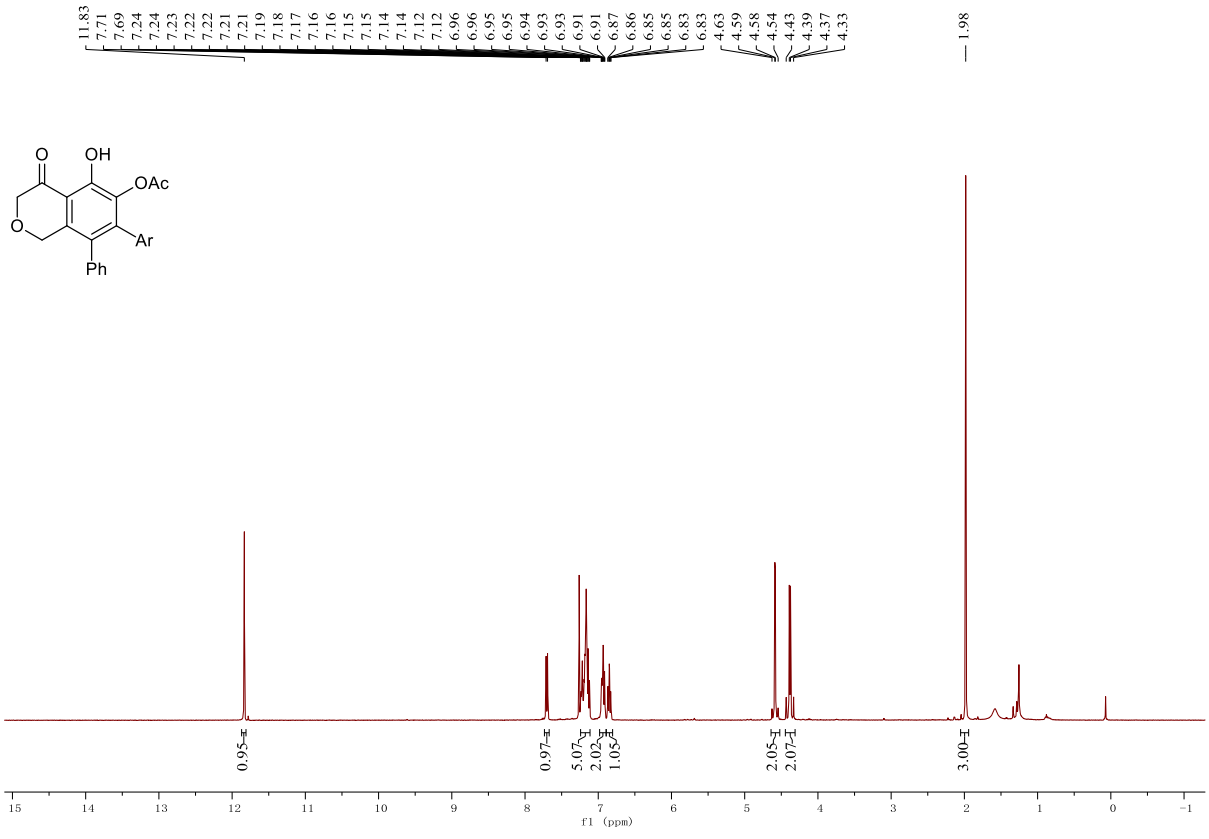
^{1}H NMR (400 MHz, $CDCl_3$) of **5n**



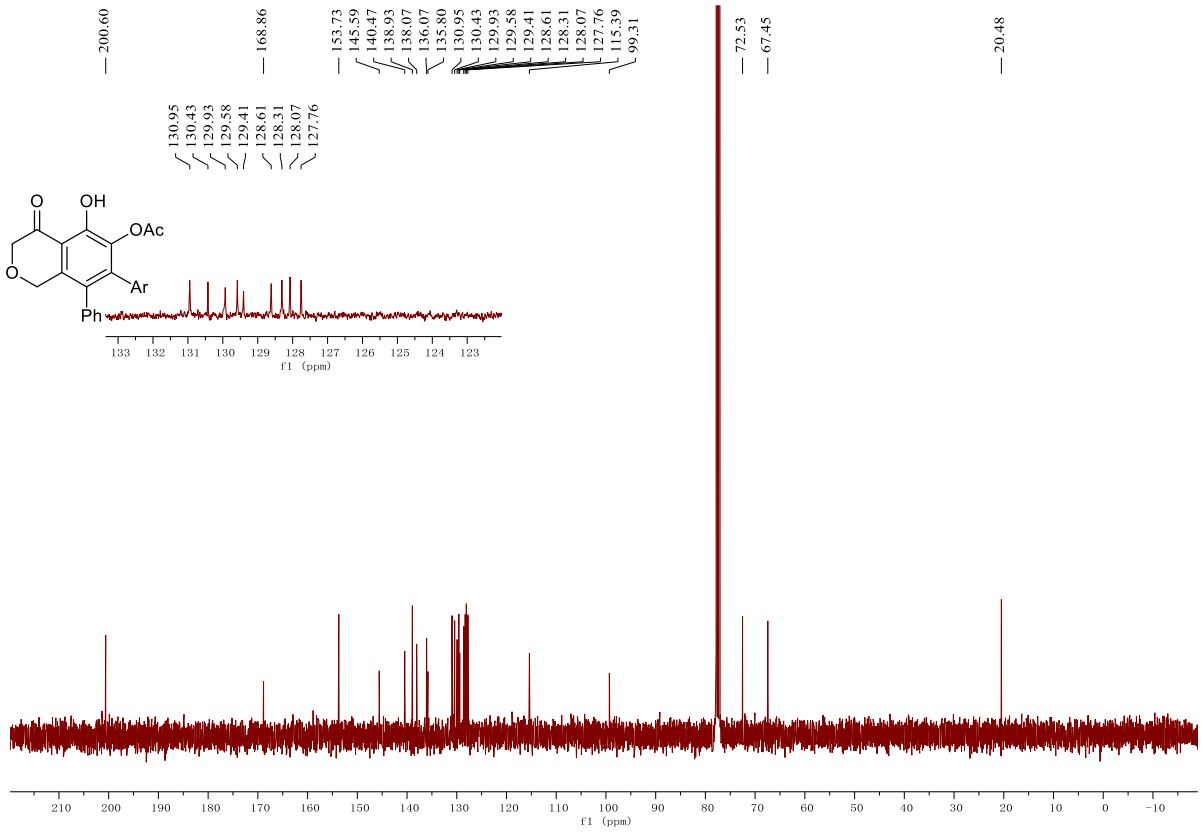
^{13}C NMR (101 MHz, $CDCl_3$) of **5n**



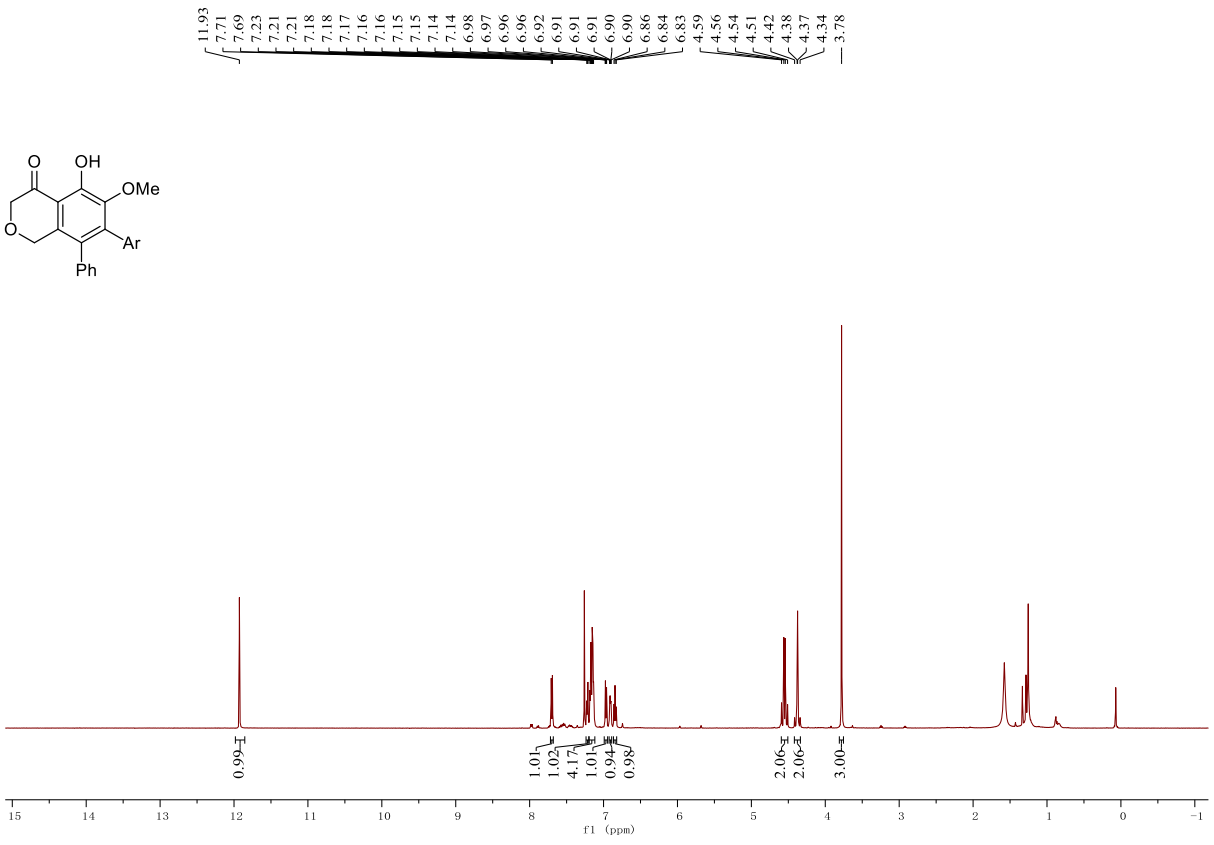
^{1}H NMR (400 MHz, $CDCl_3$) of **6**



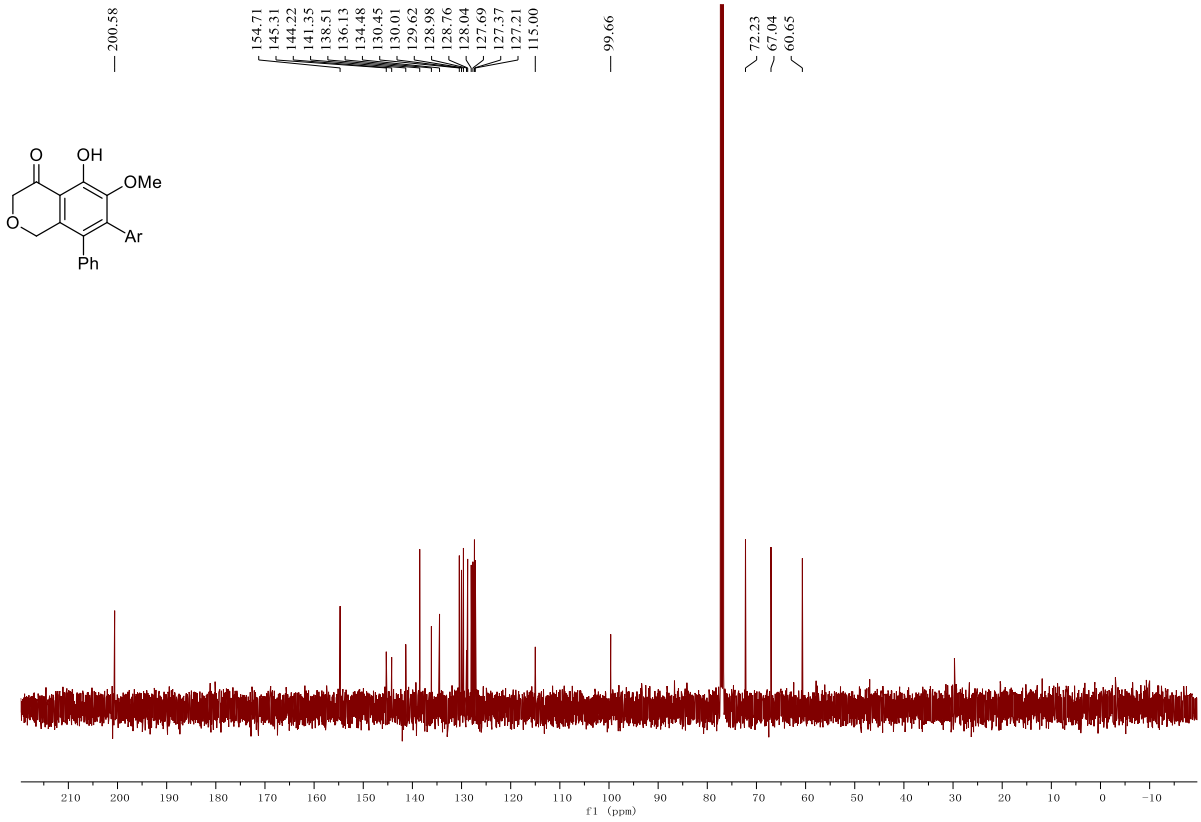
^{13}C NMR (101 MHz, $CDCl_3$) of **6**



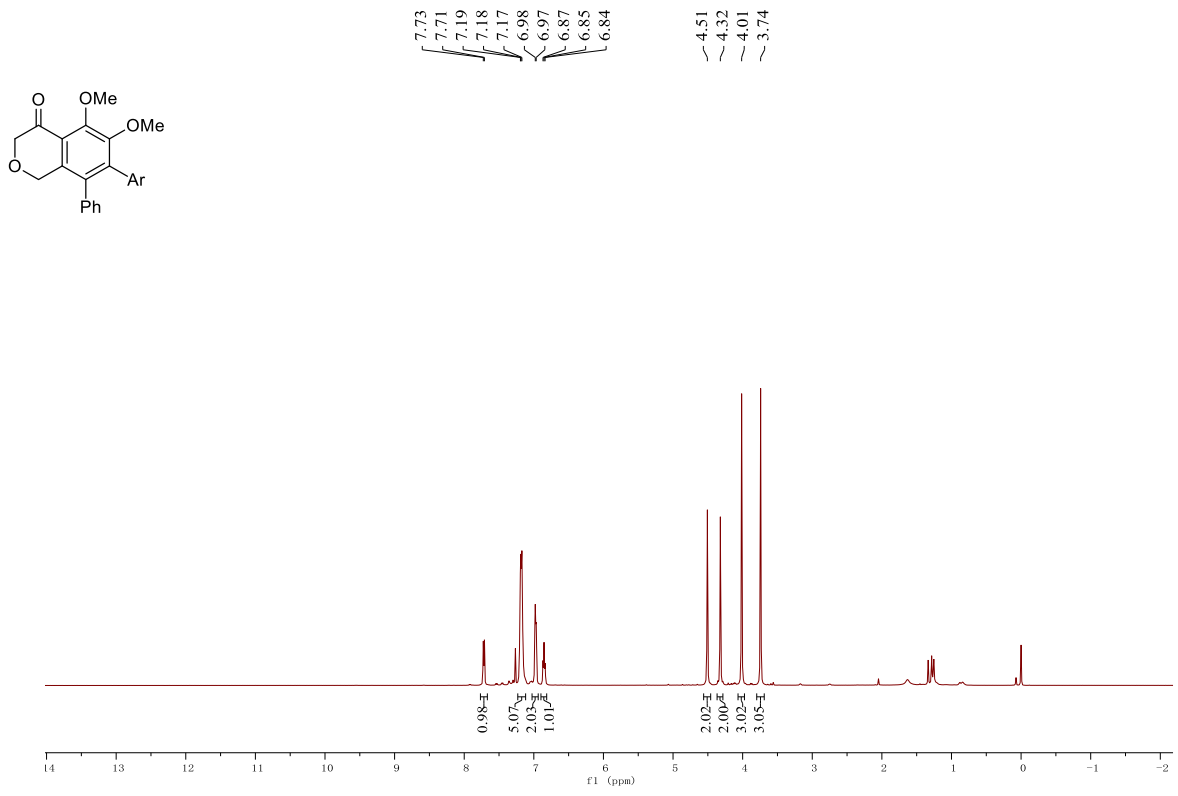
^{1}H NMR (500 MHz, $CDCl_3$) of **7**



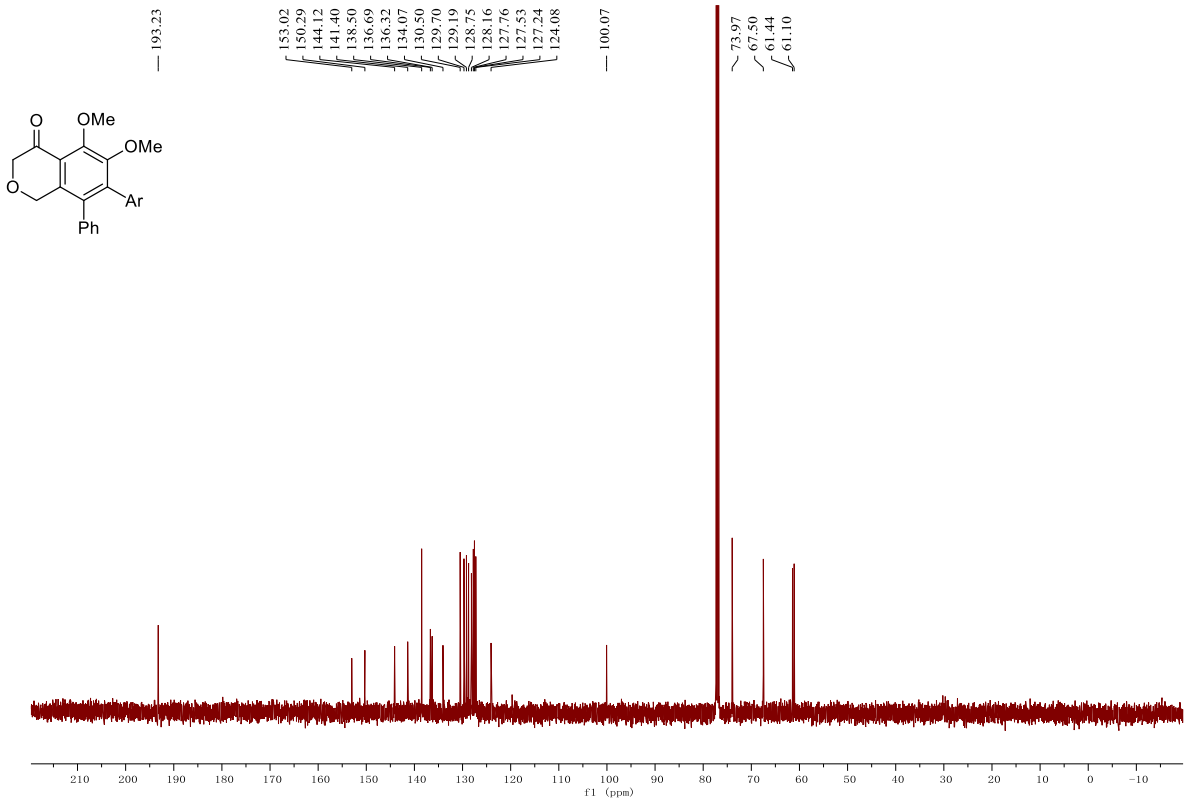
^{13}C NMR (126 MHz, $CDCl_3$) of **7**



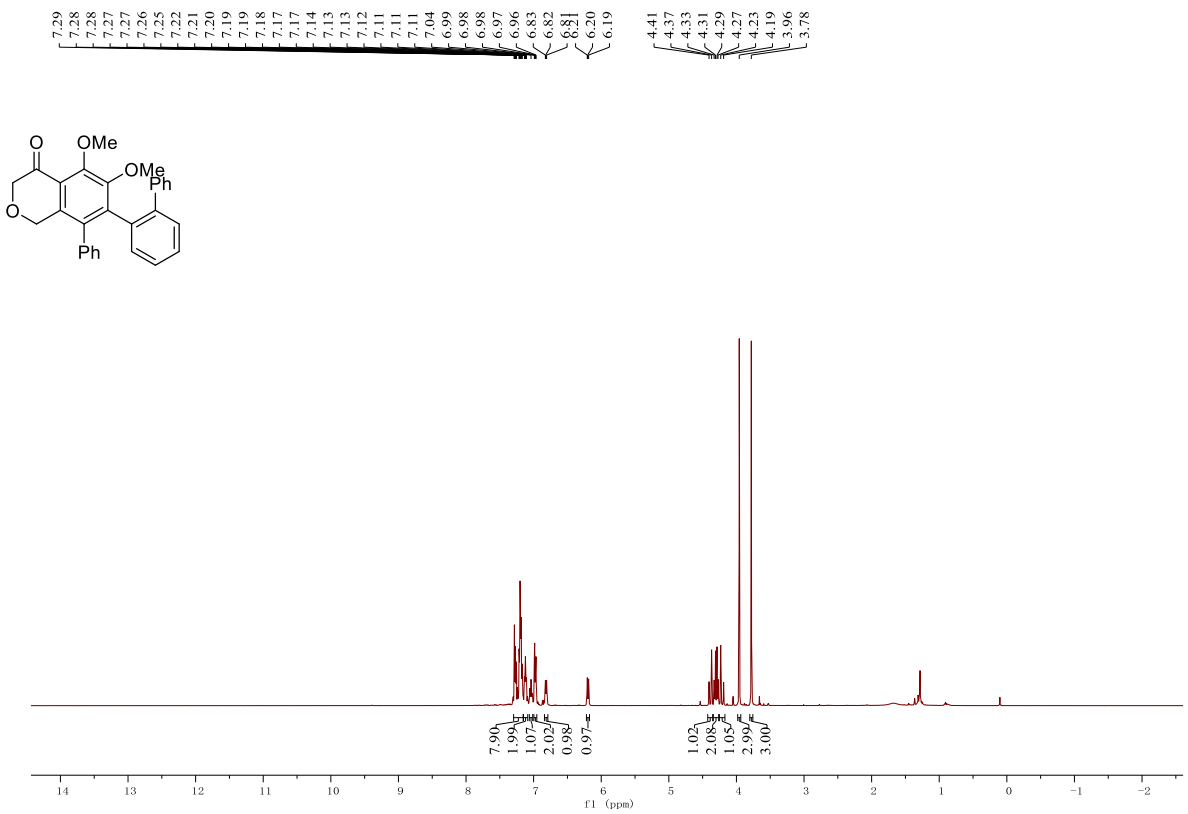
^{1}H NMR (500 MHz, $CDCl_3$) of **8**



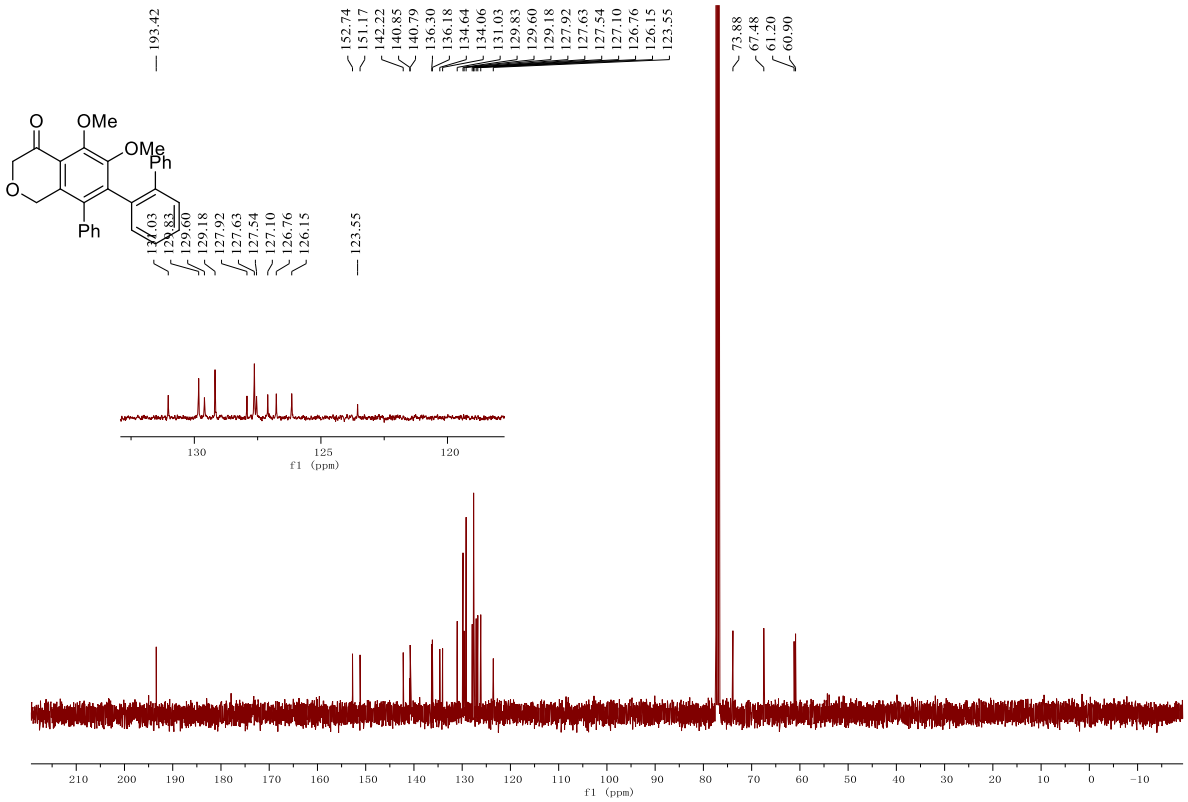
^{13}C NMR (126 MHz, $CDCl_3$) of **8**



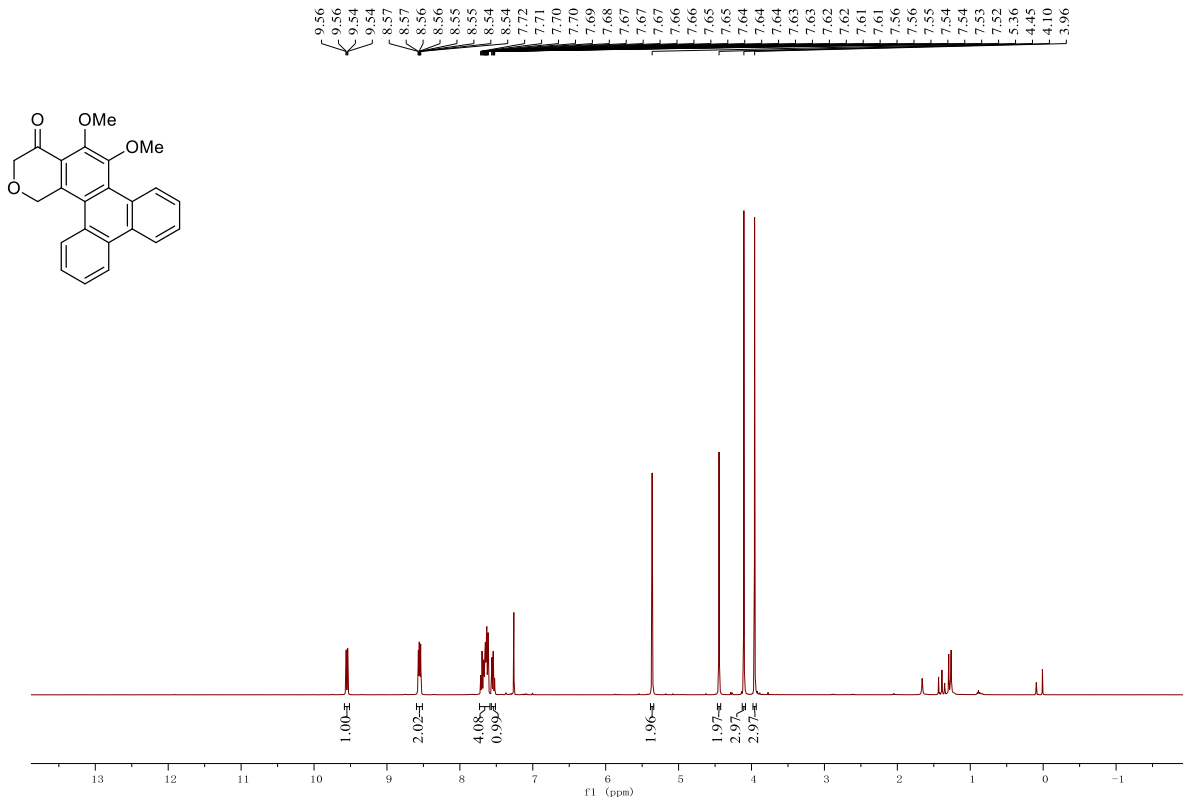
^{1}H NMR (400 MHz, $CDCl_3$) of **9**



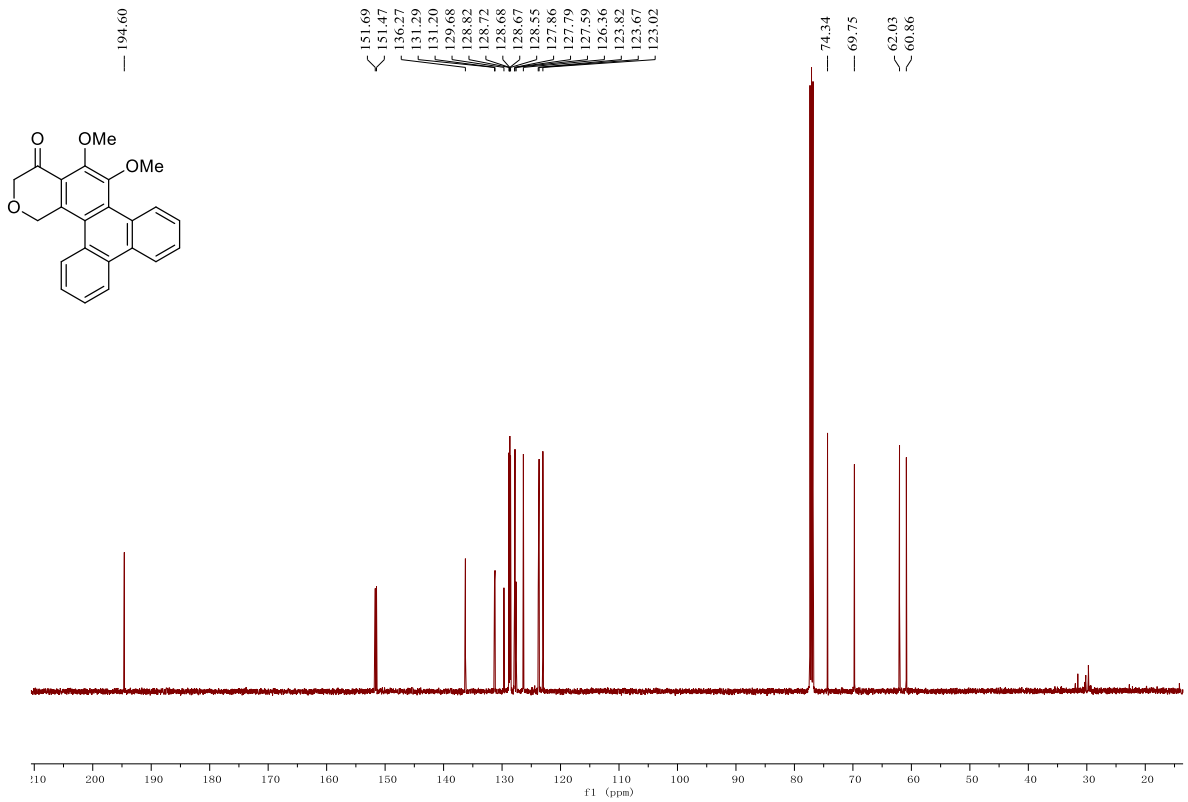
^{13}C NMR (101 MHz, $CDCl_3$) of **9**



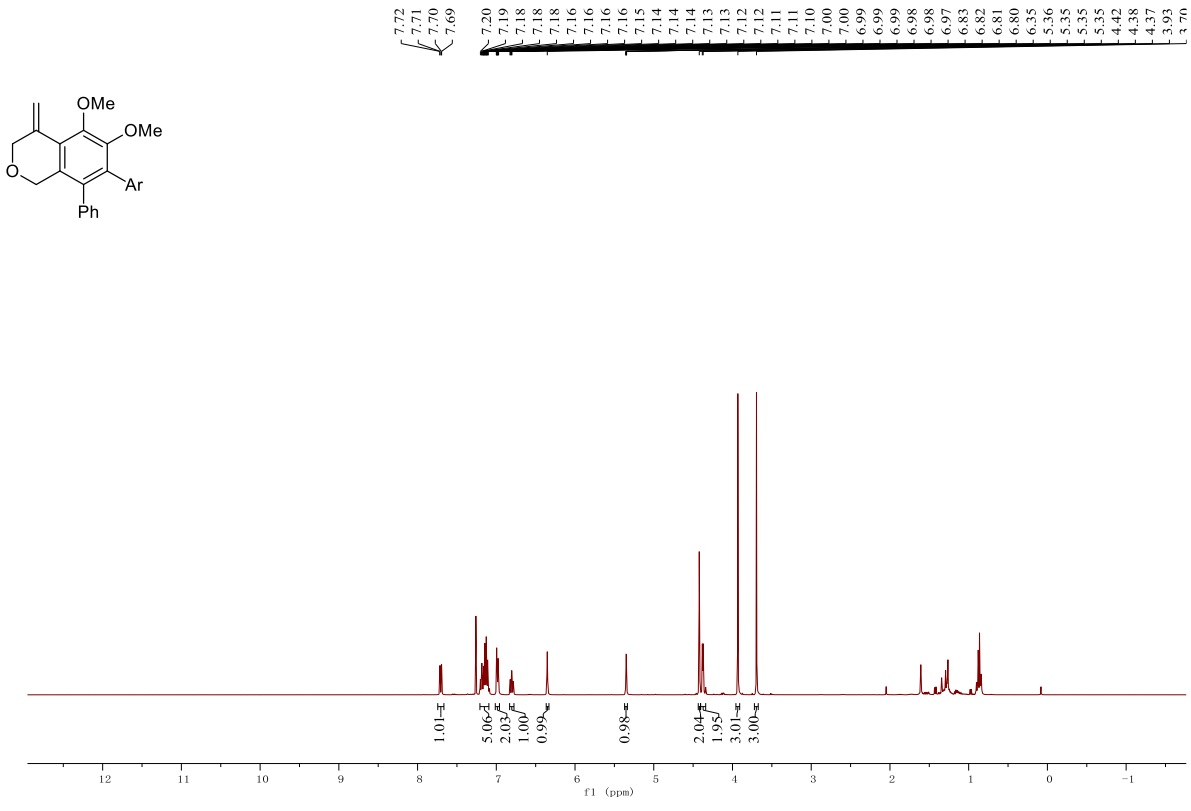
^{1}H NMR (400 MHz, $CDCl_3$) of **10**



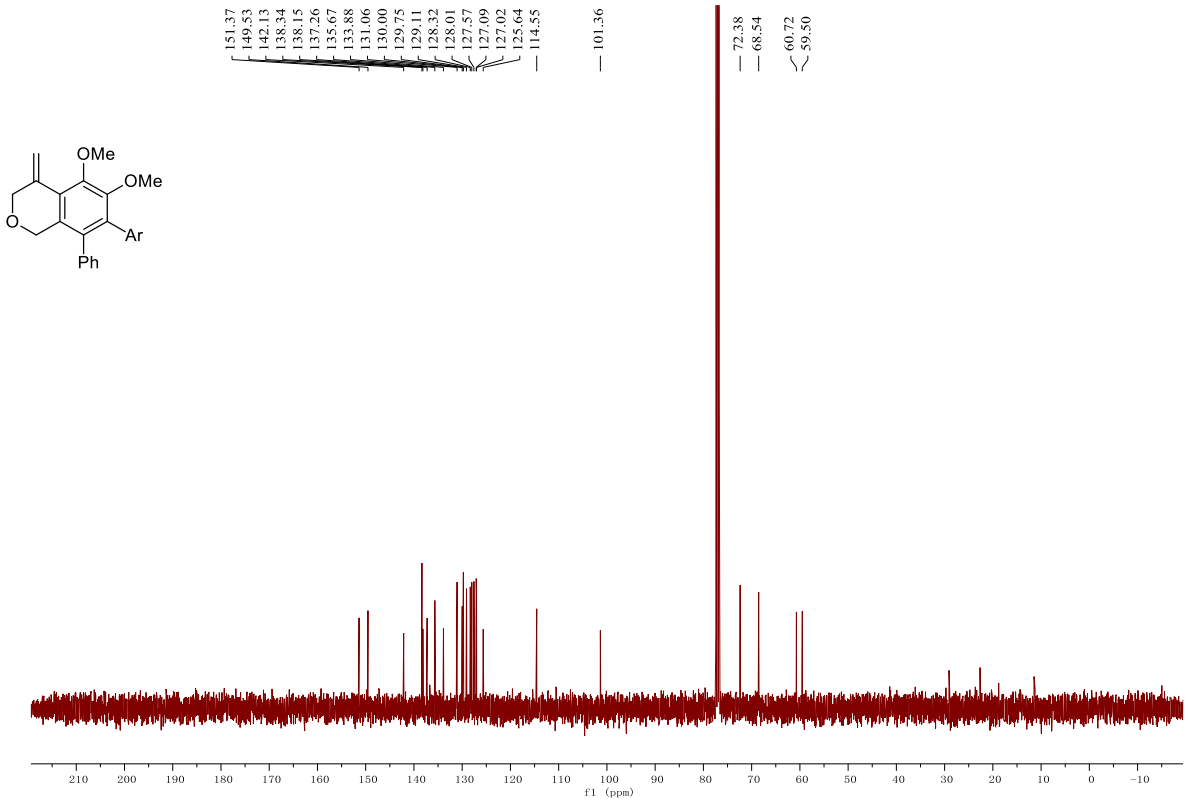
^{13}C NMR (126 MHz, $CDCl_3$) of **10**



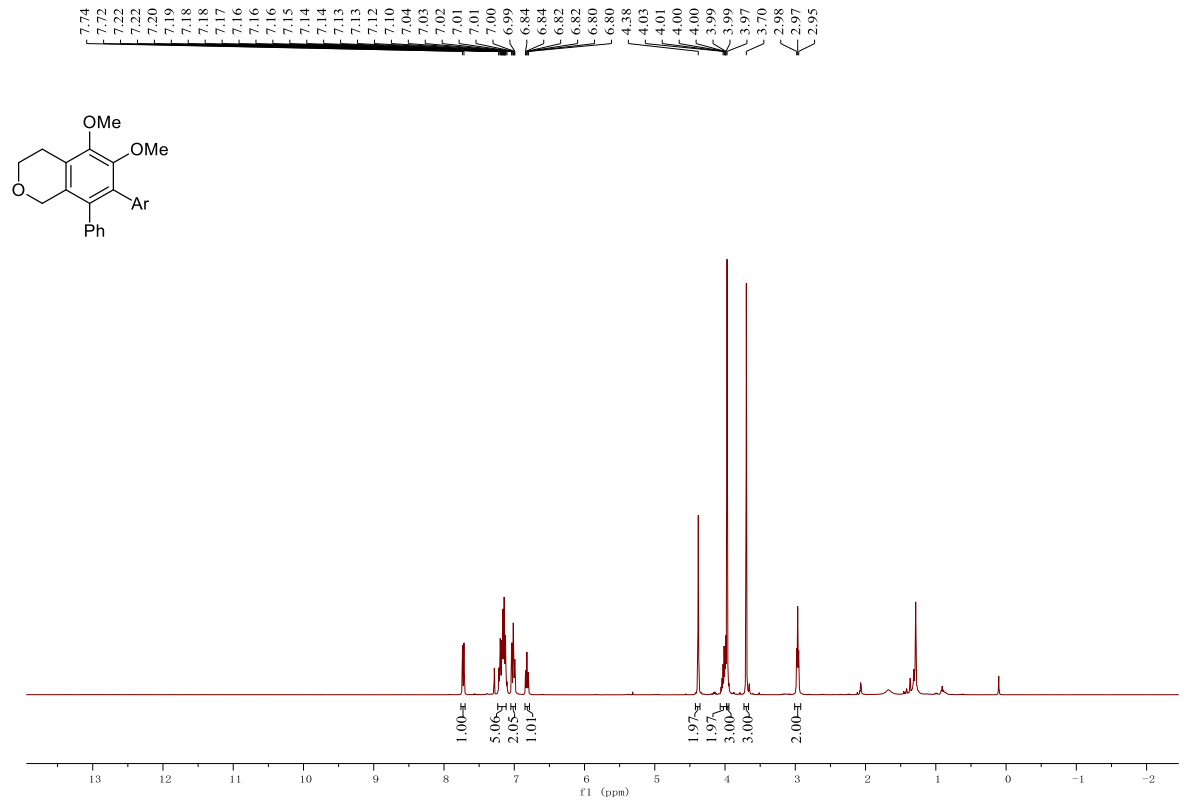
^{1}H NMR (400 MHz, $CDCl_3$) of **11**



^{13}C NMR (101MHz, $CDCl_3$) of **11**



^{1}H NMR (400 MHz, $CDCl_3$) of **12**



^{13}C NMR (101 MHz, $CDCl_3$) of **12**