Synthesis of 8-azaprotosappanin A derivatives via intramolecular palladium-catalyzed ortho C–H activation/C–C cyclization and antibacterial activity

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Supplementary data

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1. General methods and materials

Unless otherwise noted, all commercial materials and solvents were used without further purification. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity, integration, and coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift (δ ppm). The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, m = multiplet. High-resolution mass spectra (HRMS) was carried out by LC/MSD TOF using a column of C18 (rapid resolution, 3.5 μm, 2.1 mm × 30 mm) at a flow of 0.40 mL/min. IR spectra were obtained as potassium bromide pellets or as liquid films between two potassium bromide pellets with a Brucker Vector 22 spectrometer. TLC was performed using commercially prepared 100-400 mesh silica gel plates (GF254), and visualization was effected at 254 nm. All the other chemicals were purchased from Energy Chemical. Commercial reagents were used without further purification. High performance liquid chromatography (HPLC) was carried out by Shimadzu LC-20A using a column of C18 (diamonsil 5μ 250×4.6mm), at a flow (80:20 CH_3OH/3% aqueous acetic acid) of 1.0 mL/min and at λ = 254 nm.

2. General procedures for the synthesis of 2-iodophenols

For the 2-iodophenol, phenol (20 g, 212.51 mmol) and iodine (26.97 g, 106.26 mmol) in distilled water (600 ml) was added hydrogen peroxide 8 mL of a 30% (m/v) aqueous solution, (212.51 mmol). The mixture was stirred at room temperature or at 50 °C for 24 h. Then, 10% (m/v) sodium thiosulfate aqueous solution (350 ml) was added to the mixture, which was extracted with ethyl acetate (3×500 mL). The organic phase was dried over Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel using a mixture of cyclohexane/dichloromethane (1/1), affording 23.5 g of 2-iodophenol as white solid (50%). Mp. 37.9 – 39.3 °C.

For the 2-iodo-4-methoxyl-phenol, 4-methoxyphenol (25 g, 201.4 mmol) was dissolved in 420ml of methanol. Potassium iodide (33.4 g, 201.4 mmol) and sodium hydroxide (8.1 g, 201.4 mmol) were added, and the solution was cooled to 0 °C. Aqueous sodium hypochlorite (260 mL, 5.2% NaOCl) was added dropwise over 3 h at 0–3 °C. The resulting slurry was stirred for 8 h at 0–2 °C and treated with 82 mL of 10% aqueous $Na_2S_2O_3$. The mixture was neutralized using 5% aqueous HCl. Then ether (300 mL) was added. The organic layer was washed with brine (300 mL) and dried over Na_2SO_4. After filtration and rotary evaporation, 42.8 g of 2-iodo-4-methoxyphenol was

afforded, as a white solid, yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.01 (d, *J* = 2.9 Hz, 1H), 6.94 (d, *J* = 8.9 Hz, 1H), 6.80 (dd, *J* = 8.9, 2.9 Hz, 1H), 5.17 (s, 1H), 3.75 (s, 3H).

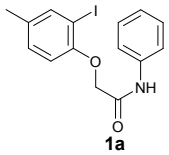
For the 2-iodo-4-methyl-phenol, 2-methylphenol (25 ml, 235.3 mmol) was dissolved in 450 ml of methanol. Potassium iodide (39.1 g, 235.3 mmol) and sodium hydroxide (9.41 g, 235.3 mmol) were added, and the solution was cooled to 0 °C. Aqueous sodium hypochlorite (290 mL, 5.2% NaOCl) was added dropwise over 3 h at 0–3 °C. The resulting slurry was stirred for 8 h at 0–2 °C and treated with 95 mL of 10% aqueous $Na_2S_2O_3$. The mixture was neutralized using 5% aqueous HCl. Then ether (350 mL) was added. The organic layer was washed with brine (350 mL) and dried over Na_2SO_4. After filtration and rotary evaporation, 49.5 g of 2-iodo-4-methyl-phenol was afforded, as a colorless liquid, yield 90%. ^{1}H NMR (400 MHz, DMSO) δ = 10.00 (s, 1H), 7.49 (d, *J* = 1.6 Hz, 1H), 6.98 (dd, *J* = 8.2, 1.6 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 2.17 (s, 3H).

For the 2-iodo-4-fluoro-phenol, 4-fluorophenol (25 g, 223 mmol) was dissolved in 430 ml of methanol. Potassium iodide (37 g, 223 mmol) and sodium hydroxide (8.92 g, 223 mmol) were added, and the solution was cooled to 0 °C. Aqueous sodium hypochlorite (275 mL, 5.2% NaOCl) was added dropwise over 3 h at 0–3 °C. The resulting slurry was stirred for 8 h at 0–2 °C and treated with 90 mL of 10% aqueous $Na_2S_2O_3$. The mixture was neutralized using 5% aqueous HCl. Then ether (325 mL) was added. The organic layer was washed with brine (325 mL) and dried over Na_2SO_4. After filtration and rotary evaporation, 43.2 g of 2-iodo-4-fluoro-phenol was afforded, as a light yellow solid, yield 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.01 – 6.91 (m, 2H), 5.11 (s, 1H).

For the 2-iodo-5-methoxy-phenol, I_2 (40.9 g, 161.1 mmol, 1 eq) was dissolved in $CHCl_3$ (850 mL) with stirring over 1.5 h. A 2 L round-bottomed flask was charged with 3-methoxyphenol (20.00 g, 161.1 mmol, 1 eq) and $AgCO_2CF_3$ (35.6 g, 40 mmol, 1 eq). The solution was added slowly into the round-bottomed flask over 3 h. The reaction was stirred at room temperature for 24 h. The mixture was filtered over celatom and the precipitate washed with $CHCl_3$. The organics were washed with 5% aqueous $Na_2S_2O_3$ (500ml), saturated $NaHCO_3$, washed with water, washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified via flash chromatography using CH_2Cl_2 to give 31.76 g of 2-iodo-5-methoxy-phenol as a white solid (79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.49 (d, *J* = 8.8 Hz, 1H), 6.59 (d, *J* = 2.8 Hz, 1H), 6.33 (dd, *J* = 8.8, 2.8 Hz, 1H), 5.24 (s, 1H), 3.77 (s, 3H).

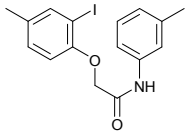
3. Synthesis and characterization of α-(2-Iodophenoxy)-N-phenylacetamide derivatives (1).

General Procedure A: The first stage of one-pot continuous reaction was to add anilines (1.0eq), anhydrous potassium carbonate (1.2eq) and appropriate amount of anhydrous DMAC (0.2 M to substrate) in a two necked flask and keep hypothermia with a rapid infusion of chloroacetyl chloride (1.02eq) into the mixture in ice bath 1 h to room temperature 20 min. After the completion of the first stage, anhydrous potassium carbonate (1.2eq) was added into the reactor and the reaction system temperature was raised up to 80 °C in water bath under nitrogen atmosphere. Then add the iodo-phenols (1.1eq) into the reactor and keep the reaction system under the adjusted conditions for 2 h. When the reaction was over, the reaction mixture was filtered and removed solvent by rotary evaporation. And the crude product was precipitated after cold 15% aqueous NaOH was added. At last, the crude product was recrystallized with alcohol to get the solid pure product. And the characterization of compounds **1** was showed as follows:



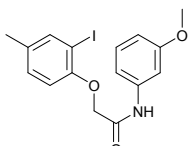
1a

Following the general procedure A. White solid (93%). Mp. 126 – 130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.74 (s, 1H), 7.63 (d, *J* = 6.3 Hz, 2H), 7.39 (d, *J* = 21.1 Hz, 3H), 7.21 – 7.05 (m, 2H), 6.81 (d, *J* = 7.3 Hz, 1H), 4.61 (s, 2H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.55, 151.31, 137.06, 133.81, 133.50, 129.40, 129.12, 124.78, 119.84, 113.78, 86.26, 68.40, 20.31. HRMS (EI) calcd for $C_{15}H_{14}INO_2$ (M+): 367.0069. Found: 367.0118. Anal.calcd for $C_{15}H_{14}INO_2$: C, 49.07; H, 3.84; I, 34.56; N, 3.81. Found: C, 49.04; H, 3.72; I, 34.59; N, 3.80. IR (KBr disc): *v*= 3365, 2917, 1685, 1542, 1288 cm^{-1}.



1b

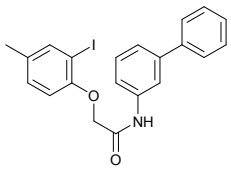
Following the general procedure A. Light yellow solid (95%). Mp. 115 – 117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.76 (s, 1H), 7.64 (s, 1H), 7.56 – 7.35 (m, 2H), 7.14 (d, *J* = 8.1 Hz, 1H), 6.97 (d, *J* = 7.7 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 4.60 (s, 2H), 2.33 (d, *J* = 32.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.30, 153.45, 139.72, 139.09, 137.05, 133.86, 130.42, 128.92, 125.60, 120.45, 116.98, 112.31, 86.27, 68.23, 21.55, 20.08. HRMS (EI) calcd for $C_{16}H_{16}INO_2$ (M+): 381.0226. Found: 381.0179. Anal.calcd for $C_{16}H_{16}INO_2$: C, 50.41; H, 4.23; I, 33.29; N, 3.67. Found: C, 50.39; H, 4.20; I, 33.32; N, 3.68. IR (KBr disc): *v*= 3379, 2913, 1683, 1548, 1241 cm^{-1}.



1c

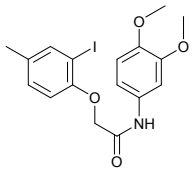
Following the general procedure A. White solid (97%). Mp. 128 – 131 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.82 (s, 1H), 7.64 (s, 1H), 7.42 (s, 1H), 7.24 (s, 1H), 7.15 (d, *J* = 7.5 Hz, 2H), 6.72 (d, *J* = 8.2 Hz, 2H), 4.60 (s, 2H), 3.83 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.33, 160.20, 153.41, 139.73, 138.35, 133.90, 130.42, 129.81, 112.32, 112.06, 110.40, 105.70, 86.26, 68.22, 55.37, 20.08. HRMS (EI) calcd for $C_{16}H_{16}INO_3$ (M+): 397.0175. Found: 397.0196. Anal.calcd for $C_{16}H_{16}INO_3$: C, 48.38; H,

4.06; I, 31.95; N, 3.53. Found: C, 48.39; H, 4.05; I, 31.92; N, 3.55. IR (KBr disc): *v*= 3373, 2909, 1692, 1556, 1288 cm^{-1}.



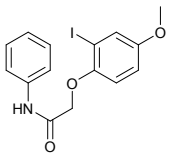
1d

Following the general procedure A. Gray solid (93%). Mp. 149 – 153 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.81 (s, 1H), 7.87 (t, *J* = 2.0 Hz, 1H), 7.62 (tt, *J* = 6.2, 1.2 Hz, 3H), 7.49 – 7.41 (m, 4H), 7.41 – 7.34 (m, 2H), 7.12 (ddd, *J* = 8.3, 2.2, 0.9 Hz, 1H), 6.84 (d, *J* = 8.3 Hz, 1H), 4.65 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.65, 151.33, 142.34, 140.63, 137.48, 133.83, 133.57, 129.49, 129.49, 129.42, 128.78, 127.56, 127.25, 123.66, 118.76, 118.62, 113.86, 86.27, 68.50, 20.30. HRMS (EI) calcd for $C_{21}H_{18}INO_2$ (M+): 443.0382. Found: 443.0401. Anal.calcd for $C_{21}H_{18}INO_2$: C, 56.90; H, 4.09; I, 28.63; N, 3.16. Found: C, 56.92; H, 4.11; I, 28.60; N, 3.15. IR (KBr disc): *v*= 3394, 2924, 1689, 1540, 1256 cm^{-1}.



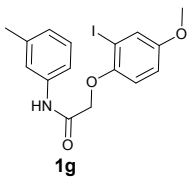
1e

Following the general procedure A. Gray solid (98%). Mp. 152 – 153 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.73 (s, 1H), 7.64 (d, *J* = 2.0 Hz, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.15 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.02 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 4.60 (s, 2H), 3.90 (d, *J* = 13.9 Hz, 6H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.14, 153.48, 149.16, 146.20, 139.72, 133.92, 130.79, 130.45, 112.41, 111.85, 111.37, 104.73, 86.25, 68.28, 56.14, 56.01, 20.08. HRMS (EI) calcd for $C_{17}H_{18}INO_4$ (M+): 427.0281. Found: 427.0243 Anal.calcd for $C_{17}H_{18}INO_4$: C, 47.79; H, 4.25; I, 29.70; N, 3.28. Found: C, 47.81; H, 4.26; I, 29.67; N, 3.29. IR (KBr disc): *v*= 3378, 2967, 1678, 1556, 1288 cm^{-1}.



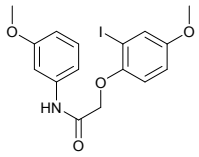
1f

Following the general procedure A. White solid (95%). Mp. 105 – 107 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.72 (s, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.22 – 7.09 (m, 2H), 6.93 – 6.78 (m, 2H), 4.59 (s, 2H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.66, 155.31, 147.79, 137.06, 129.11, 124.77, 119.84, 118.95, 115.13, 114.09, 86.01, 69.14, 55.93. HRMS (EI) calcd for $C_{15}H_{14}INO_3$ (M+): 383.0018. Found: 383.0065. Anal.calcd for $C_{15}H_{14}INO_3$: C, 47.02; H, 3.68; I, 33.12; N, 3.66. Found: C, 46.99; H, 3.69; I, 33.14; N, 3.64. IR (KBr disc): *v*= 3391, 2945, 1684, 1543, 1284 cm^{-1}.



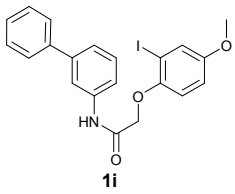
1g

Following the general procedure A. White solid (97%). Mp. 123 – 125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.67 (s, 1H), 7.47 (s, 1H), 7.41 (d, *J* = 8.1 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.16 (d, *J* = 2.5 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.91 – 6.82 (m, 2H), 4.58 (s, 2H), 3.78 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.60, 155.32, 147.83, 139.08, 136.95, 128.92, 125.60, 120.47, 118.98, 116.99, 115.14, 114.09, 86.93, 69.18, 55.93, 21.51. HRMS (EI) calcd for $C_{16}H_{16}INO_3$ (M+): 397.0175. Found: 397.0196. Anal.calcd for $C_{16}H_{16}INO_3$: C, 48.38; H, 4.06; I, 31.95; N, 3.53. Found: C, 48.37; H, 4.07; I, 31.98; N, 3.49. IR (KBr disc): *v*= 3384, 2920, 1692, 1545, 1298 cm^{-1}.



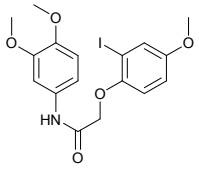
1h

Following the general procedure A. Light yellow solid (98%). Mp. 92 – 94 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.72 (s, 1H), 7.39 (s, 1H), 7.26 (t, *J* = 8.1 Hz, 1H), 7.16 (d, *J* = 2.5 Hz, 1H), 7.10 (d, *J* = 8.7 Hz, 1H), 6.91 – 6.82 (m, 2H), 6.71 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.58 (s, 2H), 3.83 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.65, 160.22, 155.35, 147.80, 138.25, 129.80, 118.97, 115.18, 114.11, 112.75, 112.06, 110.46, 85.40, 69.19, 55.93, 55.36. HRMS (EI) calcd for $C_{16}H_{16}INO_4$ (M+): 413.0124. Found: 413.0066. Anal.calcd for $C_{16}H_{16}INO_4$: C, 46.51; H, 3.90; I, 30.71; N, 3.39. Found: C, 46.54; H, 3.91; I, 30.69; N, 3.38. IR (KBr disc): *v*= 385, 2938, 1682, 1540, 1277 cm^{-1}.



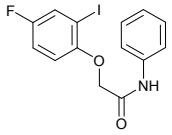
1i

Following the general procedure A. Gray solid (94%). Mp.138 – 140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.80 (s, 1H), 7.86 (s, 1H), 7.62 (t, *J* = 6.9 Hz, 3H), 7.49 – 7.41 (m, 3H), 7.37 (dd, *J* = 14.2, 6.9 Hz, 2H), 7.17 (d, *J* = 2.7 Hz, 1H), 6.93 – 6.83 (m, 2H), 4.62 (s, 2H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.76, 155.37, 147.83, 142.33, 140.62, 137.49, 129.49, 128.78, 127.56, 127.24, 123.64, 118.99, 118.76, 118.62, 115.24, 114.14, 87.63, 69.26, 55.94. HRMS (EI) calcd for $C_{21}H_{18}INO_3$ (M+): 459.0031. Found: 459.0107. Anal.calcd for $C_{21}H_{18}INO_3$: C, 54.92; H, 3.95; I, 27.63; N, 3.05. Found: C, 54.90; H, 3.97; I, 27.66; N, 3.03. IR (KBr disc): *v*= 3391, 2944, 1687, 1538, 1270 cm^{-1}.



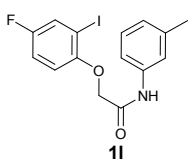
1j

Following the general procedure A. Gray solid (99%). Mp. 114 – 118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.45 (d, *J* = 2.0 Hz, 1H), 7.16 (d, *J* = 2.5 Hz, 1H), 7.00 (d, *J* = 2.1 Hz, 1H), 6.87 (dt, *J* = 12.6, 8.8 Hz, 3H), 4.58 (s, 2H), 3.91 (s, 3H), 3.88 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.46, 155.35, 149.17, 147.85, 146.23, 130.68, 118.96, 115.30, 114.12, 112.76, 111.92, 111.40, 86.77, 69.26, 56.14, 56.00, 55.93. HRMS (EI) calcd for $C_{17}H_{18}INO_5$ (M+): 443.0230. Found: 443.0266. Anal.calcd for $C_{17}H_{18}INO_5$: C, 46.07; H, 4.09; I, 28.63; N, 3.16. Found: C, 46.05; H, 4.10; I, 28.62; N, 3.15. IR (KBr disc): *v*= 3400, 2942, 1682, 1536, 1295 cm^{-1}.



1k

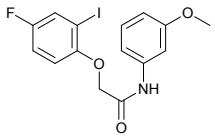
Following the general procedure A. White solid (93%). Mp. 121 – 124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.76 (s, 1H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.56 (d, *J* = 4.9 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.17 (t, *J* = 7.1 Hz, 1H), 7.10 (t, *J* = 6.8 Hz, 1H), 6.78 (dd, *J* = 8.6, 4.0 Hz, 1H), 4.60 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.91, 157.62 (d, *J* = 220 Hz), 152.16, 137.02, 129.16, 126.27 (d, *J* = 30 Hz), 124.89, 119.85, 116.30 (d, *J* = 20 Hz), 112.83 (d, *J* = 10 Hz), 86.0 (d, *J* = 10 Hz), 68.68. HRMS (EI) calcd for $C_{14}H_{11}FINO_2$ (M+): 370.9818. Found: 370.9792. Anal.calcd for $C_{14}H_{11}FINO_2$: C, 45.31; H, 2.99; F, 5.12; I, 34.19; N, 3.77. Found: C, 45.33; H, 2.97; F, 5.14; I, 34.18; N, 3.76. IR (KBr disc): *v*= 3388, 2924, 1694, 1535, 1290 cm^{-1}.



1l

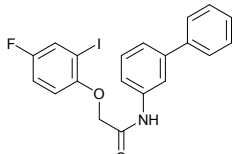
Following the general procedure A. Light yellow solid (95%). Mp. 117 – 120 °C. ^{1}H NMR (400

MHz, $CDCl_3$) δ = 8.60 (s, 1H), 7.46 (s, 1H), 7.43 – 7.31 (m, 2H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.10 – 7.01 (m, 1H), 6.98 (d, *J* = 7.3 Hz, 1H), 6.89 (dd, *J* = 8.8, 4.5 Hz, 1H), 4.60 (s, 2H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.06, 157.53 (d, *J* = 244 Hz), 150.09, 139.14, 136.82, 128.97, 125.74, 120.70 (d, *J* = 26 Hz), 120.48, 117.01, 115.38 (d, *J* = 23 Hz), 114.51 (d, *J* = 9 Hz), 86.14 (d, *J* = 8 Hz), 68.81, 21.52. HRMS (EI) calcd for $C_{15}H_{13}FINO_2$ (M+): 384.9975. Found: 384.9914. Anal.calcd for $C_{15}H_{13}FINO_2$: C, 46.77; H, 3.40; F, 4.93; I, 32.95; N, 3.64. Found: C, 46.75; H, 3.43; F, 4.94; I, 32.96; N, 3.63. IR (KBr disc): *v*= 3385, 2928, 1703, 1546, 1273 cm^{-1}.



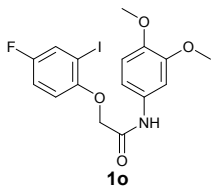
1m

Following the general procedure A. White solid (96%). Mp. 120 – 123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.74 (s, 1H), 7.55 (dd, *J* = 7.4, 3.0 Hz, 1H), 7.41 (t, *J* = 2.1 Hz, 1H), 7.16 – 7.05 (m, 2H), 6.78 (dd, *J* = 9.0, 4.4 Hz, 1H), 6.72 (ddd, *J* = 8.3, 2.5, 0.9 Hz, 1H), 4.59 (s, 2H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.90, 160.23, 157.62 (d, *J* = 245 Hz), 152.14 (d, *J* = 3 Hz), 138.21, 129.85, 126.27 (d, *J* = 25 Hz), 116.29 (d, *J* = 12 Hz), 112.82 (d, *J* = 8 Hz), 112.78, 112.06, 110.44, 105.79, 85.96 (d, *J* = 8 Hz), 68.67, 55.38. HRMS (EI) calcd for $C_{15}H_{13}FINO_3$ (M+): 400.9924. Found: 400.9962. Anal.calcd for $C_{15}H_{13}FINO_3$: C, 44.91; H, 3.27; F, 4.74; I, 31.63; N, 3.49. Found: C, 44.94; H, 3.26; F, 4.72; I, 31.58; N, 3.48. IR (KBr disc): *v*= 3380, 3913, 1685, 1550, 1285 cm^{-1}.



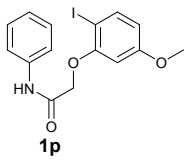
1n

Following the general procedure A. Yellow solid (91%). Mp. 138 – 141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.73 (s, 1H), 7.86 (s, 1H), 7.61 (d, *J* = 7.4 Hz, 3H), 7.49 – 7.42 (m, 3H), 7.41 – 7.34 (m, 3H), 7.10 – 7.01 (m, 1H), 6.91 (dd, *J* = 9.0, 4.6 Hz, 1H), 4.64 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.21, 157.59 (d, *J* = 244 Hz), 150.11, 142.40, 140.57, 137.35, 129.53, 128.80, 127.61, 127.24, 123.79, 120.73 (d, *J* = 26 Hz), 118.78, 118.66, 115.42 (d, *J* = 23 Hz), 114.64 (d, *J* = 8 Hz), 85.53 (d, *J* = 13 Hz), 68.91. HRMS (EI) calcd for $C_{20}H_{15}FINO_2$ (M+): 447.0131. Found: 447.0095. Anal.calcd for $C_{20}H_{15}FINO_2$: C, 53.71; H, 3.38; F, 4.25; I, 28.37; N, 3.13. Found: C, 53.68; H, 3.40; F, 4.24; I, 28.39; N, 3.42. IR (KBr disc): *v*= 3381, 2934, 1698, 1542, 1293 cm^{-1}.



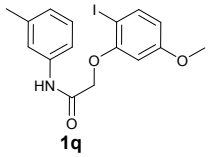
1o

Following the general procedure A. Gray solid (97%). Mp. 133 – 135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.56 (s, 1H), 7.44 (d, *J* = 2.2 Hz, 1H), 7.37 (dd, *J* = 7.6, 2.9 Hz, 1H), 7.06 (td, *J* = 8.4, 7.9, 2.9 Hz, 1H), 6.97 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.91 (dd, *J* = 9.0, 4.6 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 1H), 4.61 (s, 2H), 3.91 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.92, 158.54 (d, *J* = 244 Hz), 150.09, 149.17, 146.31, 130.50, 120.63 (d, *J* = 26 Hz), 115.42 (d, *J* = 23 Hz), 114.65 (d, *J* = 8 Hz), 111.95, 111.34, 104.78, 87.84 (d, *J* = 11 Hz), 68.87, 56.12, 56.01. HRMS (EI) calcd for $C_{16}H_{15}FINO_4$ (M+): 431.0030. Found: 431.0078. Anal. calcd for $C_{16}H_{15}FINO_4$: C, 44.47; H, 3.51; F, 4.41; I, 29.43; N, 3.25. Found: C, 44.49; H, 3.52; F, 4.41; I, 29.46; N, 3.23. IR (KBr disc): *v*= 3396, 2935, 1684, 1542, 1295 cm^{-1}.



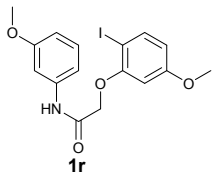
1p

Following the general procedure A. White solid (94%). Mp. 163 – 166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.83 (s, 1H), 7.72 – 7.63 (m, 3H), 7.40 – 7.34 (m, 2H), 7.16 (ddt, *J* = 8.6, 7.3, 1.2 Hz, 1H), 6.43 (d, *J* = 7.6 Hz, 2H), 4.60 (s, 2H), 3.81 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.03, 161.50, 156.08, 139.14, 137.13, 129.14, 124.80, 119.82, 108.86, 100.54, 74.94, 67.89, 55.67. HRMS (EI) calcd for $C_{15}H_{14}INO_3$ (M+): 383.0018. Found: 383.0086. Anal.calcd for $C_{15}H_{14}INO_3$: C, 47.02; H, 3.68; I, 33.12; N, 3.66. Found: C, 46.99; H, 3.68; I, 33.14; N, 3.63. IR (KBr disc): *v*= 3386, 2972, 1700, 1540, 1284 cm-1.



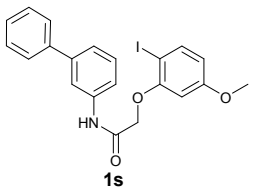
1q

Following the general procedure A. White solid (96%). Mp. 164 – 165 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.76 (s, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.51 (s, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.43 (d, J = 7.5 Hz, 2H), 4.59 (s, 2H), 3.80 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.98, 161.58, 156.10, 139.13, 139.10, 137.03, 128.93, 125.63, 120.44, 116.98, 108.87, 100.52, 74.95, 67.91, 55.66, 21.56. HRMS (EI) calcd for $C_{16}H_{16}INO_3$ (M+): 397.0175. Found: 397.0205. Anal.calcd for $C_{16}H_{16}INO_3$: C, 48.38; H, 4.06; I, 31.95; N, 3.53. Found: C, 48.36; H, 4.07; I, 31.98; N, 3.51. IR (KBr disc): *v*= 3375, 2917, 1688, 1550, 1318 cm^{-1}.



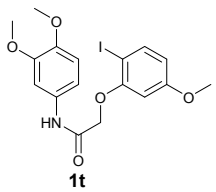
1r

Following the general procedure A. White solid (98%). Mp. 133 – 135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.82 (s, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.42 (t, *J* = 2.2 Hz, 1H), 7.30 – 7.22 (m, 1H), 7.15 (dt, *J* = 8.0, 1.4 Hz, 1H), 6.71 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.43 (d, *J* = 8.2 Hz, 2H), 4.59 (s, 2H), 3.83 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.02, 161.58, 160.20, 156.05, 139.14, 138.32, 129.82, 112.06, 110.40, 108.87, 105.71, 100.55, 74.94, 67.89, 55.66, 55.37. HRMS (EI) calcd for $C_{16}H_{16}INO_4$ (M+): 413.0124. Found: 413.0102. Anal.calcd for $C_{16}H_{16}INO_4$: C, 46.51; H, 3.90; I, 30.71; N, 3.39. Found: C, 46.53; H, 3.91; I, 30.72; N, 3.40. IR (KBr disc): *v*= 3387, 2938, 1701, 1541, 1306 cm^{-1}.



1s

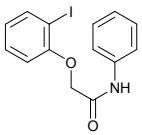
Following the general procedure A. Light yellow solid (93%). Mp. 156 – 158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.90 (s, 1H), 7.92 (t, *J* = 2.0 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.63 – 7.58 (m, 2H), 7.45 (ddd, *J* = 10.5, 6.2, 2.6 Hz, 3H), 7.41 – 7.34 (m, 2H), 6.44 (dq, *J* = 4.8, 2.6 Hz, 2H), 4.63 (s, 2H), 3.81 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.13, 161.60, 156.10, 142.34, 140.64, 139.16, 137.56, 129.50, 128.80, 127.57, 127.25, 123.69, 118.75, 118.60, 108.92, 100.60, 74.97, 67.97, 55.67. HRMS (EI) calcd for $C_{21}H_{18}INO_3$ (M+): 459.0031. Found: 459.0012. Anal.calcd for $C_{21}H_{18}INO_3$: C, 54.92; H, 3.95; I, 27.63; N, 3.05. Found: C, 54.95; H, 3.96; I, 27.63; N, 3.04. IR (KBr disc): *v*= 3391, 2910, 1704, 1543, 1307 cm^{-1}.



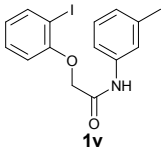
1t

Following the general procedure A. Yellow solid (99%). Mp. 154 – 157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.73 (s, 1H), 7.70 – 7.62 (m, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.02 (dd, *J* = 8.6,

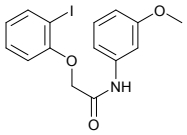
2.5 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 1H), 6.48 – 6.39 (m, 2H), 4.59 (s, 2H), 3.91 (s, 3H), 3.87 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.80, 161.59, 156.11, 149.14, 146.20, 139.13, 130.76, 111.83, 111.36, 108.88, 104.69, 100.61, 74.91, 67.94, 56.13, 56.00, 55.66. HRMS (EI) calcd for $C_{17}H_{18}INO_5$ (M+): 443.0230. Found: 443.0261. Anal. calcd for $C_{17}H_{18}INO_5$: C, 46.07; H, 4.09; I, 28.63; N, 3.16. Found: C, 46.09; H, 4.08; I, 28.65; N, 3.15. IR (KBr disc): *v*= 3379, 2939, 1685, 1546, 1236 cm^{-1}.


1u

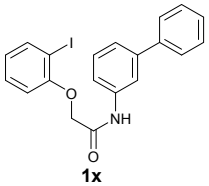
Following the general procedure A. White solid (92%). Mp. 128 – 130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.85 (s, 1H), 7.82 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 2H), 7.40 – 7.34 (m, 3H), 7.16 (t, *J* = 7.4 Hz, 1H), 6.84 (dd, *J* = 7.6, 5.4 Hz, 2H), 4.64 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.12, 155.42, 139.44, 137.13, 130.03, 129.14, 124.81, 124.11, 119.84, 112.54, 86.54, 68.01. HRMS (EI) calcd for $C_{14}H_{12}INO_2$ (M+): 352.9913. Found: 352.9886. Anal.calcd for $C_{14}H_{11}INO_2$: C, 47.61; H, 3.43; I, 35.93; N, 3.97. Found: C, 47.59; H, 3.44; I, 35.94; N, 3.97. IR (KBr disc): *v*= 3378, 2921, 1683, 1543, 1289 cm^{-1}.


1v

Following the general procedure A. White solid (95%). Mp. 134 – 138 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.77 (s, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.52 (s, 1H), 7.44 (d, *J* = 7.3 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.27 (s, 1H), 7.23 (s, 0H), 6.98 (d, *J* = 7.0 Hz, 1H), 6.83 (d, *J* = 7.2 Hz, 2H), 4.63 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.08, 155.40, 139.43, 139.11, 137.02, 130.02, 128.94, 125.65, 124.09, 120.46, 117.00, 112.52, 86.01, 68.01, 21.56. HRMS (EI) calcd for $C_{15}H_{14}INO_2$ (M+): 367.0069. Found: 367.0124. Anal.calcd for $C_{15}H_{14}INO_2$: C, 49.07; H, 3.84; I, 34.56; N, 3.81. Found: C, 49.09; H, 3.85; I, 34.57; N, 3.79. IR (KBr disc): *v*= 3379, 2914, 1687, 1549, 1285 cm^{-1}.

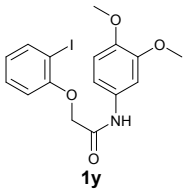

1w

Following the general procedure A. Light yellow solid (96%). Mp. 179 – 180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.83 (s, 1H), 7.82 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.43 (t, *J* = 2.1 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.26 (t, *J* = 8.1 Hz, 1H), 7.18 – 7.12 (m, 1H), 6.84 (dd, *J* = 7.6, 5.3 Hz, 2H), 6.72 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.63 (s, 2H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.13, 160.22, 155.37, 139.44, 138.31, 130.03, 129.82, 124.12, 112.55, 112.09, 110.43, 105.77, 86.48, 68.01, 55.37. HRMS (EI) calcd for $C_{15}H_{14}INO_3$ (M+): 383.0018. Found: 383.0059. Anal.calcd for $C_{15}H_{14}INO_3$: C, 47.02; H, 3.68; I, 33.12; N, 3.66. Found: C, 47.04; H, 3.67; I, 33.14; N, 3.66. IR (KBr disc): *v*= 3383, 2937, 1681, 1518, 1266 cm^{-1}.


1x

Following the general procedure A. White solid (93%). Mp. 134 – 136°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.91 (s, 1H), 7.87 (d, *J* = 33.6 Hz, 2H), 7.61 (s, 3H), 7.41 (d, *J* = 23.9 Hz, 6H), 6.85 (s, 2H), 4.67 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.24, 155.42, 142.37, 140.65,

139.46, 137.55, 130.05, 129.50, 128.80, 127.57, 127.25, 124.16, 123.71, 118.76, 118.63, 112.59, 86.52, 68.08. HRMS (EI) calcd for $C_{20}H_{16}INO_2$ (M+): 429.0226. Found: 429.0208. Anal.calcd for $C_{20}H_{16}INO_2$: C, 55.96; H, 3.76; I, 29.56; N, 3.26. Found: C, 55.93; H, 3.75; I, 29.55; N, 3.28. IR (KBr disc): *v*= 3382, 2921, 1695, 1541, 1293 cm^{-1}.

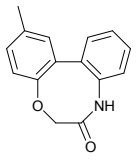


1y

Following the general procedure A. Gray solid (98%). Mp. 136 – 138 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.74 (s, 1H), 7.82 (d, *J* = 7.3 Hz, 1H), 7.50 (s, 1H), 7.37 (s, 1H), 7.02 (d, *J* = 7.7 Hz, 1H), 6.85 (d, *J* = 7.5 Hz, 3H), 4.63 (s, 2H), 3.90 (d, *J* = 14.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.93, 155.44, 149.19, 146.26, 139.43, 130.76, 130.05, 124.12, 112.63, 111.88, 111.42, 104.79, 86.46, 68.06, 56.15, 56.02. HRMS (EI) calcd for $C_{16}H_{16}INO_4$ (M+): 413.0124. Found: 413.0085. Anal.calcd for $C_{16}H_{16}INO_4$: C, 46.51; H, 3.90; I, 30.71; N, 3.39. Found: C, 46.54; H, 3.89; I, 30.68 N, 3.40. IR (KBr disc): *v*= 3379, 2936, 1686, 1542, 1283 cm^{-1}.

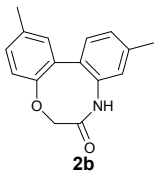
4. General procedure A for synthesis of 8-azaprotosappanin A derivatives (2).

General procedure B: The step of the reaction process was to add α-(2-Iodophenoxy)-N-phenylacetamide **1** (1eq) and appropriate amount of anhydrous DMAC (0.2 M to substrate) in a two necked flask at 120 °C in oil bath, then palladium acetate (15 mol%), anhydrous potassium carbonate (2eq) and silver trifluoroacetate (2eq) were added after the mixture was stirred for 15 min. The reaction system was kept under this condition for 10 h. The reaction progress was monitored by TLC. When the whole reaction was over, the reaction mixture was filtered and removed solvent by rotary evaporation. And the crude product was precipitated after cold water was added. At last, the crude product was recrystallized with ether to get the solid pure product. And the characterization of **2** were showed as follows:



2a

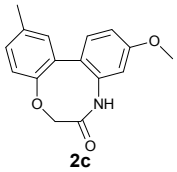
Following the general procedure B. White solid (85%). Mp. 245 – 246 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.73 (s, 1H), 7.39 (td, *J* = 7.5, 1.9 Hz, 1H), 7.33 (td, *J* = 7.4, 1.5 Hz, 1H), 7.29 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.25 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.22 – 7.15 (m, 3H), 4.85 (d, *J* = 15.8 Hz, 1H), 4.47 (d, *J* = 15.7 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 170.19, 153.57, 136.58, 134.87, 134.52, 132.74, 130.98, 130.13, 129.84, 128.69, 126.90, 125.76, 121.07, 73.56, 20.92. HRMS (EI) calcd for $C_{15}H_{13}NO_2$ (M+): 240.1025. Found: 240.0973. Anal. calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.27; H, 5.47; N, 5.85. IR (KBr disc): *v*= 3054, 2920, 1659, 1504, 1209 cm^{-1}. HPLC analysis: 98.80%.



2b

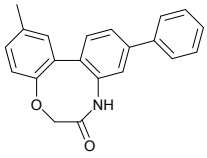
Following the general procedure B. Light yellow solid (87%). Mp. 232 – 234 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.61 (s, 1H), 7.24 – 7.15 (m, 2H), 7.12 – 7.04 (m, 1H), 4.82 (d, *J* = 15.7 Hz, 1H),

4.48 – 4.41 (m, 1H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 169.70, 153.10, 135.73, 134.32, 133.85, 133.55, 132.40, 130.38, 130.14, 129.34, 128.62, 125.17, 120.60, 73.07, 20.42, 20.38. HRMS (EI) calcd for $C_{16}H_{15}NO_2$ (M+): 254.1182. Found: 254.1166. Anal.calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.88; H, 5.95; N, 5.54. IR (KBr disc): *v*= 3069, 2948, 1648, 1512, 1207 cm^{-1}. HPLC analysis: 99.76%.



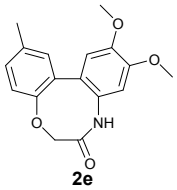
2c

Following the general procedure B. White solid (89%). Mp. 205 – 209 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.69 (s, 1H), 7.24 – 7.10 (m, 4H), 6.93 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.76 (d, *J* = 2.4 Hz, 1H), 4.85 (d, *J* = 15.7 Hz, 1H), 4.46 (d, *J* = 15.7 Hz, 1H), 3.79 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 170.27, 159.51, 153.64, 137.54, 134.72, 132.46, 130.94, 130.55, 129.98, 126.82, 121.02, 112.10, 111.62, 73.55, 55.82, 20.92. HRMS (EI) calcd for $C_{16}H_{15}NO_3$ (M+): 270.1131. Found: 270.1169. Anal.calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.38; H, 5.60; N, 5.21. IR (KBr disc): *v*= 3027, 2960, 1663, 1490, 1289 cm^{-1}. HPLC analysis: 99.88%.



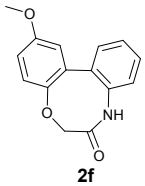
2d

Following the general procedure B. White solid (73%). Mp.219 – 224 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.81 (s, 1H), 7.72 (d, *J* = 1.5 Hz, 1H), 7.70 (s, 1H), 7.64 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 1.9 Hz, 1H), 7.42 (d, *J* = 7.4 Hz, 1H), 7.39 (d, *J* = 7.9 Hz, 1H), 7.29 – 7.22 (m, 3H), 4.91 (d, *J* = 15.8 Hz, 1H), 4.51 (d, *J* = 15.8 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 170.32, 140.61, 139.55, 137.16, 134.95, 133.44, 132.37, 131.10, 130.75, 129.83, 129.56, 128.30, 127.08, 124.99, 123.94, 121.14, 73.60, 20.95. HRMS (EI) calcd for $C_{21}H_{17}NO_2$ (M+): 316.1338. Found: 316.1374. Anal.calcd for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44. Found: C, 79.96; H, 5.44; N, 4.45. IR (KBr disc): *v*= 3064, 2963, 1662, 1517, 1221 cm^{-1}. HPLC analysis: 99.77%.



2e

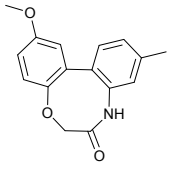
Following the general procedure B. White solid (91%). Mp. 216 – 217 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.48 (s, 1H), 7.23 – 7.15 (m, 3H), 6.82 (d, *J* = 10.9 Hz, 2H), 4.82 (d, *J* = 15.6 Hz, 1H), 4.44 (d, *J* = 15.6 Hz, 1H), 3.79 (d, *J* = 2.2 Hz, 6H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 170.05, 153.58, 148.52, 147.54, 134.59, 132.70, 130.50, 130.06, 129.21, 126.49, 121.10, 113.26, 110.22, 73.40, 56.31, 56.22, 20.94. HRMS (EI) calcd for $C_{17}H_{17}NO_4$ (M+): 300.1237. Found: 300.1265. Anal. calcd for $C_{17}H_{17}NO_4$: C, 68.22; H, 5.72; N, 4.68. Found: C, 68.25; H, 5.71; N, 4.68. IR (KBr disc): *v*= 3046, 2938, 1657, 1516, 1256 cm^{-1}. HPLC analysis: 98.93%.



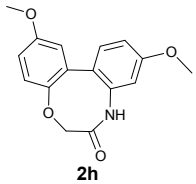
2f

Following the general procedure B. White solid (86%). Mp. 198 – 200 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.72 (s, 1H), 7.43 – 7.32 (m, 3H), 7.26 (d, *J* = 8.8 Hz, 1H), 7.20 (d, *J* = 7.7 Hz, 1H), 7.00 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.92 (d, *J* = 3.0 Hz, 1H), 4.83 (d, *J* = 15.9 Hz, 1H), 4.47 (d, *J* = 15.8 Hz, 1H), 3.79 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 169.83, 156.28, 148.85, 136.05, 133.92, 133.44,

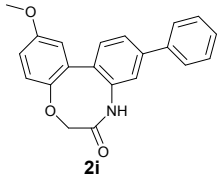
129.68, 128.34, 126.39, 125.34, 121.77, 115.47, 113.45, 73.34, 55.49. HRMS (EI) calcd for $C_{15}H_{13}NO_3$ (M+): 256.0974. Found: 256.0933. Anal.calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.56; H, 5.13; N, 5.52. IR (KBr disc): *v*= 3028, 2942, 1660, 1517, 1267 cm^{-1}. HPLC analysis: 98.80%.


2g

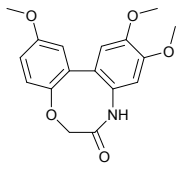
Following the general procedure B. White solid (88%). Mp. 206 – 209 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.66 (s, 1H), 7.26 – 7.18 (m, 2H), 7.17 – 7.13 (m, 1H), 7.02 – 6.95 (m, 2H), 6.88 (d, *J* = 3.0 Hz, 1H), 4.81 (d, *J* = 15.8 Hz, 1H), 4.45 (d, *J* = 15.8 Hz, 1H), 3.78 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 170.31, 156.70, 149.36, 138.32, 136.28, 133.90, 131.50, 129.99, 127.44, 126.28, 122.21, 115.69, 113.94, 73.80, 55.96, 21.01. HMS (EI) calcd for $C_{16}H_{15}NO_4$ (M+): 270.1131. Found: 270.1085. Anal.calcd for $C_{16}H_{15}NO_4$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.34; H, 5.61; N, 5.20. IR (KBr disc): *v*= 3052, 2954, 1661, 1519, 1204 cm^{-1}. HPLC analysis: 99.25%.


2h

Following the general procedure B. White solid (92%). Mp. 205 – 206 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.69 (s, 1H), 7.23 (dd, *J* = 8.6, 4.0 Hz, 2H), 6.94 (td, *J* = 10.1, 9.5, 2.8 Hz, 2H), 6.87 (d, *J* = 3.0 Hz, 1H), 6.76 (d, *J* = 2.4 Hz, 1H), 4.83 (d, *J* = 15.8 Hz, 1H), 4.46 (d, *J* = 15.8 Hz, 1H), 3.78 (d, *J* = 7.5 Hz, 6H). ^{13}C NMR (100 MHz, DMSO) δ = 170.39, 159.60, 156.68, 149.42, 137.50, 133.68, 130.97, 126.69, 122.18, 115.50, 114.04, 112.06, 111.69, 73.83, 55.95, 55.85. HRMS (EI) calcd for $C_{16}H_{15}NO_4$ (M+): 286.1080. Found: 286.1109. Anal.calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.39; H, 5.31; N, 4.90. IR (KBr disc): *v*= 3066, 2958, 1657, 1516, 1203 cm^{-1}. HPLC analysis: 99.48%.

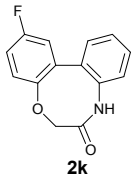

2i

Following the general procedure B. Yellow solid (77%). Mp. 222 – 223 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.82 (s, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.62 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.45 (s, 0H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.34 (t, *J* = 8.4 Hz, 1H), 6.97 (d, *J* = 2.4 Hz, 0H), 6.90 (dd, *J* = 8.5, 2.5 Hz, 0H), 4.93 (d, *J* = 15.7 Hz, 1H), 4.57 (d, *J* = 15.7 Hz, 1H), 3.82 (s, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 169.71, 160.77, 156.25, 139.80, 139.12, 136.73, 132.75, 130.42, 129.77, 129.05, 127.74, 126.56, 124.49, 124.14, 123.36, 111.52, 106.30, 72.74, 55.49. HRMS (EI) calcd for $C_{21}H_{17}NO_3$ (M+): 332.1287. Found: 332.1324. Anal.calcd for $C_{21}H_{17}NO_3$: C, 76.12; H, 5.17; N, 4.23. Found: C, 76.09; H, 5.18; N, 4.24. IR (KBr disc): *v*= 3027, 2920, 1657, 1519, 1269 cm^{-1}. HPLC analysis: 99.24%.


2j

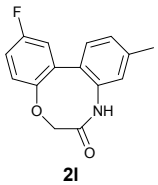
Following the general procedure B. Light yellow solid (92%). Mp. 212 – 214 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.46 (s, 1H), 7.22 (d, *J* = 8.7 Hz, 1H), 6.99 – 6.91 (m, 2H), 6.87 (s, 1H), 6.81 (s, 1H), 4.80 (d, *J* = 15.7 Hz, 1H), 4.44 (d, *J* = 15.7 Hz, 1H), 3.79 (d, *J* = 4.3 Hz, 9H). ^{13}C NMR (100 MHz, DMSO) δ = 169.69, 156.14, 148.89, 148.16, 147.02, 133.45, 128.70, 125.86, 121.74, 114.87, 113.83, 112.88, 109.82, 73.19, 55.86, 55.75, 55.50. HRMS (EI) calcd for $C_{17}H_{17}NO_5$ (M+): 316.1186. Found:

316.1126. Anal.calcd for $C_{17}H_{17}NO_5$: C, 64.75; H, 5.43; N, 4.44. Found: C, 64.78; H, 5.42; N, 4.43. IR (KBr disc): *v*= 3066, 2958, 1662, 1519, 1207 cm^{-1}. HPLC analysis: 99.48%.



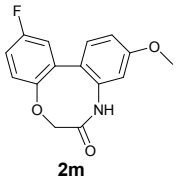
2k

Following the general procedure B. Light yellow solid (79%). Mp. 211 – 213 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.78 (s, 1H), 7.47 – 7.32 (m, 4H), 7.32 – 7.26 (m, 2H), 7.22 (dd, *J* = 7.9, 1.2 Hz, 1H), 4.89 (d, *J* = 15.9 Hz, 1H), 4.53 (d, *J* = 15.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 166.99, 159.37 (d, *J* = 240 Hz), 151.97 (d, *J* = 3 Hz), 136.5, 134.86 (d, *J* = 9 Hz), 133.41 (d, *J* = 1 Hz), 130.2, 129.2, 127.06, 126.0, 123.27 (d, *J* = 9 Hz), 117.07 (d, *J* = 24 Hz), 115.84 (d, *J* = 24 Hz), 73.73. HRMS (EI) calcd for $C_{14}H_{10}FNO_2$ (M+): 244.0775. Found: 244.0792. Anal.calcd for $C_{14}H_{10}FNO_2$: C, 69.13; H, 4.14; F, 7.81; N, 5.76. Found: C, 69.10; H, 4.13; F, 7.79; N, 5.75. IR (KBr disc): *v*= 3059, 2954, 1659, 1574, 1262 cm^{-1}. HPLC analysis: 99.69%.



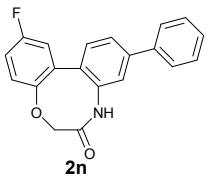
2l

Following the general procedure B. White solid (81%). Mp. 229 – 231 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.71 (s, 1H), 7.38 (dd, *J* = 8.7, 4.9 Hz, 1H), 7.30 – 7.15 (m, 4H), 7.03 (s, 1H), 4.87 (d, *J* = 15.8 Hz, 1H), 4.51 (d, *J* = 15.8 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 169.99, 159.34 (d, *J* = 240 Hz), 151.99 (d, *J* = 2 Hz), 138.8, 136.3, 134.85 (d, *J* = 9 Hz), 130.54 (d, *J* = 1 Hz), 130.05, 127.60, 126.5, 123.22 (d, *J* = 9 Hz), 116.82 (d, *J* = 23 Hz), 115.82 (d, *J* = 23 Hz), 73.7, 21.0. HRMS (EI) calcd for $C_{15}H_{12}FNO_2$ (M+): 258.0931. Found: 258.0896. Anal.calcd for $C_{15}H_{12}FNO_2$: C, 70.03; H, 4.70; F, 7.38; N, 5.44. Found: C, 70.05; H, 4.69; F, 7.39; N, 5.45. IR (KBr disc): *v*= 3076, 2954, 1662, 1518, 1261 cm^{-1}. HPLC analysis: 99.86%.



2m

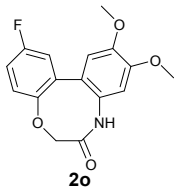
Following the general procedure B. Light yellow solid (84%). Mp. 221 – 225 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.71 (s, 1H), 7.38 (dd, *J* = 8.8, 5.0 Hz, 1H), 7.30 – 7.19 (m, 3H), 7.17 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.03 (d, *J* = 1.6 Hz, 1H), 4.87 (d, *J* = 15.8 Hz, 1H), 4.51 (d, *J* = 15.8 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 169.99, 159.34 (d, *J* = 243 Hz), 151.99 (d, *J* = 2 Hz), 138.83, 136.25, 134.96 (d, *J* = 9 Hz), 130.53, 130.05, 127.60, 126.45, 123.22 (d, *J* = 9 Hz), 116.82 (d, *J* = 23 Hz), 115.80 (d, *J* = 23 Hz), 73.71, 21.02. HRMS (EI) calcd for $C_{15}H_{12}FNO_3$ (M+): 273.0801 Found: 273.0842 Anal.calcd for $C_{15}H_{12}FNO_3$: C, 65.93; H, 4.43; F, 6.95; N, 5.13. Found: C, 65.95; H, 4.42; F, 6.96; N, 5.14. IR (KBr disc): *v*= 3074, 2953, 1662, 1568, 1261 cm^{-1}. HPLC analysis: 99.28%.



2n

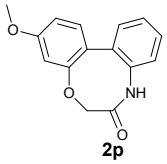
Following the general procedure B. White solid (62%). Mp. 267 – 268 °C. ^{1}H NMR (400 MHz, DMSO) δ= 9.84 (s, 1H), 7.74 – 7.69 (m, 2H), 7.65 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.49 – 7.38 (m, 5H), 7.38 – 7.30 (m, 2H), 4.95 (d, *J* = 15.8 Hz, 1H), 4.56 (d, *J* = 15.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 170.11, 159.41 (d, *J* = 240 Hz), 152.06 (d, *J* = 3 Hz), 141.1, 139.4, 137.1, 134.50 (d, *J* = 9 Hz), 132.30, 130.85, 129.58, 128.41, 127.13, 125.09, 124.17, 123.34 (d, *J* = 10

Hz), 117.19 (d, *J* = 23 Hz), 115.86 (d, *J* = 24 Hz), 73.8. HRMS (EI) calcd for $C_{20}H_{14}FNO_2$ (M+): 320.1088. Found: 320.1148. Anal.calcd for $C_{20}H_{14}FNO_2$: C, 75.22; H, 4.42; F, 5.95; N, 4.39. Found: C, 75.26; H, 4.44; F, 5.91; N, 4.37. IR (KBr disc): *v*= 3065, 2925, 1660, 1555, 1261 cm^{-1}. HPLC analysis: 99.27%.



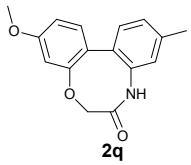
2o

Following the general procedure B. Yellow solid (86%). Mp. 243 – 247 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.54 (s, 1H), 7.36 (dd, *J* = 8.8, 5.0 Hz, 1H), 7.27 (td, *J* = 8.8, 3.1 Hz, 2H), 6.89 (s, 1H), 6.83 (s, 1H), 4.86 (d, *J* = 15.7 Hz, 1H), 4.50 (d, *J* = 15.8 Hz, 1H), 3.80 (d, *J* = 2.9 Hz, 6H). ^{13}C NMR (100 MHz, DMSO) δ = 169.87, 159.26 (d, *J* = 240 Hz), 152.00, 148.89, 147.56, 134.86 (d, *J* = 9 Hz), 129.18, 125.31, 123.23 (d, *J* = 9 Hz), 116.55 (d, *J* = 23 Hz), 116.06 (d, *J* = 23 Hz), 113.32, 110.33, 73.55, 56.32, 56.24. HRMS (EI) calcd for $C_{16}H_{14}FNO_4$ (M+): 304.0986. Found: 304.0962. Anal.calcd for $C_{16}H_{14}FNO_4$: C, 63.36; H, 4.65; F, 6.26; N, 4.62. Found: C, 63.38; H, 4.64; F, 6.27; N, 4.63. IR (KBr disc): *v*= 3057, 2943, 1656, 1519, 1260 cm^{-1}. HPLC analysis: 99.97.



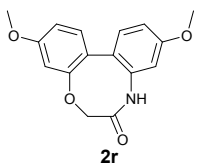
2p

Following the general procedure B. Light white solid (86%). Mp. 201 – 203 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.75 (s, 1H), 7.40 – 7.31 (m, 2H), 7.30 – 7.24 (m, 2H), 7.17 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.94 (d, *J* = 2.5 Hz, 1H), 6.87 (dd, *J* = 8.5, 2.5 Hz, 1H), 4.88 (d, *J* = 15.6 Hz, 1H), 4.53 (d, *J* = 15.6 Hz, 1H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 170.06, 161.15, 156.63, 136.65, 134.30, 130.31, 130.24, 128.36, 126.88, 125.67, 125.00, 111.91, 106.72, 73.18, 55.97. HRMS (EI) calcd for $C_{15}H_{13}NO_3$ (M+): 256.0974. Found: 256.0943. Anal.calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.61; H, 5.12; N, 5.50. IR (KBr disc): *v*= 3054, 2959, 1663, 1514, 1259 cm^{-1}. HPLC analysis: 99.78%.



2q

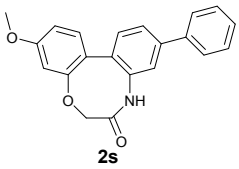
Following the general procedure B. White solid (89%). Mp. 253 – 254 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.69 (s, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 1.0 Hz, 2H), 6.98 (s, 1H), 6.91 (d, *J* = 2.5 Hz, 1H), 6.85 (dd, *J* = 8.5, 2.5 Hz, 1H), 4.86 (d, *J* = 15.5 Hz, 1H), 4.50 (d, *J* = 15.5 Hz, 1H), 3.79 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 170.04, 160.97, 156.62, 137.80, 136.41, 131.42, 130.28, 130.17, 127.48, 126.11, 124.88, 111.80, 106.68, 73.12, 55.94, 20.98. HRMS (EI) calcd for $C_{16}H_{15}NO_3$ (M+): 270.1131. Found: 270.1141. Anal.calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.38; H, 5.60; N, 5.21. IR (KBr disc): *v*= 3061, 2961, 1655, 1564, 1257 cm^{-1}. HPLC analysis: 99.83%.



2r

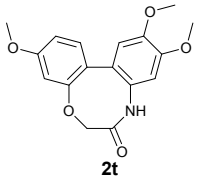
Following the general procedure B. White solid (90%). Mp. 182 – 184 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.72 (s, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.16 (d, *J* = 8.5 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.6 Hz, 2H), 6.84 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.75 (d, *J* = 2.6 Hz, 1H), 4.88 (d, *J* = 15.5 Hz, 1H), 4.51 (d, *J* = 15.5 Hz, 1H), 3.79 (d, *J* = 2.2 Hz, 6H). ^{13}C NMR (100 MHz, DMSO) δ = 170.11, 160.83, 159.28, 156.64, 137.57, 131.11, 130.40, 126.62, 124.65, 112.15, 111.77, 111.48, 106.65, 73.16, 55.93, 55.81. HRMS (EI) calcd for

$C_{16}H_{15}NO_4$ (M+): 286.1080. Found: 286.1036. Anal.calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.39; H, 5.29;N, 4.90. IR (KBr disc): *v*= 3003, 2958, 1663, 1567, 1287 cm^{-1}. HPLC analysis: 99.91%.



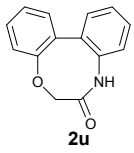
2s

Following the general procedure B. White solid (79%). Mp. 225 – 226 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.82 (s, 1H), 7.73 – 7.67 (m, 2H), 7.62 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.45 (d, *J* = 1.9 Hz, 1H), 7.41 (d, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 2.5 Hz, 1H), 6.90 (dd, *J* = 8.5, 2.5 Hz, 1H), 4.93 (d, *J* = 15.7 Hz, 1H), 4.57 (d, *J* = 15.7 Hz, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 170.20, 161.25, 156.73, 140.28, 139.60, 137.21, 133.23, 130.90, 130.25, 129.55, 128.24, 127.05, 124.98, 124.63, 123.85, 112.02, 106.79, 73.23, 55.99. HRMS (EI) calcd for $C_{21}H_{17}NO_3$ (M+): 332.1287. Found: 332.1316. Anal.calcd for $C_{21}H_{17}NO_3$: C, 76.12; H, 5.17; N, 4.23. Found: C, 76.15; H, 5.16; N, 4.23. IR (KBr disc): *v*= 3058, 2918, 1657, 1549, 1269 cm^{-1}. HPLC analysis: 99.25%.



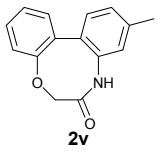
2t

Following the general procedure B. Yellow solid (94%). Mp. 184 – 186 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.52 (s, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 6.90 (d, *J* = 2.6 Hz, 1H), 6.84 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.79 (s, 2H), 4.85 (d, *J* = 15.4 Hz, 1H), 4.50 (s, 1H), 3.82 – 3.75 (m, 9H). ^{13}C NMR (100 MHz, DMSO) δ = 169.90, 160.78, 156.59, 148.34, 147.52, 130.56, 129.26, 126.31, 124.87, 113.48, 111.63, 110.10, 106.66, 72.96, 56.27, 56.22, 55.94. HRMS (EI) calcd for $C_{17}H_{17}NO_5$ (M+): 316.1186. Found: 316.1150. Anal.calcd for $C_{17}H_{17}NO_5$: C, 64.75; H, 5.43; N, 4.44. Found: C, 64.73; H, 5.43; N, 4.43. IR (KBr disc): *v*= 3063, 2961, 1663, 1523, 1253 cm^{-1}. HPLC analysis: 99.78%.



2u

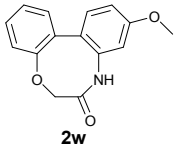
Following the general procedure B. White solid (84%). Mp. 189 – 192 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.75 (s, 1H), 7.49 – 7.28 (m, 7H), 7.24 – 7.16 (m, 1H), 4.90 (d, *J* = 15.7 Hz, 1H), 4.52 (d, *J* = 15.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 170.08, 155.73, 136.57, 134.43, 133.06, 130.60, 130.22, 129.57, 128.79, 126.99, 125.80, 125.76, 121.42, 73.50. HRMS (EI) calcd for $C_{14}H_{11}NO_2$ (M+): 226.0869. Found: 226.0846. Anal.calcd for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.62; H, 4.93; N, 6.23. IR (KBr disc): *v*= 3057, 2957, 1663, 1503, 1203 cm^{-1}. HPLC analysis: 99.32%.



2v

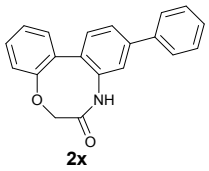
Following the general procedure B. White solid (85%). Mp. 219 – 223 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.70 (s, 1H), 7.43 (ddd, *J* = 8.2, 7.1, 1.9 Hz, 1H), 7.35 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.29 (ddd, *J* = 14.5, 7.6, 1.2 Hz, 2H), 7.17 (d, *J* = 2.1 Hz, 2H), 7.01 (s, 1H), 4.88 (d, *J* = 15.7 Hz, 1H), 4.50 (d, *J* = 15.6 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 170.08, 155.75, 138.29, 136.34, 132.99, 131.55, 130.35, 130.08, 129.60, 127.58, 126.25, 125.66, 121.38, 73.46, 21.01. HRMS (EI) calcd for $C_{15}H_{13}NO_2$ (M+): 240.1025. Found: 240.0992. Anal.calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.33; H, 5.49; N, 5.83.

IR (KBr disc): *v*= 3027, 2954, 1660, 1515, 1202 cm^{-1}. HPLC analysis: 99.48%.



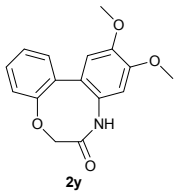
2w

Following the general procedure B. Light yellow solid (88%). Mp. 187 – 189 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.72 (s, 1H), 7.44 – 7.39 (m, 1H), 7.35 – 7.26 (m, 3H), 7.21 (d, *J* = 8.4 Hz, 1H), 6.94 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.77 (d, *J* = 2.4 Hz, 1H), 4.90 (d, *J* = 15.6 Hz, 1H), 4.50 (d, *J* = 15.7 Hz, 1H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 170.16, 159.59, 155.80, 137.55, 132.76, 131.06, 130.15, 129.72, 126.72, 125.63, 121.36, 112.19, 111.67, 73.48, 55.84. HRMS (EI) calcd for $C_{15}H_{13}NO_3$ (M+): 226.0974. Found: 256.0938. Anal.calcd for $C_{15}H_{13}NO_3$: C, 70.51; H, 5.20; N, 5.57. Found: C, 70.49; H, 5.21; N, 5.52. IR (KBr disc): *v*= 3065, 2921, 1663, 1516, 1206 cm^{-1}. HPLC analysis: 99.97%.



2x

Following the general procedure B. White solid (74%). Mp. 256 – 258 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.86 (s, 1H), 7.76 – 7.63 (m, 3H), 7.56 – 7.39 (m, 6H), 7.32 (dq, *J* = 8.8, 5.2, 4.3 Hz, 2H), 4.94 (d, *J* = 16.1 Hz, 1H), 4.57 (d, *J* = 15.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 170.22, 155.82, 140.72, 139.53, 137.15, 133.34, 132.70, 130.84, 130.70, 129.57, 128.32, 127.10, 125.84, 125.09, 123.98, 121.49, 73.55. HRMS (EI) calcd for $C_{20}H_{15}NO_2$ (M+): 302.1182. Found: 302.1138. Anal.calcd for $C_{20}H_{15}NO_2$: C, 79.63; H, 5.13; N, 4.71. Found: C, 79.66; H, 5.12; N, 4.70. IR (KBr disc): *v*= 3066, 2901, 1658, 1525, 1211 cm^{-1}. HPLC analysis: 99.34%.



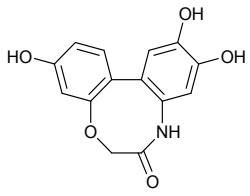
2y

Following the General procedure B. White solid (90%). Mp. 215 – 218 °C. ^{1}H NMR (400 MHz, DMSO) δ = 9.51 (s, 1H), 7.42 – 7.36 (m, 2H), 7.29 (dd, *J* = 7.7, 2.3 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 4.87 (d, *J* = 15.5 Hz, 1H), 4.48 (d, *J* = 15.5 Hz, 1H), 3.79 (s, 6H). ^{13}C NMR (100 MHz, DMSO) δ = 169.95, 155.75, 148.62, 147.59, 132.98, 130.11, 129.87, 129.23, 126.38, 125.48, 121.43, 113.38, 110.23, 73.30, 56.30, 56.23. HRMS (EI) calcd for $C_{16}H_{15}NO_4$ (M+): 286.1180. Found: 286.1235. Anal.calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.39; H, 5.29; N, 4.90. IR (KBr disc): *v*= 3057, 2959, 1659, 1515, 1256 cm^{-1}. HPLC analysis: 99.19%.

5. Synthesis of 8-azaprotosappanin A

Added **2t** (1 mmol), 40% HBr (4 equiv) and HOAc (1.2 equiv) in the flask. The mixture was stirred for 20 h at 110 °C under inert atmosphere and then cooled down to room temperature. The mixture was poured into ice water and adjusted pH ≈ 5-6. Which was extracted with ethyl acetate three times. The organic phase was dried over Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure. 8-azaprotosappanin A was obtained by flash silica gel column chromatography eluting with a petroleum ether/ethyl acetate gradient (95:5,

v/v). Yeild 80%, light yellow solid.



2t'

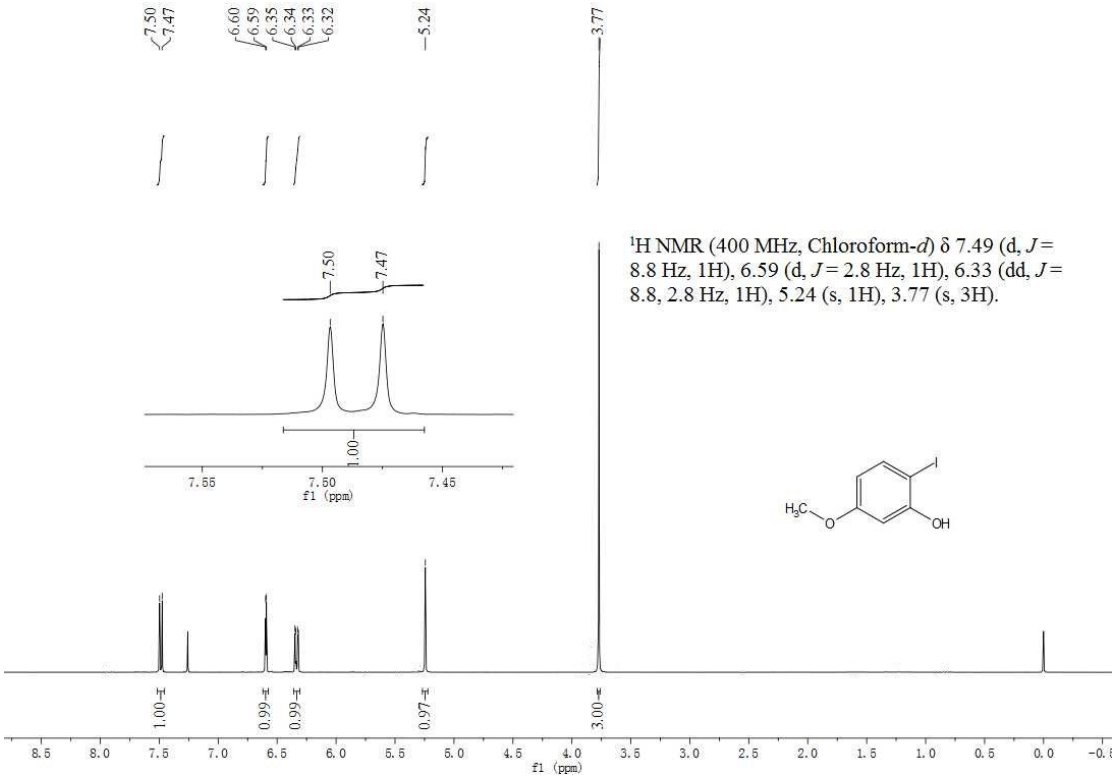
Light yellow solid (80%). Mp. 276 – 278 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 9.68 (s, 1H), 9.52 (s, 1H), 8.93 (s, 1H), 8.91 (s, 1H), 7.19 (d, *J* = 8.5 Hz, 1H), 6.84 (s, 1H), 6.78 (s, 1H), 6.75 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.69 (d, *J* = 2.5 Hz, 1H), 4.85 (d, *J* = 15.4 Hz, 1H), 4.49 (d, *J* = 15.4 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 169.69 , 160.78 , 153.58 , 148.52 , 147.54 , 131.11 , 130.40 , 126.62 , 124.65 , 114.87 , 113.83 , 112.88 , 109.82 , 73.80. HRMS (EI) calcd for $C_{14}H_{11}NO_5$ (M+): 273.0637. Found: 273.0586. Anal.calcd for $C_{14}H_{11}NO_5$: C, 61.54; H, 4.06; N, 5.13. Found: C, 61.58; H, 4.05; N, 5.12. IR (KBr disc): *v*= 3318, 3048, 2895, 1677, 1527, 1239 cm^{-1}. HPLC analysis: 99.54%.

6. Antibacterial studies

Staphylococcus aureus (ATCC 25923), methicillin-resistant Staphylococcus aureus (MRSA, clinical isolate), Staphylococcus epidermidis (ATCC 12228) Enterococcus faecalis (ATCC 29212) and E. coli (ATCC 25922) were used as the antibacterial test strains. The in vitro antibacterial activity of the compounds was tested by using the test bacteria maintained on the nutrient agar (NA) medium at 37 °C. The bacteria were cultured in LB culture medium with 96 holes plate. The compound concentration was diluted by double fold and was kept at 32, 16, 8, 4, 2, 1, 0.5, 0.25, 0.125, 0.062, 0.031, 0 (μg/mL), then the plate was cultured at 37 °C for 24 h. The 96 holes plate was scan in a MULTISKAN EX microplate reader and the growth of bacteria was showed by UV absorption. The lowest concentration of the compound without bacteria growth was assigned to be the MIC value. Most compounds exhibited excellent in vitro antibacterial activity against Gram-positive.

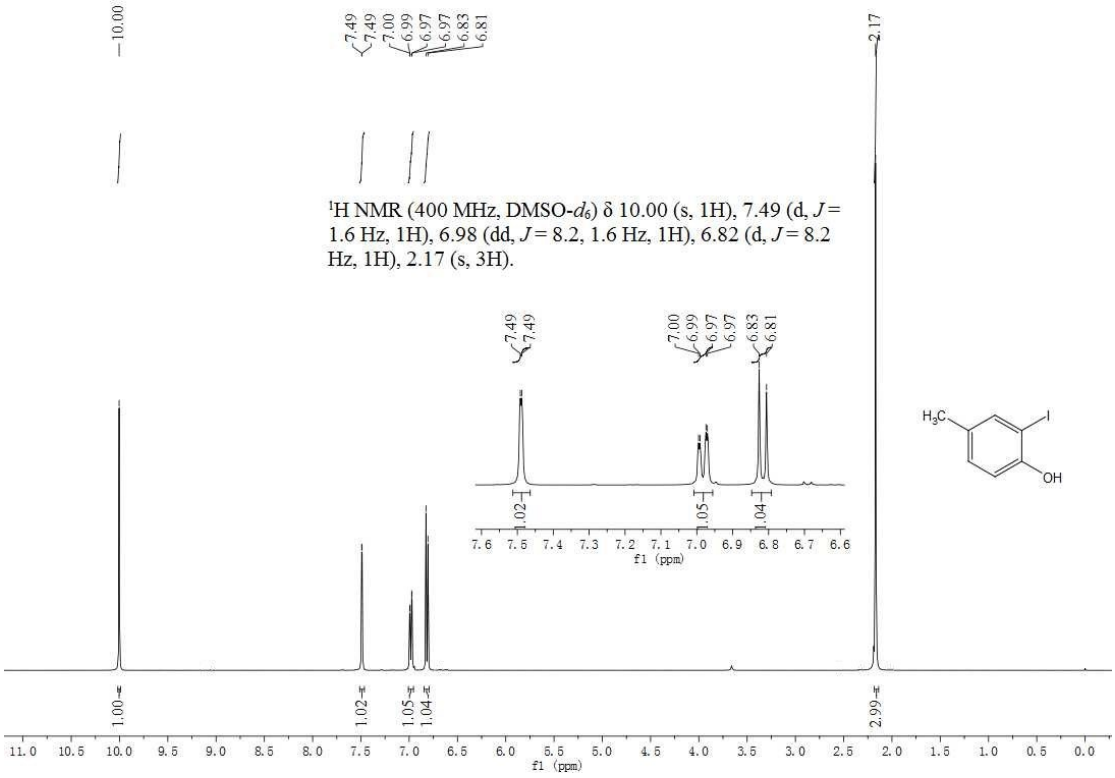
7. Characterization of 2-iodophenols

[1]HNMR spectra of 2-iodo-5-methoxyl-phenol



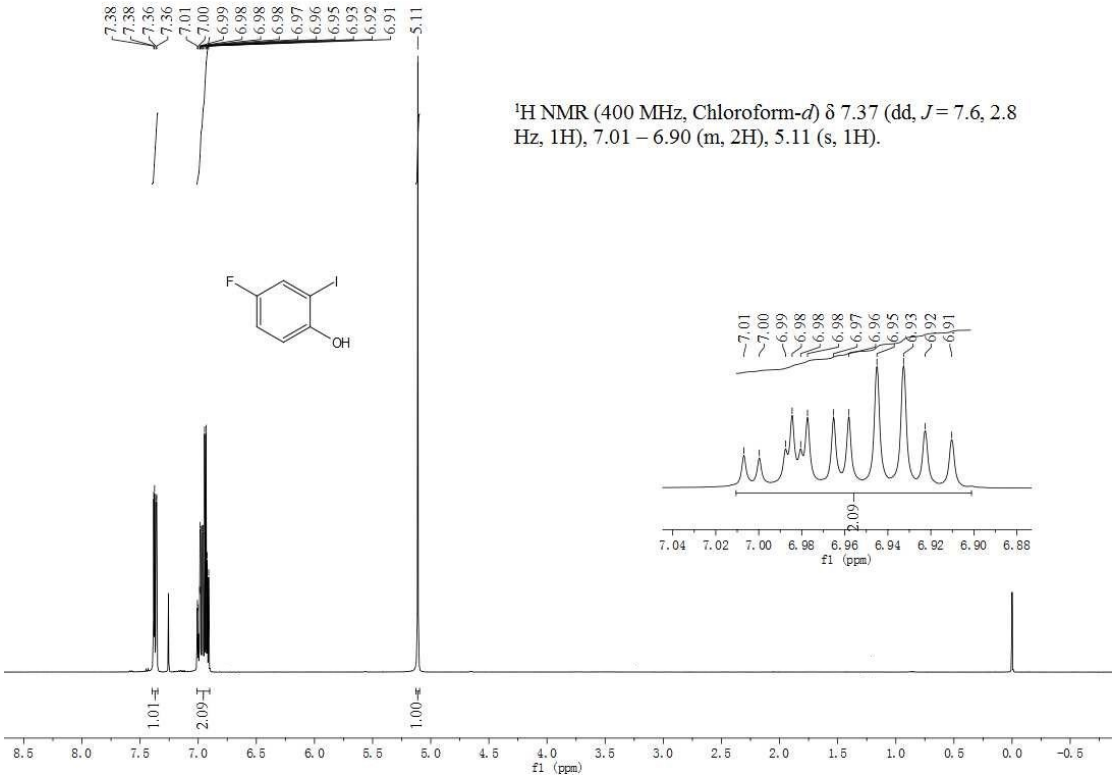
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 8.8 Hz, 1H), 6.59 (d, *J* = 2.8 Hz, 1H), 6.33 (dd, *J* = 8.8, 2.8 Hz, 1H), 5.24 (s, 1H), 3.77 (s, 3H).

[1]H NMR spectra of 2-iodo-4-methyl-phenol



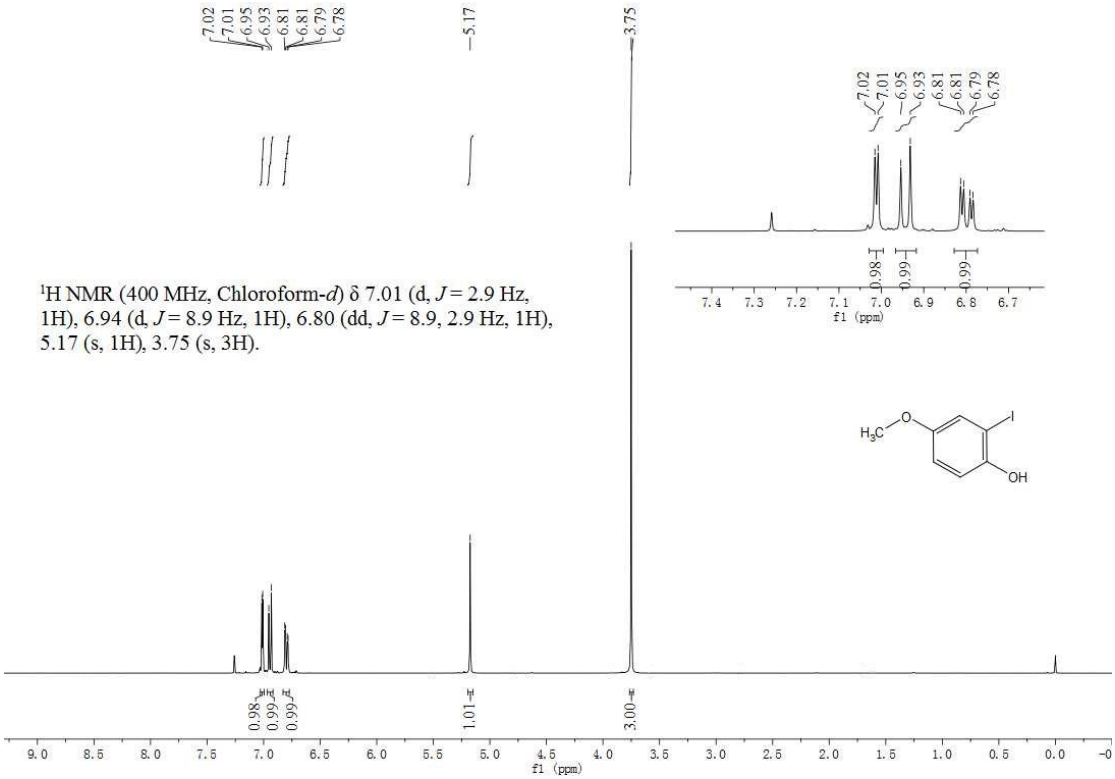
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.00 (s, 1H), 7.49 (d, *J* = 1.6 Hz, 1H), 6.98 (dd, *J* = 8.2, 1.6 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 2.17 (s, 3H).

^{1}H NMR spectra of 2-iodo-4-fluoro-phenol



^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.01 – 6.90 (m, 2H), 5.11 (s, 1H).

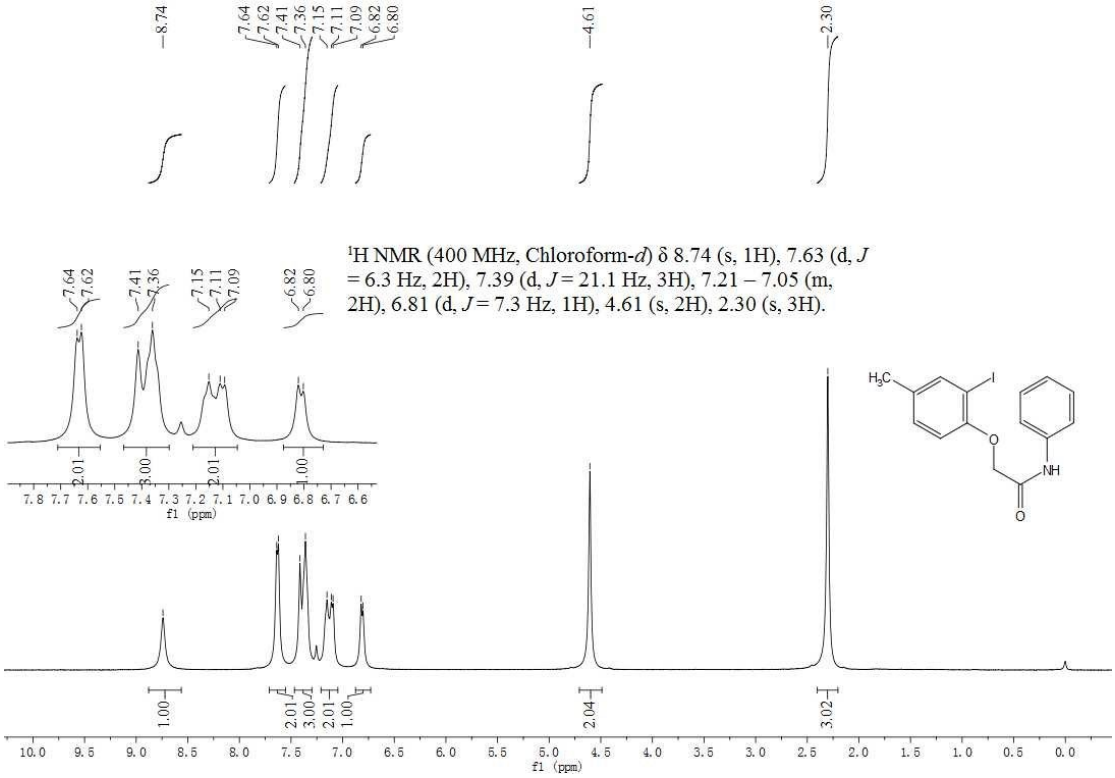
^{1}H NMR spectra of 2-iodo-4-methoxyl-phenol

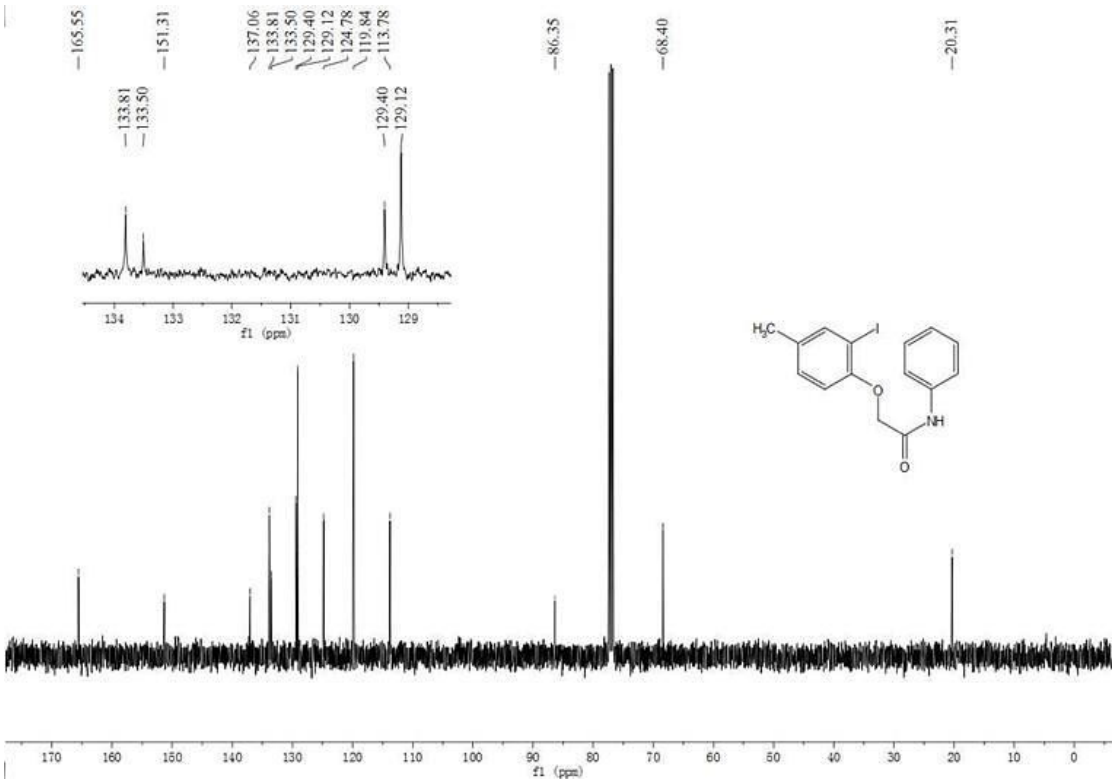


^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.01 (d, *J* = 2.9 Hz, 1H), 6.94 (d, *J* = 8.9 Hz, 1H), 6.80 (dd, *J* = 8.9, 2.9 Hz, 1H), 5.17 (s, 1H), 3.75 (s, 3H).

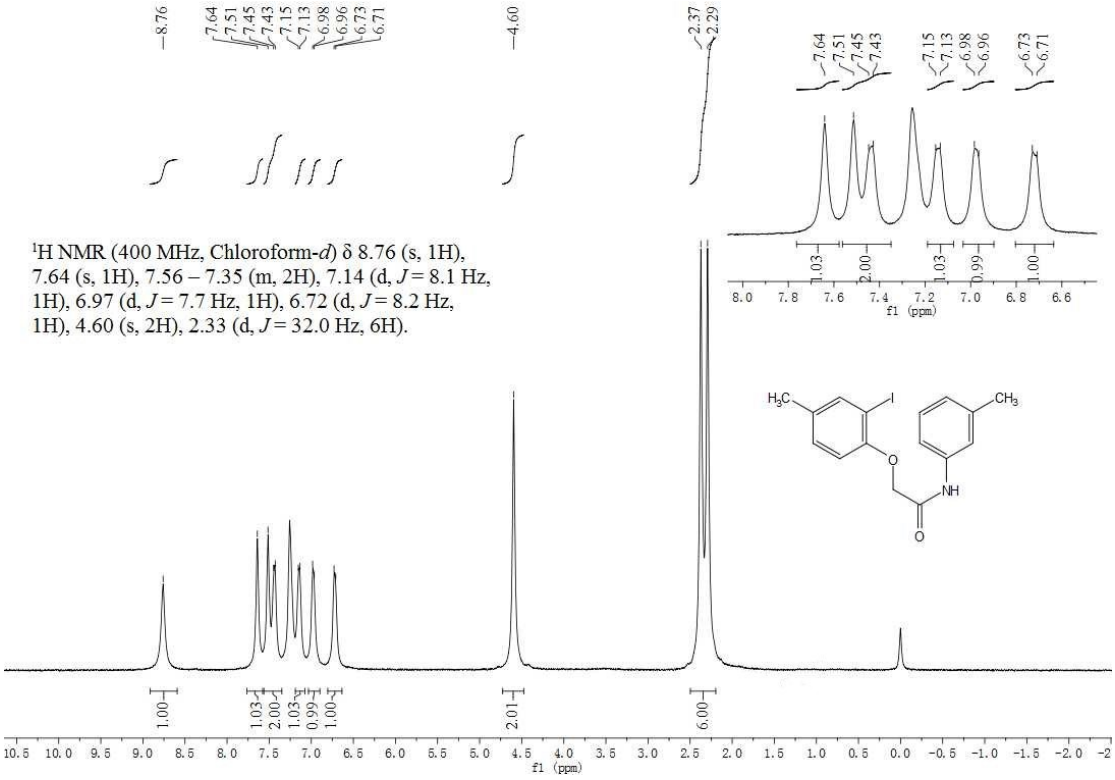
8.^{1}H and ^{13}C NMR spectra for α-(2-Iodophenoxy)-N-phenylacetamide derivatives (1)

NMR spectra of **1a**

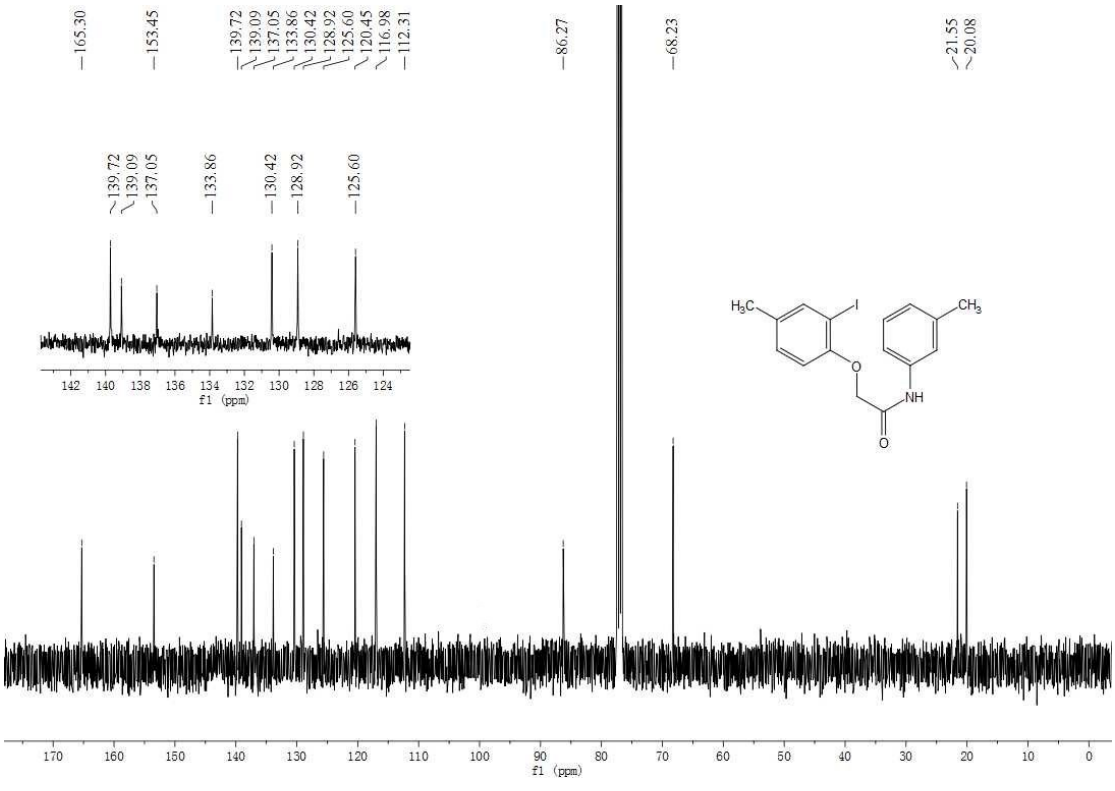




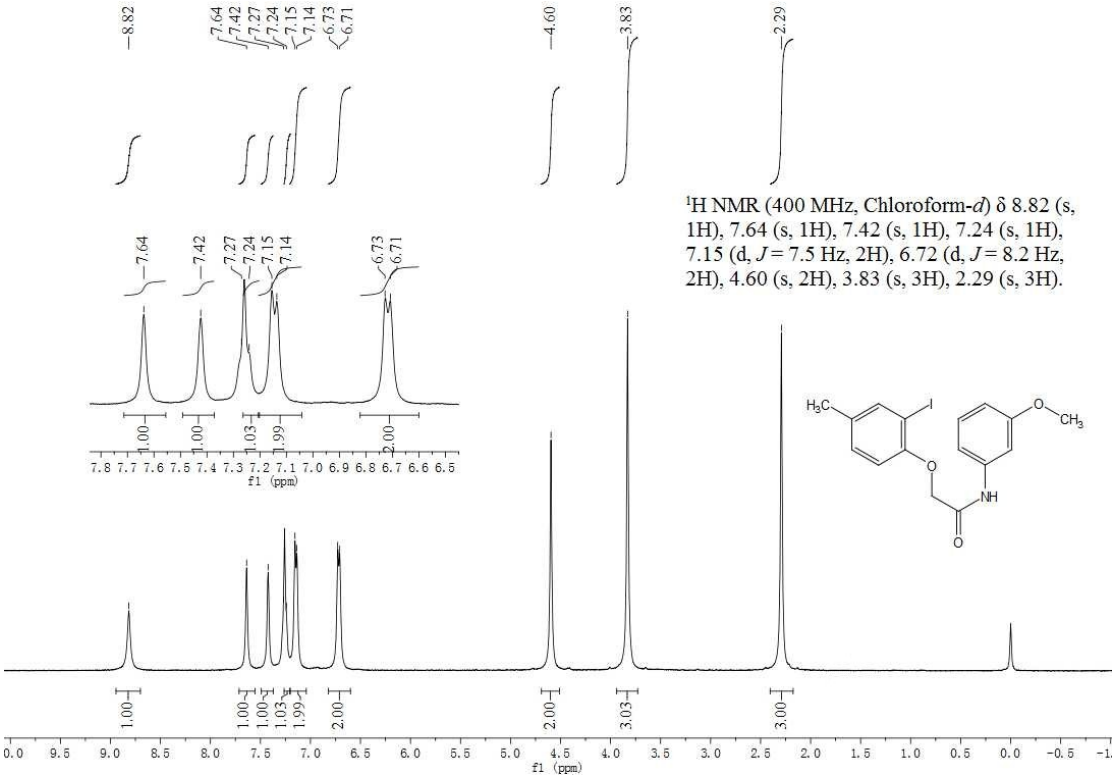
NMR spectra of **1b**



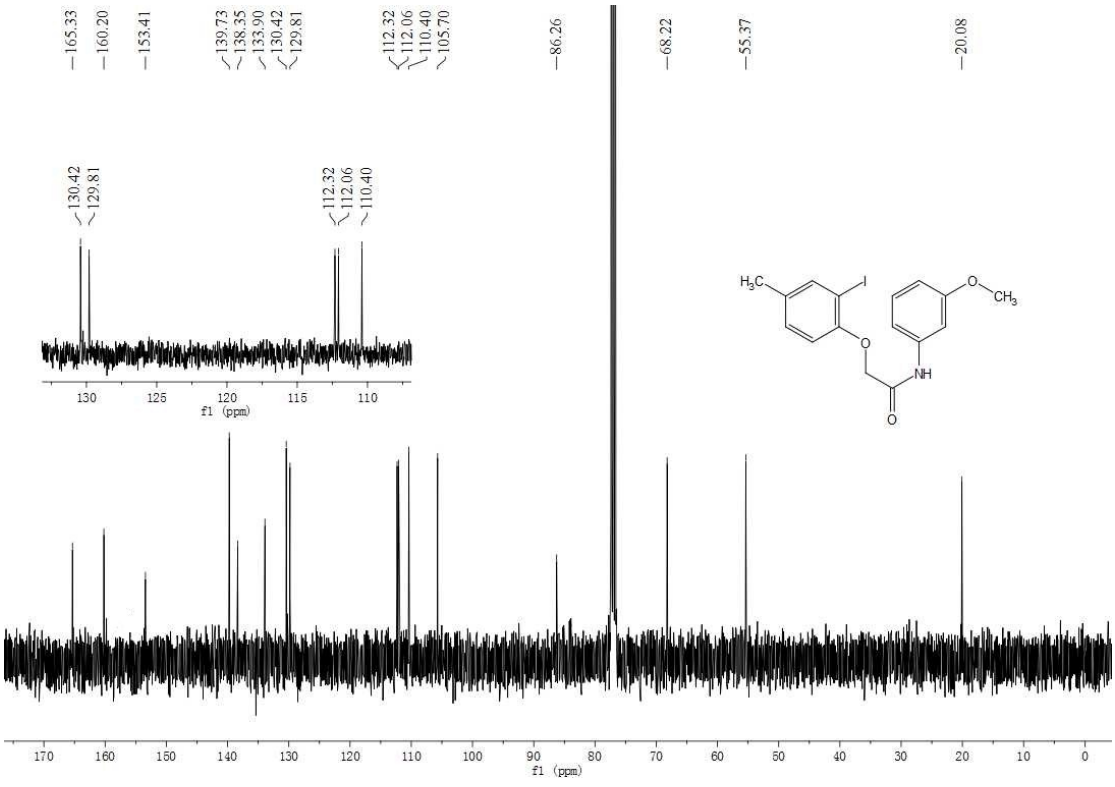
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.76 (s, 1H), 7.64 (s, 1H), 7.56 – 7.35 (m, 2H), 7.14 (d, *J* = 8.1 Hz, 1H), 6.97 (d, *J* = 7.7 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 4.60 (s, 2H), 2.33 (d, *J* = 32.0 Hz, 6H).



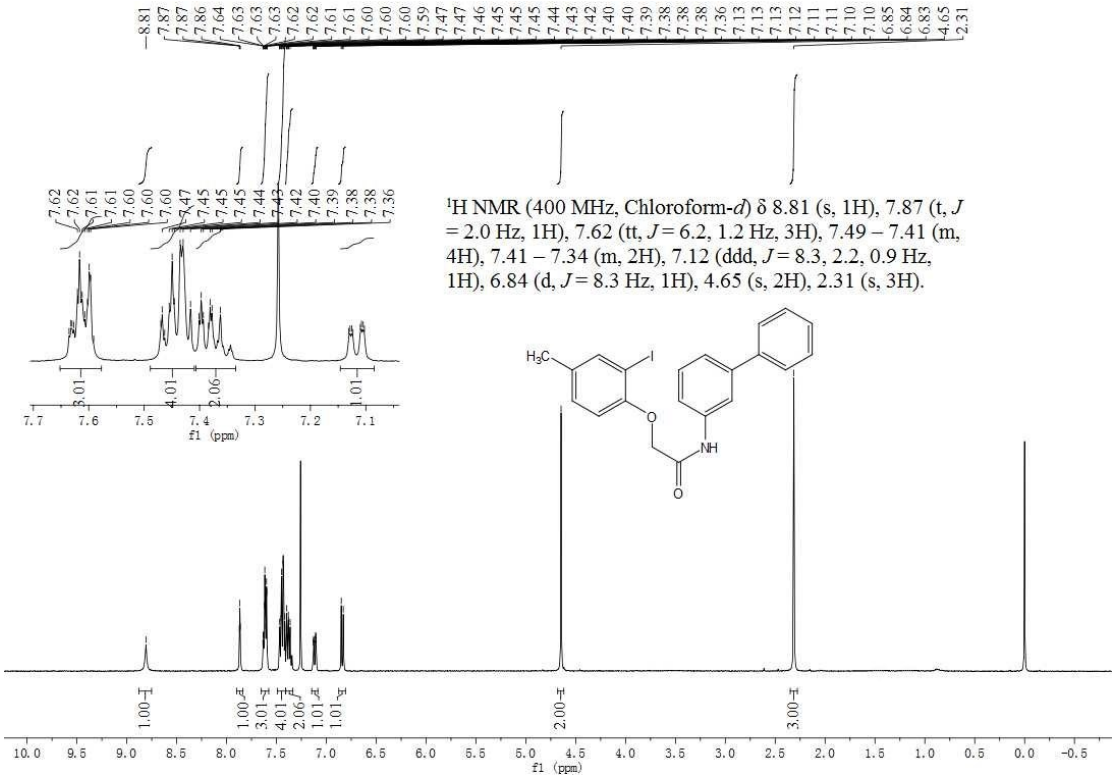
NMR spectra of **1c**

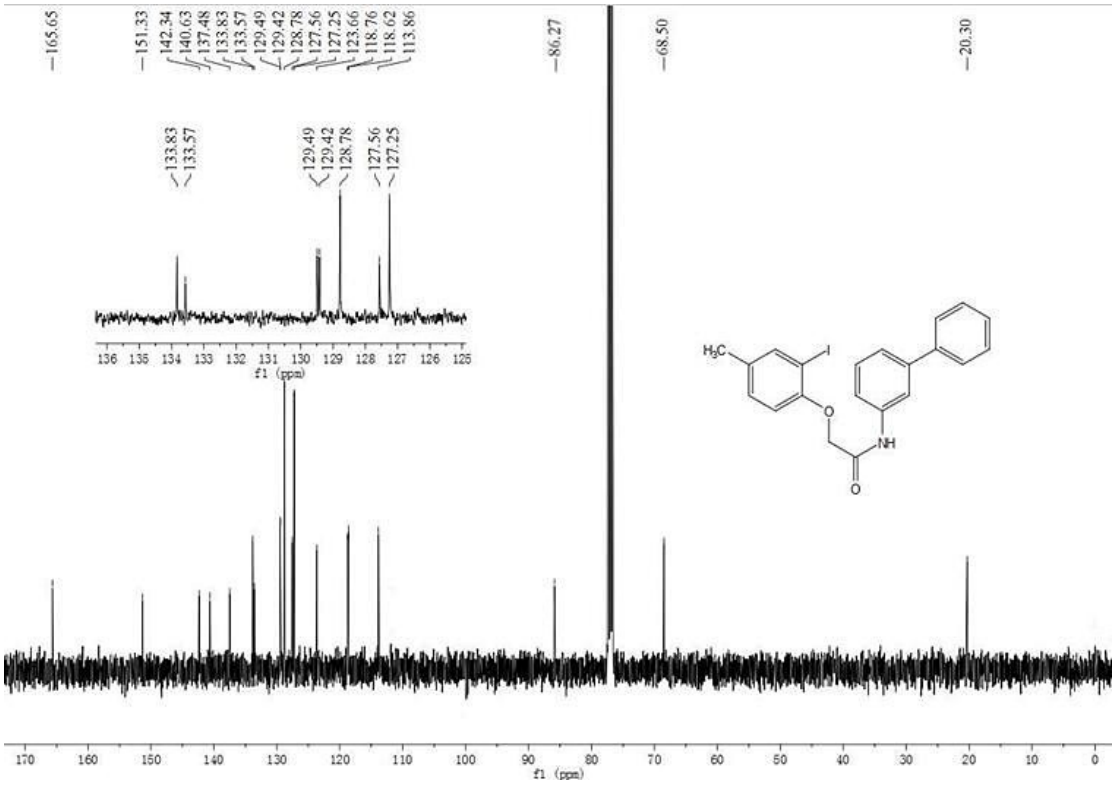


^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.82 (s, 1H), 7.64 (s, 1H), 7.42 (s, 1H), 7.24 (s, 1H), 7.15 (d, *J* = 7.5 Hz, 2H), 6.72 (d, *J* = 8.2 Hz, 2H), 4.60 (s, 2H), 3.83 (s, 3H), 2.29 (s, 3H).

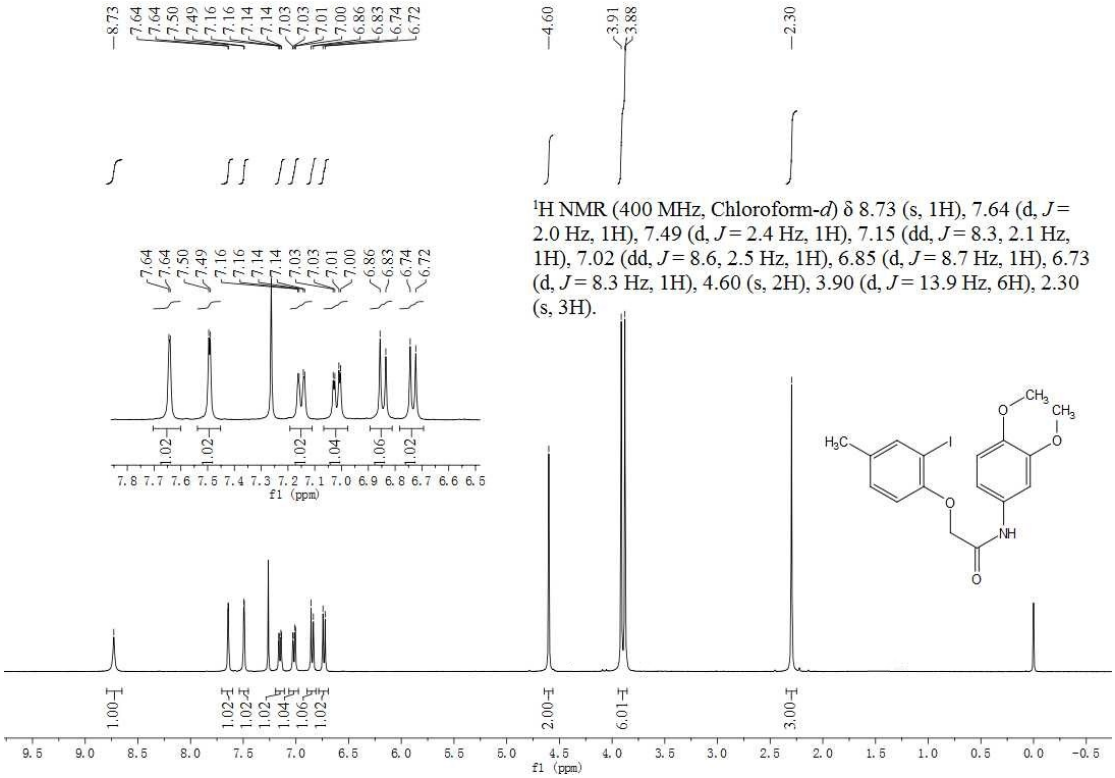


NMR spectra of **1d**

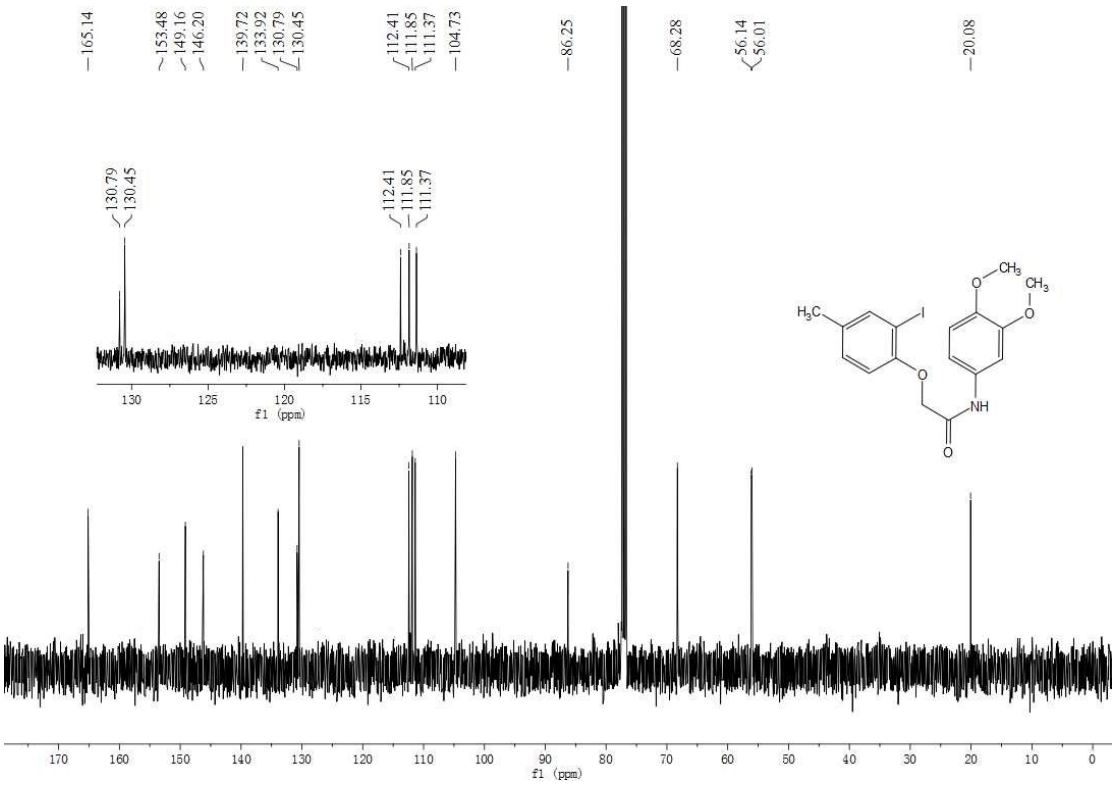




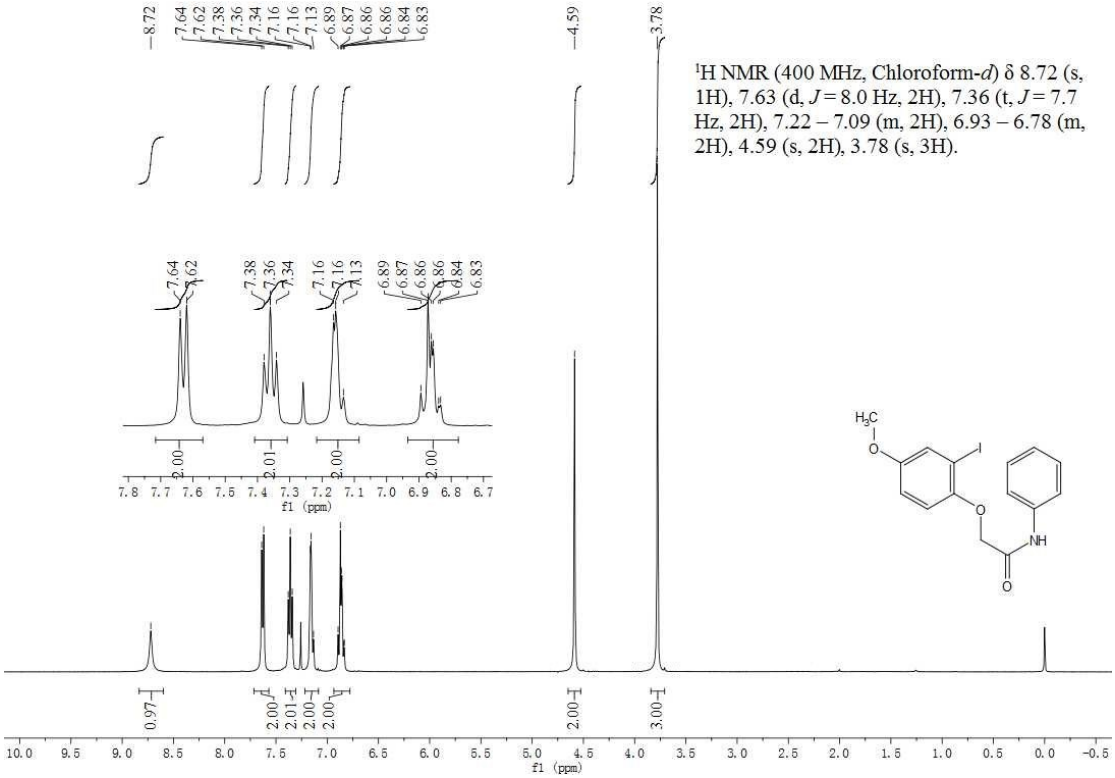
NMR spectra of **1e**



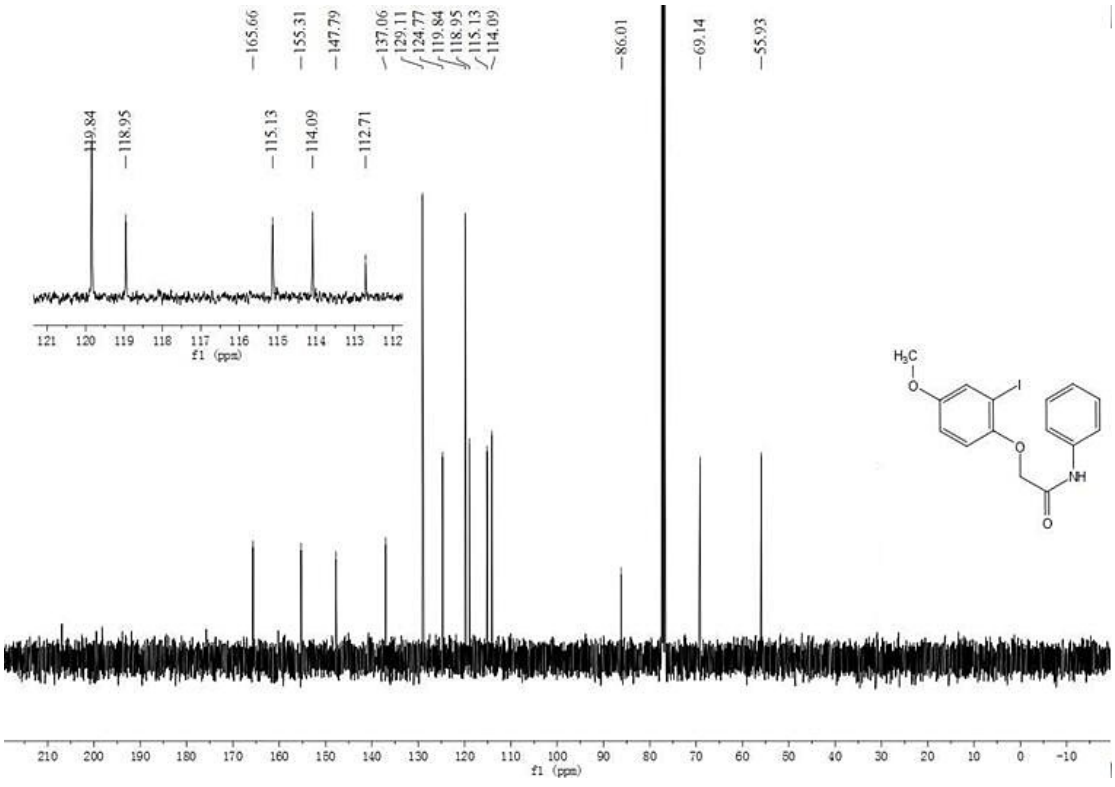
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 7.64 (d, *J* = 2.0 Hz, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.15 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.02 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 4.60 (s, 2H), 3.90 (d, *J* = 13.9 Hz, 6H), 2.30 (s, 3H).



NMR spectra of **1f**

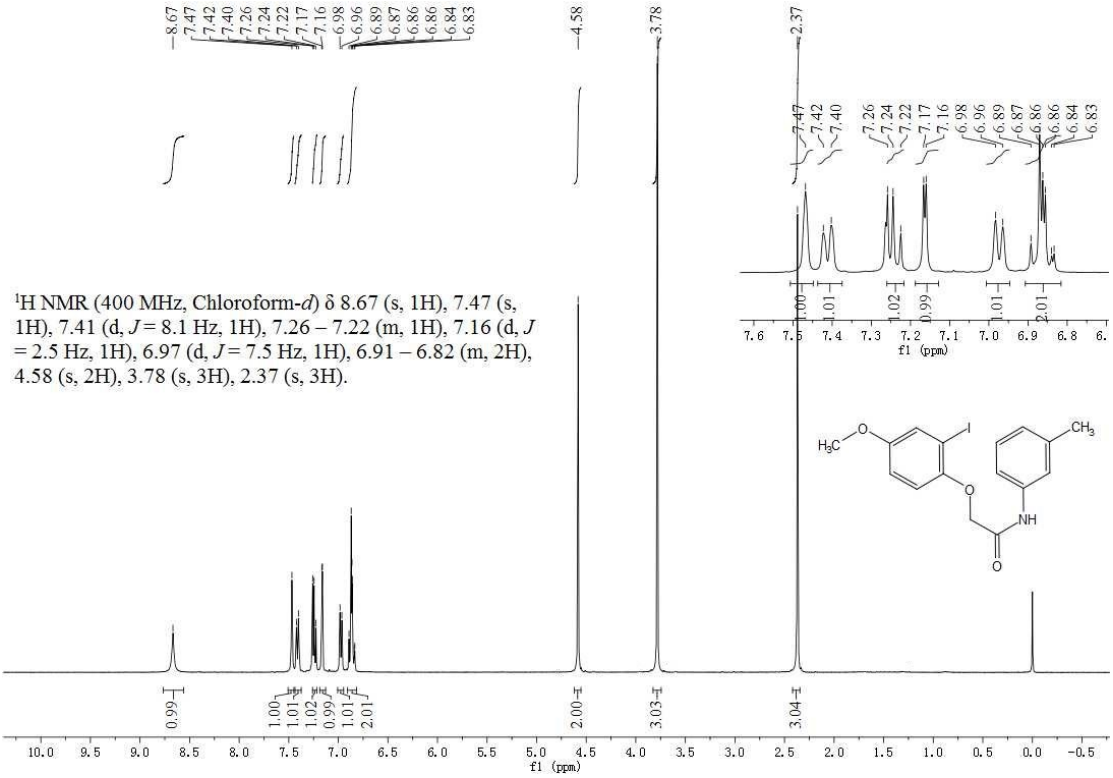


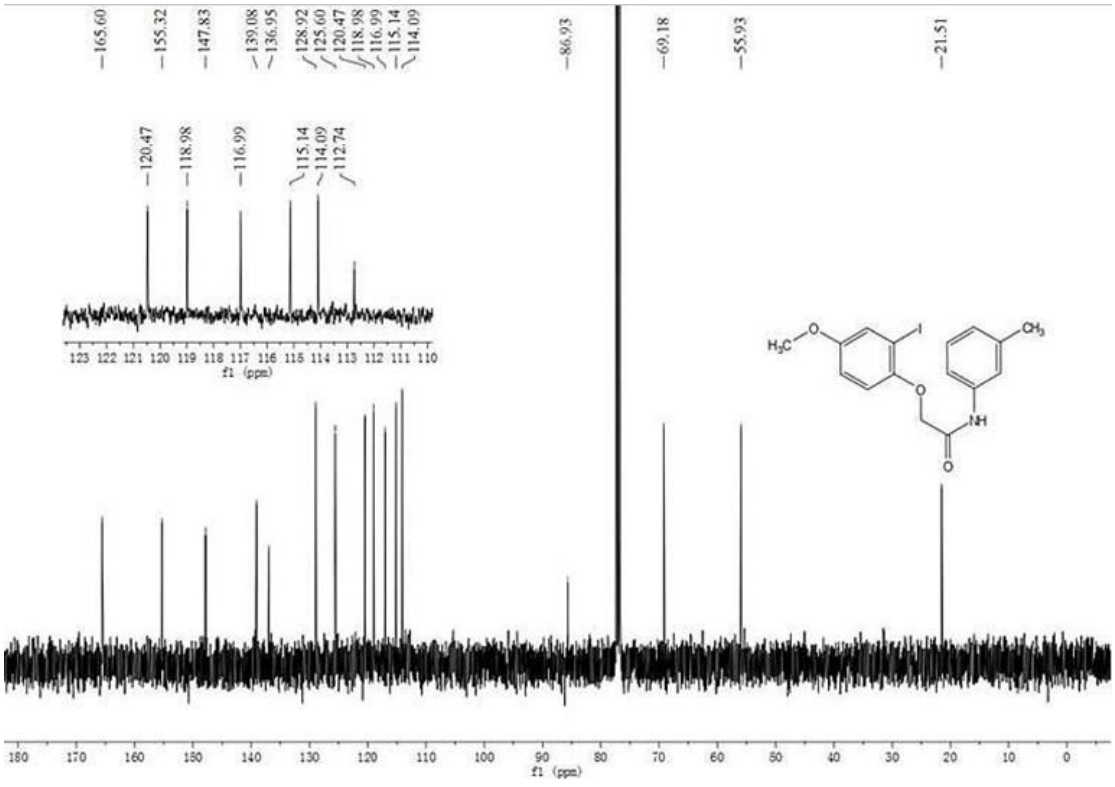
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.72 (s, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.22 – 7.09 (m, 2H), 6.93 – 6.78 (m, 2H), 4.59 (s, 2H), 3.78 (s, 3H).



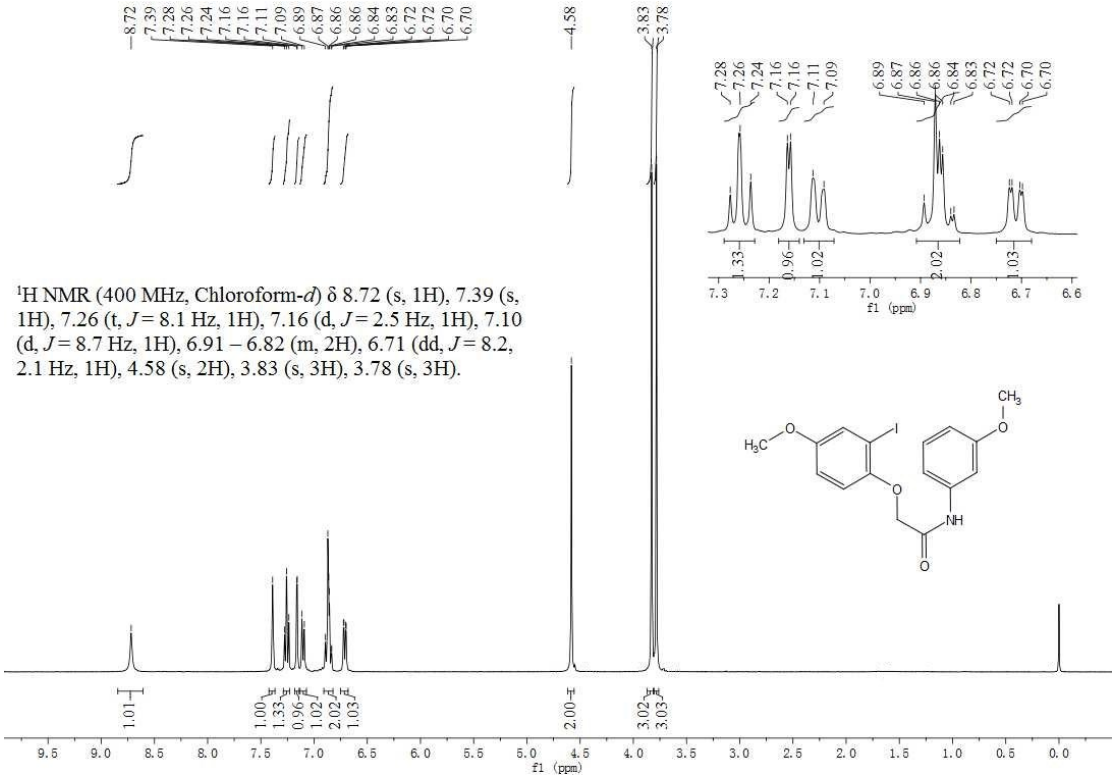
NMR spectra of **1g**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.67 (s, 1H), 7.47 (s, 1H), 7.41 (d, *J* = 8.1 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.16 (d, *J* = 2.5 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.91 – 6.82 (m, 2H), 4.58 (s, 2H), 3.78 (s, 3H), 2.37 (s, 3H).

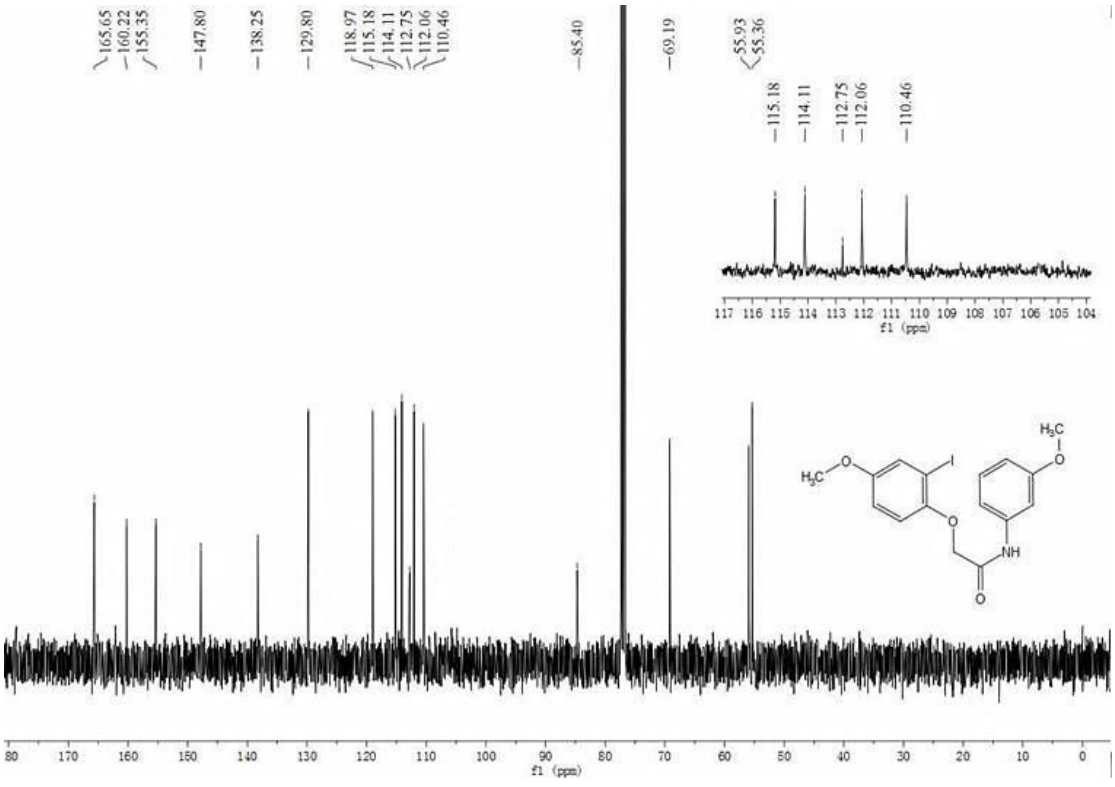




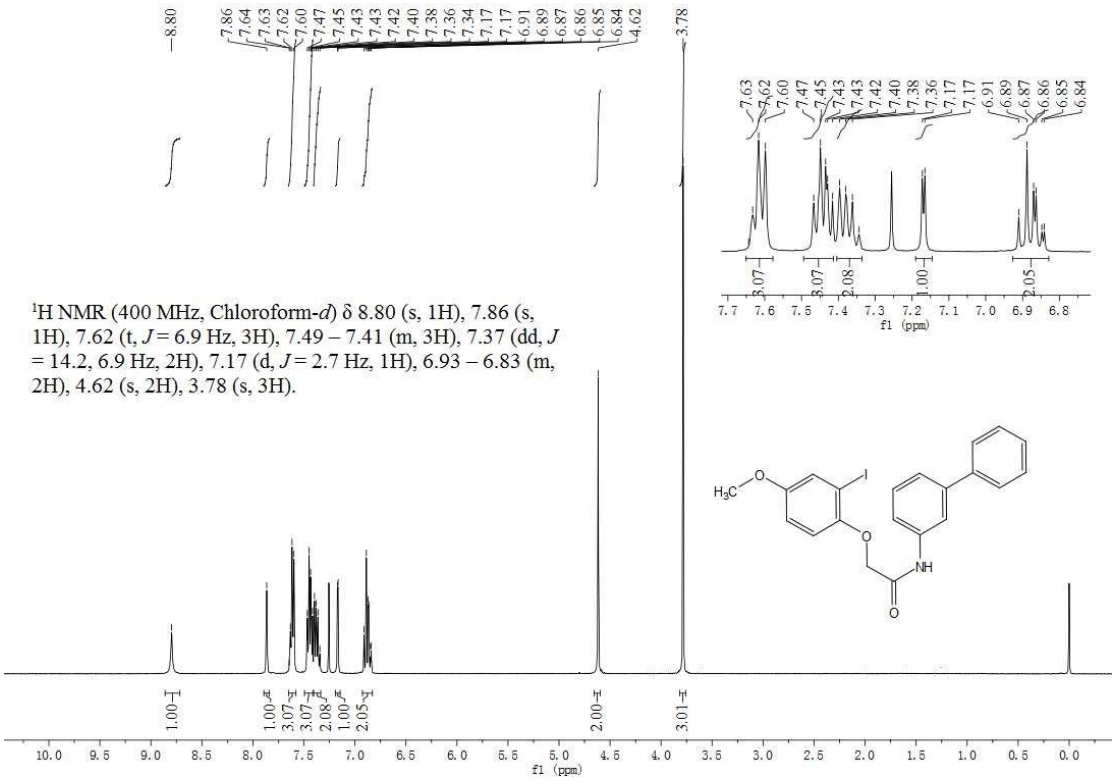
NMR spectra of **1h**



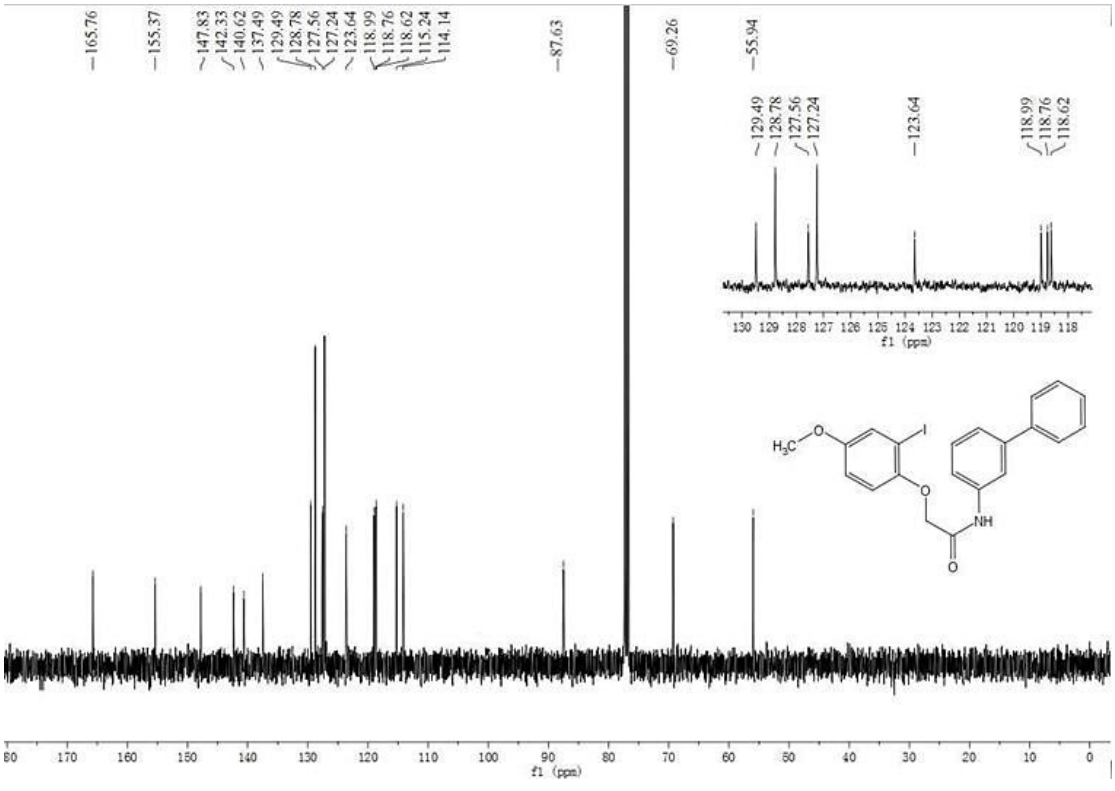
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.72 (s, 1H), 7.39 (s, 1H), 7.26 (t, *J* = 8.1 Hz, 1H), 7.16 (d, *J* = 2.5 Hz, 1H), 7.10 (d, *J* = 8.7 Hz, 1H), 6.91 – 6.82 (m, 2H), 6.71 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.58 (s, 2H), 3.83 (s, 3H), 3.78 (s, 3H).



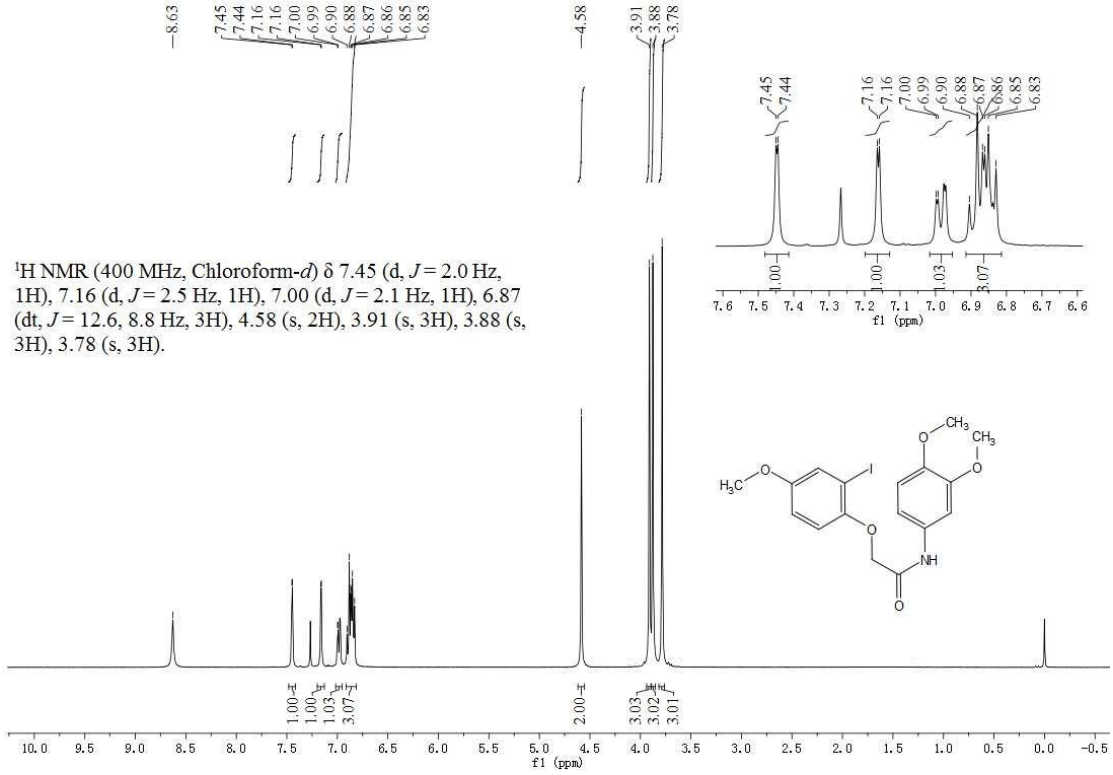
NMR spectra of **1i**



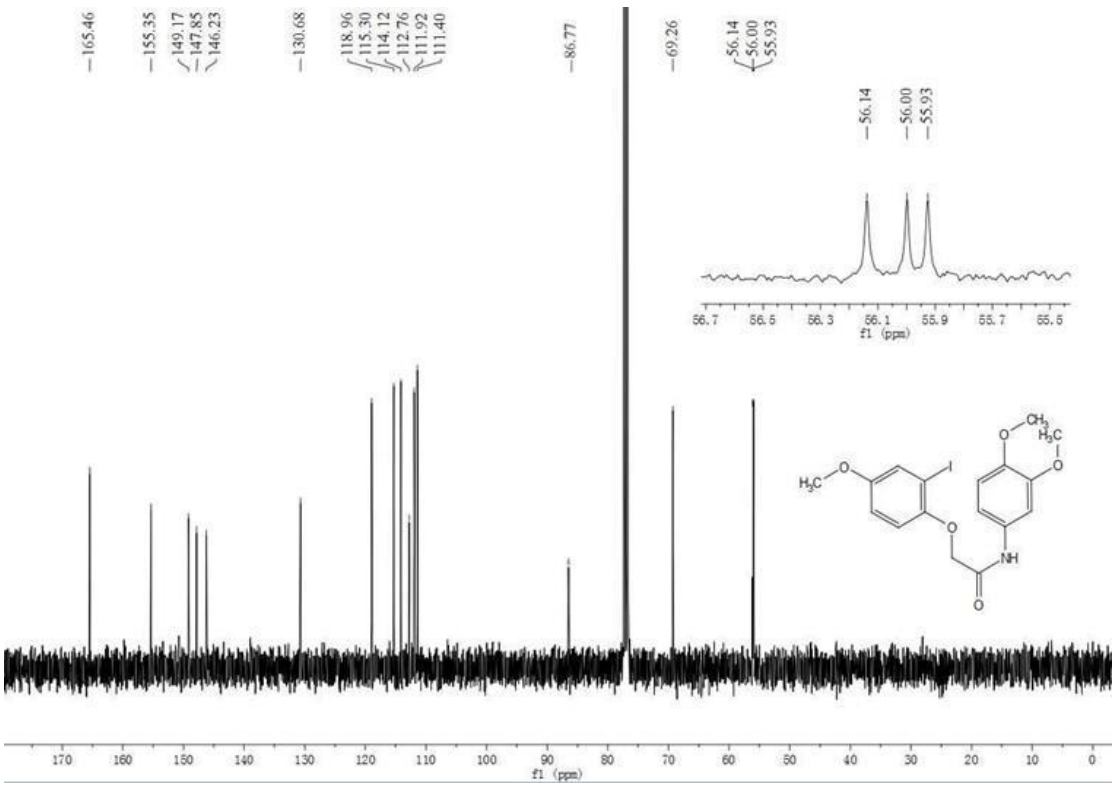
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.80 (s, 1H), 7.86 (s, 1H), 7.62 (t, *J* = 6.9 Hz, 3H), 7.49 – 7.41 (m, 3H), 7.37 (dd, *J* = 14.2, 6.9 Hz, 2H), 7.17 (d, *J* = 2.7 Hz, 1H), 6.93 – 6.83 (m, 2H), 4.62 (s, 2H), 3.78 (s, 3H).



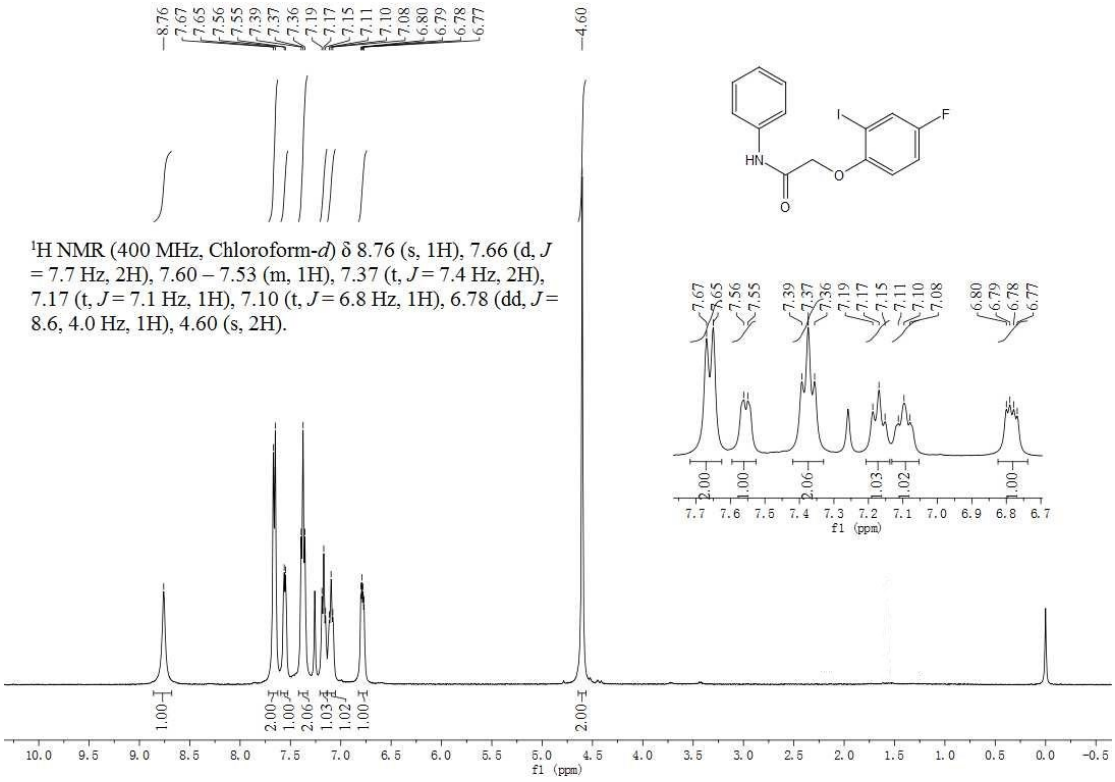
NMR spectra of **1j**



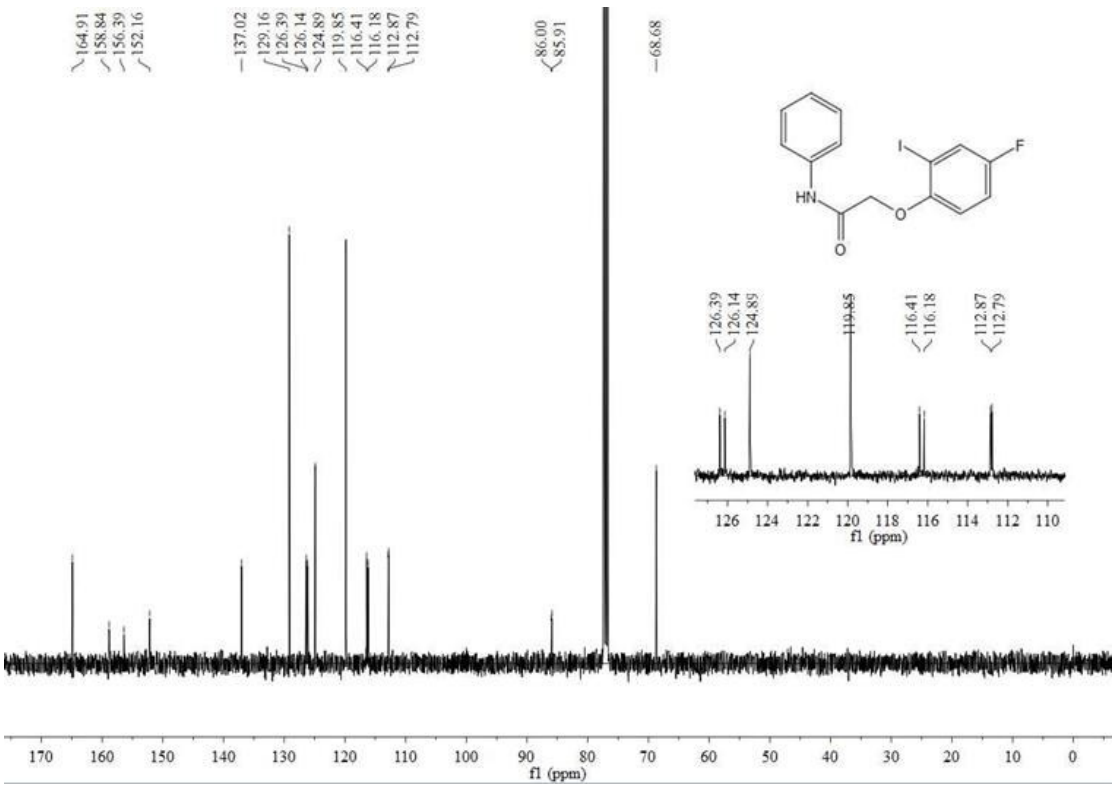
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 2.0 Hz, 1H), 7.16 (d, *J* = 2.5 Hz, 1H), 7.00 (d, *J* = 2.1 Hz, 1H), 6.87 (dt, *J* = 12.6, 8.8 Hz, 3H), 4.58 (s, 2H), 3.91 (s, 3H), 3.88 (s, 3H), 3.78 (s, 3H).



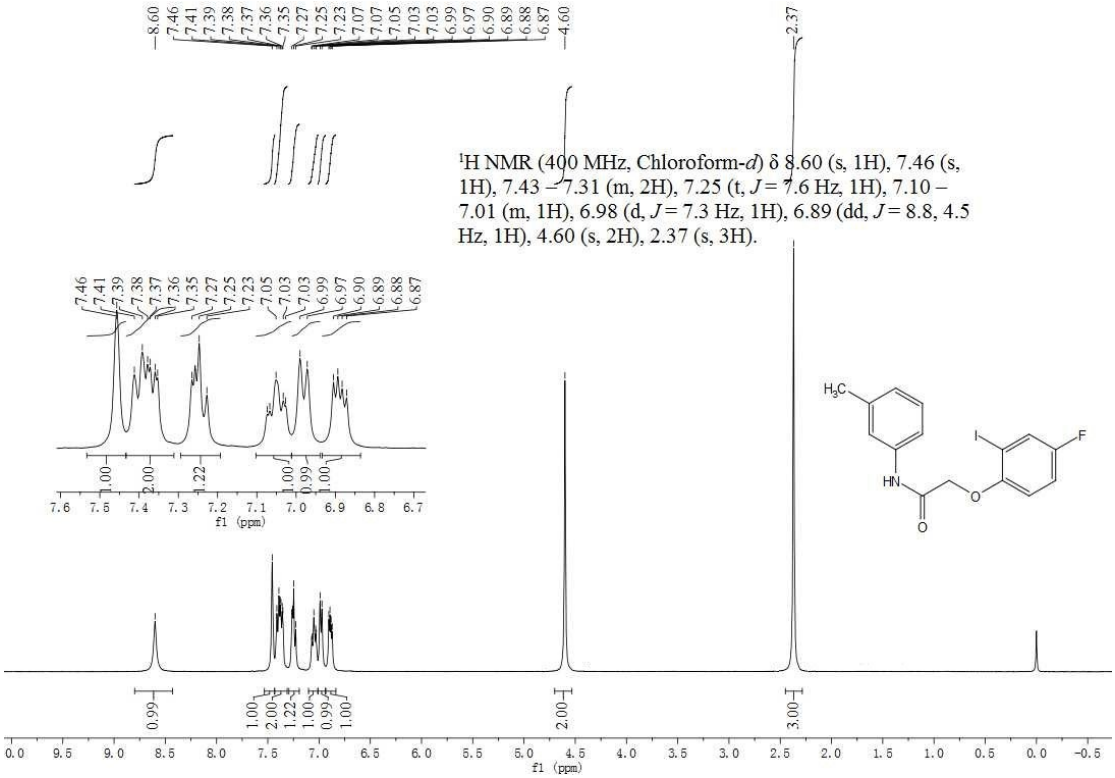
NMR spectra of **1k**



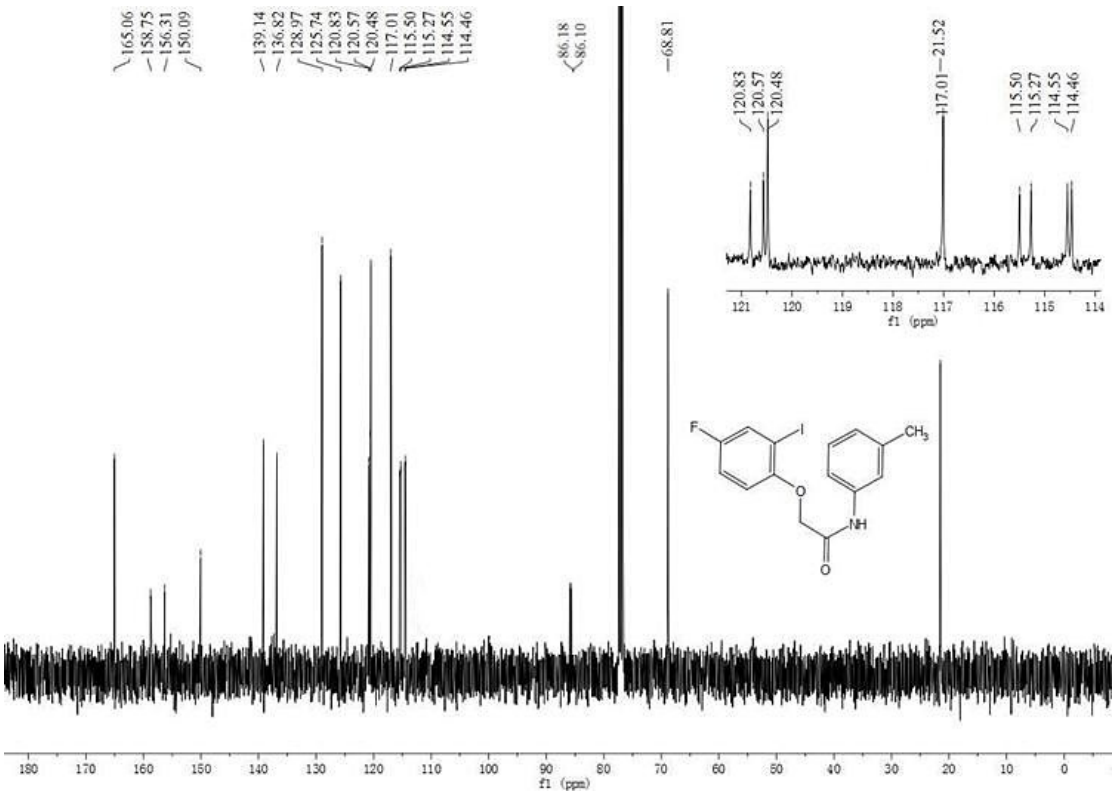
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.76 (s, 1H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.60 – 7.53 (m, 1H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.17 (t, *J* = 7.1 Hz, 1H), 7.10 (t, *J* = 6.8 Hz, 1H), 6.78 (dd, *J* = 8.6, 4.0 Hz, 1H), 4.60 (s, 2H).



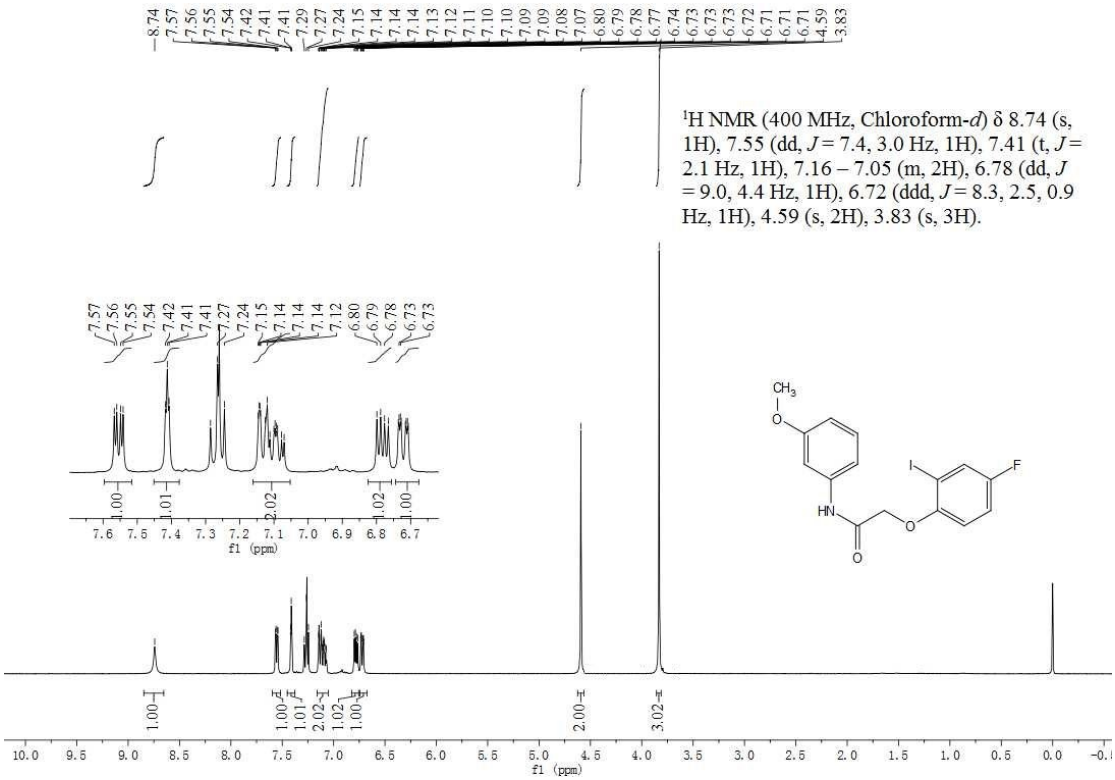
NMR spectra of **1l**



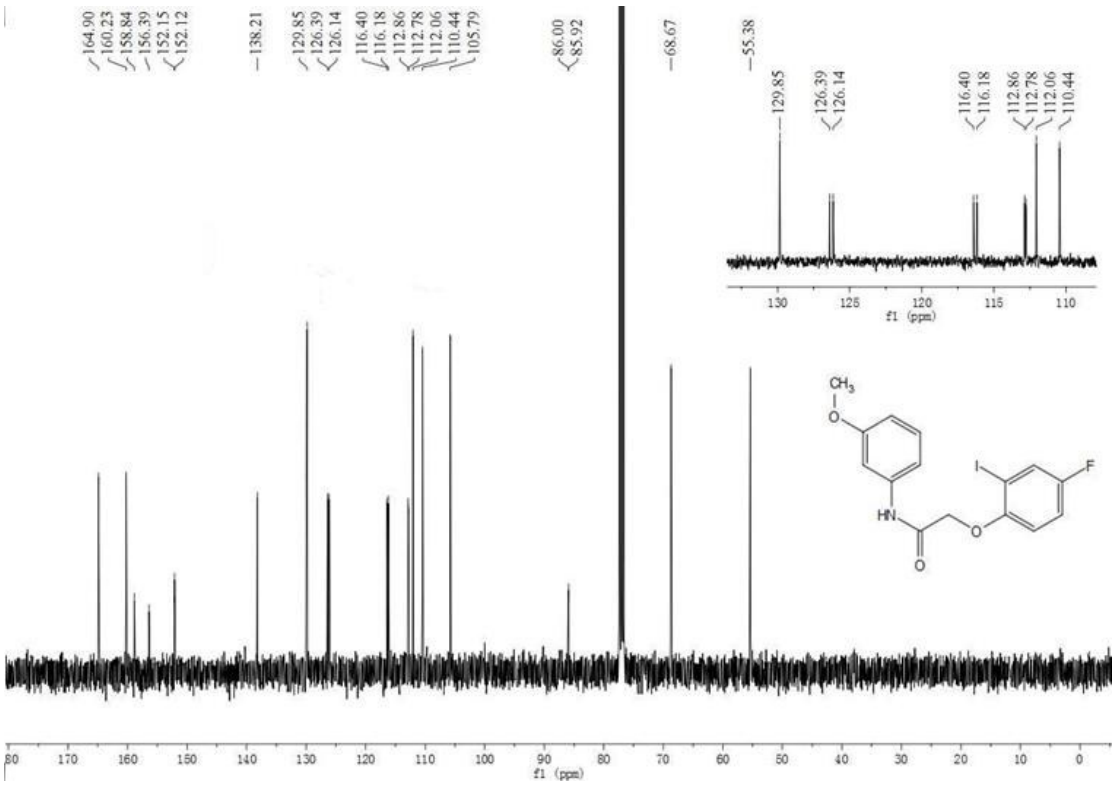
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.60 (s, 1H), 7.46 (s, 1H), 7.43 – 7.31 (m, 2H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.10 – 7.01 (m, 1H), 6.98 (d, *J* = 7.3 Hz, 1H), 6.89 (dd, *J* = 8.8, 4.5 Hz, 1H), 4.60 (s, 2H), 2.37 (s, 3H).



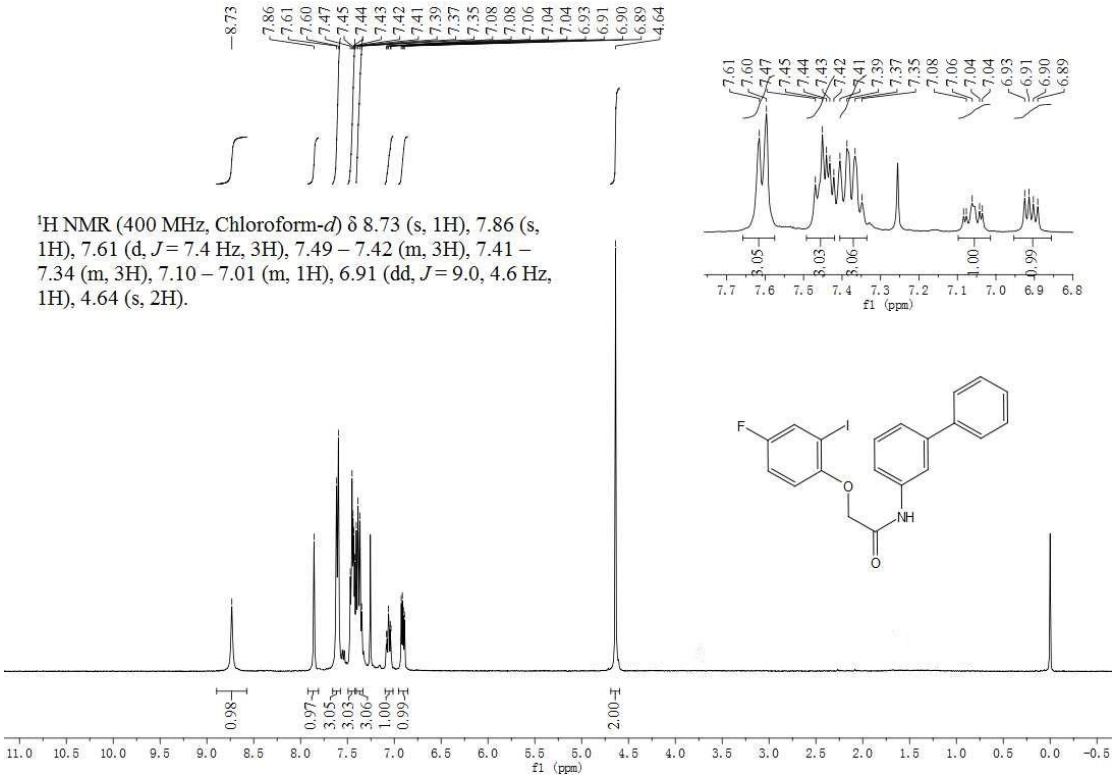
NMR spectra of **1m**



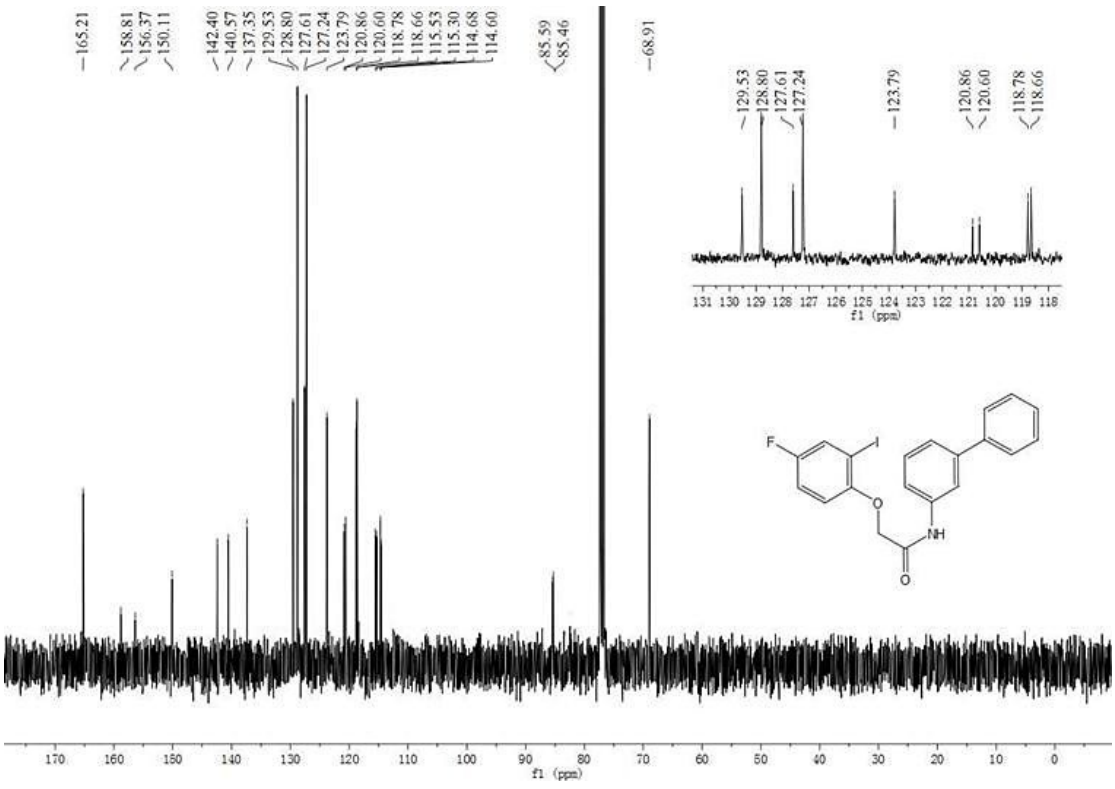
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.74 (s, 1H), 7.55 (dd, *J* = 7.4, 3.0 Hz, 1H), 7.41 (t, *J* = 2.1 Hz, 1H), 7.16 – 7.05 (m, 2H), 6.78 (dd, *J* = 9.0, 4.4 Hz, 1H), 6.72 (ddd, *J* = 8.3, 2.5, 0.9 Hz, 1H), 4.59 (s, 2H), 3.83 (s, 3H).



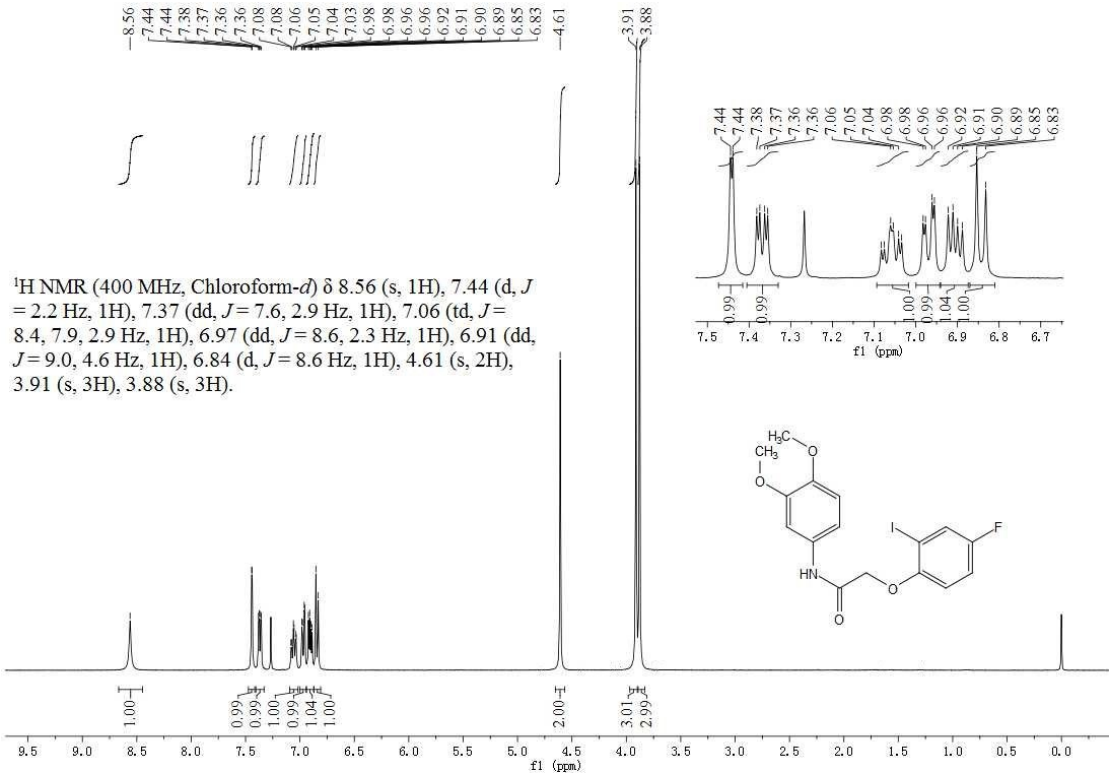
NMR spectra of **1n**



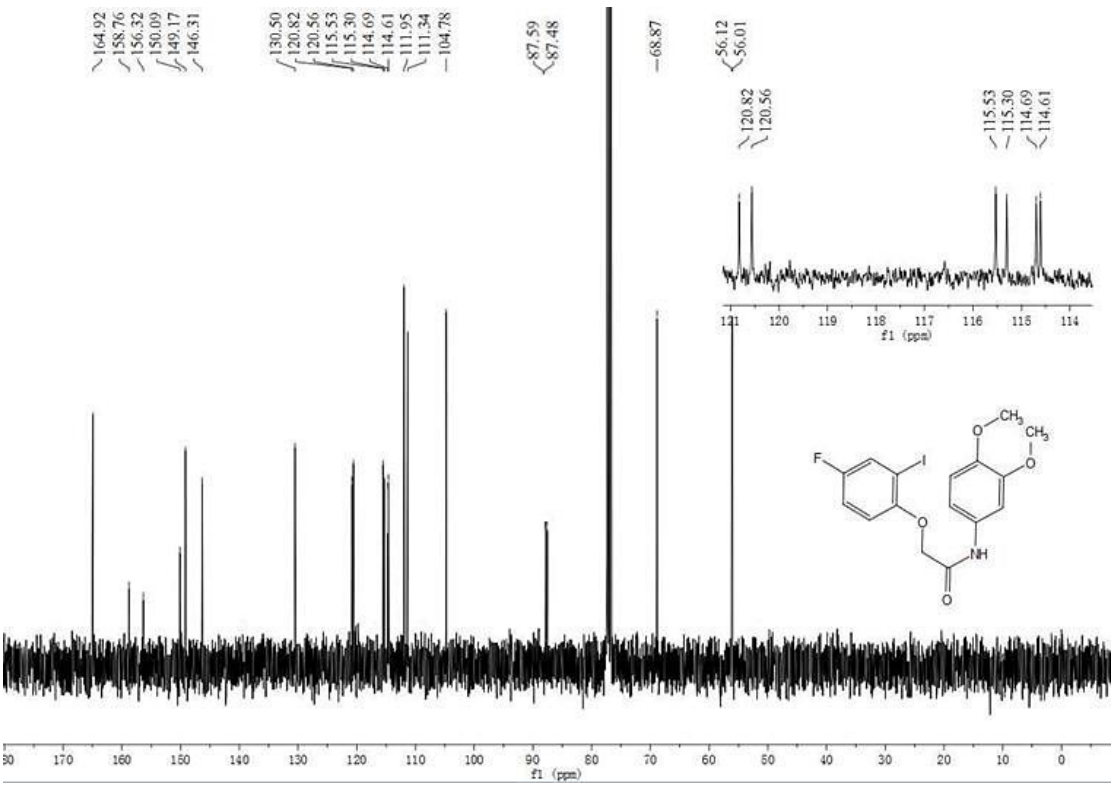
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 7.86 (s, 1H), 7.61 (d, *J* = 7.4 Hz, 3H), 7.49 – 7.42 (m, 3H), 7.41 – 7.34 (m, 3H), 7.10 – 7.01 (m, 1H), 6.91 (dd, *J* = 9.0, 4.6 Hz, 1H), 4.64 (s, 2H).



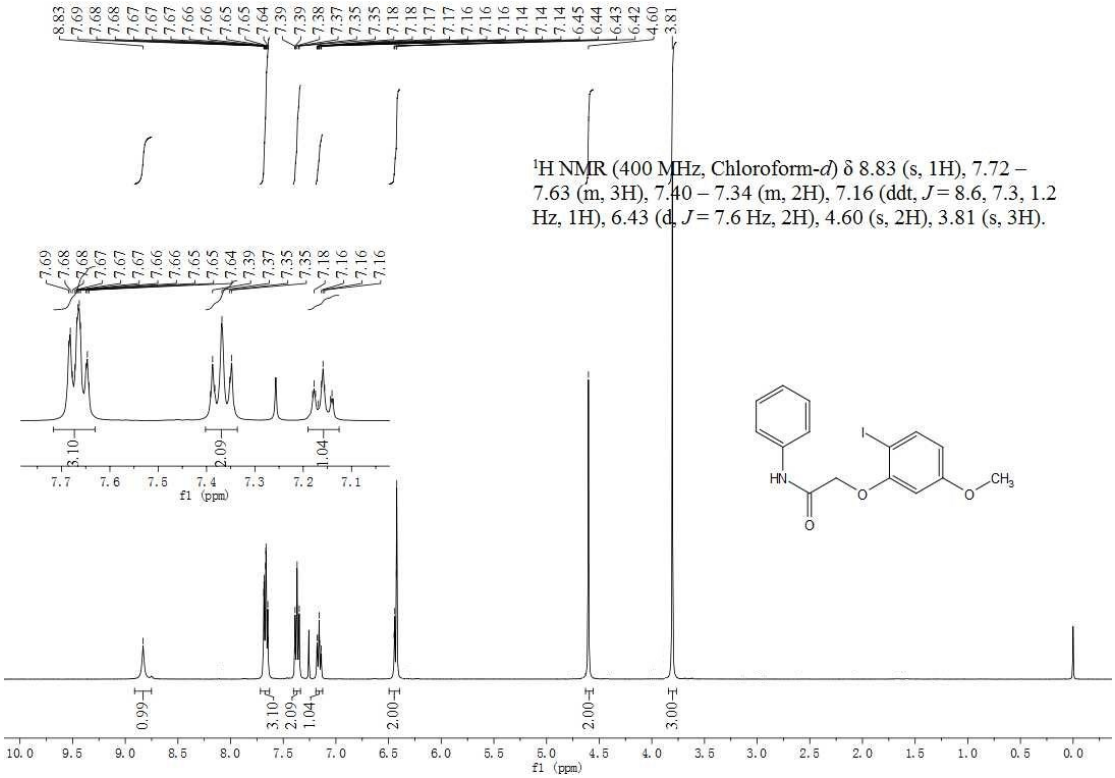
NMR spectra of **1o**



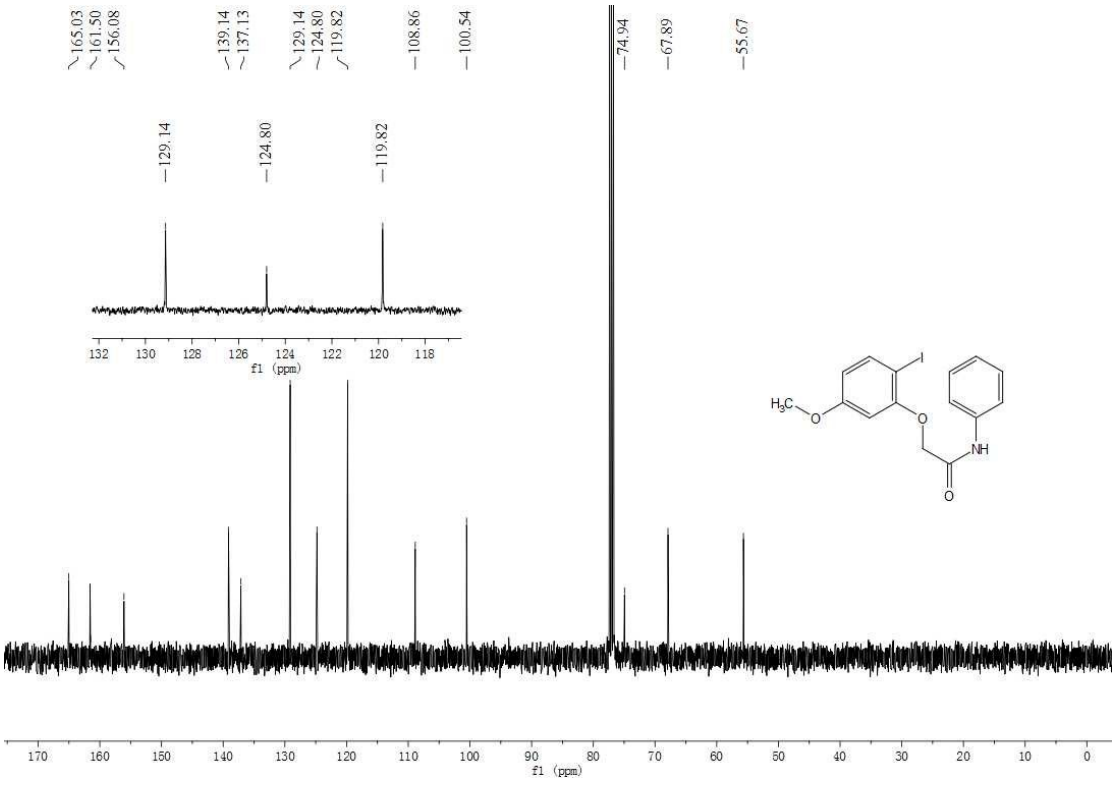
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.56 (s, 1H), 7.44 (d, *J* = 2.2 Hz, 1H), 7.37 (dd, *J* = 7.6, 2.9 Hz, 1H), 7.06 (td, *J* = 8.4, 7.9, 2.9 Hz, 1H), 6.97 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.91 (dd, *J* = 9.0, 4.6 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 1H), 4.61 (s, 2H), 3.91 (s, 3H), 3.88 (s, 3H).



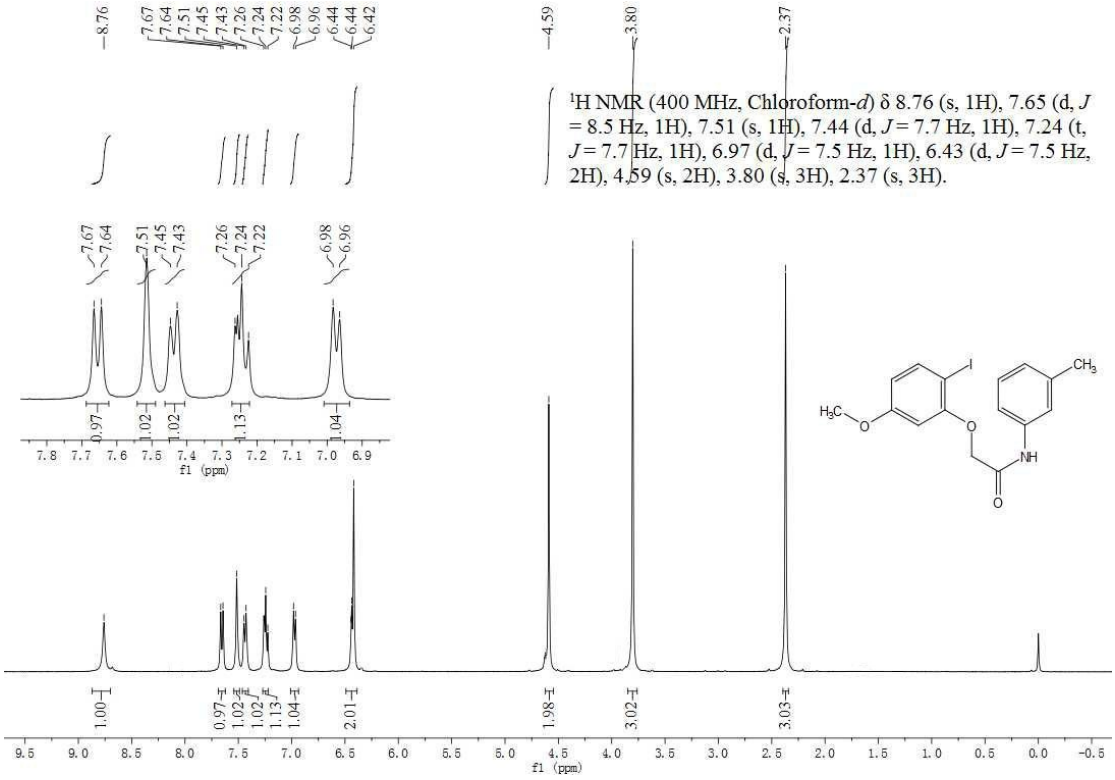
NMR spectra of **1p**



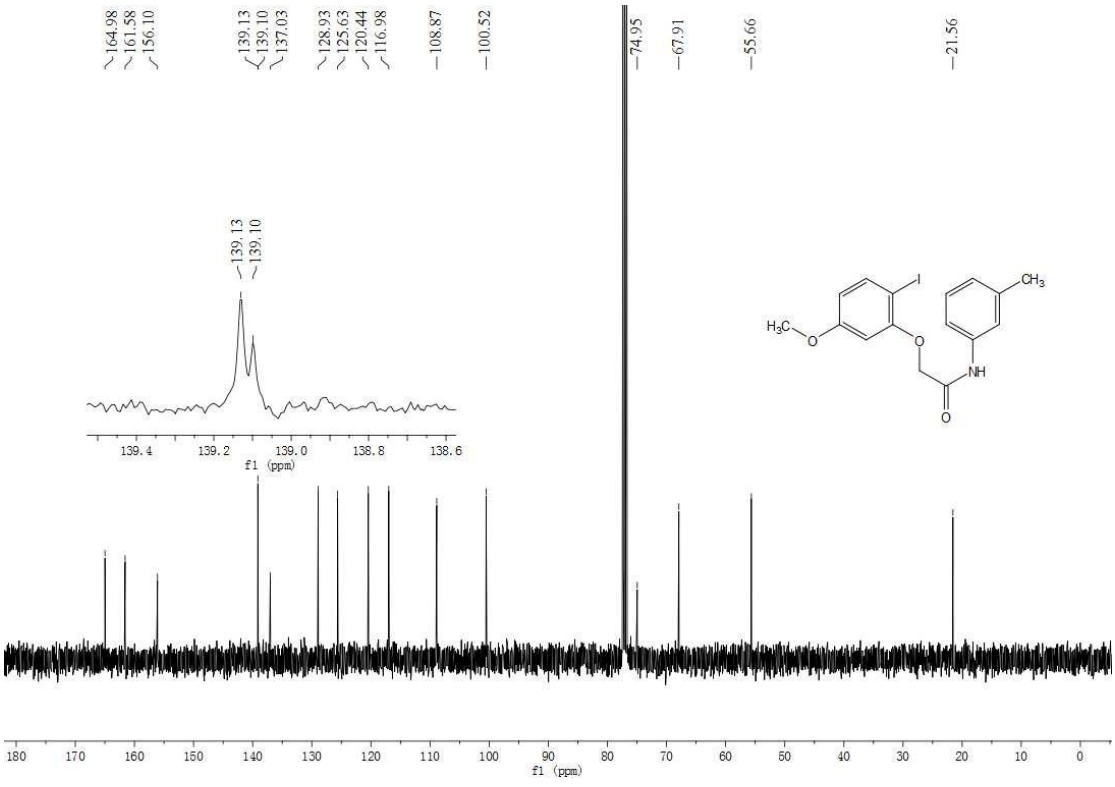
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.83 (s, 1H), 7.72 – 7.63 (m, 3H), 7.40 – 7.34 (m, 2H), 7.16 (ddt, *J* = 8.6, 7.3, 1.2 Hz, 1H), 6.43 (d, *J* = 7.6 Hz, 2H), 4.60 (s, 2H), 3.81 (s, 3H).



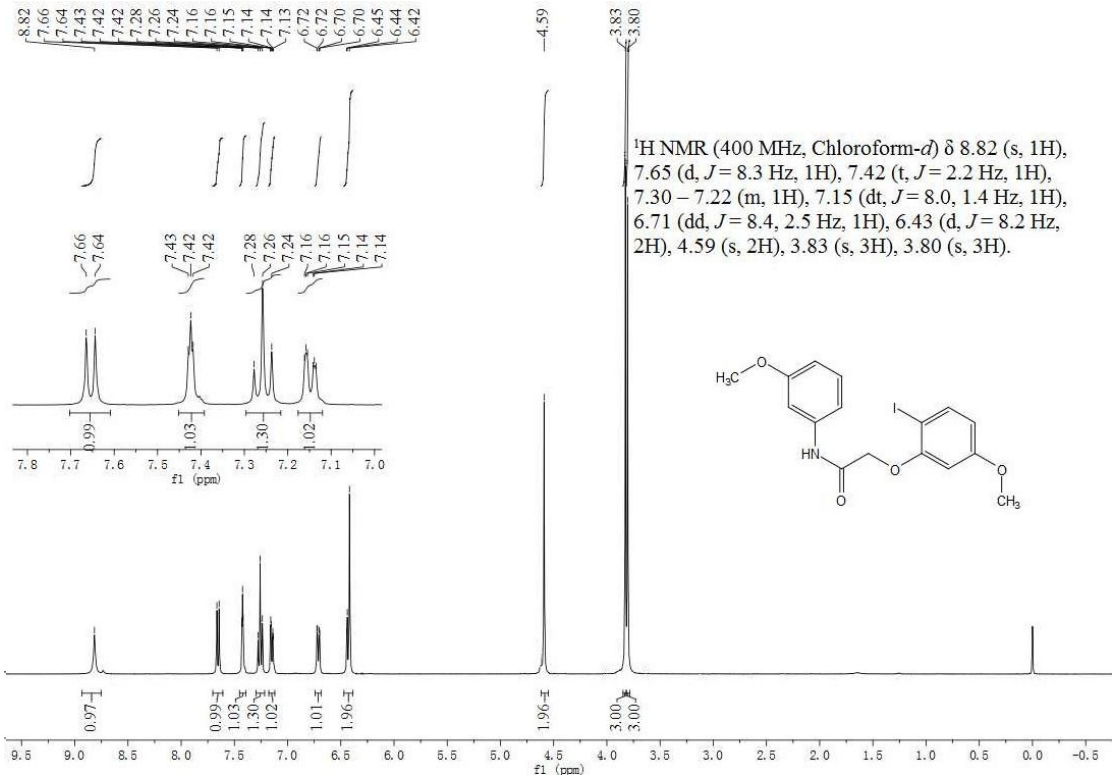
NMR spectra of **1q**



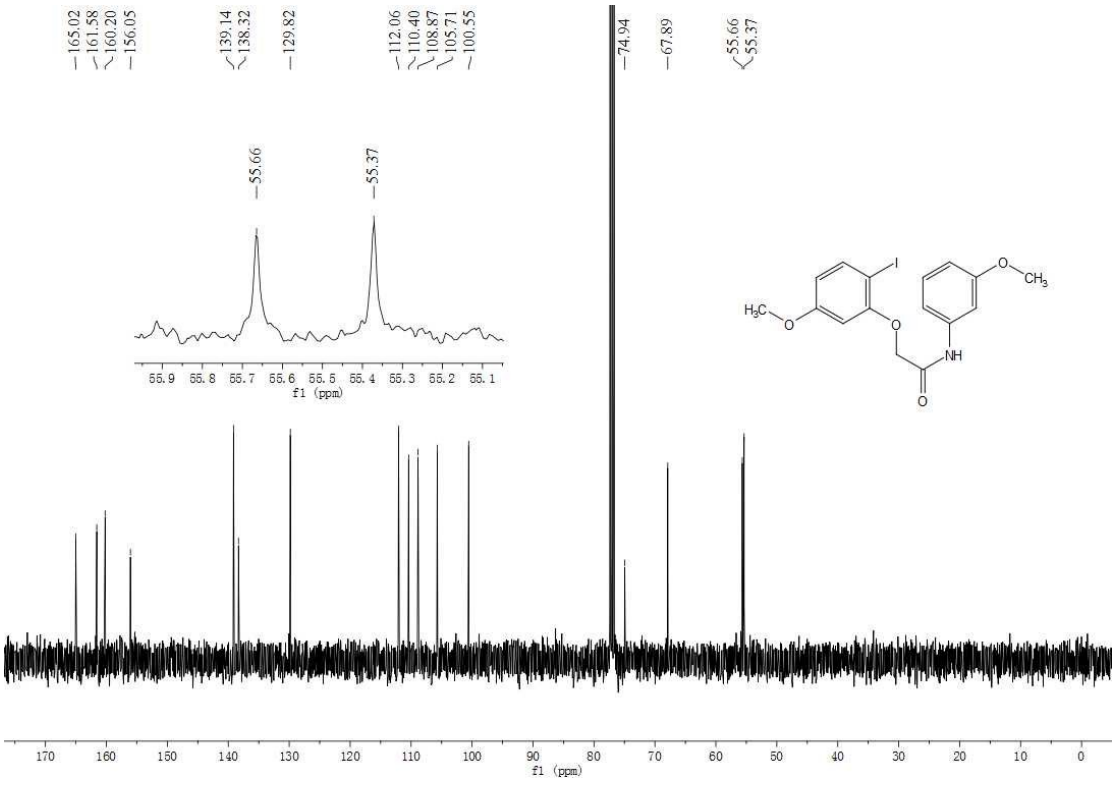
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.76 (s, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.51 (s, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.43 (d, *J* = 7.5 Hz, 2H), 4.59 (s, 2H), 3.80 (s, 3H), 2.37 (s, 3H).



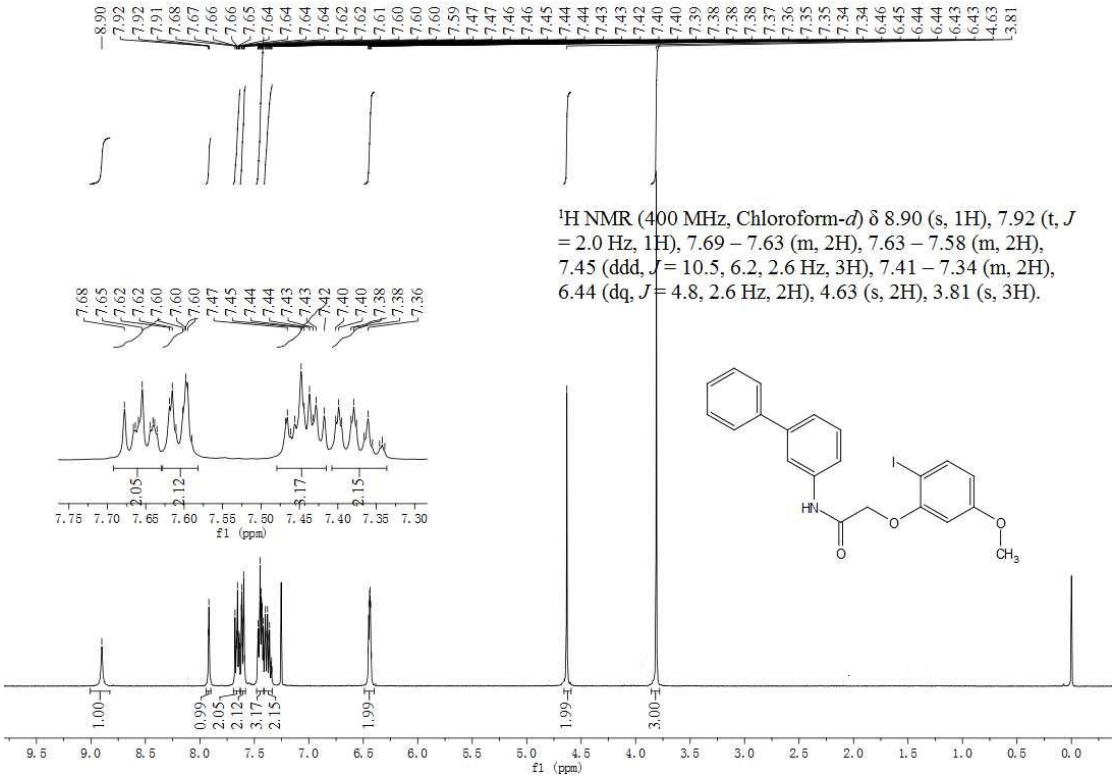
NMR spectra of **1r**



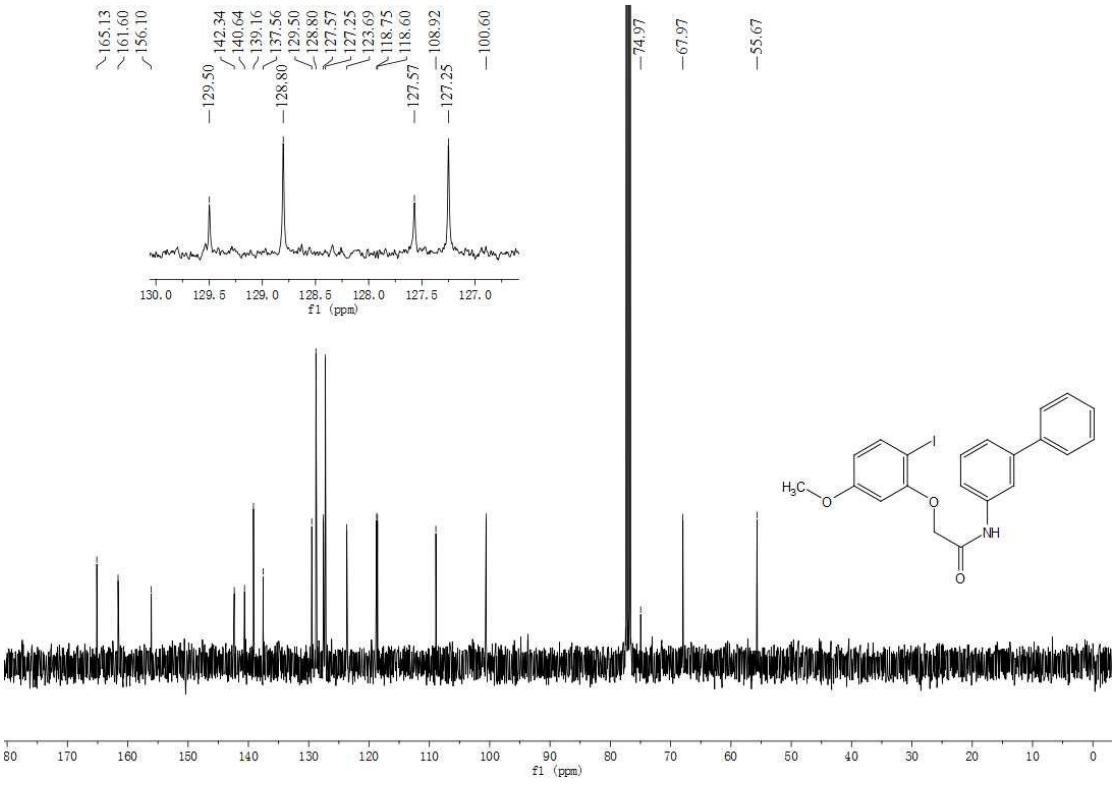
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.82 (s, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.42 (t, *J* = 2.2 Hz, 1H), 7.30 – 7.22 (m, 1H), 7.15 (dt, *J* = 8.0, 1.4 Hz, 1H), 6.71 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.43 (d, *J* = 8.2 Hz, 2H), 4.59 (s, 2H), 3.83 (s, 3H), 3.80 (s, 3H).



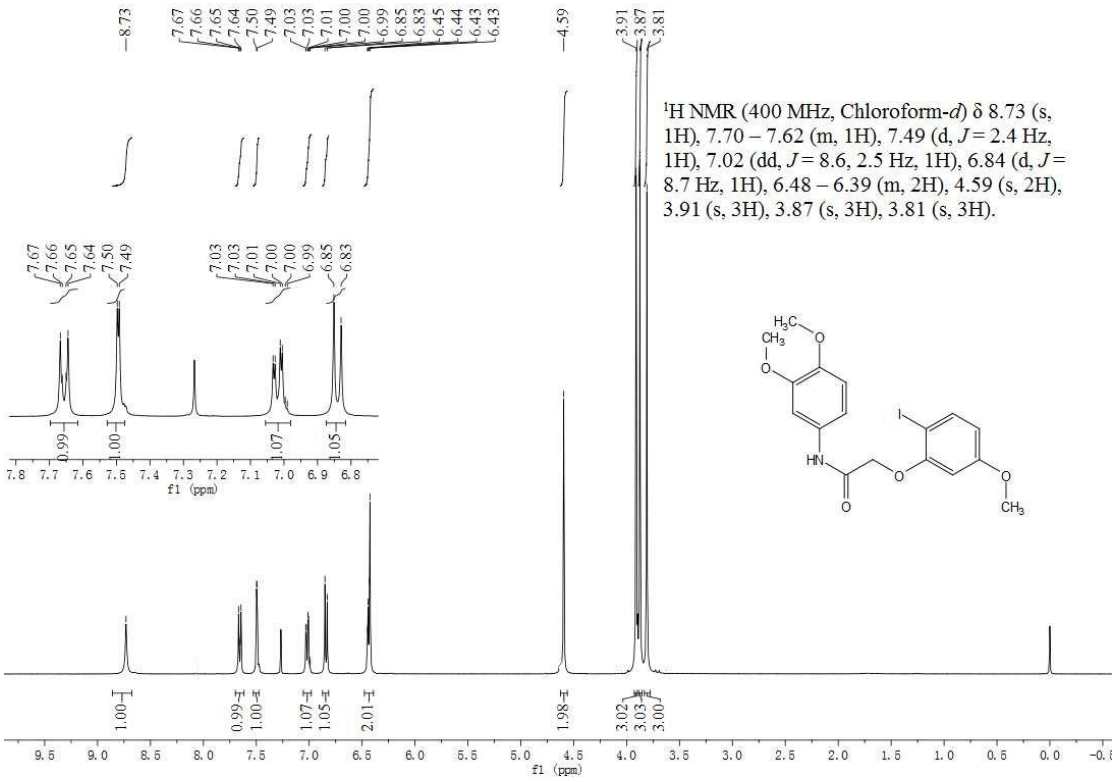
NMR spectra of **1s**



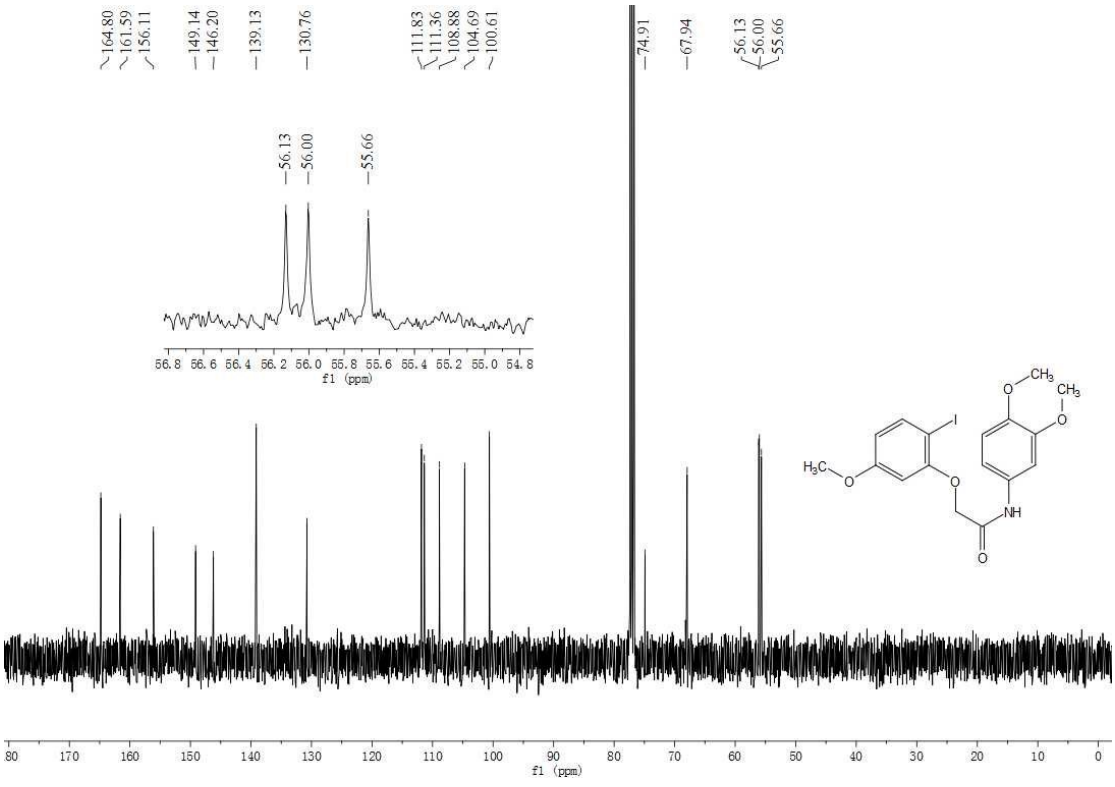
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.90 (s, 1H), 7.92 (t, *J* = 2.0 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.63 – 7.58 (m, 2H), 7.45 (ddd, *J* = 10.5, 6.2, 2.6 Hz, 3H), 7.41 – 7.34 (m, 2H), 6.44 (dq, *J* = 4.8, 2.6 Hz, 2H), 4.63 (s, 2H), 3.81 (s, 3H).



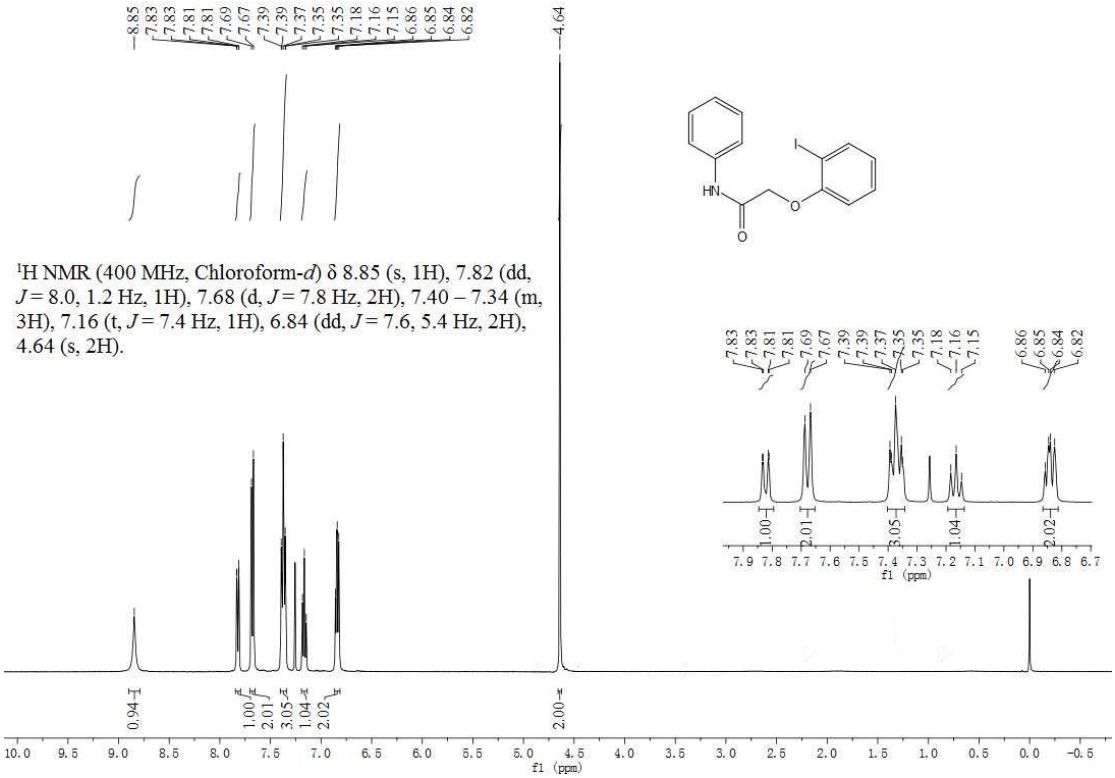
NMR spectra of **1t**



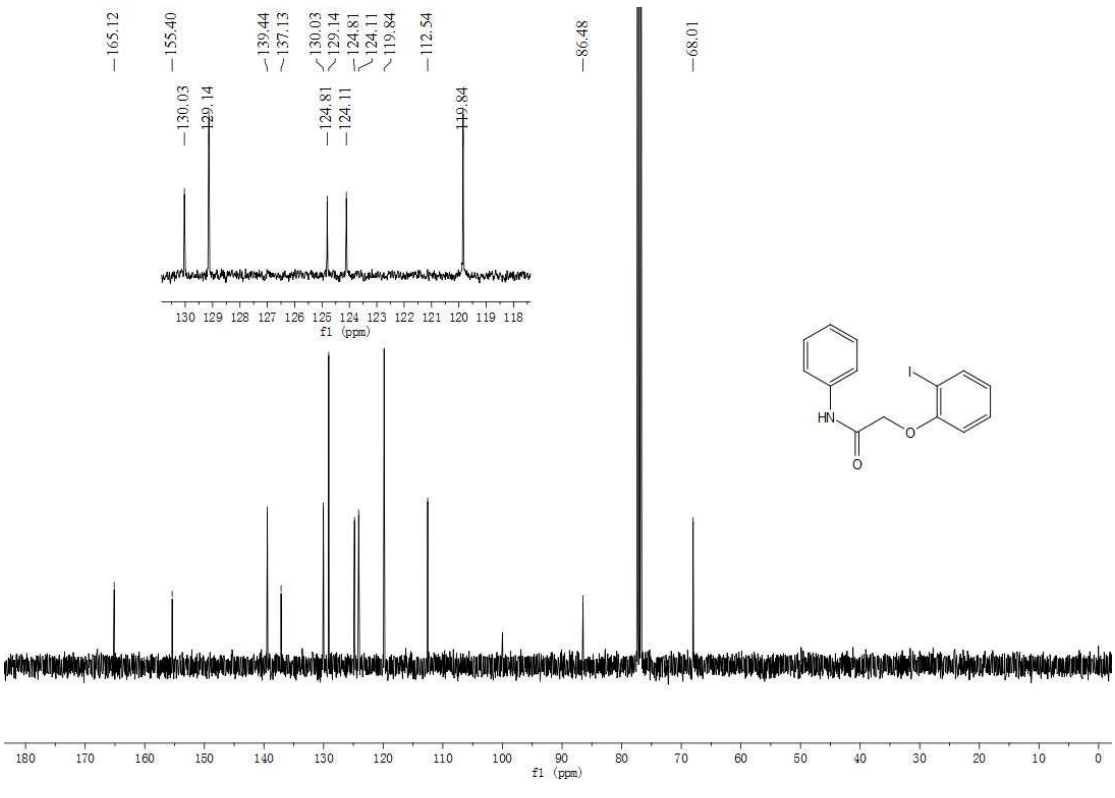
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 (s, 1H), 7.70 – 7.62 (m, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.02 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 1H), 6.48 – 6.39 (m, 2H), 4.59 (s, 2H), 3.91 (s, 3H), 3.87 (s, 3H), 3.81 (s, 3H).



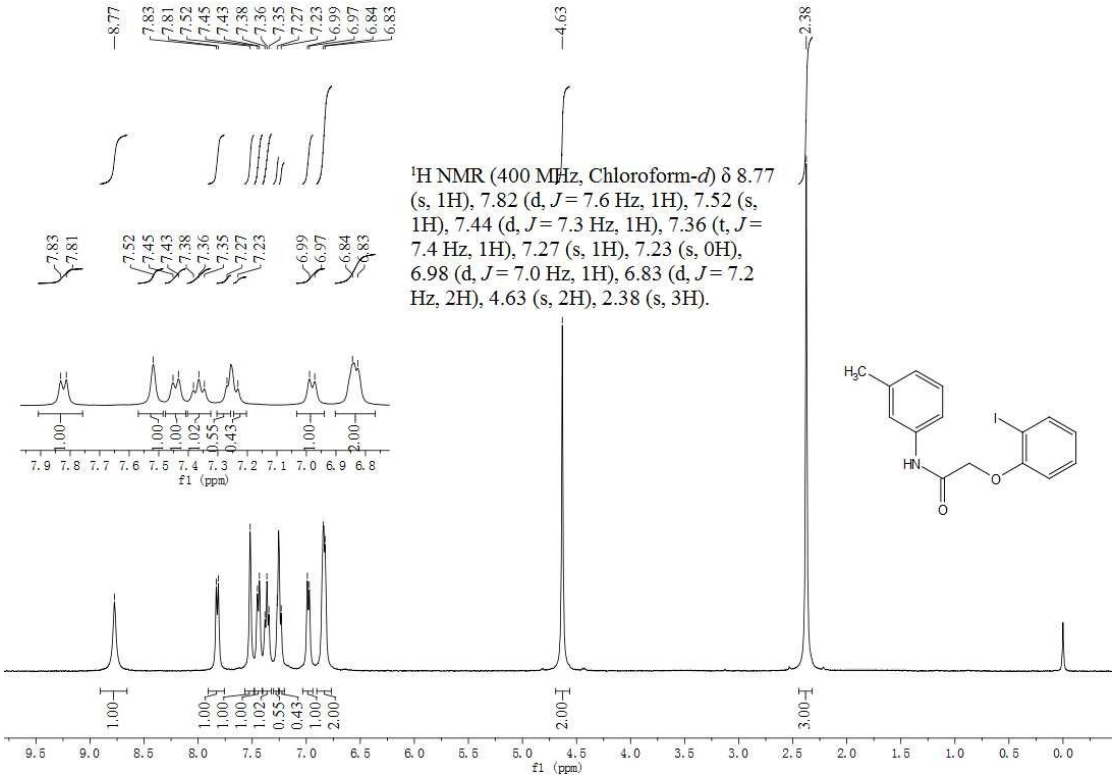
NMR spectra of **1u**



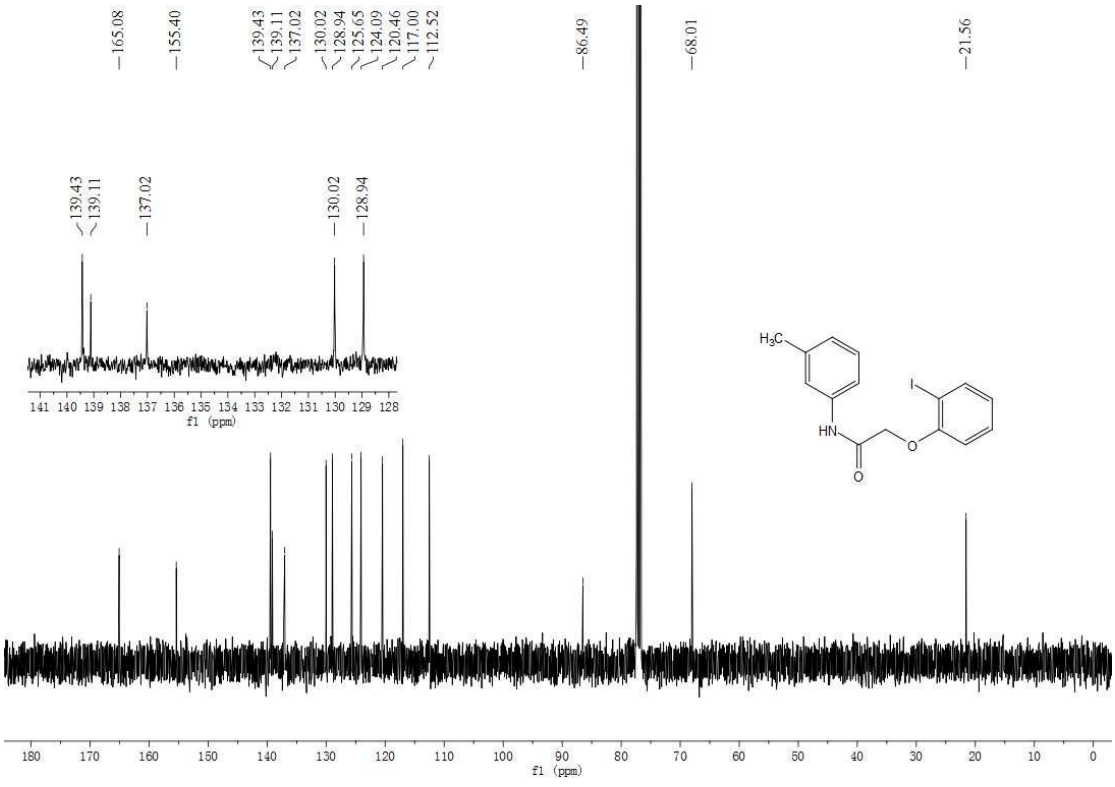
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.85 (s, 1H), 7.82 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 2H), 7.40 – 7.34 (m, 3H), 7.16 (t, *J* = 7.4 Hz, 1H), 6.84 (dd, *J* = 7.6, 5.4 Hz, 2H), 4.64 (s, 2H).



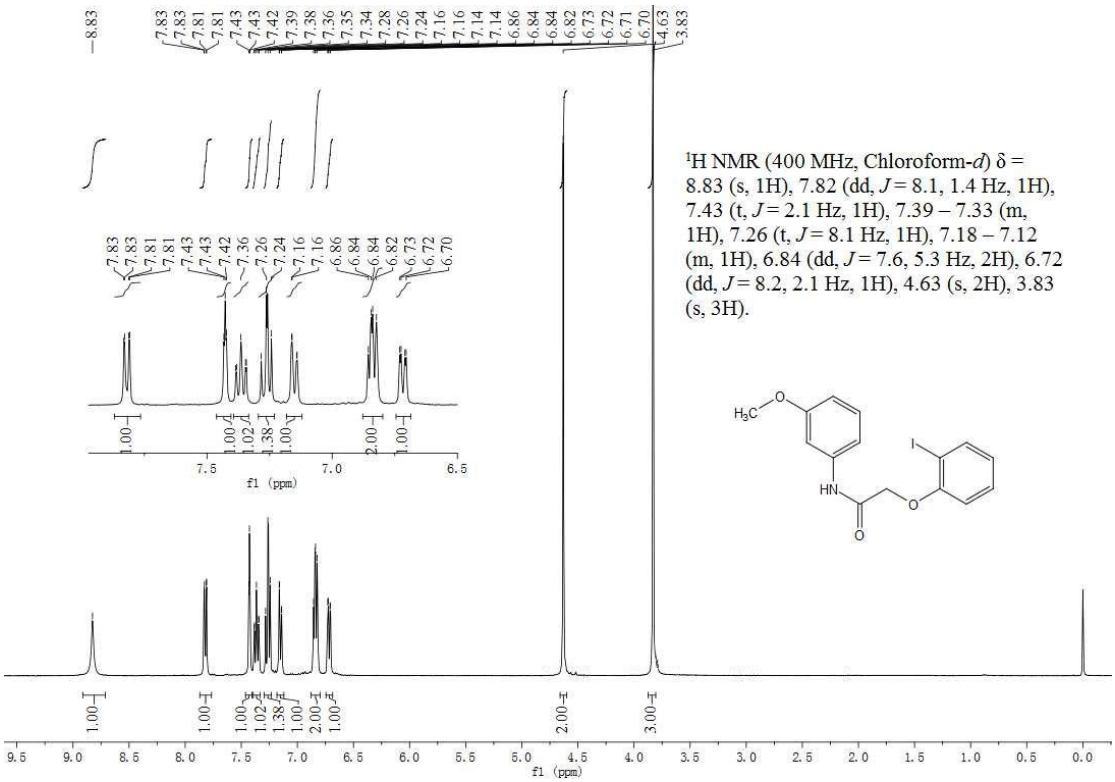
NMR spectra of **1v**



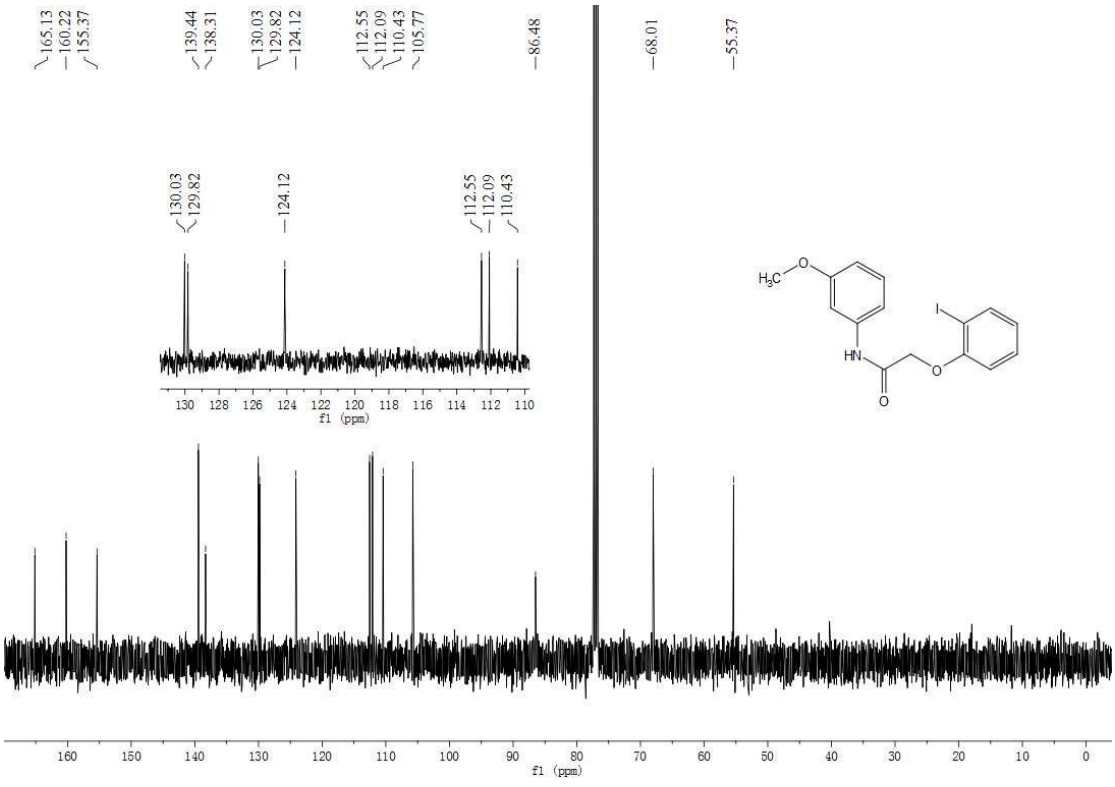
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.77 (s, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.52 (s, 1H), 7.44 (d, *J* = 7.3 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.27 (s, 1H), 7.23 (s, 0H), 6.98 (d, *J* = 7.0 Hz, 1H), 6.83 (d, *J* = 7.2 Hz, 2H), 4.63 (s, 2H), 2.38 (s, 3H).



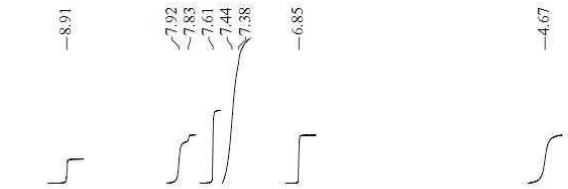
NMR spectra of **1w**



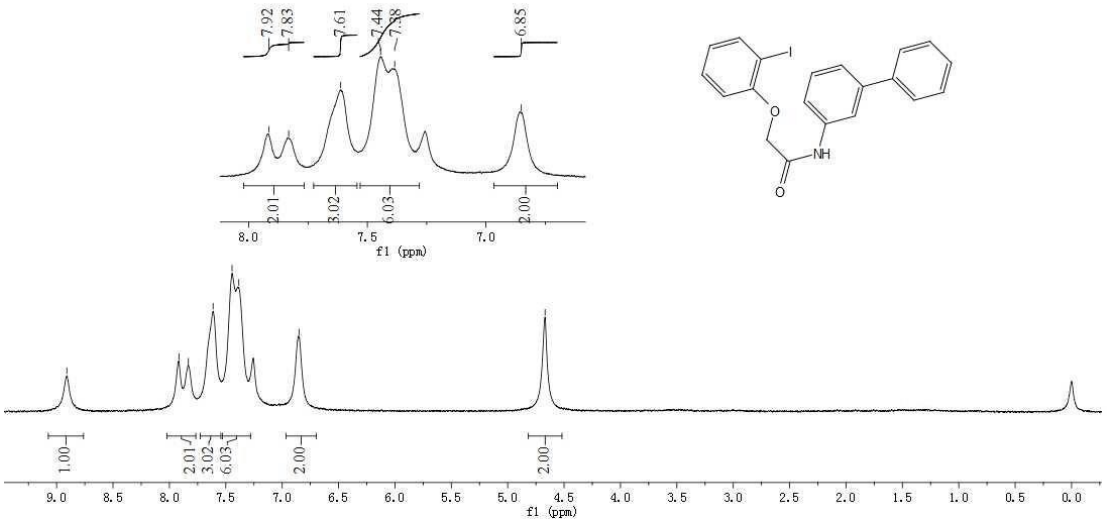
^{1}H NMR (400 MHz, Chloroform-*d*) δ = 8.83 (s, 1H), 7.82 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.43 (t, *J* = 2.1 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.26 (t, *J* = 8.1 Hz, 1H), 7.18 – 7.12 (m, 1H), 6.84 (dd, *J* = 7.6, 5.3 Hz, 2H), 6.72 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.63 (s, 2H), 3.83 (s, 3H).

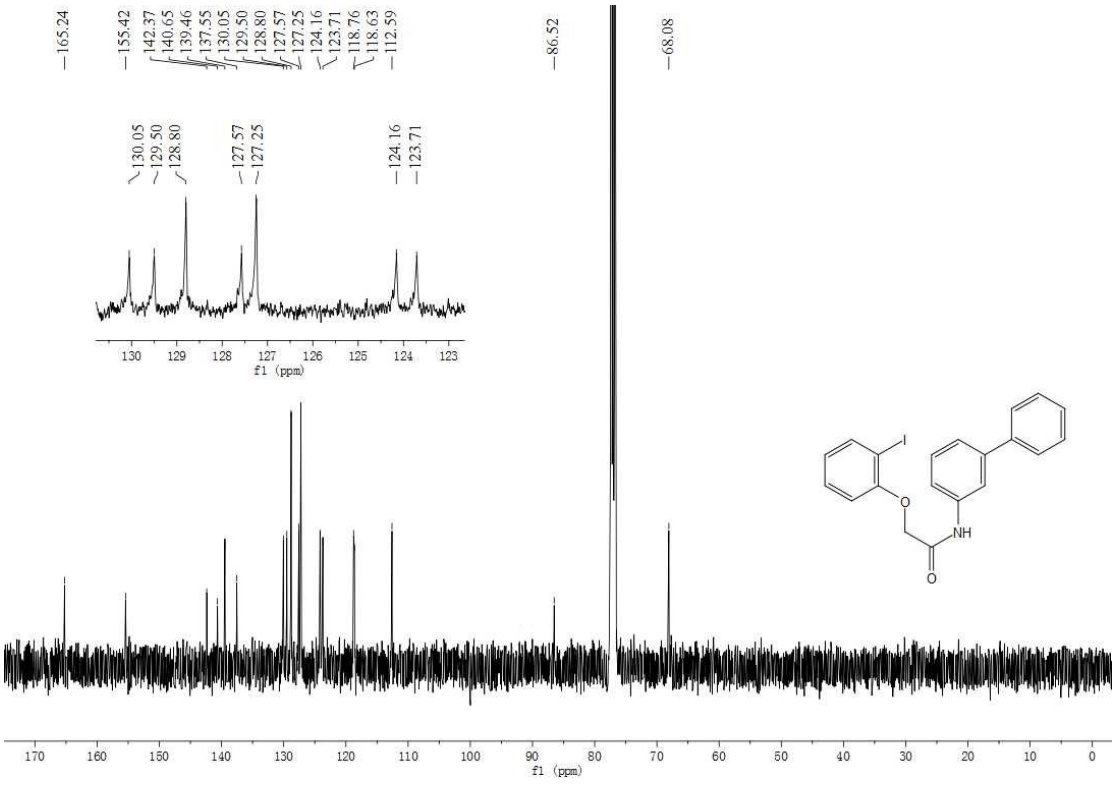


NMR spectra of **1x**

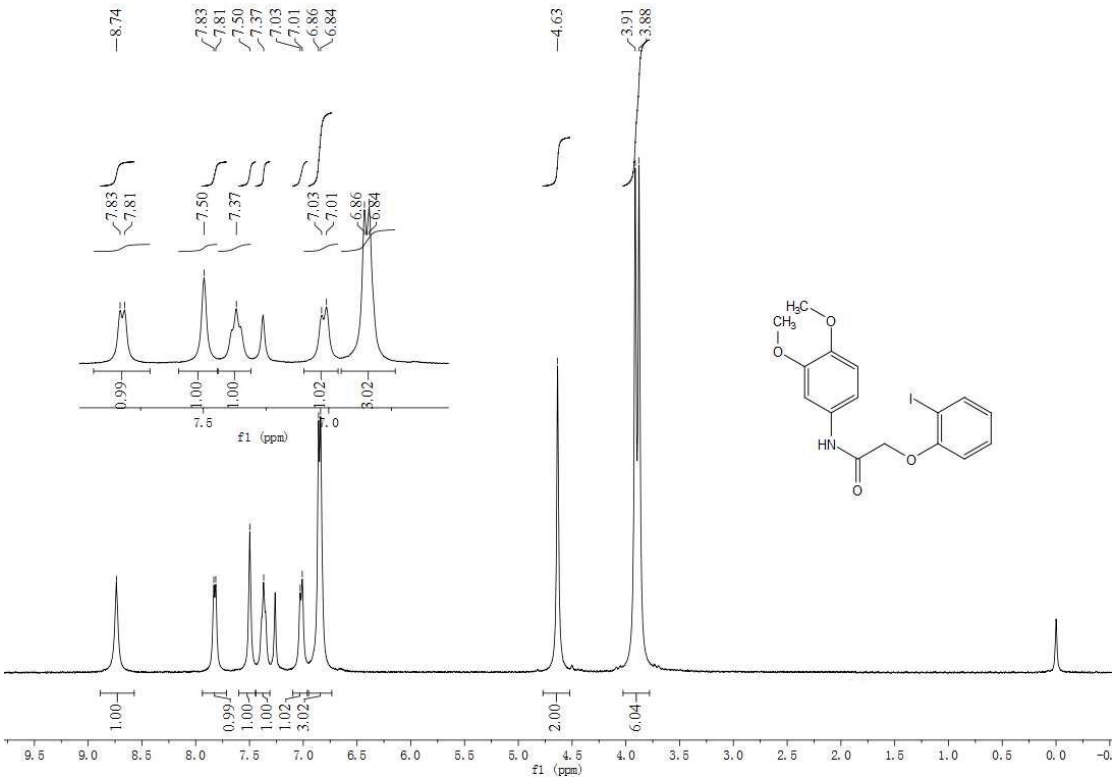


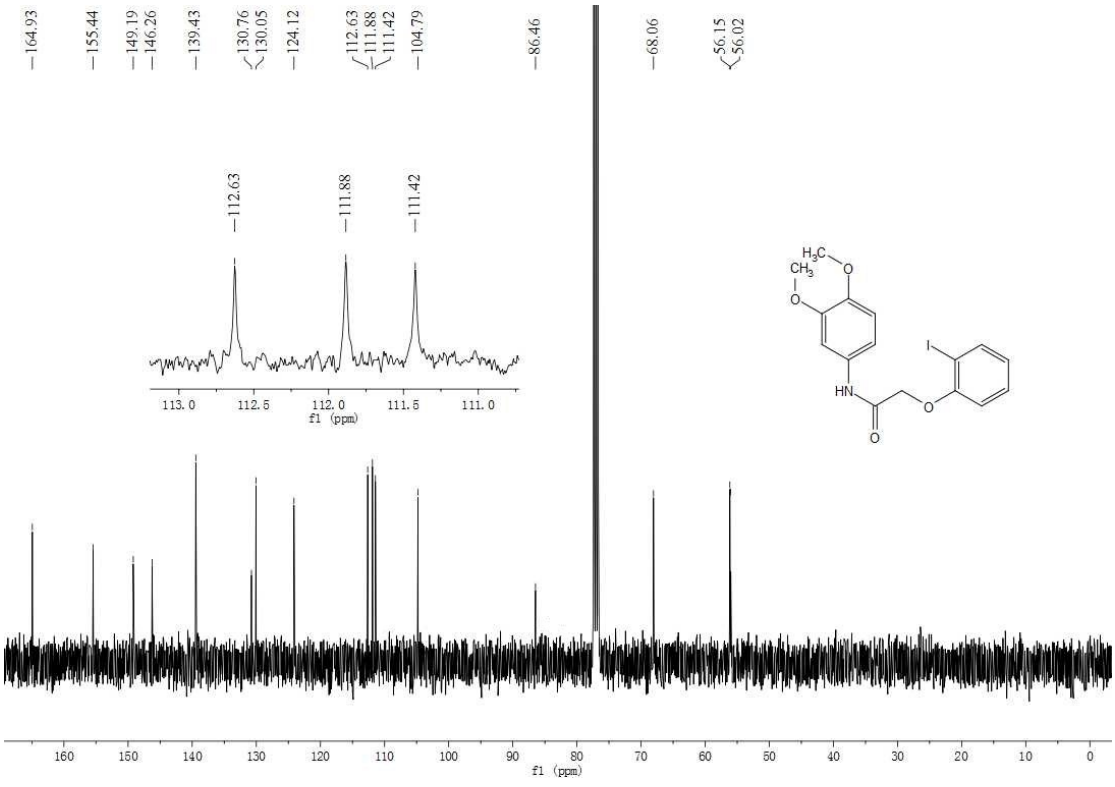
^{1}H NMR (400 MHz, Chloroform-*d*) δ = 8.91 (s, 1H), 7.87 (d, *J* = 33.6 Hz, 2H), 7.61 (s, 3H), 7.41 (d, *J* = 23.9 Hz, 6H), 6.85 (s, 2H), 4.67 (s, 2H).





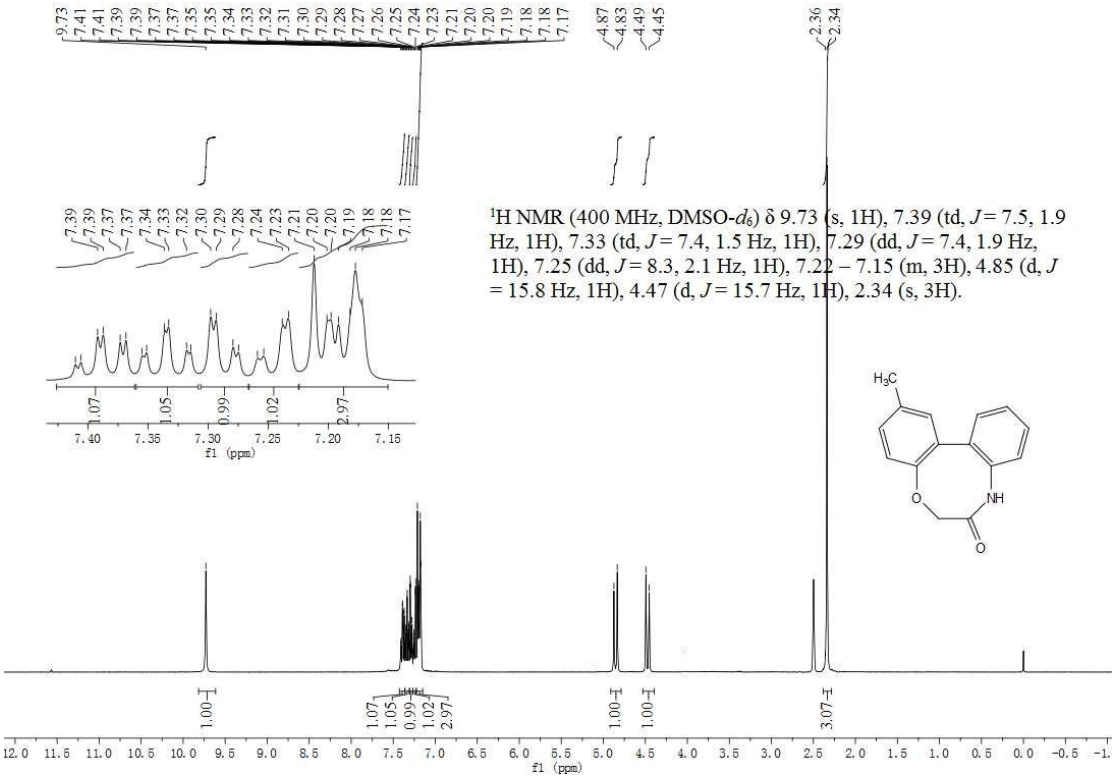
NMR spectra of **1y**

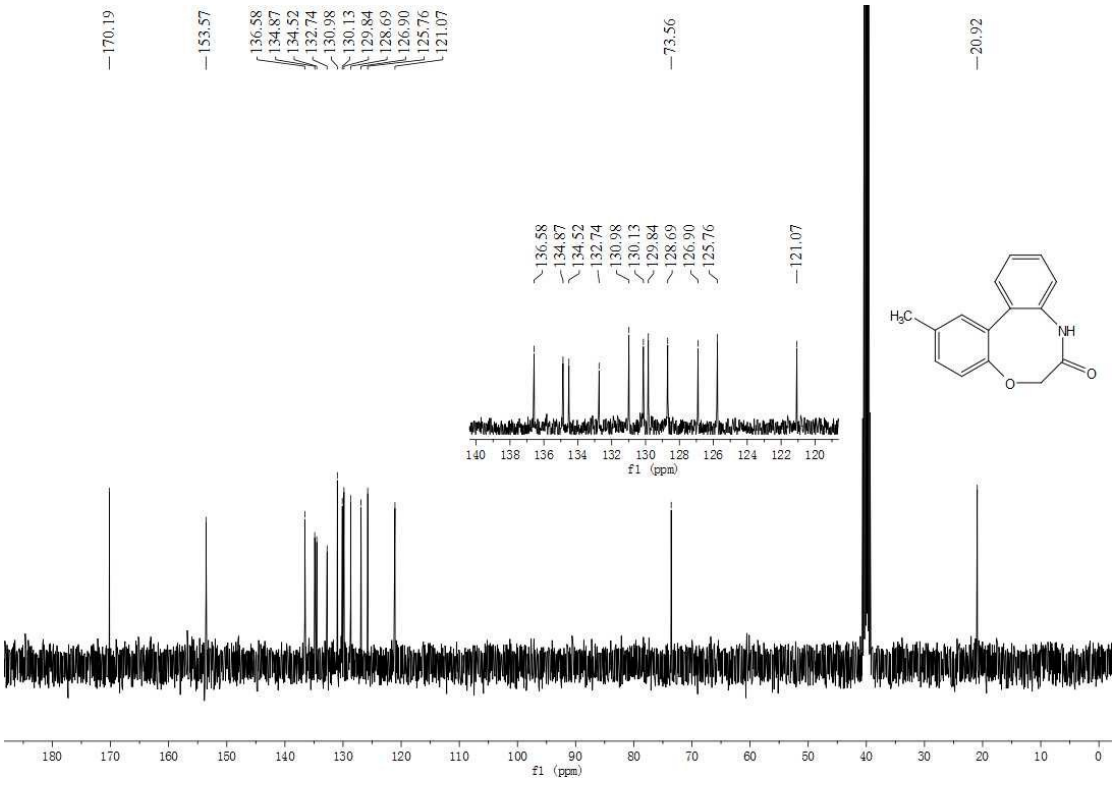




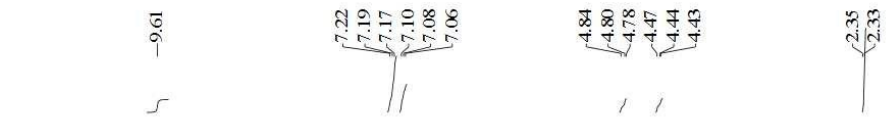
9.^{1}H and ^{13}C NMR spectra for 8-azaprotosappanin A and derivatives (2)

NMR spectra of **2a**

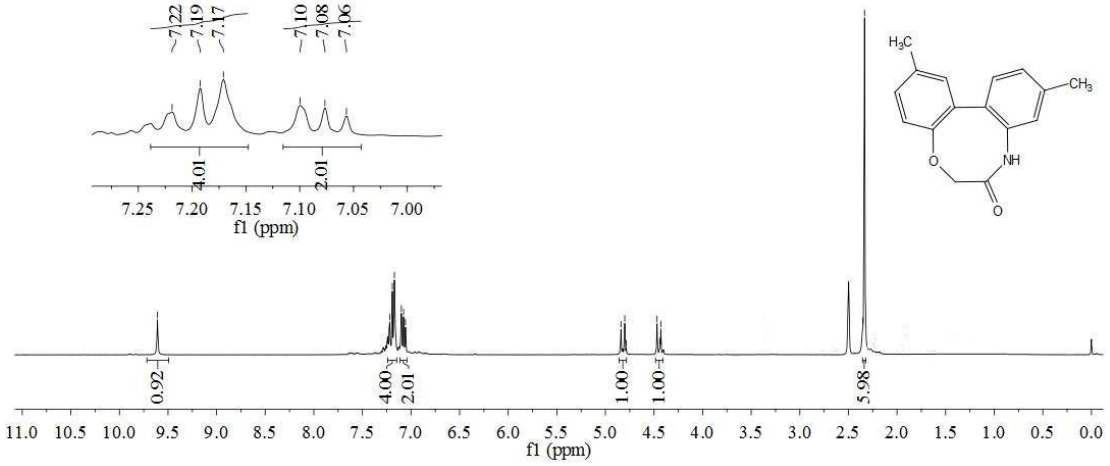


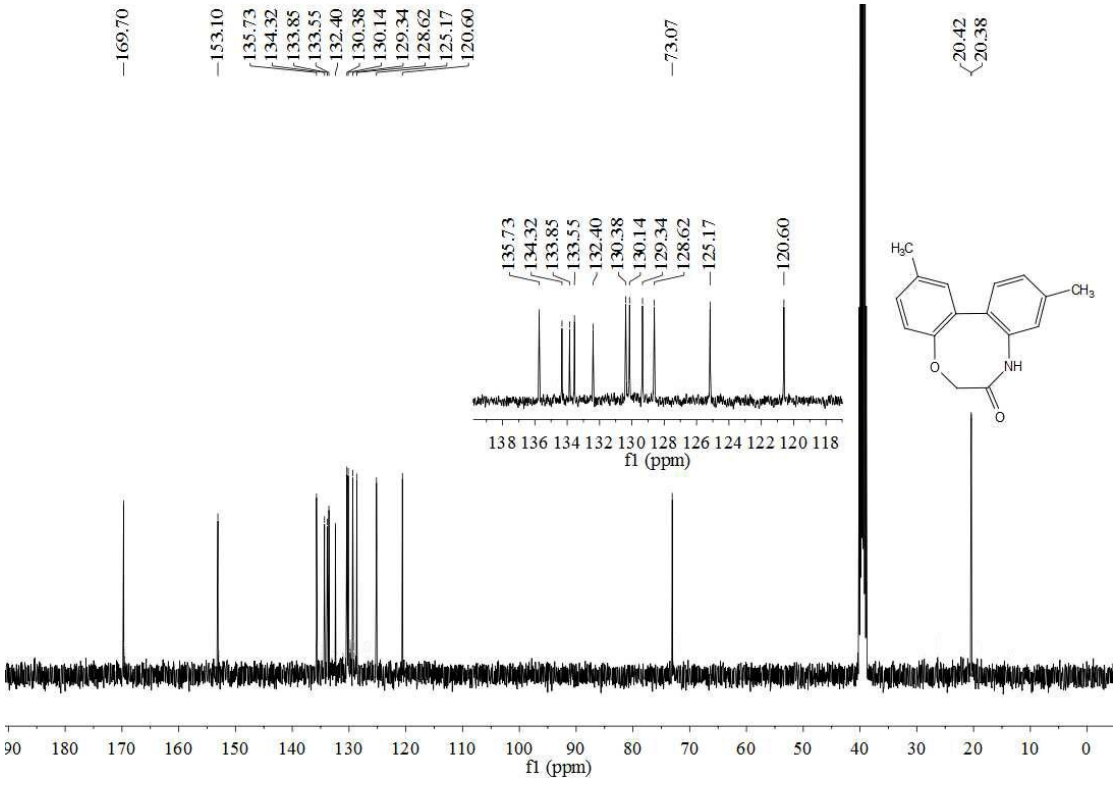


NMR spectra of **2b**

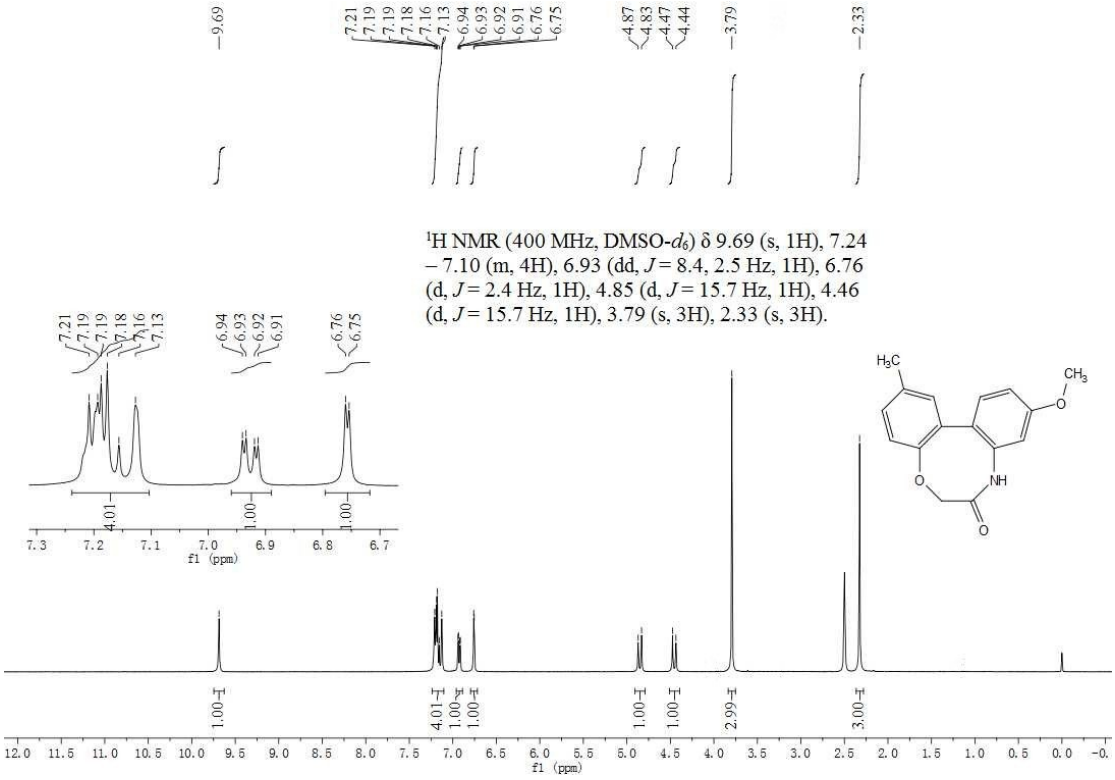


^{1}H NMR (400 MHz, DMSO-d_6) δ 9.61 (s, 0H), 7.24 – 7.15 (m, 2H), 7.12 – 7.04 (m, 1H), 4.82 (d, J = 15.7 Hz, 1H), 4.48 – 4.41 (m, 1H), 2.33 (s, 3H).

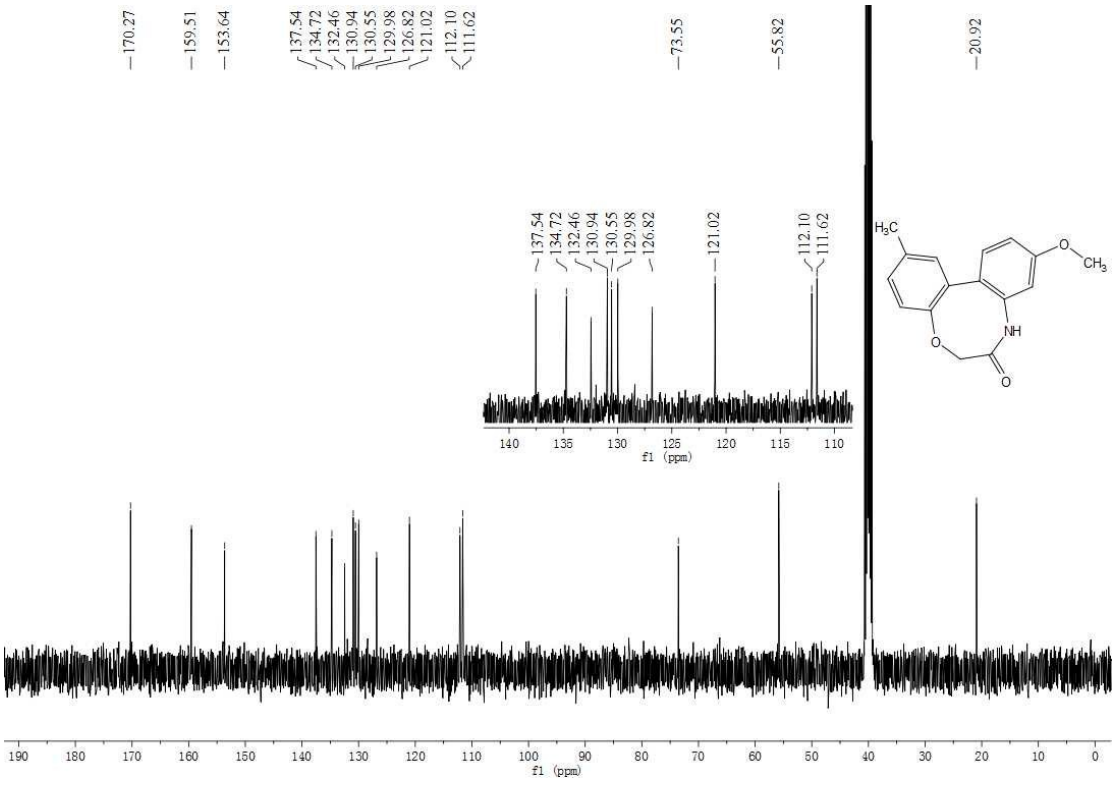




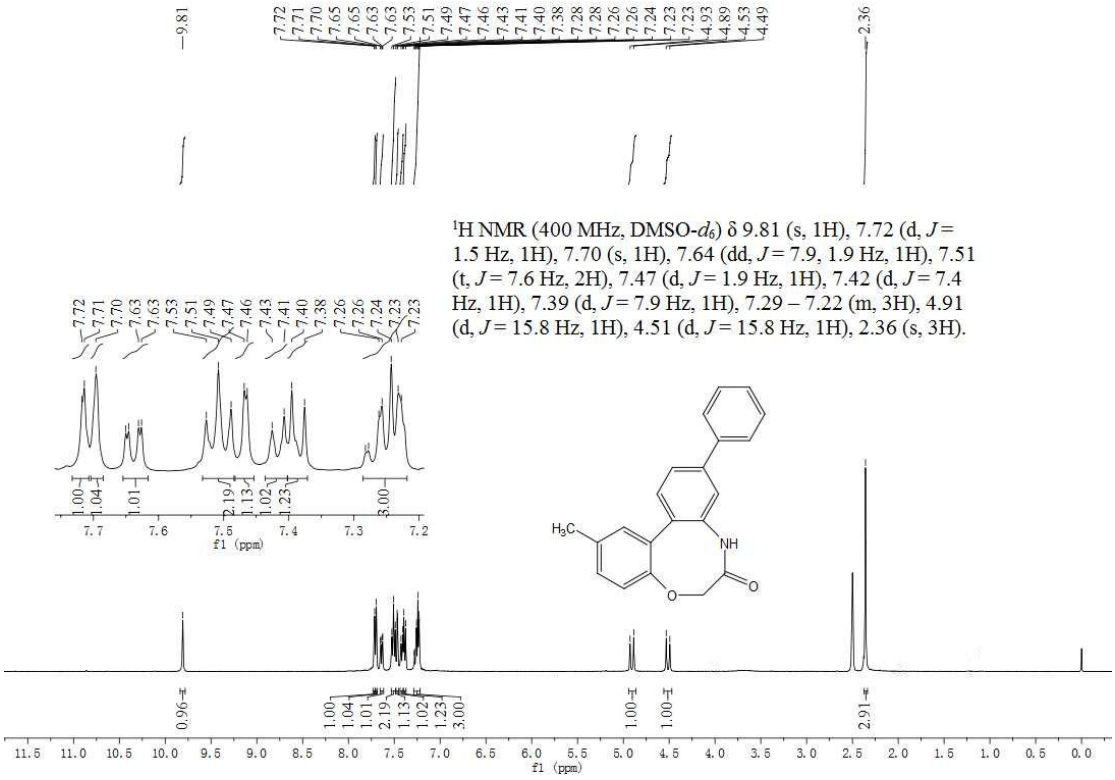
NMR spectra of **2c**



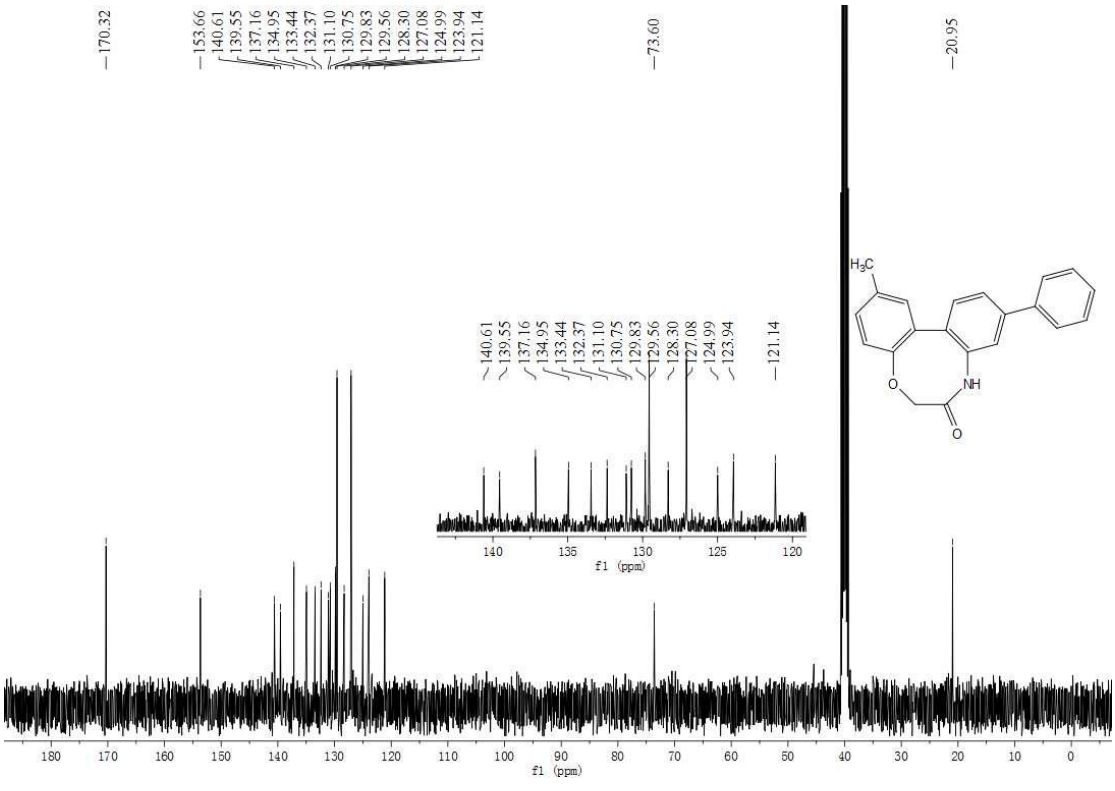
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.69 (s, 1H), 7.24 – 7.10 (m, 4H), 6.93 (dd, J = 8.4, 2.5 Hz, 1H), 6.76 (d, J = 2.4 Hz, 1H), 4.85 (d, J = 15.7 Hz, 1H), 4.46 (d, J = 15.7 Hz, 1H), 3.79 (s, 3H), 2.33 (s, 3H).



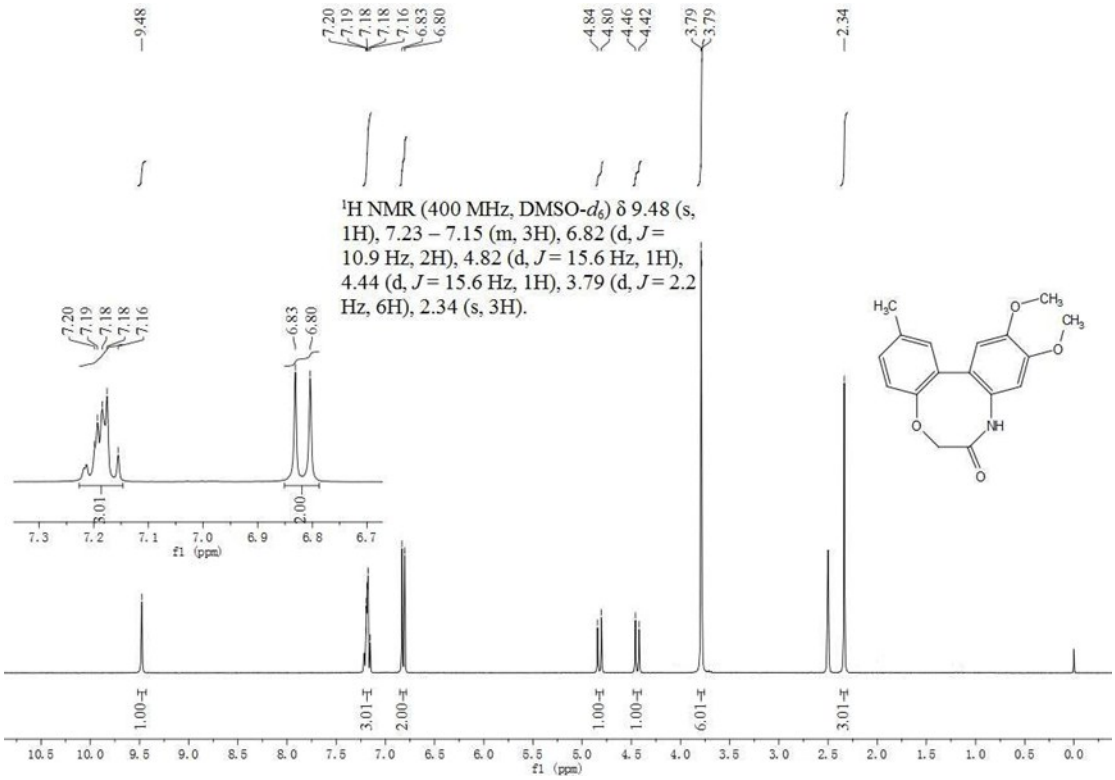
NMR spectra of **2d**

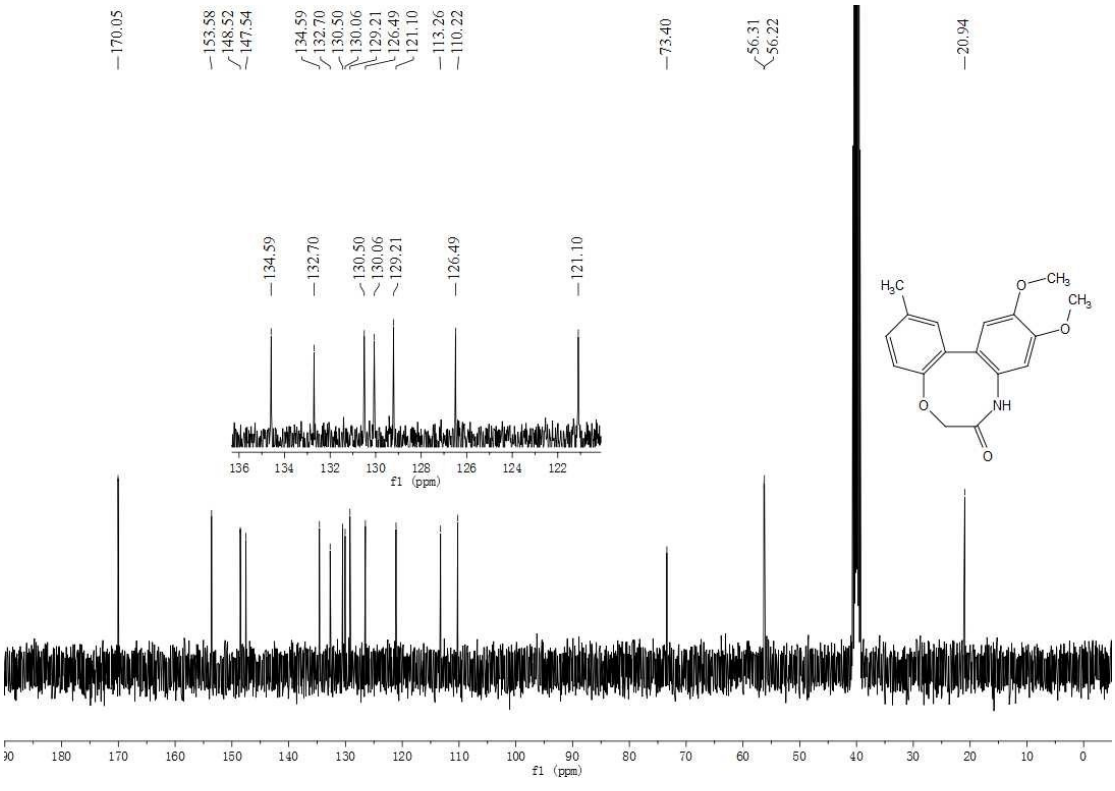


^{1}H NMR (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 7.72 (d, J = 1.5 Hz, 1H), 7.70 (s, 1H), 7.64 (dd, J = 7.9, 1.9 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.47 (d, J = 1.9 Hz, 1H), 7.42 (d, J = 7.4 Hz, 1H), 7.39 (d, J = 7.9 Hz, 1H), 7.29 – 7.22 (m, 3H), 4.91 (d, J = 15.8 Hz, 1H), 4.51 (d, J = 15.8 Hz, 1H), 2.36 (s, 3H).

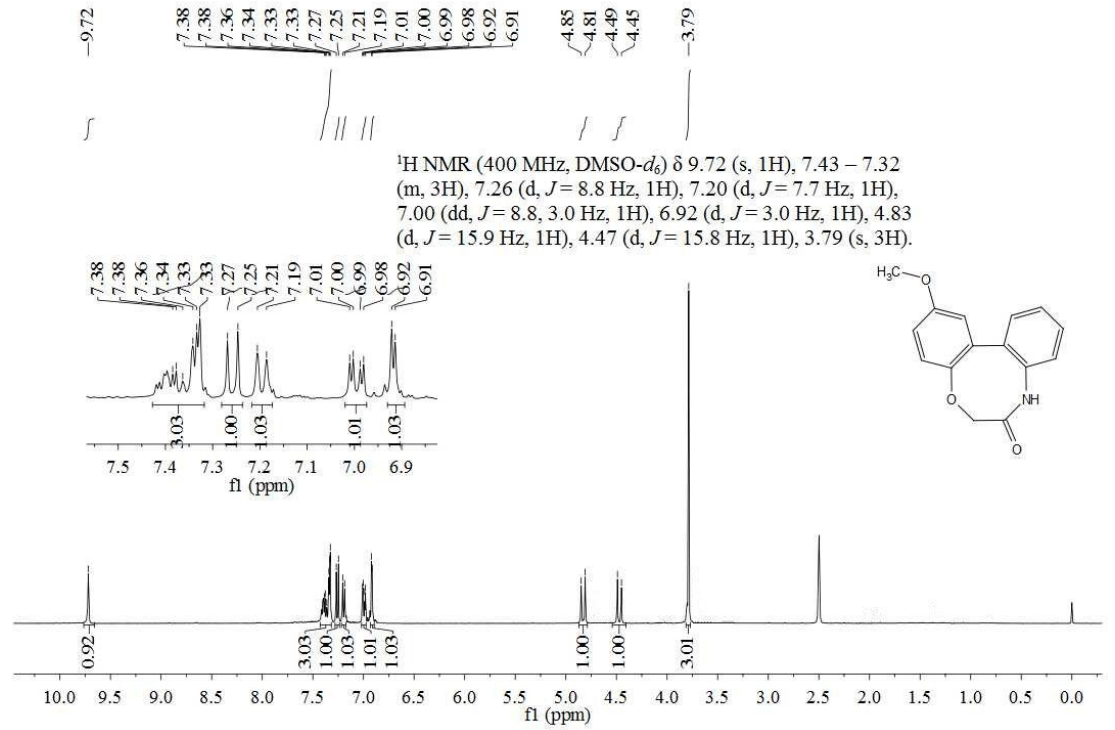


NMR spectra of **2e**

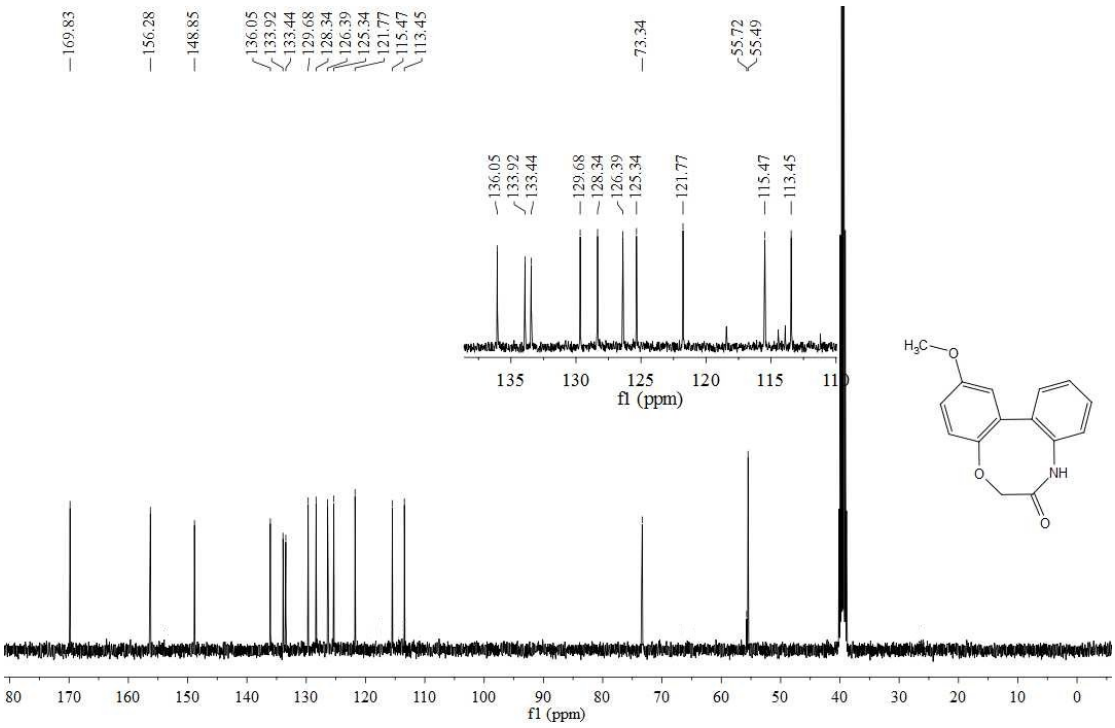




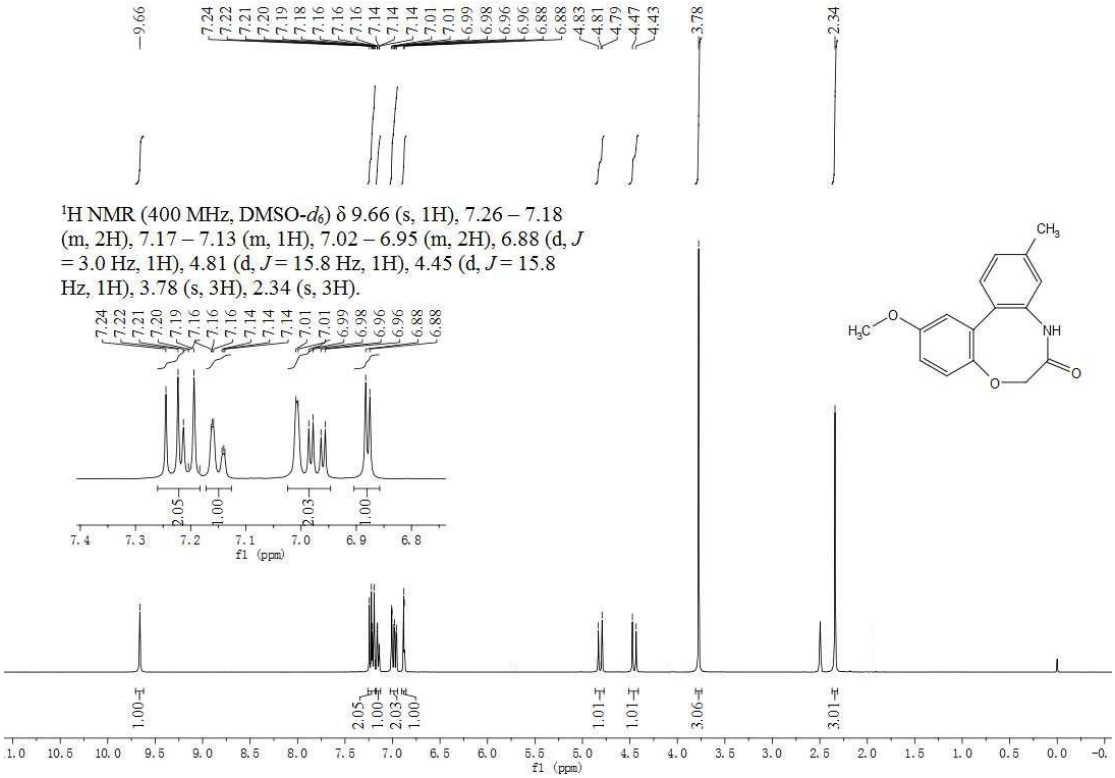
NMR spectra of **2f**



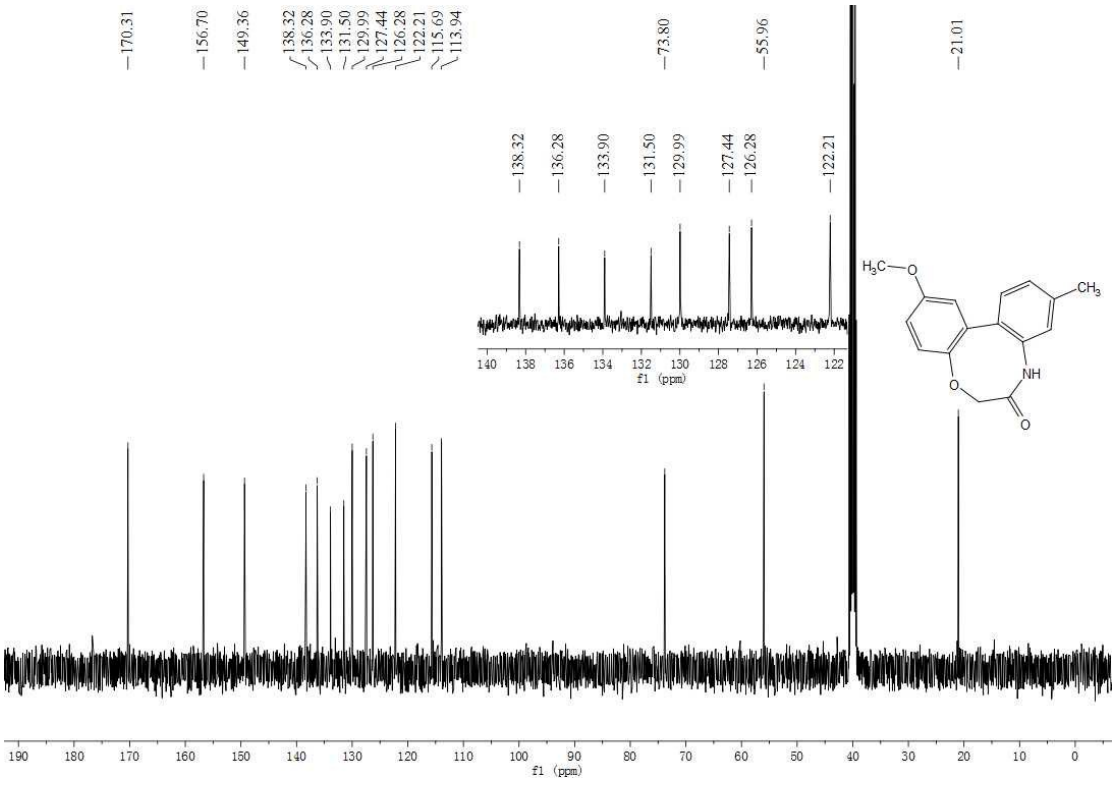
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.72 (s, 1H), 7.43 – 7.32 (m, 3H), 7.26 (d, J = 8.8 Hz, 1H), 7.20 (d, J = 7.7 Hz, 1H), 7.00 (dd, J = 8.8, 3.0 Hz, 1H), 6.92 (d, J = 3.0 Hz, 1H), 4.83 (d, J = 15.9 Hz, 1H), 4.47 (d, J = 15.8 Hz, 1H), 3.79 (s, 3H).



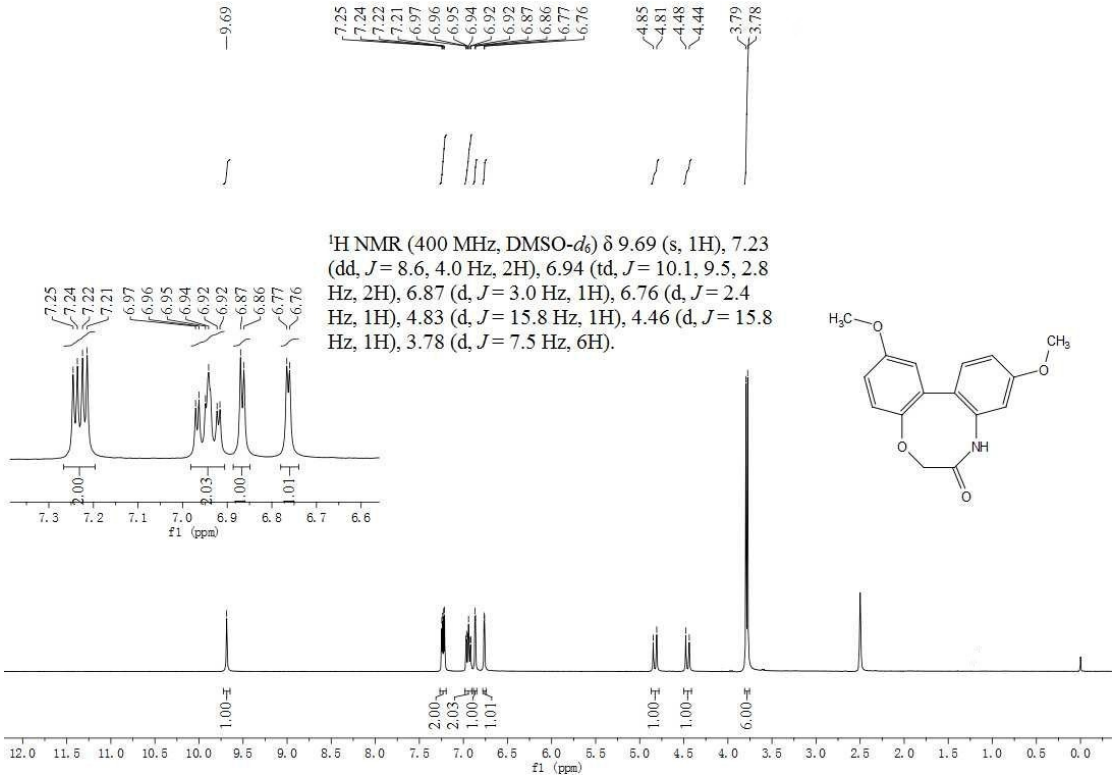
NMR spectra of **2g**

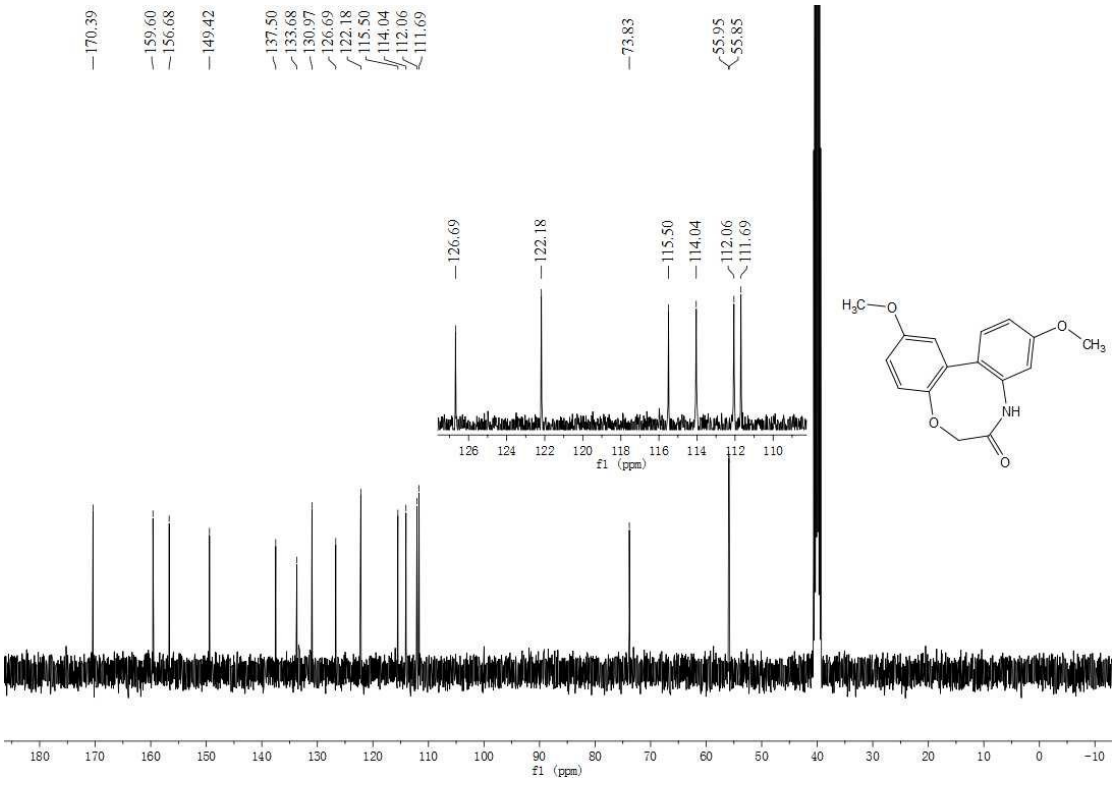


^{1}H NMR (400 MHz, DMSO-d_6) δ 9.66 (s, 1H), 7.26 – 7.18 (m, 2H), 7.17 – 7.13 (m, 1H), 7.02 – 6.95 (m, 2H), 6.88 (d, J = 3.0 Hz, 1H), 4.81 (d, J = 15.8 Hz, 1H), 4.45 (d, J = 15.8 Hz, 1H), 3.78 (s, 3H), 2.34 (s, 3H).

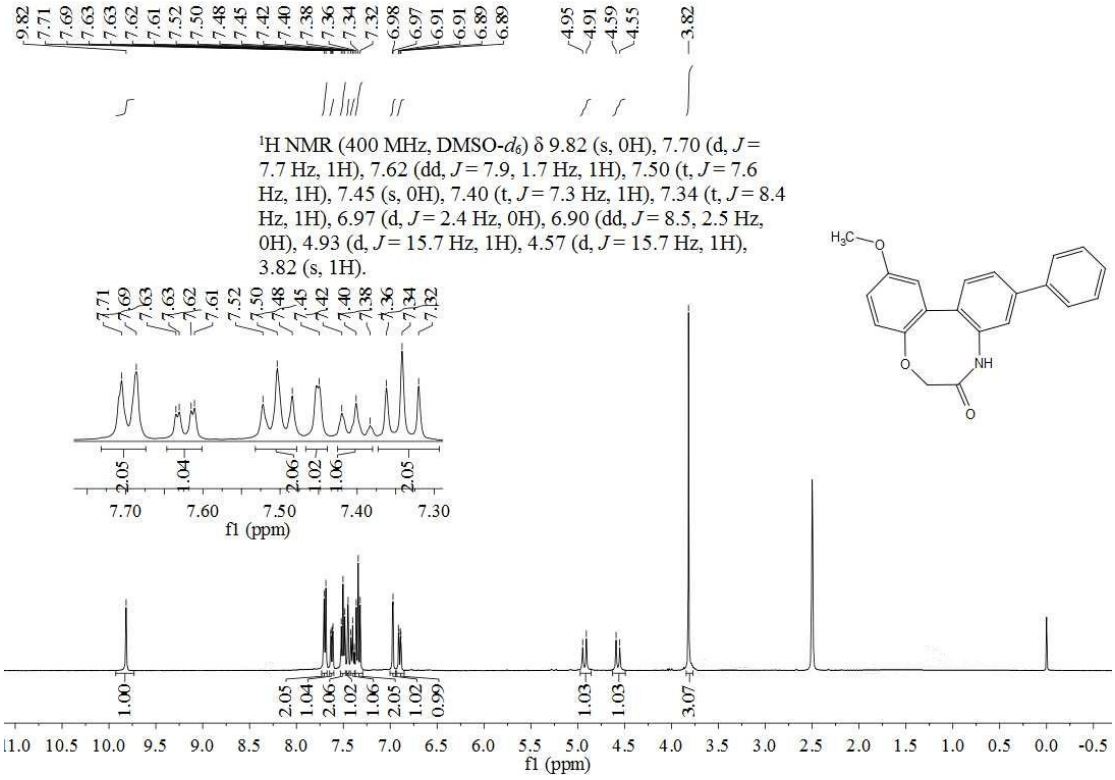


NMR spectra of **2h**

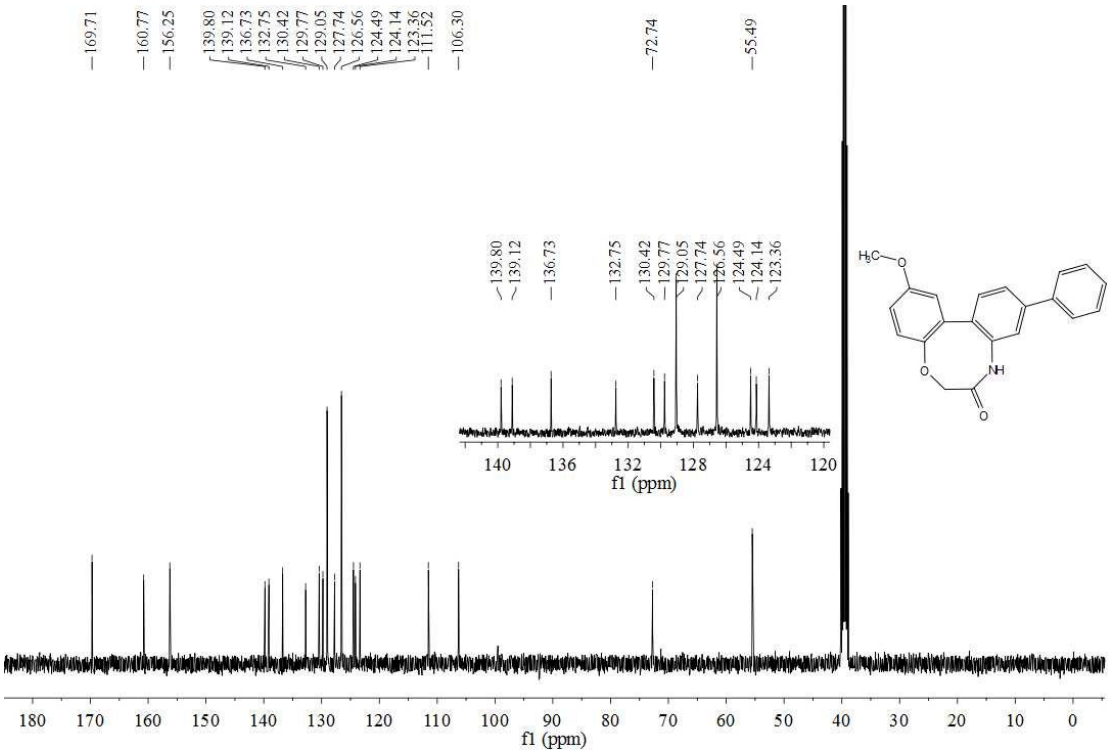




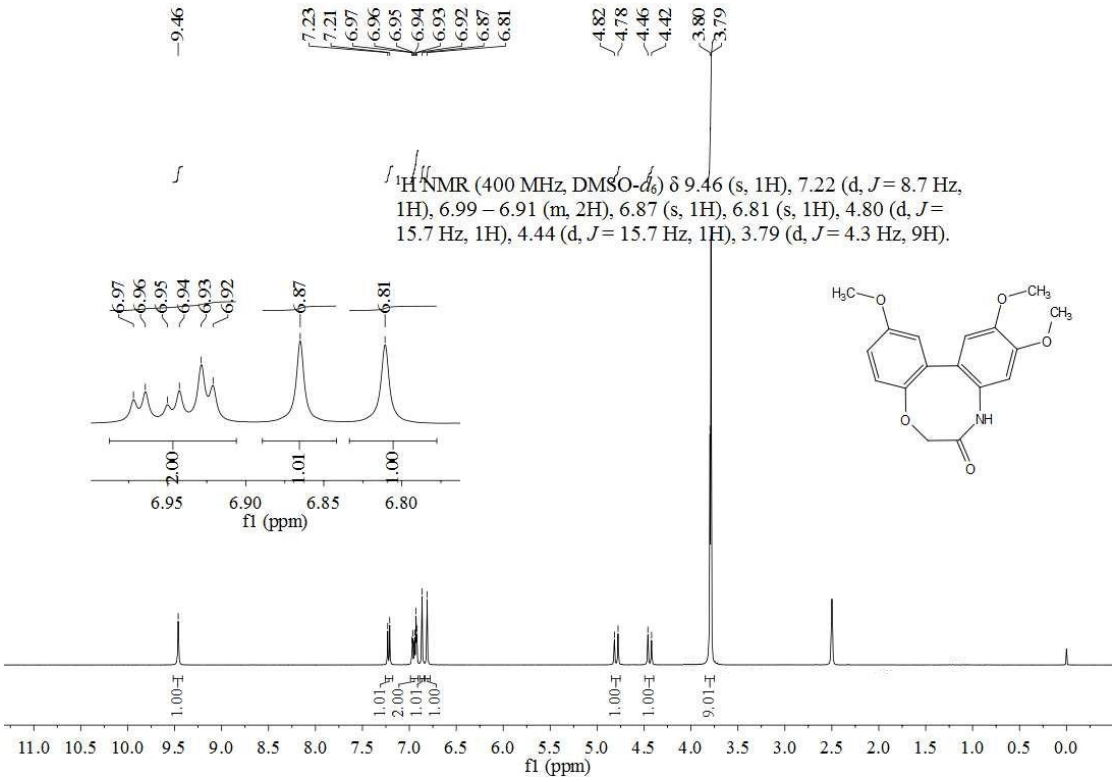
NMR spectra of **2i**

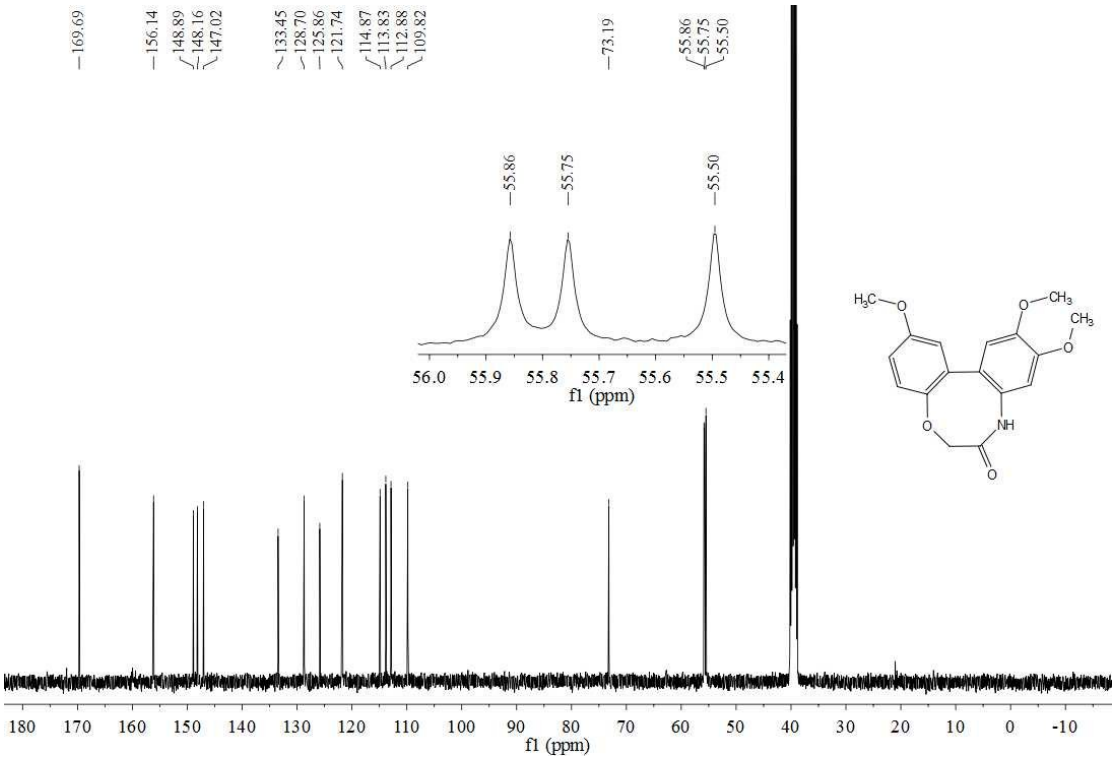


^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 0H), 7.70 (d, J = 7.7 Hz, 1H), 7.62 (dd, J = 7.9, 1.7 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.45 (s, 0H), 7.40 (t, J = 7.3 Hz, 1H), 7.34 (t, J = 8.4 Hz, 1H), 6.97 (d, J = 2.4 Hz, 0H), 6.90 (dd, J = 8.5, 2.5 Hz, 0H), 4.93 (d, J = 15.7 Hz, 1H), 4.57 (d, J = 15.7 Hz, 1H), 3.82 (s, 1H).

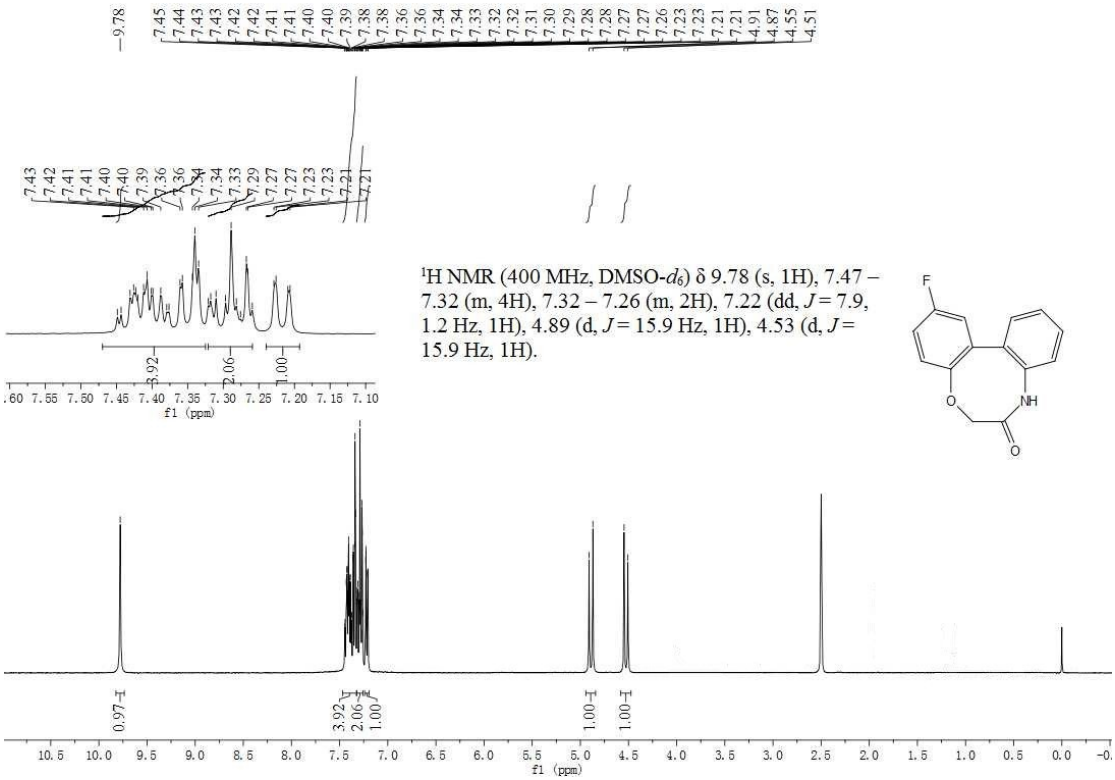


NMR spectra of **2j**

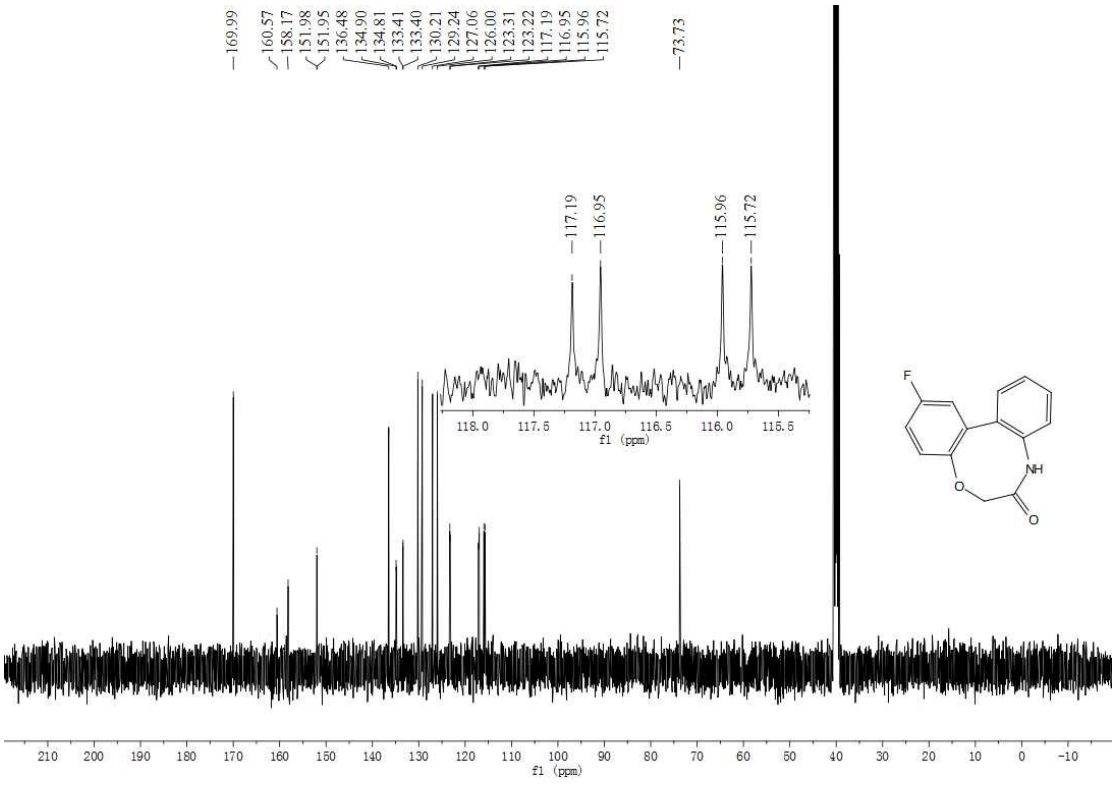




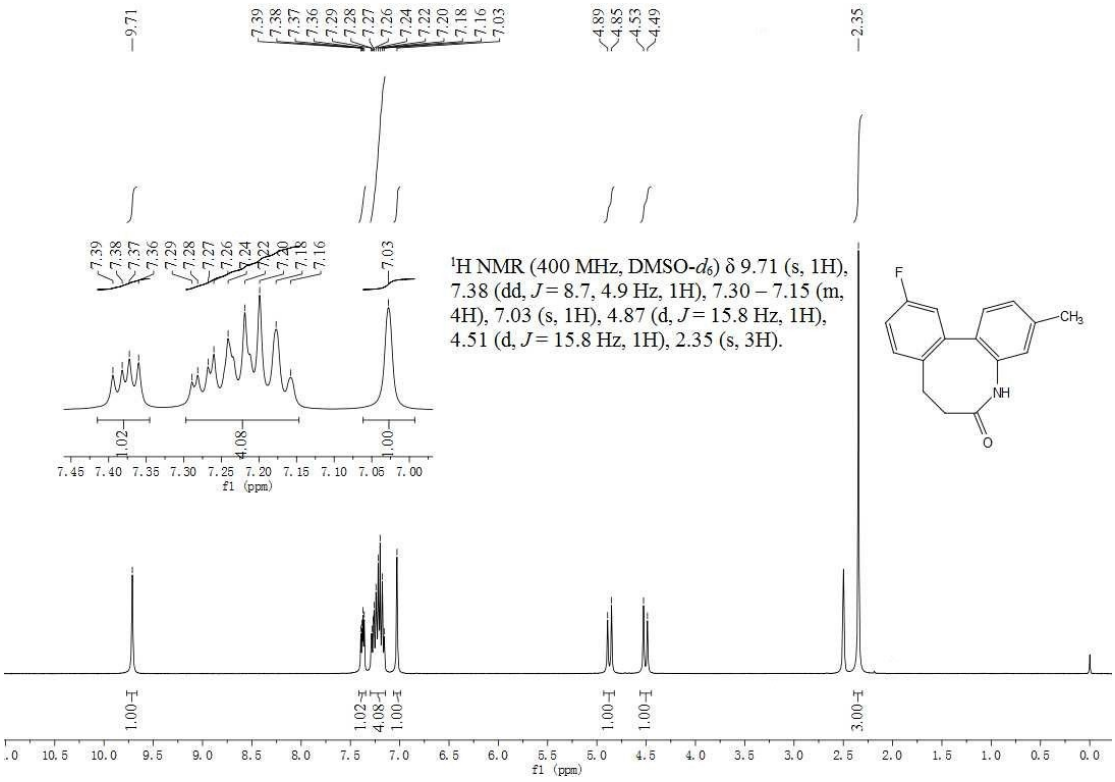
NMR spectra of **2k**



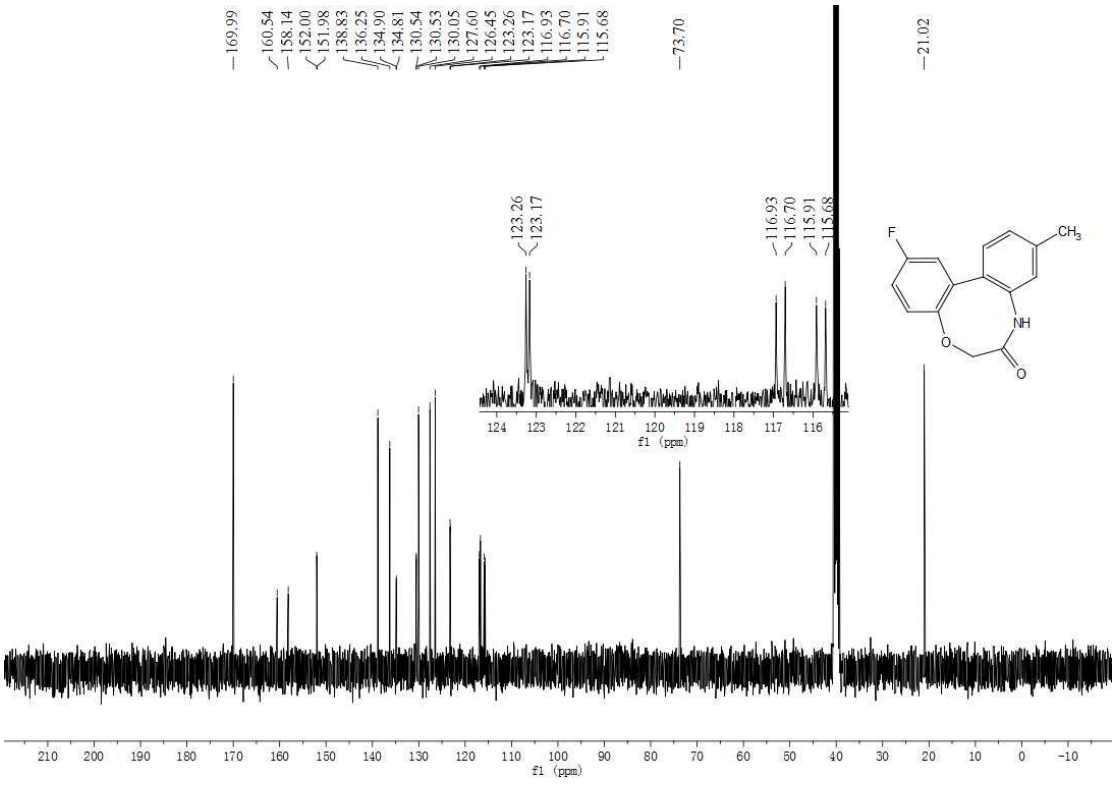
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 7.47 – 7.32 (m, 4H), 7.32 – 7.26 (m, 2H), 7.22 (dd, J = 7.9, 1.2 Hz, 1H), 4.89 (d, J = 15.9 Hz, 1H), 4.53 (d, J = 15.9 Hz, 1H).



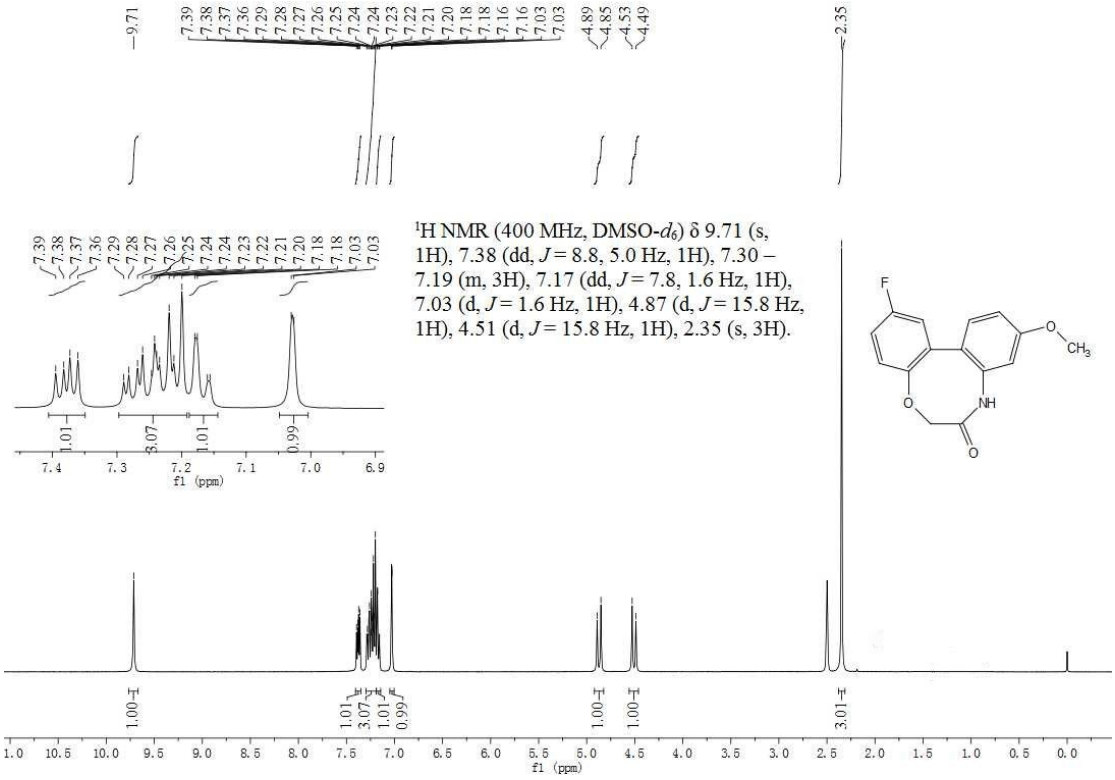
NMR spectra of **2l**



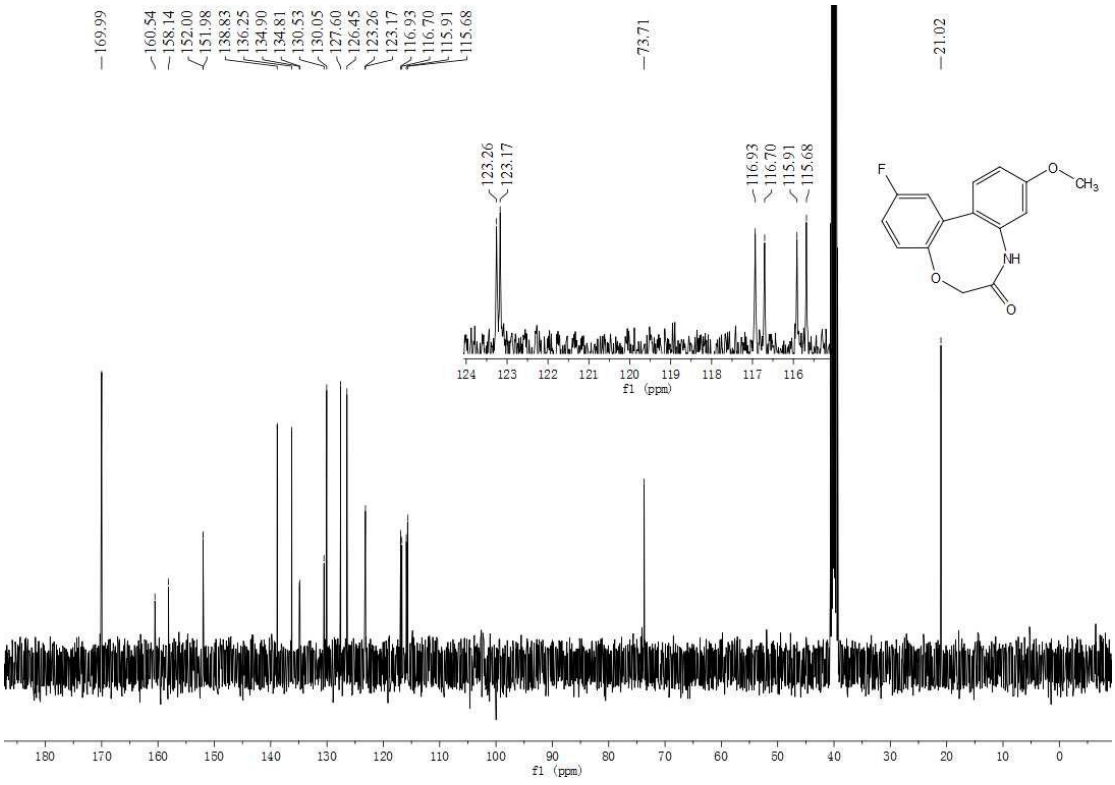
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.71 (s, 1H), 7.38 (dd, J = 8.7, 4.9 Hz, 1H), 7.30 – 7.15 (m, 4H), 7.03 (s, 1H), 4.87 (d, J = 15.8 Hz, 1H), 4.51 (d, J = 15.8 Hz, 1H), 2.35 (s, 3H).



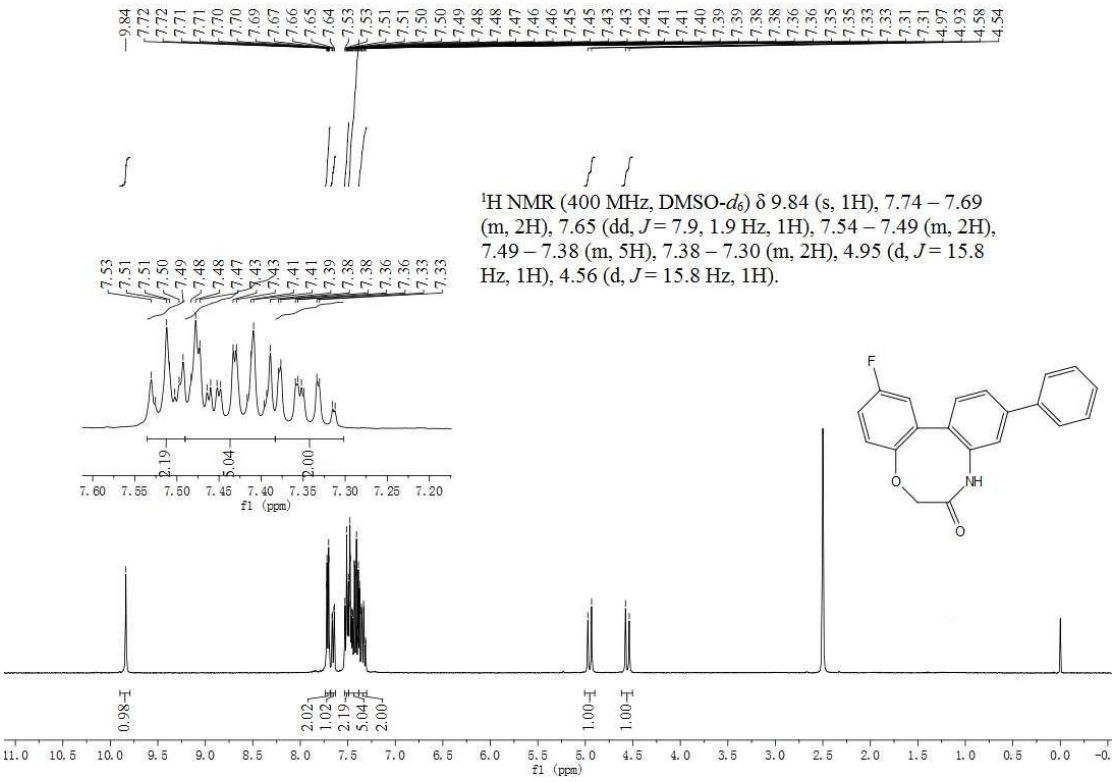
NMR spectra of **2m**



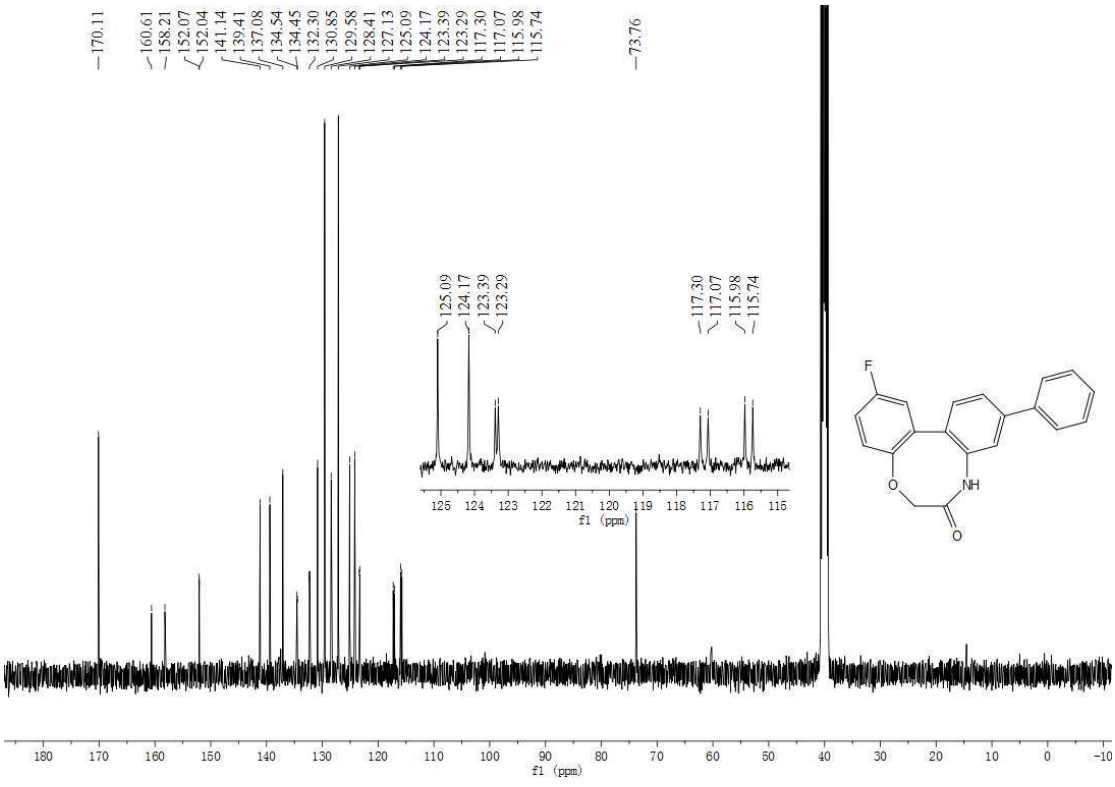
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.71 (s, 1H), 7.38 (dd, J = 8.8, 5.0 Hz, 1H), 7.30 – 7.19 (m, 3H), 7.17 (dd, J = 7.8, 1.6 Hz, 1H), 7.03 (d, J = 1.6 Hz, 1H), 4.87 (d, J = 15.8 Hz, 1H), 4.51 (d, J = 15.8 Hz, 1H), 2.35 (s, 3H).



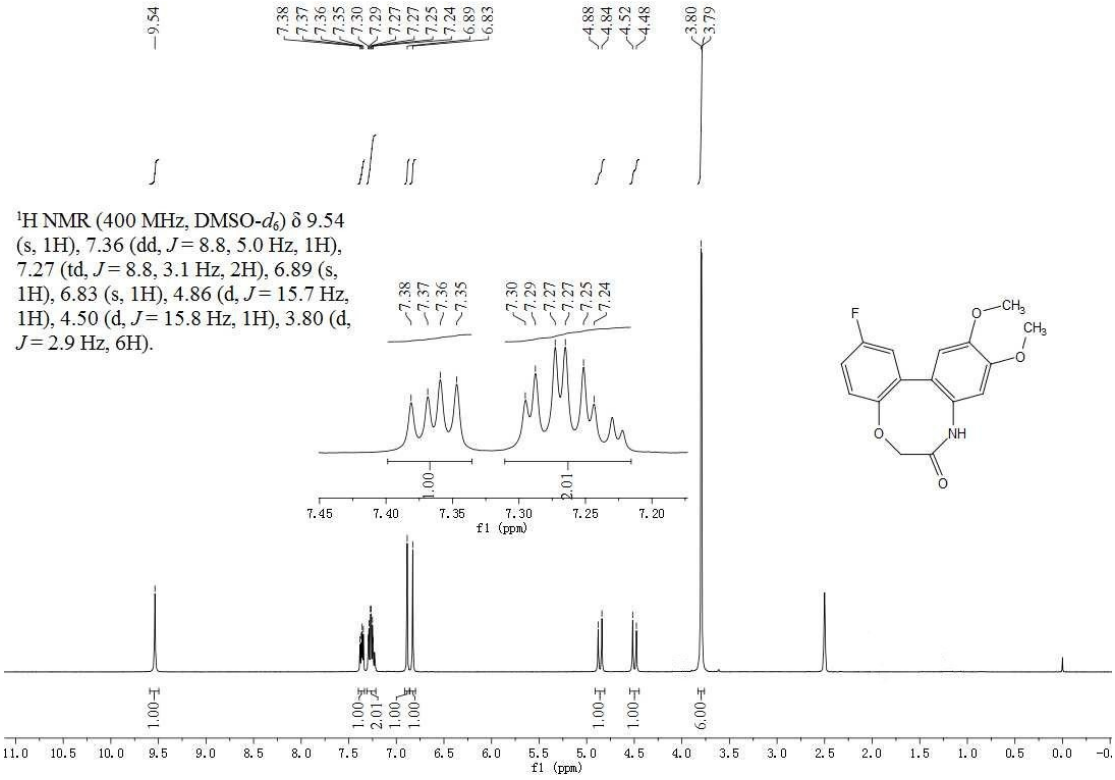
NMR spectra of **2n**

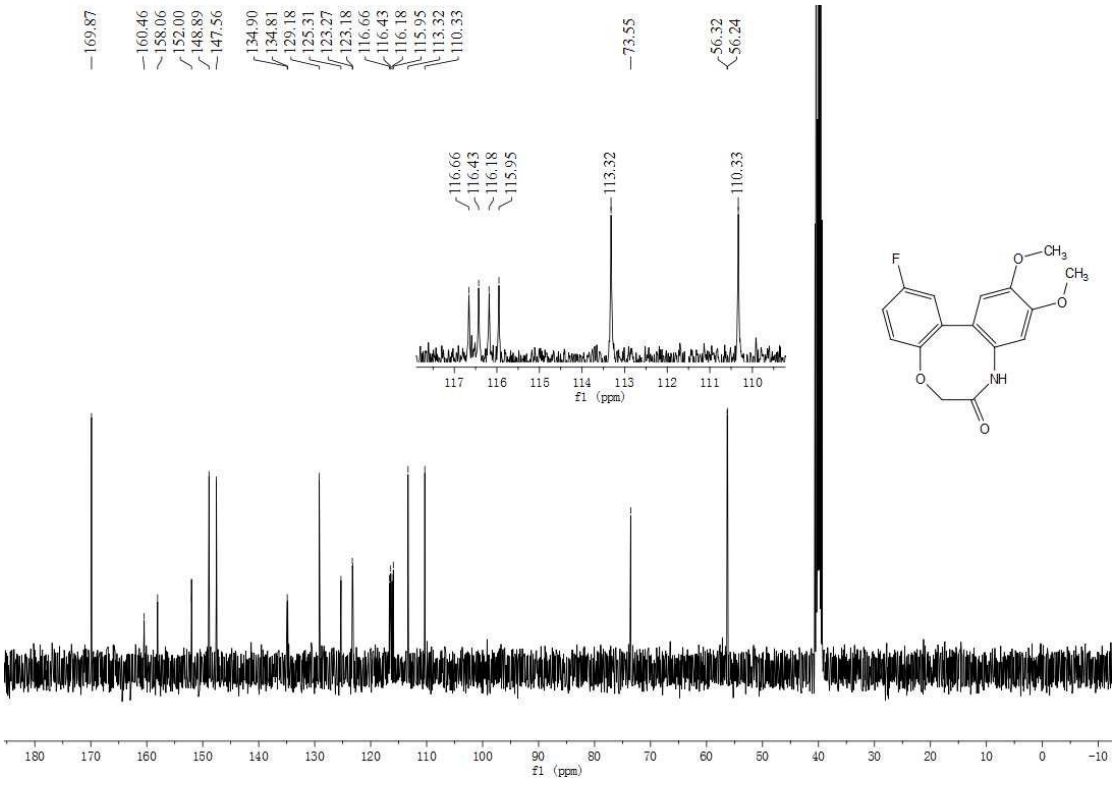


^{1}H NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 7.74 – 7.69 (m, 2H), 7.65 (dd, J = 7.9, 1.9 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.49 – 7.38 (m, 5H), 7.38 – 7.30 (m, 2H), 4.95 (d, J = 15.8 Hz, 1H), 4.56 (d, J = 15.8 Hz, 1H).



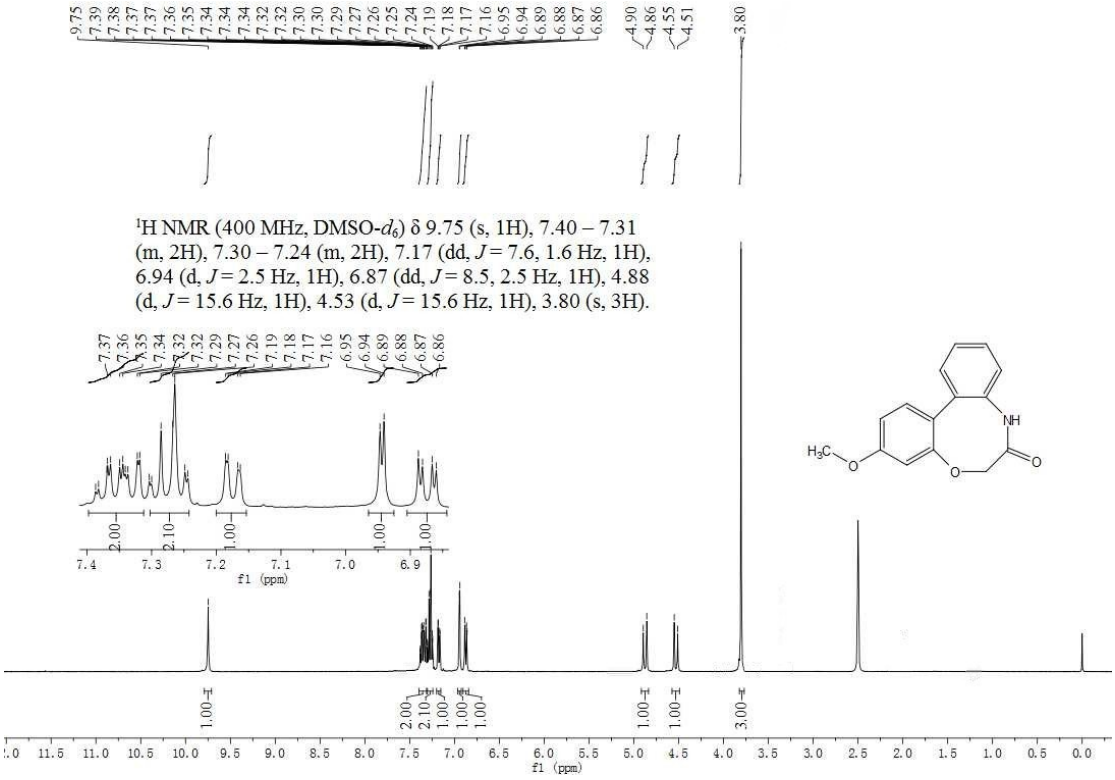
NMR spectra of **2o**

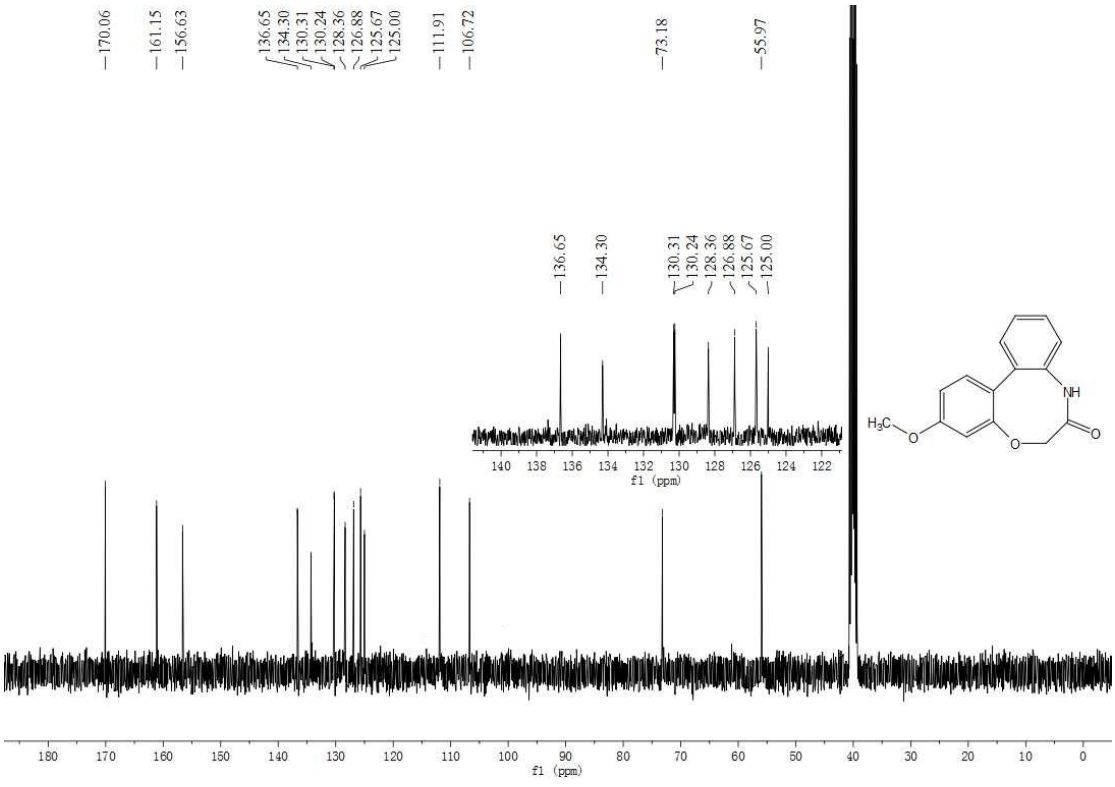




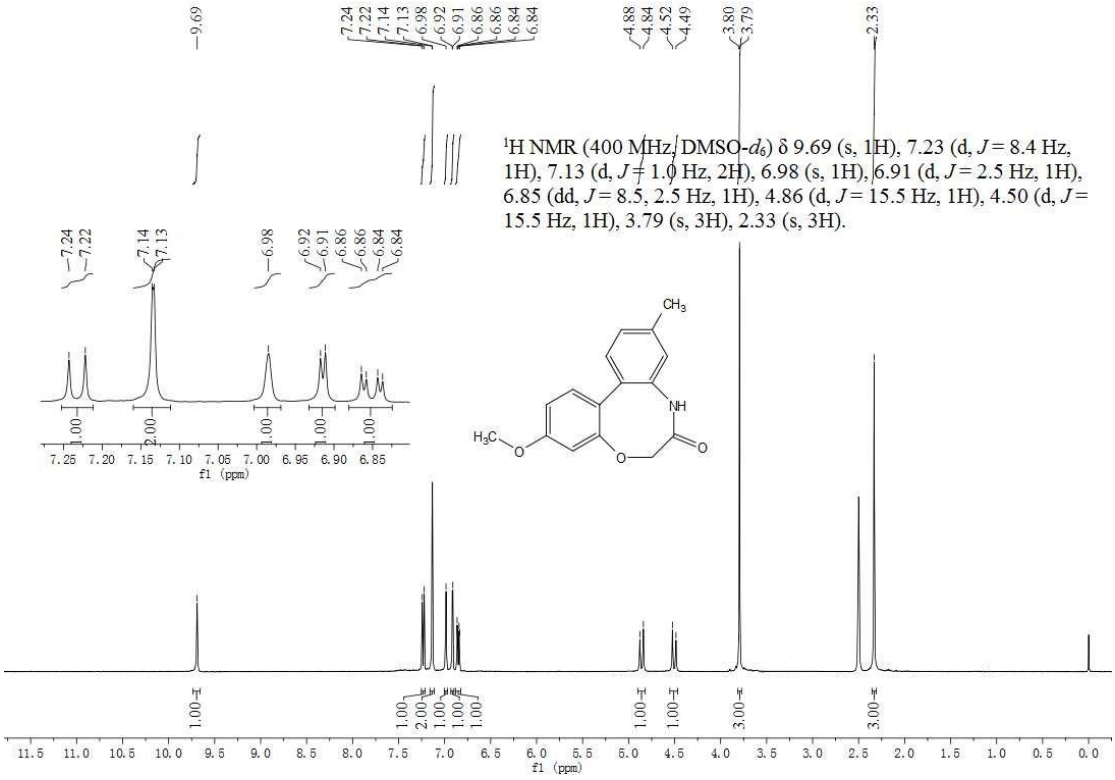
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.54 (s, 1H), 7.36 (dd, J = 8.8, 5.0 Hz, 1H), 7.27 (td, J = 8.8, 3.1 Hz, 2H), 6.89 (s, 1H), 6.83 (s, 1H), 4.86 (d, J = 15.7 Hz, 1H), 4.50 (d, J = 15.8 Hz, 1H), 3.80 (d, J = 2.9 Hz, 6H).

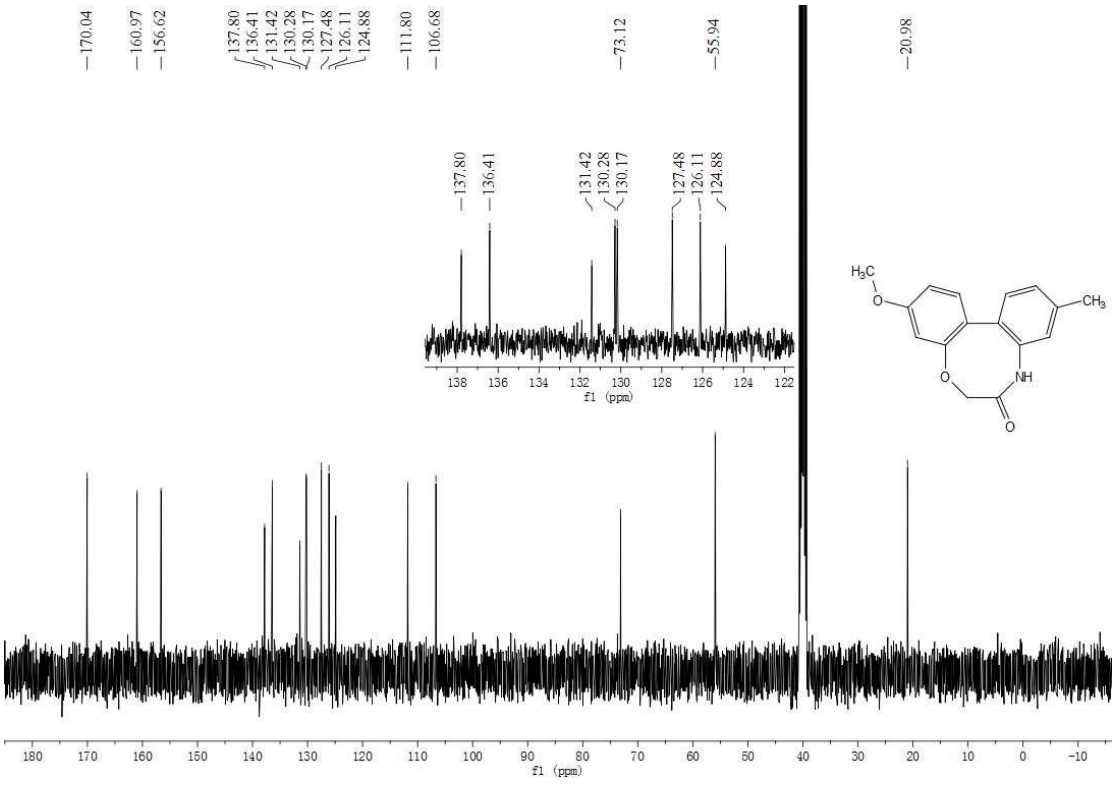
NMR spectra of **2p**



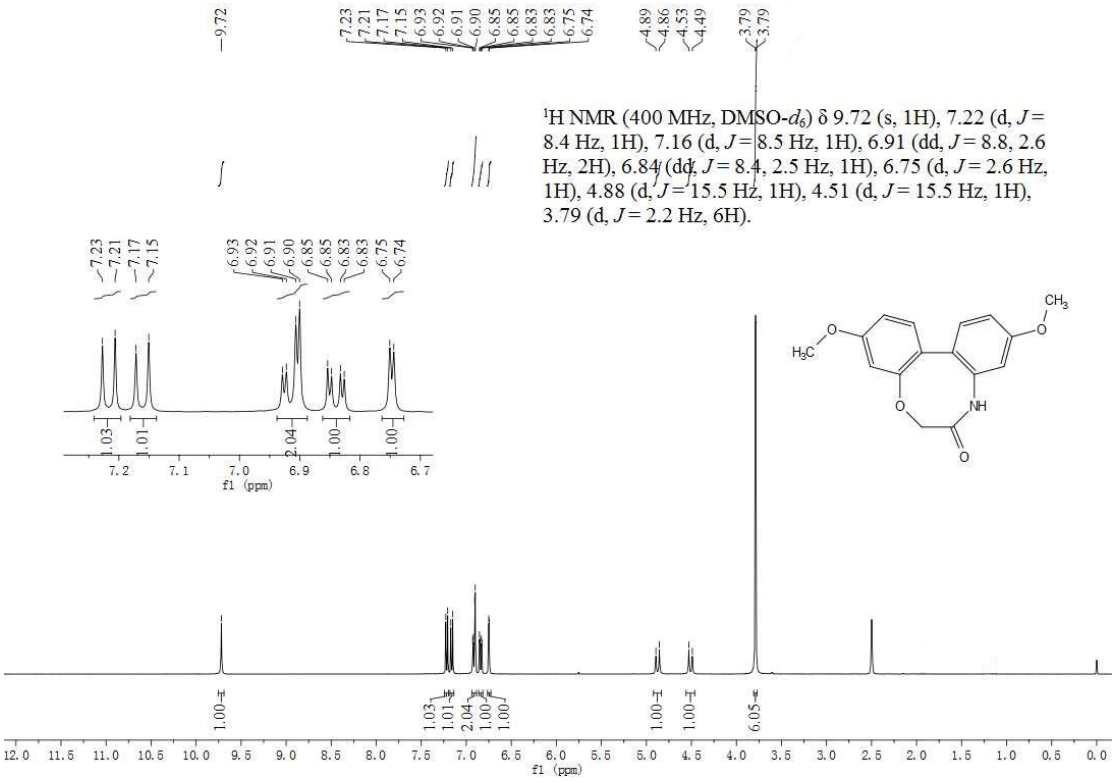


NMR spectra of **2q**

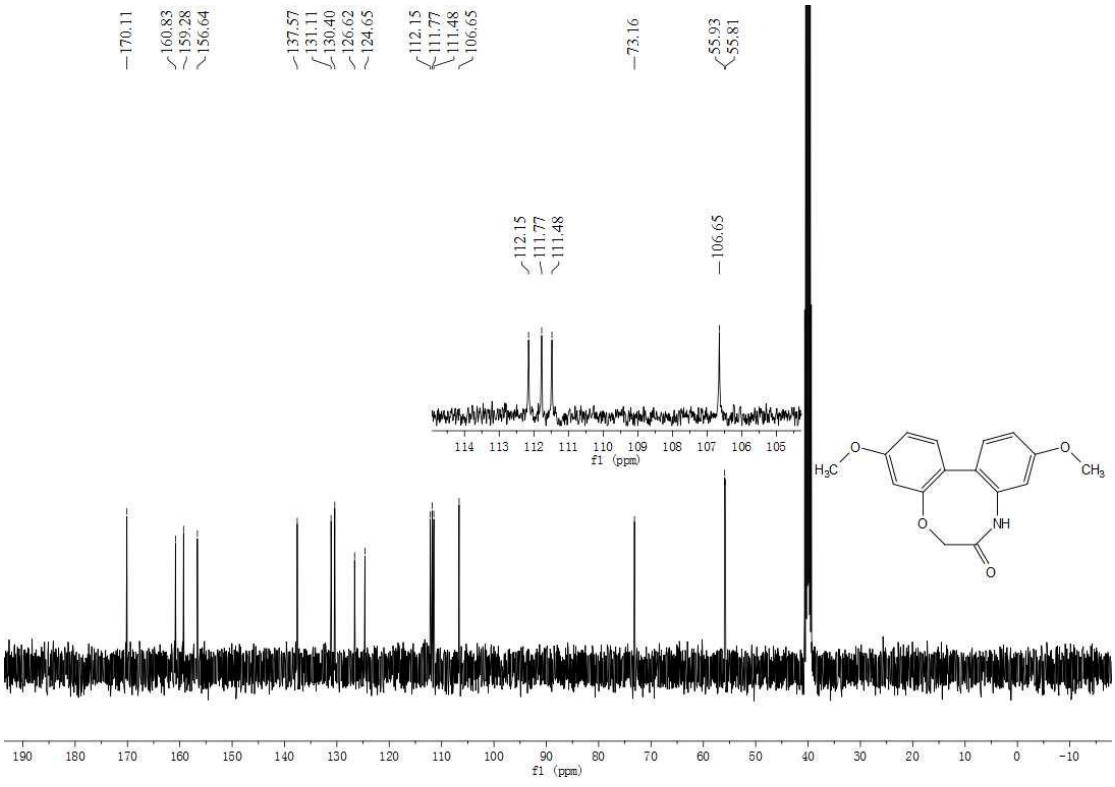




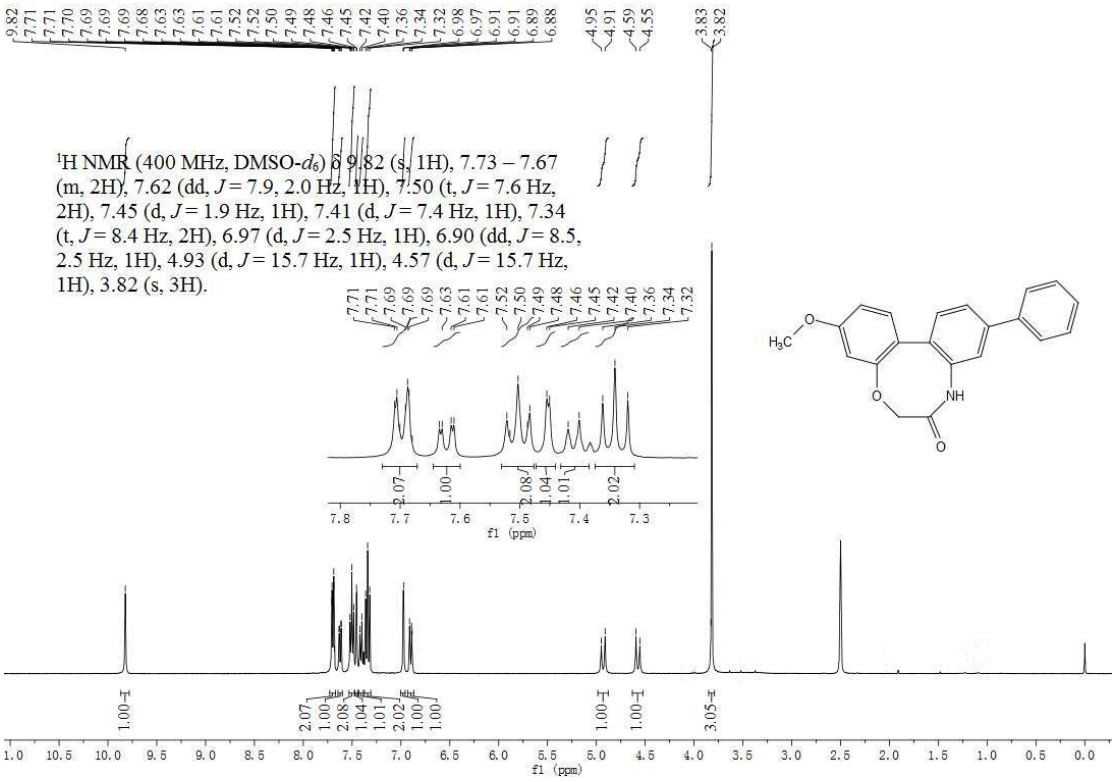
NMR spectra of **2r**



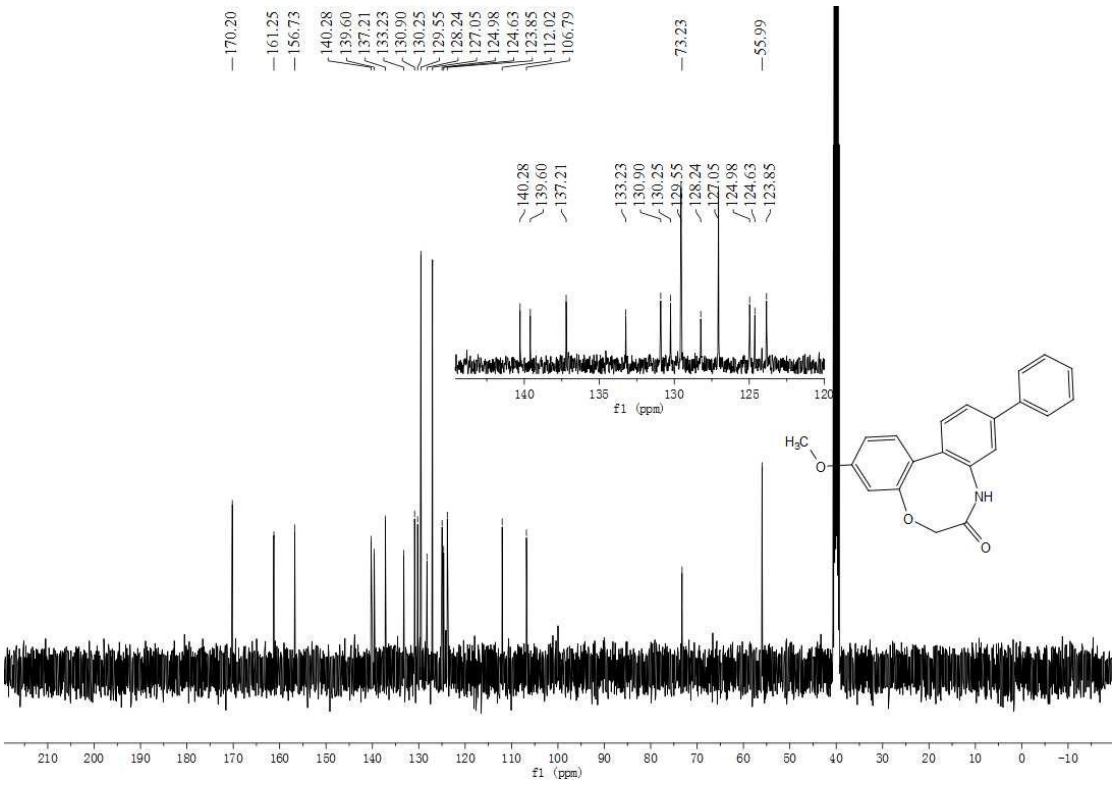
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.72 (s, 1H), 7.22 (d, J = 8.4 Hz, 1H), 7.16 (d, J = 8.5 Hz, 1H), 6.91 (dd, J = 8.8, 2.6 Hz, 2H), 6.84 (dd, J = 8.4, 2.5 Hz, 1H), 6.75 (d, J = 2.6 Hz, 1H), 4.88 (d, J = 15.5 Hz, 1H), 4.51 (d, J = 15.5 Hz, 1H), 3.79 (d, J = 2.2 Hz, 6H).



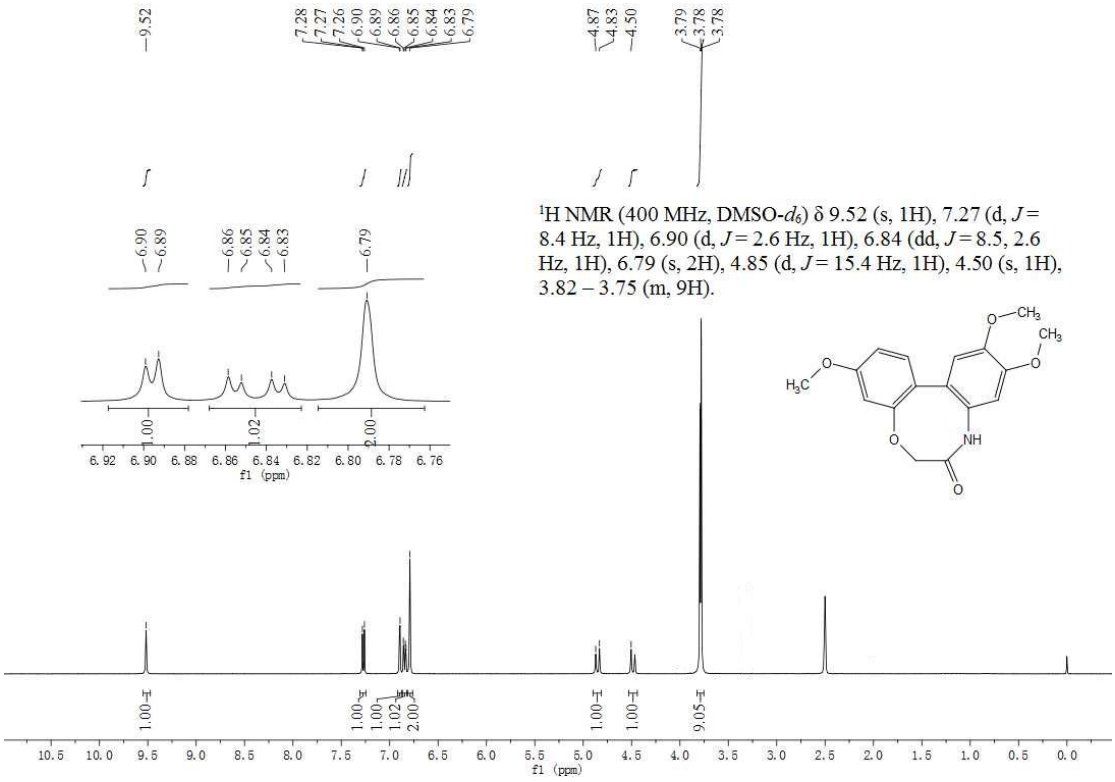
NMR spectra of **2s**



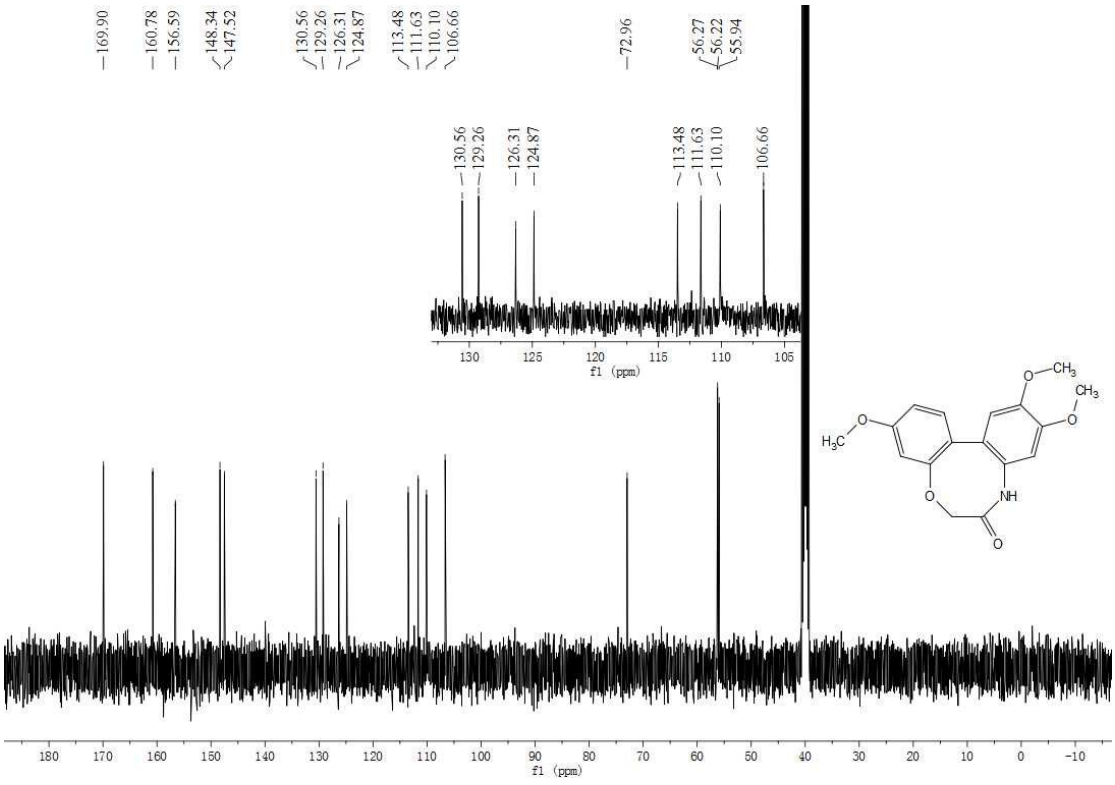
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.73 – 7.67 (m, 2H), 7.62 (dd, J = 7.9, 2.0 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.45 (d, J = 1.9 Hz, 1H), 7.41 (d, J = 7.4 Hz, 1H), 7.34 (t, J = 8.4 Hz, 2H), 6.97 (d, J = 2.5 Hz, 1H), 6.90 (dd, J = 8.5, 2.5 Hz, 1H), 4.93 (d, J = 15.7 Hz, 1H), 4.57 (d, J = 15.7 Hz, 1H), 3.82 (s, 3H).



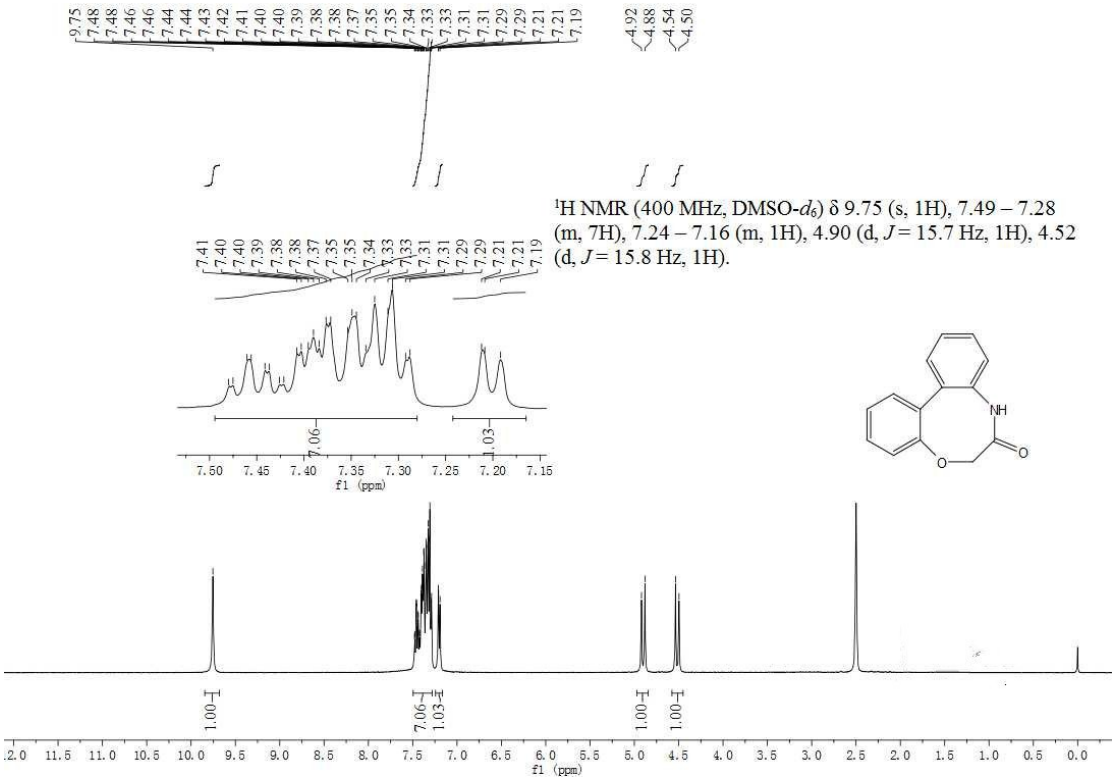
NMR spectra of **2t**



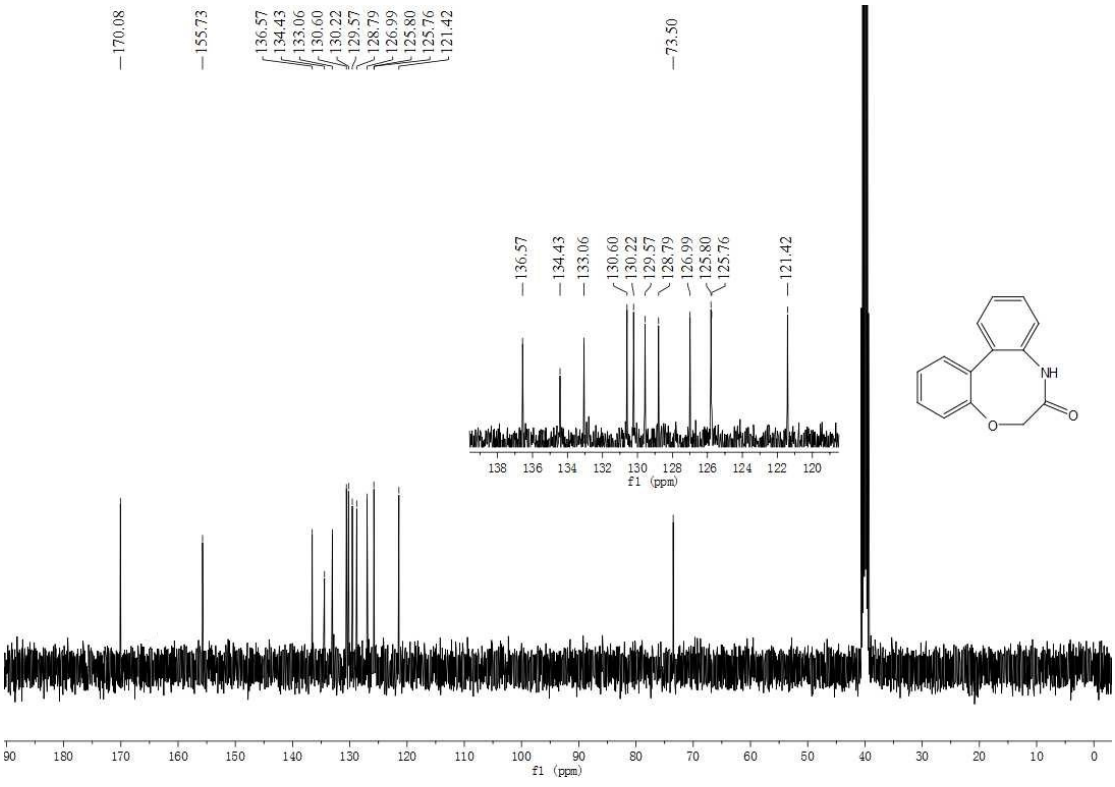
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.52 (s, 1H), 7.27 (d, J = 8.4 Hz, 1H), 6.90 (d, J = 2.6 Hz, 1H), 6.84 (dd, J = 8.5, 2.6 Hz, 1H), 6.79 (s, 2H), 4.85 (d, J = 15.4 Hz, 1H), 4.50 (s, 1H), 3.82 – 3.75 (m, 9H).



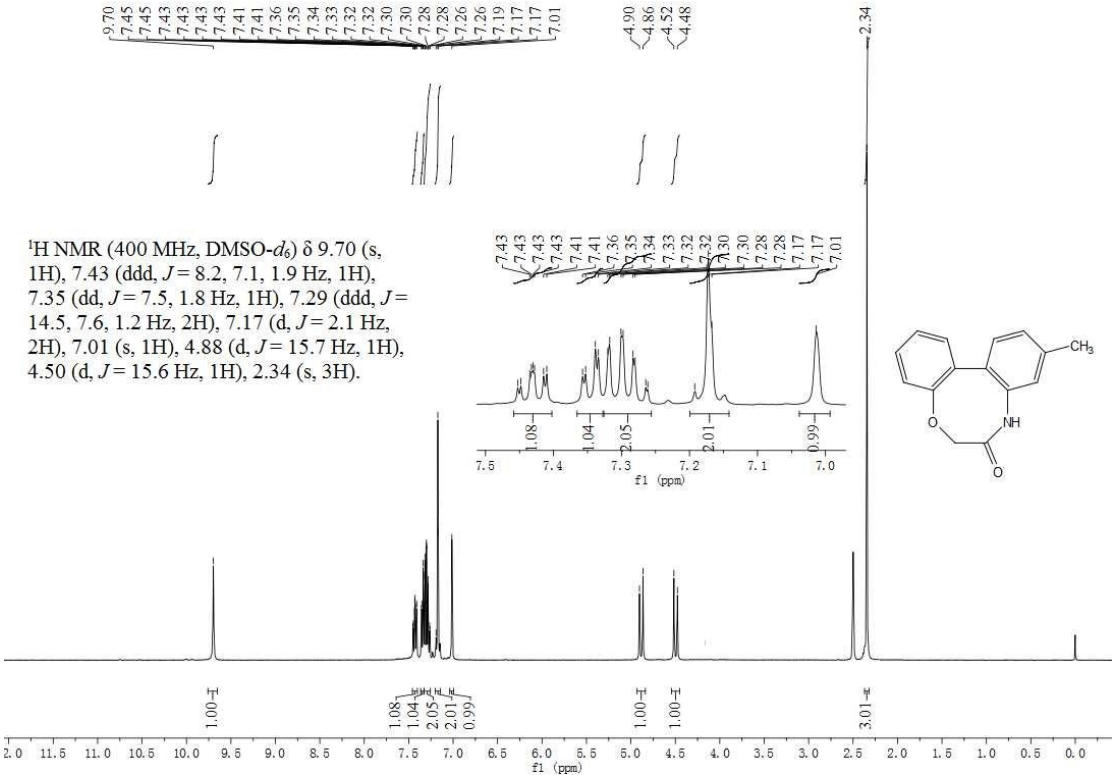
NMR spectra of **2u**



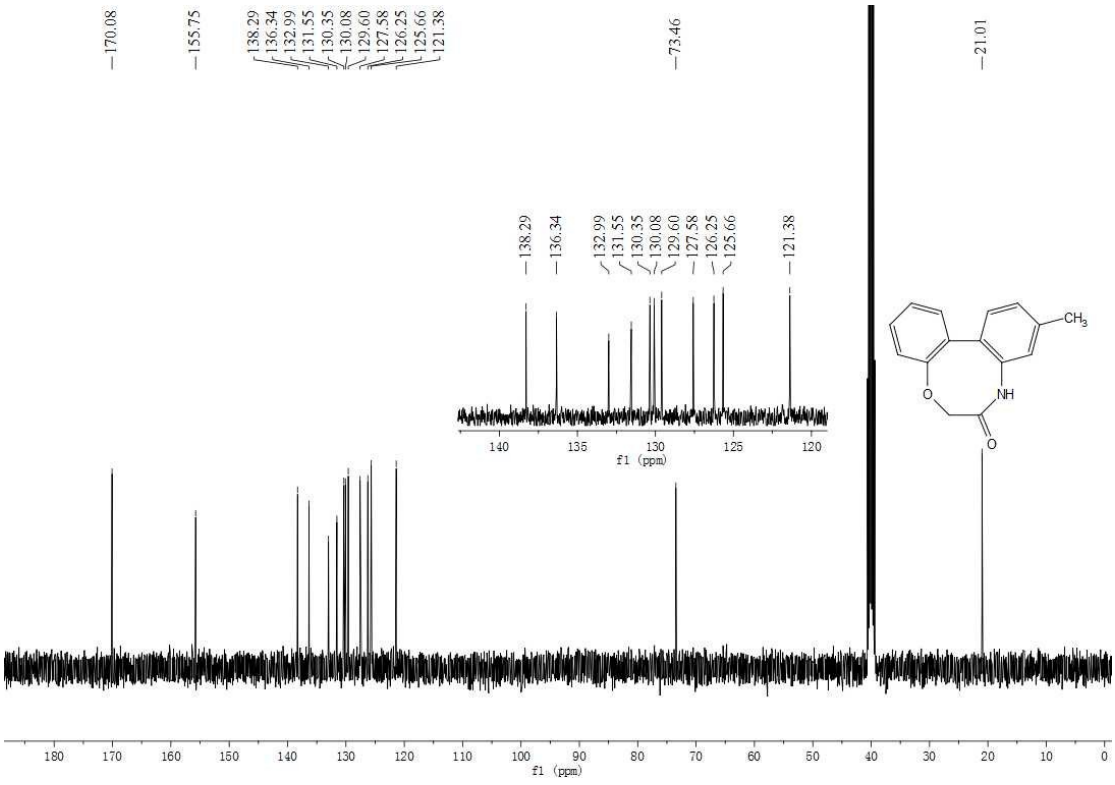
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 7.49 – 7.28 (m, 7H), 7.24 – 7.16 (m, 1H), 4.90 (d, J = 15.7 Hz, 1H), 4.52 (d, J = 15.8 Hz, 1H).



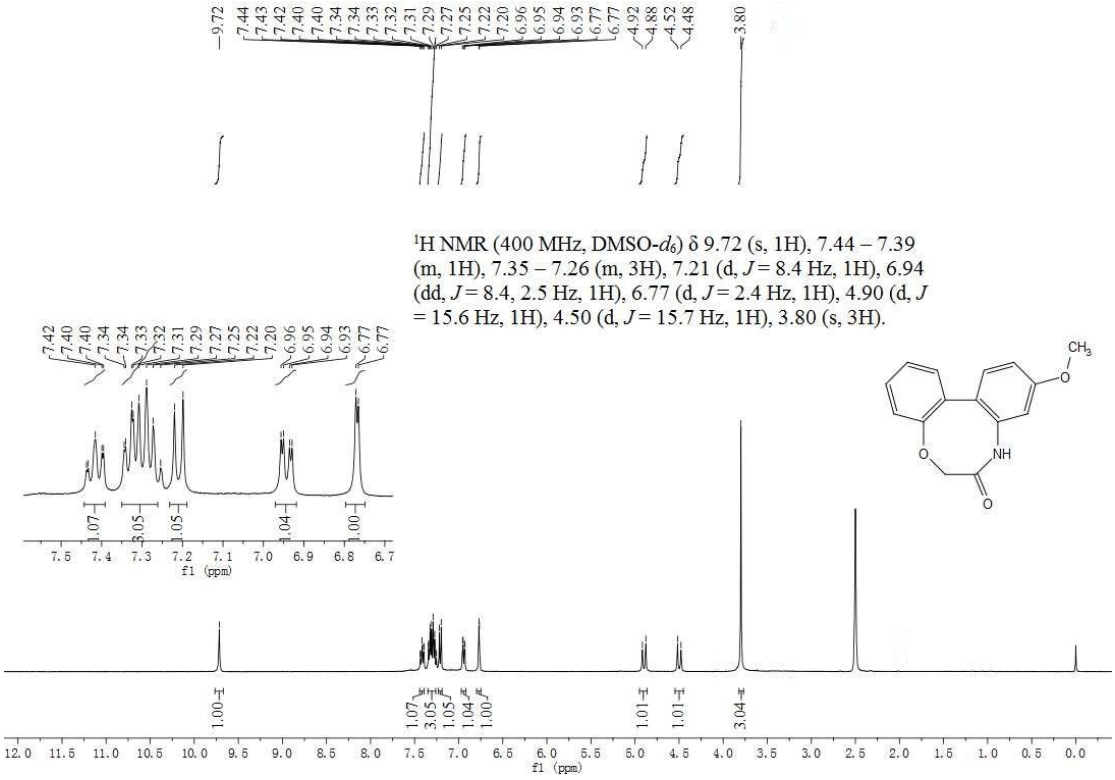
NMR spectra of **2v**



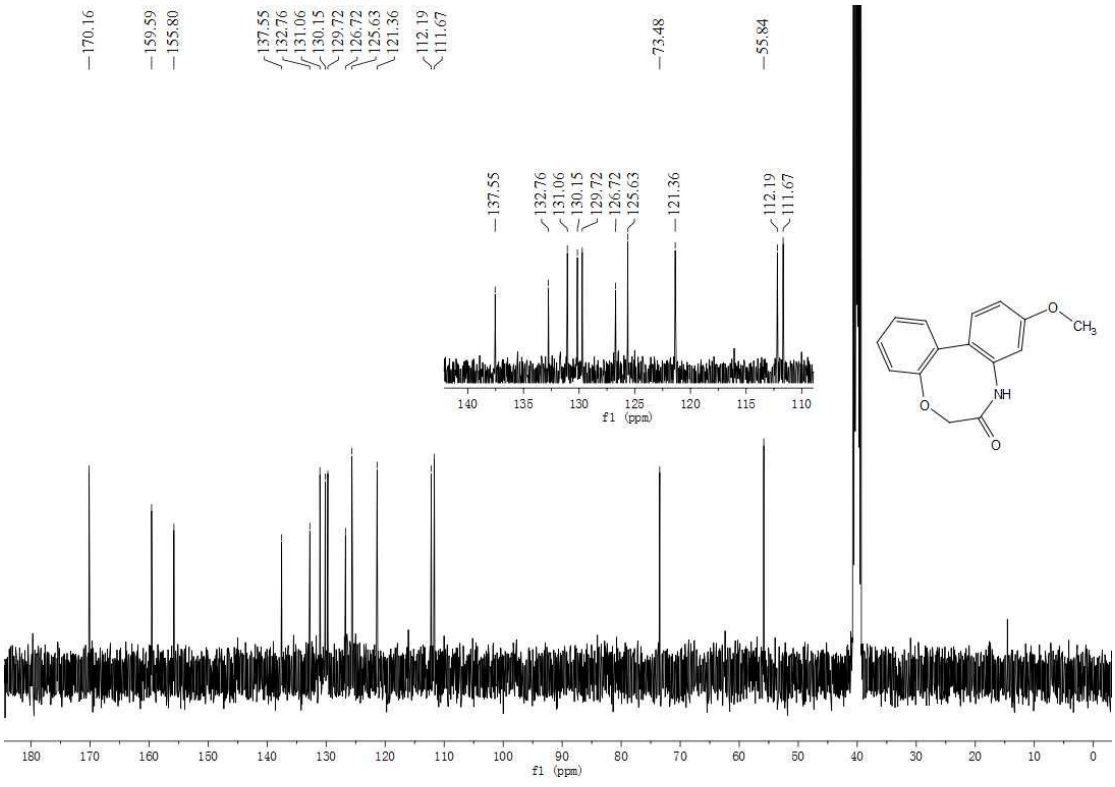
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.70 (s, 1H), 7.43 (ddd, J = 8.2, 7.1, 1.9 Hz, 1H), 7.35 (dd, J = 7.5, 1.8 Hz, 1H), 7.29 (ddd, J = 14.5, 7.6, 1.2 Hz, 2H), 7.17 (d, J = 2.1 Hz, 2H), 7.01 (s, 1H), 4.88 (d, J = 15.7 Hz, 1H), 4.50 (d, J = 15.6 Hz, 1H), 2.34 (s, 3H).



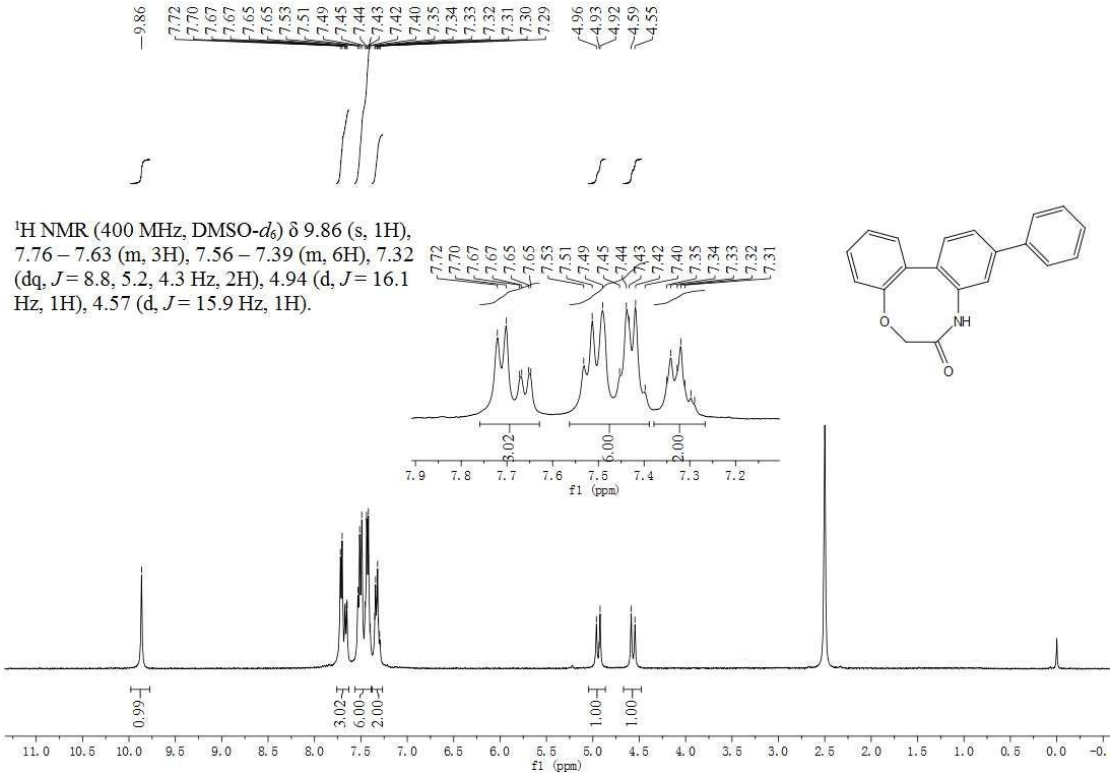
NMR spectra of **2w**



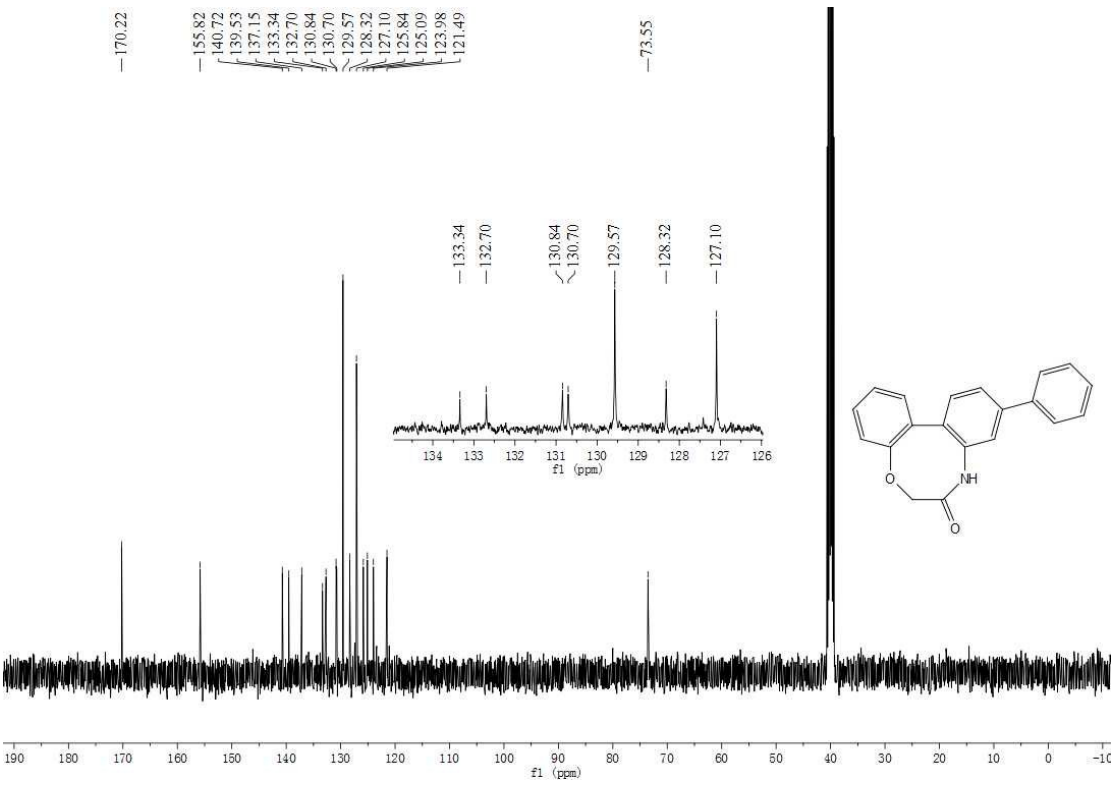
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.72 (s, 1H), 7.44 – 7.39 (m, 1H), 7.35 – 7.26 (m, 3H), 7.21 (d, J = 8.4 Hz, 1H), 6.94 (dd, J = 8.4, 2.5 Hz, 1H), 6.77 (d, J = 2.4 Hz, 1H), 4.90 (d, J = 15.6 Hz, 1H), 4.50 (d, J = 15.7 Hz, 1H), 3.80 (s, 3H).



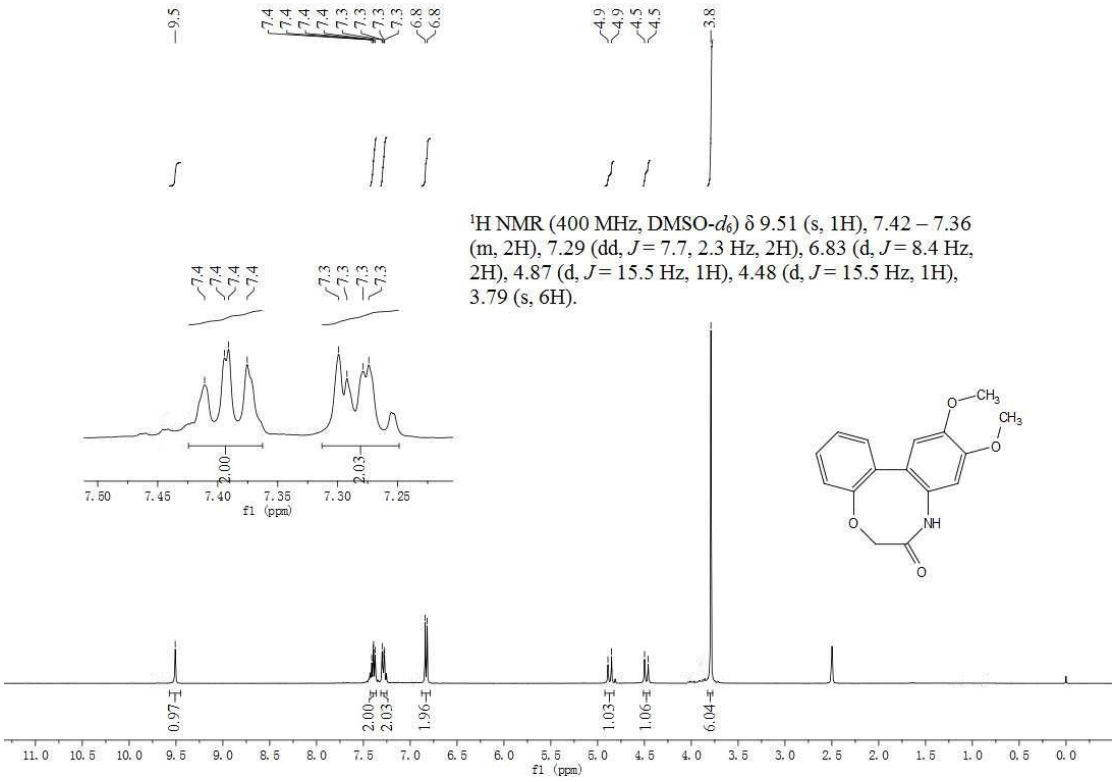
NMR spectra of **2x**



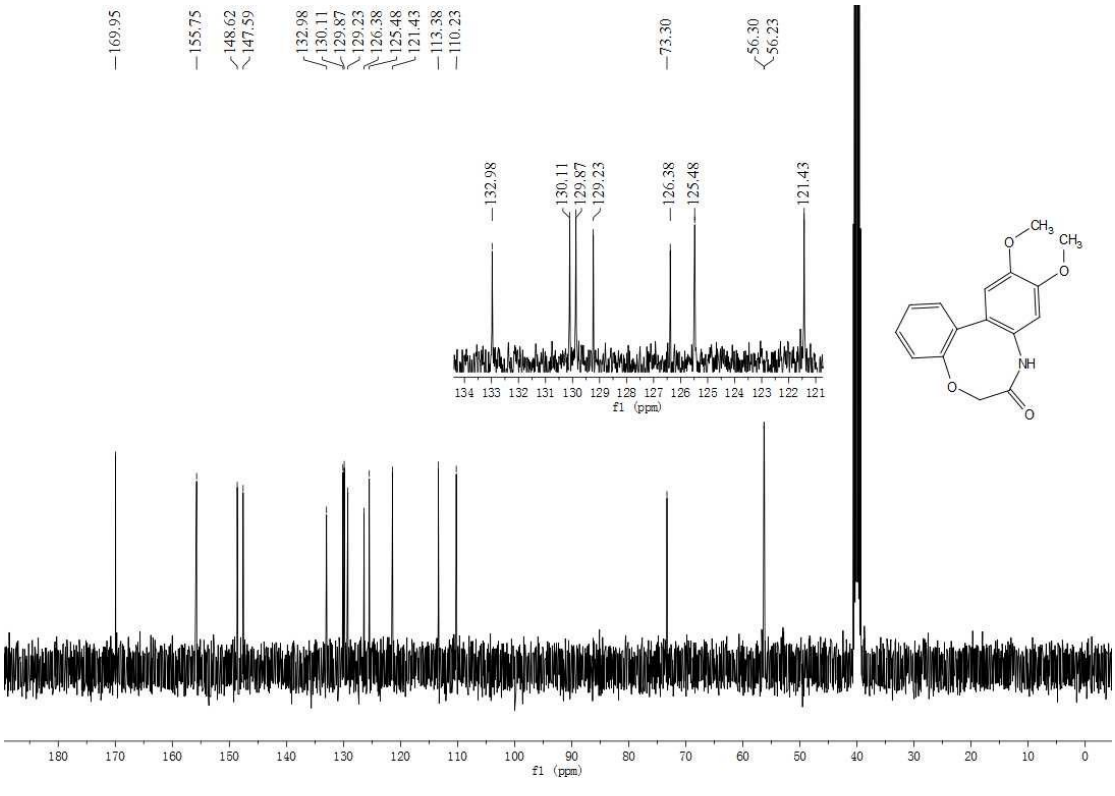
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.86 (s, 1H), 7.76 – 7.63 (m, 3H), 7.56 – 7.39 (m, 6H), 7.32 (dq, J = 8.8, 5.2, 4.3 Hz, 2H), 4.94 (d, J = 16.1 Hz, 1H), 4.57 (d, J = 15.9 Hz, 1H).



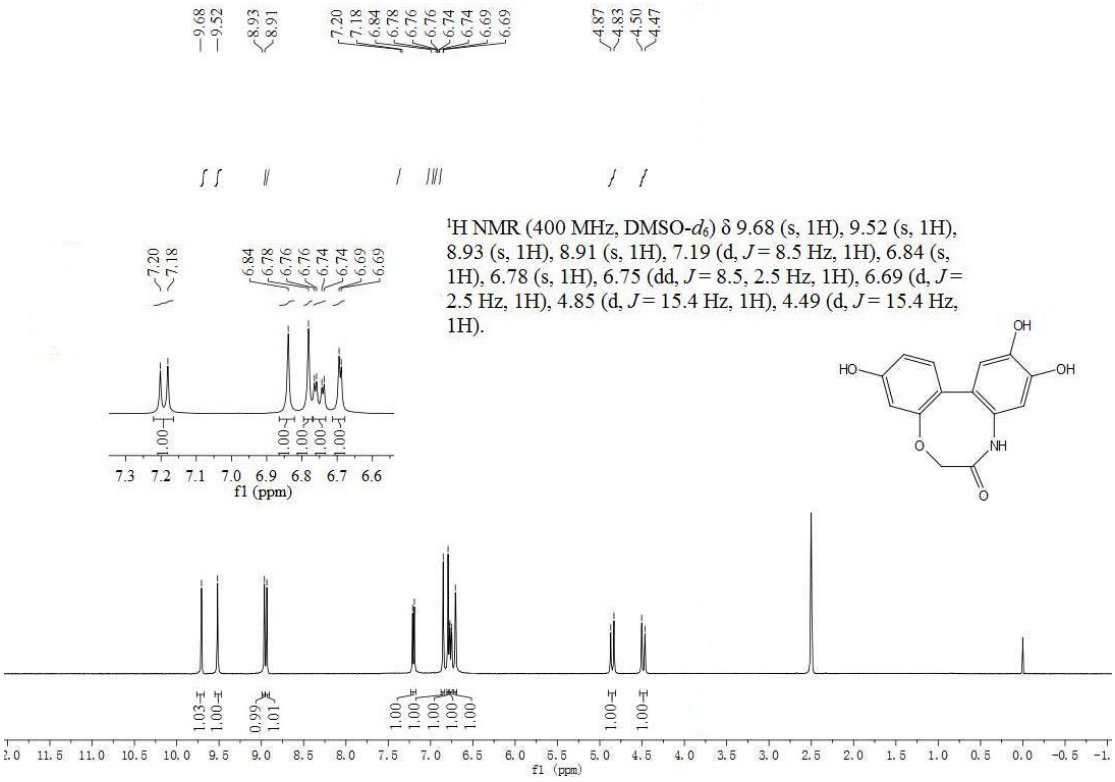
NMR spectra of **2y**



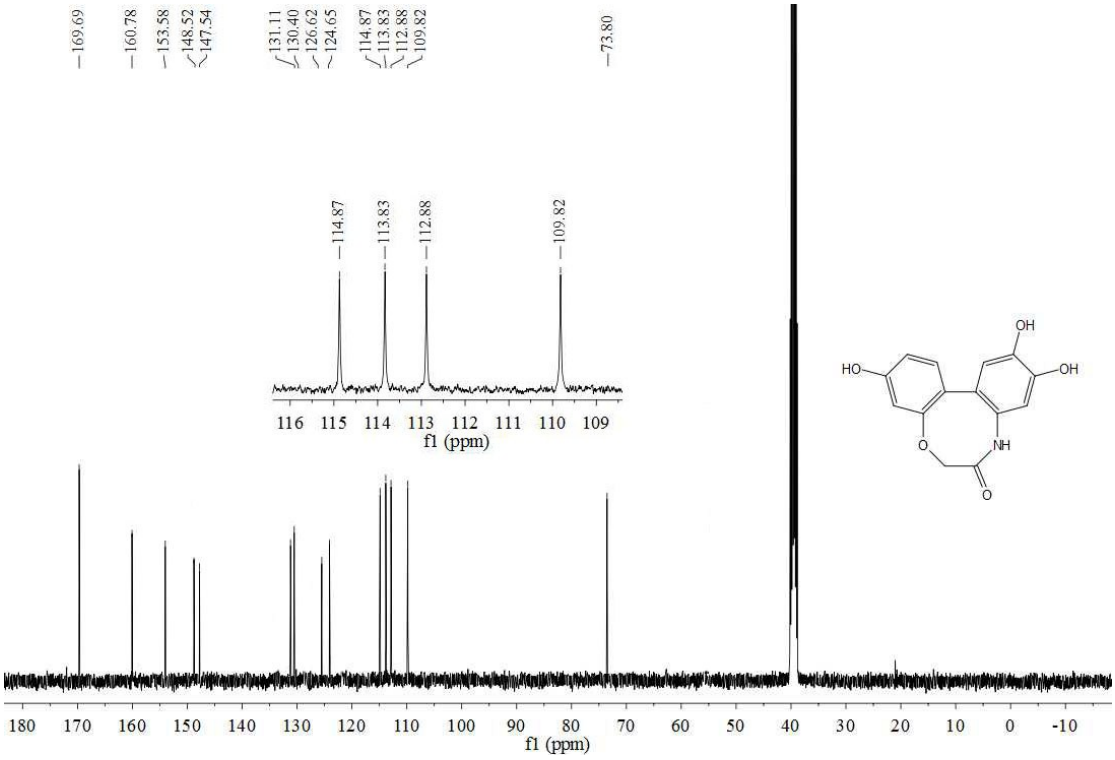
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.51 (s, 1H), 7.42 – 7.36 (m, 2H), 7.29 (dd, J = 7.7, 2.3 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 4.87 (d, J = 15.5 Hz, 1H), 4.48 (d, J = 15.5 Hz, 1H), 3.79 (s, 6H).



NMR spectra of **2t'**

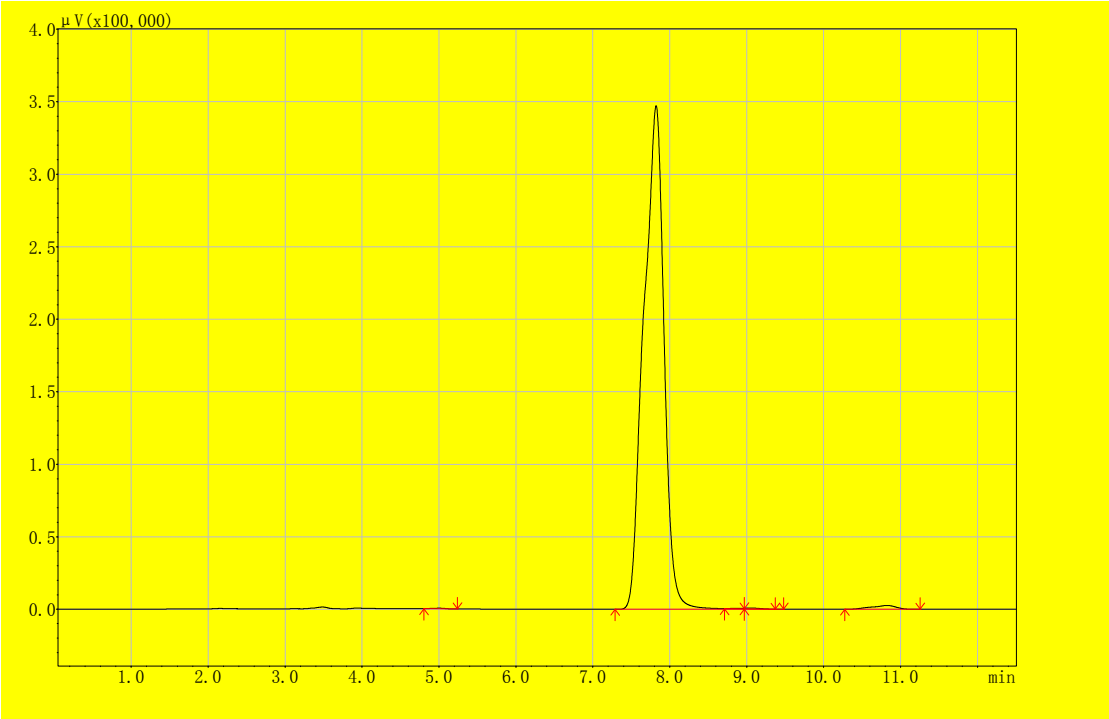


^{1}H NMR (400 MHz, DMSO-d_6) δ 9.68 (s, 1H), 9.52 (s, 1H), 8.93 (s, 1H), 8.91 (s, 1H), 7.19 (d, J = 8.5 Hz, 1H), 6.84 (s, 1H), 6.78 (s, 1H), 6.75 (dd, J = 8.5, 2.5 Hz, 1H), 6.69 (d, J = 2.5 Hz, 1H), 4.85 (d, J = 15.4 Hz, 1H), 4.49 (d, J = 15.4 Hz, 1H).



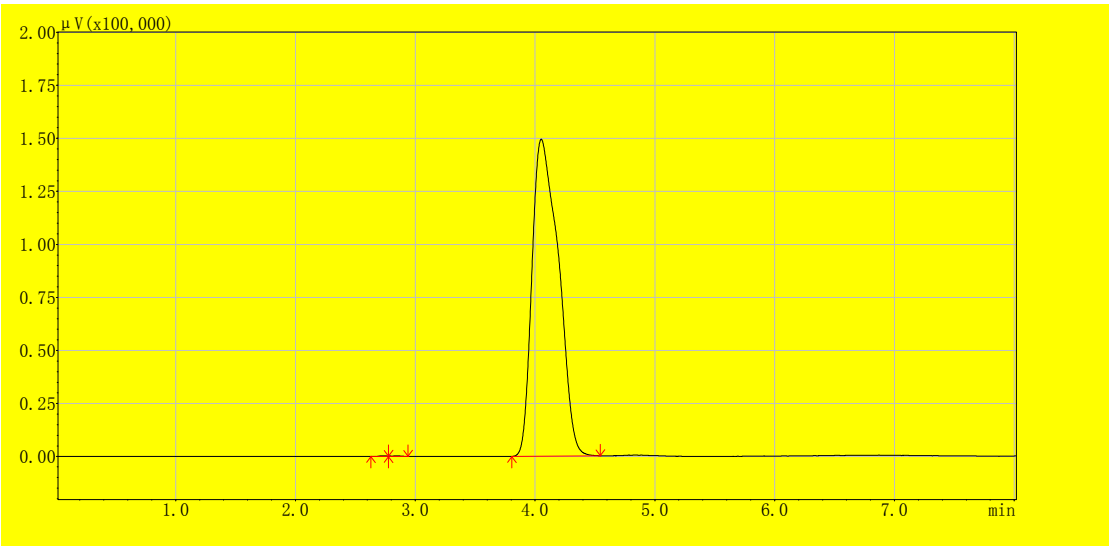
10. HPLC spectra for 8-azaprotosappanin A and derivatives (2)

HPLC spectra of product **2a**



Peak#	Ret. Time	Area	Area%	Height	Height%
1	5.005	5341.8	0.0830	461.4	0.1313
2	7.822	6359694.4	98.7974	347298.4	98.8451
3	8.895	3439.3	0.0534	326.0	0.0928
4	9.060	7180.9	0.1116	584.4	0.1663
5	10.823	61447.4	0.9546	2686.0	0.7645

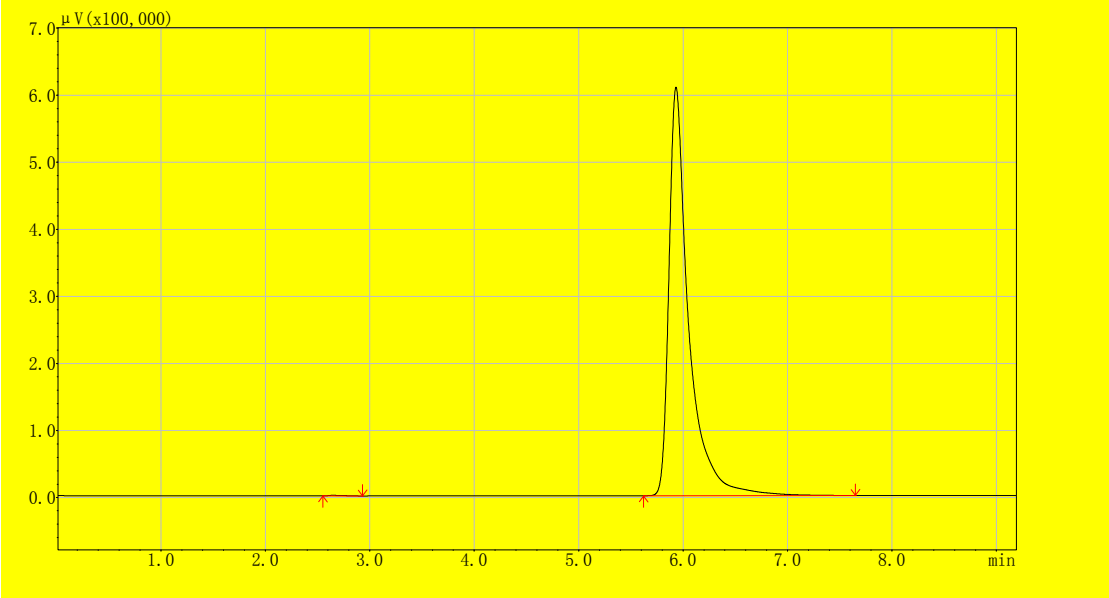
HPLC spectra of product **2b**



Peak#	Ret. Time	Area	Area%	Height	Height%
1	2.715	2434.0	0.1062	421.6	0.2807

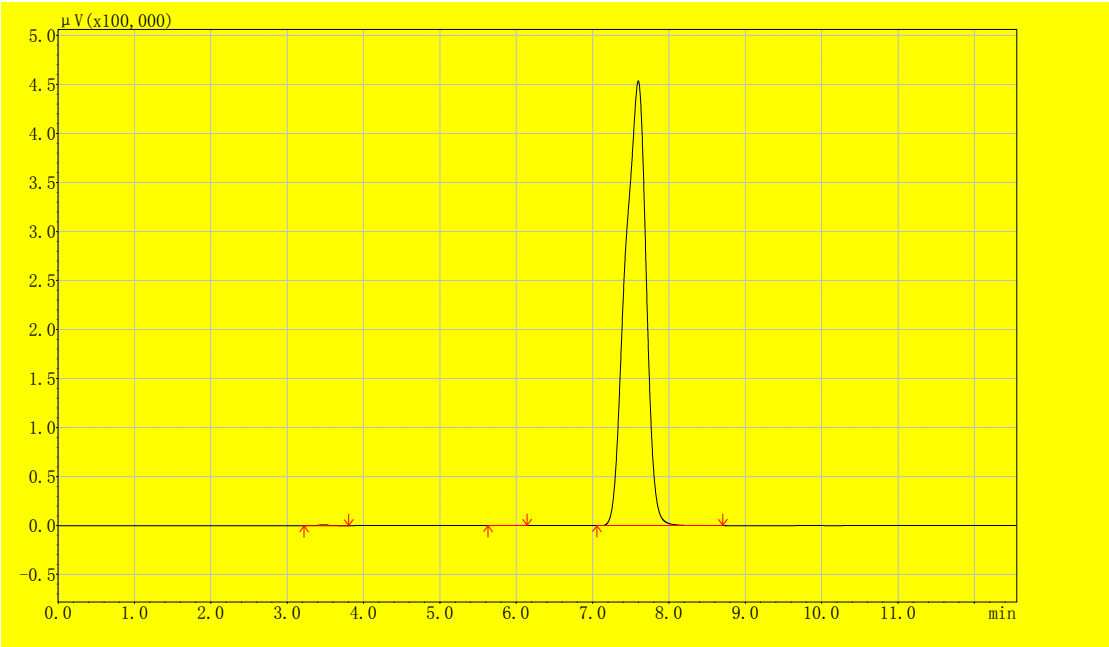
2	2.840	3040.0	0.1326	430.4	0.2865
3	4.051	2287125.0	99.7612	149375.5	99.4328

HPLC spectra of product **2c**



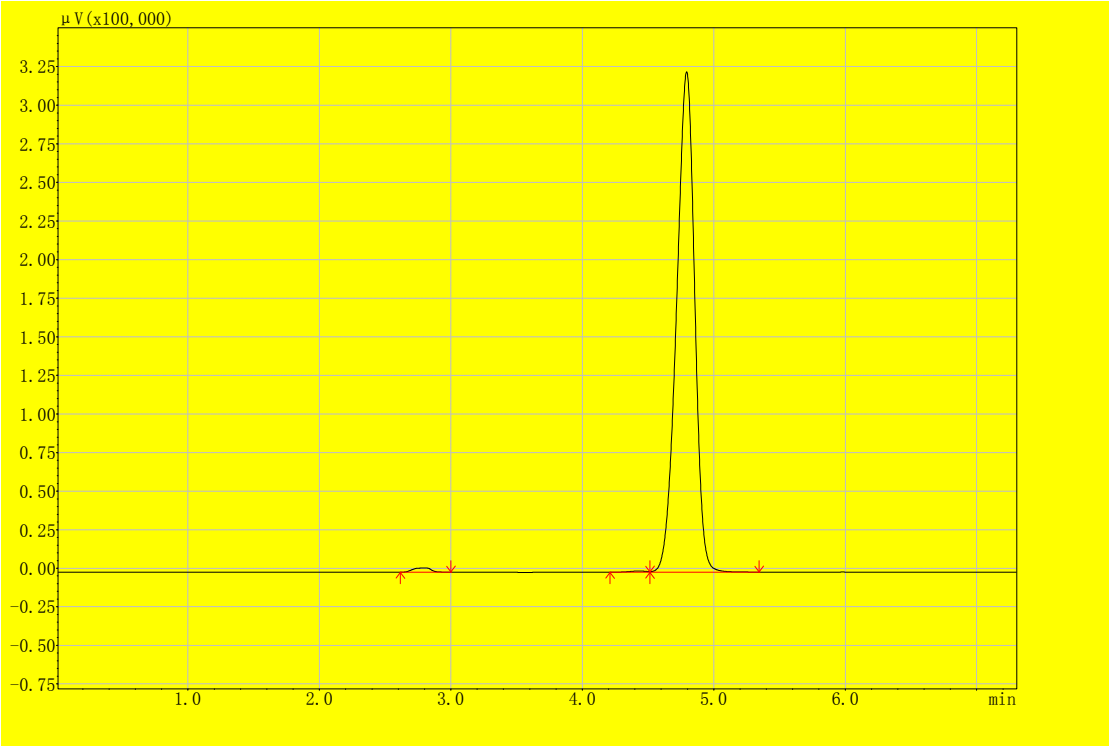
Peak#	Ret. Time	Area	Area%	Height	Height%
1	2.649	9505.8	0.1188	842.1	0.1382
2	5.932	7994238.7	99.8812	608624.8	99.8618

HPLC spectra of product **2d**



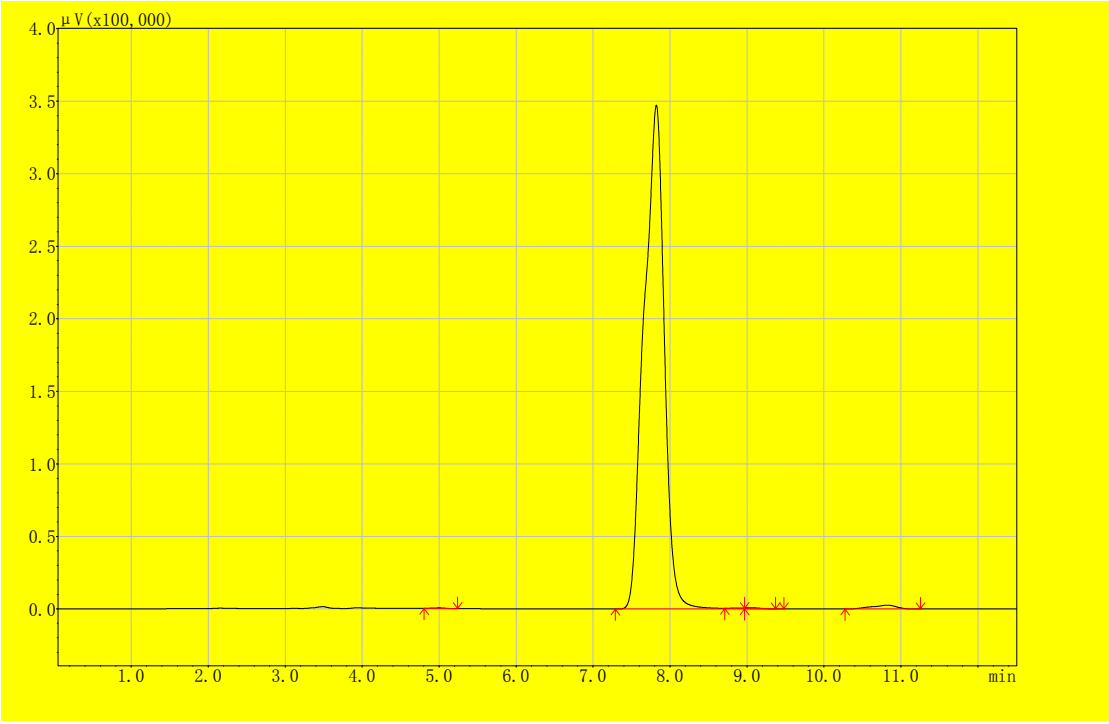
Peak#	Ret. Time	Area	Area%	Height	Height%
1	3.482	14483.7	0.1685	1187.8	0.2608
2	5.892	5180.5	0.0603	353.3	0.0776
3	7.598	8575936.1	99.7712	453897.2	99.6616

HPLC spectra of product **2e**



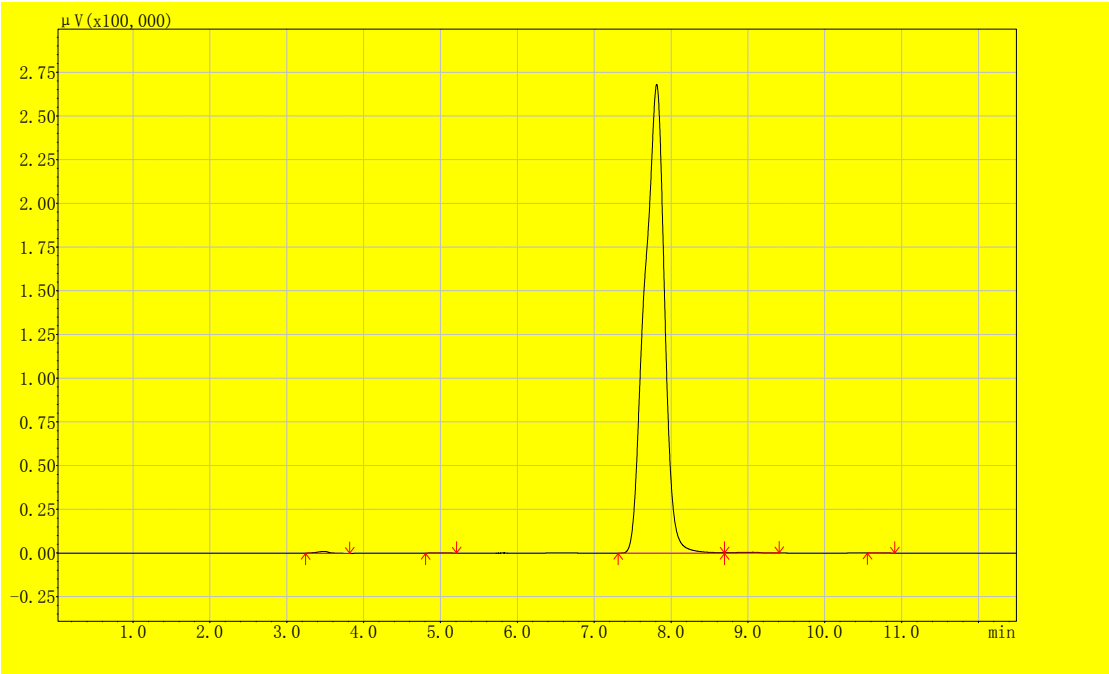
Peak#	Ret. Time	Area	Area%	Height	Height%
1	2.809	26518.0	0.8446	2928.0	0.8928
2	4.432	7101.2	0.2262	791.0	0.2412
3	4.794	3106005.6	98.9292	324229.1	98.8660

HPLC spectra of product **2f**



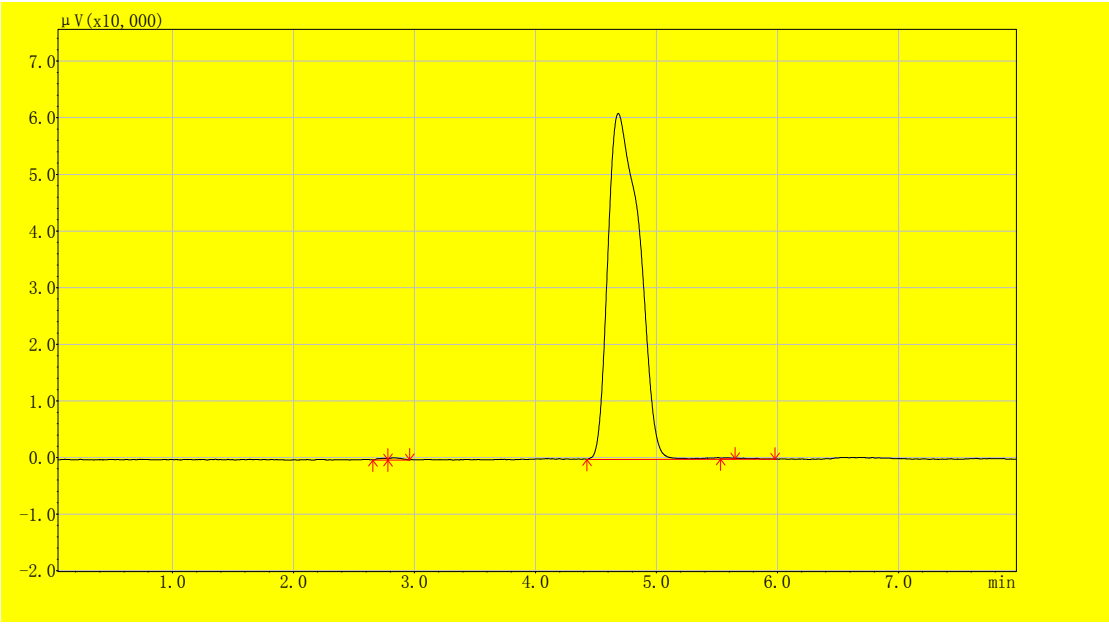
Peak#	Ret. Time	Area	Area%	Height	Height%
1	5.005	5341.8	0.0830	461.4	0.1313
2	7.822	6359694.4	98.7974	347298.4	98.8451

HPLC spectra of product **2g**



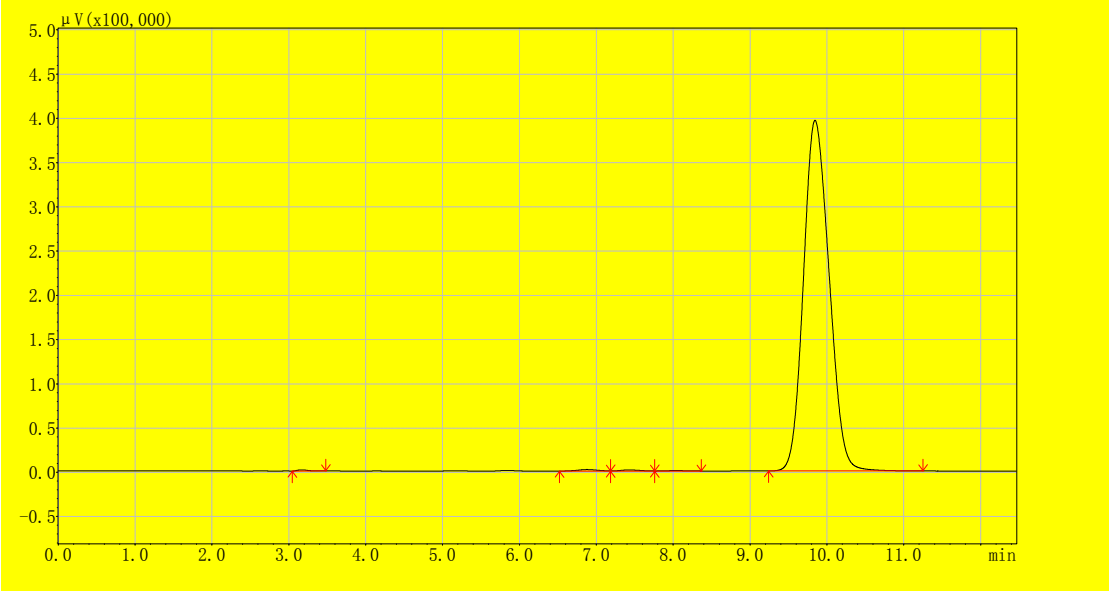
Peak#	Ret. Time	Area	Area%	Height	Height%
1	3.480	15119.5	0.3131	1210.6	0.4476
2	5.016	3632.1	0.0752	317.2	0.1173
3	7.813	4792365.0	99.2488	268178.5	99.1426
4	9.063	15730.3	0.3258	637.8	0.2358
5	10.668	1790.3	0.0371	153.5	0.0567

HPLC spectra of product **2h**



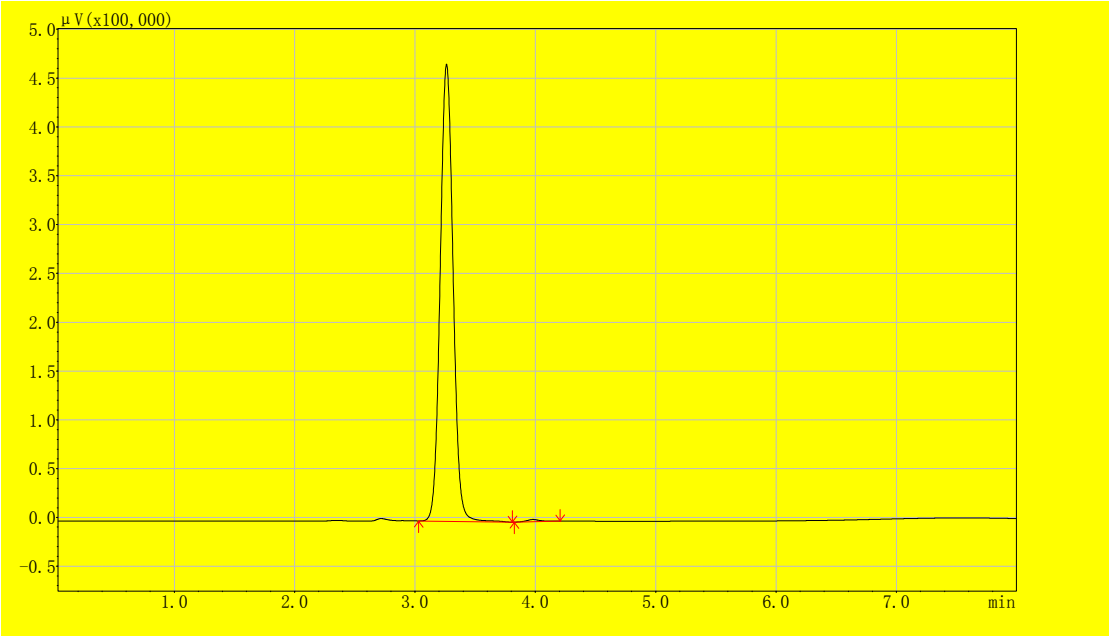
Peak#	Ret. Time	Area	Area%	Height	Height%
1	2.738	1631.4	0.1487	298.5	0.4811
2	2.829	2742.6	0.2499	409.6	0.6602
3	4.684	1091759.1	99.4837	61128.4	98.5250
4	5.576	1291.6	0.1177	207.0	0.3337

HPLC spectra of product **2i**



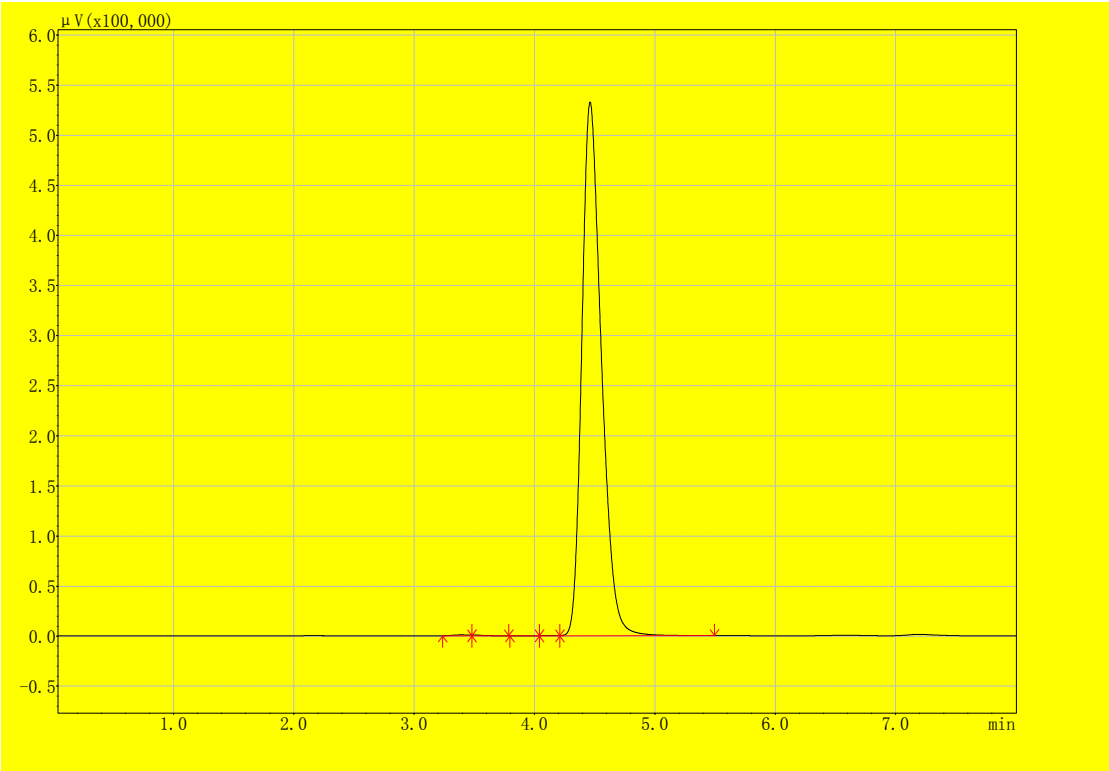
Peak#	Ret. Time	Area	Area%	Height	Height%
1	3.168	12144.2	0.1318	1264.9	0.3156
2	6.878	29980.4	0.3254	1680.3	0.4193
3	7.421	20661.4	0.2243	1244.5	0.3105
4	8.020	7557.7	0.0820	435.7	0.1087
5	9.845	9142845.3	99.2365	396164.6	98.8459

HPLC spectra of product **2j**



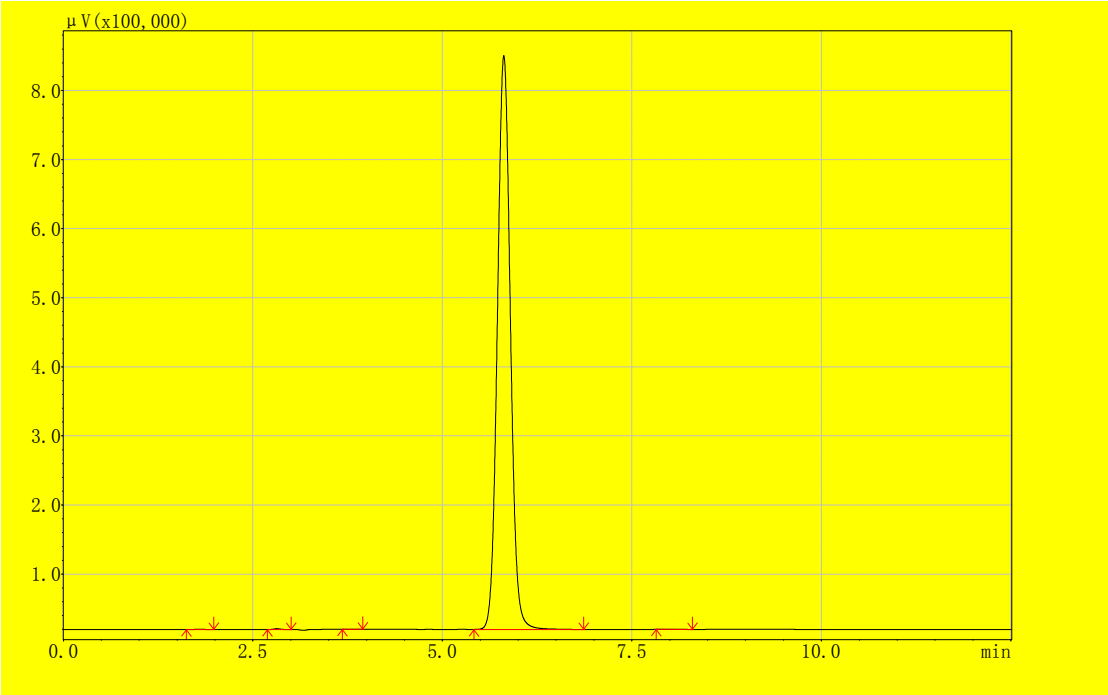
Peak#	Ret. Time	Area	Area%	Height	Height%
1	3.262	3493612.1	99.4815	468106.9	99.5088
2	3.979	18208.6	0.5185	2310.5	0.4912

HPLC spectra of product **2k**



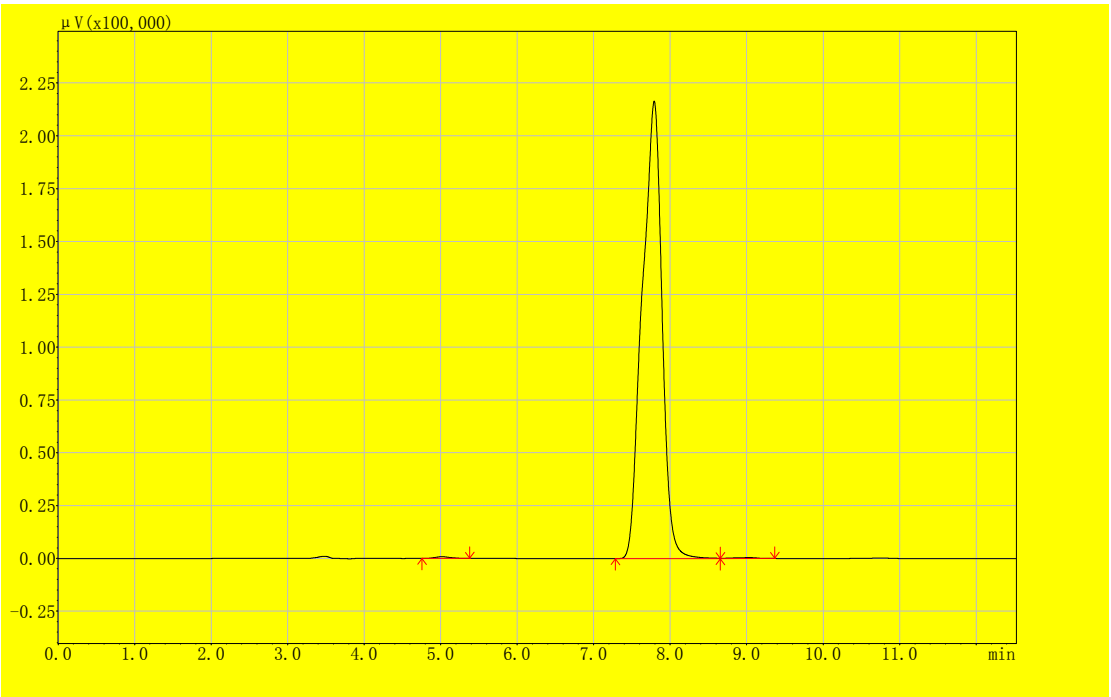
Peak#	Ret. Time	Area	Area%	Height	Height%
1	3.393	8541.4	0.1419	945.4	0.1768
2	3.514	5276.7	0.0876	731.0	0.1367
3	3.960	1805.9	0.0300	169.2	0.0316
4	4.150	2770.4	0.0460	321.7	0.0602
5	4.462	6001996.9	99.6945	532427.3	99.5946

HPLC spectra of product **2l**



Peak#	Ret. Time	Area	Area%	Height	Height%
1	1.778	2497.5	0.0252	228.4	0.0274
2	2.818	6903.4	0.0697	1149.7	0.1382
3	3.811	1519.8	0.0154	201.5	0.0242
4	5.810	9887438.2	99.8633	830383.4	99.7886
5	8.004	2613.4	0.0264	179.8	0.0216

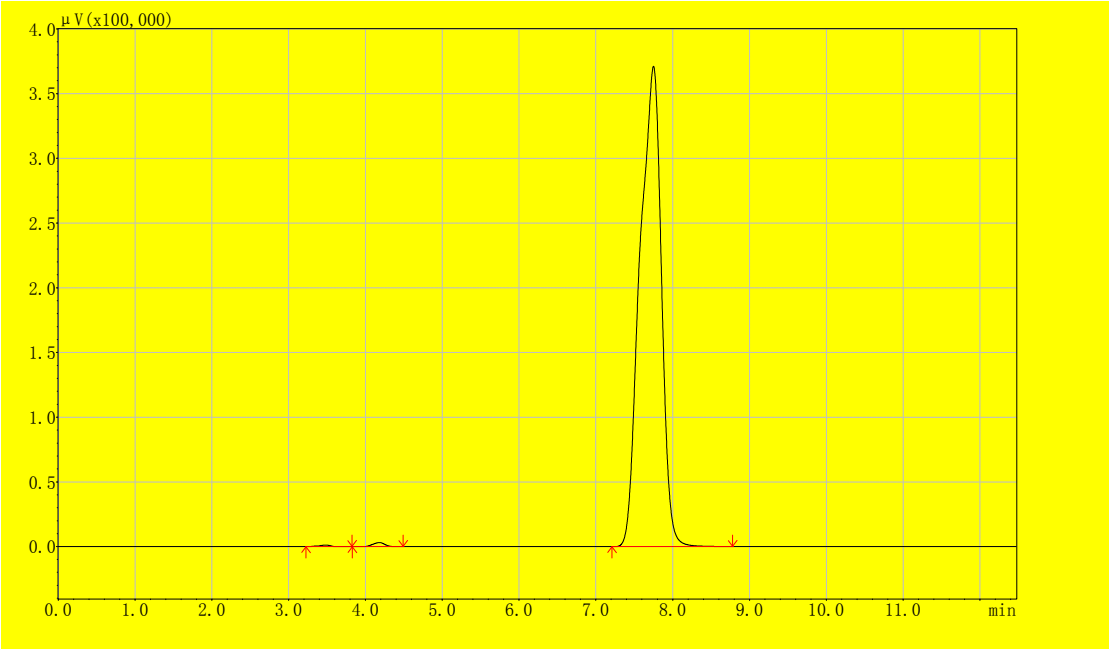
HPLC spectra of product **2m**



Peak#	Ret. Time	Area	Area%	Height	Height%

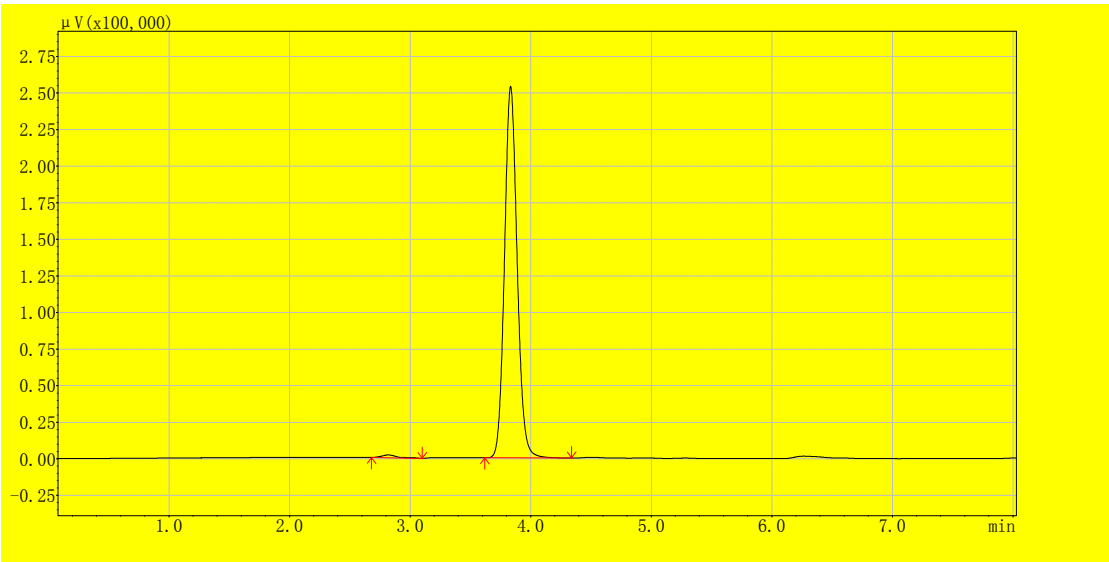
1	5.018	13985.5	0.3561	922.8	0.4232
2	7.791	3899354.8	99.2784	216509.2	99.3045
3	9.037	14357.1	0.3655	593.5	0.2722

HPLC spectra of product **2n**



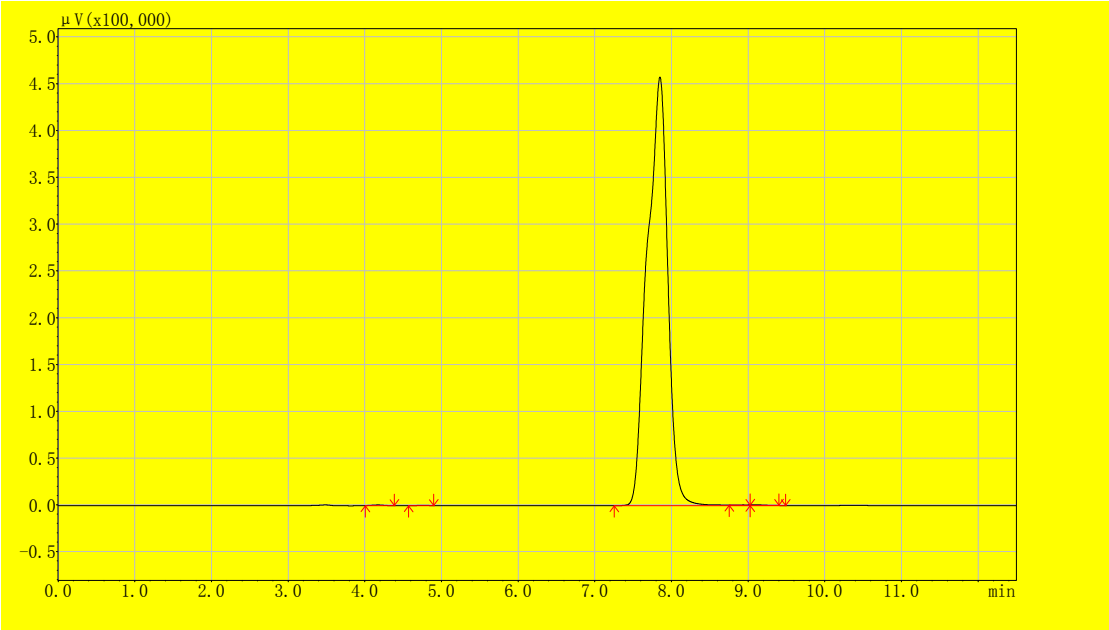
Peak#	Ret. Time	Area	Area%	Height	Height%
1	3.484	15716.0	0.2171	1308.2	0.3482
2	4.182	37309.4	0.5154	3294.5	0.8769
3	7.750	7185485.7	99.2675	371085.2	98.7749

HPLC spectra of product **2o**



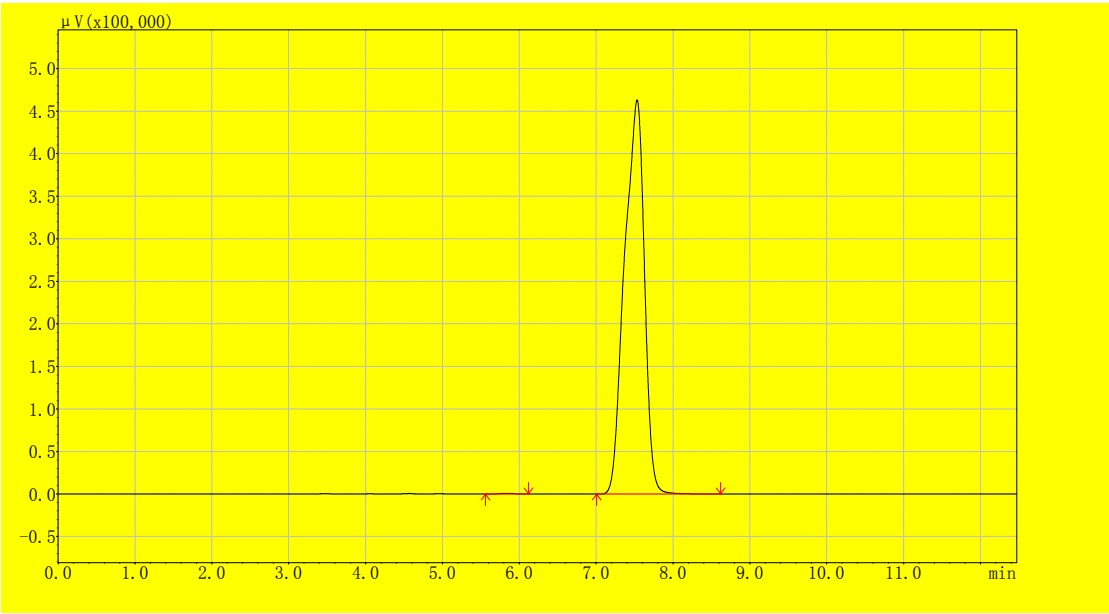
Peak#	Ret. Time	Area	Area%	Height	Height%
1	2.817	17744.4	0.9394	1940.7	0.7562
2	3.833	1850514.4	97.9718	253695.5	98.8584
3	14.065	20564.9	1.0888	988.9	0.3854

HPLC spectra of product **2p**



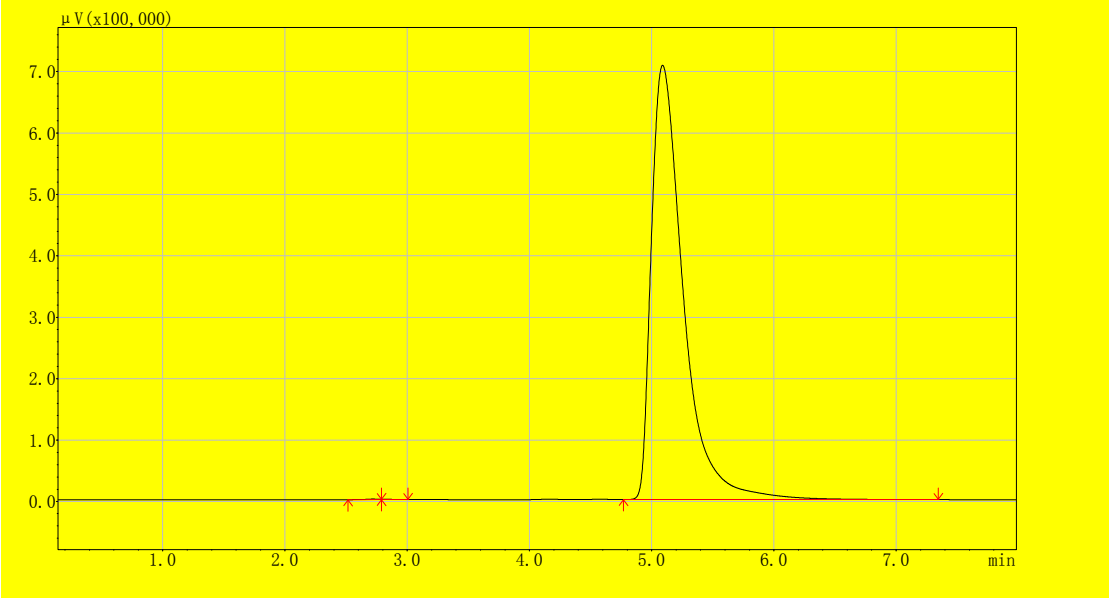
Peak#	Ret. Time	Area	Area%	Height	Height%
1	4.176	7529.3	0.0882	746.3	0.1623
2	4.770	2126.5	0.0249	213.1	0.0464
3	7.850	8522284.2	99.7814	458063.4	99.6277
4	8.915	3069.8	0.0359	253.2	0.0551
5	9.113	5948.5	0.0696	498.9	0.1085

HPLC spectra of product **2q**



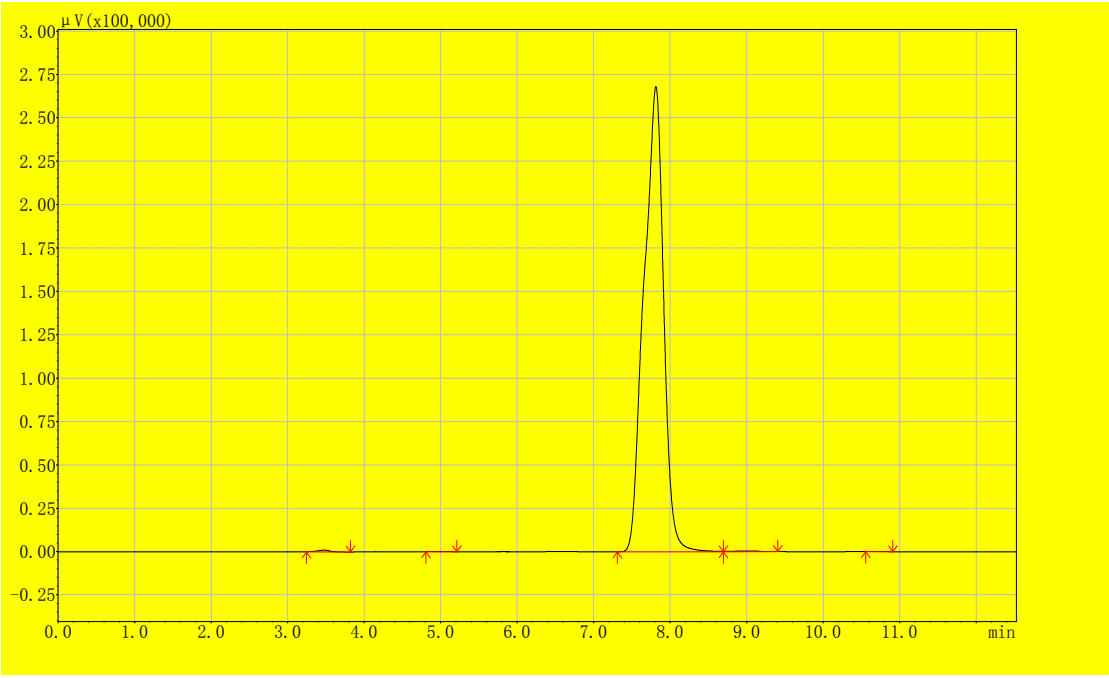
Peak#	Ret. Time	Area	Area%	Height	Height%
1	5.857	14455.4	0.1734	1015.7	0.2188
2	7.532	8323202.1	99.8266	463191.7	99.7812

HPLC spectra of product **2r**



Peak#	Ret. Time	Area	Area%	Height	Height%
1	2.718	7361.3	0.0572	932.2	0.1315
2	2.820	4323.2	0.0336	778.3	0.1098
3	5.089	12850417.5	99.9092	707180.4	99.7587

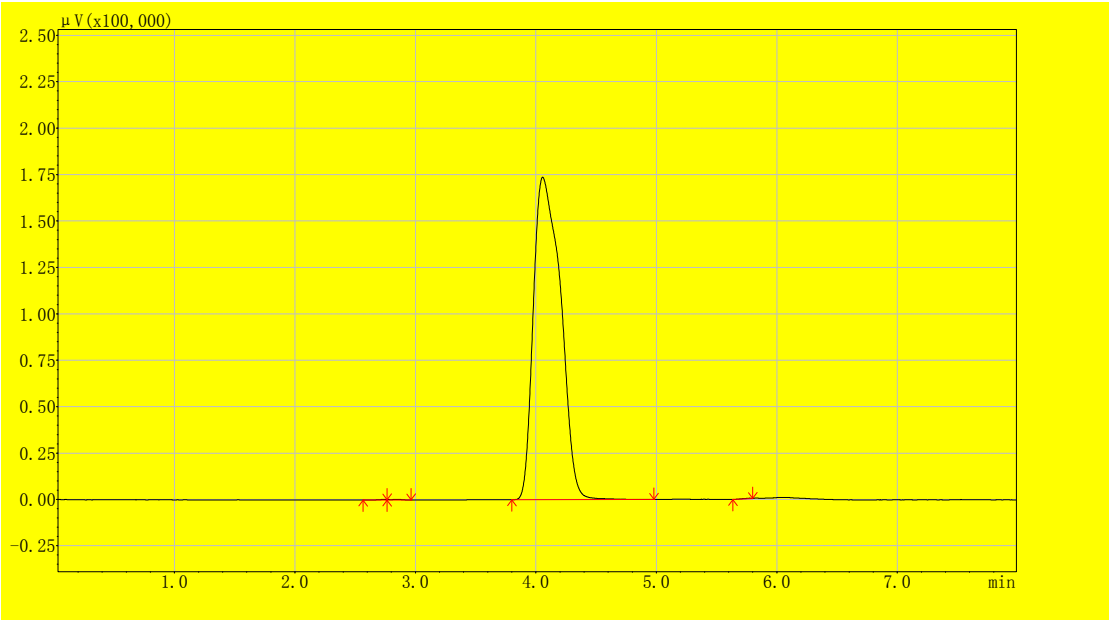
HPLC spectra of product **2s**



Peak#	Ret. Time	Area	Area%	Height	Height%
1	3.480	15119.5	0.3131	1210.6	0.4476
2	5.016	3632.1	0.0752	317.2	0.1173
3	7.813	4792365.0	99.2488	268178.5	99.1426
4	9.063	15730.3	0.3258	637.8	0.2358

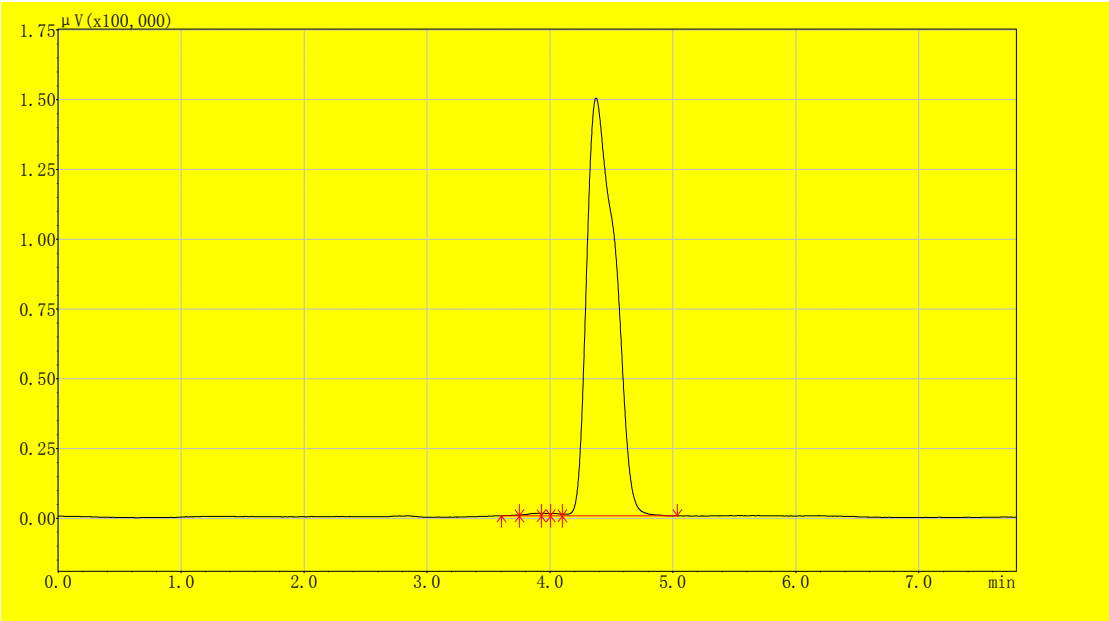
5	10.668	1790.3	0.0371	153.5	0.0567

HPLC spectra of product **2t**



Peak#	Ret. Time	Area	Area%	Height	Height%
1	2.730	1463.7	0.0537	293.6	0.1681
2	2.855	2513.2	0.0921	318.3	0.1822
3	4.056	2721986.9	99.7835	173737.4	99.4570
4	5.775	1928.7	0.0707	336.5	0.1926

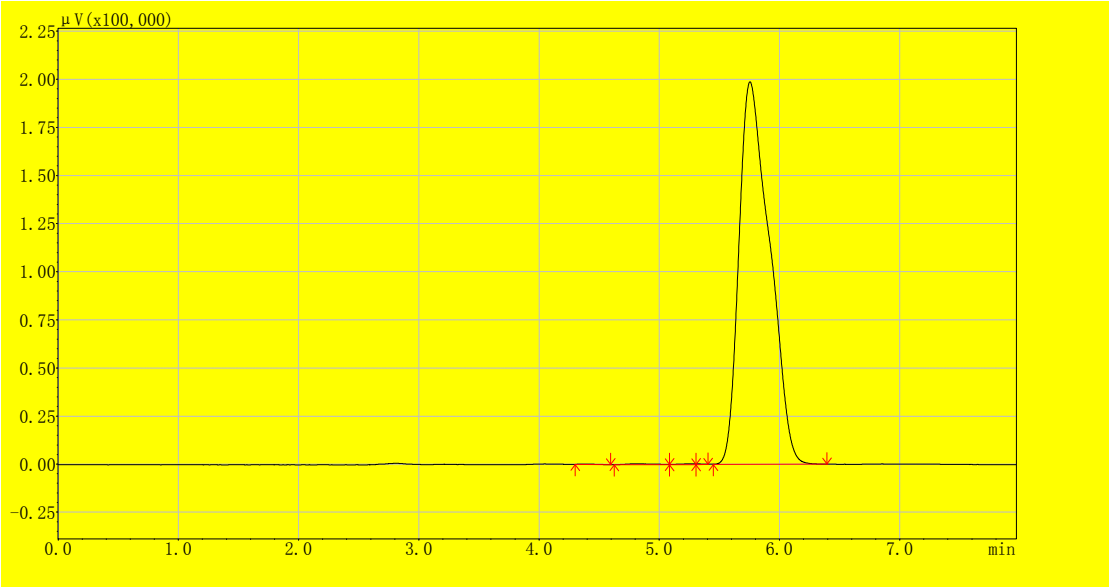
HPLC spectra of product **2u**



Peak#	Ret. Time	Area	Area%	Height	Height%
1	3.724	1168.2	0.0489	261.5	0.1714
2	3.898	6975.6	0.2917	904.3	0.5925
3	3.955	3800.6	0.1589	877.3	0.5748
4	4.028	4336.2	0.1813	878.6	0.5756

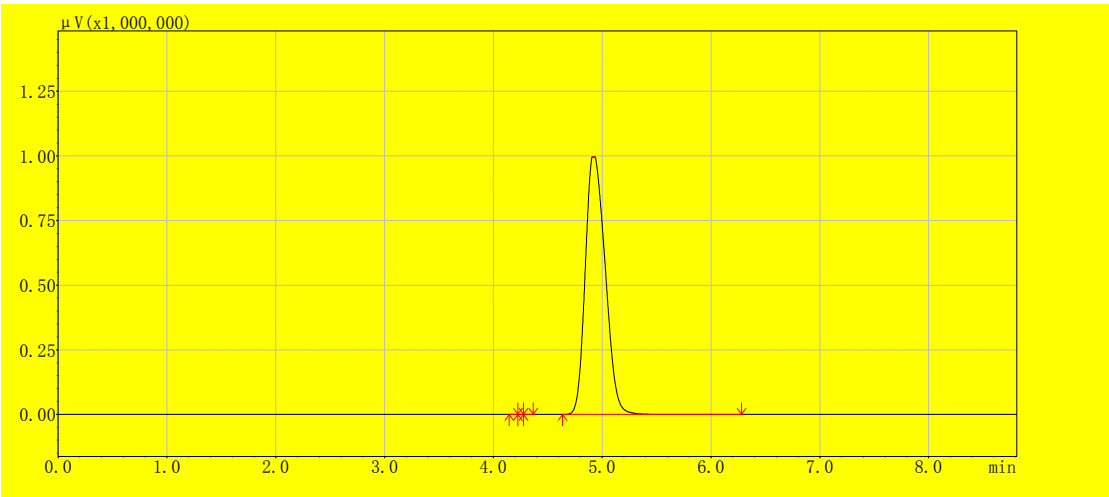
5	4.375	2375153.0	99.3192	149705.7	98.0857

HPLC spectra of product **2v**



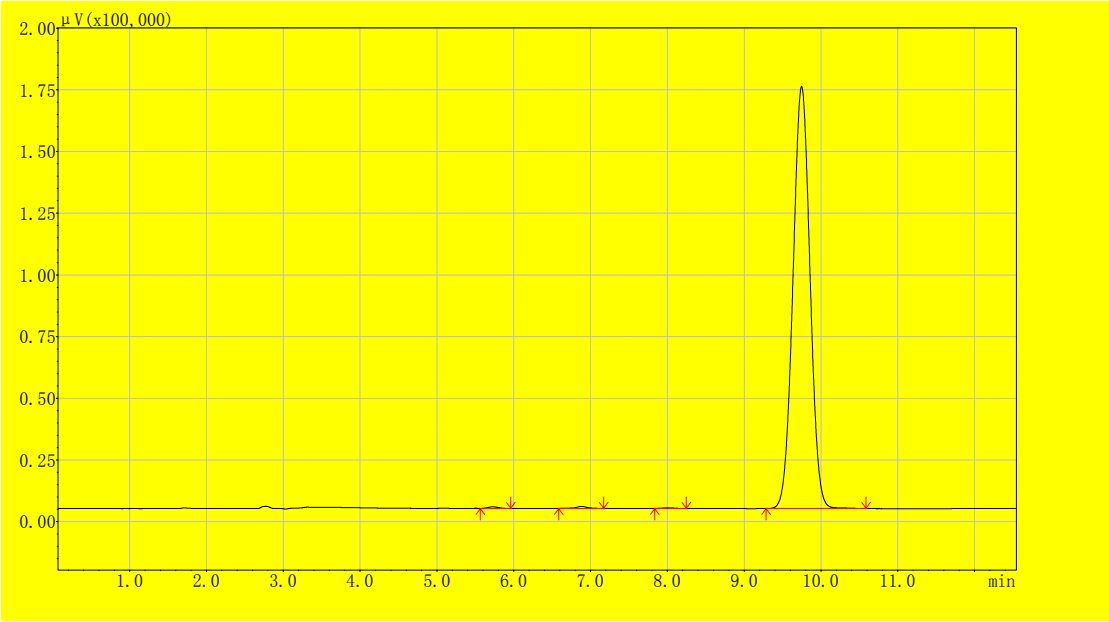
Peak#	Ret. Time	Area	Area%	Height	Height%
1	4.391	2149.8	0.0608	232.8	0.1160
2	4.808	9648.7	0.2727	662.4	0.3299
3	5.233	4441.1	0.1255	551.1	0.2745
4	5.330	2335.3	0.0660	462.4	0.2303
5	5.754	3519882.2	99.4751	198862.6	99.0493

HPLC spectra of product **2w**



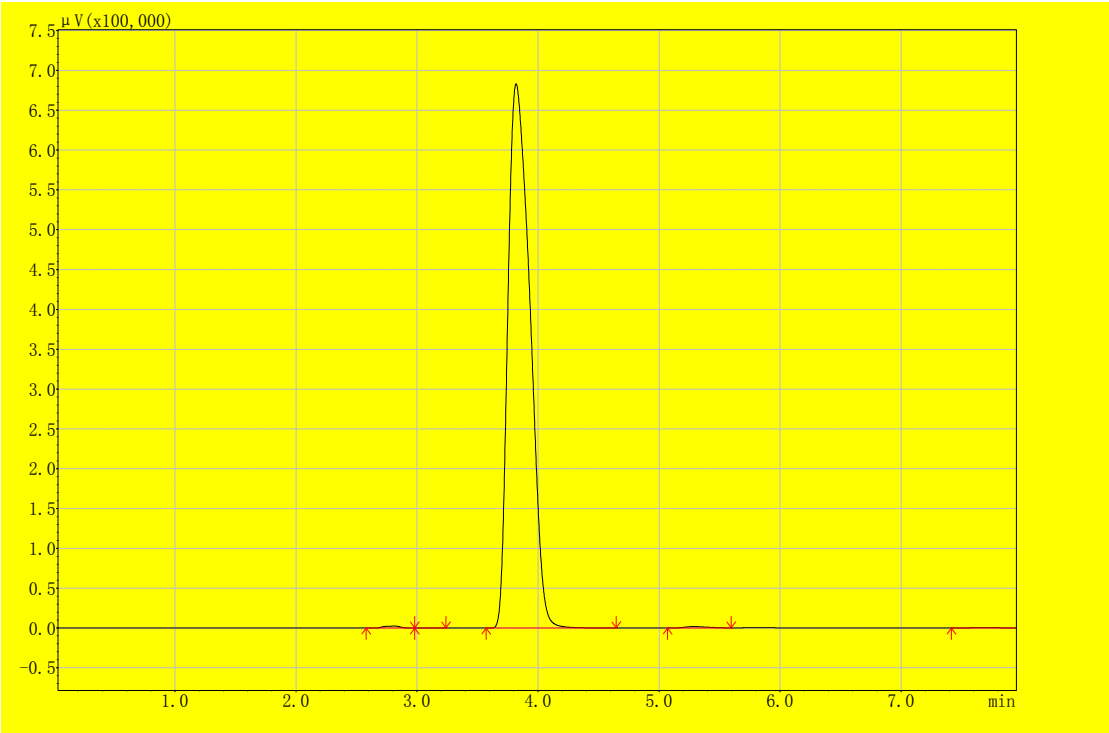
Peak#	Ret. Time	Area	Area%	Height	Height%
1	4.192	1962.2	0.0154	465.3	0.0467
2	4.230	1065.1	0.0084	425.3	0.0427
3	4.289	1238.7	0.0097	351.1	0.0352
4	4.931	12728506.7	99.9665	995570.8	99.8754

HPLC spectra of product **2x**



Peak#	Ret. Time	Area	Area%	Height	Height%
1	5.727	6061.2	0.2287	647.8	0.3750
2	6.880	8469.4	0.3195	799.1	0.4626
3	8.003	2993.9	0.1130	269.1	0.1558
4	9.747	2632929.0	99.3388	171023.0	99.0066

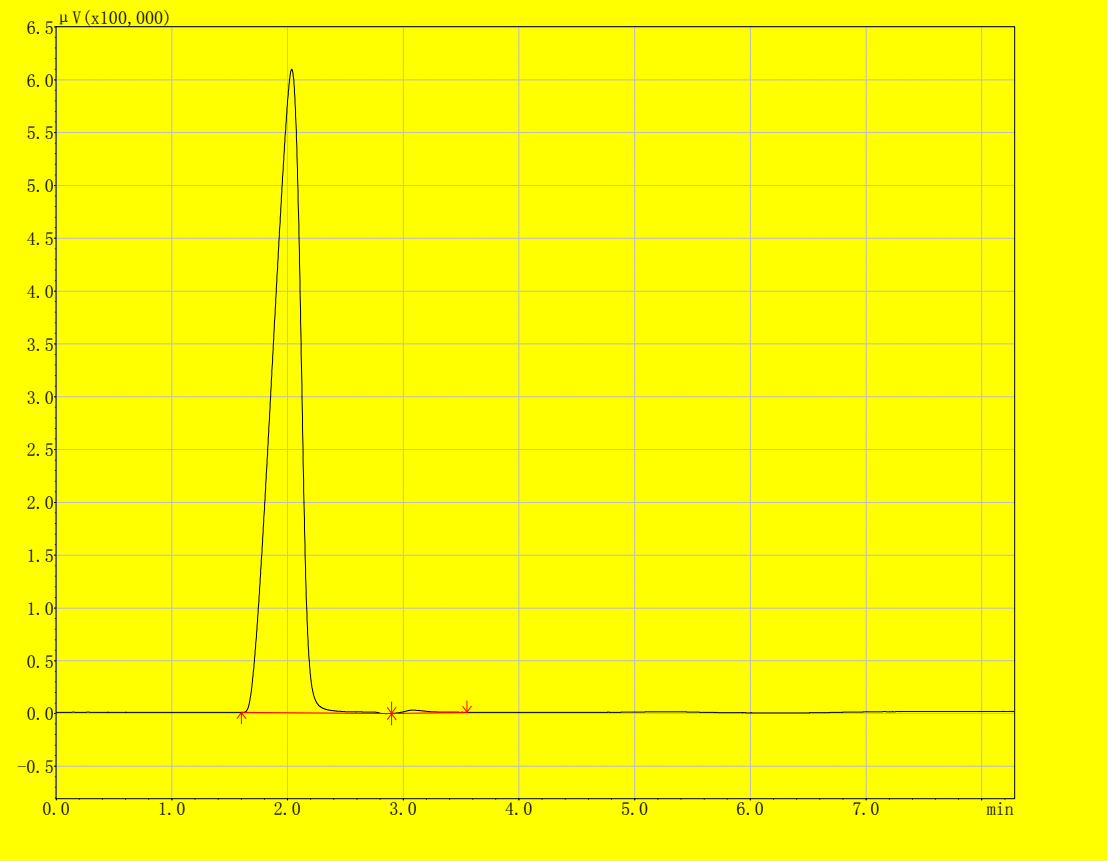
HPLC spectra of product **2y**



Peak#	Ret. Time	Area	Area%	Height	Height%
1	2.813	28304.6	0.3262	2773.3	0.4025
2	3.057	1226.0	0.0141	155.1	0.0225

3	3.819	8606698.3	99.1942	683371.8	99.1866
4	5.286	22738.0	0.2621	1766.1	0.2563
5	7.672	17644.2	0.2034	910.0	0.1321

HPLC spectra of product **2t'**



Peak#	Ret. Time	Area	Area%	Height	Height%
1	2.026	10089000.0	99.5392	600936.7	99.5088
2	3.090	46708.4	0.4608	2966.2	0.4912