

Supporting Information

**Transition Metal- and Oxidant-free [3+2] Cyclization of Azomethine Imines Utilizing
Vinylene Carbonate as Dual Synthons**

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1. General considerations

Unless otherwise noted, commercial reagents were purchased from Alfa Aesar, TCI, *J&K* or Adamas and used without further purification. All reactions were carried out using oven-dried glassware and all catalytic reactions proceeded without special care. Column chromatography was performed on 200-300 mesh silica gel (Huanghai, China).

^1H , ^{19}F and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded on a Bruker Ascend 400 MHz spectrometer and Bruker Ultrashield 300MHz at ambient temperature. ^1H NMR spectra are referred to the TMS signal ($\delta = 0$ ppm) and ^{13}C NMR spectra are referred to the residual solvent signal ($\delta = 77.16$ ppm). Data for ^1H NMR are reported as follows: chemical shifts (δ ppm), multiplicities (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (Hz), integration.

The data of HRMS was carried out on a Agilent 7250 GC/Q-TOF high-resolution mass spectrometer. Melting point were recorded using a SGW X-4 Melting Point Apparatus.

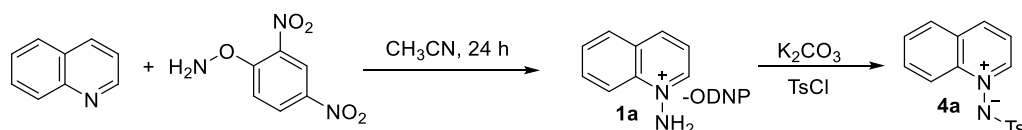
2. Experimental procedures and characterization data

2.1 Experimental procedures

Synthesis of compounds **1** according to the following procedure¹⁻³:

Synthesis of compounds **1**, **4** and **7** according to the following procedure:

The substrates azomethine imines are known and were prepared according to the procedures in the literature.¹⁻³ As exemplified for **1a** and **4a**:

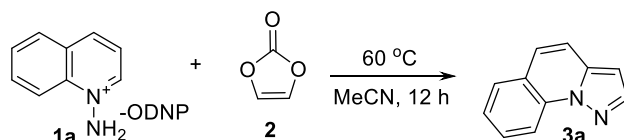


To a solution of quinoline (0.77 g, 6.0 mmol) in acetonitrile (25 mL) was added *O*-(2,4-dinitrophenyl)hydroxylamine (1.3 g, 6.6 mmol). The reaction flask was sealed with rubber plug, and the reaction mixture was stirred for 24 h at room temperature, then upon filtering off the solvent. The orange solid **1a** was obtained, which was carried out to the next step without further purification.

The orange precipitate was dissolved in THF/ H₂O (30 mL, 1/1, v/v). The reaction mixture was added K₂CO₃ (2.9 g, 21.0 mmol) at room temperature, and 4-toluenesulfonyl chloride (2.3 g, 12.0 mmol) was slowly added. After 12 h, the reaction was diluted with 20 mL of H₂O and extracted three times with DCM (30 mL). The combined organic phases were dried over anhydrous Na₂SO₄, concentrated under reduced pressure, and purified by column chromatography on silica gel (DCM/CH₃OH = 20/1, v/v) to afford corresponding product **4a**.

Synthesis of products **3** according to the following procedure:

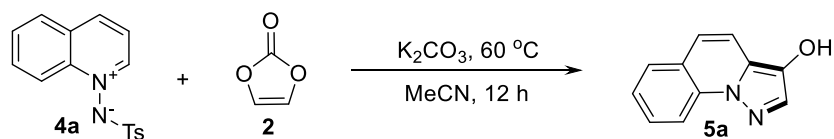
As exemplified for **3a**:



A test tube with 2.0 mL acetonitrile was charged with a stirring bar, *N*-quinolinium 2,4-(dinitro)phenolate (**1a**, 98.4 mg, 0.3 mmol), vinylene carbonate (**2**, 38.7 mg, 0.45 mmol) were added. The reaction was heated with a heating mantle at 60 °C for 12 h. After cooling to room temperature, the solvent was volatilized and the crude product was purified by flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v), and the target compound **3a** was obtained.

Synthesis of products 5 and 7 according to the following procedure:

As exemplified for **5a**:



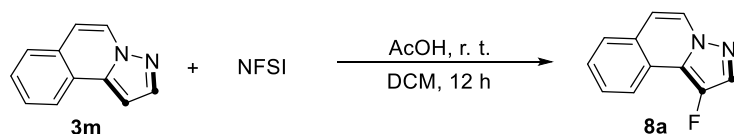
A test tube with 2.0 mL acetonitrile was charged with a stirring bar, K_2CO_3 (82.4 mg, 0.6 mmol) *N*-iminoquinolinium ylides (**4a**, 89.4 mg, 0.3 mmol), vinylene carbonate (**2**, 38.7 mg, 0.45 mmol) were added. The reaction was heated with a heating mantle at $60\text{ }^\circ\text{C}$ for 12 h. After cooling to room temperature, the solvent was volatilized and the crude product was purified by flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v), and the target compound **5a** was obtained.

Large-scale reactions for **3a** and **5a**: As exemplified for **3a**

A pressure tube was charged with *N*-quinolinium 2,4-(dinitro)phenolate (**1a**, 98.4 mg, 1 mmol), vinylene carbonate (**2**, 129.0 mg, 1.5 mmol) and MeCN (20.0 mL) was added and the mixtures were heated with a heating mantle at $60\text{ }^\circ\text{C}$ for 12 h, then cooled to room temperature. The solvent was volatilized and the crude product was separated by column chromatography (PE:EA = 5:1) to give a pure sample of **3a** in 49% yield (82.3 mg).

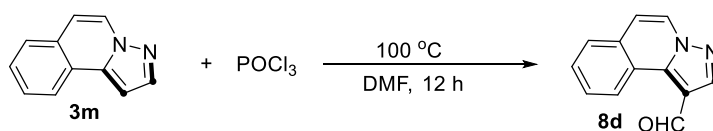
Synthesis of products **8a-8c** according to the following procedure⁴:

As exemplified for **8a**:



A mixture of the pyrazolo[5,1-*a*]isoquinoline **3m** (50.4 mg, 0.3 mmol), NFSI (129.0 mg, 0.5 mmol) and AcOH (0.1 mmol) in DCM (2 mL) was stirred overnight at rt. The resulting mixture was filtered, and the filtrate was evaporated in vacuo. The residue was purified by flash column chromatography (PE:EA = 5:1), affording the corresponding halogenated product **8a**.

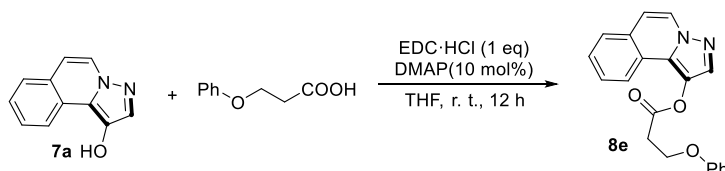
Synthesis of product **8d** according to the following procedure⁴:



A test tube with 2.0 mL DMF was charged with a stirring bar, pyrazolo[5,1-*a*]isoquinoline **3m** (50.4 mg, 0.3 mmol), POCl₃ (68.9 mg, 0.3 mmol) were added. The reaction was heated with a heating mantle at 100 °C for 12 h. The phases were separated and the aqueous phase was extracted with DCM (25 mL ×2) and the combined organic layer was dried over anhydrous MgSO₄, filtered, and concentrated in vacuo. Finally, the crude product was purified by flash column chromatography on silica gel (PE:EA = 5:1), affording the corresponding product **8d**.

Synthesis of products **8e** and **8f** according to the following procedure⁵:

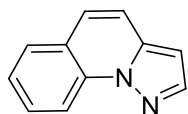
As exemplified for **8e**:



A mixture of the carboxylic acid (0.3 mmol), pyrazolo[5,1-*a*]isoquinolin-1-ol **7a** (55.2 mg, 0.3 mmol), DMAP (0.1 mmol), and 1-ethyl-3-(3-(dimethylamino)propyl)carbodiimide hydrochloride (EDC·HCl, 57.3 mg, 0.3 mmol) in THF (2 mL) was stirred overnight at 25 °C. The resulting mixture was filtered, and the filtrate was evaporated in vacuo. The residue was purified by flash column chromatography (PE:EA = 5:1), affording the corresponding ester **8e**.

2.2 Characterization data

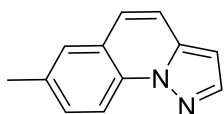
Pyrazolo[1,5-*a*]quinoline (3a)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3a**.

Yellow liquid (42.3 mg, 84%). ¹H NMR (400 MHz, CDCl₃) δ 8.59 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 1.7 Hz, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.67 (t, *J* = 7.8 Hz, 1H), 7.49 – 7.39 (m, 3H), 6.62 (d, *J* = 1.9 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 141.2, 138.1, 134.9, 129.5, 128.5, 124.8, 124.7, 123.4, 116.8, 115.6, 99.9. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₈N₂ [M]: 168.0687, found: 168.0693.

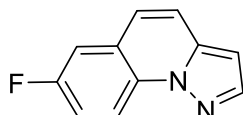
7-Methylpyrazolo[1,5-*a*]quinoline (3b)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3b**.

Red liquid (44.2 mg, 81%). ¹H NMR (400 MHz, CDCl₃) δ 8.47 (d, *J* = 8.5 Hz, 1H), 8.00 (d, *J* = 2.0 Hz, 1H), 7.54 (s, 1H), 7.51 – 7.47 (m, 1H), 7.42 (d, *J* = 9.3 Hz, 1H), 7.35 (d, *J* = 9.3 Hz, 1H), 6.59 (d, *J* = 2.1 Hz, 1H), 2.50 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 140.9, 137.9, 134.5, 133.1, 130.9, 128.1, 124.6, 123.4, 116.7, 115.4, 99.6, 21.3. HRMS GC/QTOF (*m/z*): calcd for C₁₂H₁₀N₂ [M]: 182.0844, found: 182.0849.

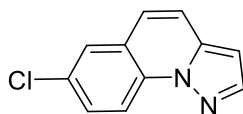
7-Fluoropyrazolo[1,5-*a*]quinoline (3c)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3c**.

Brown solid (41.8mg, 75%), mp 131.8-132.7 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.57 (dd, *J* = 8.7, 4.9 Hz, 1H), 8.00 (s, 1H), 7.50 (d, *J* = 9.3 Hz, 1H), 7.40 (dd, *J* = 15.0, 5.8 Hz, 2H), 7.37 – 7.30 (m, 1H), 6.63 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 141.2, 137.8, 131.6 (d, *J* = 5.1 Hz), 124.5 (d, *J* = 8.7 Hz), 123.9 (d, *J* = 3.3 Hz), 118.2, 117.8, 117.7, 117.6 (d, *J* = 2.2 Hz), 113.3, 113.0, 100.2, 94.8. ¹⁹F NMR (376 MHz, CDCl₃) δ -117.31. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₇FN₂ [M]: 186.0593, found: 186.0600.

7-Chloropyrazolo[1,5-*a*]quinoline (3d)

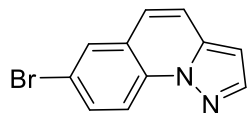


Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3d**.

Yellow solid (53.9 mg, 89%), mp 160.9-161.8 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.48 (d, *J* = 8.9 Hz, 1H), 8.00 (d, *J* = 1.7 Hz, 1H), 7.69 (d, *J* = 1.9 Hz, 1H), 7.58 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.44 (d, *J* = 9.3 Hz, 1H), 7.28 – 7.25 (m, 1H), 6.61 (d, *J* = 1.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 141.5,

137.8, 133.4, 130.3, 129.6, 127.5, 124.4, 123.5, 118.1, 117.1, 100.3. HRMS GC/QTOF (m/z): calcd for $C_{11}H_7CIN_2$ [M]: 202.0298, found: 202.0298.

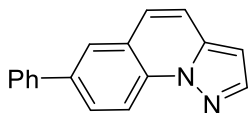
7-Bromopyrazolo[1,5-a]quinoline (3e)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3e**.

Yellow solid (60.3 mg, 82%), mp 165.7-166.3 °C. 1H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, J = 8.9 Hz, 1H), 8.01 (d, J = 1.7 Hz, 1H), 7.88 (d, J = 1.8 Hz, 1H), 7.77 – 7.66 (m, 1H), 7.46 (d, J = 9.3 Hz, 1H), 7.29 (d, J = 9.3 Hz, 1H), 6.62 (d, J = 1.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 137.2, 133.8, 132.4, 130.6, 124.8, 123.4, 118.1, 117.9, 117.4, 100.4. HRMS GC/QTOF (m/z): calcd for $C_{11}H_7BrN_2$ [M]: 245.9793, found: 245.9789.

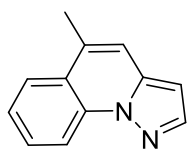
7-Phenylpyrazolo[1,5-a]quinoline (3f)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3f**.

Yellow solid (65.1 mg, 89%), mp 182.1-183.0 °C. 1H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 8.6 Hz, 1H), 7.95 (d, J = 1.9 Hz, 1H), 7.87 – 7.79 (m, 2H), 7.60 (d, J = 7.7 Hz, 2H), 7.45 – 7.34 (m, 4H), 7.31 (dd, J = 14.1, 6.6 Hz, 1H), 6.53 (d, J = 1.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 140.3, 138.1, 137.8, 134.3, 129.1, 128.6, 127.6, 127.3, 126.6, 124.8, 123.7, 117.2, 116.0, 99.9. HRMS GC/QTOF (m/z): calcd for $C_{17}H_{12}N_2$ [M]: 244.1000, found: 244.0996.

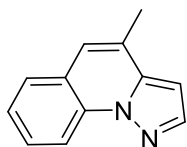
5-Methylpyrazolo[1,5-a]quinoline (3g)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3g**. Red

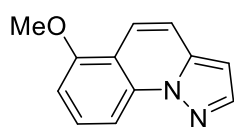
solid (36.6 mg, 67%), mp 134.1-134.9 °C. 1H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 8.3 Hz, 1H), 7.90 (s, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.47 – 7.37 (m, 1H), 7.19 (s, 1H), 6.42 (s, 1H), 2.52 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 134.7, 131.5, 129.3, 128.8, 125.3, 124.6, 123.7, 116.0, 115.8, 98.8, 19.3. HRMS GC/QTOF (m/z): calcd for $C_{12}H_{10}N_2$ [M]: 182.0844, found: 182.0842.

4-Methylpyrazolo[1,5-a]quinoline (3h)



Flash column chromatography on silica gel (eluent:eluent: PE/EA = 5/1, v/v) to afford **3h**. Brown solid (45.3 mg, 83%), mp 77.6-78.5 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.53 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 1.9 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.17 (s, 1H), 6.60 (d, *J* = 2.0 Hz, 1H), 2.49 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 141.1, 139.8, 133.8, 128.4, 127.7, 126.3, 124.8, 123.8, 122.8, 115.4, 98.6, 18.6. HRMS GC/QTOF (m/z): calcd for C₁₂H₁₀N₂ [M]: 182.0844, found: 182.0852.

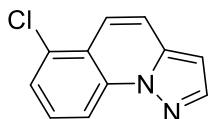
6-Methoxypyrazolo[1,5-*a*]quinoline (**3i**)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3i**.

Yellow solid (46.3 mg, 78%), mp 143.3-144.2 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.19 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* = 1.9 Hz, 1H), 7.85 (d, *J* = 9.5 Hz, 1H), 7.60 (t, *J* = 8.3 Hz, 1H), 7.43 (d, *J* = 9.5 Hz, 1H), 6.88 (d, *J* = 8.1 Hz, 1H), 6.61 (d, *J* = 2.0 Hz, 1H), 4.01 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 156.3, 141.2, 138.4, 135.7, 129.9, 119.1, 115.4, 114.4, 108.1, 104.8, 99.5, 56.0. HRMS GC/QTOF (m/z): calcd for C₁₂H₁₀N₂O [M]: 198.0793, found: 198.0799.

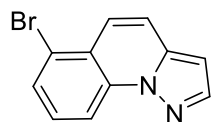
6-Chloropyrazolo[1,5-*a*]quinoline (**3j**)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3j**.

Yellow solid (45.4 mg, 75%), mp 134.2-135.1 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.53 (d, *J* = 8.3 Hz, 1H), 8.04 (s, 1H), 7.83 (d, *J* = 9.6 Hz, 1H), 7.54 (dt, *J* = 14.5, 7.8 Hz, 3H), 6.65 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 141.9, 137.9, 136.0, 132.7, 129.4, 125.3, 121.4, 120.8, 117.8, 114.6, 100.3. HRMS GC/QTOF (m/z): calcd for C₁₁H₇ClN₂ [M]: 202.0298, found: 202.0306.

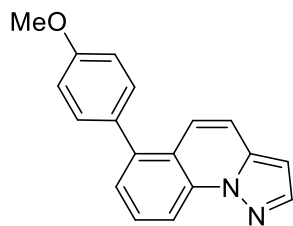
2-(4-Methoxyphenyl)-[1,2,4]triazolo[1,5-*a*]quinoline (**3k**)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3k**.

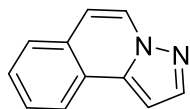
Brown solid (58.1 mg, 79%), mp 157.2-158.1. ¹H NMR (400 MHz, CDCl₃) δ 8.57 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 1.9 Hz, 1H), 7.79 (d, *J* = 9.6 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.50 (dd, *J* = 16.7, 8.8 Hz, 2H), 6.64 (d, *J* = 2.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 141.9, 137.8, 135.9, 129.8, 128.8, 123.5, 123.0, 122.7, 118.0, 115.3, 100.3. HRMS GC/QTOF (m/z): calcd for C₁₁H₇BrN₂ [M]: 245.9793, found: 245.9789.

6-(4-Methoxyphenyl)pyrazolo[1,5-*a*]quinoline (**3l**)



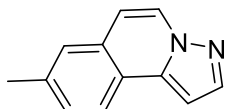
Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3l**. Yellow solid (69.9 mg, 85%), mp 194.2-195.1 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.62 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 1.8 Hz, 1H), 7.68 (t, *J* = 7.9 Hz, 1H), 7.50 (d, *J* = 9.6 Hz, 1H), 7.38 (dd, *J* = 8.8, 3.5 Hz, 4H), 7.04 (d, *J* = 8.5 Hz, 2H), 6.60 (d, *J* = 1.8 Hz, 1H), 3.90 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 159.4, 141.4, 141.2, 137.7, 135.43, 132.3, 131.2, 128.9, 126.1, 122.8, 121.5, 116.4, 114.6, 113.9, 99.6, 55.5. HRMS GC/QTOF (*m/z*): calcd for C₁₈H₁₄N₂O [M]: 274.1106, found: 274.1101.

Pyrazolo[5,1-*a*]isoquinoline (3m)



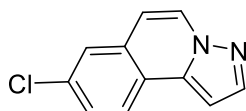
Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3m**. Yellow solid (40.8 mg, 81%), mp 80.5-81.3 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.27 (d, *J* = 7.4 Hz, 1H), 8.10 (d, *J* = 7.4 Hz, 1H), 7.98 (d, *J* = 1.8 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.56 (dq, *J* = 7.3, 5.8 Hz, 2H), 7.00 (dd, *J* = 4.4, 2.7 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 141.3, 138.5, 128.8, 128.0, 127.8, 127.3, 126.5, 124.7, 123.8, 112.3, 97.7. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₈N₂ [M]: 168.0687, found: 168.0690.

8-Methylpyrazolo[5,1-*a*]isoquinoline (3n)



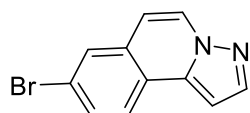
Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3n**. Yellow solid (45.3 mg, 83%), mp 117.6-118.5. ¹H NMR (400 MHz, CDCl₃) δ 8.15 (d, *J* = 7.4 Hz, 1H), 7.89 (dd, *J* = 13.4, 4.8 Hz, 2H), 7.42 (s, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 6.85 (d, *J* = 7.1 Hz, 2H), 2.43 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 141.2, 138.6, 138.1, 129.3, 129.0, 127.1, 126.5, 123.7, 122.5, 112.1, 97.1, 21.7. HRMS GC/QTOF (*m/z*): calcd for C₁₂H₁₀N₂ [M]: 182.0844, found: 182.0848.

8-Chloropyrazolo[5,1-*a*]isoquinoline (3o)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3o**. Yellow solid (47.9 mg, 79%), mp 181.1-182.0 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.28 (d, *J* = 6.5 Hz, 1H), 8.05 – 7.94 (m, 2H), 7.71 (s, 1H), 7.53 (d, *J* = 8.3 Hz, 1H), 7.01 – 6.87 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 141.7, 137.9, 133.8, 130.1, 128.2, 127.6, 126.6, 125.3, 123.1, 111.1, 97.9. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₇ClN₂ [M]: 202.0298, found: 202.0292.

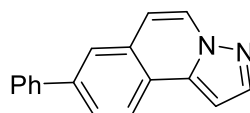
8-Bromopyrazolo[5,1-*a*]isoquinoline (**3p**)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3p**.

Yellow solid (61.7 mg, 84%), mp 163.5-164.3. ¹H NMR (400 MHz, CDCl₃) δ 8.25 (d, *J* = 7.4 Hz, 1H), 7.98 (d, *J* = 1.5 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.84 (d, *J* = 1.4 Hz, 1H), 7.63 (dd, *J* = 8.5, 1.6 Hz, 1H), 6.96 (s, 1H), 6.87 (d, *J* = 7.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 141.6, 137.9, 130.8, 130.3, 129.6, 127.6, 125.4, 123.3, 121.9, 111.0, 97.9. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₇BrN₂ [M]: 245.9793, found: 245.9802.

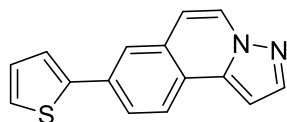
8-Phenylpyrazolo[5,1-*a*]isoquinoline (**3q**)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3q**.

White solid (59.3 mg, 81%), mp 182.1-183.1 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.29 (d, *J* = 7.4 Hz, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 1.6 Hz, 1H), 7.91 (s, 1H), 7.81 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.69 (d, *J* = 7.4 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 7.01 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 141.4, 140.9, 140.4, 138.4, 129.3, 129.1, 127.9, 127.4, 127.1, 126.8, 125.5, 124.4, 123.7, 112.4, 97.8. HRMS GC/QTOF (*m/z*): calcd for C₁₇H₁₂N₂ [M]: 244.1000, found: 244.1008.

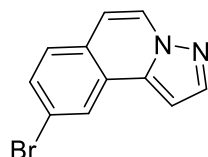
8-(Thiophen-2-yl)pyrazolo[5,1-*a*]isoquinoline (**3r**)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford

3r. Yellow solid (54.8 mg, 73%), mp 238.8-239.5 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 2.0 Hz, 1H), 7.91 (s, 1H), 7.82 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.44 (d, *J* = 3.6 Hz, 1H), 7.36 (d, *J* = 5.1 Hz, 1H), 7.14 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.99 (dd, *J* = 11.4, 4.7 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 143.6, 141.4, 138.3, 134.1, 129.4, 128.4, 127.0, 125.8, 125.8, 124.5, 124.0, 123.9, 123.7, 112.2, 97.8. HRMS GC/QTOF (*m/z*): calcd for C₁₅H₁₀N₂S [M]: 250.0565, found: 250.0559.

9-Bromopyrazolo[5,1-*a*]isoquinoline (**3s**)

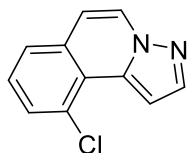


Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3s**.

Yellow solid (64.7 mg, 88%), mp 133.9-134.8 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.23 (d,

$J = 7.4$ Hz, 1H), 8.17 (s, 1H), 7.97 (d, $J = 1.6$ Hz, 1H), 7.58 (dd, $J = 8.5, 1.5$ Hz, 1H), 7.52 (d, $J = 8.5$ Hz, 1H), 6.93 (d, $J = 1.3$ Hz, 1H), 6.89 (d, $J = 7.4$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 141.5, 137.2, 131.0, 128.7, 127.4, 126.8, 126.3, 126.0, 121.5, 111.5, 98.1. HRMS GC/QTOF (m/z): calcd for $\text{C}_{11}\text{H}_7\text{BrN}_2$ [M]: 245.9793, found: 245.9789.

10-Chloropyrazolo[5,1-*a*]isoquinoline (3t)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3t**.

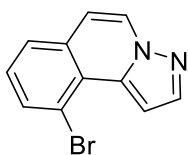
Yellow solid (52.7 mg, 87%), mp 179.3-180.2 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.27 (d,

$J = 7.2$ Hz, 1H), 8.02 (s, 1H), 7.66 (s, 1H), 7.58 (t, $J = 8.2$ Hz, 2H), 7.40 (t, $J = 7.6$ Hz,

1H), 6.93 (d, $J = 7.1$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 141.3, 135.8, 131.4, 130.8, 129.5, 127.8, 127.5,

126.1, 123.0, 112.0, 103.6. HRMS GC/QTOF (m/z): calcd for $\text{C}_{11}\text{H}_7\text{ClN}_2$ [M]: 202.0298, found: 202.0292.

10-Bromopyrazolo[5,1-*a*]isoquinoline (3u)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3u**.

Yellow solid (61.0 mg, 83%), mp 174.1-174.9 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.28 (d,

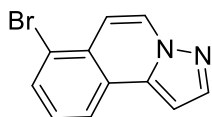
$J = 7.3$ Hz, 1H), 8.02 (d, $J = 2.0$ Hz, 1H), 7.93 (d, $J = 1.7$ Hz, 1H), 7.84 (d, $J = 7.8$ Hz,

1H), 7.65 (d, $J = 7.7$ Hz, 1H), 7.33 (t, $J = 7.8$ Hz, 1H), 6.95 (d, $J = 7.3$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3)

δ 140.9, 136.6, 133.5, 131.7, 128.1, 127.5, 126.9, 124.5, 119.7, 112.2, 103.4. HRMS GC/QTOF (m/z): calcd

for $\text{C}_{11}\text{H}_7\text{BrN}_2$ [M]: 245.9793, found: 245.9801.

7-Bromopyrazolo[5,1-*a*]isoquinoline (3v)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3v**.

Yellow solid (66.2 mg, 90%), mp 157.2-158.1 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.27

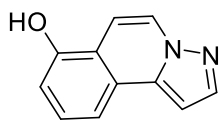
(d, $J = 7.7$ Hz, 1H), 7.98 (t, $J = 10.7$ Hz, 1H), 7.73 (d, $J = 7.7$ Hz, 1H), 7.34 (td, $J = 7.9,$

3.3 Hz, 1H), 6.95 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 141.8, 137.8, 137.8, 131.8, 128.3, 128.3, 127.6,

126.0, 123.2, 122.3, 110.8, 98.3. HRMS GC/QTOF (m/z): calcd for $\text{C}_{11}\text{H}_7\text{BrN}_2$ [M]: 245.9793, found:

245.9789.

Pyrazolo[5,1-*a*]isoquinolin-7-ol (3w)



Flash column chromatography on silica gel (eluent: PE/EA = 5/1, v/v) to afford **3w**.

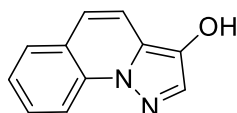
Yellow solid (33.7 mg, 61%), mp 171.7-172.6 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.26

(d, *J* = 7.5 Hz, 1H), 8.00 (s, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.48 – 7.38 (m, 2H), 6.98 (s,

2H). ¹³C NMR (100 MHz, CDCl₃) δ 152.4, 141.0, 138.4, 128.6, 126.0, 125.3, 118.7, 115.9, 112.6, 106.9, 97.9.

HRMS GC/QTOF (m/z): calcd for C₁₁H₈N₂O [M]: 184.0637, found: 184.0629.

Pyrazolo[1,5-*a*]quinolin-3-ol (**5a**)



Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **5a**.

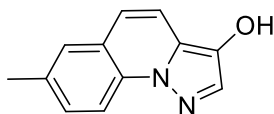
Brown solid (43.6 mg, 79%), mp 192.6-193.4 °C. ¹H NMR (400 MHz, Methanol-D₄)

δ 8.25 (d, *J* = 8.3 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.59 – 7.49 (m, 1H), 7.42 – 7.27 (m, 2H), 7.16 (d, *J* = 9.3

Hz, 1H). ¹³C NMR (100 MHz, Methanol-D₄) δ 136.5, 135.8, 130.4, 130.2, 129.7, 127.5, 125.7, 124.9, 122.8,

115.8, 115.1. HRMS GC/QTOF (m/z): calcd for C₁₁H₈N₂O [M]: 184.0637, found: 184.0629.

7-Methylpyrazolo[1,5-*a*]quinolin-3-ol (**5b**)



Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **5b**.

Brown solid (40.4 mg, 68%), mp 220.4-221.3 °C. ¹H NMR (400 MHz,

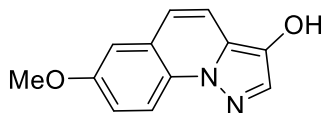
Methanol-D₄) δ 8.16 (d, *J* = 8.4 Hz, 1H), 7.60 (s, 1H), 7.48 (s, 1H), 7.42 – 7.30 (m, 2H), 7.17 (d, *J* = 9.3 Hz,

1H), 2.40 (s, 3H). ¹³C NMR (100 MHz, Methanol-D₄) δ 136.4, 135.8, 133.9, 131.5, 129.9, 129.4, 127.4,

125.0, 122.8, 115.7, 115.0, 21.1. HRMS GC/QTOF (m/z): calcd for C₁₂H₁₀N₂O [M]: 198.0793, found:

198.0792.

7-Methoxypyrazolo[1,5-*a*]quinolin-3-ol (**5c**)



Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to

afford **5c**. Yellow solid (46.2 mg, 72%), mp 193.2-194.1 °C. ¹H NMR (400

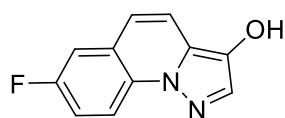
MHz, Acetone-D₆) δ 8.33 (d, *J* = 9.1 Hz, 1H), 7.62 (d, *J* = 6.2 Hz, 1H), 7.47 (d, *J* = 9.4 Hz, 1H), 7.31 (d, *J* =

2.6 Hz, 1H), 7.27 – 7.22 (m, 2H), 3.90 (s, 3H). ¹³C NMR (100 MHz, Acetone-D₆) δ 157.6, 136.0, 130.4,

129.4, 125.9, 125.5, 121.6, 118.7, 116.5, 116.4, 110.8, 55.9. HRMS GC/QTOF (m/z): calcd for C₁₂H₁₀N₂O₂

[M]: 214.0742, found: 214.0745.

7-Fluoropyrazolo[1,5-*a*]quinolin-3-ol (**5d**)

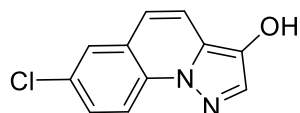


Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford

5d. Yellow solid (44.2 mg, 73%), mp 215.6-216.5 °C. ¹H NMR (400 MHz,

Methanol-D₄) δ 8.24 (dd, *J* = 8.5, 4.7 Hz, 1H), 7.60 (s, 1H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 8.7 Hz, 1H), 7.13 (d, *J* = 9.2 Hz, 1H). ¹³C NMR (100 MHz, Methanol-D₄) δ 160.9 (d, *J* = 242.4 Hz), 136.8, 132.5, 130.3, 127.1, 126.3 (d, *J* = 8.9 Hz), 121.8 (d, *J* = 3.1 Hz), 17.9 (d, *J* = 24.8 Hz), 117.3, 117.2, 117.2, 114.3 (d, *J* = 23.1 Hz). ¹⁹F NMR (376 MHz, Methanol-D₄) δ -119.63 (m). HRMS GC/QTOF (*m/z*): calcd for C₁₁H₇FN₂O [M]: 202.0542, found: 202.0534.

7-Chloropyrazolo[1,5-*a*]quinolin-3-ol (5e)

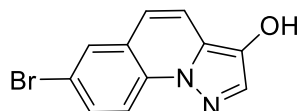


Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford

5e. Yellow solid (42.5 mg, 65%), mp 225.4-225.8 °C. ¹H NMR (400 MHz,

Acetone-D₆) δ 8.38 (d, *J* = 8.9 Hz, 1H), 8.28 (s, 1H), 7.84 (d, *J* = 2.0 Hz, 1H), 7.70 (s, 1H), 7.62 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.53 (d, *J* = 9.4 Hz, 1H), 7.26 (d, *J* = 9.4 Hz, 1H). ¹³C NMR (100 MHz, Acetone-D₆) δ 136.6, 134.4, 130.9, 130.2, 129.9, 128.4, 126.2, 125.8, 120.7, 117.4, 117.0. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₇ClN₂O [M]: 218.0247, found: 218.0240.

7-Bromopyrazolo[1,5-*a*]quinolin-3-ol (5f)

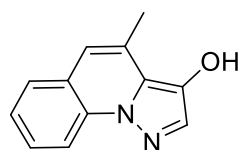


Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford

5f. Brown solid (55.6 mg, 71%), mp 219.3-219.9. ¹H NMR (400 MHz,

Methanol-D₄) δ 8.25 – 8.09 (m, 1H), 7.61 (dt, *J* = 28.6, 13.9 Hz, 2H), 7.52 – 7.43 (m, 1H), 7.37 (dd, *J* = 10.7, 8.2 Hz, 1H), 7.04 (dd, *J* = 31.8, 29.0 Hz, 1H). ¹³C NMR (100 MHz, Methanol-D₄) δ 136.9, 134.4, 131.1, 130.8, 130.1, 128.7, 127.1, 126.2, 121.5, 117.3, 116.8. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₇BrN₂O [M]: 261.9742, found: 261.9741.

4-Methylpyrazolo[1,5-*a*]quinolin-3-ol (5g)



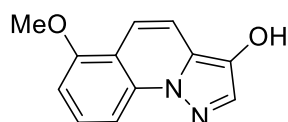
Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **5g**.

Yellow solid (42.8 mg, 72%), mp 185.6-186.4 °C. ¹H NMR (400 MHz, Methanol-D₄)

δ 8.21 (d, *J* = 8.3 Hz, 1H), 7.58 (d, *J* = 10.0 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.47 (t,

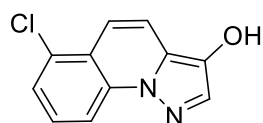
$J = 7.7$ Hz, 1H), 7.29 (t, $J = 7.5$ Hz, 1H), 6.84 (s, 1H), 2.56 (s, 3H). ^{13}C NMR (100 MHz, Methanol-D4) δ 137.9, 134.7, 130.7, 129.1, 128.8, 128.7, 127.7, 125.7, 125.4, 121.3, 114.9, 18.3. HRMS GC/QTOF (m/z): calcd for $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}$ [M]: 198.0793, found: 198.0786.

6-Methoxypyrazolo[1,5-*a*]quinolin-3-ol (5h)



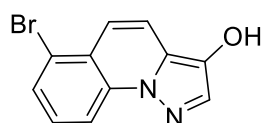
Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **5h**. Yellow solid (44.3 mg, 69%), mp 223.4-224.2 °C. ^1H NMR (400 MHz, Methanol-D4) δ 7.87 (d, $J = 8.5$ Hz, 1H), 7.65 (s, 1H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.50 (t, $J = 8.3$ Hz, 1H), 7.35 (dd, $J = 9.3, 4.3$ Hz, 1H), 6.89 (t, $J = 7.1$ Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (100 MHz, Methanol-D4) δ 157.7, 136.5, 136.2, 130.9, 130.5, 127.7, 116.9, 115.5, 114.4, 107.6, 106.1, 56.5. HRMS GC/QTOF (m/z): calcd for $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_2$ [M]: 214.0742, found: 214.0736.

6-Chloropyrazolo[1,5-*a*]quinolin-3-ol (5i)



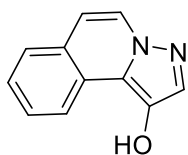
Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **5i**. Yellow solid (47.7 mg, 73%), mp 227.8-228.6 °C. ^1H NMR (400 MHz, Methanol-D4) δ 7.94 (d, $J = 4.4$ Hz, 1H), 7.46 – 7.32 (m, 1H), 7.30 – 7.05 (m, 4H). ^{13}C NMR (100 MHz, Methanol-D4) δ 137.0, 136.9, 133.5, 131.3, 130.3, 126.9, 126.2, 122.7, 118.1, 117.2, 114.3. HRMS GC/QTOF (m/z): calcd for $\text{C}_{17}\text{H}_{13}\text{BrN}_3$ [M]: 218.0247, found: 218.0239.

6-Bromopyrazolo[1,5-*a*]quinolin-3-ol (5j)



Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **5j**. Yellow solid (50.9 mg, 65%), mp 238.1-239.0 °C. ^1H NMR (400 MHz, Methanol-D4) δ 8.29 (d, $J = 8.3$ Hz, 1H), 7.66 (s, 1H), 7.61 (t, $J = 8.4$ Hz, 1H), 7.50 (t, $J = 7.5$ Hz, 2H), 7.43 (dd, $J = 14.5, 6.5$ Hz, 1H). ^{13}C NMR (100 MHz, Methanol-D4) δ 137.0, 131.4, 130.8, 129.9, 127.2, 126.9, 124.1, 123.8, 120.9, 117.5, 115.1. HRMS GC/QTOF (m/z): calcd for $\text{C}_{17}\text{H}_{13}\text{BrN}_3$ [M]: 261.9742, found: 261.9749.

Pyrazolo[5,1-*a*]isoquinolin-1-ol (7a)

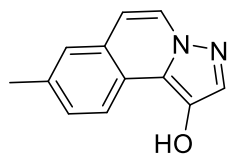


Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **7a**.

Yellow solid (39.2 mg, 71%), mp 228.2-229.1 °C. ¹H NMR (400 MHz, Acetone-D6) δ 8.57 – 8.46 (m, 2H), 8.08 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.9 Hz, 1H), 7.65 (s, 1H), 7.57

(t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 7.3 Hz, 1H). ¹³C NMR (100 MHz, Acetone-D6) δ 137.7, 130.5, 129.0, 128.3, 127.6, 127.6, 127.6, 126.6, 124.2, 123.9, 112.0. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₈N₂O [M]: 184.0637, found: 184.0628.

8-Methylpyrazolo[5,1-*a*]isoquinolin-1-ol (**7b**)

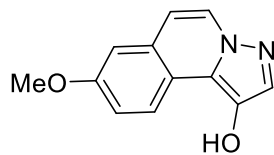


Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **7b**.

Brown solid (42.8 mg, 72%), mp 243.2-244.1 °C. ¹H NMR (400 MHz, Methanol-D4) δ 8.14 (d, *J* = 8.2 Hz, 1H), 7.71 (t, *J* = 6.9 Hz, 1H), 7.39 (s, 1H), 7.19 – 7.10 (m, 2H),

6.57 (d, *J* = 7.5 Hz, 1H), 2.22 (s, 3H). ¹³C NMR (101 MHz, Methanol-D4) δ 138.3, 137.7, 131.5, 130.1, 129.9, 129.6, 127.6, 126.8, 125.6, 124.4, 112.9, 21.6. HRMS GC/QTOF (*m/z*): calcd for C₁₂H₁₀N₂O [M]: 198.0793, found: 198.0786.

8-Methoxy pyrazolo[5,1-*a*]isoquinolin-1-ol (**7c**)

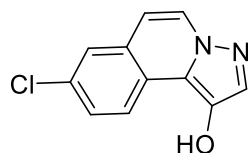


Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **7c**.

Yellow solid (47.5 mg, 74%), mp 201.9-202.7 °C. ¹H NMR (400 MHz, Acetone-D6) δ 8.42 (d, *J* = 8.8 Hz, 1H), 8.05 (d, *J* = 7.5 Hz, 1H), 7.62 (s, 1H),

7.25 (d, *J* = 5.5 Hz, 1H), 7.22 – 7.14 (m, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 3.89 (s, 3H). ¹³C NMR (100 MHz, Acetone-D6) δ 159.5, 136.5, 130.7, 130.6, 127.9, 125.4, 124.5, 120.5, 117.1, 111.7, 109.5, 55.7. HRMS GC/QTOF (*m/z*): calcd for C₁₂H₁₀N₂O₂ [M]: 214.0742, found: 214.0734.

8-Chloropyrazolo[5,1-*a*]isoquinolin-1-ol (**7d**)

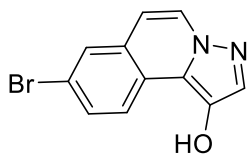


Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **7d**.

Yellow solid (44.5 mg, 68%), mp 301.2-301.9 °C. ¹H NMR (400 MHz, Methanol-D4) δ 7.83 (d, *J* = 7.4 Hz, 1H), 7.58 (s, 1H), 7.39 (dd, *J* = 11.0, 8.2 Hz,

2H), 7.22 (t, *J* = 7.8 Hz, 1H), 6.65 (d, *J* = 7.4 Hz, 1H). ¹³C NMR (100 MHz, Methanol-D4) δ 138.4, 133.1, 133.0, 131.2, 130.2, 128.8, 128.4, 127.0, 125.6, 123.2, 112.5. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₇ClN₂O [M]: 218.0247, found: 218.0242.

8-Bromopyrazolo[5,1-*a*]isoquinolin-1-ol (**7e**)



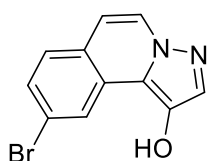
Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **7e**.

Yellow solid (49.3 mg, 63%), mp 258.7-259.8 °C. ¹H NMR (400 MHz, Acetone-D₆)

δ 8.77 (s, 1H), 8.39 (d, *J* = 8.5 Hz, 1H), 8.13 (d, *J* = 7.5 Hz, 1H), 7.95 (s, 1H), 7.74 –

7.63 (m, 2H), 6.94 (d, *J* = 7.5 Hz, 1H). ¹³C NMR (100 MHz, Acetone-D₆) δ 137.9, 131.1, 130.8, 130.6, 129.8, 128.8, 125.7, 125.4, 123.5, 120.6, 110.8. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₇BrN₂O [*M*]: 261.9742, found: 261.9737.

9-Bromopyrazolo[5,1-*a*]isoquinolin-1-ol (**7f**)



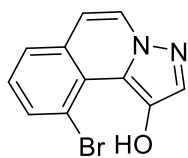
Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **7f**.

Yellow solid (48.5 mg, 62%), mp 259.2-260.1 °C. ¹H NMR (400 MHz, Acetone-D₆) δ

8.87 (s, 1H), 8.61 (s, 1H), 8.12 (d, *J* = 7.5 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.61 (d, *J* = 8.5

Hz, 1H), 6.96 (d, *J* = 7.4 Hz, 1H). ¹³C NMR (100 MHz, Acetone-D₆) δ 138.2, 130.4, 129.5, 128.2, 128.1, 127.8, 126.1, 122.8, 121.5, 111.3, 101.0. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₇BrN₂O [*M*]: 261.9742, found: 261.9749.

10-Bromopyrazolo[5,1-*a*]isoquinolin-1-ol (**7g**)



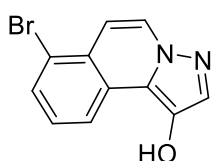
Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **7g**.

Yellow solid (46.2 mg, 59%), mp 230.1-231.0 °C. ¹H NMR (400 MHz, Methanol-D₄) δ

7.86 (d, *J* = 7.3 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.58 (s, 1H), 7.49 (d, *J* = 7.7 Hz, 1H),

7.20 (t, *J* = 7.7 Hz, 1H), 6.69 (d, *J* = 7.3 Hz, 1H). ¹³C NMR (100 MHz, Methanol-D₄) δ 138.5, 135.1, 133.6, 133.2, 129.2, 128.5, 127.6, 127.5, 124.0, 118.2, 112.6. HRMS GC/QTOF (*m/z*): calcd for C₁₁H₇BrN₂O [*M*]: 261.9742, found: 261.9734.

7-Bromopyrazolo[5,1-*a*]isoquinolin-1-ol (**7h**)



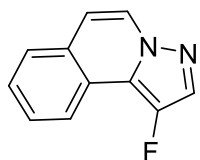
Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **7h**.

Yellow solid (47.8 mg, 61%), mp 281.1-290.0 °C. ¹H NMR (400 MHz, Acetone-D₆) δ

8.52 (d, *J* = 8.0 Hz, 1H), 8.22 (d, *J* = 7.7 Hz, 1H), 7.77 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.71 (s,

1H), 7.49 (t, $J = 7.9$ Hz, 1H), 7.20 (d, $J = 7.7$ Hz, 1H). ^{13}C NMR (100 MHz, Acetone- D_6) δ 138.2, 131.4, 131.0, 129.4, 129.27, 128.3, 127.9, 123.6, 123.1, 121.7, 110.0. HRMS GC/QTOF (m/z): calcd for $\text{C}_{11}\text{H}_7\text{BrN}_2\text{O}$ [M]: 261.9742, found: 261.9738.

1-Fluoropyrazolo[5,1-*a*]isoquinoline (8a)

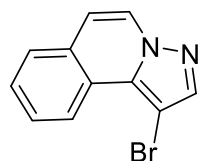


Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford 8a.

Yellow solid (26.2 mg, 47%), mp 98.3-99.2 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.26 (d, $J = 7.9$ Hz, 1H), 8.06 (d, $J = 7.4$ Hz, 1H), 7.85 (d, $J = 3.6$ Hz, 1H), 7.71 (d, $J = 7.8$ Hz, 1H),

7.58 (dt, $J = 23.5, 7.3$ Hz, 2H), 6.95 (d, $J = 7.4$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 144.2 (d, $J = 247.8$ Hz), 142.9, 128.4, 128.1, 127.9 (d, $J = 12.9$ Hz), 127.1, 126.5, 123.8 (d, $J = 6.1$ Hz), 123.7, 123.6, 112.5. ^{19}F NMR (376 MHz, CDCl_3) δ -176.52. HRMS GC/QTOF (m/z): calcd for $\text{C}_{11}\text{H}_7\text{FN}_2$ [M]: 186.0593, found: 186.0586.

1-Bromopyrazolo[5,1-*a*]isoquinoline (8b)

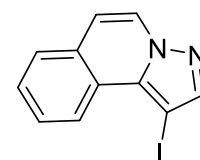


Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford 8b.

Yellow solid (62.5 mg, 85%), mp 140.5-141.4 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.91 (d, 1H), 8.11 (d, $J = 7.4$ Hz, 1H), 7.90 (s, 1H), 7.65 – 7.61 (m, 1H), 7.58 – 7.47 (m, 2H),

6.91 (d, $J = 7.4$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.4, 133.3, 129.2, 128.3, 127.6, 127.1, 126.5, 124.4, 123.2, 112.9, 86.5. HRMS GC/QTOF (m/z): calcd for $\text{C}_{11}\text{H}_7\text{BrN}_2$ [M]: 245.9793, found: 245.9787.

1-Iodopyrazolo[5,1-*a*]isoquinoline (8c)

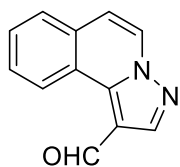


Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford 8c.

Yellow solid (76.5 mg, 87%), mp 133.4-134.1 °C. ^1H NMR (400 MHz, CDCl_3) δ 9.14 (d, $J = 8.0$ Hz, 1H), 8.15 (t, $J = 8.2$ Hz, 1H), 7.94 (s, 1H), 7.63 (t, $J = 8.4$ Hz, 1H), 7.55 (dt,

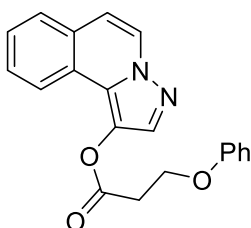
$J = 14.2, 6.9$ Hz, 2H), 6.94 (d, $J = 7.4$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 147.5, 134.8, 129.3, 128.4, 127.3, 127.2, 126.5, 124.7, 123.0, 113.0, 48.5. HRMS GC/QTOF (m/z): calcd for $\text{C}_{11}\text{H}_7\text{IN}_2$ [M]: 293.9654, found: 293.9651.

Pyrazolo[5,1-*a*]isoquinoline-1-carbaldehyde (8d)



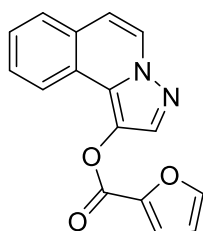
Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **8d**. Yellow solid (42.9 mg, 73%), mp 183.1-183.9 °C. ¹H NMR (400 MHz, CDCl₃) δ 10.15 (s, 1H), 9.72 – 9.60 (m, 1H), 8.45 (s, 1H), 8.33 (d, *J* = 7.3 Hz, 1H), 7.79 (dd, *J* = 13.0, 9.8 Hz, 1H), 7.76 – 7.64 (m, 2H), 7.29 (d, *J* = 7.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 183.2, 148.6, 137.9, 130.9, 130.4, 128.5, 128.0, 127.1, 126.2, 124.4, 117.5, 115.8. HRMS GC/QTOF (*m/z*): calcd for C₁₂H₈N₂O [M]: 196.0637, found: 196.0634.

Pyrazolo[5,1-*a*]isoquinolin-1-yl 3-phenoxypropanoate (**8e**)



Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **8e**. Yellow solid (66.7 mg, 69%), mp 190.7-191.5 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.28 (d, *J* = 8.0 Hz, 1H), 8.16 (s, 1H), 8.11 (d, *J* = 7.4 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.9 Hz, 2H), 6.98 (dt, *J* = 10.2, 7.5 Hz, 4H), 4.48 (t, *J* = 6.1 Hz, 2H), 3.23 (t, *J* = 6.1 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 168.5, 158.5, 133.4, 129.7, 129.2, 128.9, 128.1, 127.9, 127.2, 127.0, 126.5, 124.1, 123.7, 121.5, 114.7, 112.6, 63.3, 35.1. HRMS GC/QTOF (*m/z*): calcd for C₂₀H₁₆N₂O₃ [M]: 332.1161, found: 332.1154.

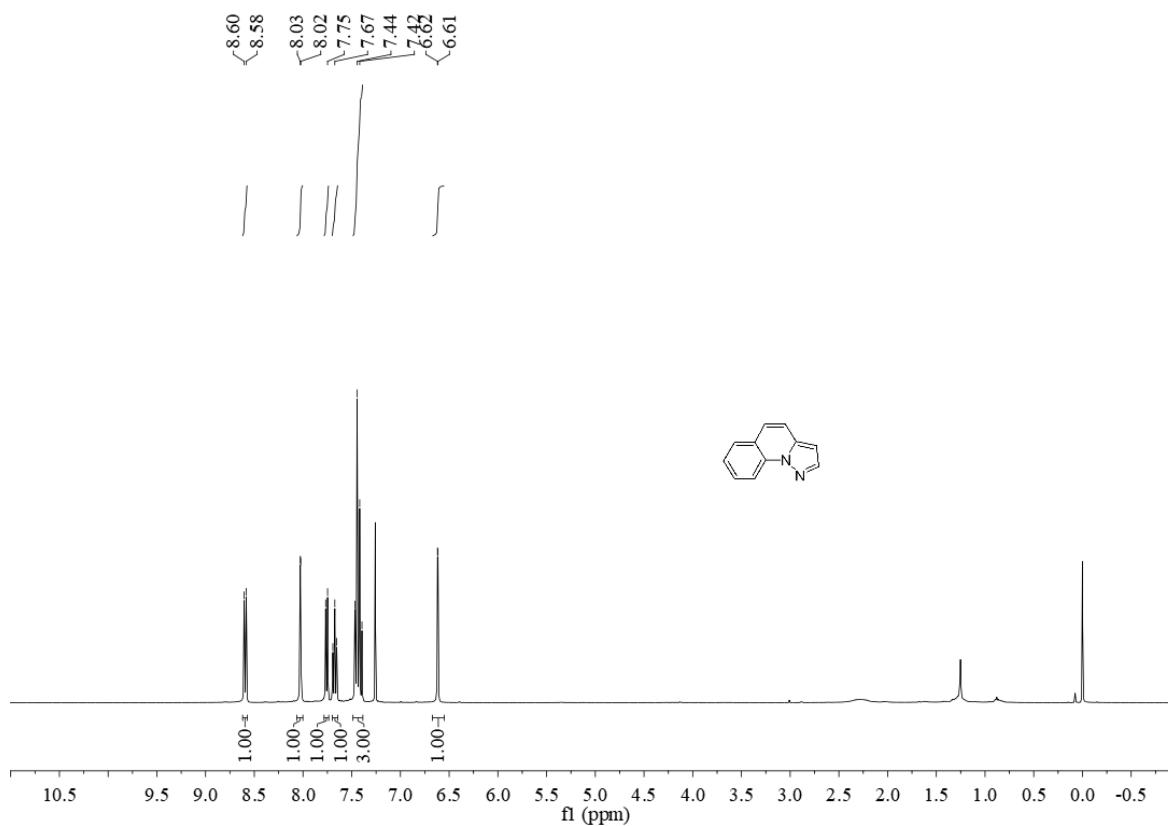
Pyrazolo[5,1-*a*]isoquinolin-1-yl furan-2-carboxylate (**8f**)



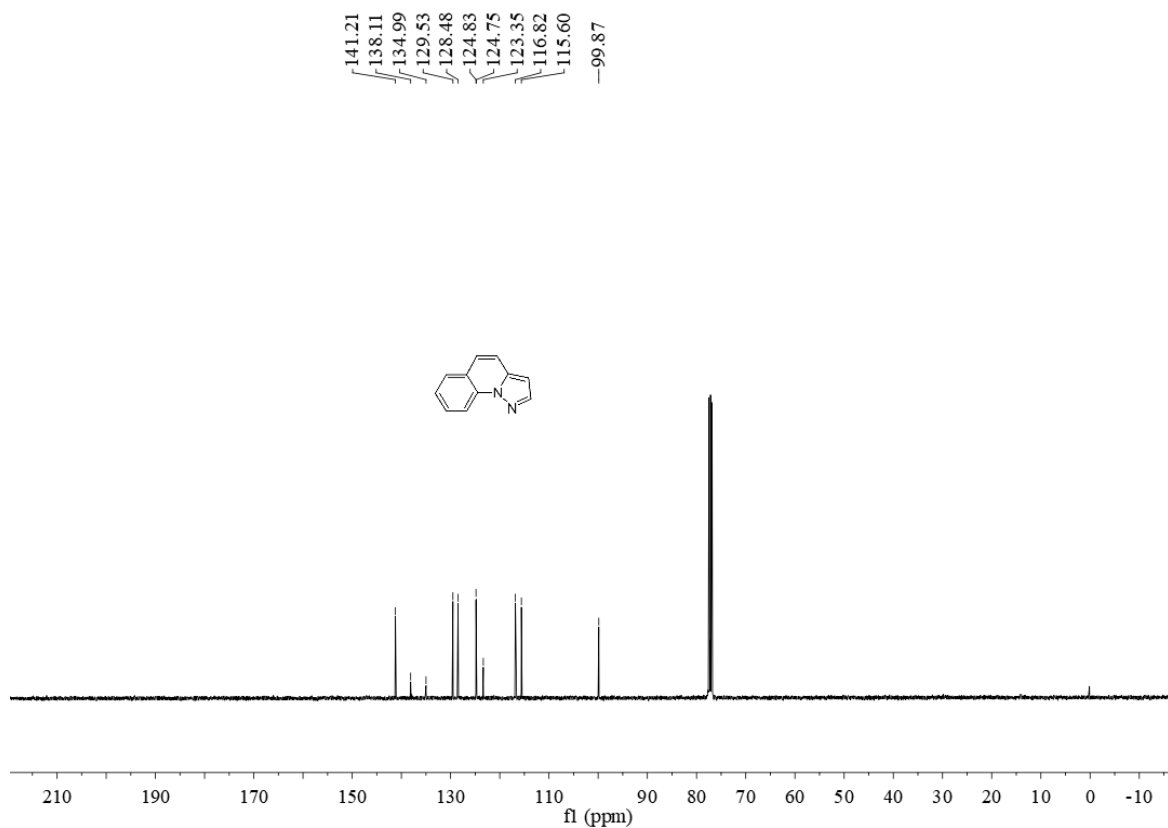
Flash column chromatography on silica gel (eluent: PE/EA = 2/1, v/v) to afford **8f**. Yellow solid (70.1 mg, 84%), mp 182.5-183.4 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.33 (s, 1H), 8.21 (d, *J* = 4.9 Hz, 2H), 8.09 (d, *J* = 7.4 Hz, 1H), 7.70 – 7.63 (m, 1H), 7.57 (s, 1H), 7.55 – 7.47 (m, 2H), 6.97 (d, *J* = 1.0 Hz, 1H), 6.91 (d, *J* = 7.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 160.3, 148.9, 144.5, 133.5, 128.9, 127.9, 127.7, 127.3, 127.2, 127.0, 126.4, 123.9, 123.3, 118.5, 112.4, 110.1. HRMS GC/QTOF (*m/z*): calcd for C₁₆H₁₀N₂O₃ [M]: 278.0691, found: 278.0686.

3. NMR spectra for new compounds

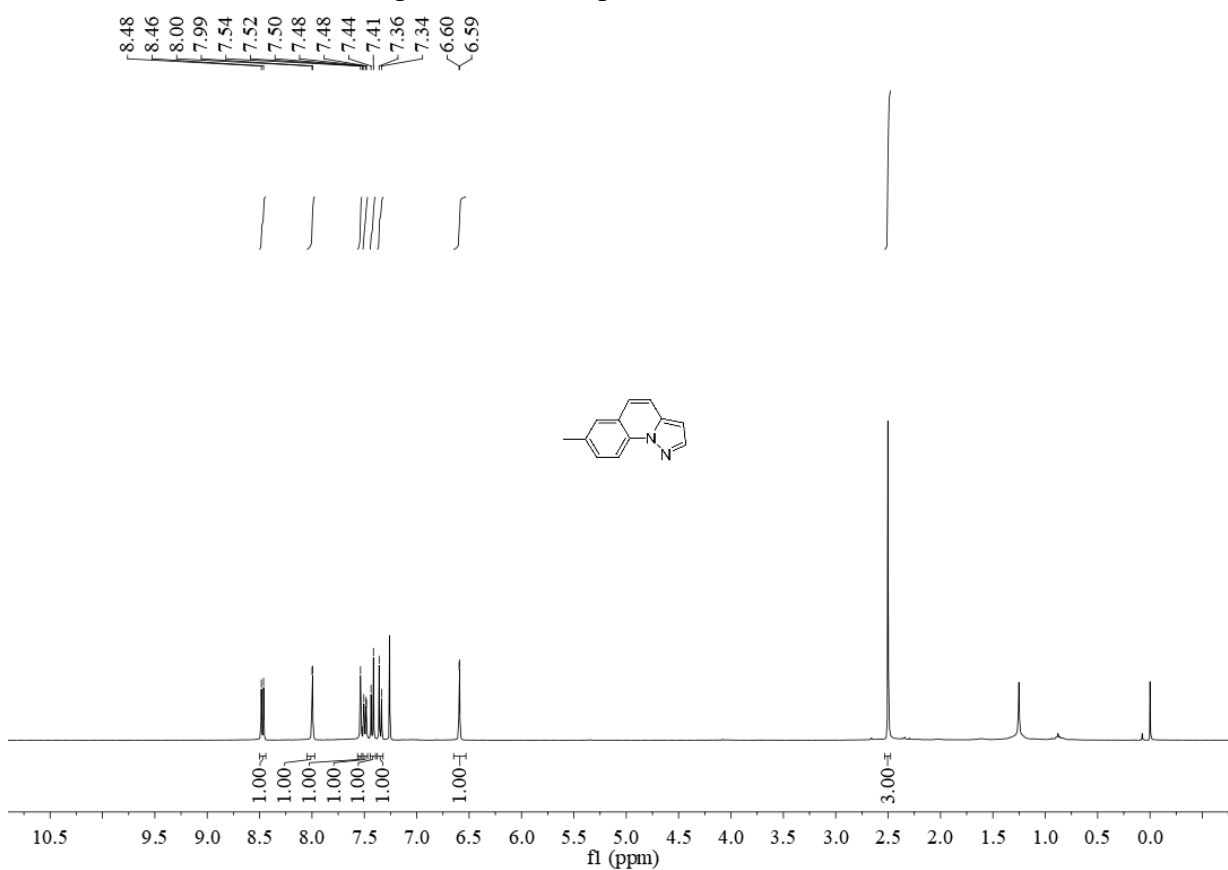
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3a**



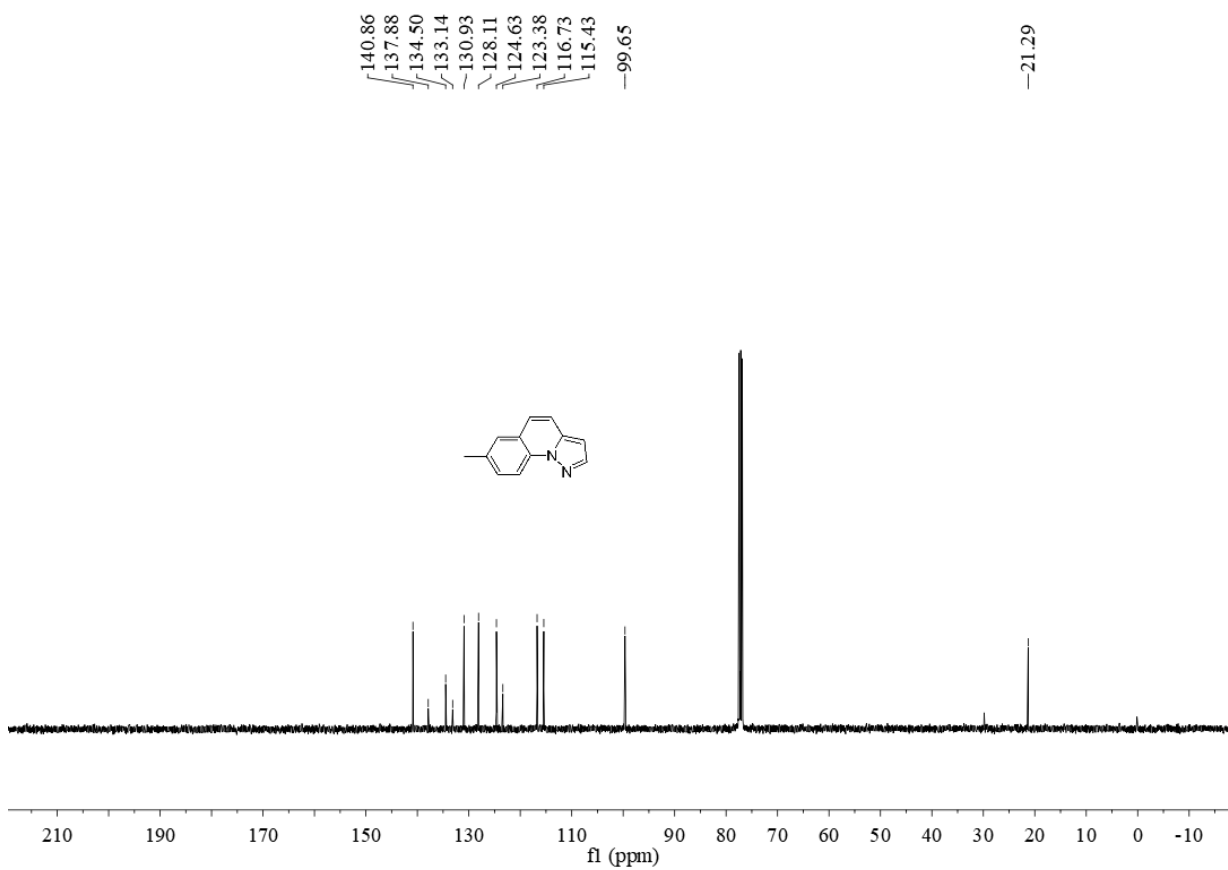
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3a**



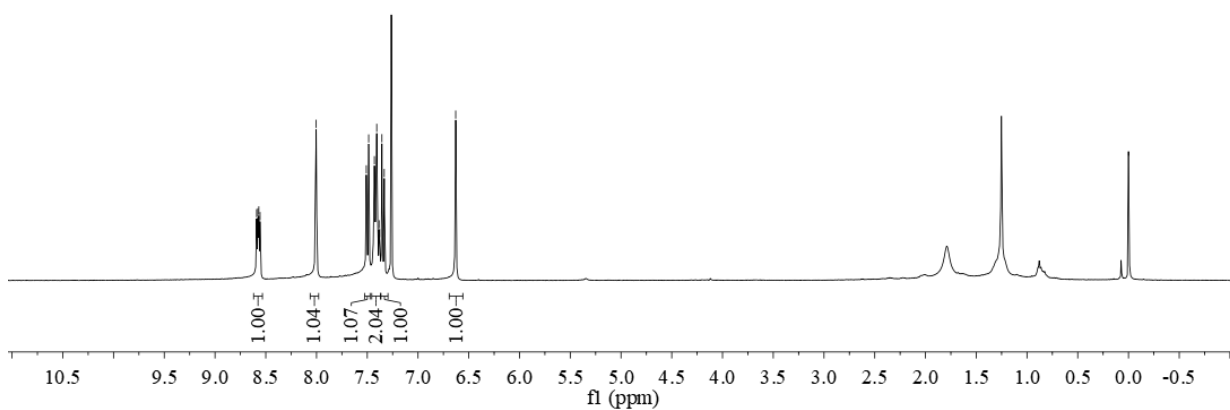
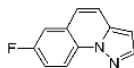
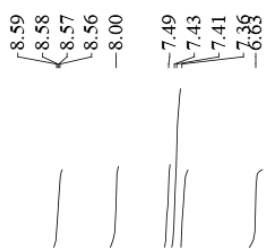
¹H NMR (400 MHz, CDCl₃) spectrum of compound **3b**



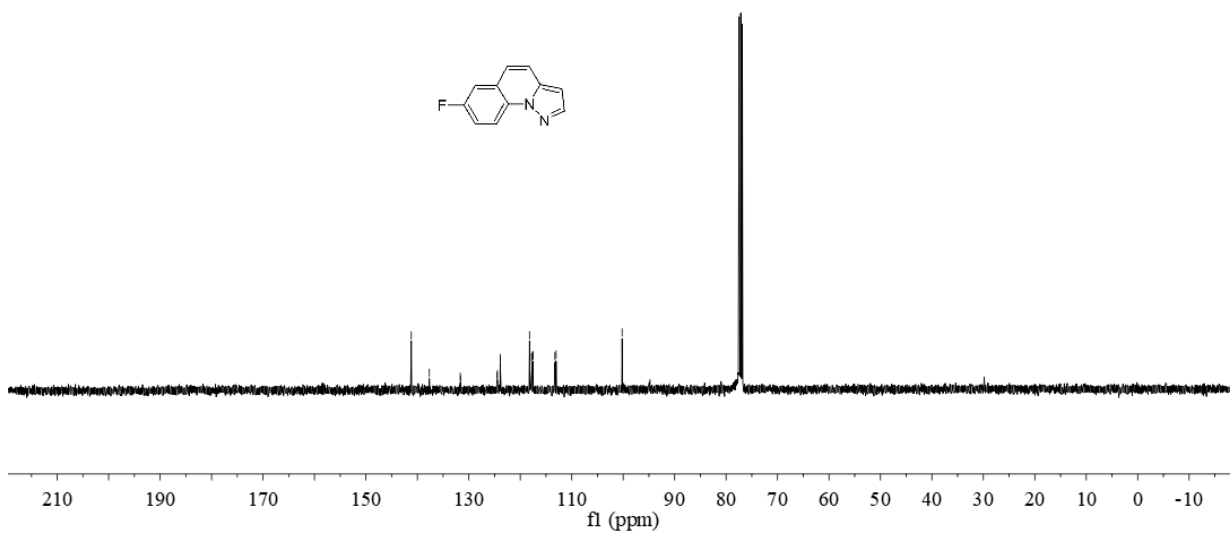
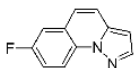
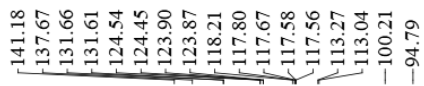
¹³C NMR (100 MHz, CDCl₃) spectrum of compound **3b**



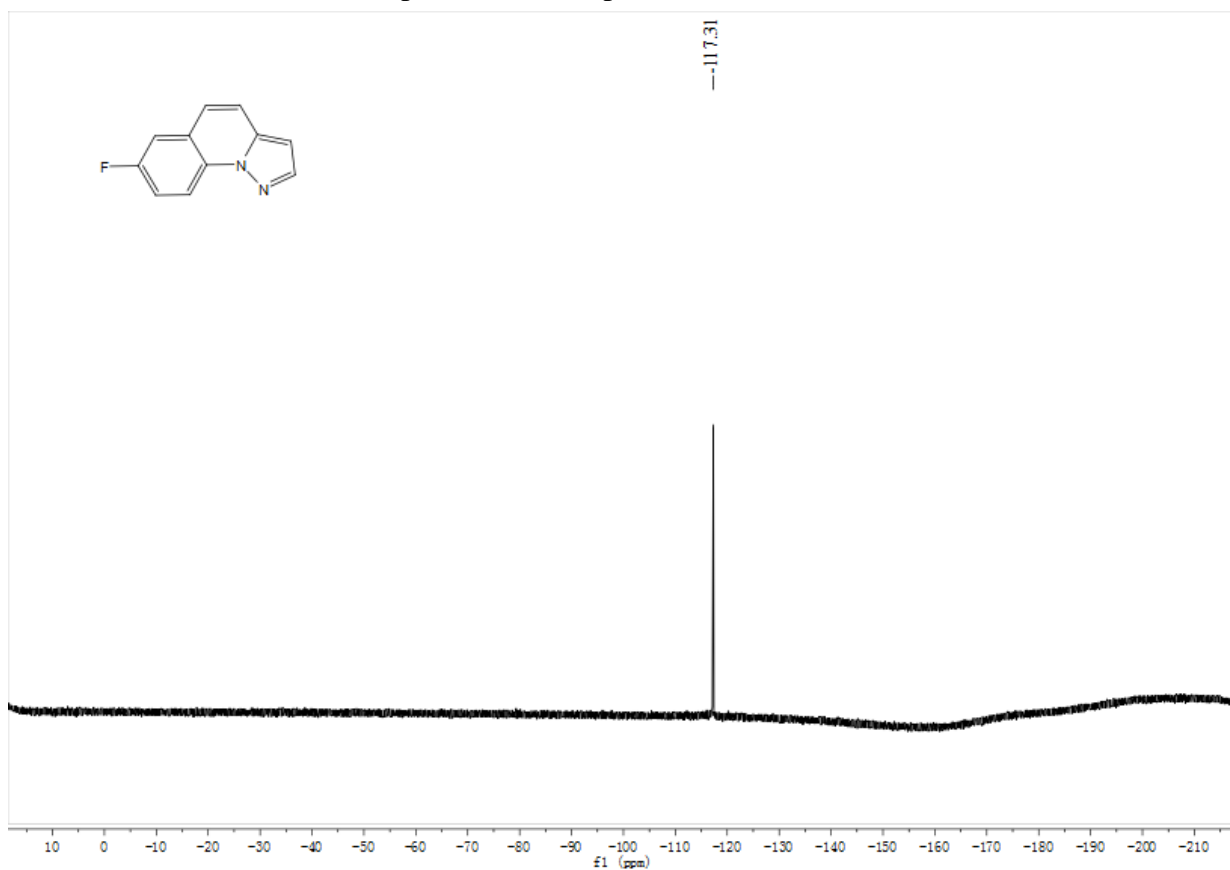
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3c**



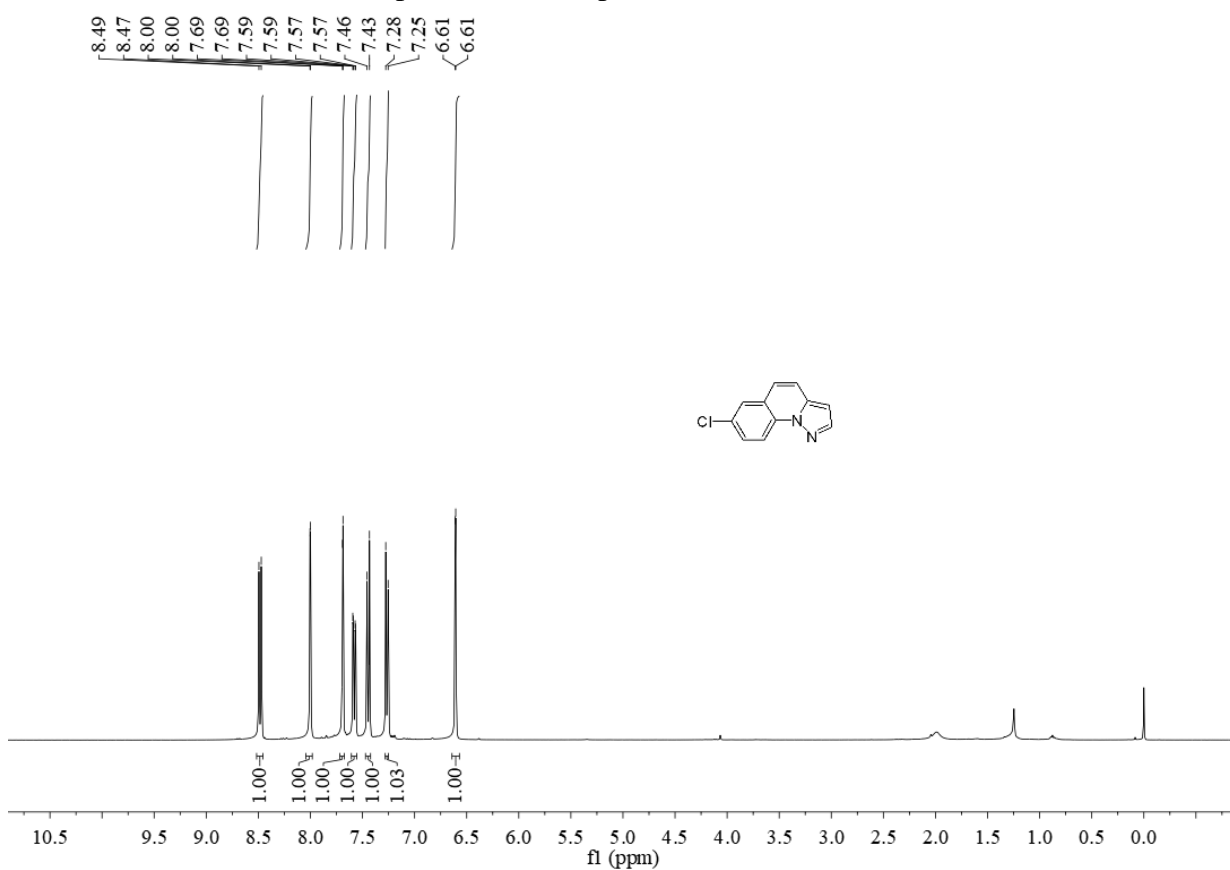
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3c**



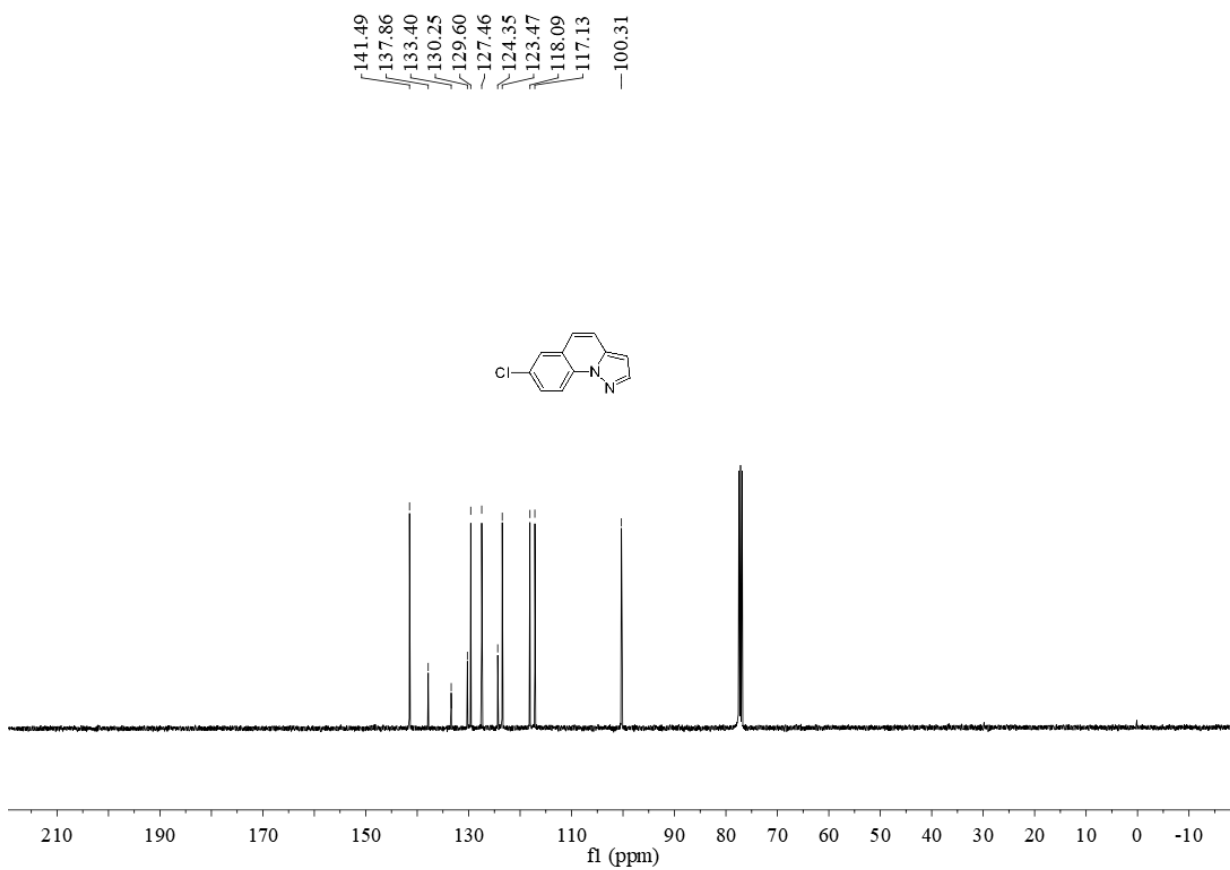
^{19}F NMR (376 MHz, CDCl_3) spectrum of compound **3c**



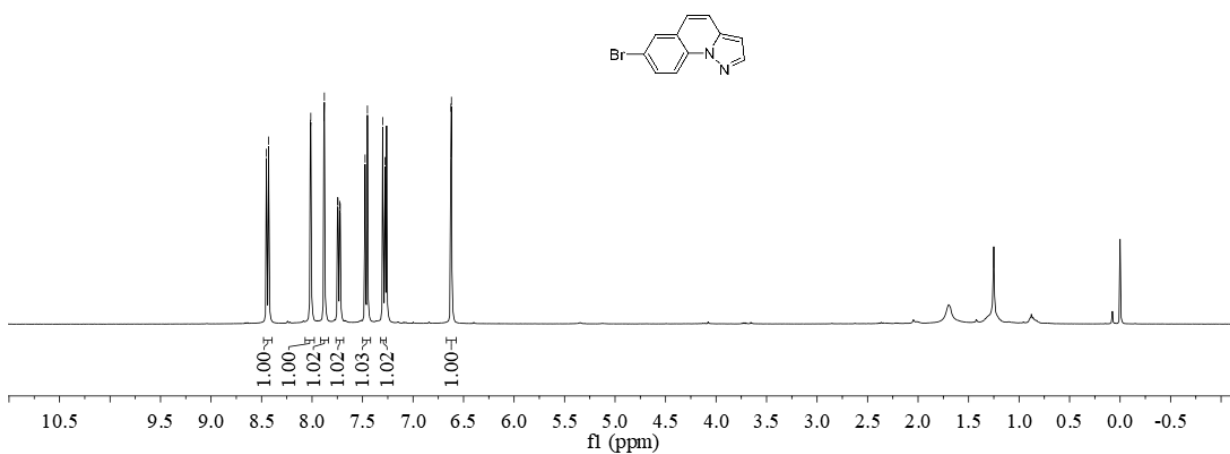
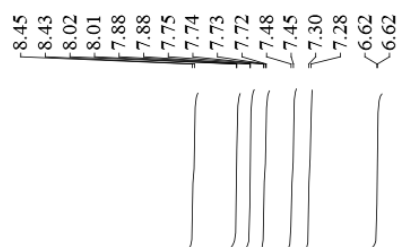
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3d**



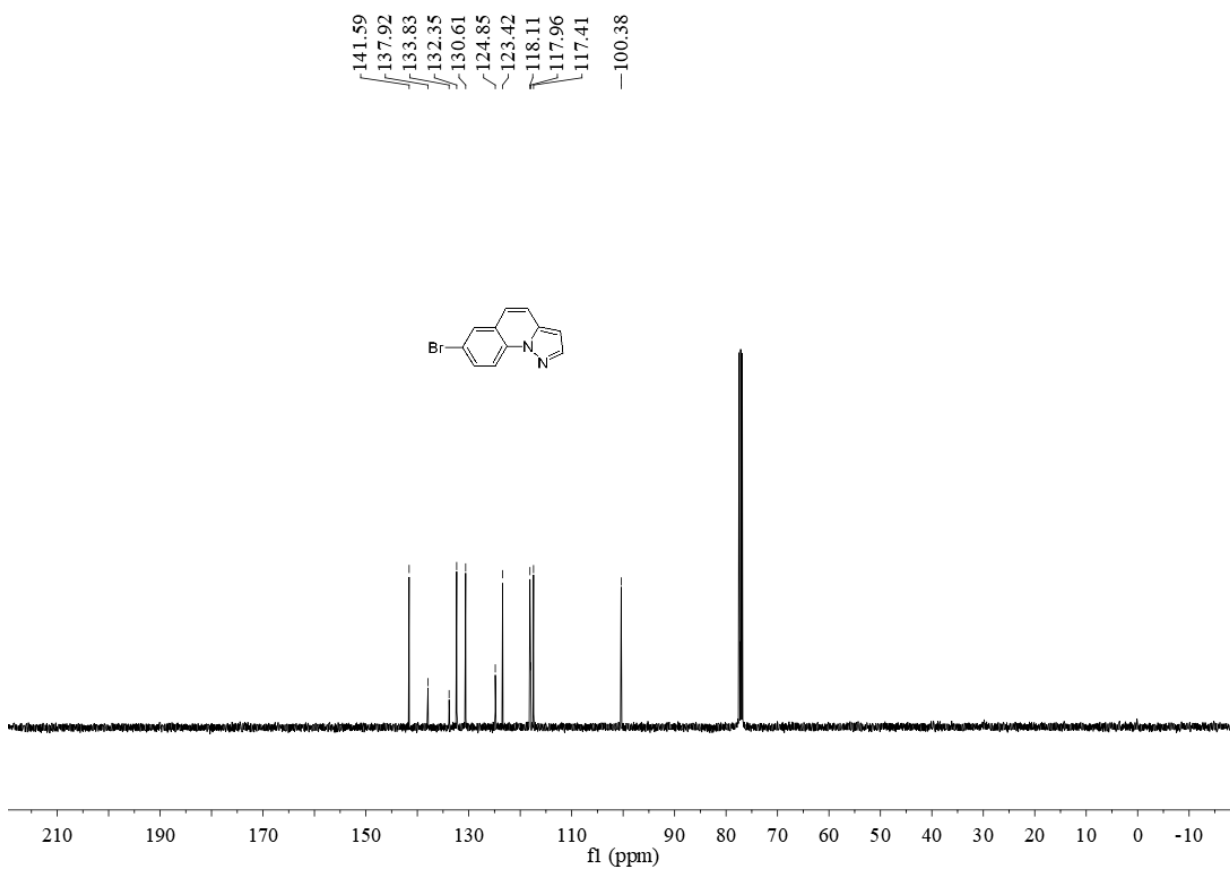
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3d**



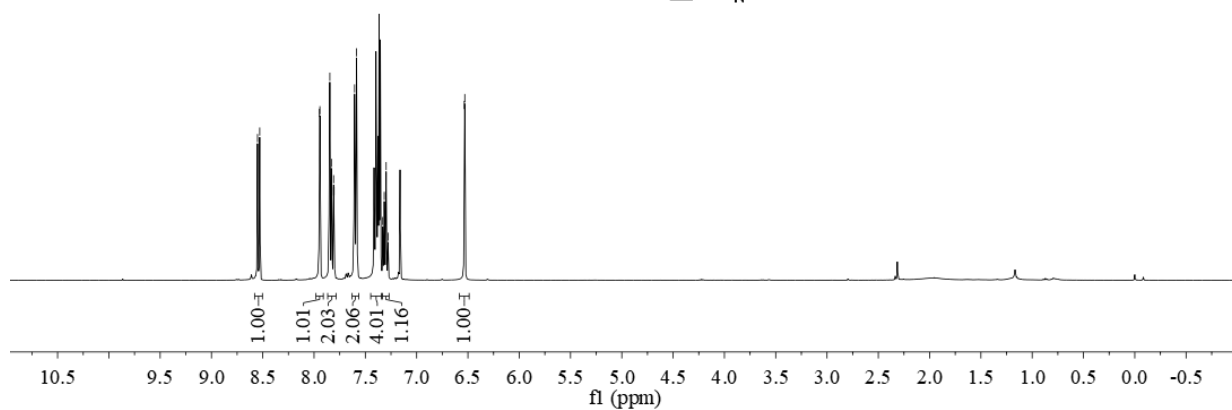
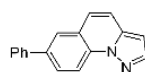
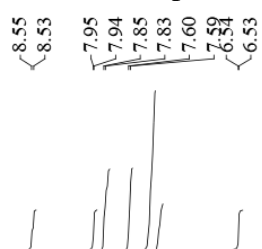
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3e**



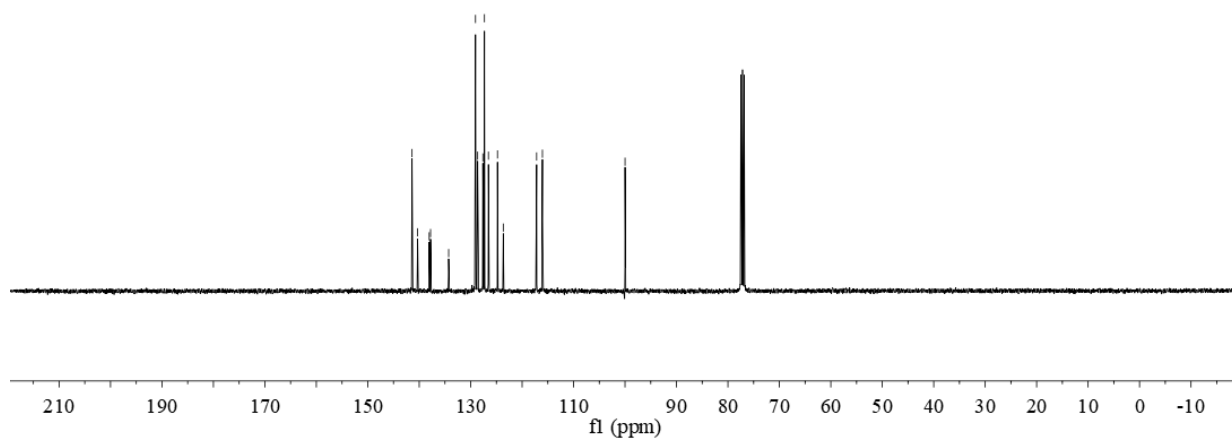
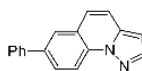
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3e**



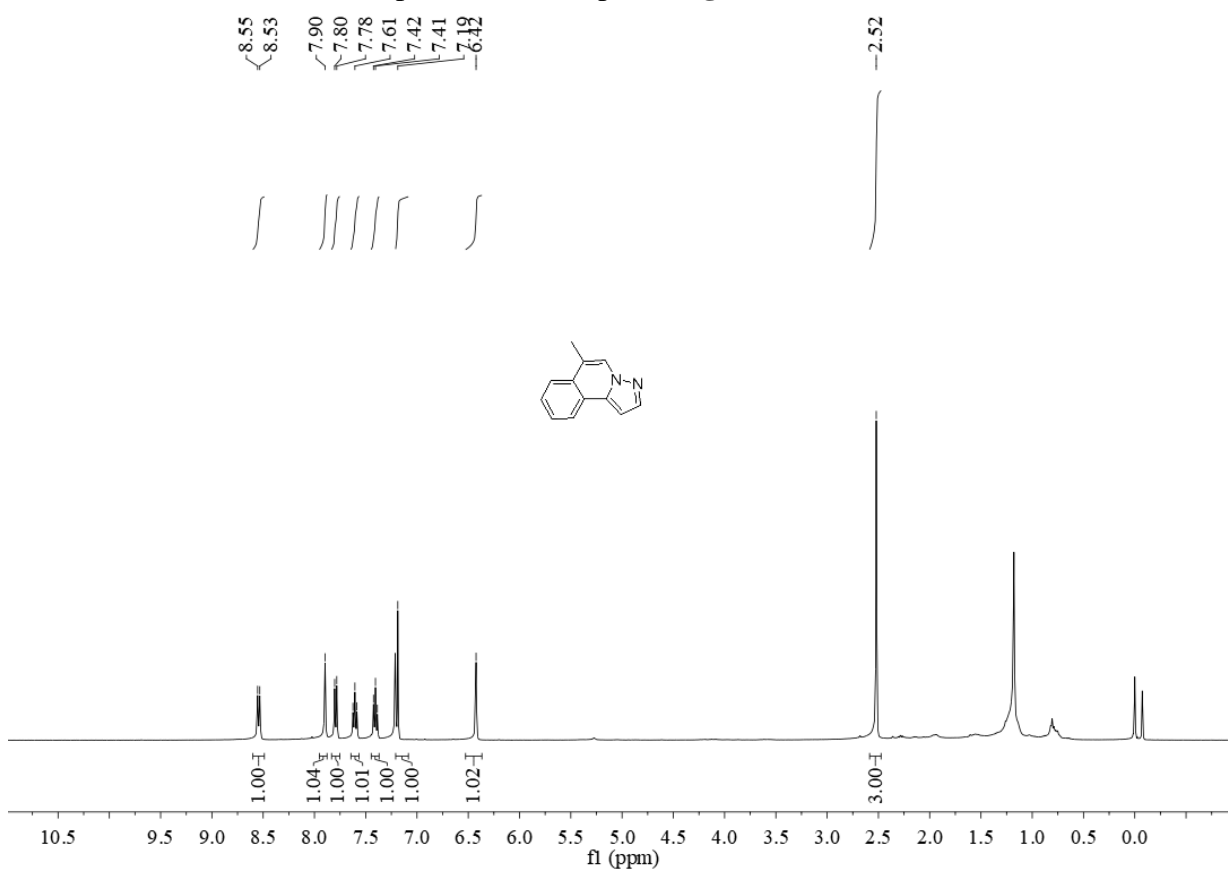
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3f**



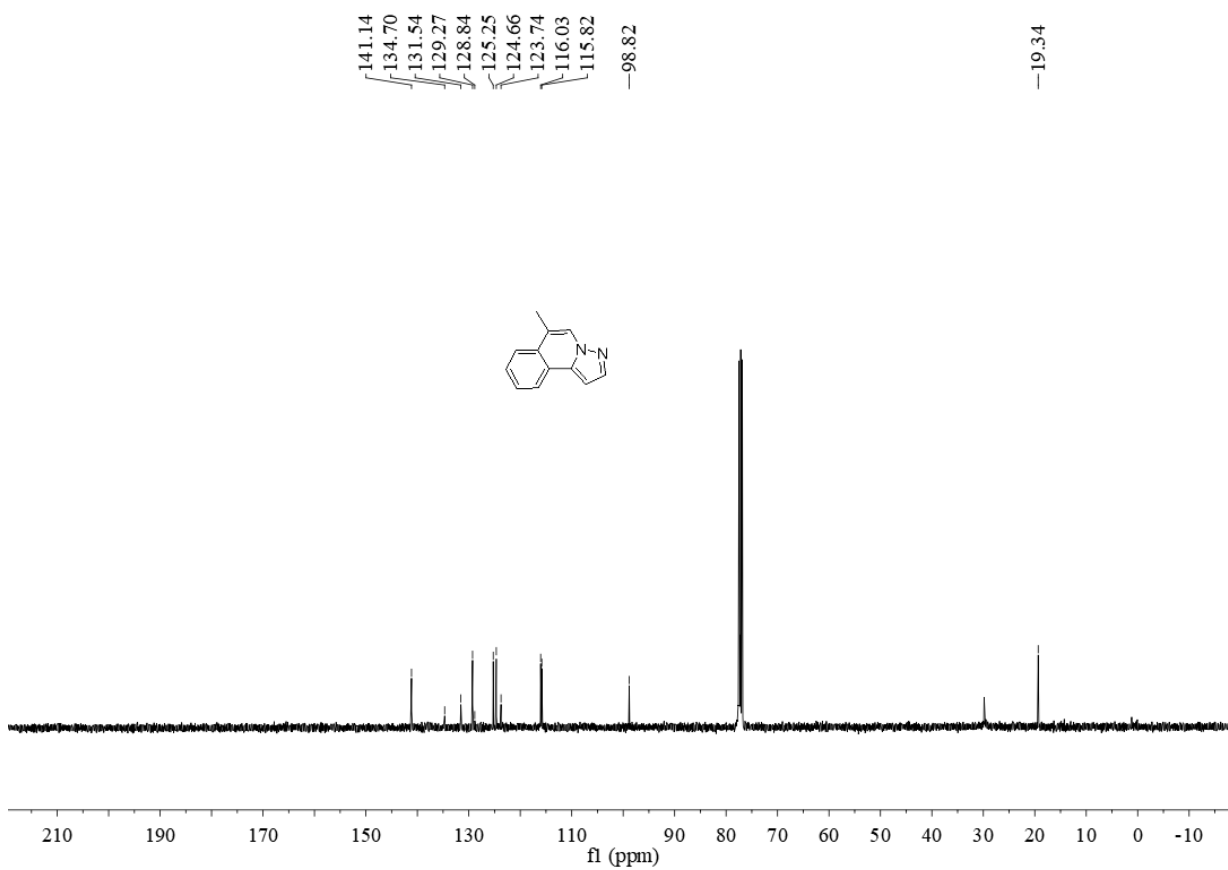
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3f**



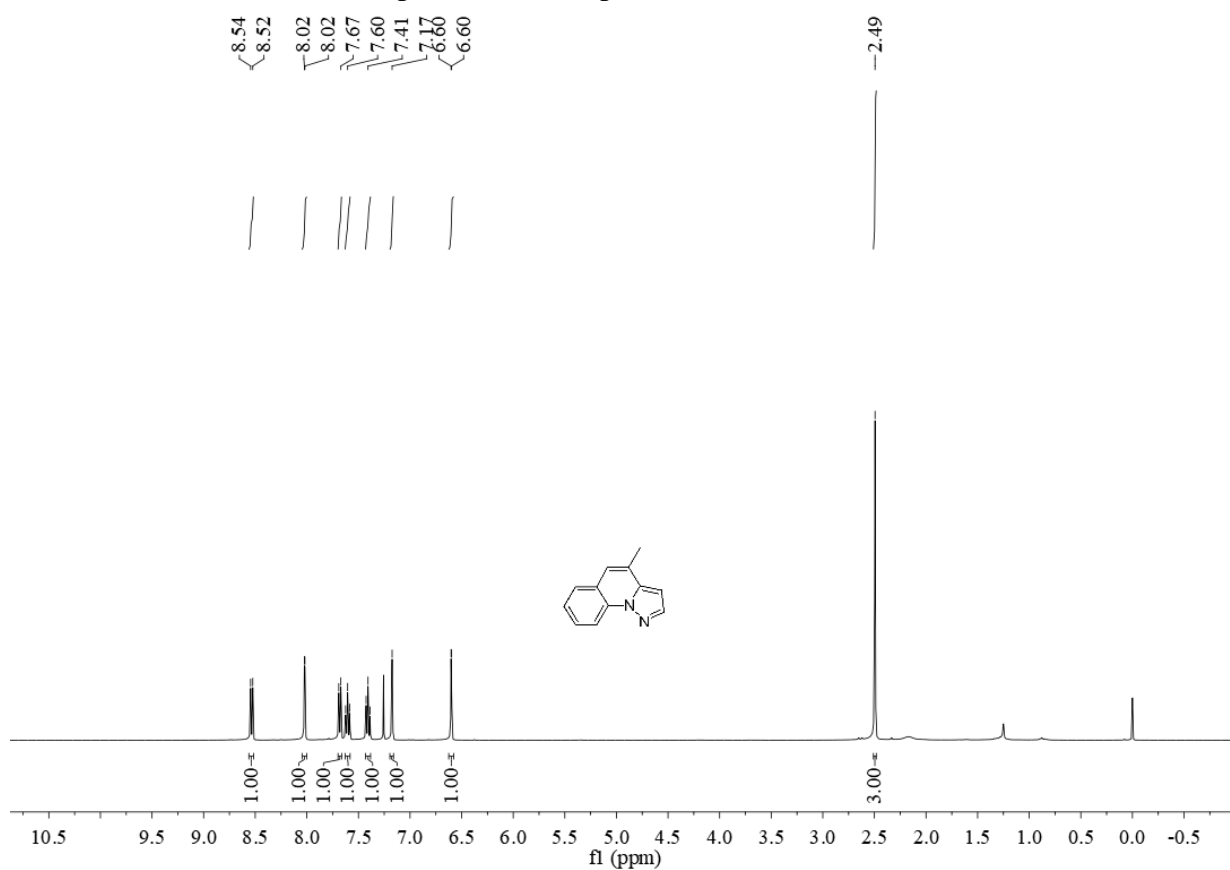
¹H NMR (400 MHz, CDCl₃) spectrum of compound **3g**



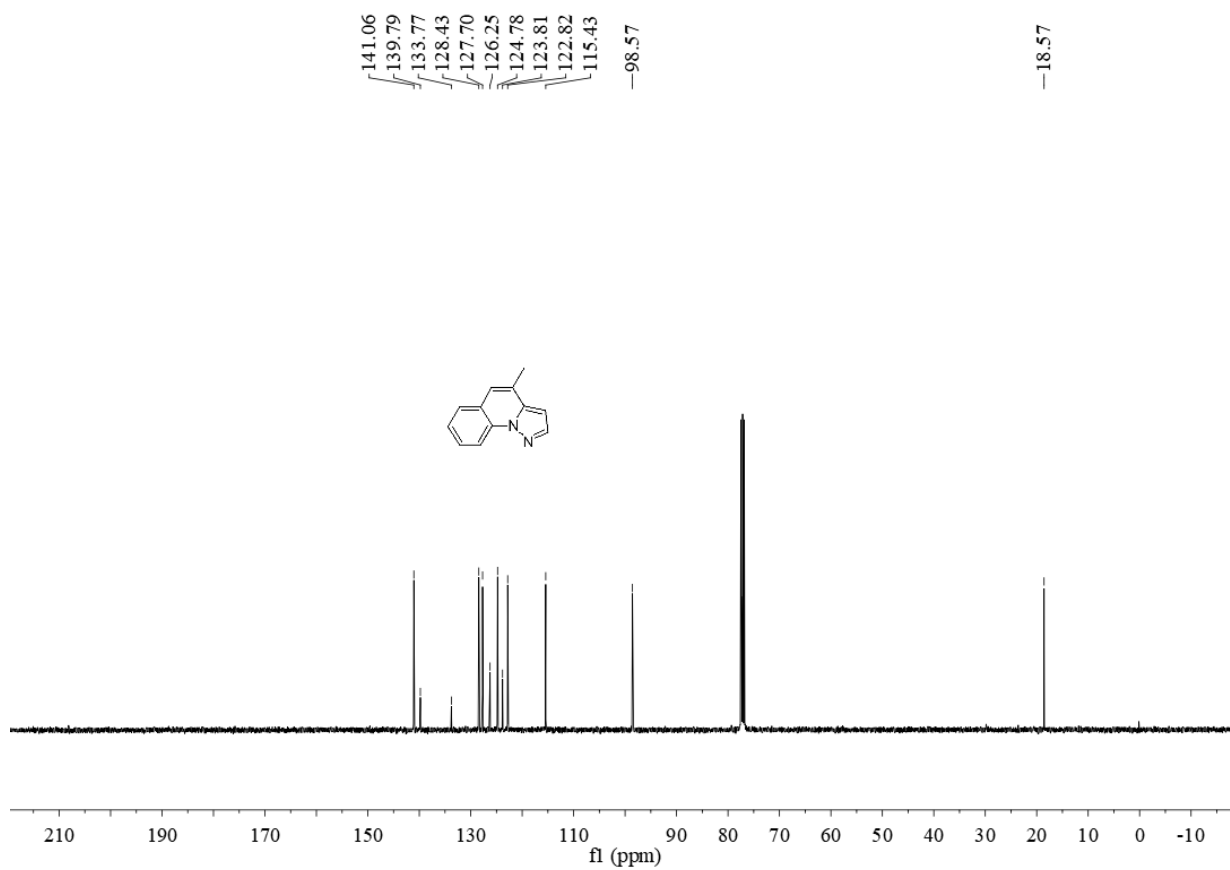
¹³C NMR (100 MHz, CDCl₃) spectrum of compound **3g**



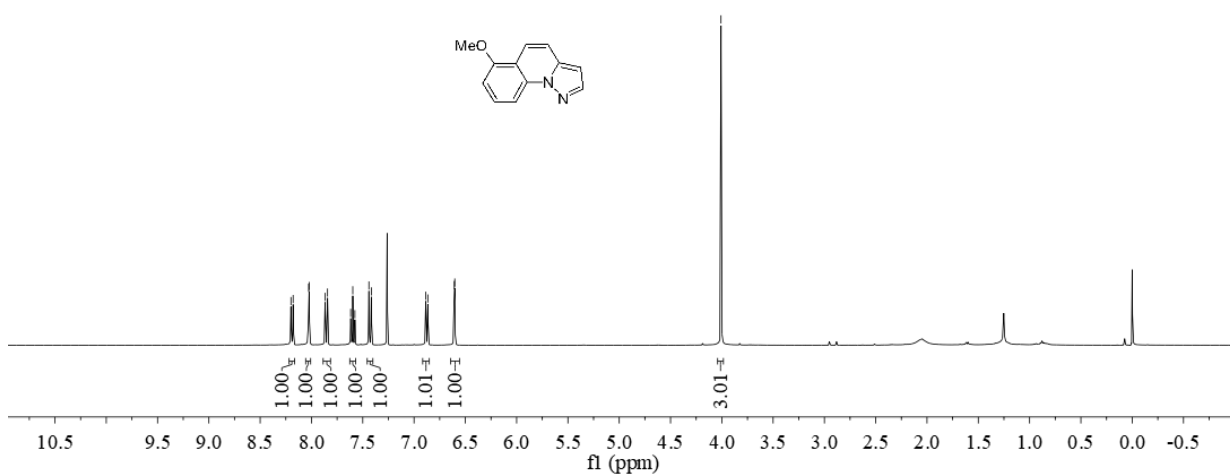
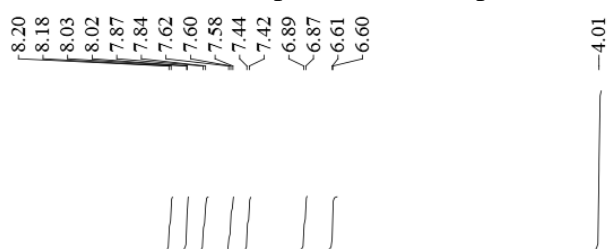
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3h**



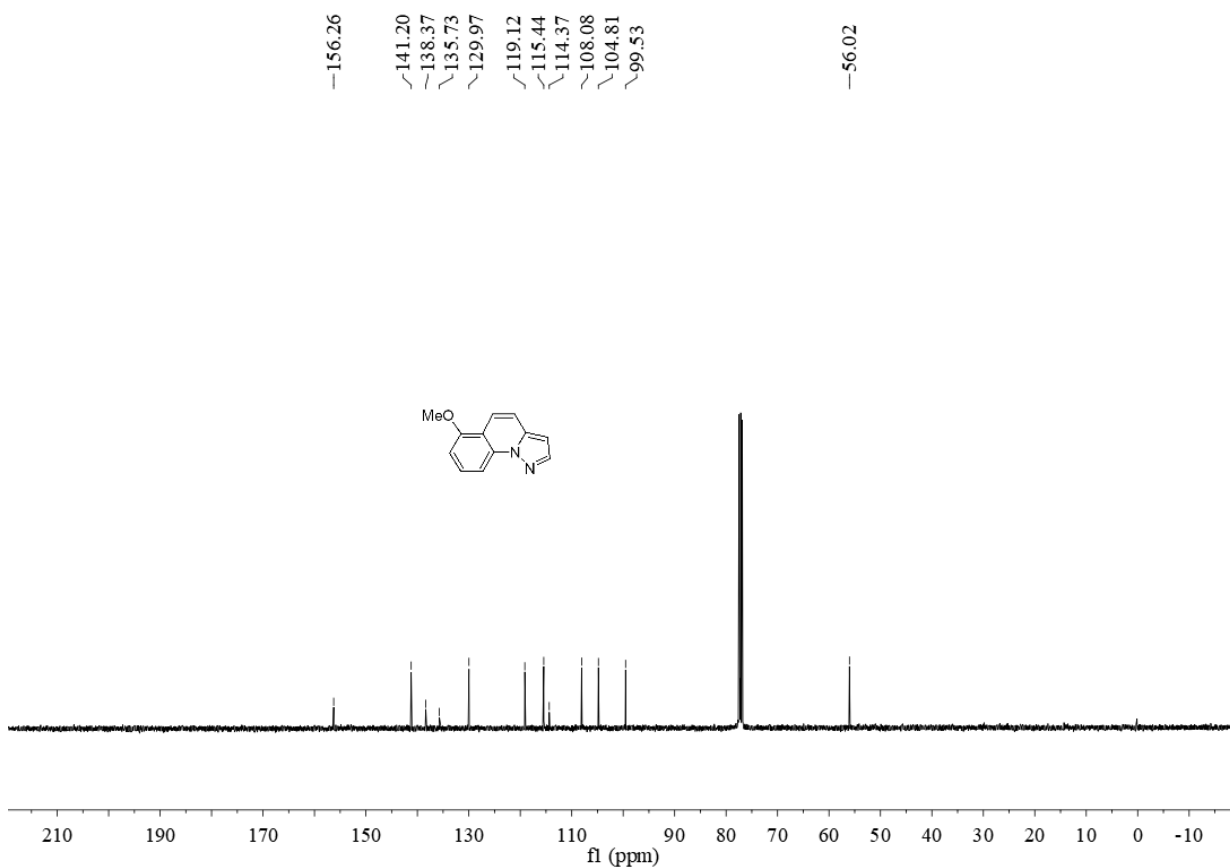
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3h**



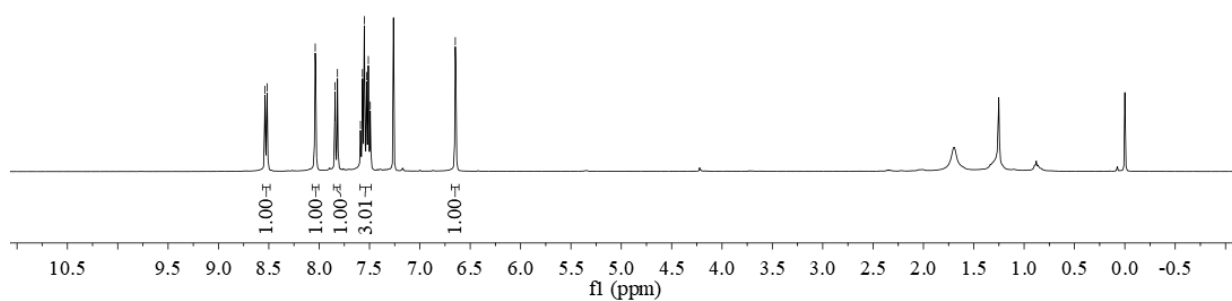
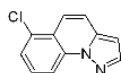
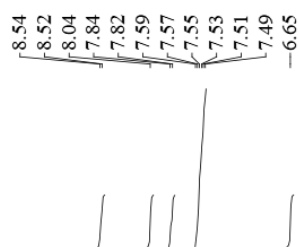
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3i**



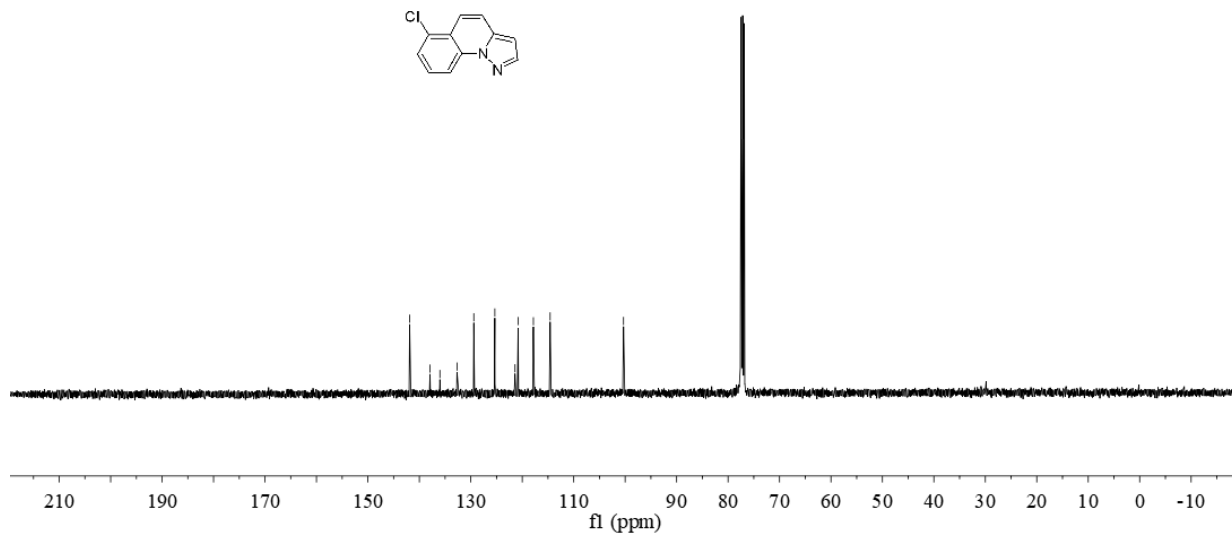
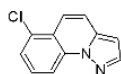
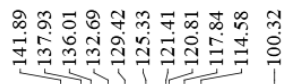
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3i**



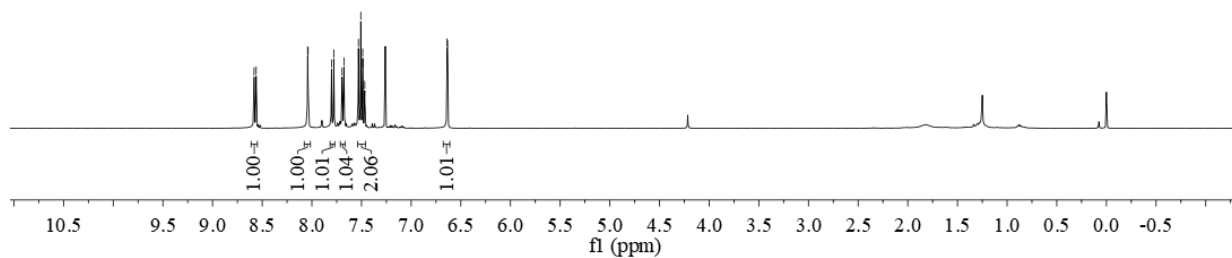
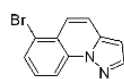
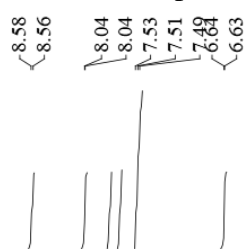
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3j**



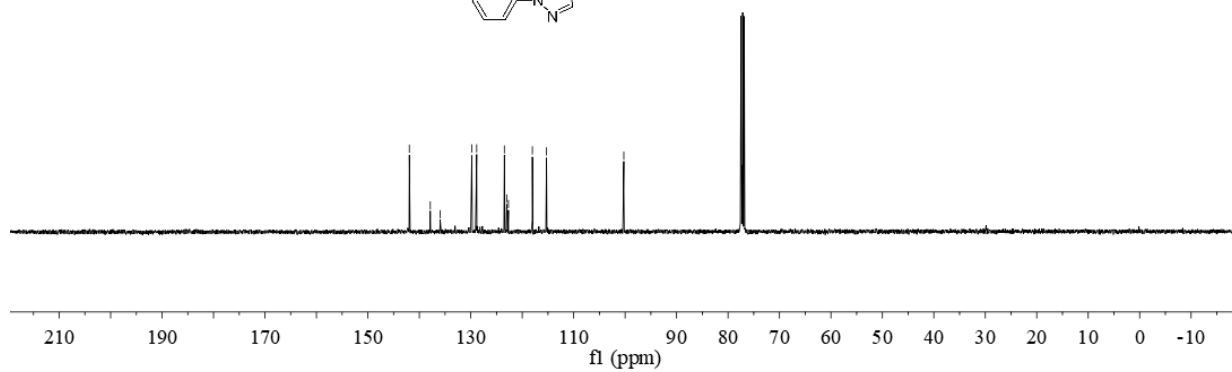
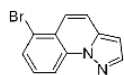
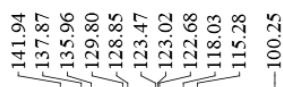
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3j**



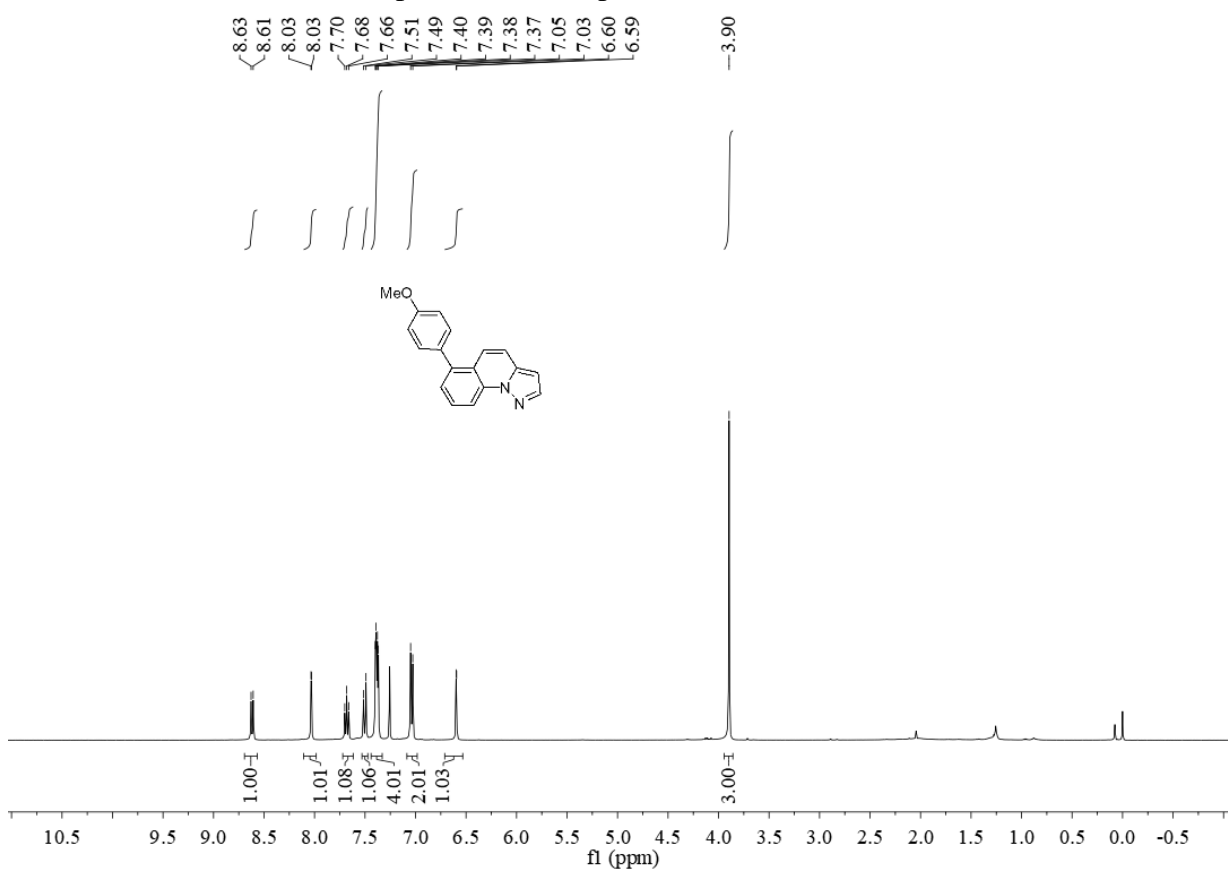
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3k**



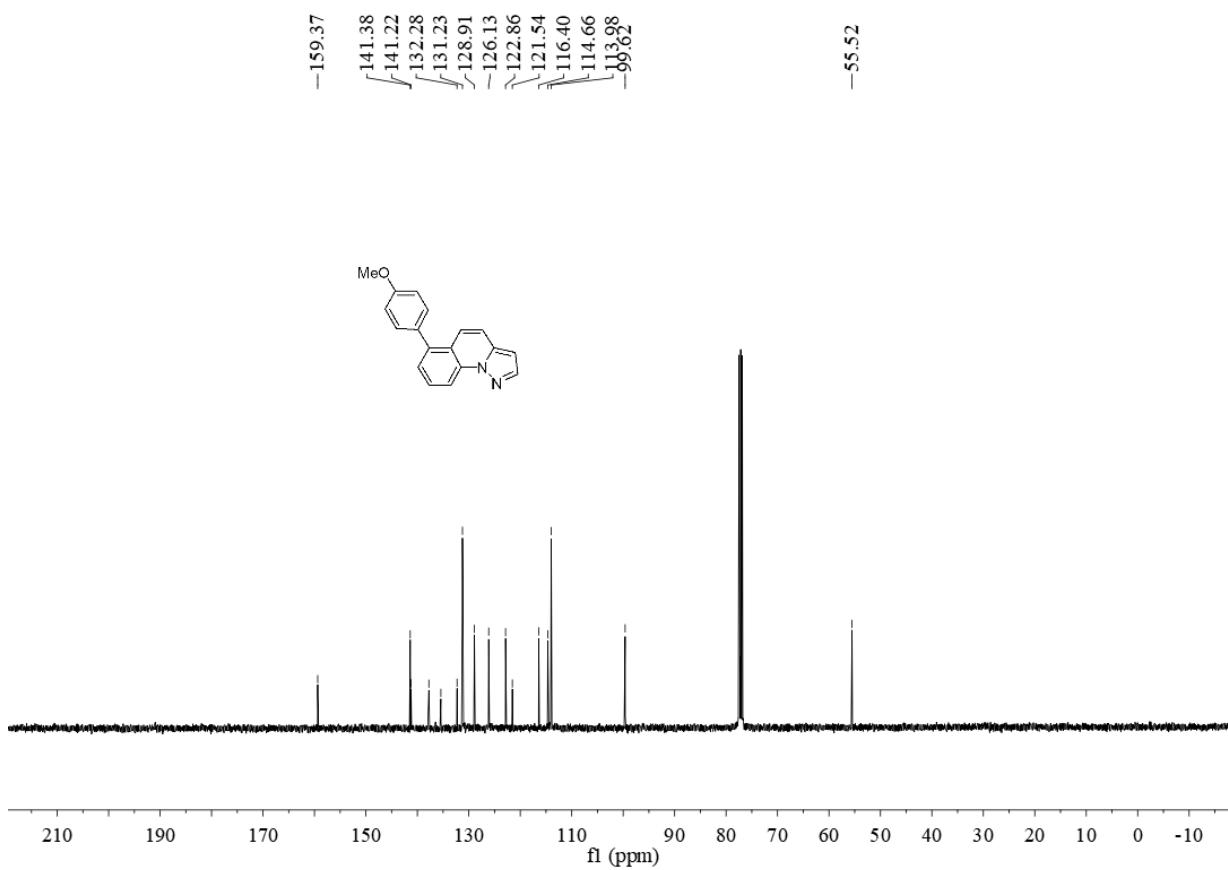
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3k**



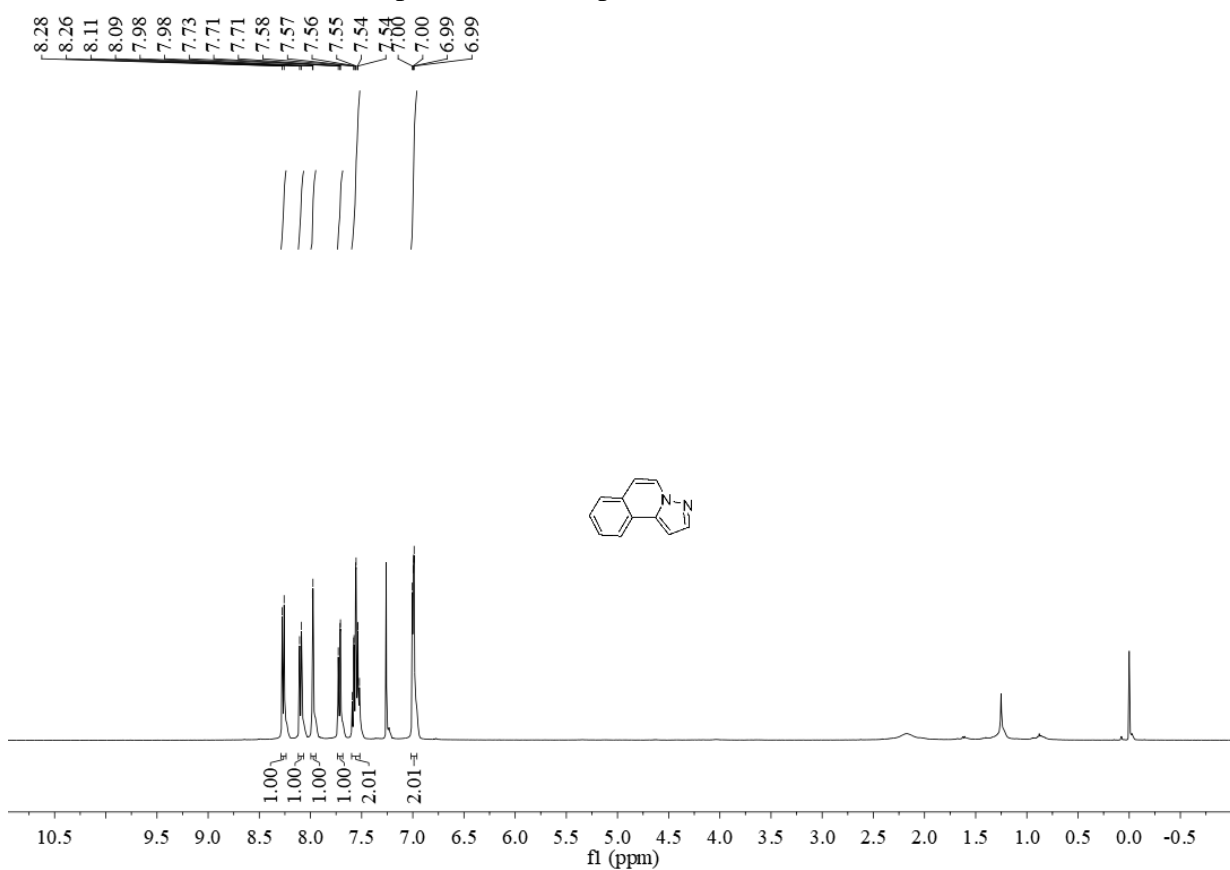
¹H NMR (400 MHz, CDCl₃) spectrum of compound **31**



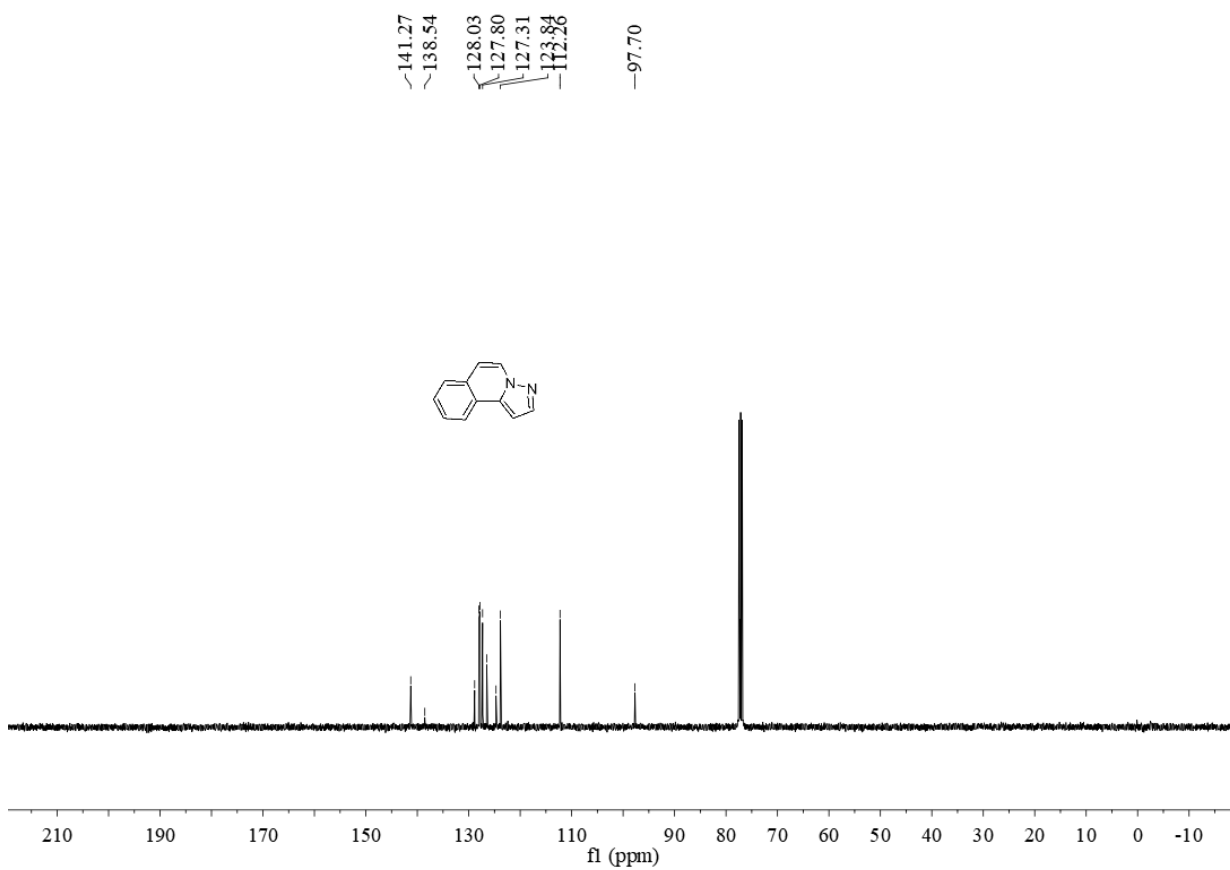
¹³C NMR (100 MHz, CDCl₃) spectrum of compound **31**



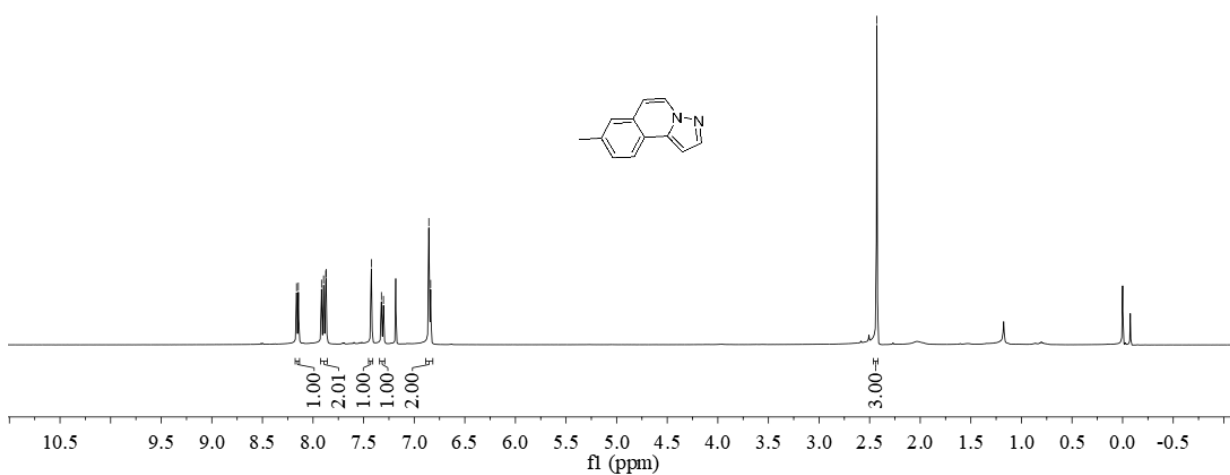
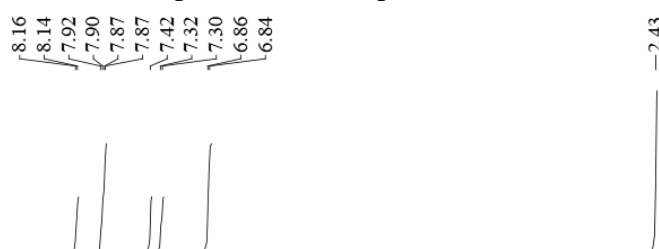
¹H NMR (400 MHz, CDCl₃) spectrum of compound **3m**



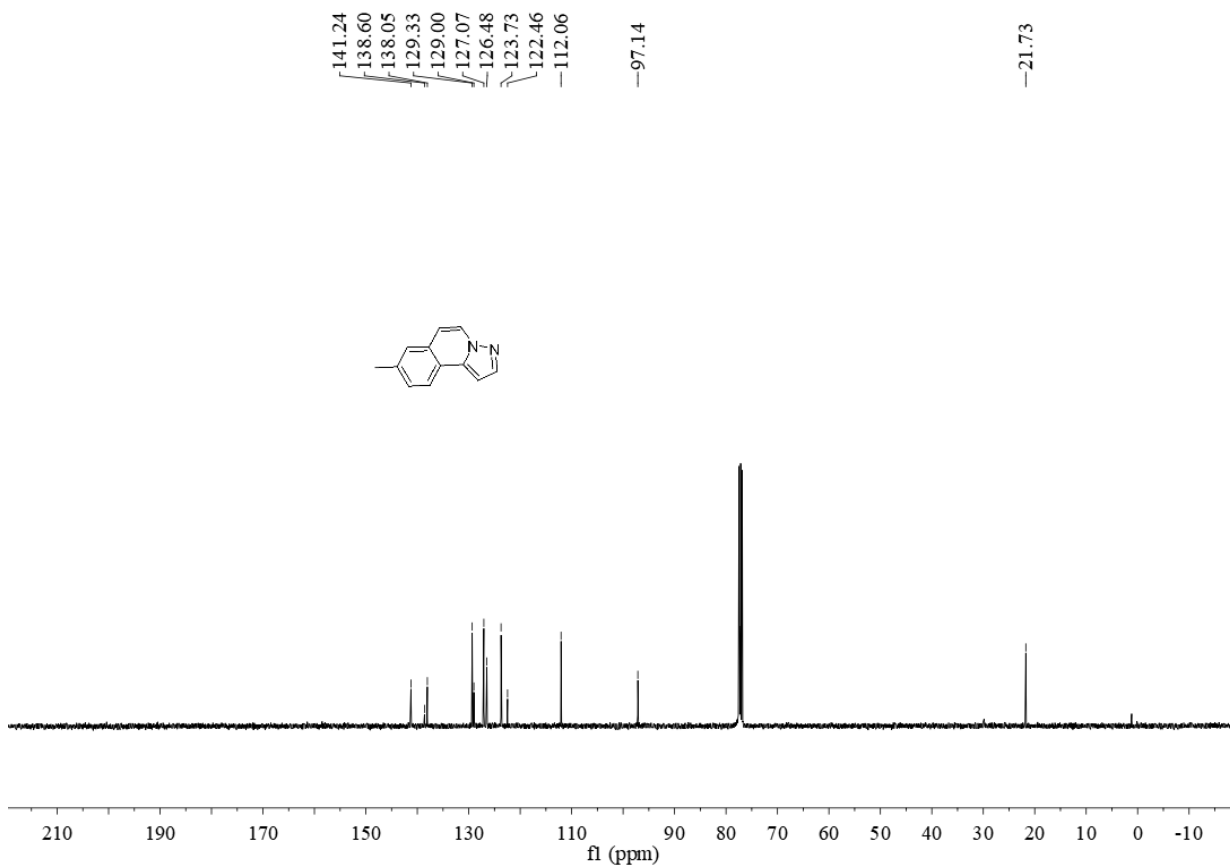
¹³C NMR (100 MHz, CDCl₃) spectrum of compound **3m**



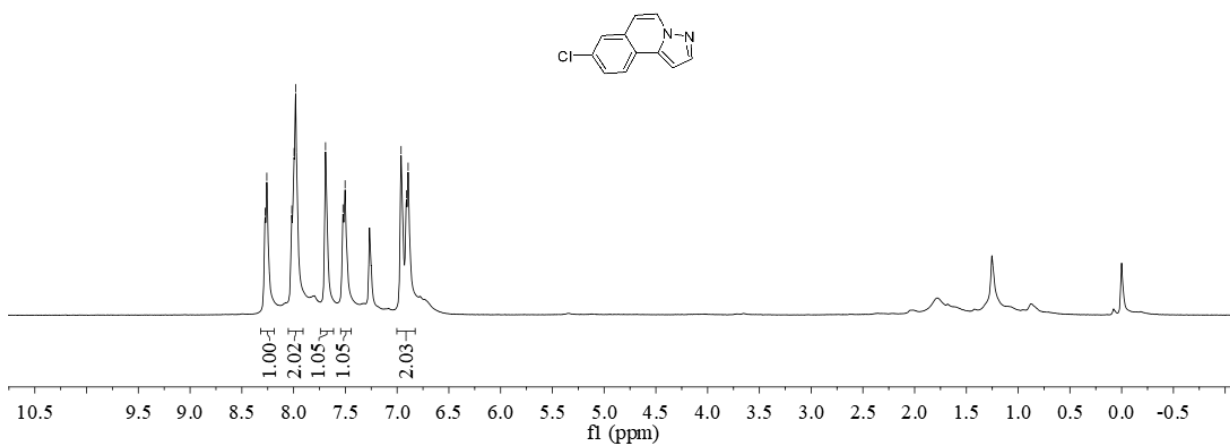
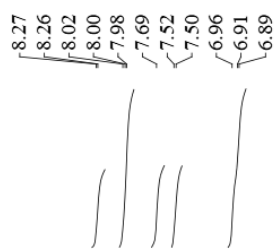
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3n**



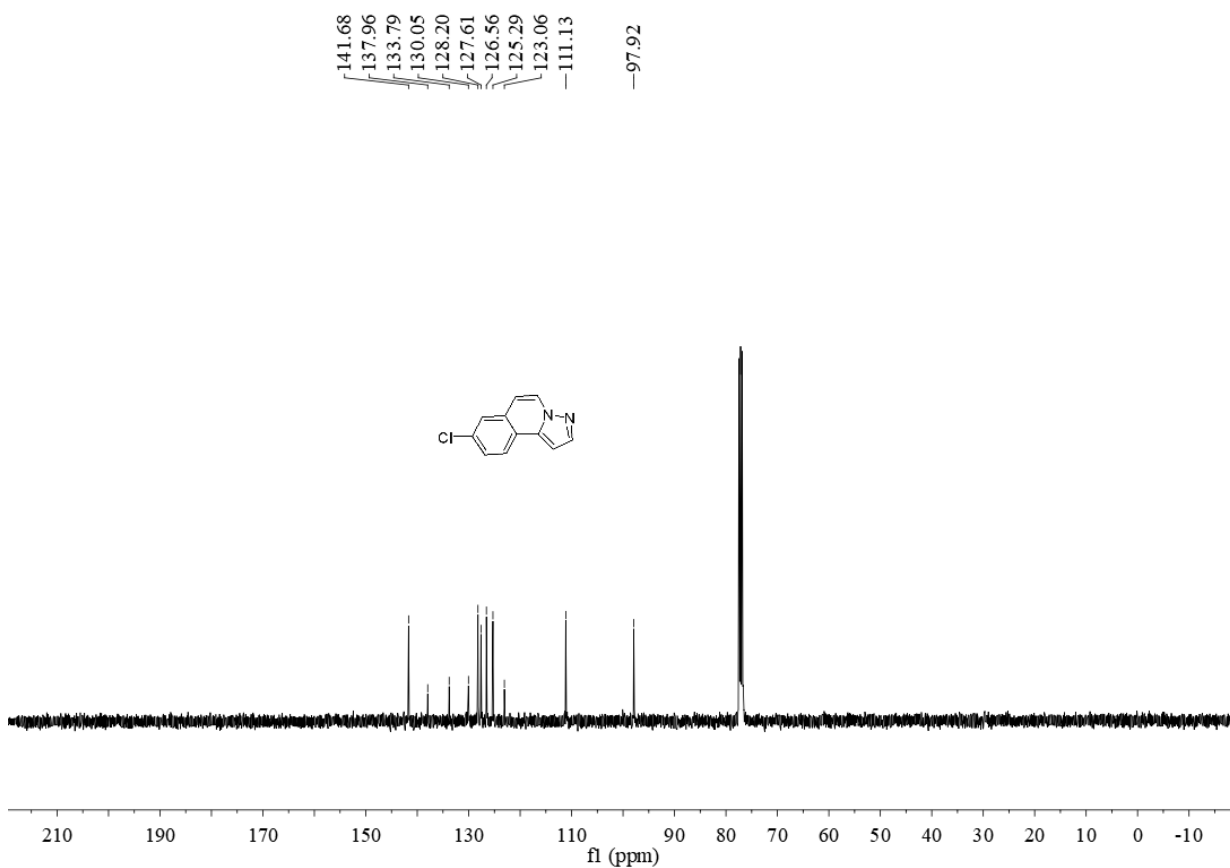
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3n**



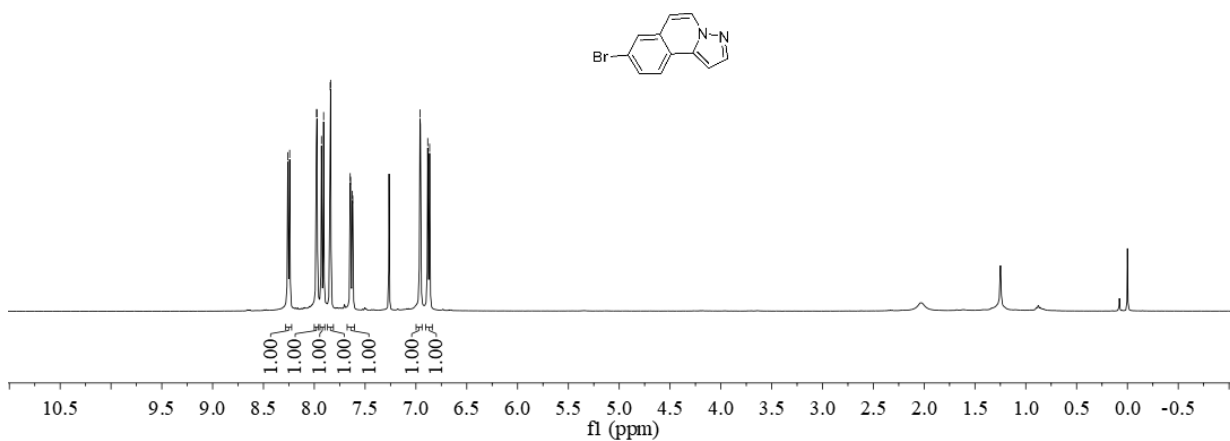
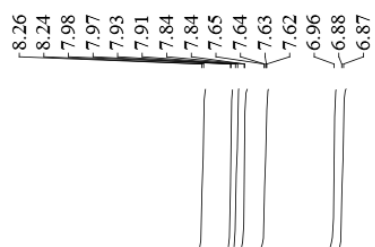
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3o**



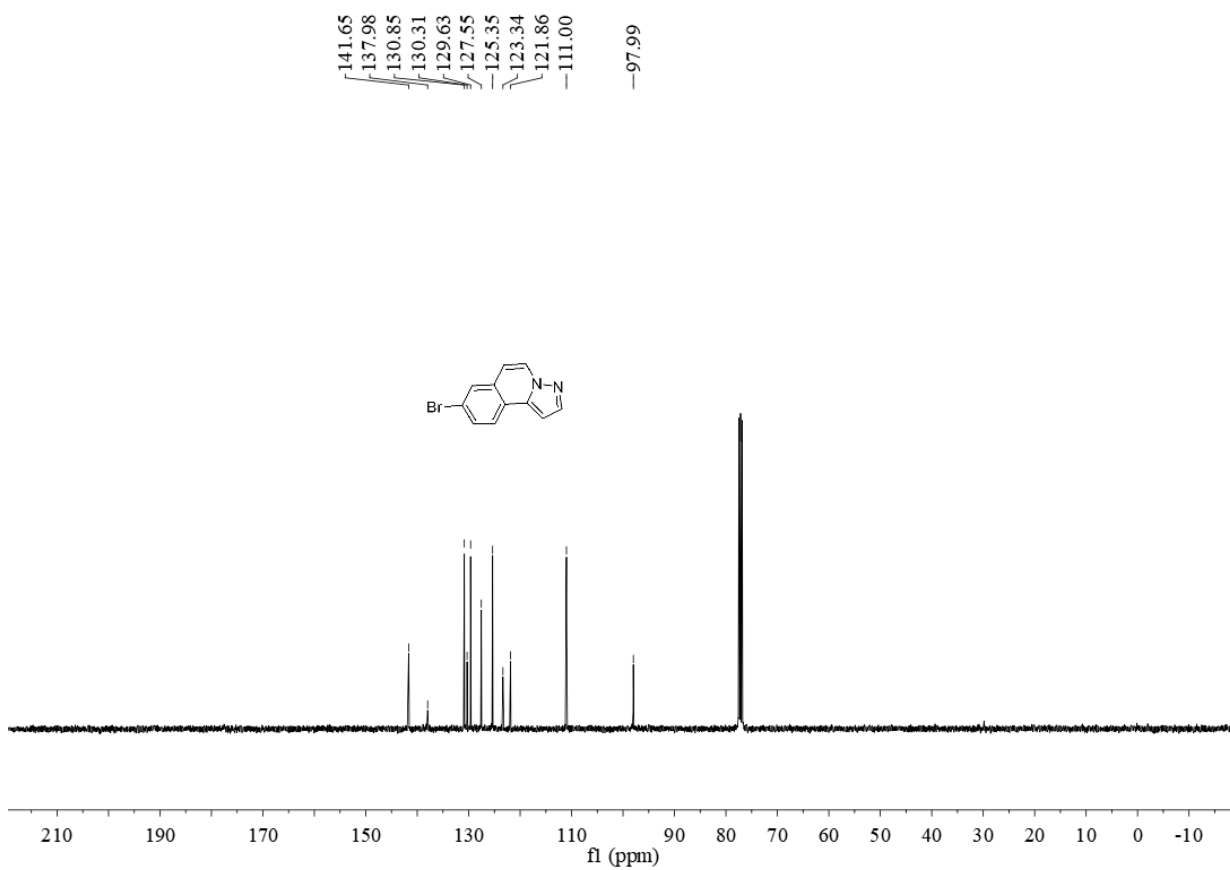
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3o**



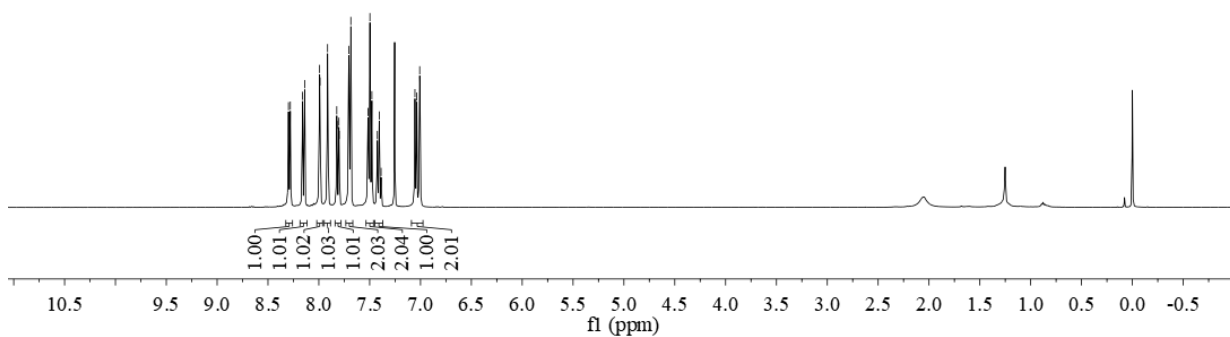
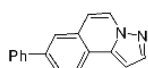
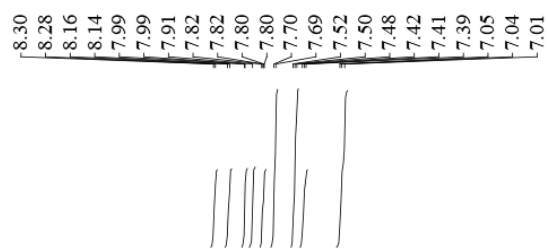
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3p**



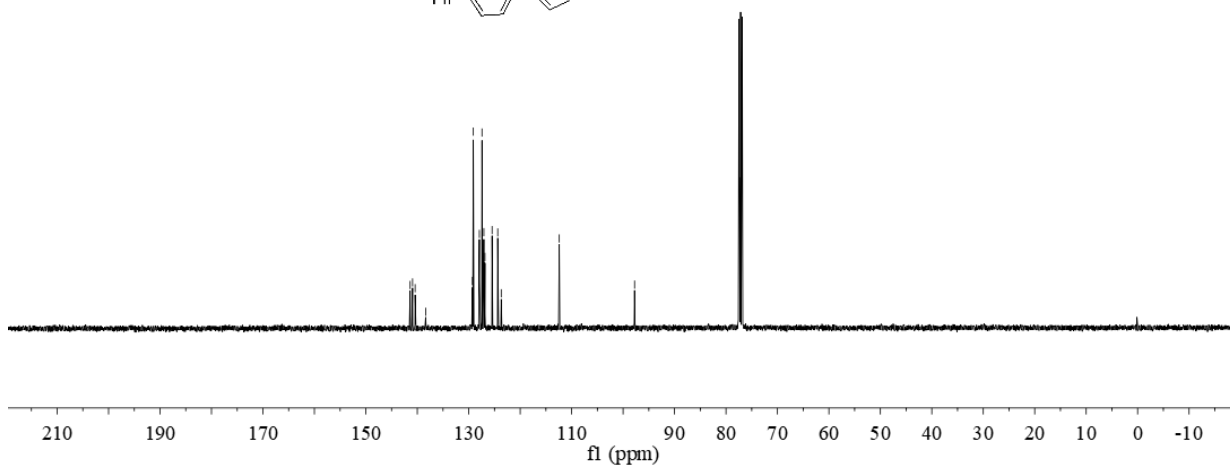
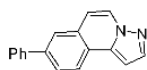
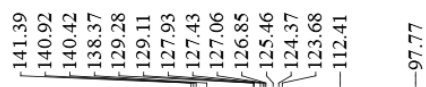
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3p**



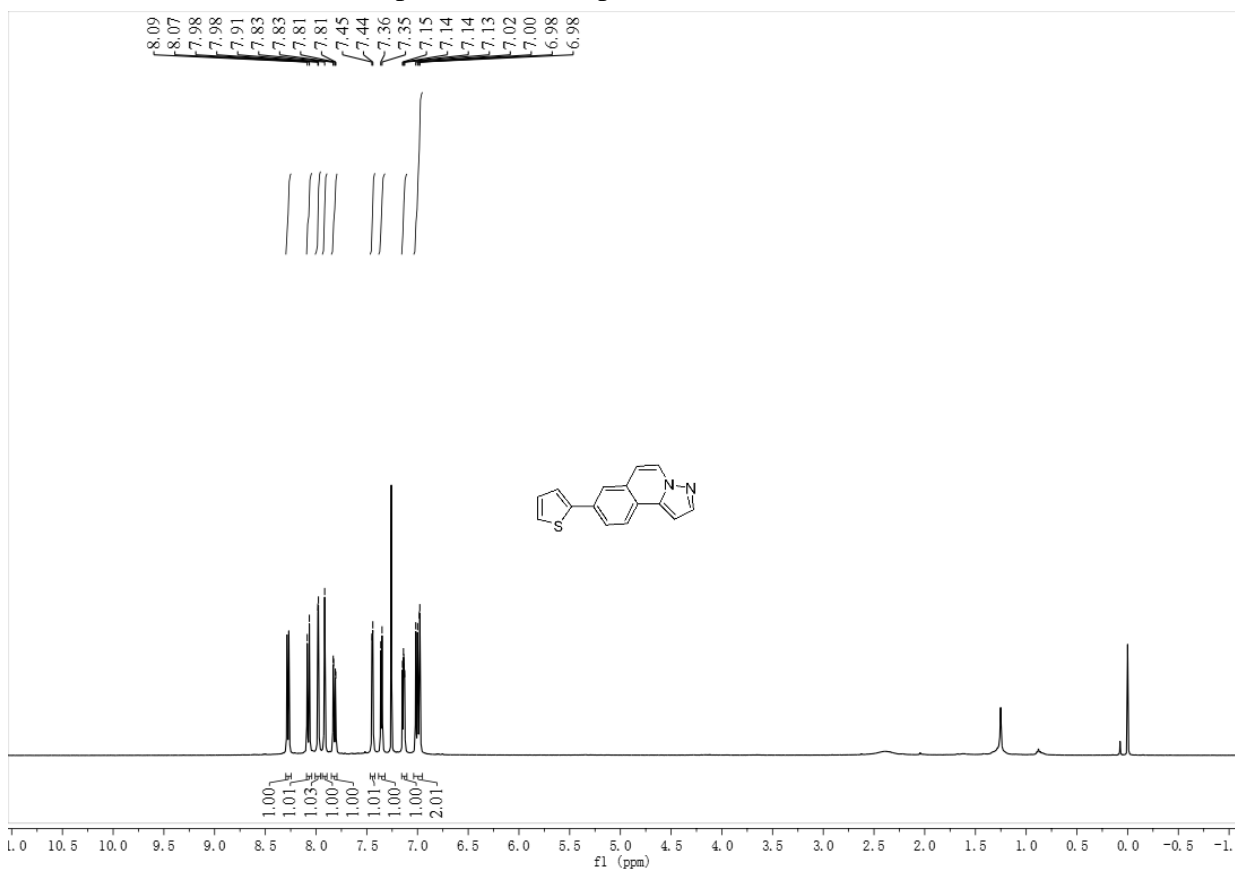
¹H NMR (400 MHz, CDCl₃) spectrum of compound **3q**



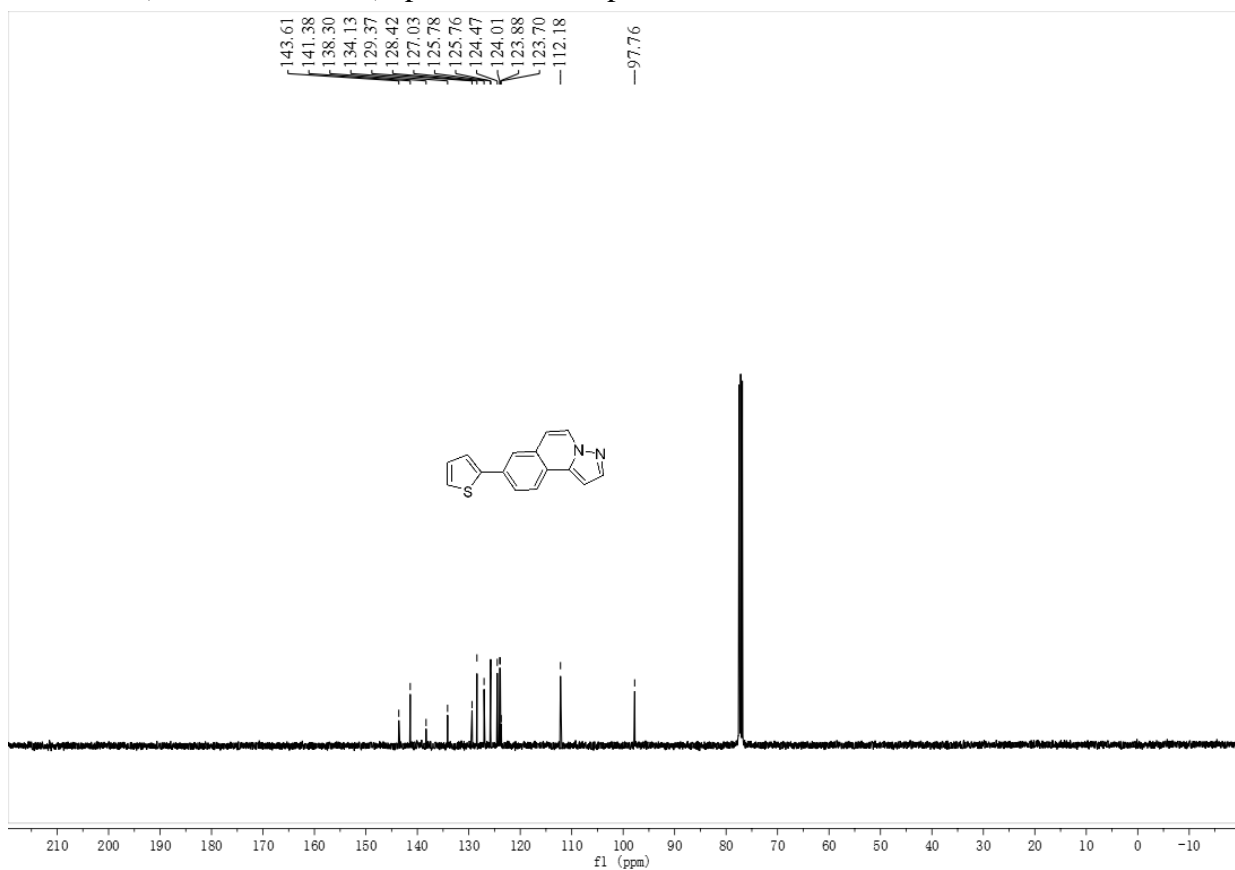
¹³C NMR (100 MHz, CDCl₃) spectrum of compound **3q**



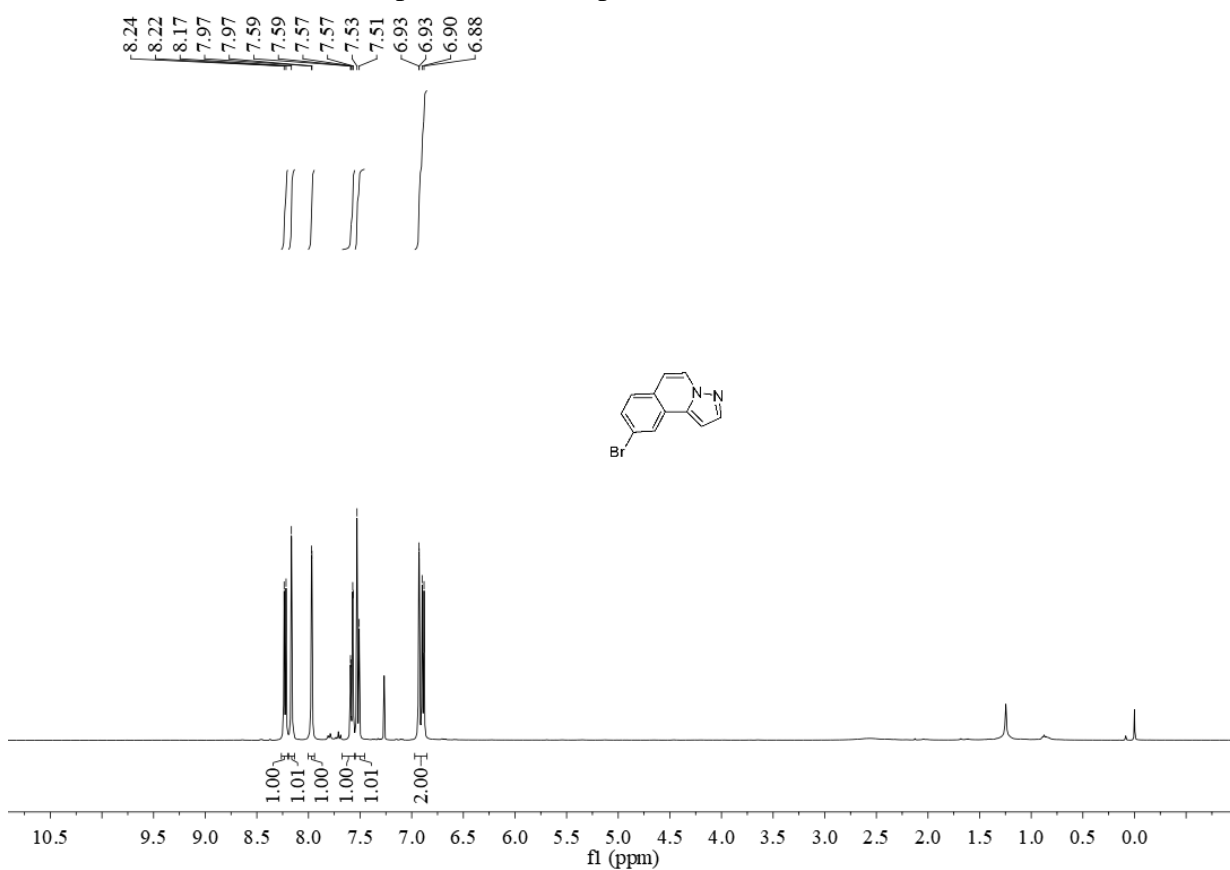
¹H NMR (400 MHz, CDCl₃) spectrum of compound **3r**



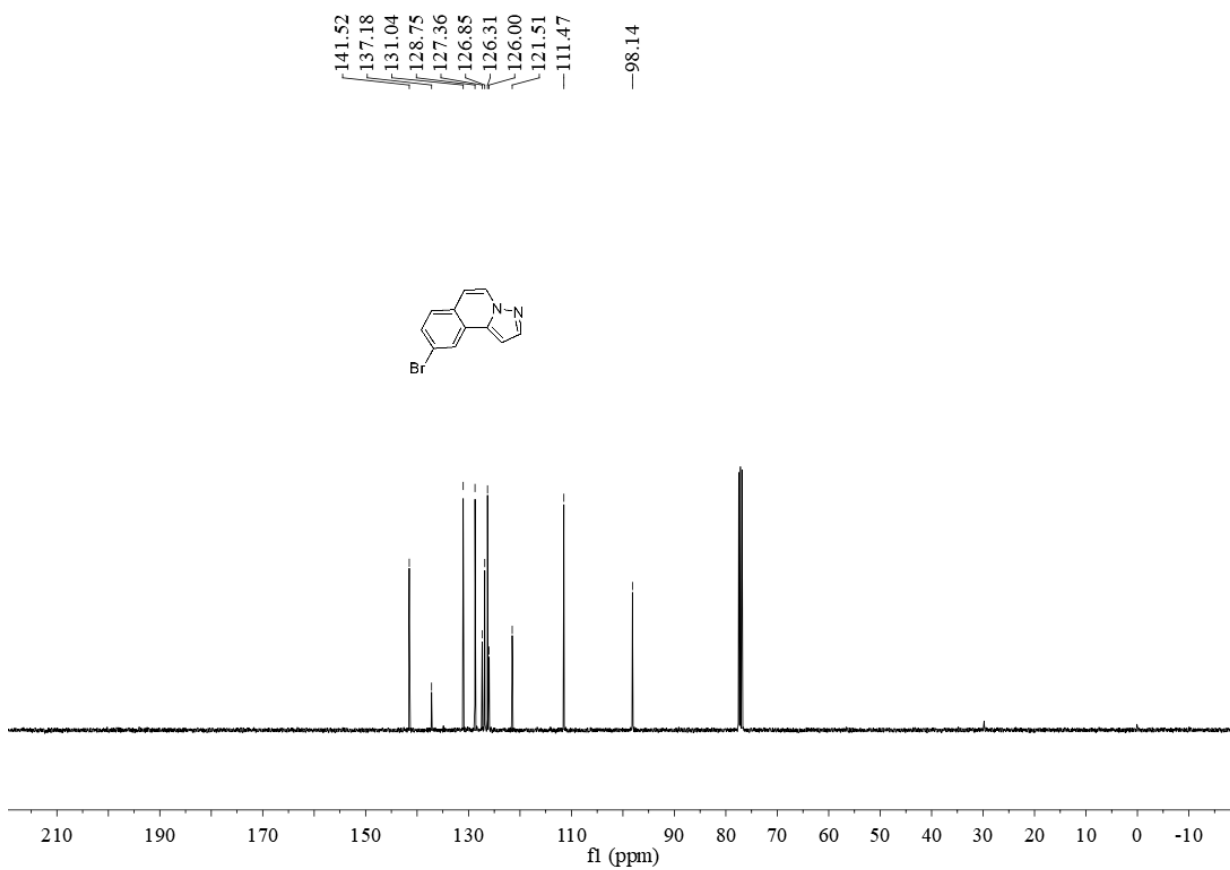
¹³C NMR (100 MHz, CDCl₃) spectrum of compound **3r**



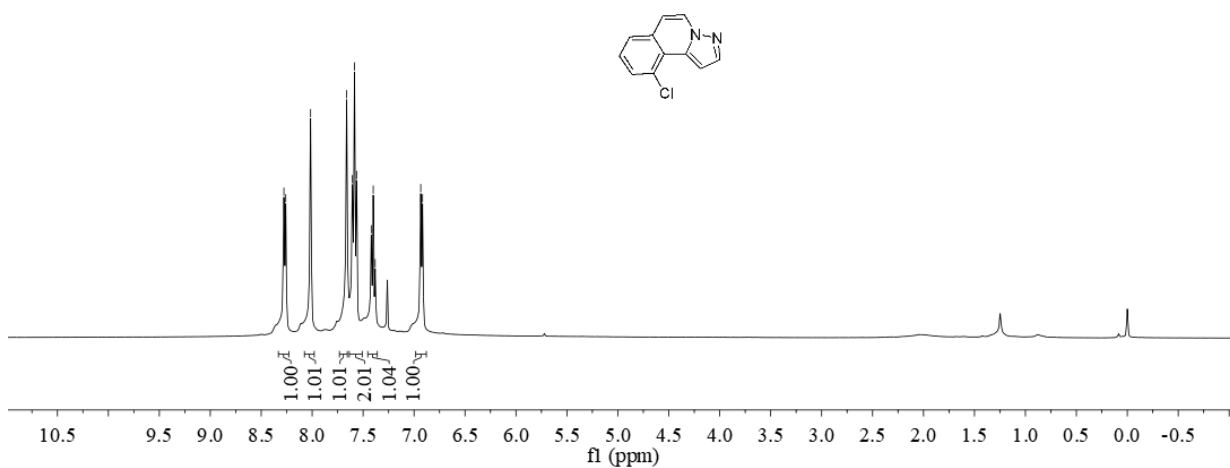
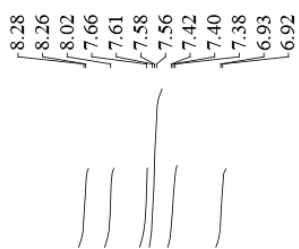
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3s**



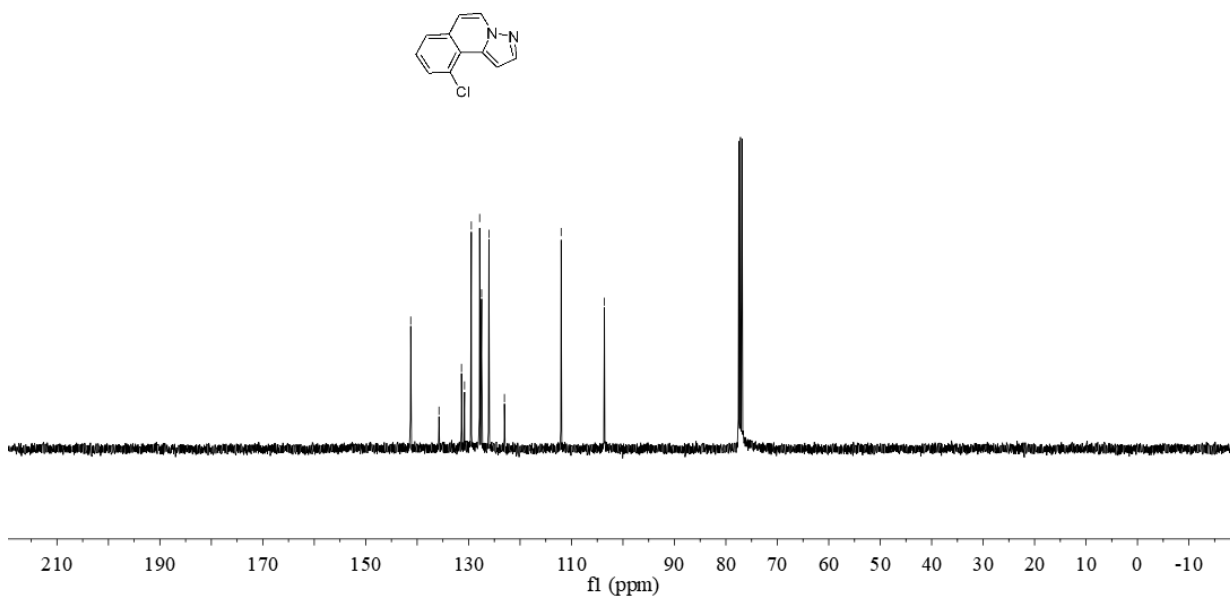
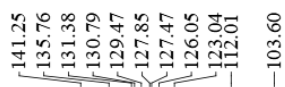
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3s**



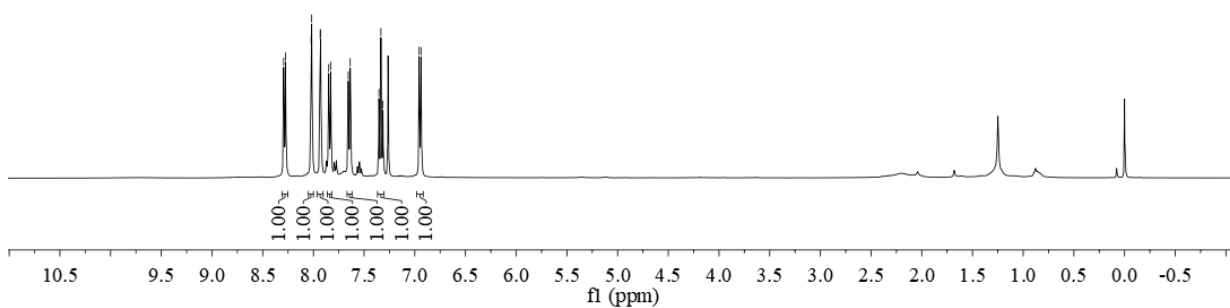
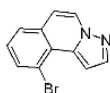
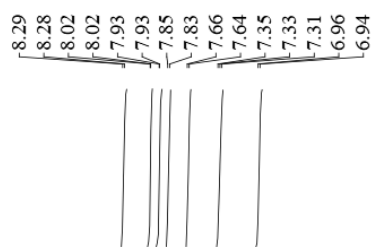
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3t**



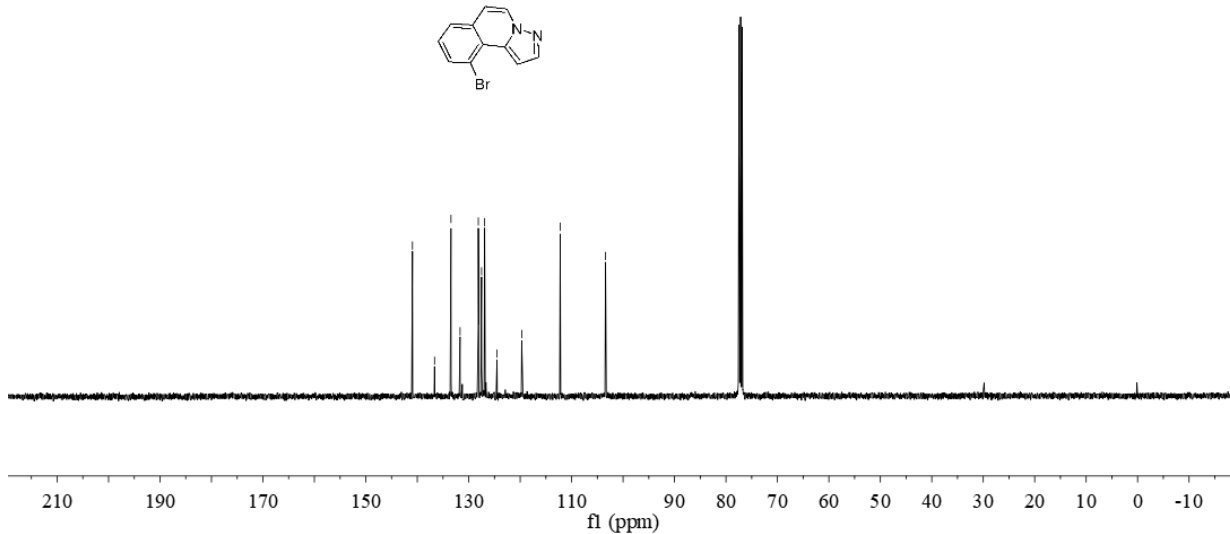
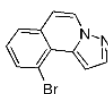
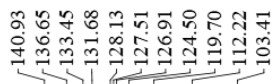
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3t**



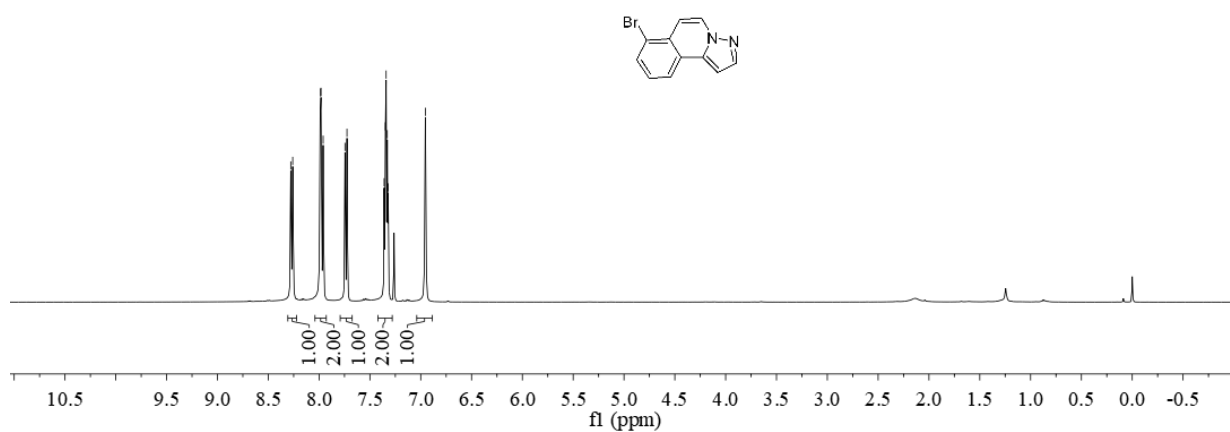
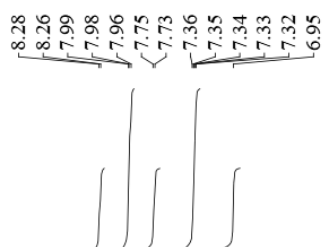
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3u**



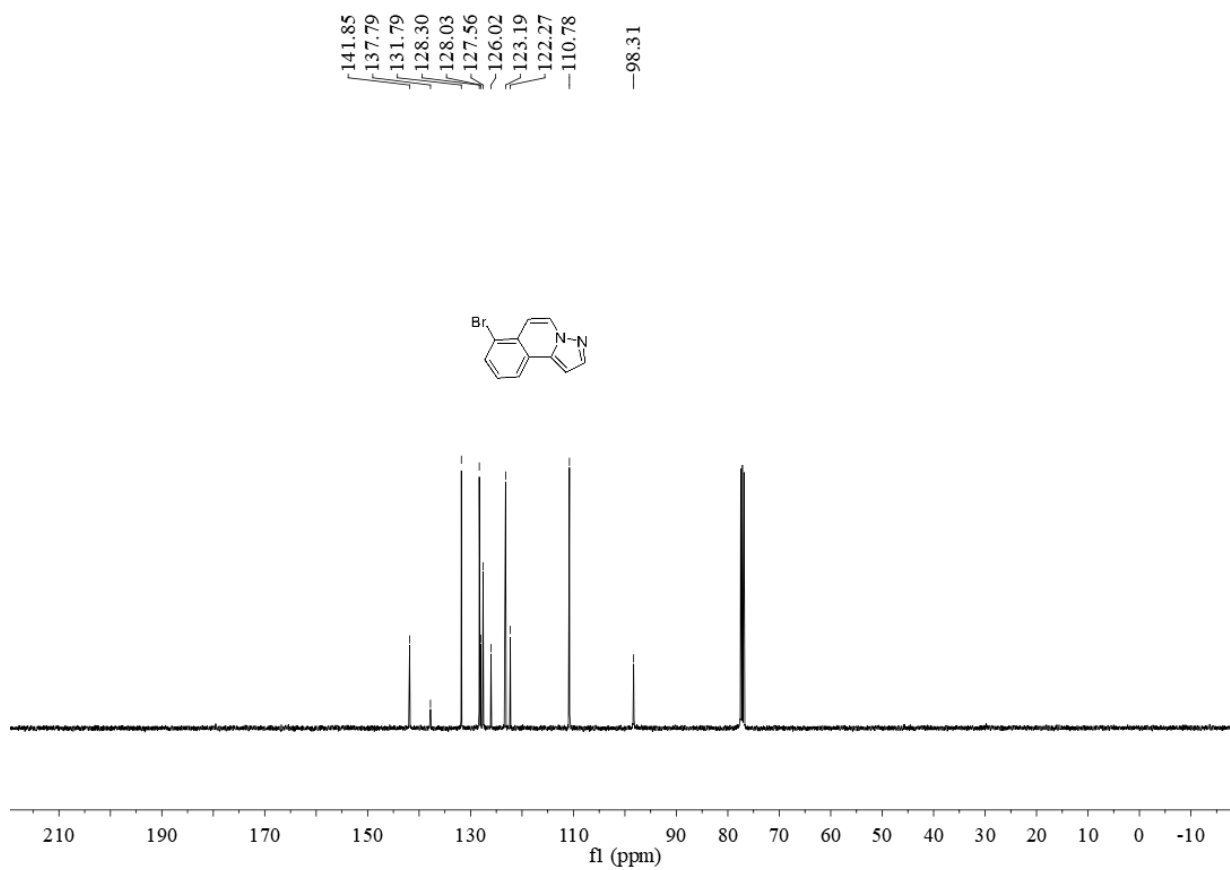
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3u**



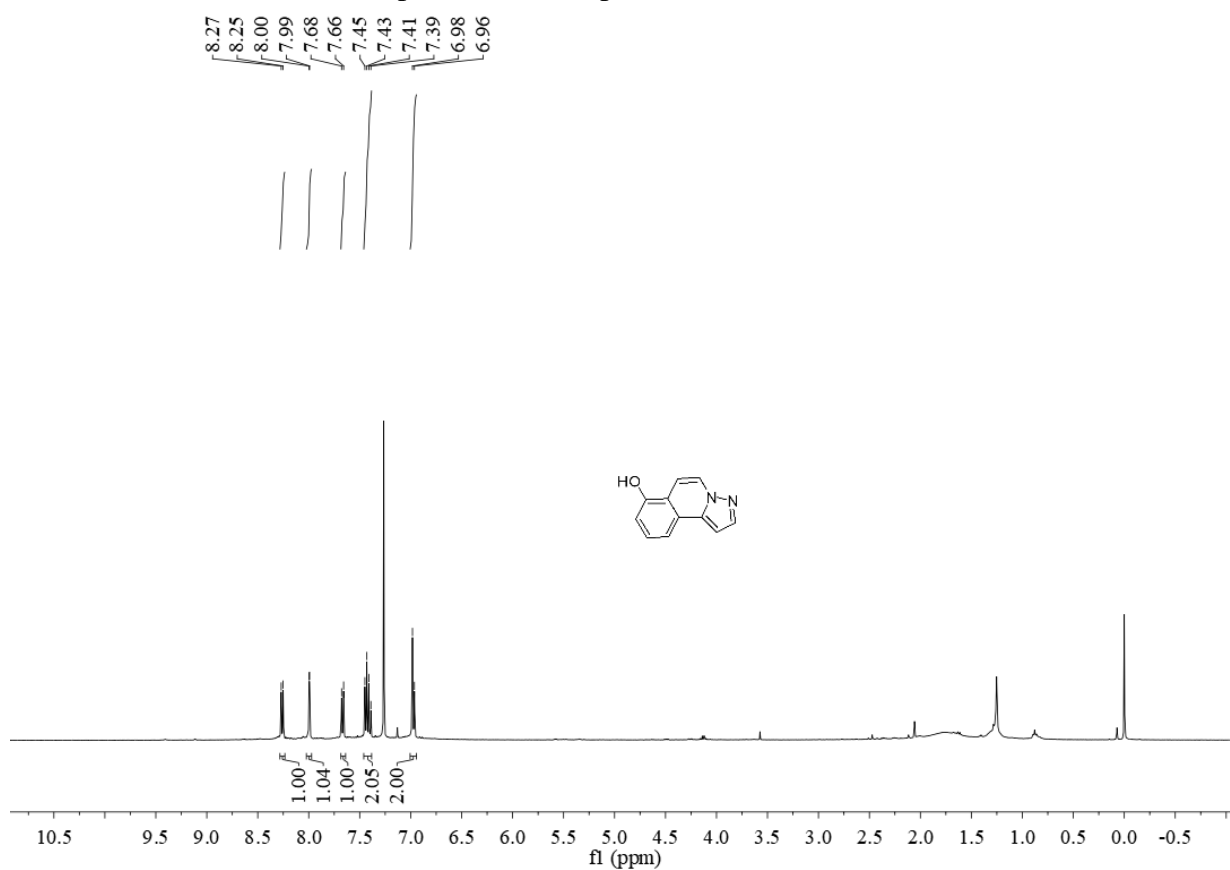
^1H NMR (400 MHz, CDCl_3) spectrum of compound **3v**



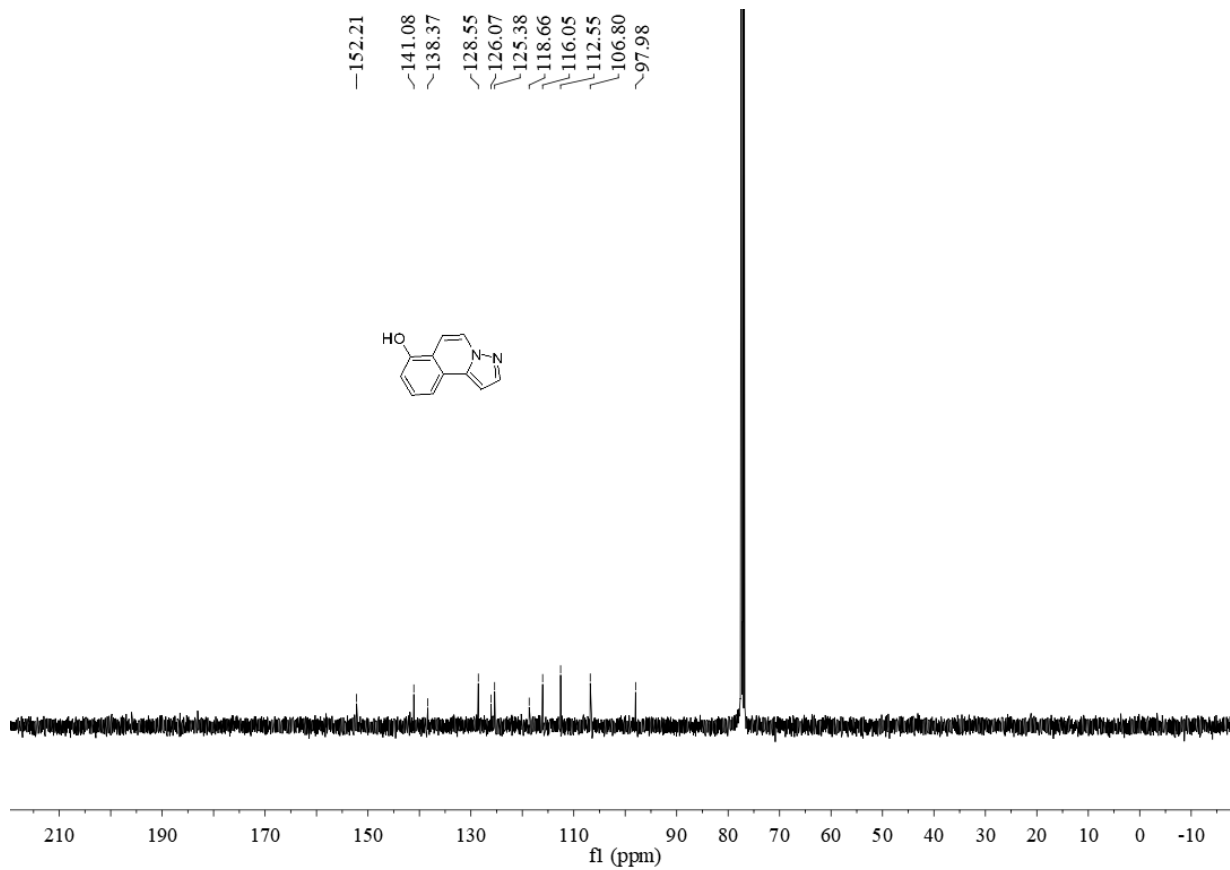
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3v**



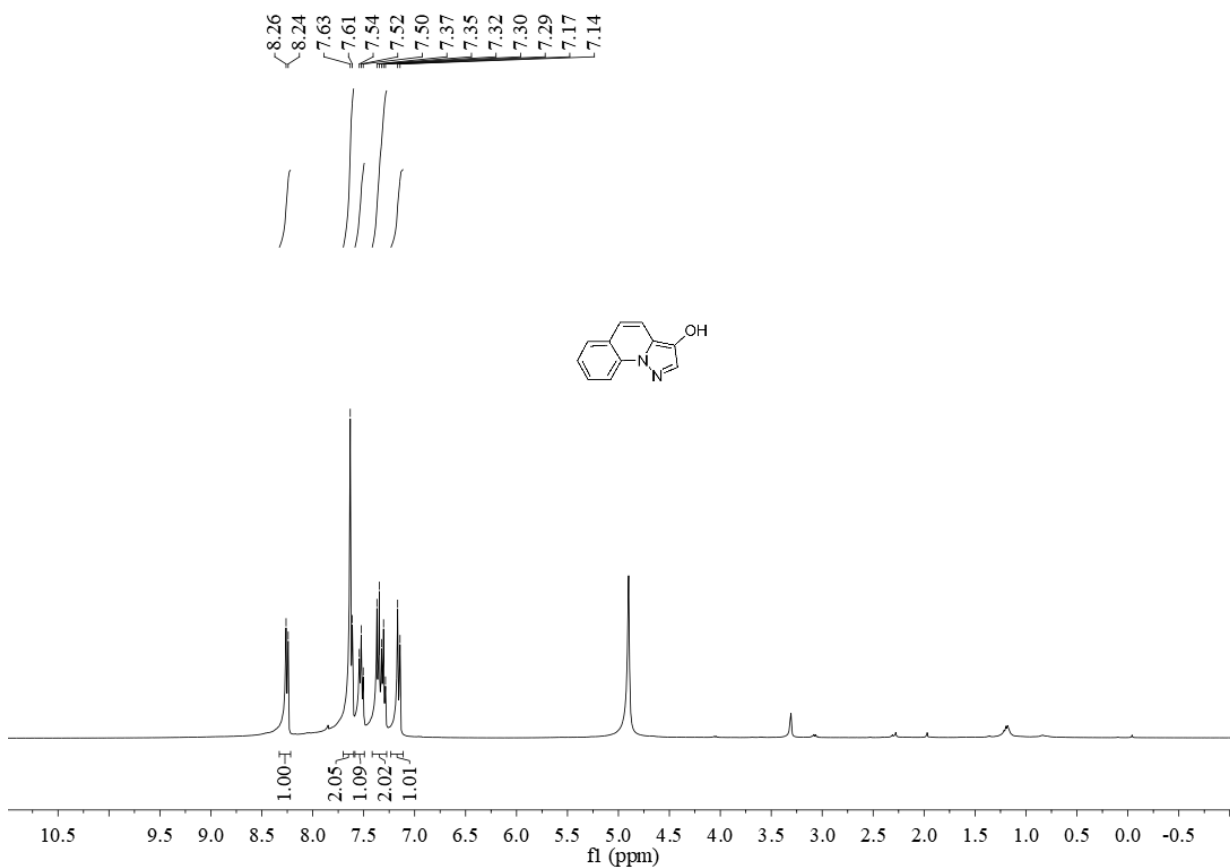
¹H NMR (400 MHz, CDCl₃) spectrum of compound **3w**



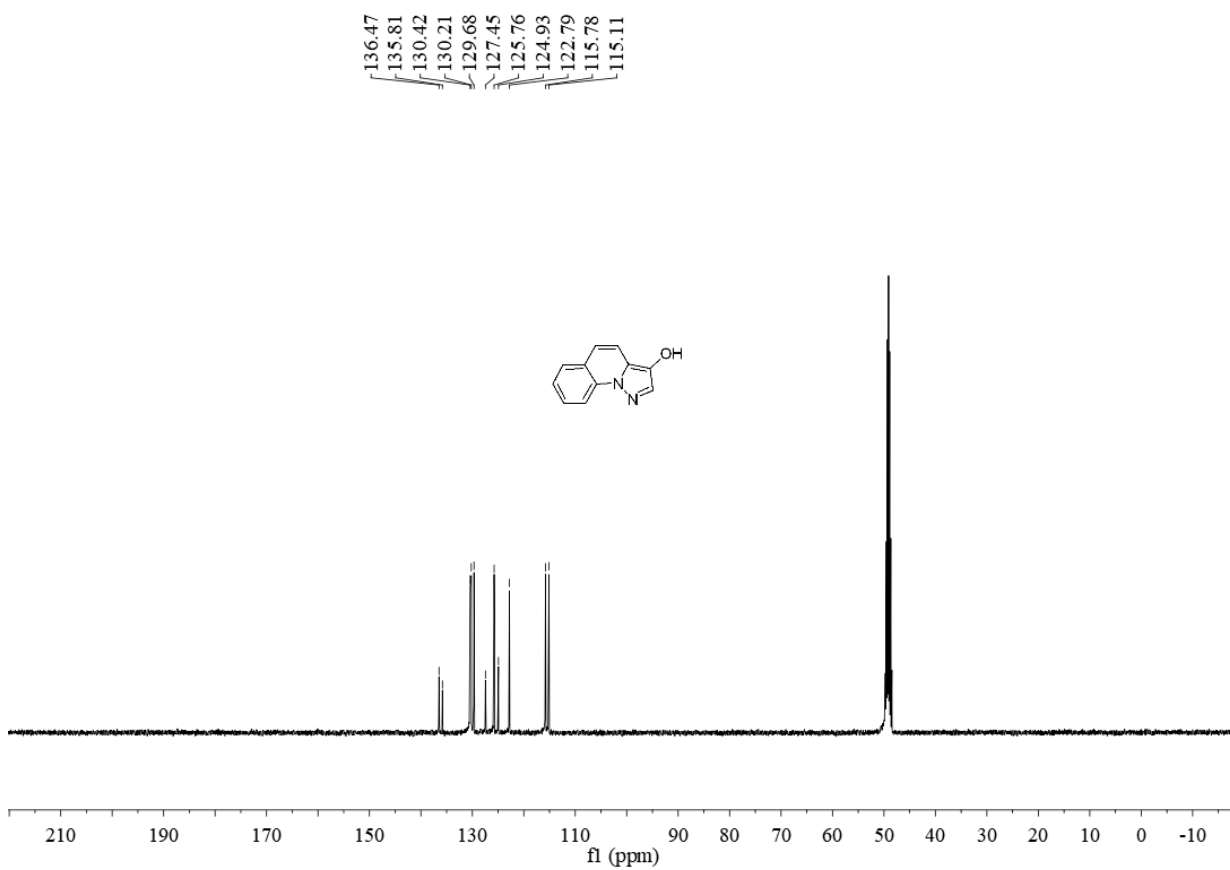
¹³C NMR (100 MHz, CDCl₃) spectrum of compound **3w**



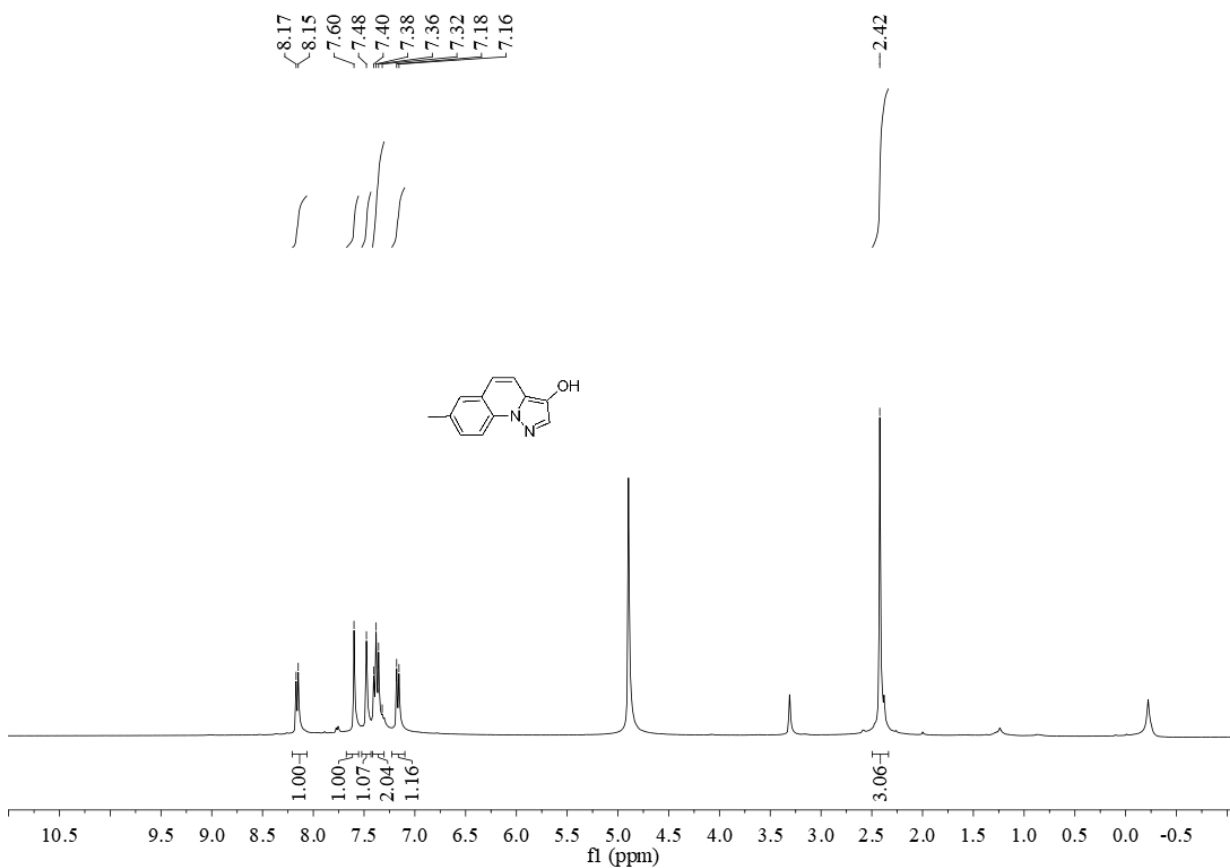
¹H NMR (400 MHz, Acetone-D₆) spectrum of compound **5a**



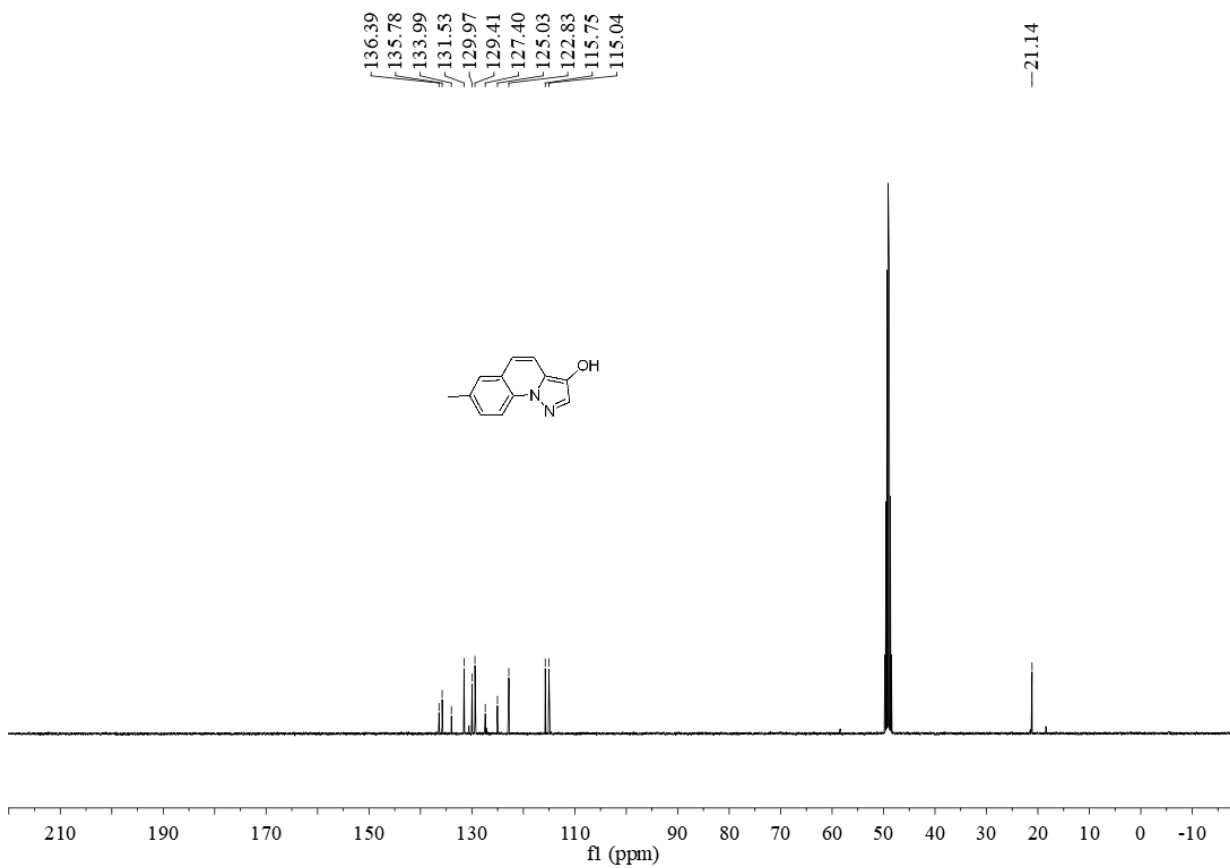
¹³C NMR (100 MHz, Acetone-D₆) spectrum of compound **5a**



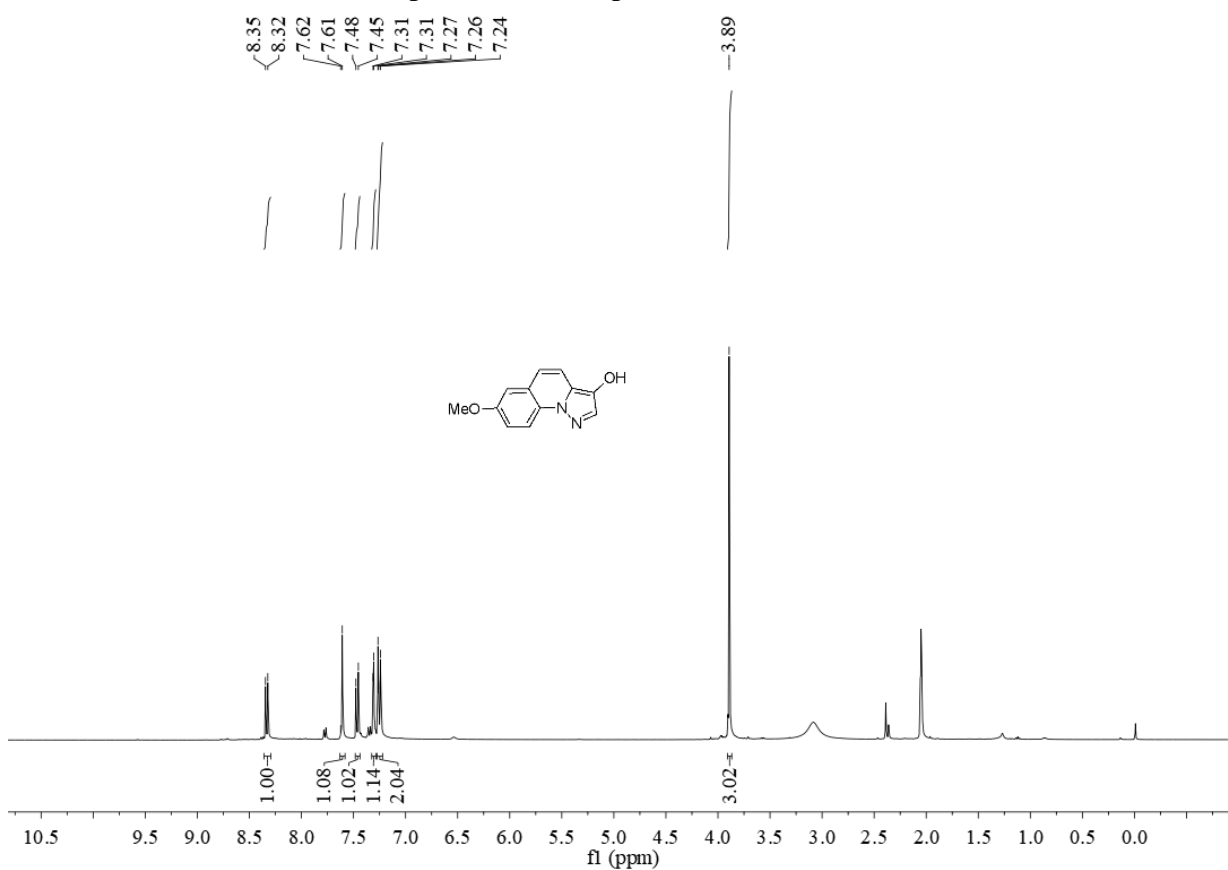
¹H NMR (400 MHz, Methanol-D₄) spectrum of compound **5b**



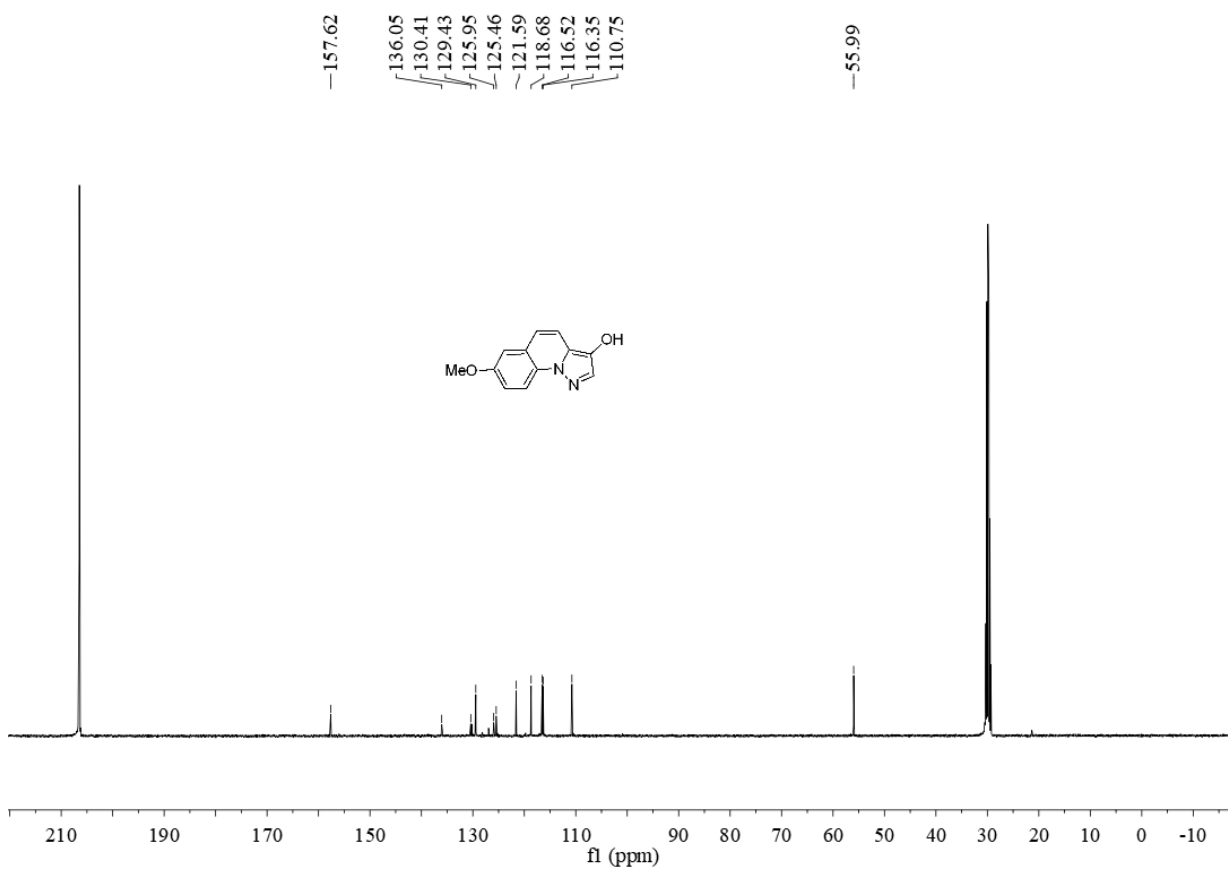
¹³C NMR (100 MHz, Methanol-D₄) spectrum of compound **5b**



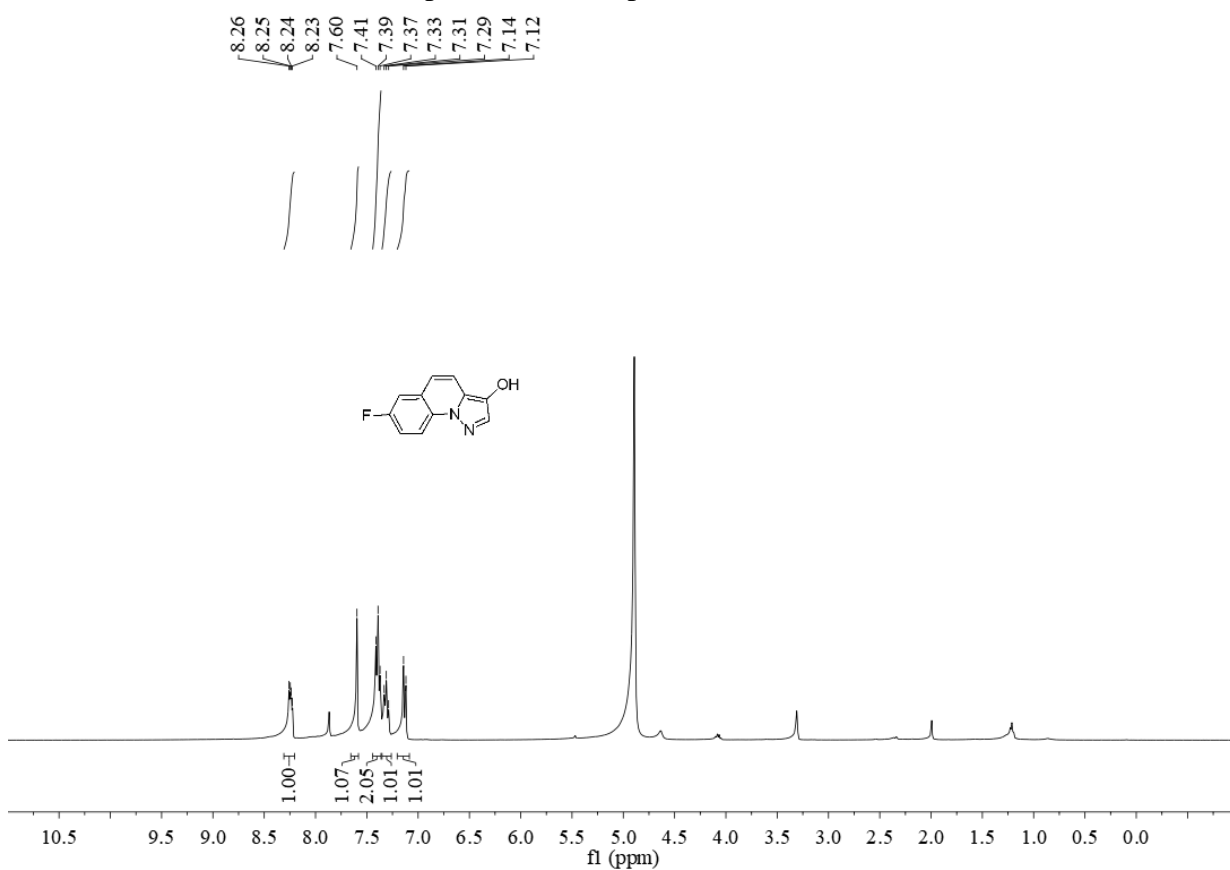
¹H NMR (400 MHz, Acetone-D₆) spectrum of compound **5c**



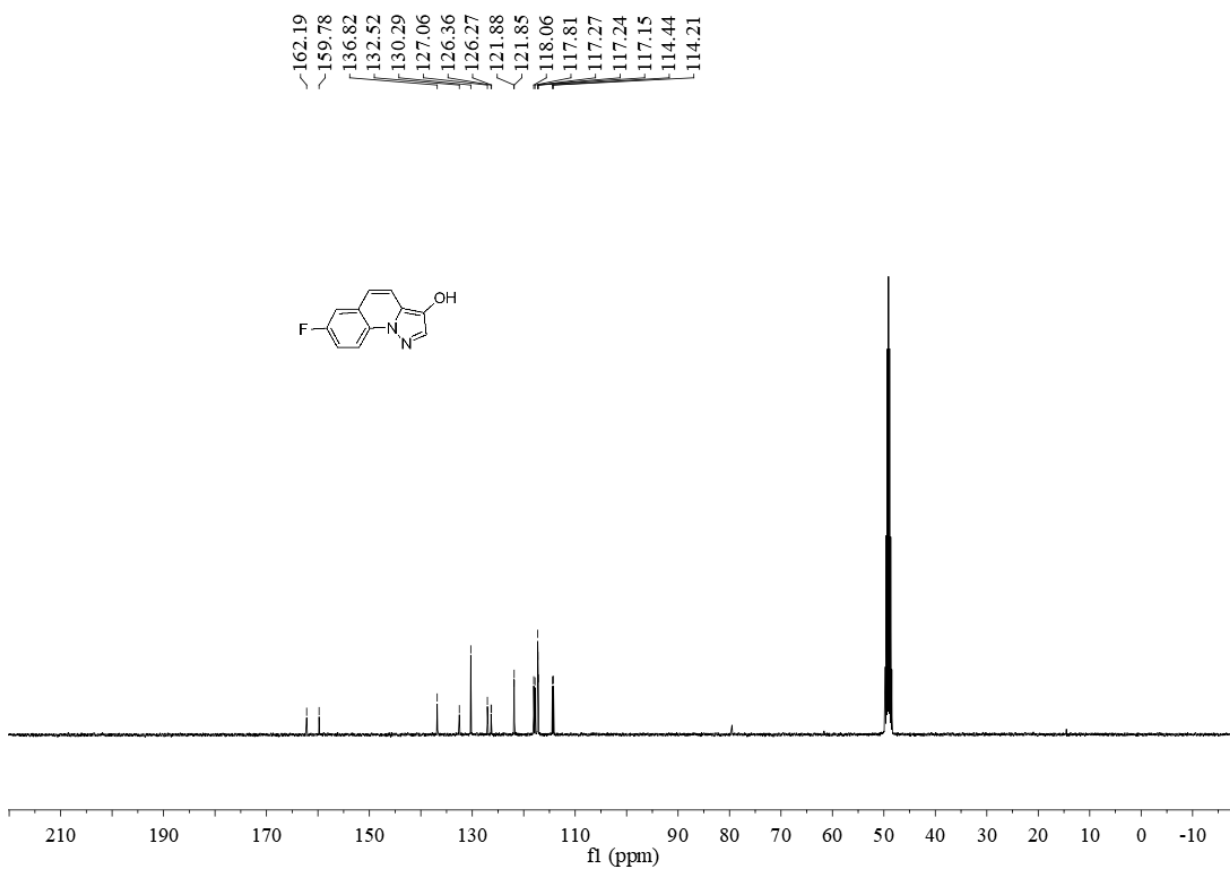
¹³C NMR (100 MHz, Acetone-D₆) spectrum of compound **5c**



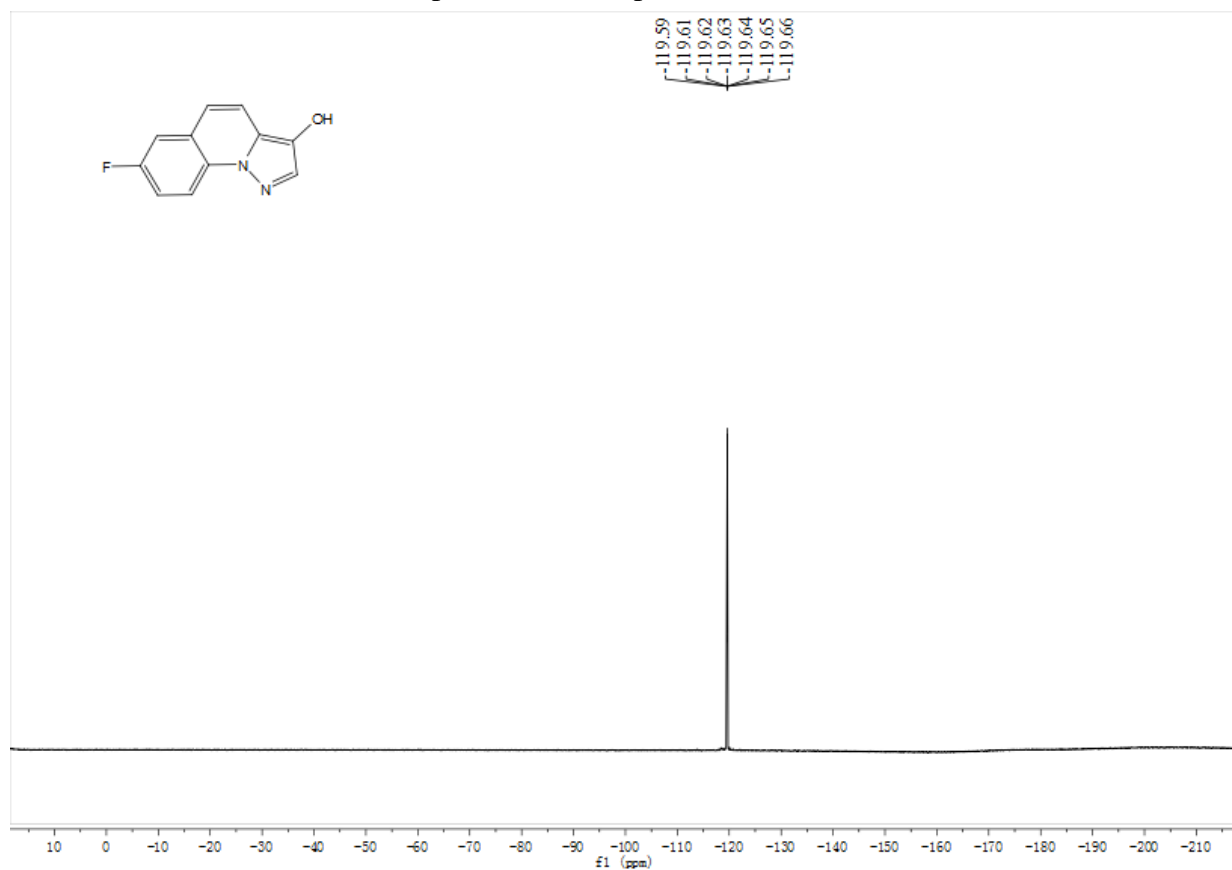
¹H NMR (400 MHz, Methanol-D4) spectrum of compound **5d**



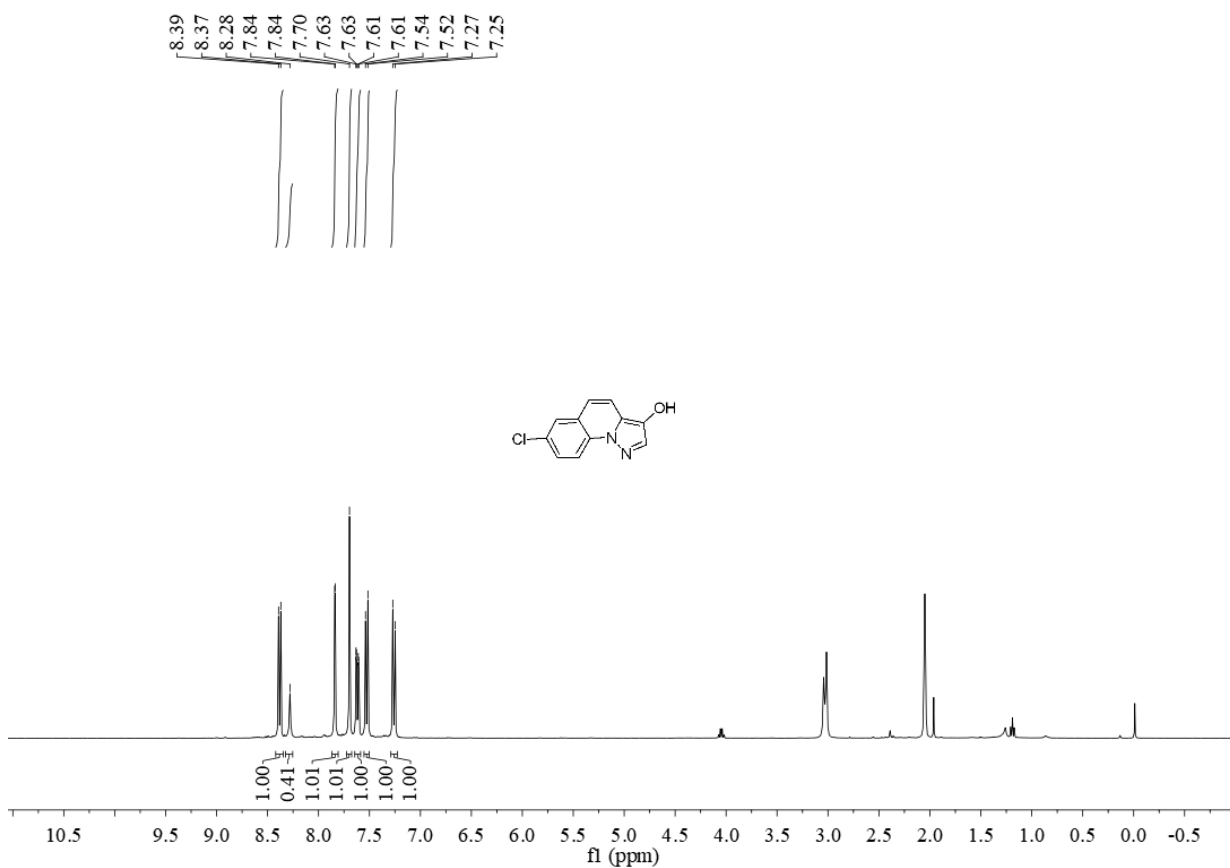
¹³C NMR (100 MHz, Methanol-D4) spectrum of compound **5d**



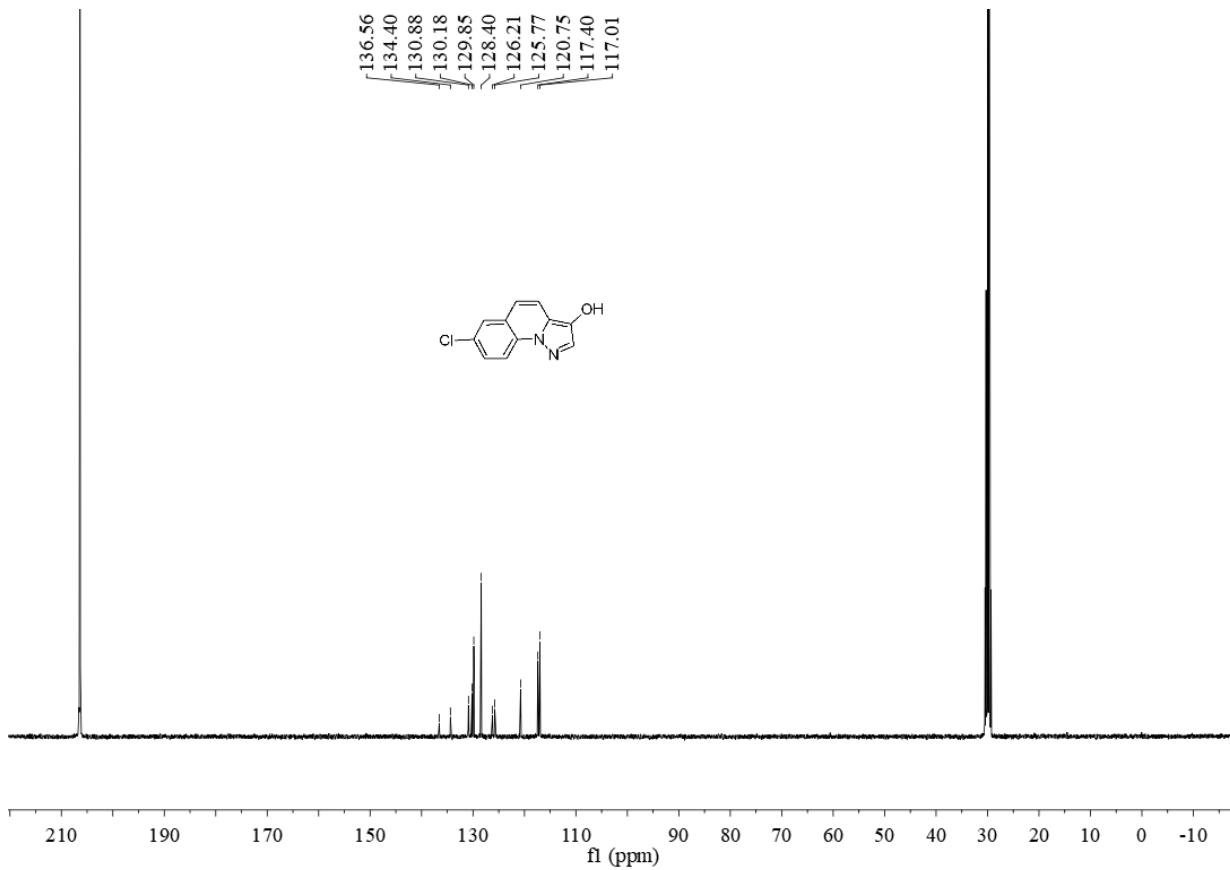
^{19}F NMR (376 MHz, Methanol-D₄) spectrum of compound **5d**



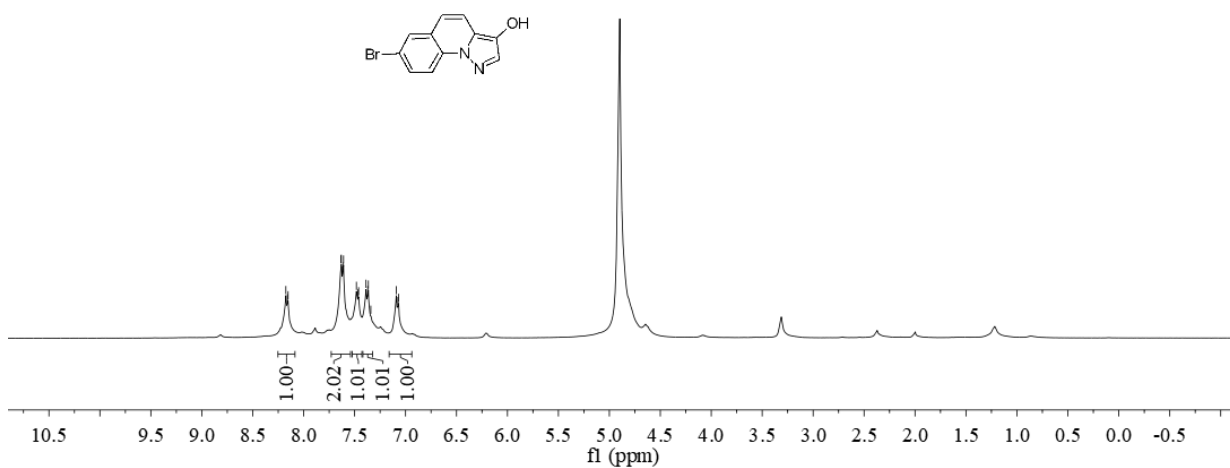
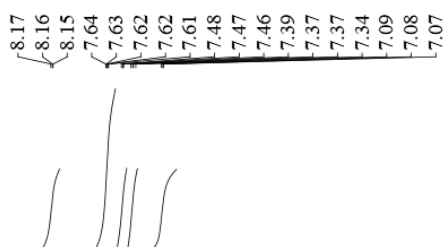
¹H NMR (400 MHz, Acetone-D6) spectrum of compound **5e**



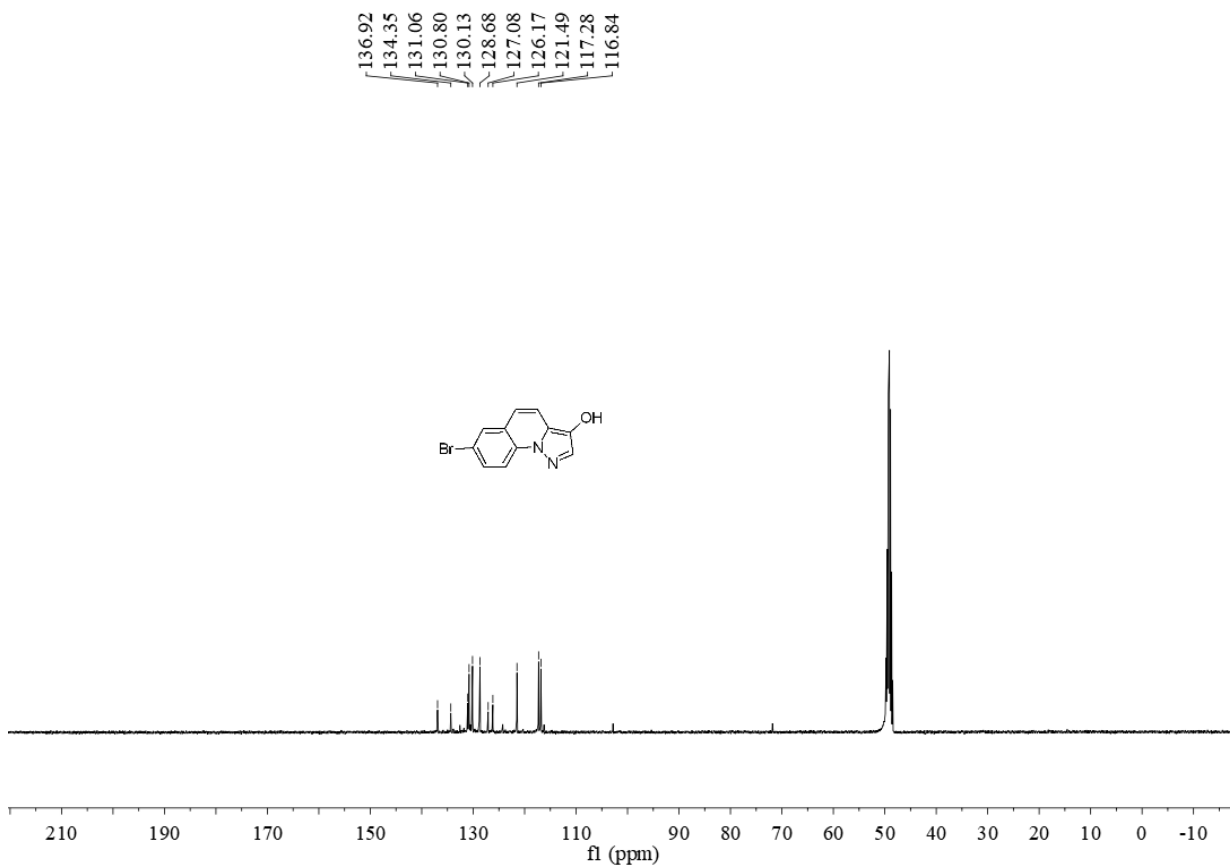
¹³C NMR (100 MHz, Acetone-D6) spectrum of compound **5e**



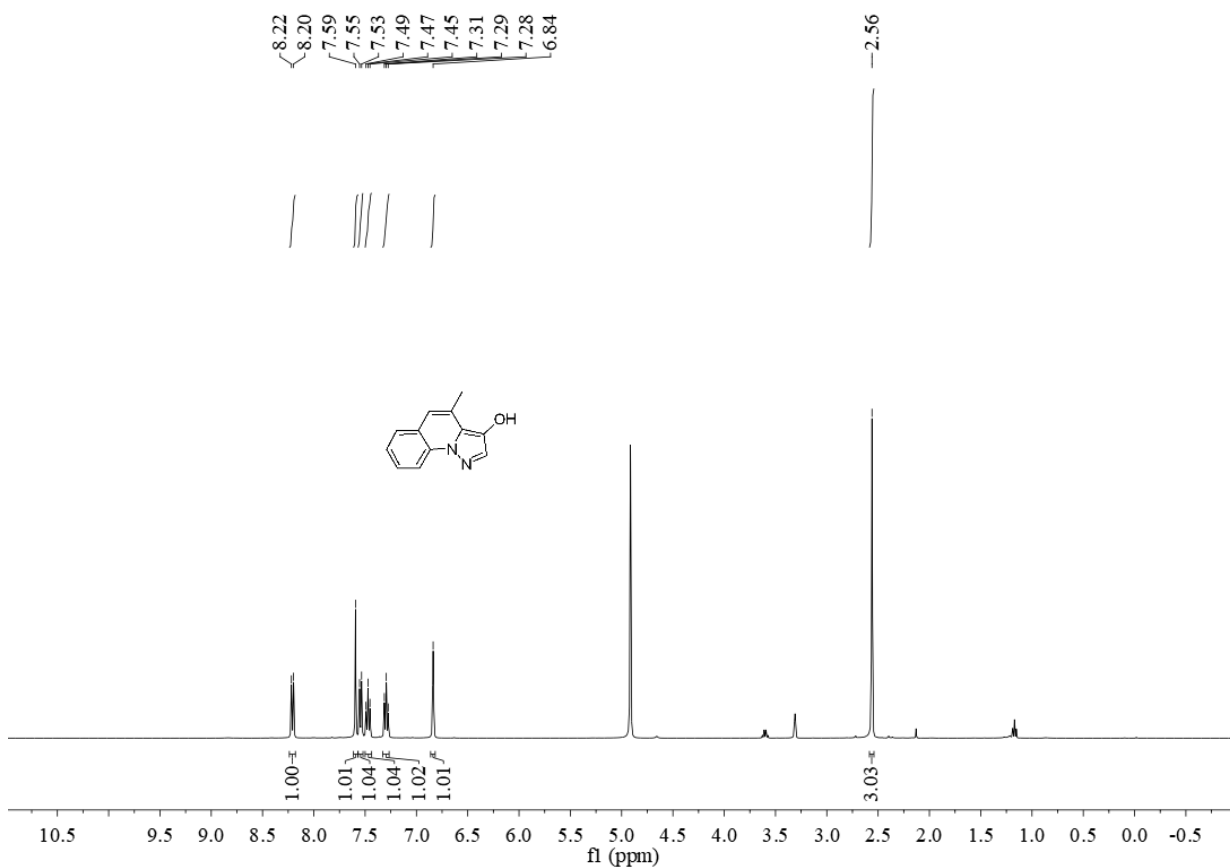
¹H NMR (400 MHz, Methanol-D4) spectrum of compound **5f**



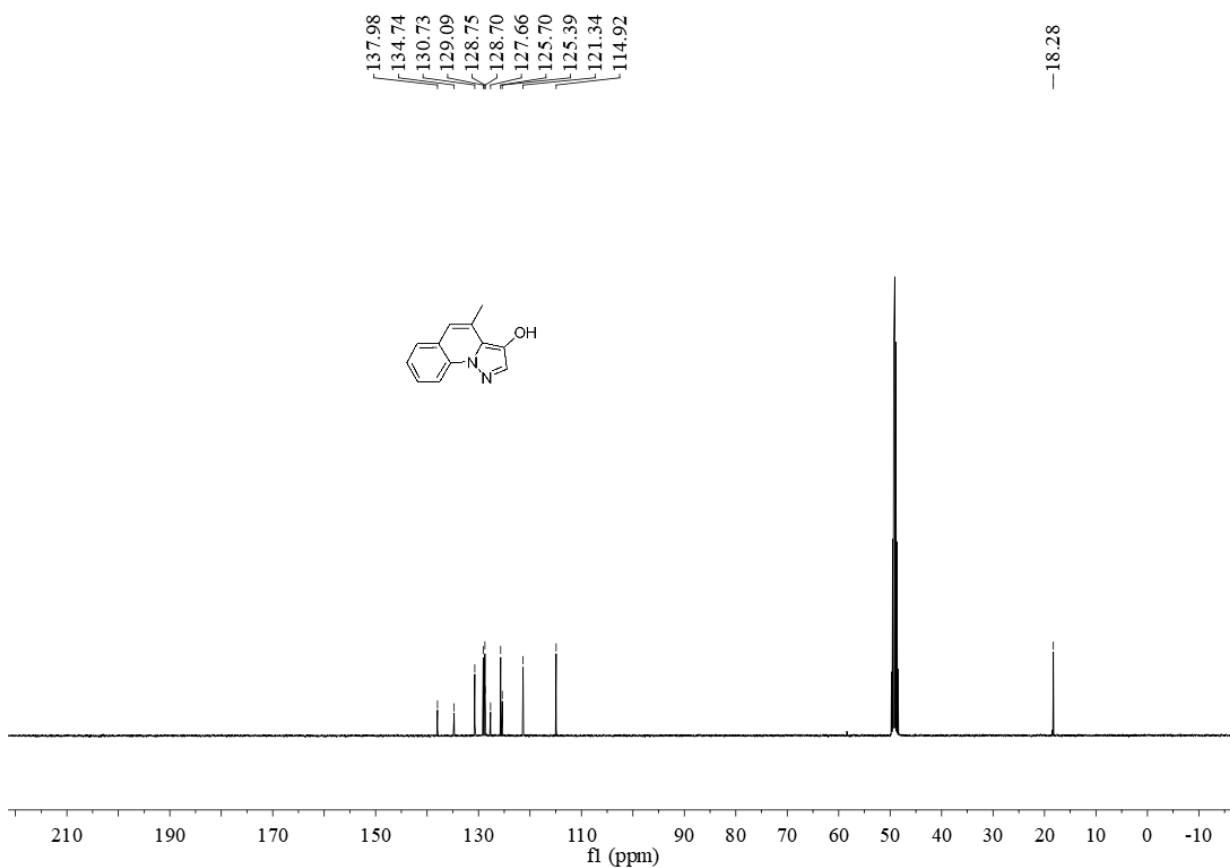
¹³C NMR (100 MHz, Methanol-D4) spectrum of compound **5f**



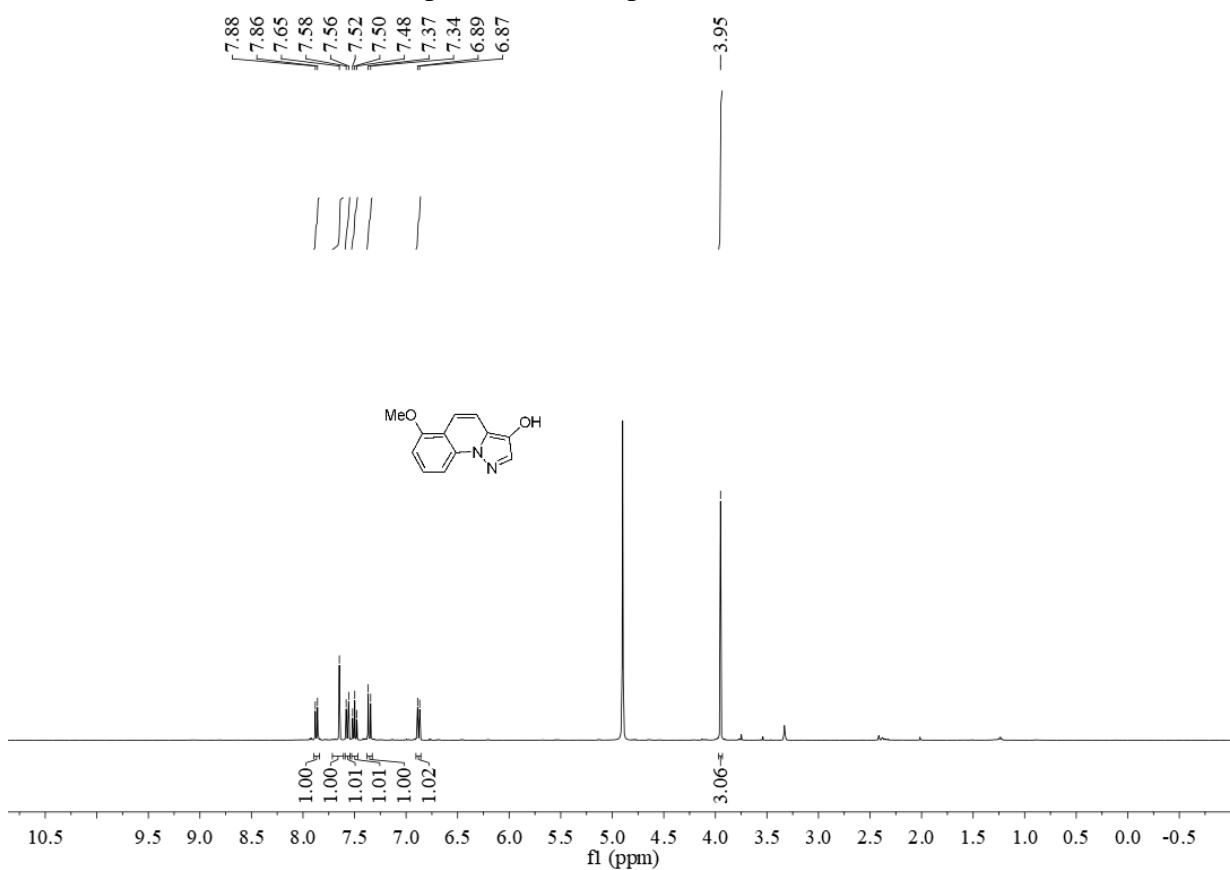
¹H NMR (400 MHz, Methanol-D4) spectrum of compound **5g**



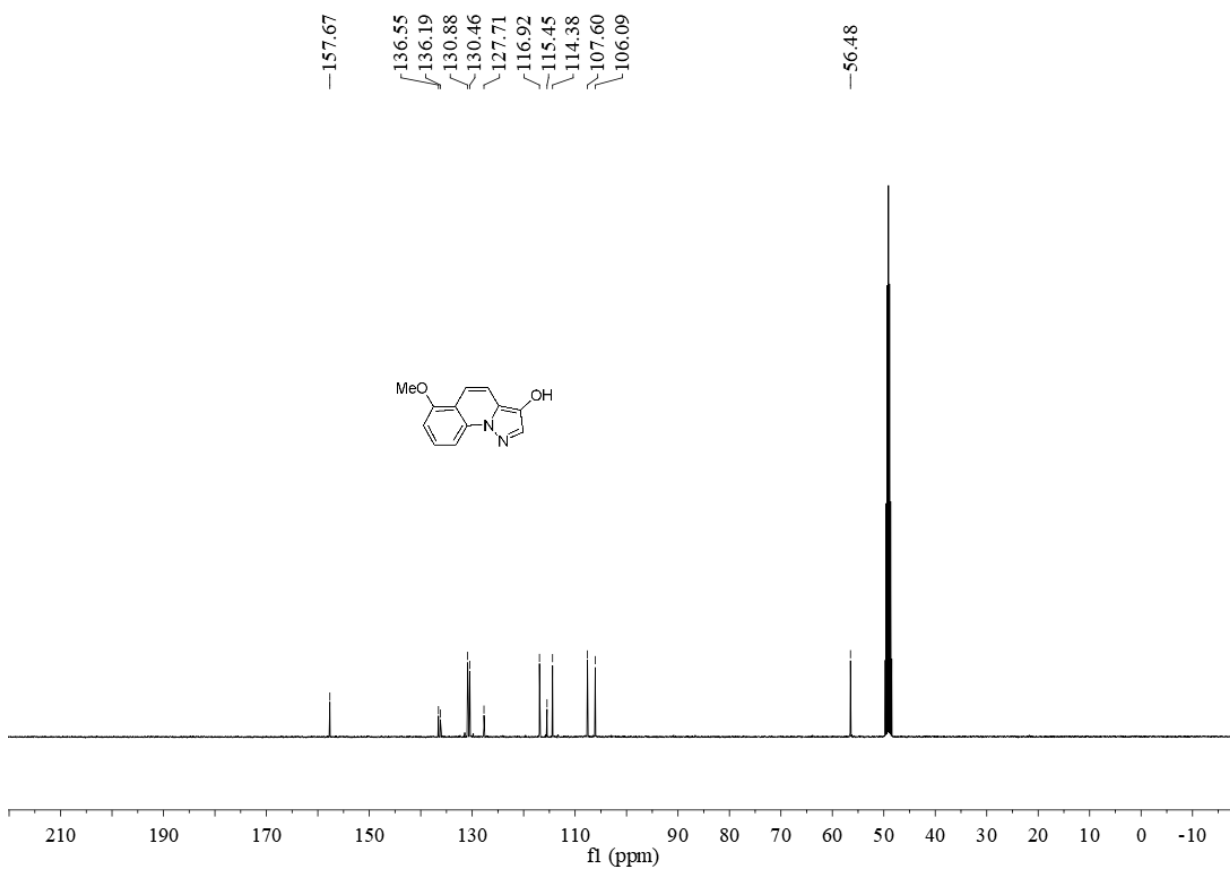
¹³C NMR (100 MHz, Methanol-D4) spectrum of compound **5g**



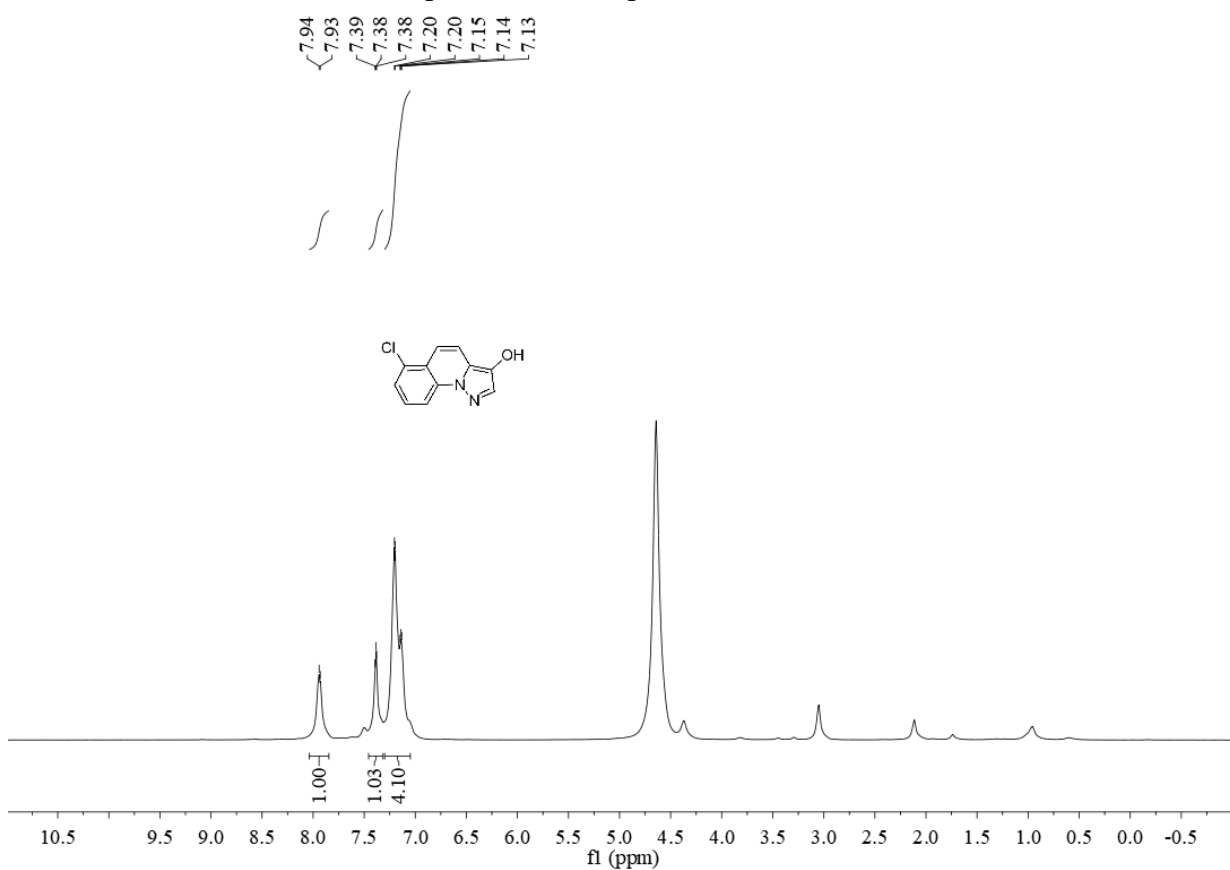
¹H NMR (400 MHz, Methanol-D4) spectrum of compound **5h**



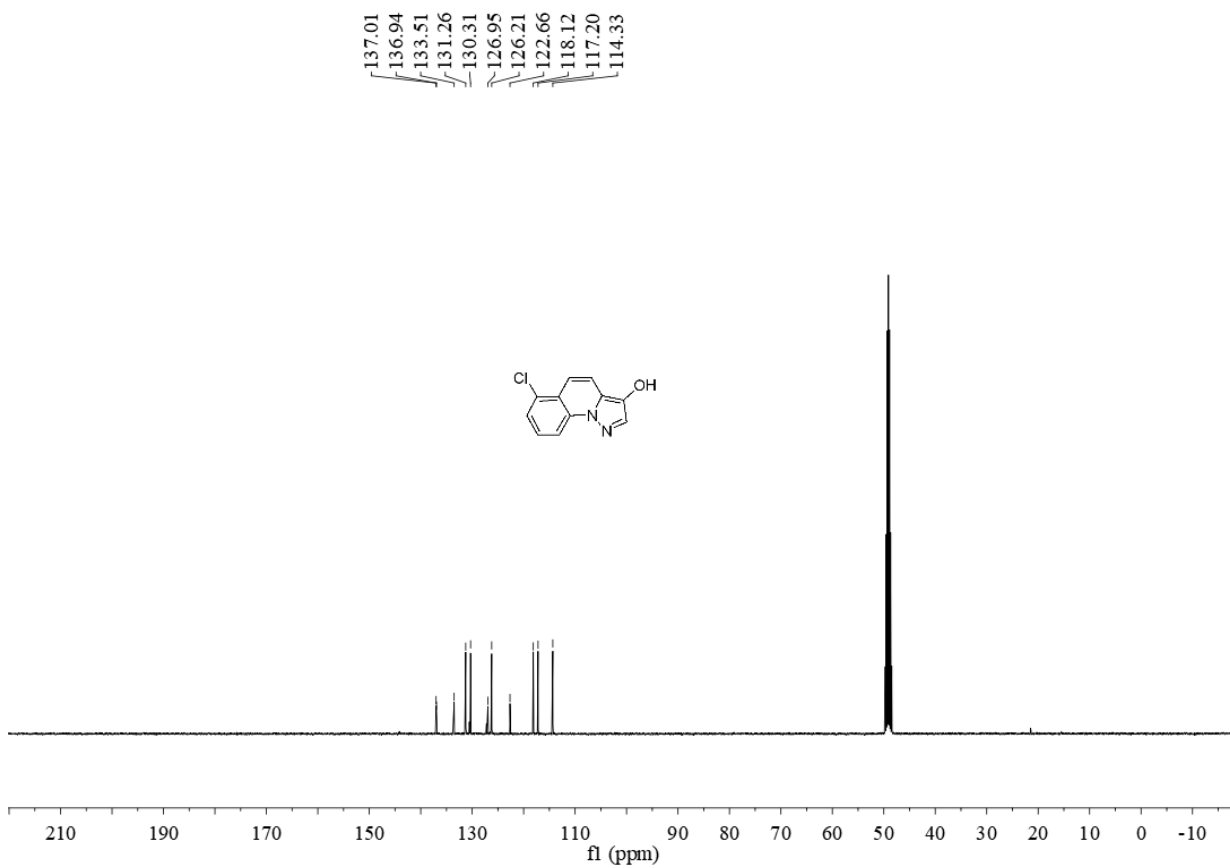
¹³C NMR (100 MHz, Methanol-D4) spectrum of compound **5h**



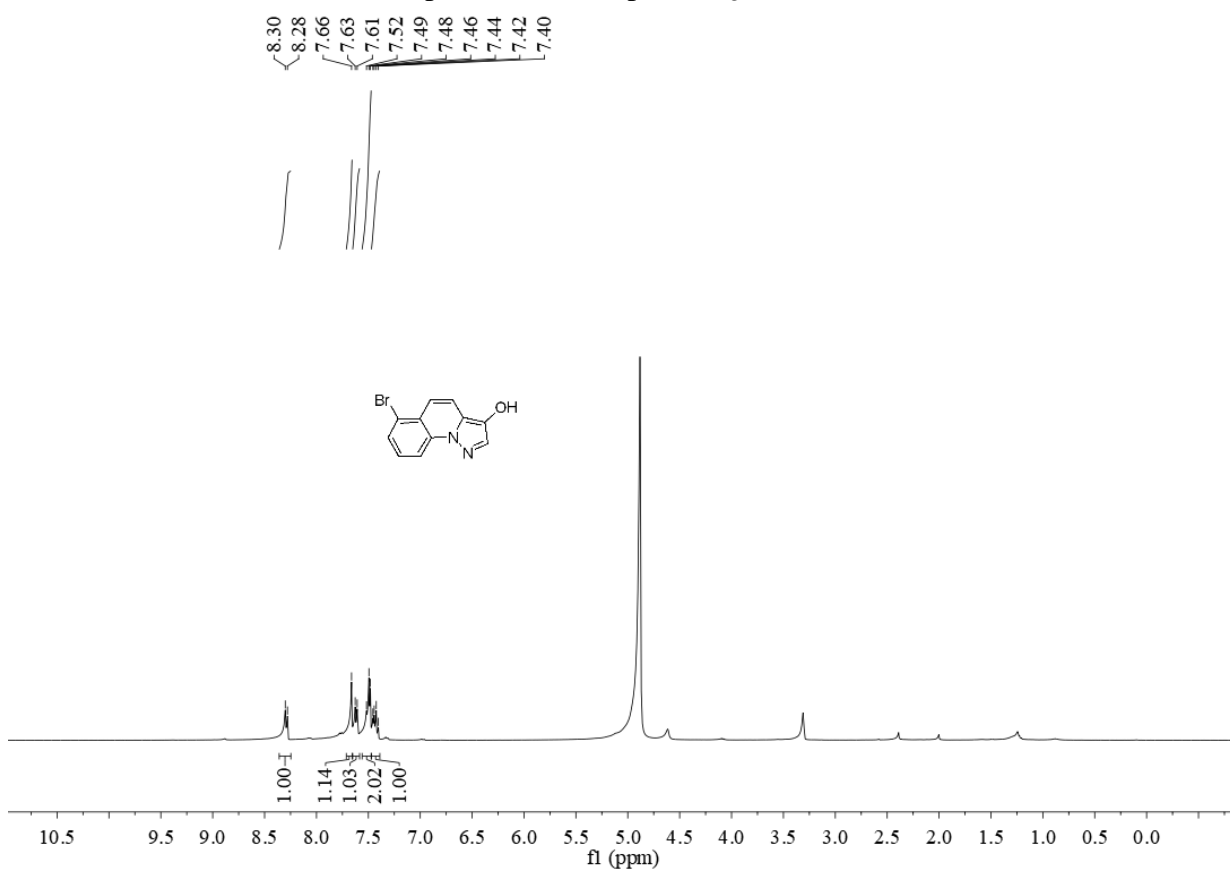
¹H NMR (400 MHz, Methanol-D₄) spectrum of compound **5i**



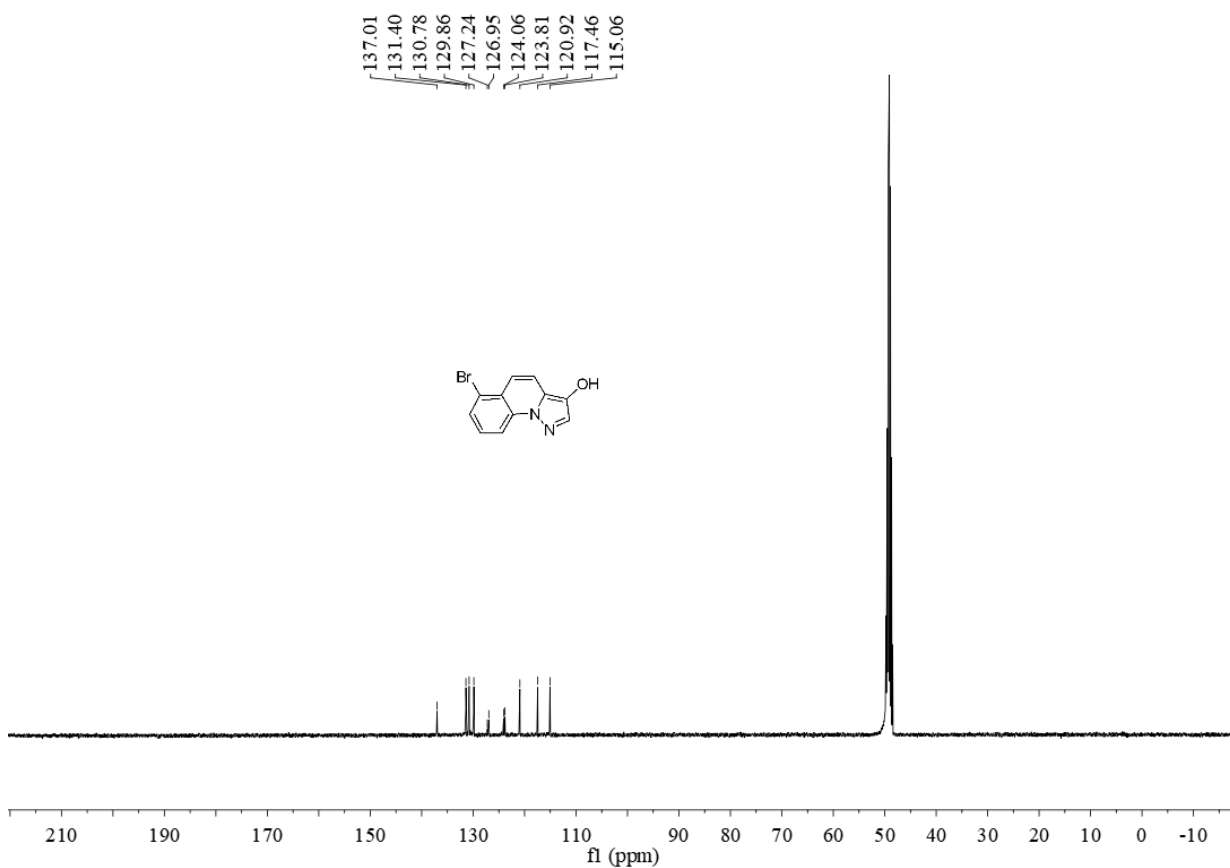
¹³C NMR (100 MHz, Methanol-D₄) spectrum of compound **5i**



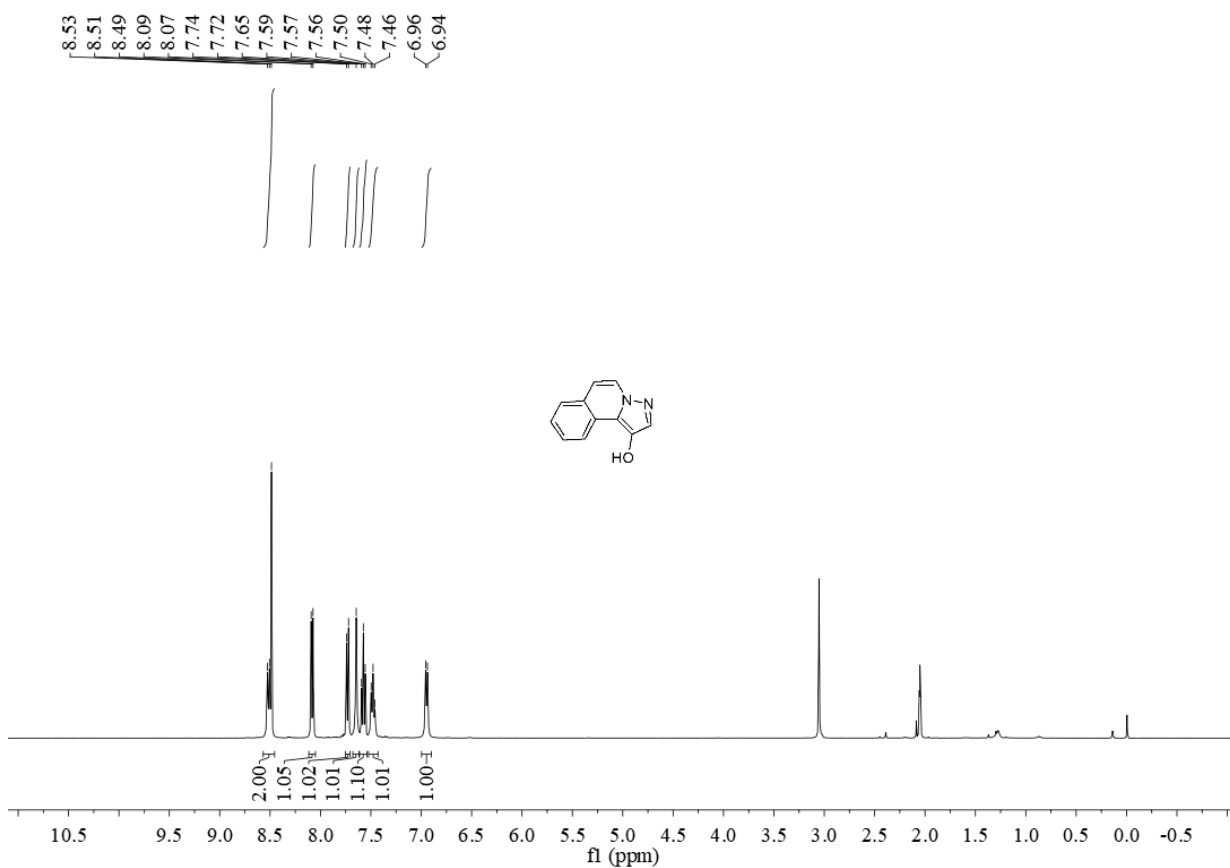
¹H NMR (400 MHz, Methanol-D₄) spectrum of compound **5j**



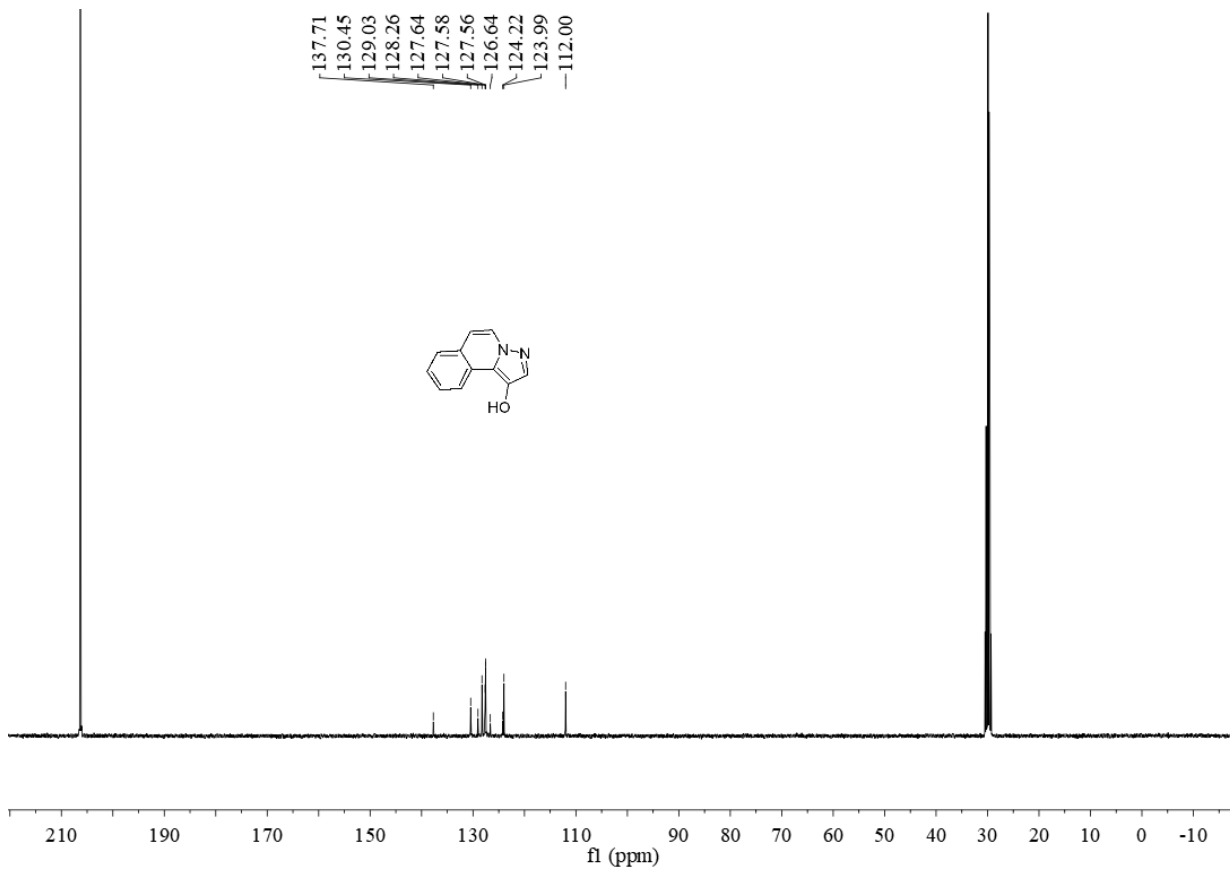
¹³C NMR (100 MHz, Methanol-D₄) spectrum of compound **5j**



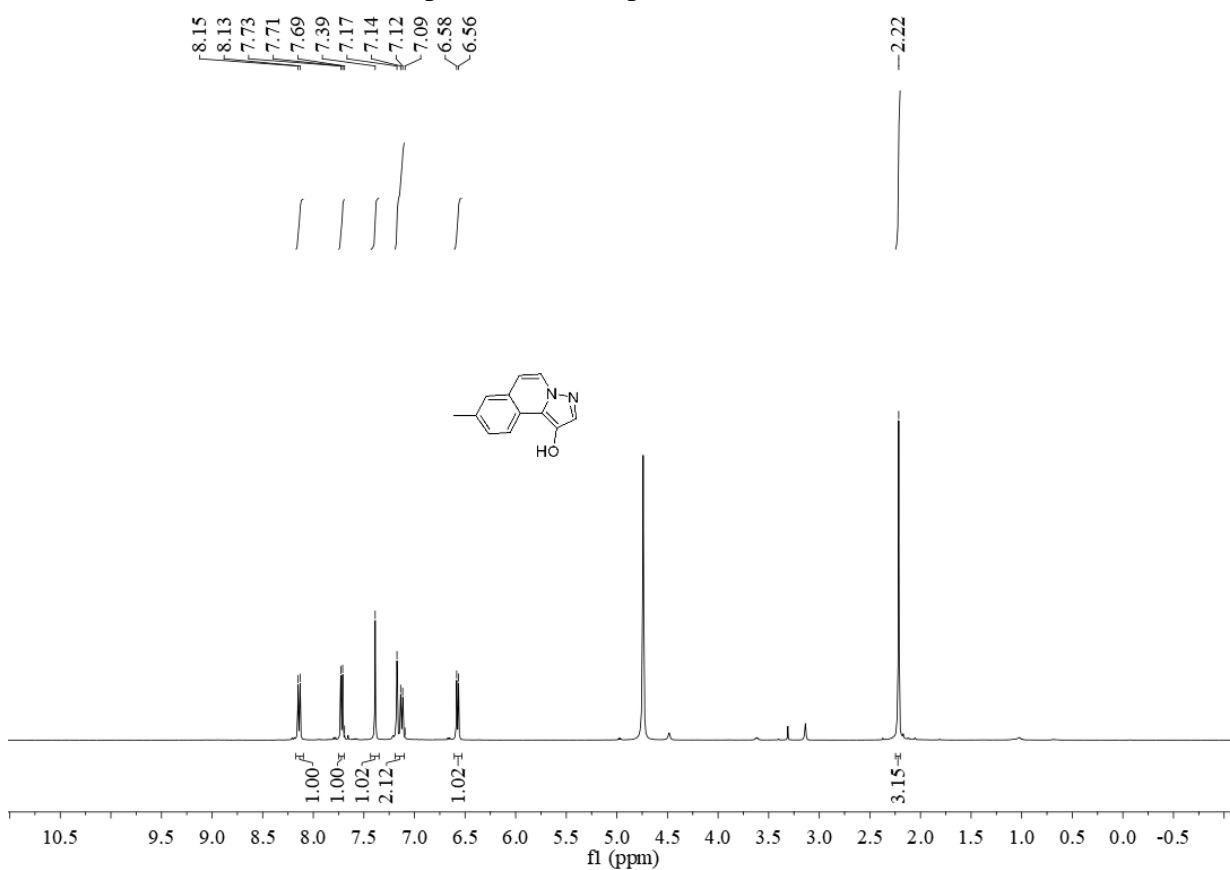
¹H NMR (400 MHz, Acetone-D₆) spectrum of compound **7a**



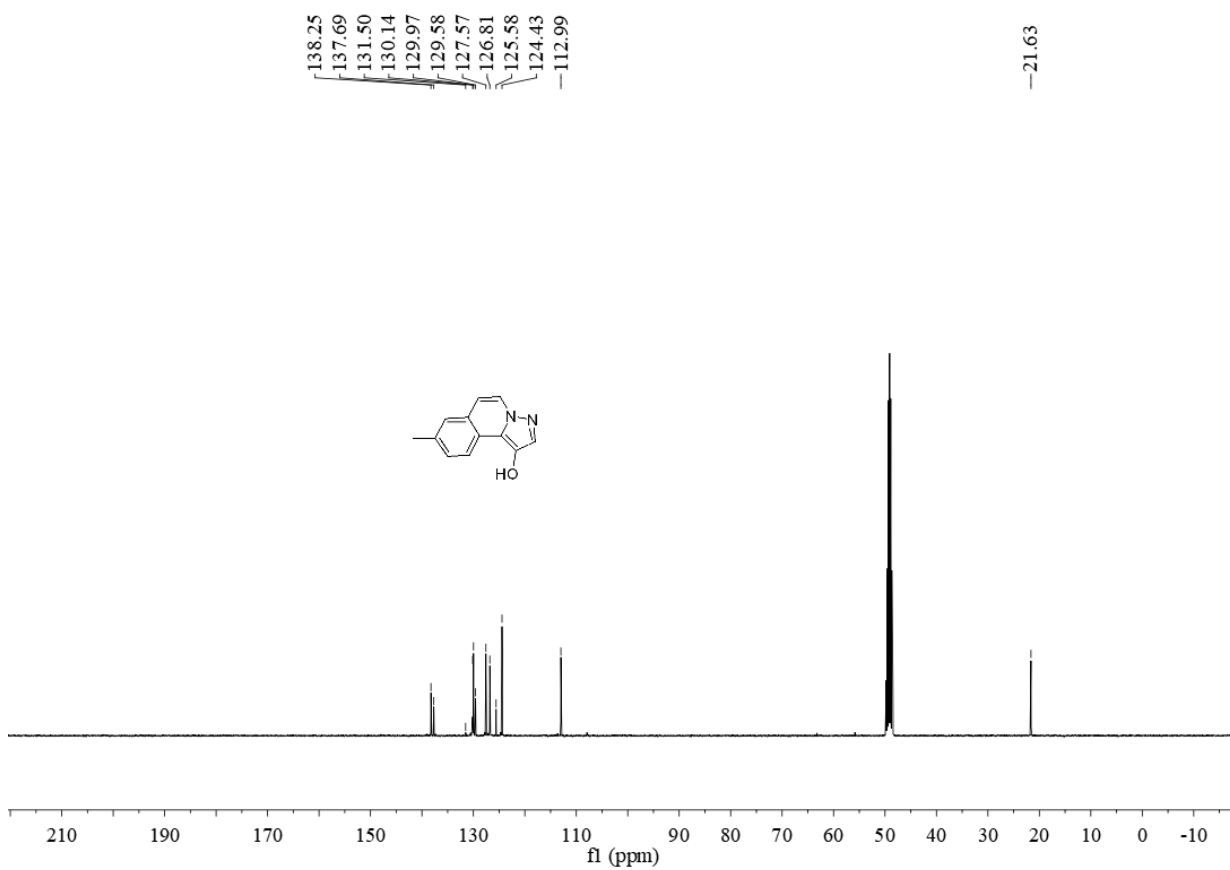
¹³C NMR (100 MHz, Acetone-D₆) spectrum of compound **7a**



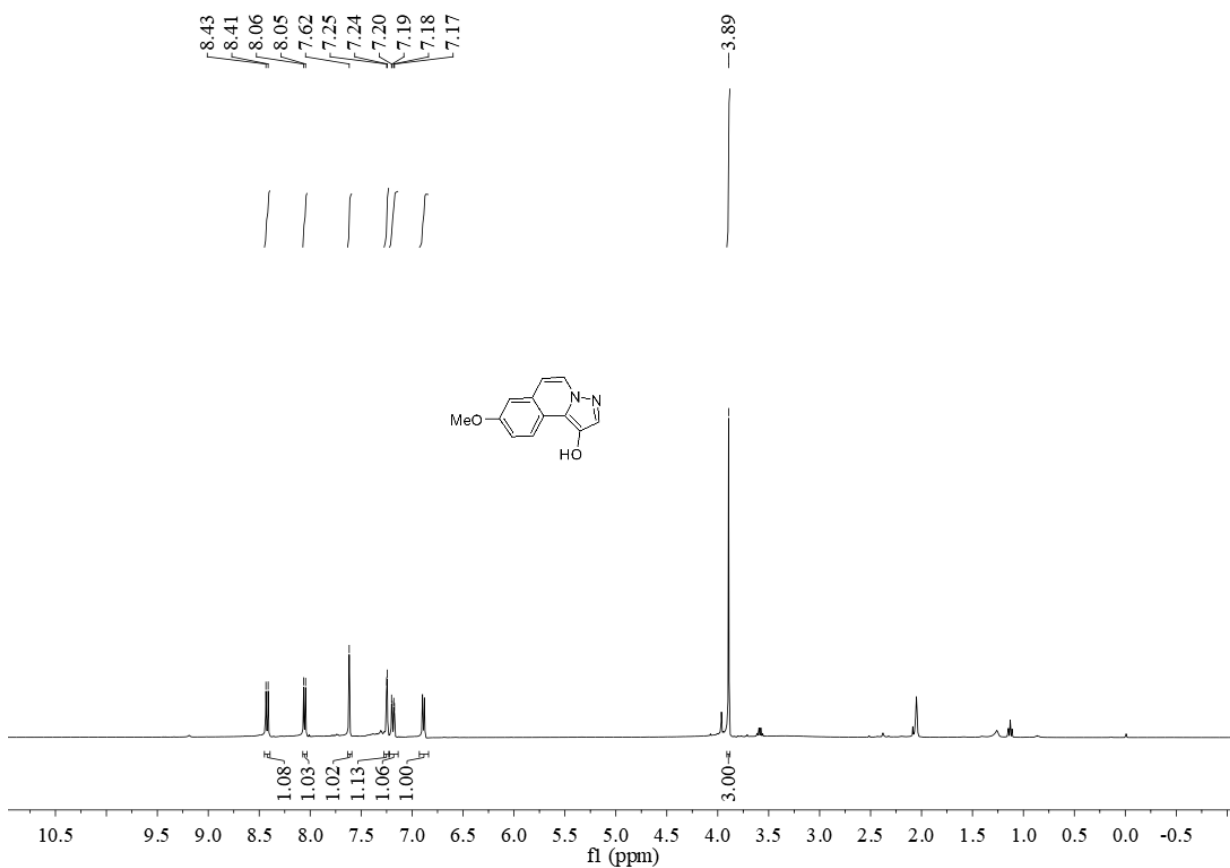
¹H NMR (400 MHz, Methanol-D4) spectrum of compound **7b**



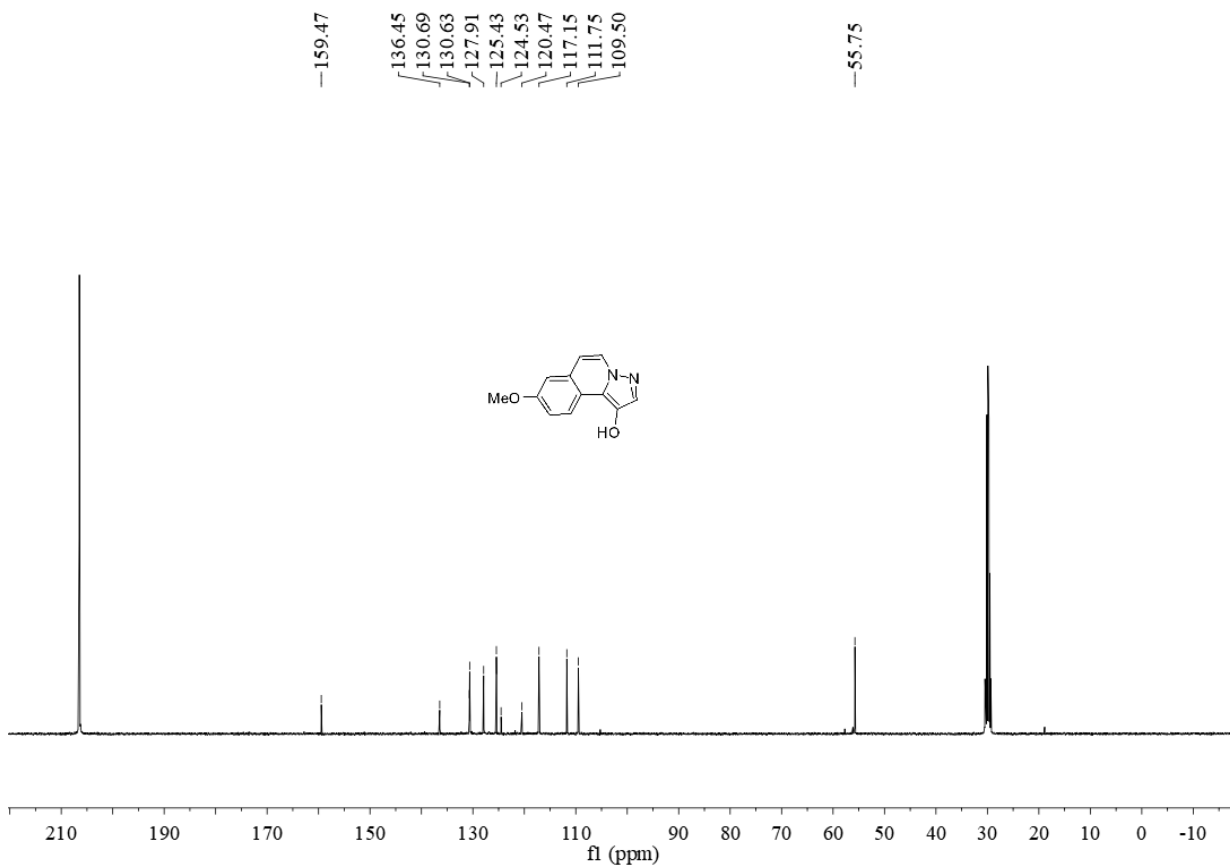
¹³C NMR (100 MHz, Methanol-D4) spectrum of compound **7b**



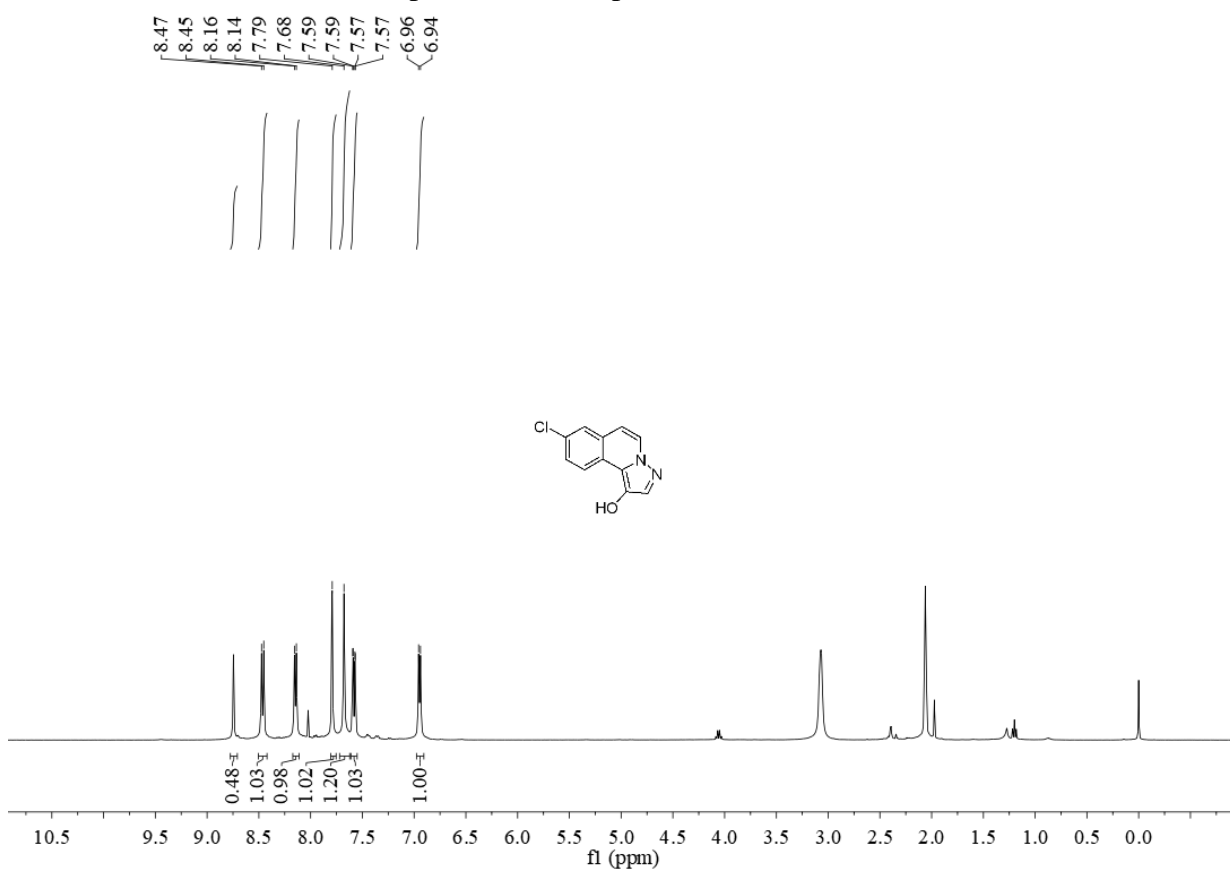
¹H NMR (400 MHz, Acetone-D₆) spectrum of compound **7c**



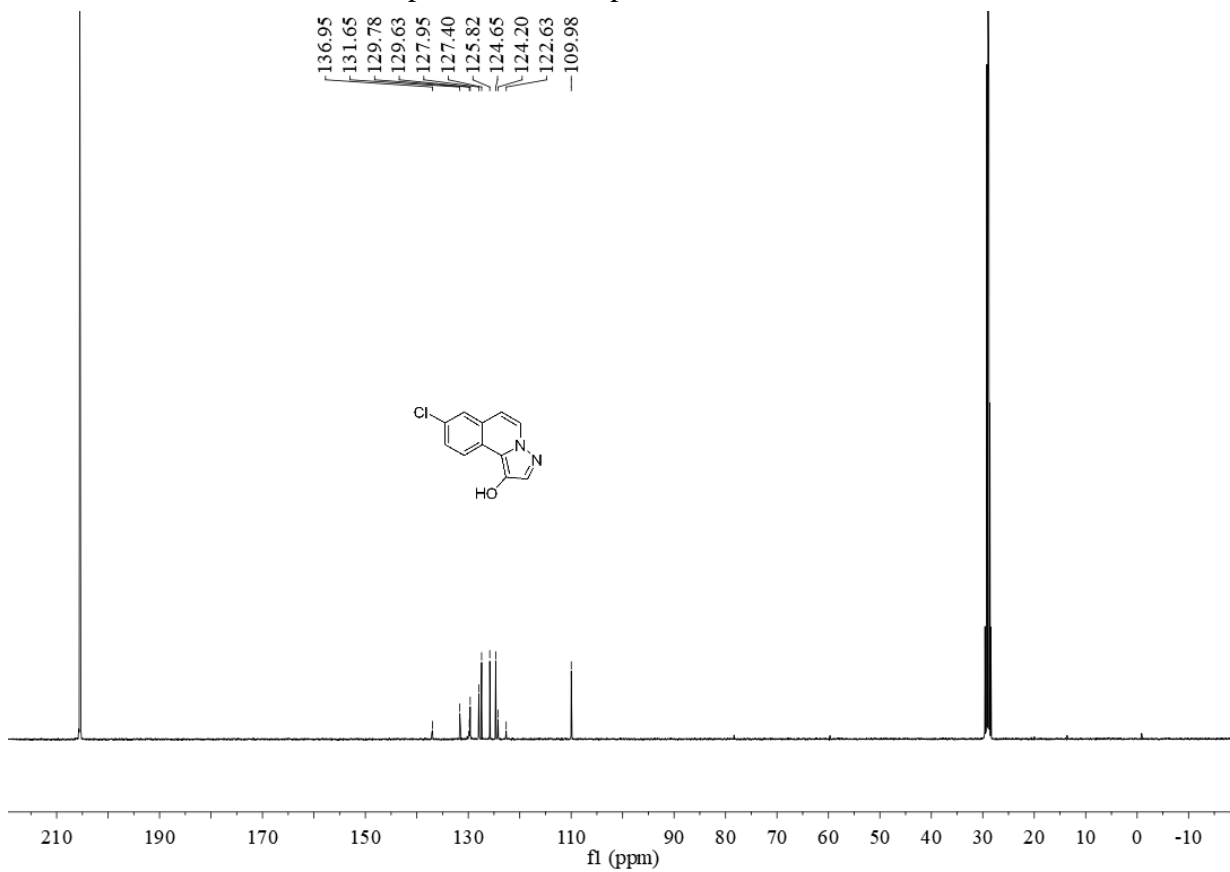
¹³C NMR (100 MHz, Acetone-D₆) spectrum of compound **7c**



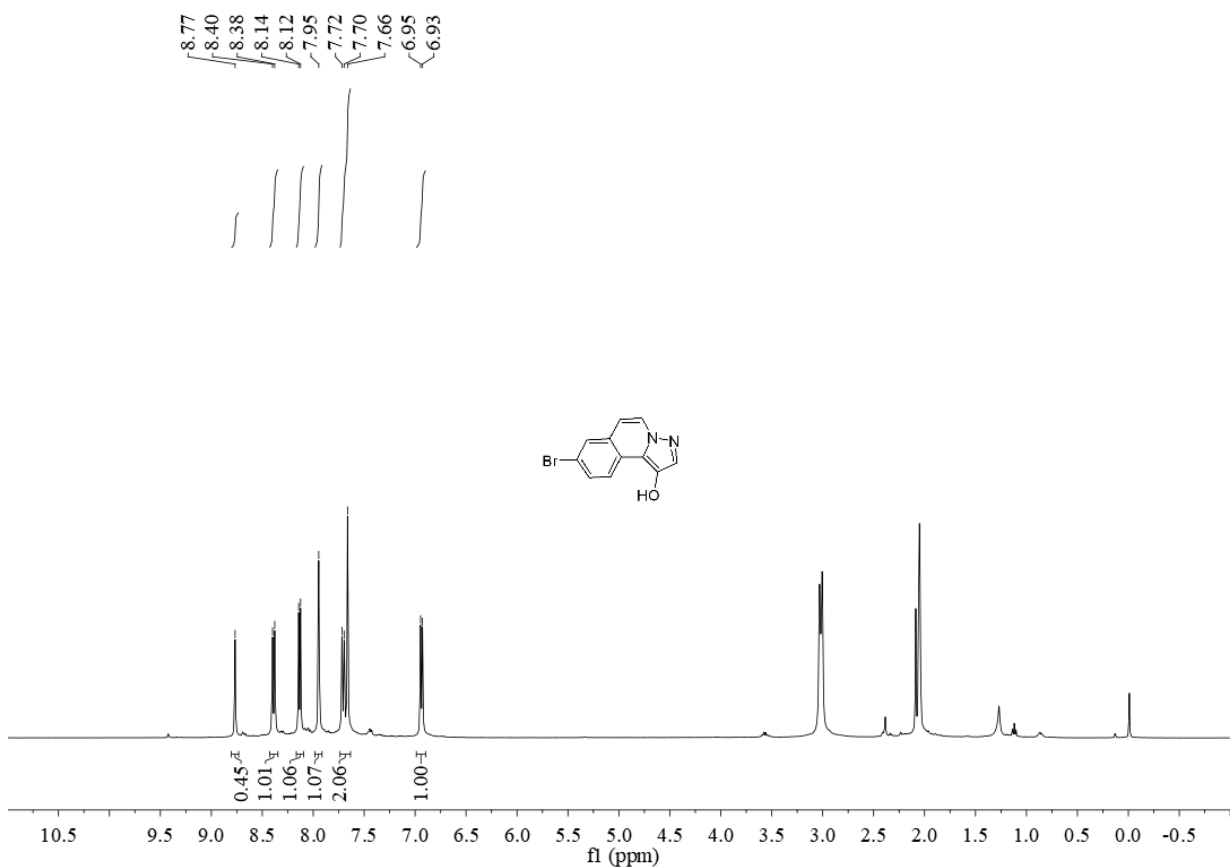
¹H NMR (400 MHz, Acetone-D6) spectrum of compound **7d**



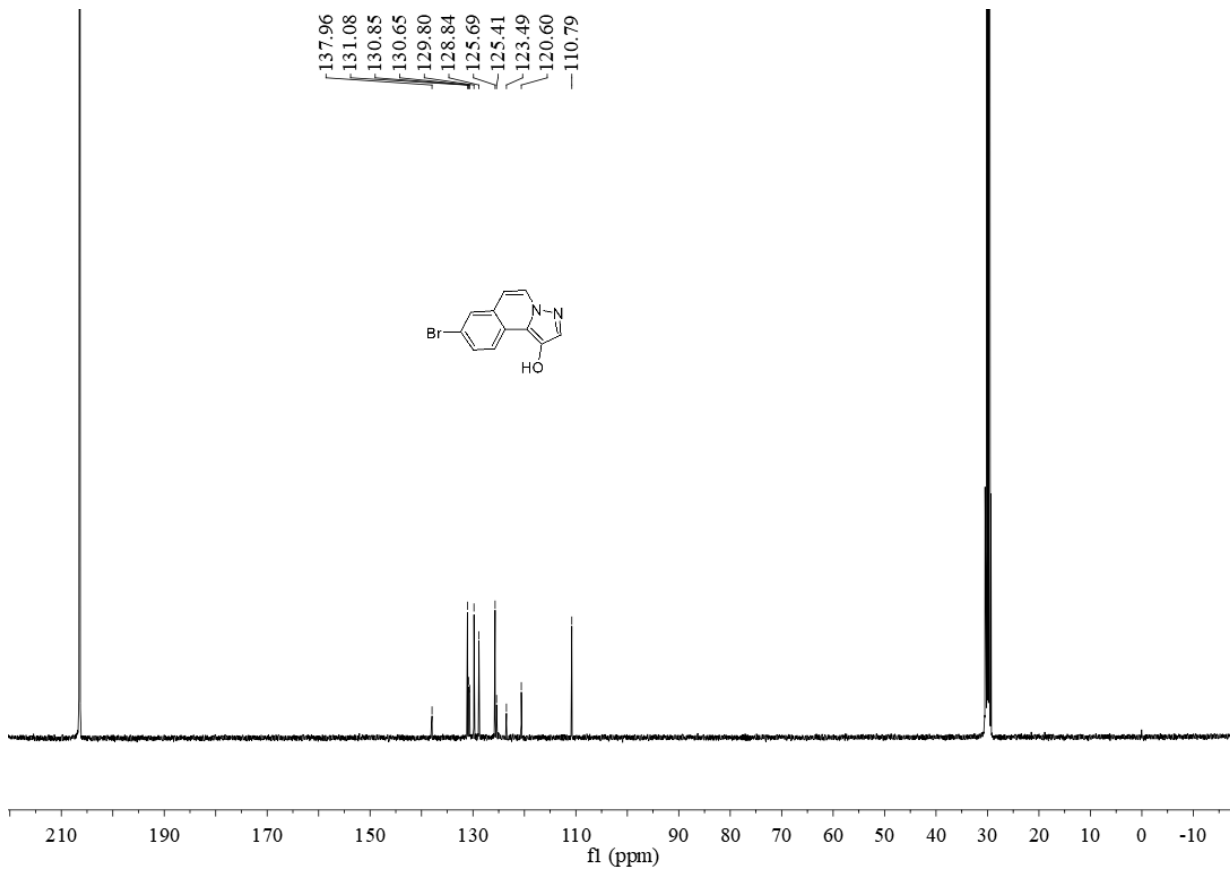
¹³C NMR (100 MHz, Acetone-D6) spectrum of compound **7d**



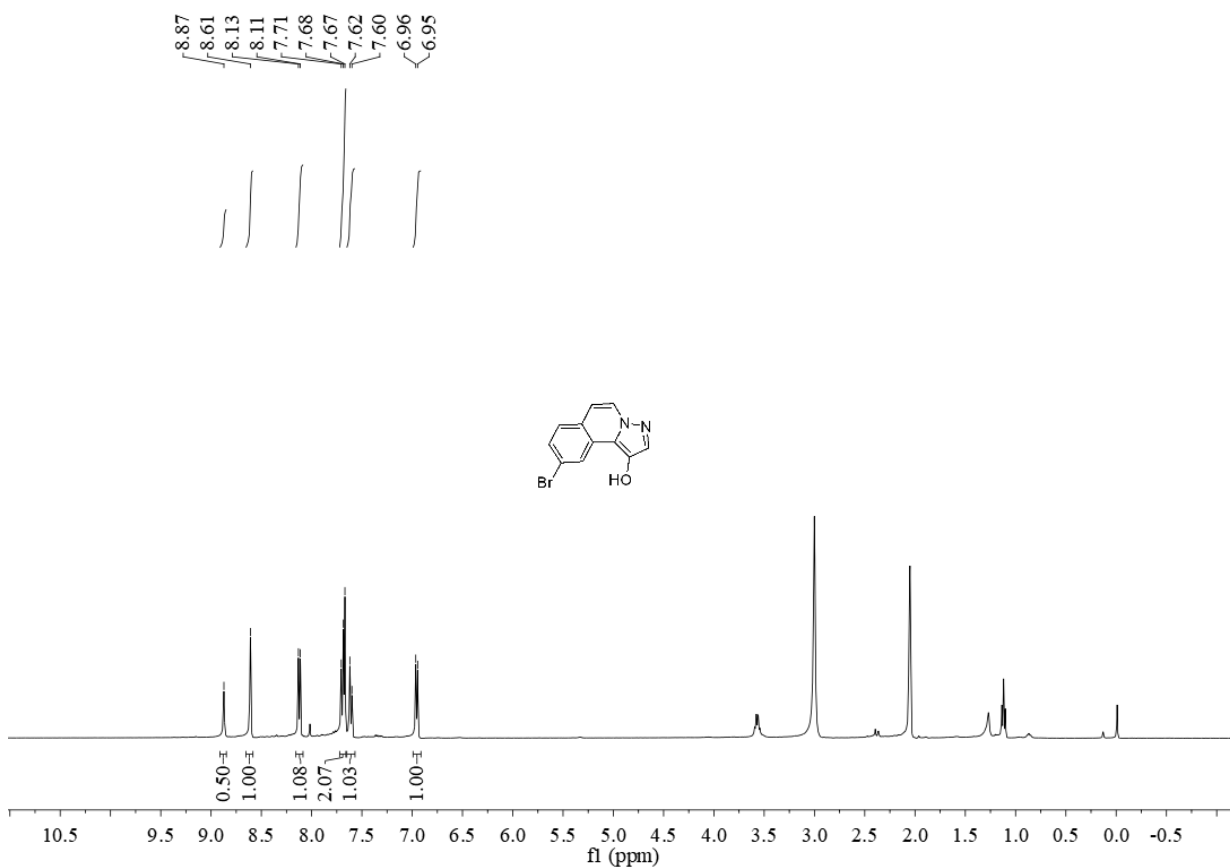
¹H NMR (400 MHz, Acetone-D₆) spectrum of compound **7e**



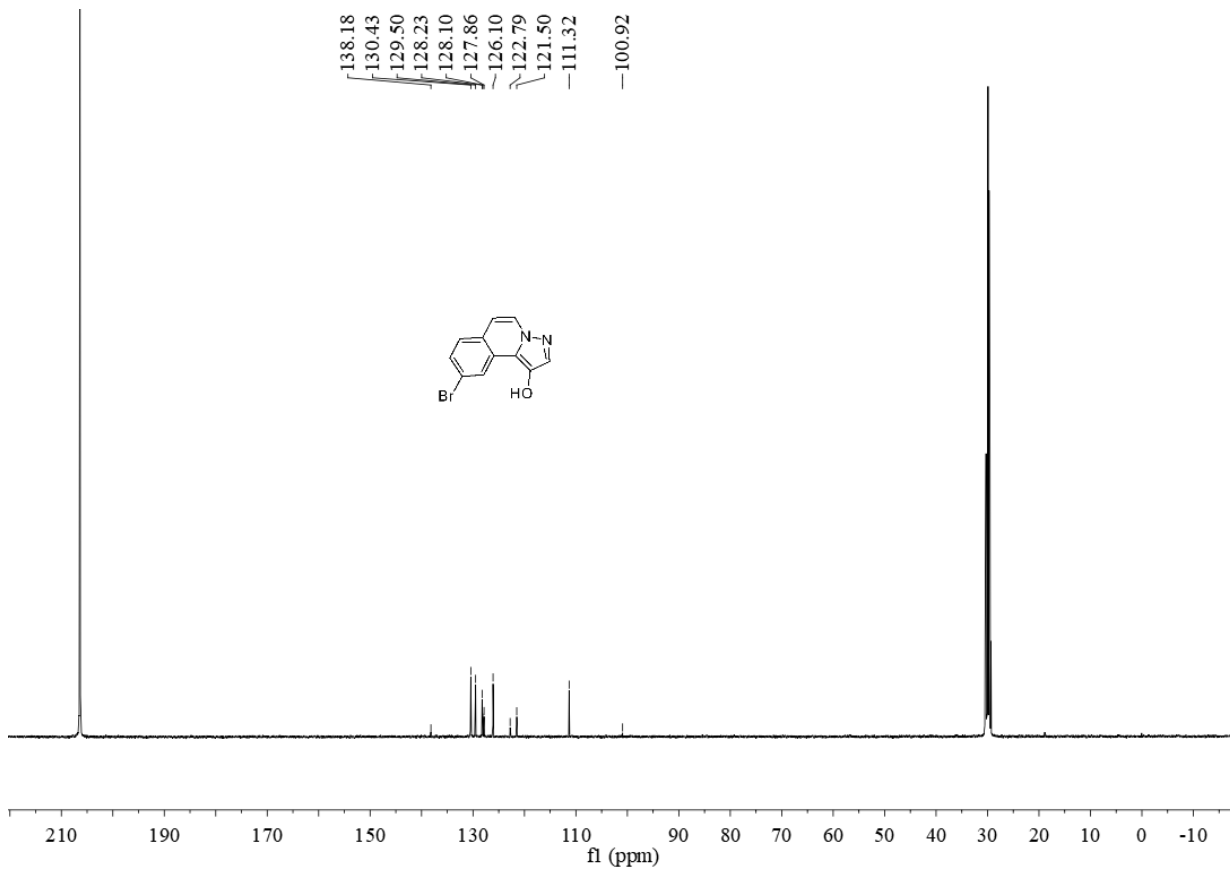
¹³C NMR (100 MHz, Acetone-D₆) spectrum of compound **7e**



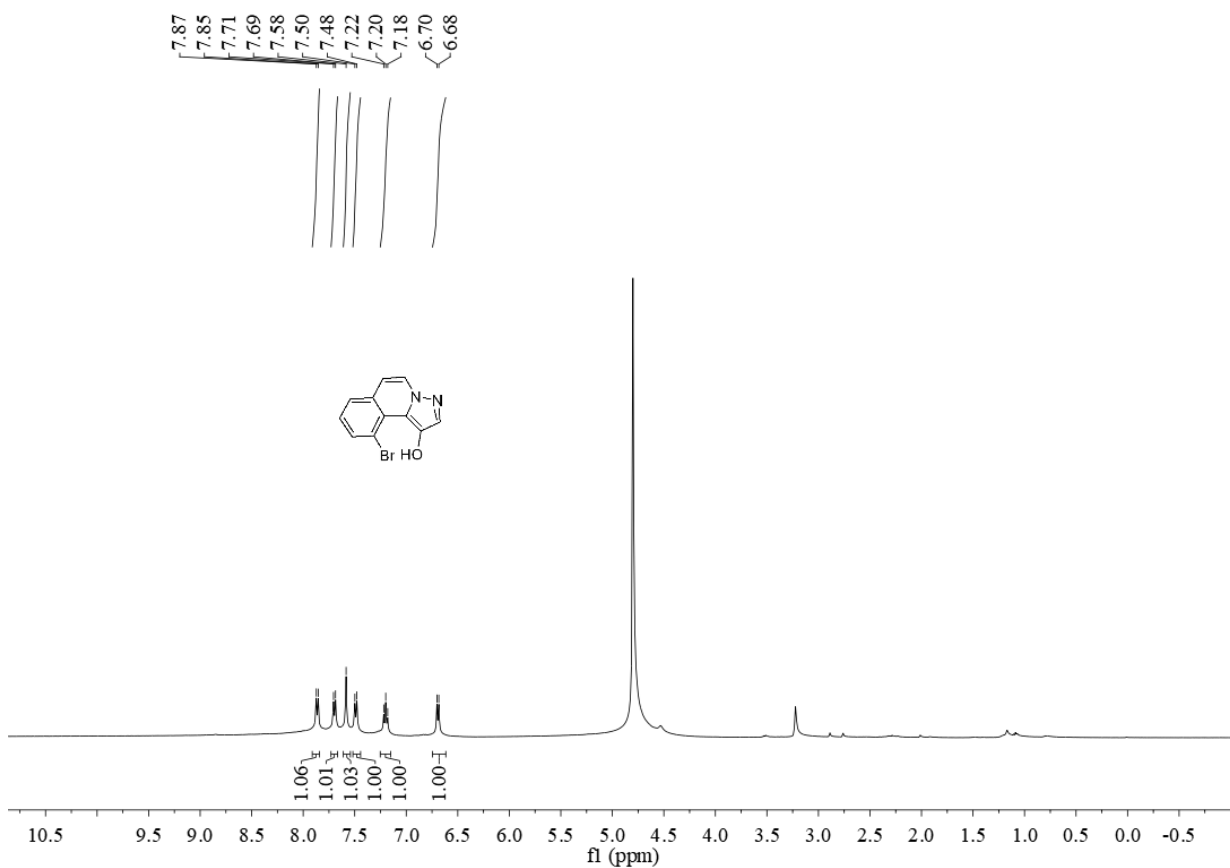
^1H NMR (400 MHz, Acetone- D_6) spectrum of compound **7f**



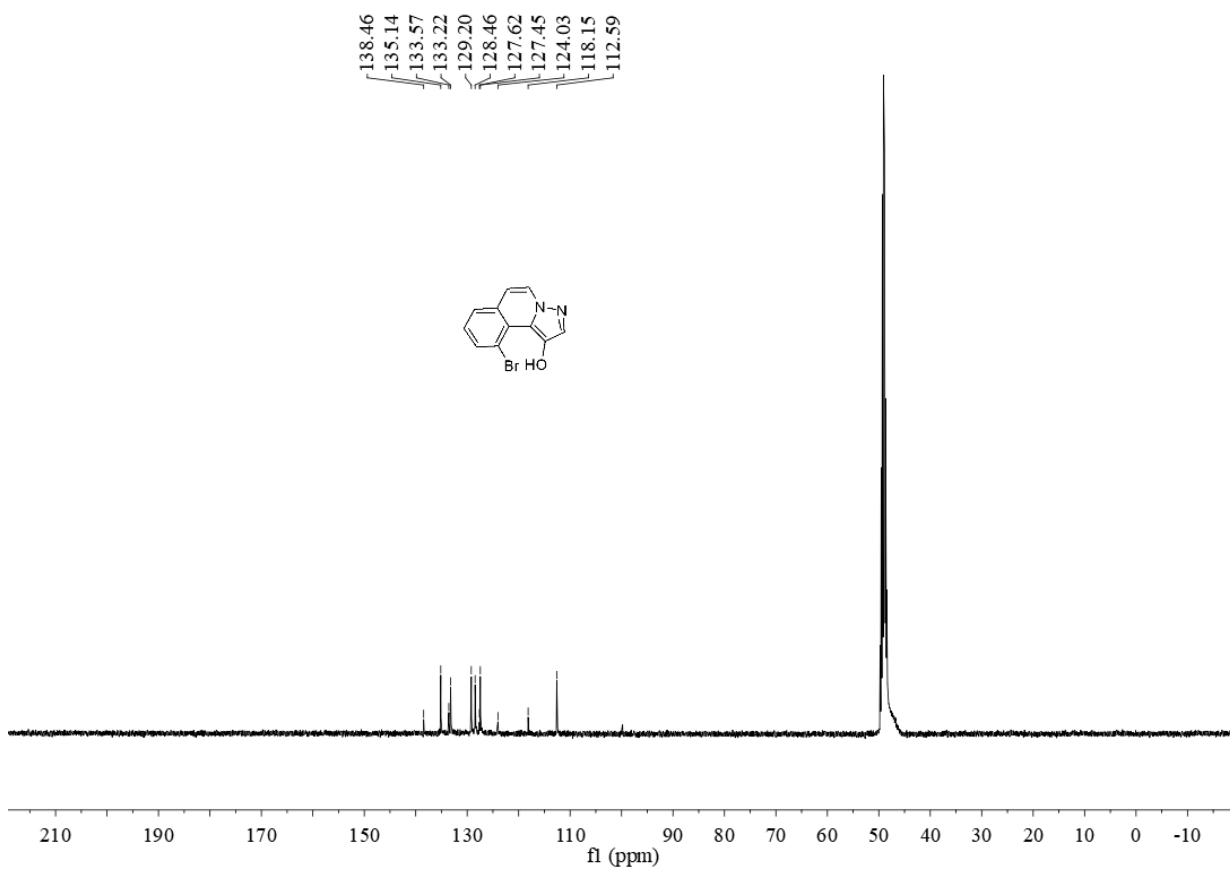
^{13}C NMR (100 MHz, Acetone- D_6) spectrum of compound **7f**



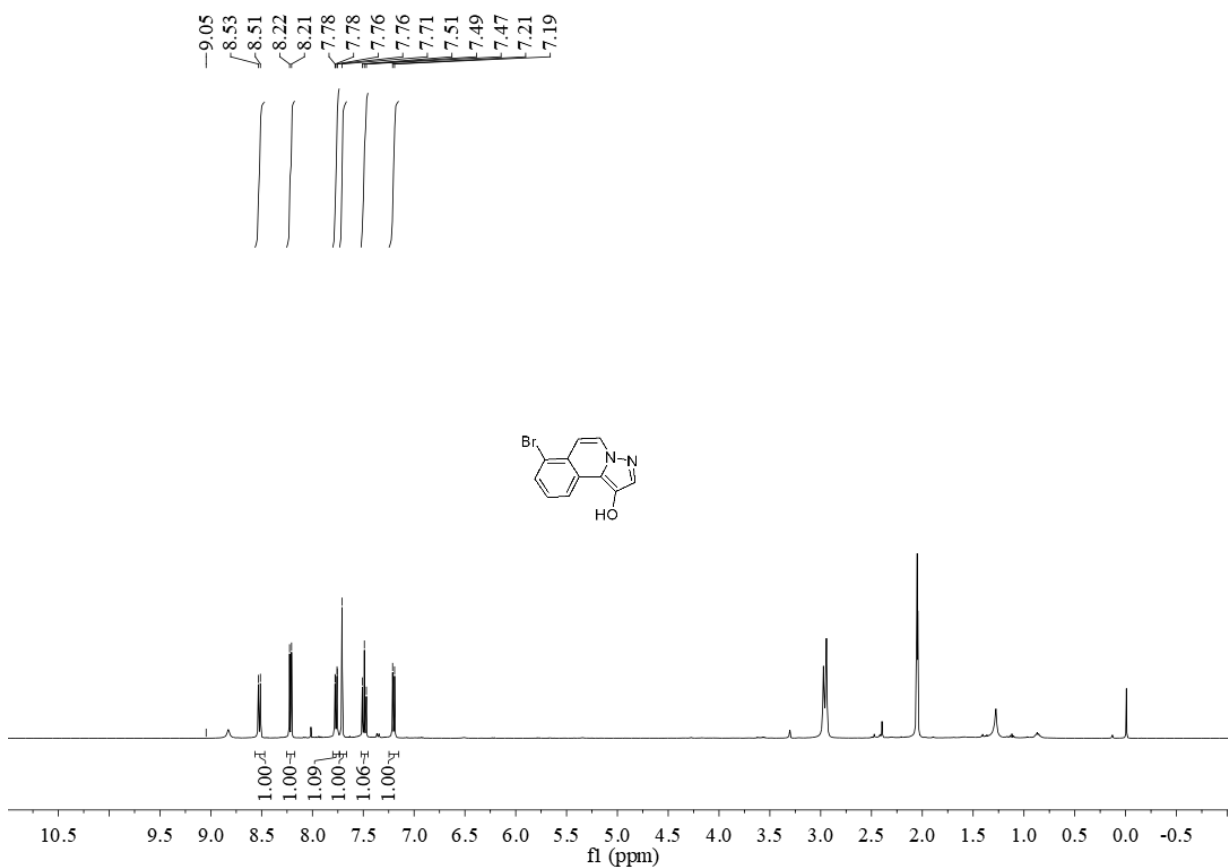
¹H NMR (400 MHz, Methanol-D4) spectrum of compound **7g**



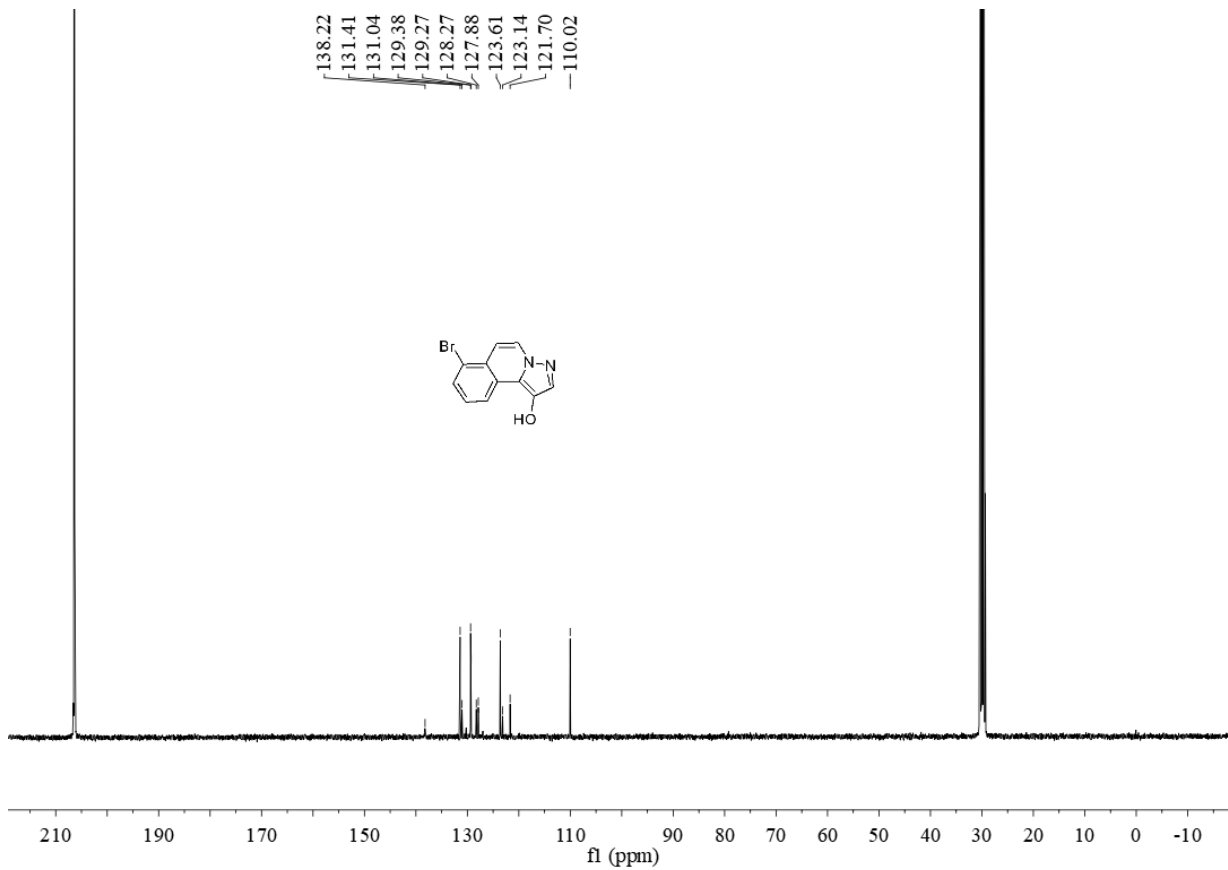
¹³C NMR (400 MHz, Methanol-D4) spectrum of compound **7g**



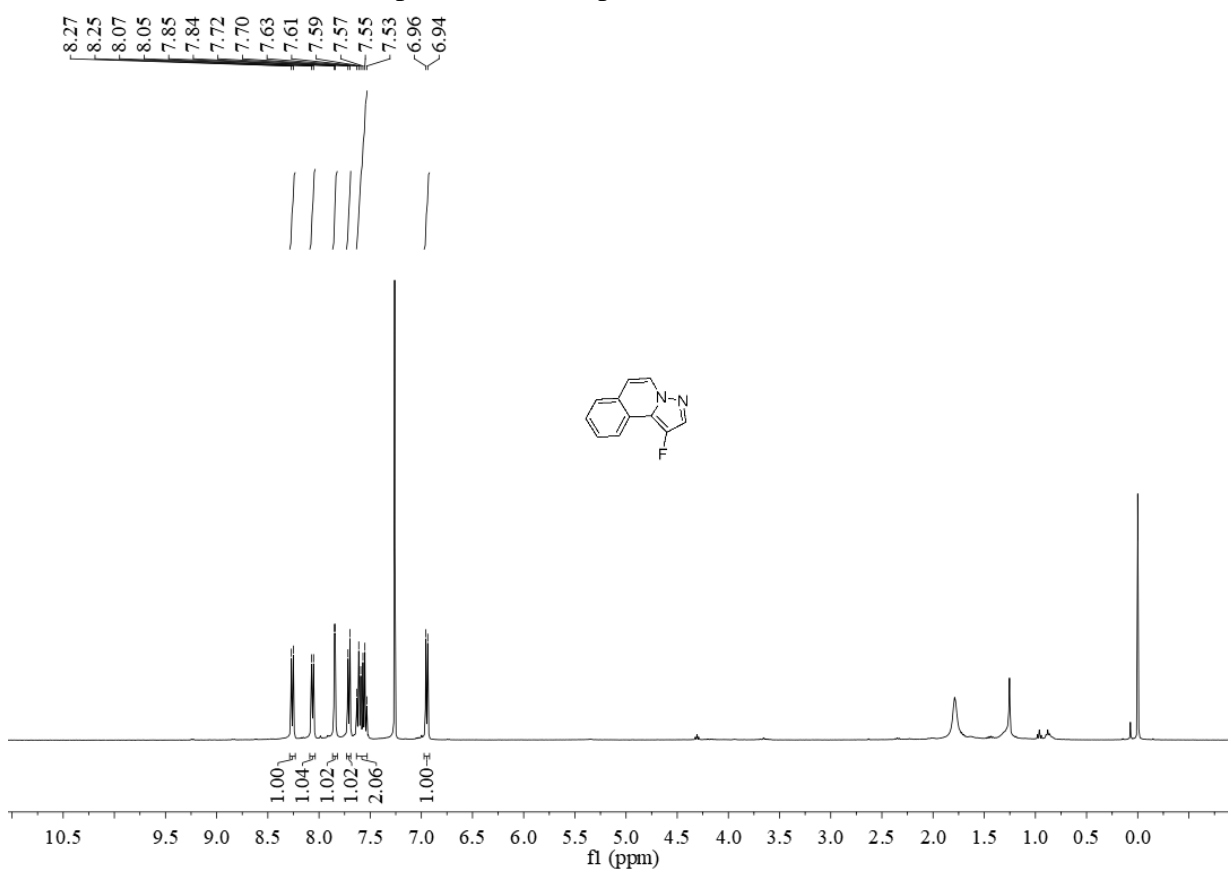
¹H NMR (400 MHz, Acetone-D6) spectrum of compound **7h**



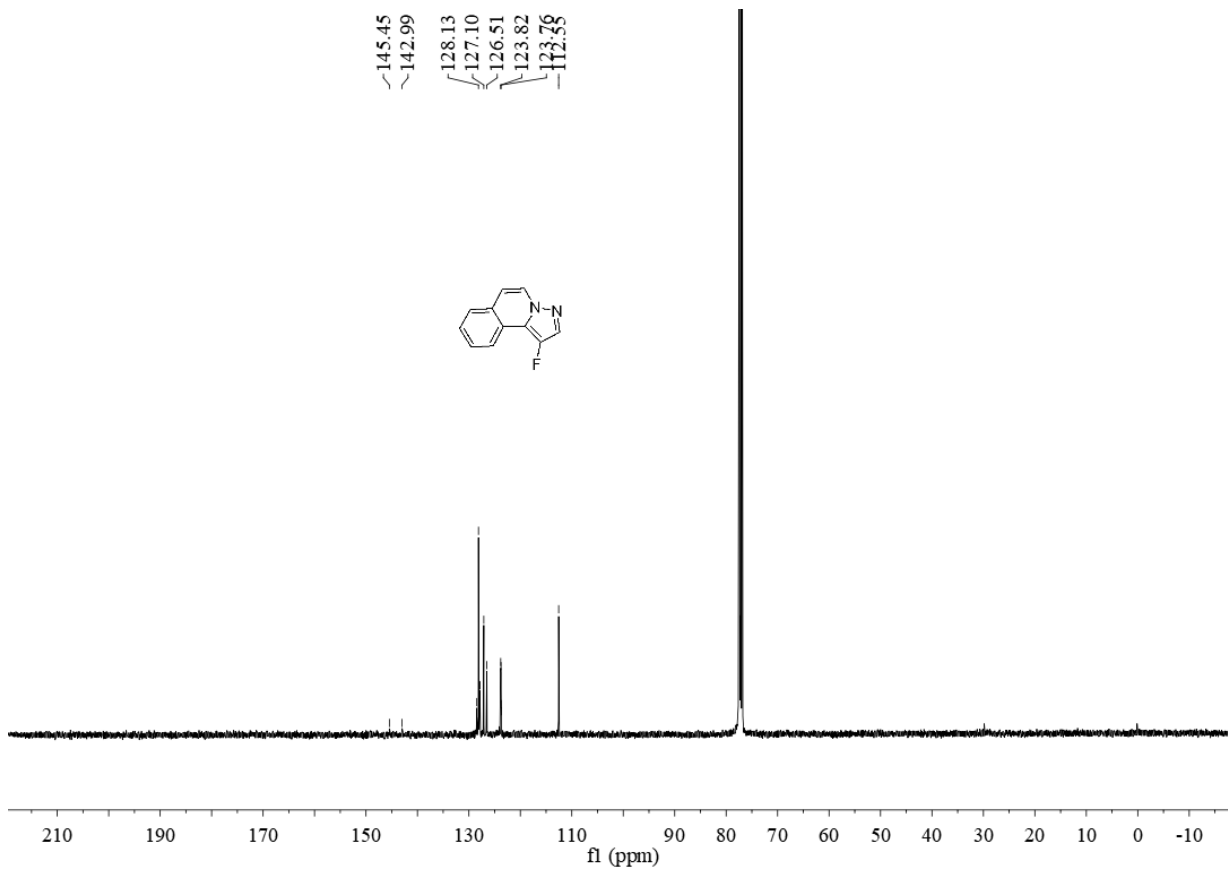
¹³C NMR (100 MHz, Acetone-D6) spectrum of compound **7h**



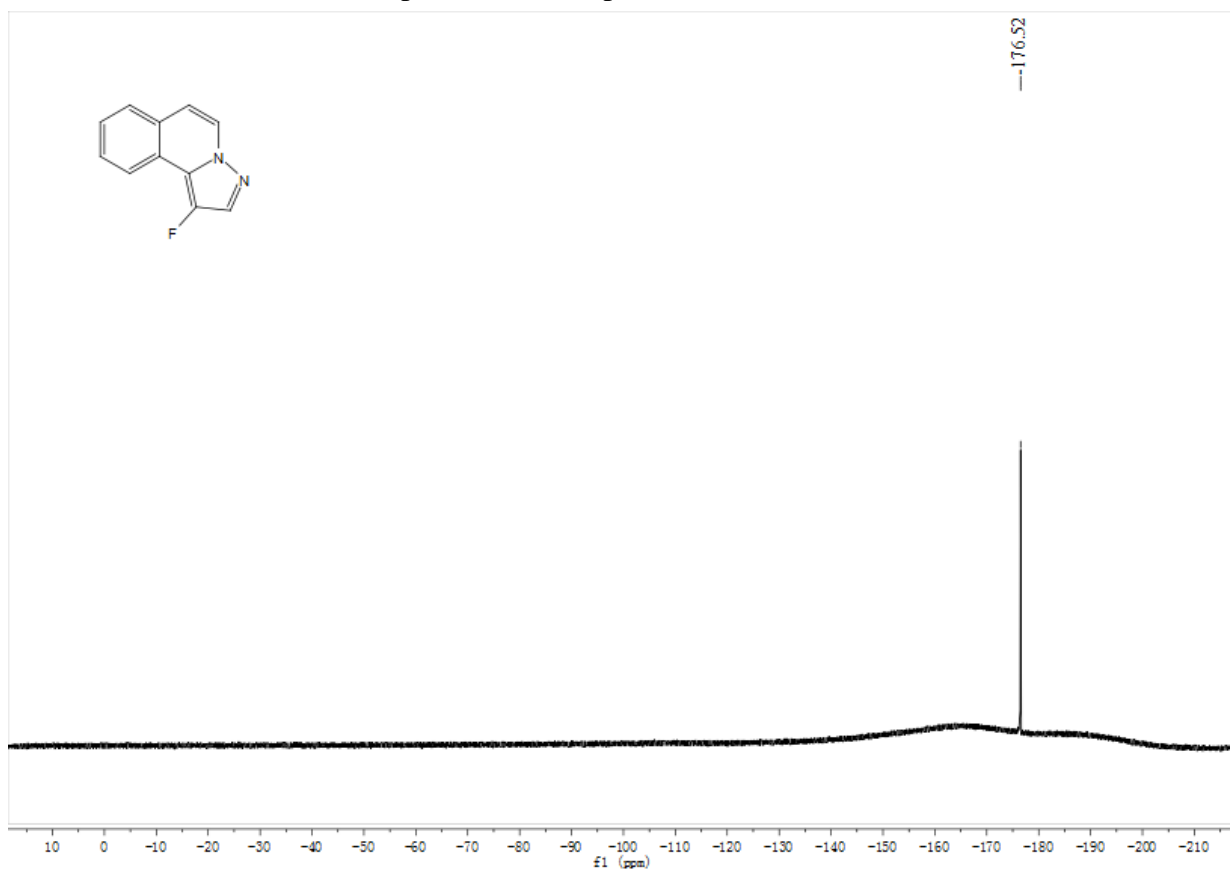
¹H NMR (400 MHz, CDCl₃) spectrum of compound **8a**



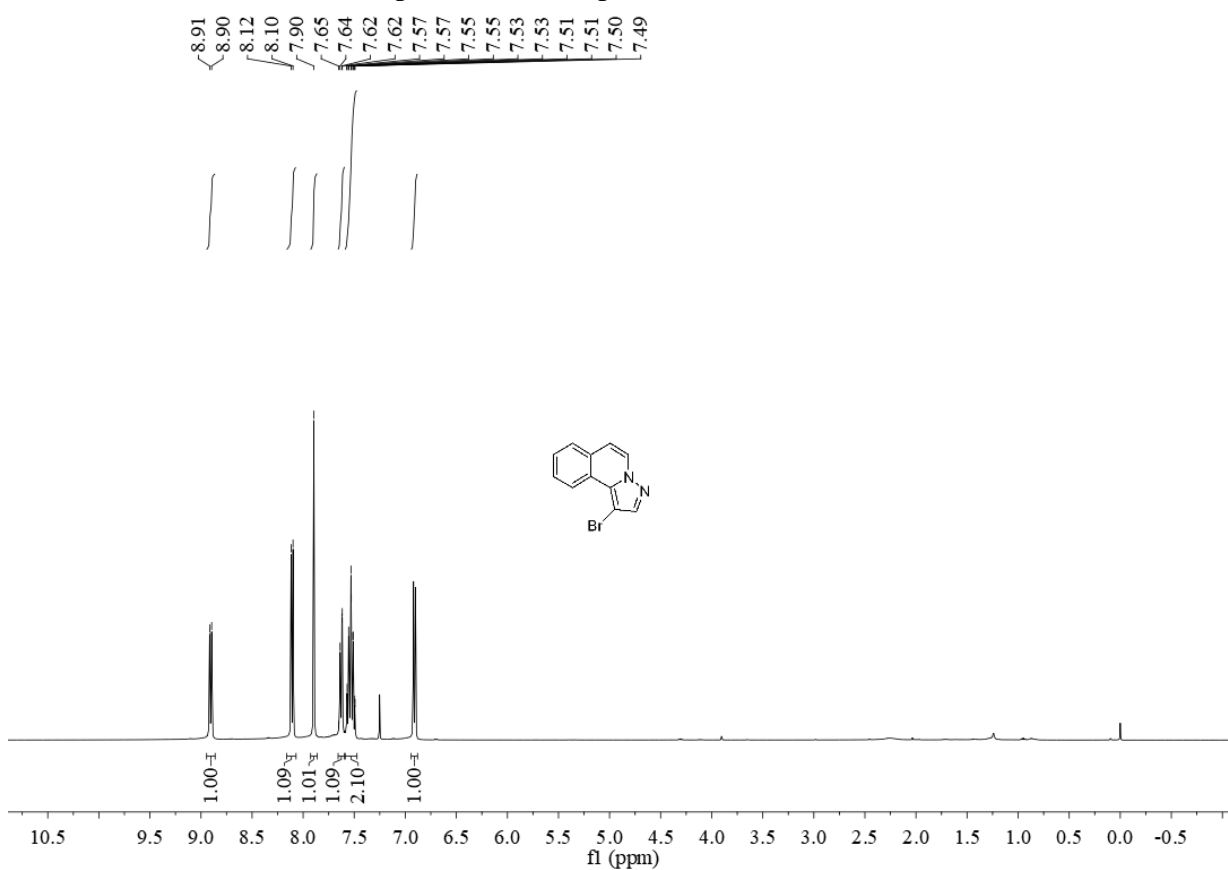
¹³C NMR (100 MHz, CDCl₃) spectrum of compound **8a**



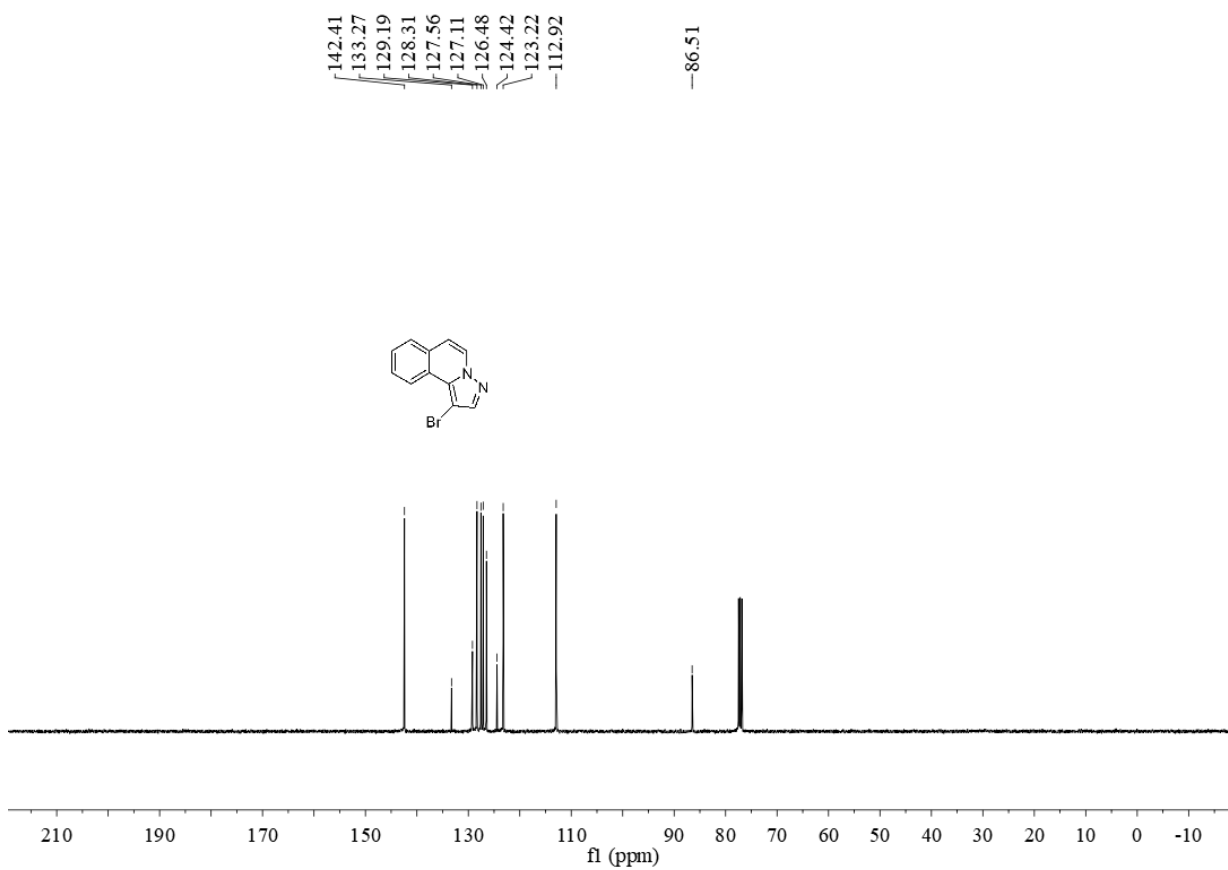
^{19}F NMR (376 MHz, CDCl_3) spectrum of compound **8a**



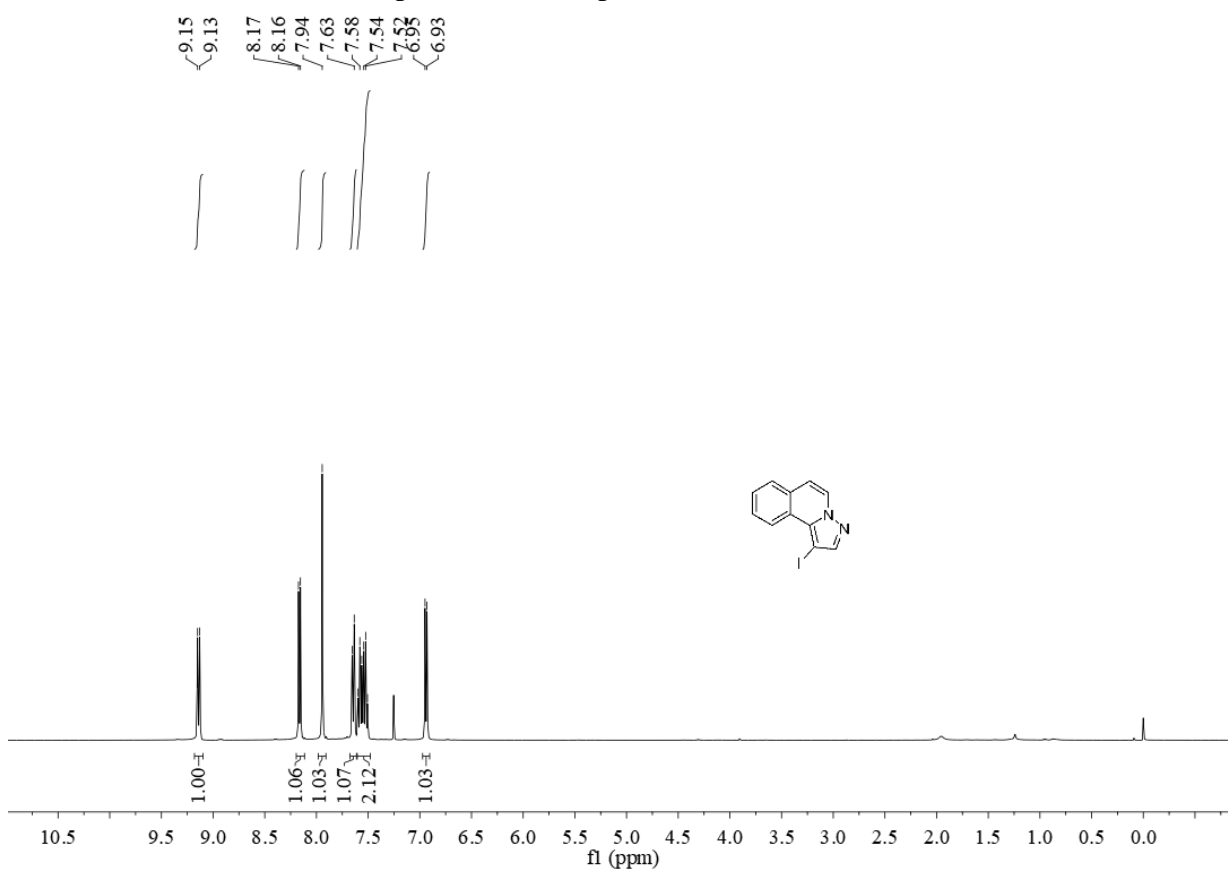
¹H NMR (400 MHz, CDCl₃) spectrum of compound **8b**



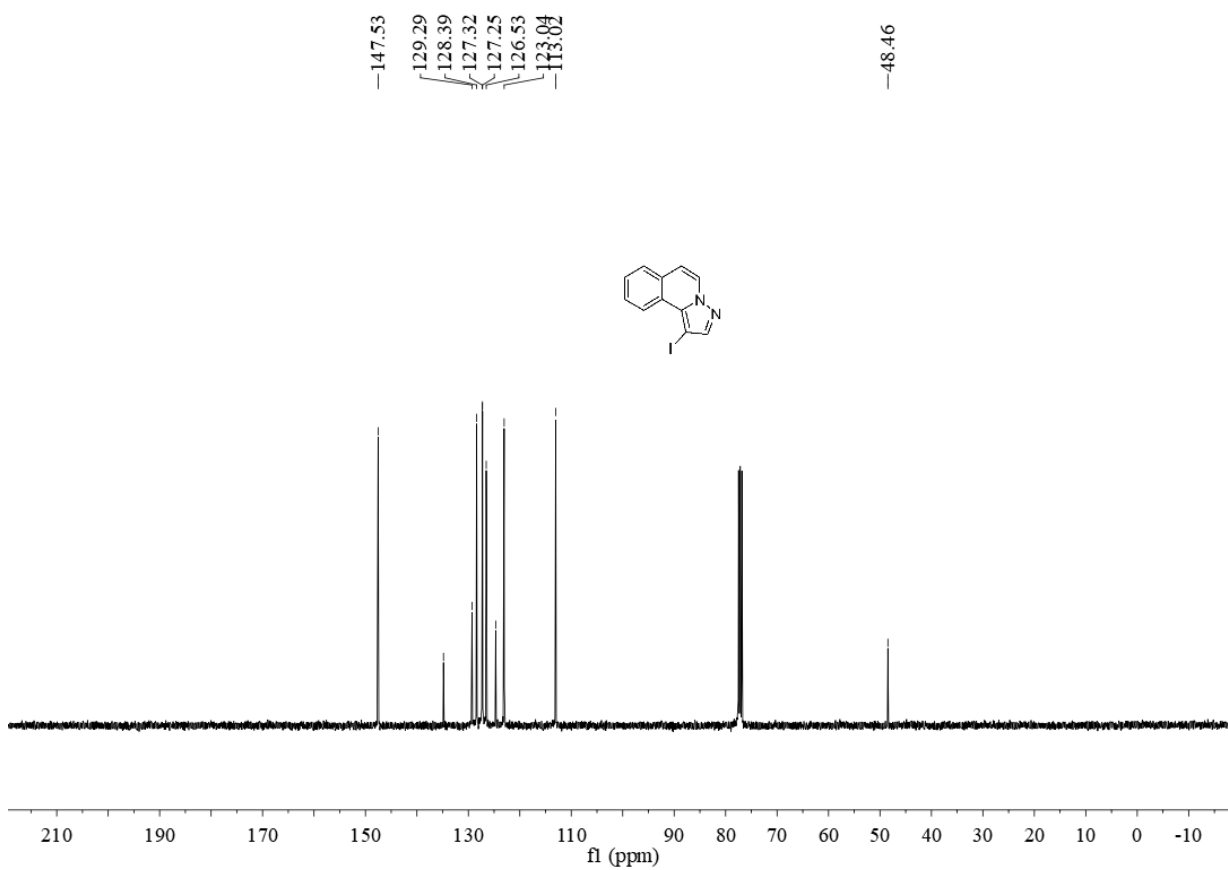
¹³C NMR (100 MHz, CDCl₃) spectrum of compound **8b**



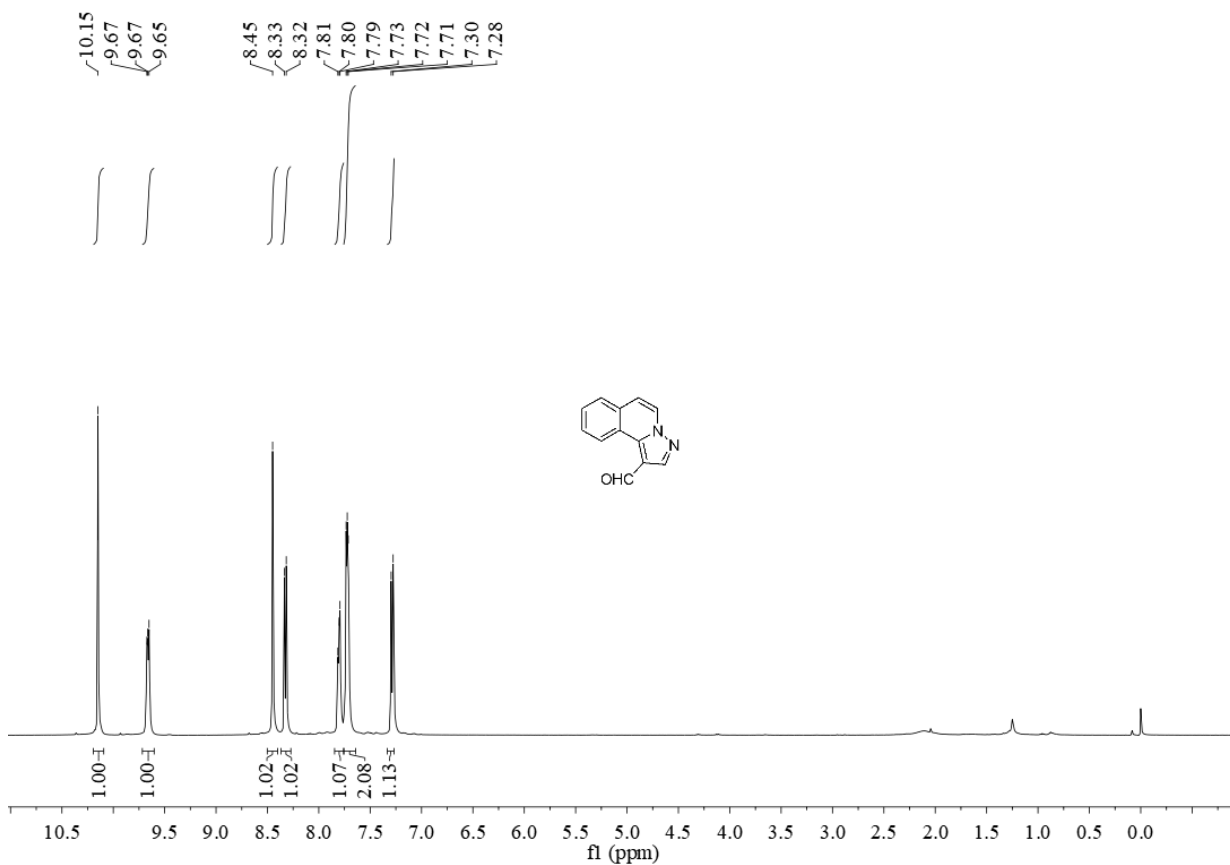
^1H NMR (400 MHz, CDCl_3) spectrum of compound **8c**



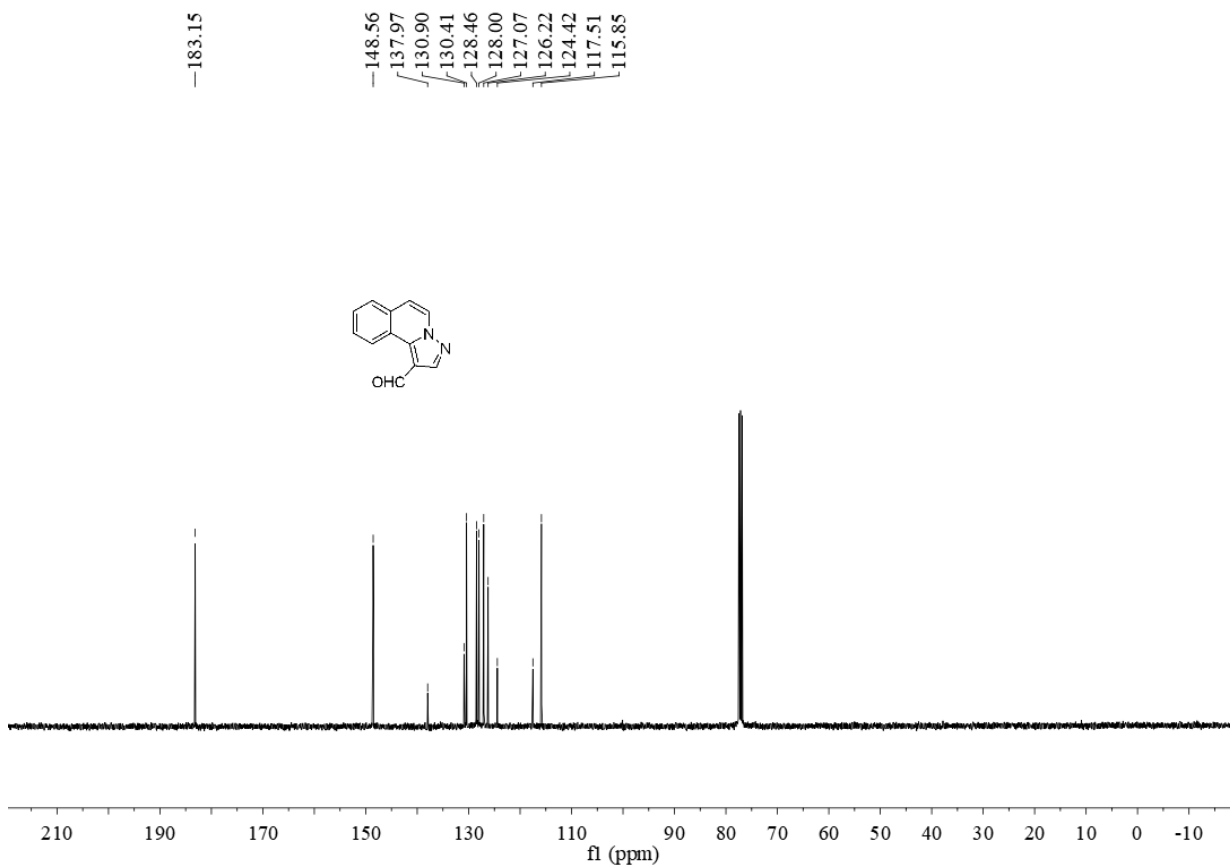
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **8c**



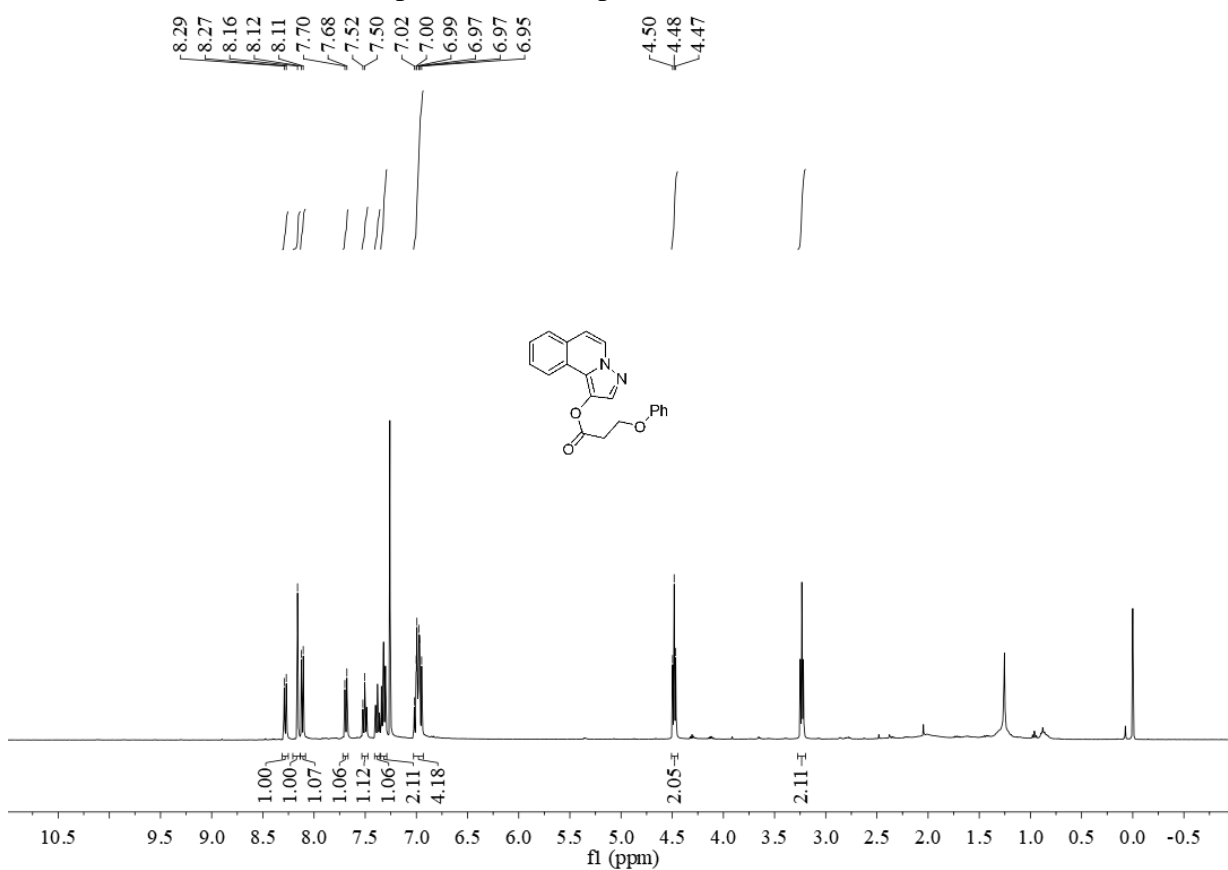
^1H NMR (400 MHz, CDCl_3) spectrum of compound **8d**



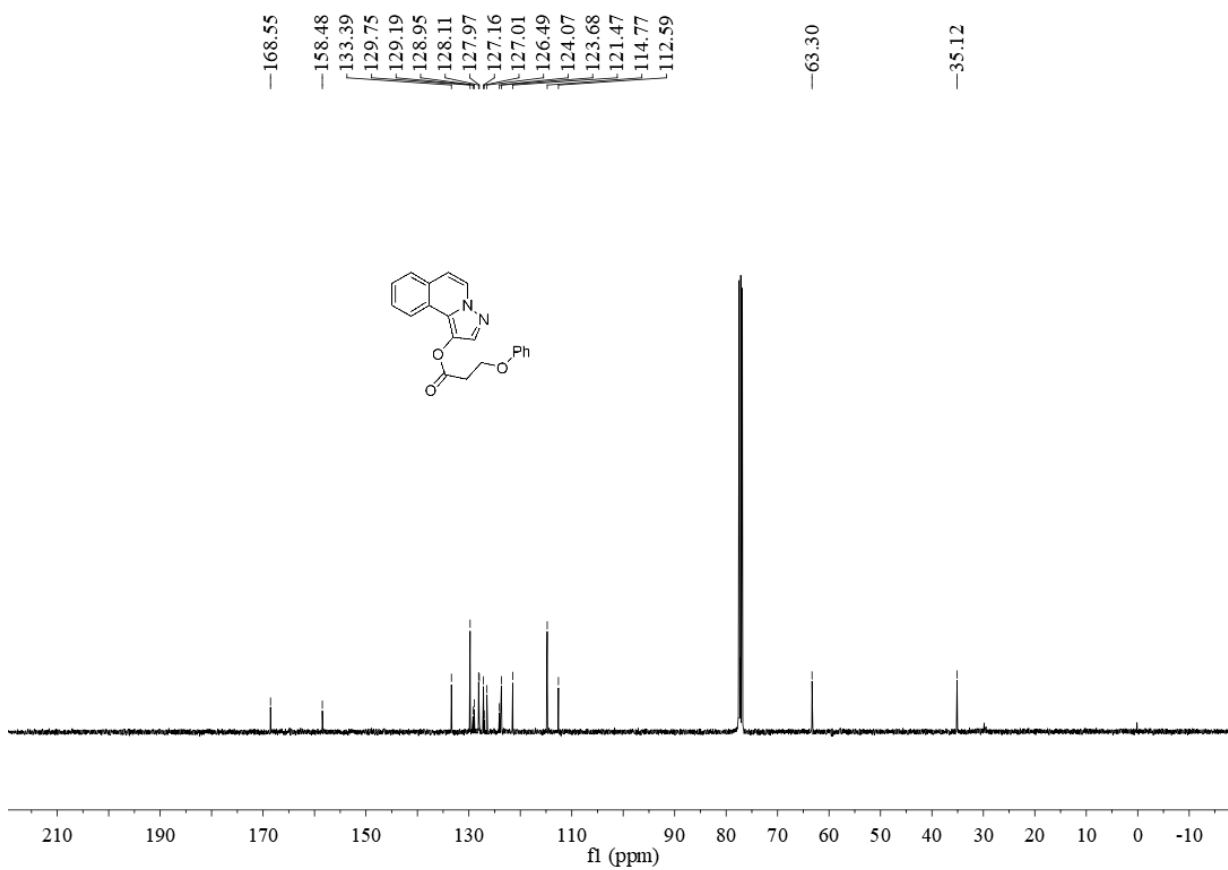
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **8d**



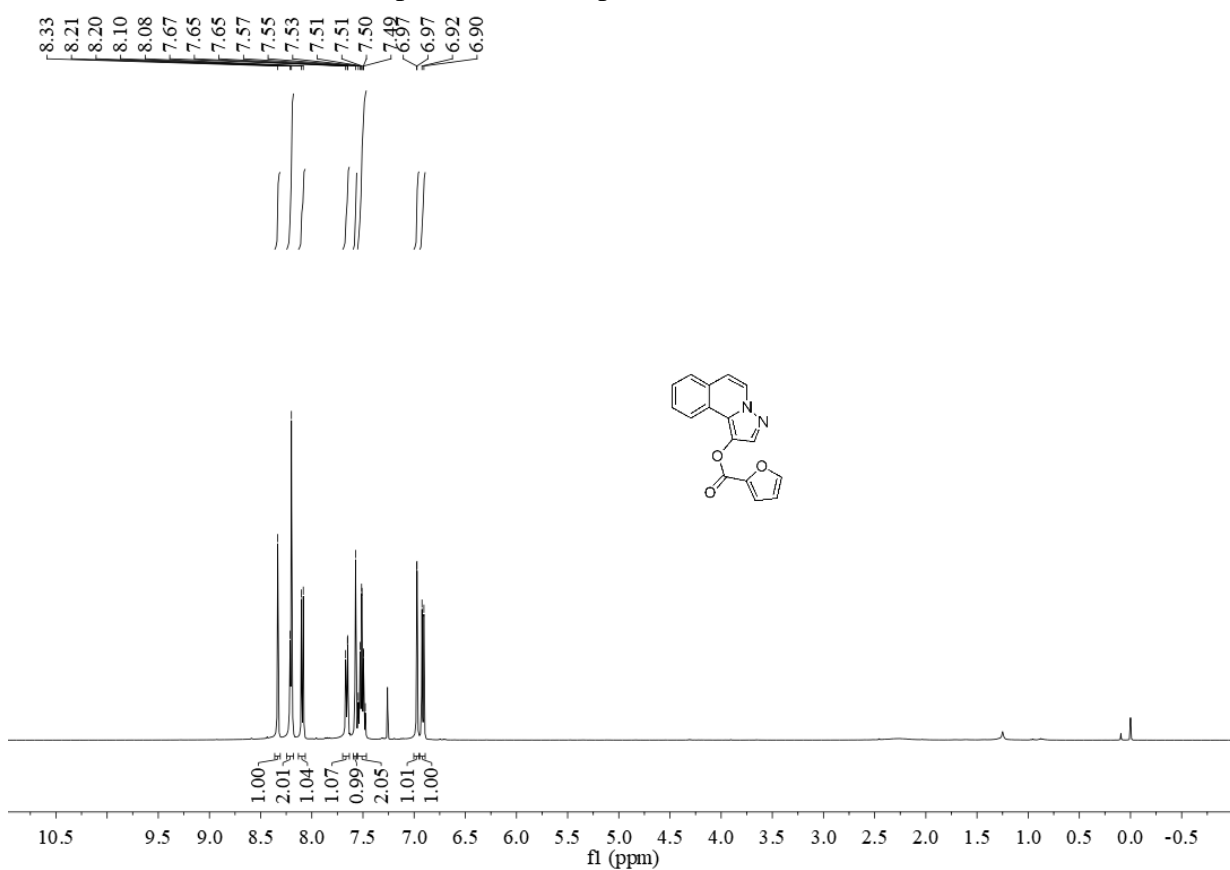
^1H NMR (400 MHz, CDCl_3) spectrum of compound **8e**



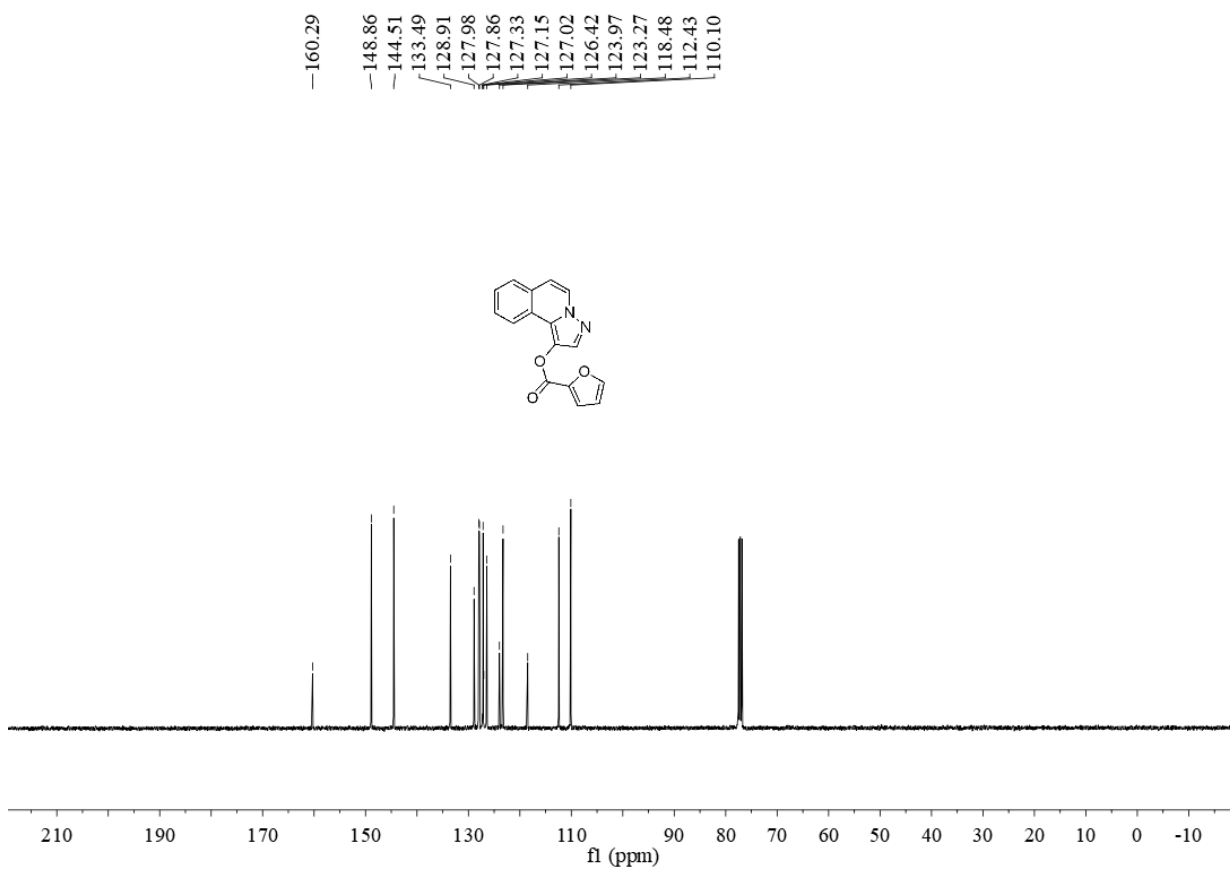
^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **8e**



^1H NMR (400 MHz, CDCl_3) spectrum of compound **8f**

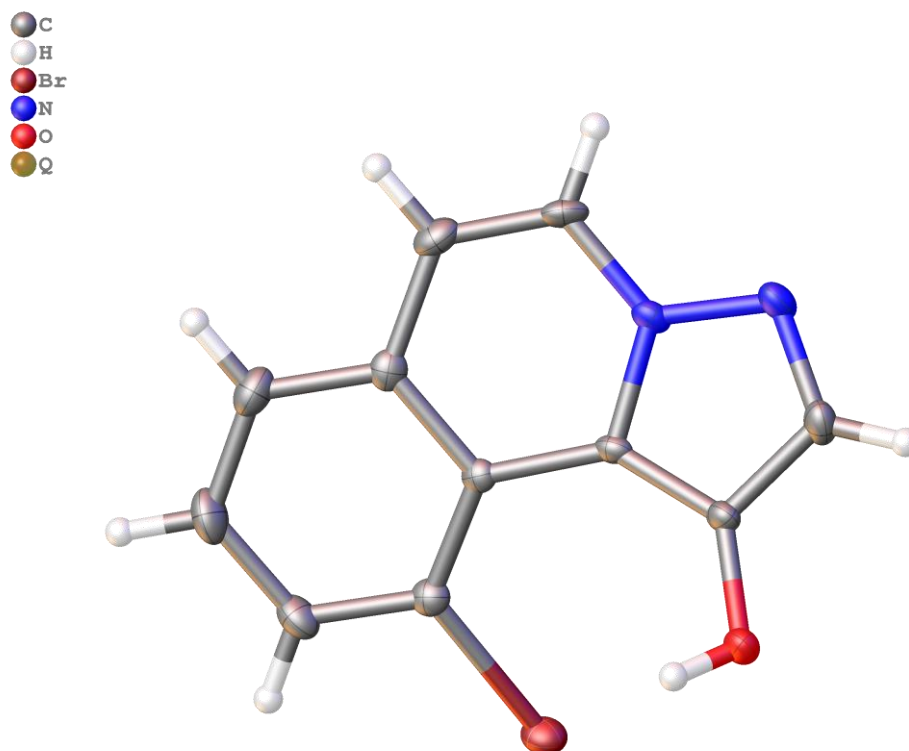


^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **8f**



4. X-ray crystallographic data

Figure S1 X-ray single crystal structure of **7g**



Single crystals of **7g** were grown by slow evaporation of its EA/PE solution. Single-crystal X-ray diffraction data were collected with a 'multiwire proportional' diffractometer. The crystal was kept at 219.99 K during data collection. Using Olex2, the structure was solved with the olex2.solve structure solution program using Charge Flipping and refined with the olex2.refine refinement package using Least Squares minimization. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center (CCDC 2121364).

Table S1 Crystal data and structure refinement for **7g**

Identification code	7g
Empirical formula	C ₁₁ H ₇ BrN ₂ O
Formula weight	263.10
Temperature/K	219.99(10)
Crystal system	monoclinic
Space group	P2 ₁ /n
a/Å	8.5927(13)
b/Å	10.6826(11)
c/Å	11.0184(16)
α/°	90
β/°	110.950(16)
γ/°	90
Volume/Å ³	944.5(2)
Z	4

$\rho_{\text{calc}}/\text{cm}^3$	1.850
μ/mm^{-1}	4.321
F(000)	520.0
Crystal size/ mm^3	$0.14 \times 0.12 \times 0.1$
Radiation	Mo K α ($\lambda = 0.71073$)
2Θ range for data collection/ $^\circ$	5.202 to 49.98
Index ranges	$-10 \leq h \leq 9, -12 \leq k \leq 12, -13 \leq l \leq 12$
Reflections collected	3803
Independent reflections	1667 [$R_{\text{int}} = 0.0337, R_{\text{sigma}} = 0.0538$]
Data/restraints/parameters	1667/0/137
Goodness-of-fit on F^2	1.047
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0345, wR_2 = 0.0610$
Final R indexes [all data]	$R_1 = 0.0501, wR_2 = 0.0651$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	0.40/-0.43

Table S2 Bond Lengths for **7g**

Atom	Atom	Length/ \AA	Atom	Atom	Length/ \AA
Br1	C5	1.895(4)	C2	C3	1.377(5)
O1	C10	1.363(4)	C3	C4	1.373(5)
N1	N2	1.348(4)	C4	C5	1.376(5)
N1	C8	1.372(4)	C5	C6	1.409(4)
N1	C9	1.402(4)	C6	C9	1.444(4)
N2	C11	1.329(4)	C7	C8	1.326(5)
C1	C2	1.403(5)	C9	C10	1.389(4)
C1	C6	1.413(5)	C10	C11	1.391(4)
C1	C7	1.450(4)			

Table S3 Bond Angles for **7g**

Atom	Atom	Atom	Angle/ $^\circ$	Atom	Atom	Atom	Angle/ $^\circ$
N2	N1	C8	122.6(3)	C1	C6	C9	117.7(3)
N2	N1	C9	112.4(3)	C5	C6	C1	116.5(3)
C8	N1	C9	123.8(3)	C5	C6	C9	125.8(3)
C11	N2	N1	105.0(2)	C8	C7	C1	120.8(3)
C2	C1	C6	120.7(3)	C7	C8	N1	119.7(3)
C2	C1	C7	119.6(3)	N1	C9	C6	116.6(3)
C6	C1	C7	119.6(3)	C10	C9	N1	104.0(3)
C3	C2	C1	119.8(4)	C10	C9	C6	139.2(3)
C4	C3	C2	120.3(3)	O1	C10	C9	131.2(3)
C3	C4	C5	120.3(3)	O1	C10	C11	122.2(3)
C4	C5	Br1	116.0(3)	C9	C10	C11	106.5(3)

C4	C5	C6	121.6(3)	N2	C11	C10	112.0(3)
C6	C5	Br1	122.0(3)				

5. References

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