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Supporting Information

Pd-Catalyzed C-H arylation of benzothioamides with boronic acids using thioamides as directing groups

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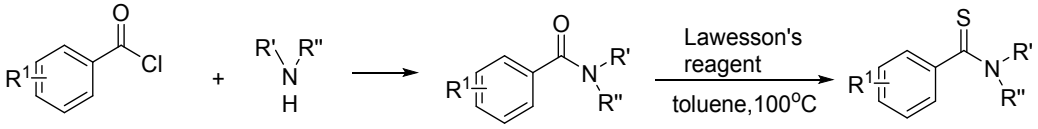
1. General information

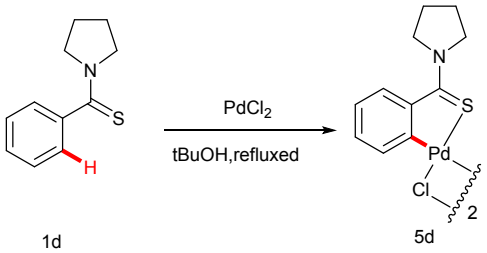
All solvents and chemicals were used directly without further purification. Flash chromatography was performed on silica gel (200-300 mesh). ^{1}H NMR spectra were recorded on Bruker AV-300 instrument (300 MHz). The following abbreviations (or combinations thereof) were used to explain multiplicities: singlet (s), doublet (d), doublet of doublets (dd), multiplet (m), triplet (t). Coupling constants, *J*, were reported in Hertz unit (Hz). ^{13}C NMR spectra were recorded on Bruker AV-300 instrument (75 MHz). Chemical shifts were reported in ppm referenced to the center line of a triplet peak at 77.0 ppm of CDCl3. High-resolution mass spectra (HRMS) were recorded using ESI-TOF (electrospray ionization-time of flight).

2. General procedure for the preparation of thioamides substrates

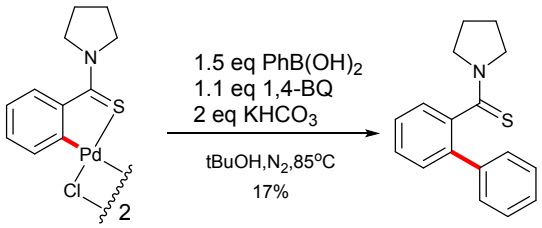


To a 100 ml flask charged with a magnetic stirbar was added an *N,N*-disubstituted amine (1.1 eq, 11 mmol). Dichloromethane (50 ml, 0.2 M) was added and the mixture was cooled to 0°C with an ice bath. Triethylamine(2.8 ml, 1.25 eq, 20 mmol) was added in one portion. an benzoyl chloride derivative (1.0 eq, 10 mmol) was then added dropwise and the reaction was stirred for 1-2h before quenching with sat. NaHCO3. The organic layer was separated, washed with brine, dried over anhydrous magnesium sulfate, and filtered to the crude amide,[1] which was used without further purification. The crude amide was added to a 250 ml flask equipped with a magnetic stirbar. Toluene (50 ml) and Lawesson's reagent (2.43g, 0.6 eq, 6 mmol) were added. After the mixture was refluxed overnight., The reaction was cooled to room temperature and then concentrated in vacuo. The product was then purified by flash chromatography with ethyl acetate/petroleum ether as the eluent to ensure elimination of sulfur contaminants.[2]

3. Synthesis and reactivity of palladacycle intermediate



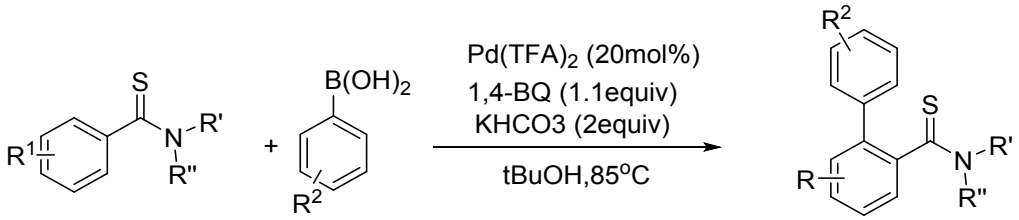
To a 10 ml round bottom equipped with a magnetic stirbar was added thioamide **1d** (65 mg, 0.34 mmol, 1.2 eq), $PdCl_2$ (50 mg, 0.28 mmol, 1.0 eq), and *t*BuOH (5 ml). The mixture was refluxed, with rapid stirring for 3 hour. A pale yellow precipitate formed in the reaction mixture. The reaction was cooled to room temperature and the precipitate was collected, washed with methanol, and dried to provide the palladacycle **5d** (79 mg, 85% yield) as an air-stable pale yellow solid. 1H NMR (400 MHz, CDCl3) δ= 7.61 (dd, *J* = 6.8, 2.8 Hz, 2H), 7.45 (q, *J* = 3.6 Hz, 2H), 4.26 – 4.08 (m, 2H), 3.56 – 3.35 (m, 2H), 2.23 – 2.02 (m, 2H), 2.00 – 1.84 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.91, 130.24, 128.73, 128.56, 128.19, 128.05, 127.53, 55.45, 54.63, 25.77, 25.13.



5d **3d**

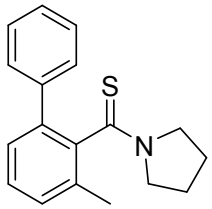
A mixture of the the palladacycle 5d (66 mg, 0.2 mmol of monomer,1.0 eq), arylboronic acid (3mmol, 1.5 eq), 1,4-benzoquinone (24 mg, 0.22 mmol, 1.1 eq), potassium bicarbonate (40 mg, 0.4 mmol, 2.0 eq), and *tert*-butyl alcohol (5.0 ml, non-anhydrous) was added to a oven-dried round-bottomed flask (25 mL) equipped with a reflux condenser. The flask was stirred rapidly and heated in an oil bath at 85 °C under N_2. The reaction was cooled to room temperature and diluted with 2 ml EtOAc. The mixture was filtered through a pad of celite. The celite was washed thoroughly with EtOAc and dichloromethane and the combined organics were concentrated *in vacuo*. The crude residue was purified by by flash column chromatography (petroleum ether/ethyl acetate = 60:1) to afford the desired products.

4. General procedure for arylation of C(sp2)-H bonds



A mixture of the thioamide (0.1 mmol, 1.0 eq), arylboronic acid (1.5 mmol, 1.5 eq), 1,4-benzoquinone (12 mg, 0.11 mmol, 1.1 eq, unless otherwise noted), potassium bicarbonate (20 mg, 0.2 mmol, 2.0 eq), palladium(II) trifluoroacetate (0.02 mmol, 0.2 eq), and tert-butyl alcohol (5.0 ml, non-anhydrous) was added to a oven-dried round-bottomed flask (25 mL) equipped with a reflux condenser. The flask was stirred rapidly at room temperature for several minutes, providing a deep red reaction mixture and then heated in an oil bath at 85 °C under N_2. The reaction was cooled to room temperature and diluted with 2 ml EtOAc. The mixture was filtered through a pad of celite. The celite was washed thoroughly with EtOAc and dichloromethane and the combined organics were concentrated *in vacuo*. The crude residue was purified by by flash column chromatography (petroleum ether/ethyl acetate = 60:1) to afford the desired products.

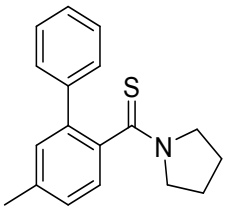
5. Analytical data of products



(3-methyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (3a)

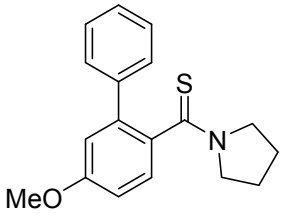
Yellow solid(24mg, 84%); mp: 74-77 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.64 – 7.56 (m, 2H), 7.40 – 7.33 (m, 2H), 7.33 – 7.27 (m, 2H), 7.24 – 7.17 (m, 2H), 3.94 – 3.81 (m, 1H), 3.58 – 3.45 (m, 1H), 3.14 – 3.01 (m, 1H), 2.86 – 2.74 (m, 1H), 2.38 (s, 3H), 1.92 – 1.78 (m, 1H), 1.78 – 1.64 (m, 1H), 1.54 – 1.46 (m, 1H), 1.44 – 1.33 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.68, 142.16, 140.02, 137.53, 133.31, 130.04, 129.67, 128.69, 128.64, 128.32, 127.29, 52.85, 52.46, 25.87, 24.27, 21.07. HRMS (ESI) m/z Calcd for $C_{18}H_{19}NS$ ($M+H^+$): 282.1311, found: 282.1312.

Followed by the aforementioned general procedure, compounds **3b-3h** (except **3g**) **and 4b-4q** were synthesized on 0.1 mmol scale using Pd(TFA)2 as a catalyst, respectively, as indicated in the Table 2 and 3 (see main text for details). The physical characterization data for these biaryl compounds were outlined in the following section.



(5-methyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (3b)

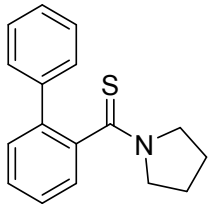
Yellow solid(19mg, 68%); mp: 118-120 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.61 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.43 – 7.29 (m, 4H), 7.17 (d, *J* = 7.4 Hz, 2H), 3.88 (dt, *J* = 14.8, 7.6 Hz, 1H), 3.57 – 3.45 (m, 1H), 3.07 (dt, *J* = 12.3, 6.2 Hz, 1H), 2.80 (dt, *J* = 12.7, 7.3 Hz, 1H), 2.39 (s, 3H), 1.92 – 1.78 (m, 1H), 1.74 – 1.63 (m, 1H), 1.55 – 1.45 (m, 1H), 1.37 (dq, *J* = 11.7, 5.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.82, 140.21, 139.82, 139.02, 135.96, 130.29, 128.98, 128.69, 128.28, 127.94, 127.42, 52.83, 52.44, 25.84, 24.26, 21.23. HRMS (ESI) m/z Calcd for $C_{18}H_{19}NS$ ($M+H^+$): 282.1311, found: 282.1311.



(5-methoxy-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (3c)

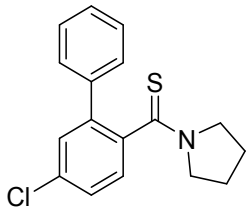
Yellow solid(13mg, 43%); mp: 87-89 °C . ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.62 (d, *J* = 8.1 Hz, 2H), 7.47 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.42 – 7.28 (m, 3H), 6.90 (dt, *J* = 8.3, 2.1 Hz, 1H), 6.86 (d, *J* = 2.2 Hz, 1H), 3.94 – 3.87 (m, 1H), 3.85 (s, 3H), 3.56 – 3.44 (m, 1H), 3.15 – 3.02 (m, 1H), 2.85 – 2.71 (m, 1H), 1.91 – 1.80 (m, 1H), 1.74 – 1.63 (m, 1H), 1.55 – 1.45 (m, 1H), 1.45 – 1.34 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.63, 160.04, 140.07, 137.65, 135.45, 129.93, 128.60, 128.34, 127.65, 114.86,

113.06, 55.46, 52.94, 52.45, 25.84, 24.28. HRMS (ESI) m/z Calcd for $C_{18}H_{19}NOS$ ($M+H^+$): 298.1260, found: 298.1258.



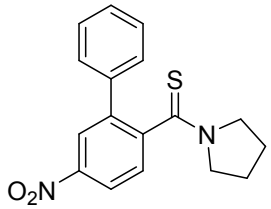
[1,1'-biphenyl]-2-yl(pyrrolidin-1-yl)methanethione (3d)

Yellow solid(18mg, 69%); mp: 87-90 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.56 – 7.45 (m, 2H), 7.42 – 7.32 (m, 5H), 3.95 – 3.82 (m, 1H), 3.58 – 3.46 (m, 1H), 3.13 – 3.02 (m, 1H), 2.87 – 2.75 (m, 1H), 1.93 – 1.81 (m, 1H), 1.77 – 1.66 (m, 1H), 1.64 – 1.57 (m, 1H), 1.47 – 1.35 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 195.23, 140.80, 138.74, 134.77, 129.66, 129.57, 128.86, 128.58, 128.49, 128.14, 128.09, 127.66, 52.87, 52.45, 25.87, 24.21. HRMS (ESI) m/z Calcd for $C_{17}H17NS$ ($M+H^+$): 268.1154, found: 268.1152.



(5-chloro-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (3e)

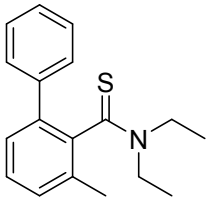
Yellow solid(22mg, 72%); mp: 84-87 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.61 (dd, *J* = 8.0, 1.7 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.40 (s, 1H), 7.36 (d, *J* = 6.1 Hz, 3H), 3.93 – 3.81 (m, 1H), 3.57 – 3.44 (m, 1H), 3.14 – 3.00 (m, 1H), 2.86 – 2.73 (m, 1H), 1.94 – 1.81 (m, 1H), 1.76 – 1.66 (m, 1H), 1.55 – 1.47 (m, 1H), 1.46 – 1.37 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.23, 140.80, 138.74, 129.66, 129.57, 128.86, 128.58, 128.49, 128.14, 128.09, 127.66, 52.87, 52.45, 25.87, 24.21. HRMS (ESI) m/z Calcd for $C_{17}H_{16}ClNS$ ($M+H^+$): 302.0765, found: 302.0770.



(5-nitro-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (3f)

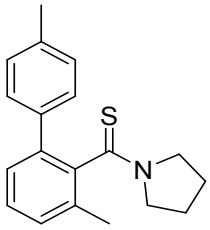
Yellow solid(21mg, 66%); mp: 110-112 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 8.22 (d, *J* = 17.4 Hz, 2H), 7.66 (d, *J* = 7.6 Hz, 3H), 7.43 (d, *J* = 7.5 Hz, 3H), 3.96 – 3.81 (m, 1H), 3.61 – 3.46 (m, 1H), 3.16 – 3.03 (m, 1H), 2.90 – 2.74 (m, 1H), 1.99 – 1.84 (m, 1H), 1.84 – 1.71 (m, 1H), 1.71 – 1.60 (m, 1H), 1.51 – 1.39 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 193.52, 147.55, 137.75, 137.50, 129.40, 128.74, 128.71,

128.62, 128.39, 125.02, 122.41, 52.78, 52.42, 25.92, 24.09. HRMS (ESI) m/z Calcd for $C_{17}H_{16}N_2O_2S$ ($M+H^+$): 313.1005, found: 313.1005.



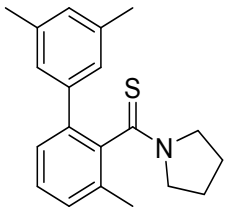
N,N-diethyl-3-methyl-[1,1'-biphenyl]-2-carbothioamide (3h)

Yellow solid(8mg, 29%); mp: 74-76 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.57 (dd, *J* = 7.8, 1.9 Hz, 2H), 7.35 – 7.26 (m, 3H), 7.24 (d, *J* = 3.0 Hz, 1H), 7.21 (d, *J* = 5.2 Hz, 1H), 7.10 (dd, *J* = 7.2, 1.8 Hz, 1H), 4.51 – 4.37 (m, 1H), 3.44 – 3.35 (m, 1H), 3.35 – 3.25 (m, 1H), 2.94 – 2.80 (m, 1H), 2.40 (s, 3H), 0.88 (t, *J* = 7.2 Hz, 3H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 197.62, 140.80, 140.23, 136.55, 132.88, 129.96, 129.51, 127.78, 127.66, 127.59, 127.19, 46.94, 44.36, 20.21, 12.74, 9.98. HRMS (ESI) m/z Calcd for $C_{18}H_{21}NS$ ($M+H^+$): 284.1467, found: 284.1471.



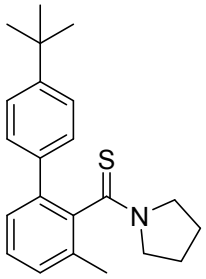
(3,4'-dimethyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4b)

Yellow solid(22mg, 76%); mp: 113-115 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.49 (d, *J* = 8.1 Hz, 2H), 7.31 (s, 1H), 7.21 (d, *J* = 3.2 Hz, 2H), 7.17 (d, *J* = 7.7 Hz, 2H), 3.95 – 3.83 (m, 1H), 3.61 – 3.49 (m, 1H), 3.14 – 3.03 (m, 1H), 2.86 – 2.76 (m, 1H), 2.37 (s, 3H), 2.36 (s, 3H), 1.93 – 1.80 (m, 1H), 1.76 – 1.67 (m, 1H), 1.67 – 1.57 (m, 1H), 1.48 – 1.39 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.89, 142.16, 137.14, 136.95, 133.33, 129.92, 129.62, 129.00, 128.68, 128.57, 128.53, 52.78, 52.38, 25.86, 24.26, 21.16, 21.00. HRMS (ESI) m/z Calcd for $C_{19}H_{21}NS$ ($M+H^+$): 296.1467, found: 296.1467.



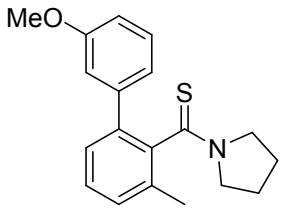
pyrrolidin-1-yl(3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)methanethione (4c)

Yellow solid(19mg, 60%); mp: 123-126°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.30 (s, 1H), 7.23 (s, 3H), 7.18 (d, *J* = 7.7 Hz, 1H), 6.93 (s, 1H), 3.95 – 3.84 (m, 1H), 3.57 – 3.46 (m, 1H), 3.12 – 3.02 (m, 1H), 2.89 – 2.78 (m, 1H), 2.37 (s, 3H), 2.32 (s, 6H), 1.93 – 1.83 (m, 1H), 1.76 – 1.66 (m, 1H), 1.65 – 1.57 (m, 1H), 1.48 – 1.38 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.93, 142.18, 139.89, 137.70, 137.18, 133.46, 129.86, 129.55, 128.83, 128.57, 126.41, 52.89, 52.45, 25.87, 24.27, 21.33, 21.02. HRMS (ESI) m/z Calcd for $C_{20}H_{23}NS$ ($M+H^+$): 310.1624, found: 310.1629.



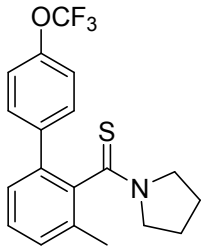
(4'-(tert-butyl)-3-methyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4d)

Yellow solid(22mg, 65%); mp: 91-93 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.59 – 7.53 (m, 2H), 7.44 – 7.38 (m, 2H), 7.34 (d, *J* = 2.7 Hz, 1H), 7.28 (s, 1H), 7.22 (dd, *J* = 8.2, 1.9 Hz, 1H), 3.94 – 3.82 (m, 1H), 3.63 – 3.51 (m, 1H), 3.12 – 3.01 (m, 1H), 2.87 – 2.76 (m, 1H), 2.40 (s, 3H), 1.93 – 1.82 (m, 1H), 1.76 – 1.64 (m, 1H), 1.56 – 1.46 (m, 1H), 1.46 – 1.36 (m, 1H), 1.34 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.92, 150.29, 142.19, 137.18, 137.03, 133.24, 129.97, 129.47, 128.67, 128.36, 125.10, 52.85, 52.33, 34.53, 31.33, 25.80, 24.27, 21.01. HRMS (ESI) m/z Calcd for $C_{22}H_{27}NS$ ($M+H^+$): 338.1937, found: 338.1936.



(3'-methoxy-3-methyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4e)

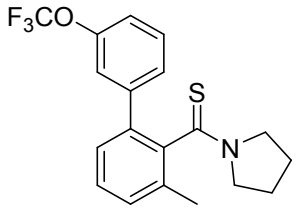
Yellow solid(15mg, 47%); mp: 98-101°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.30 (d, *J* = 8.3 Hz, 3H), 7.25 (s, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 6.85 (dd, *J* = 7.9, 2.2 Hz, 1H), 3.95 – 3.85 (m, 1H), 3.82 (s, 3H), 3.61 – 3.48 (m, 1H), 3.14 – 3.03 (m, 1H), 2.92 – 2.80 (m, 1H), 2.39 (s, 3H), 1.93 – 1.81 (m, 1H), 1.77 – 1.69 (m, 1H), 1.67 – 1.58 (m, 1H), 1.50 – 1.42 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.79, 159.40, 142.22, 141.43, 137.60, 133.30, 129.93, 129.56, 129.33, 128.54, 120.86, 113.88, 113.48, 77.49, 77.07, 76.64, 55.52, 52.85, 52.40, 25.90, 24.27, 21.02. HRMS (ESI) m/z Calcd for $C_{19}H_{21}NOS$ ($M+H^+$): 312.1417, found: 312.1419.



(3-methyl-4'-(trifluoromethoxy)-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4f)

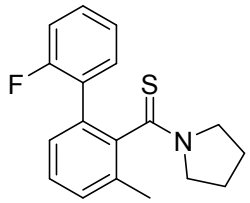
Yellow solid(20mg, 54%); mp: 81-83°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.67 (dd, *J* = 8.7, 1.7 Hz, 2H), 7.33 (s, 1H), 7.28 (d, *J* = 1.6 Hz, 1H), 7.25 – 7.20 (m, 3H), 3.96 – 3.83 (m, 1H), 3.61 – 3.49 (m, 1H), 3.17 – 3.06 (m, 1H), 2.85 – 2.72 (m, 1H), 2.41 (s, 3H), 1.98 – 1.85 (m, 1H), 1.83 – 1.70 (m, 1H), 1.69 –

1.59 (m, 1H), 1.52 – 1.41 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.43, 148.45, 142.31, 138.76, 138.10, 131.77, 130.17, 130.05, 129.52, 122.16, 120.68, 120.46(d, *J* =255.0Hz)，52.81, 52.46, 25.88, 24.21, 21.02. HRMS (ESI) m/z Calcd for $C_{19}H_{18}F_3NOS$ ($M+H^+$): 366.1134, found: 366.1135.



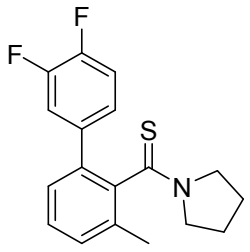
(3-methyl-3'-(trifluoromethoxy)-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4g)

Yellow solid(26mg, 70%); mp: 85-87°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.59 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.46 (s, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.30 (s, 1H), 7.22 (d, *J* = 1.2 Hz, 2H), 7.17 (d, *J* = 8.3 Hz, 1H), 3.92 – 3.80 (m, 1H), 3.61 – 3.49 (m, 1H), 3.17 – 3.07 (m, 1H), 2.86 – 2.75 (m, 1H), 2.39 (s, 3H), 1.96 – 1.83 (m, 1H), 1.82 – 1.70 (m, 1H), 1.68 – 1.58 (m, 1H), 1.52 – 1.42 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.21, 149.12, 142.35, 142.14, 138.34, 131.63, 130.02, 129.63, 129.56, 128.53, 127.35, 121.25, 120.48(d, *J*=255.8 Hz), 119.82, 52.73, 52.51, 25.88, 24.22, 21.02. HRMS (ESI) m/z Calcd for $C_{19}H_{18}F_3NOS$ ($M+H^+$): 366.1134, found: 366.1135.



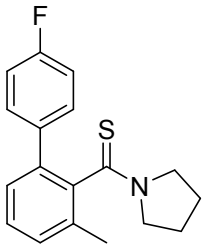
(2'-fluoro-3-methyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4h)

Yellow solid(20mg, 69%); mp: 128-132 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.64 (t, *J* = 7.7 Hz, 1H), 7.26 – 7.20 (m, 3H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 8.5 Hz, 1H), 7.06 (d, *J* = 8.6 Hz, 1H), 3.92 – 3.76 (m, 1H), 3.55 – 3.41 (m, 1H), 3.28 – 3.15 (m, 1H), 3.15 – 3.02 (m, 1H), 2.40 – 2.28 (m, 3H), 1.95 – 1.81 (m, 1H), 1.81 – 1.72 (m, 1H), 1.71 – 1.62 (m, 1H), 1.60 – 1.53 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.07, 159.36(d, *J*=245.4 Hz) 143.05, 138.10, 132.09 (d, *J* = 3.0 Hz), 131.03 (d, *J* = 2.7 Hz), 129.28, 129.20, 129.17, 127.80, 127.31, 127.30(d, *J*=14.2 Hz), 123.82 (d, *J* = 3.6 Hz), 115.48 (d, *J* = 22.6 Hz), 52.66, 52.59, 52.56, 26.04, 24.34, 21.15. HRMS (ESI) m/z Calcd for $C_{18}H_{18}FNS$ ($M+H^+$): 300.1217, found: 300.1221.



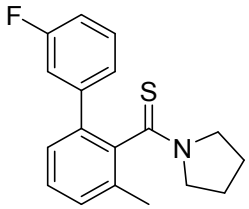
(3',4'-difluoro-3-methyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4i)

Yellow solid(23mg, 71%); mp: 89-92 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.51 – 7.35 (m, 2H), 7.28 (d, *J* = 1.1 Hz, 1H), 7.25 – 7.11 (m, 3H), 4.00 – 3.87 (m, 1H), 3.65 – 3.53 (m, 1H), 3.22 – 3.10 (m, 1H), 2.89 – 2.77 (m, 1H), 2.40 (s, 3H), 2.03 – 1.90 (m, 1H), 1.88 – 1.77 (m, 1H), 1.77 – 1.68 (m, 1H), 1.68 – 1.59 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.28, 151.45 (dd, *J* = 20.5, 13.0 Hz), 148.16 (dd, *J* = 20.9, 12.7 Hz), 142.29, 138.27, 137.04 (dd, *J* = 9.2, 2.6 Hz), 131.07, 129.99, 129.55, 128.39, 124.96 (dd, *J* = 5.8, 3.7 Hz), 117.59 (d, *J* = 17.8 Hz), 117.07 (d, *J* = 17.1 Hz) , 52.77, 52.52, 25.97, 24.27, 21.00. HRMS (ESI) m/z Calcd for $C_{18}H_{17}F_2NS$ ($M+H^+$): 318.1123, found: 318.1121.



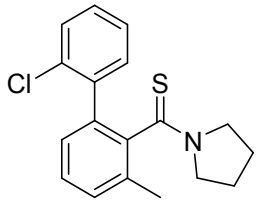
(4'-fluoro-3-methyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4j)

Yellow solid(22mg, 74%); mp: 87-89 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.59 (dd, *J* = 8.5, 5.5 Hz, 2H), 7.29 (s, 1H), 7.20 (s, 2H), 7.06 (t, *J* = 8.7 Hz, 2H), 3.96 – 3.82 (m, 1H), 3.60 – 3.44 (m, 1H), 3.16 – 3.03 (m, 1H), 2.86 – 2.71 (m, 1H), 2.38 (s, 3H), 1.96 – 1.83 (m, 1H), 1.81 – 1.68 (m, 1H), 1.67 – 1.58 (m, 1H), 1.52 – 1.41 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.58, 162.14 (d, *J* = 246.7 Hz), 142.25, 137.68, 136.05 (d, *J* = 3.2 Hz), 132.19, 130.39 (d, *J* = 7.9 Hz), 129.80 (d, *J* = 29.3 Hz), 128.49, 115.36, 115.08, 52.78, 52.45, 25.91, 24.26, 21.02. HRMS (ESI) m/z Calcd for $C_{18}H_{18}FNS$ ($M+H^+$): 300.1217, found: 300.1218.



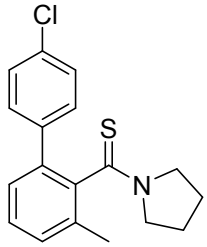
(3'-fluoro-3-methyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4k)

Yellow solid(23mg, 76%); mp: 83-85 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.42 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.37 – 7.32 (m, 1H), 7.30 (d, *J* = 5.0 Hz, 2H), 7.22 (d, *J* = 0.9 Hz, 2H), 7.00 (tdd, *J* = 8.4, 2.7, 1.1 Hz, 1H), 3.95 – 3.82 (m, 1H), 3.63 – 3.50 (m, 1H), 3.17 – 3.06 (m, 1H), 2.88 – 2.76 (m, 1H), 2.38 (s, 3H), 1.95 – 1.83 (m, 1H), 1.83 – 1.70 (m, 1H), 1.69 – 1.58 (m, 1H), 1.55 – 1.43 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.37, 162.61 (d, *J* = 245.8 Hz), 142.28 (d, *J* = 7.5Hz), 138.14, 131.95, 130.02, 129.75 (d, *J* = 8.3 Hz), 129.58, 128.55, 124.52 (d, *J* = 2.9 Hz), 115.47 (d, *J* = 22.1 Hz), 114.14 (d, *J* = 21.0 Hz), 52.83, 52.50, 25.94, 24.27, 21.05. HRMS (ESI) m/z Calcd for $C_{18}H_{18}FNS$ ($M+H^+$): 300.1217, found: 300.1214.



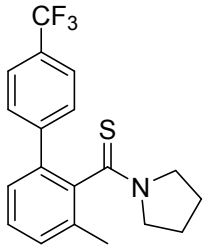
(2'-chloro-3-methyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4l)

Yellow solid(21mg, 66%); mp: 84-86 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.76 (s, 1H), 7.48 – 7.42 (m, 1H), 7.30 (d, *J* = 3.1 Hz, 1H), 7.29 – 7.24 (m, 3H), 7.22 (d, *J* = 7.8 Hz, 1H), 3.95 – 3.81 (m, 1H), 3.54 – 3.39 (m, 1H), 3.34 – 3.19 (m, 2H), 2.42 (s, 3H), 1.99 – 1.86 (m, 1H), 1.86 – 1.76 (m, 1H), 1.75 – 1.58 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 195.83, 142.93, 138.09, 137.84, 132.75, 132.73, 131.36, 129.69, 128.84, 128.79, 127.88, 127.83, 126.39, 77.47, 77.05, 76.63, 52.68, 52.64, 26.03, 24.28, 21.19. HRMS (ESI) m/z Calcd for $C_{18}H_{18}ClNS$ ($M+H^+$): 316.0921, found: 316.0923.



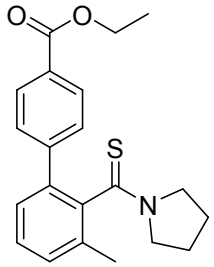
(4'-chloro-3-methyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4m)

Yellow solid(21mg, 65%); mp: 139-141 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.56 (d, *J* = 8.4 Hz, 2H), 7.38 – 7.27 (m, 3H), 7.20 (s, 2H), 3.97 – 3.82 (m, 1H), 3.61 – 3.48 (m, 1H), 3.16 – 3.05 (m, 1H), 2.86 – 2.72 (m, 1H), 2.38 (s, 3H), 1.96 – 1.83 (m, 1H), 1.82 – 1.69 (m, 1H), 1.69 – 1.59 (m, 1H), 1.54 – 1.43 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.45, 142.21, 138.51, 137.96, 133.33, 131.99, 130.03, 129.55, 128.52, 128.48, 52.80, 52.48, 25.92, 24.26, 21.04. HRMS (ESI) m/z Calcd for $C_{18}H_{18}ClNS$ ($M+H^+$): 316.0921, found: 316.0927.



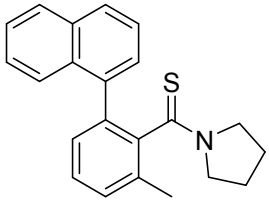
(3-methyl-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)(pyrrolidin-1-yl)methanethione (4n)

Yellow solid(25mg, 71%); mp: 172-175 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.80 (d, *J* = 8.1 Hz, 2H), 7.68 (d, *J* = 7.1 Hz, 2H), 7.36 (s, 1H), 7.28 (s, 2H), 4.01 – 3.85 (m, 1H), 3.66 – 3.51 (m, 1H), 3.27 – 3.10 (m, 1H), 2.90 – 2.73 (m, 1H), 2.45 (s, 3H), 2.02 – 1.88 (m, 1H), 1.88 – 1.72 (m, 1H), 1.71 – 1.61 (m, 1H), 1.56 – 1.45 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.25, 143.74, 142.35, 138.56, 131.79, 129.88 (d, *J* = 30.3 Hz), 129.55, 129.06, 128.52, 125.96, 125.18 (q, *J* = 3.8 Hz), 120.55 (d, *J* = 272.2 Hz), 52.80, 52.53, 25.91, 24.22, 21.06. HRMS (ESI) m/z Calcd for $C_{19}H_{18}F_3NS$ ($M+H^+$): 350.1185, found: 350.1190.



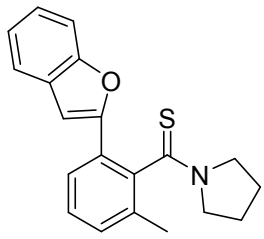
ethyl 3'-methyl-2'-(pyrrolidine-1-carbonothioyl)-[1,1'-biphenyl]-4-carboxylate (4o)

Yellow solid(24mg, 67%); mp: 92-94 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 8.04 (dd, *J* = 7.6, 3.1 Hz, 2H), 7.68 (dd, *J* = 8.7, 2.2 Hz, 2H), 7.31 (s, 1H), 7.25 – 7.18 (m, 2H), 4.46 – 4.32 (m, 2H), 3.94 – 3.81 (m, 1H), 3.59 – 3.44 (m, 1H), 3.16 – 3.03 (m, 1H), 2.84 – 2.68 (m, 1H), 2.39 (s, 3H), 1.93 – 1.80 (m, 1H), 1.80 – 1.66 (m, 1H), 1.63 – 1.48 (m, 2H), 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.36, 166.42, 144.67, 142.33, 138.36, 132.27, 130.00, 129.63, 129.52, 129.23, 128.66, 128.59, 61.01, 52.77, 52.49, 25.90, 24.20, 21.05, 14.31. HRMS (ESI) m/z Calcd for $C_{21}H_{23}NO_2S$ ($M+H^+$): 354.1522, found: 354.1522.



(2-methyl-6-(naphthalen-1-yl)phenyl)(pyrrolidin-1-yl)methanethione (4p)

Yellow solid(19mg, 58%); mp: 128-131 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.94 (t, *J* = 7.5 Hz, 2H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.61 – 7.37 (m, 4H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 2.6 Hz, 1H), 7.26 (s, 1H), 3.91 – 3.75 (m, 1H), 3.46 – 3.31 (m, 1H), 3.24 – 3.07 (m, 1H), 2.94 – 2.74 (m, 1H), 2.48 (s, 3H), 1.85 – 1.72 (m, 1H), 1.56 – 1.46 (m, 1H), 1.46 – 1.28 (m, 1H), 1.14 – 0.89 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.48, 143.78, 137.57, 136.24, 133.96, 131.85, 131.56, 131.43, 128.82, 128.73, 128.65, 128.39, 127.76, 126.01, 125.40, 125.25, 124.87, 52.50, 52.46, 25.56, 23.98, 21.15. HRMS (ESI) m/z Calcd for $C_{22}H_{21}NS$ ($M+H^+$):332.1467, found: 332.1468.



(2-(benzofuran-2-yl)-6-methylphenyl)(pyrrolidin-1-yl)methanethione (4q)

Yellow solid(7mg, 21%); mp: 155-157 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.83 (d, *J* = 8.1 Hz, 1H), 7.56 (dd, *J* = 7.6, 2.1 Hz, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.30 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.26 – 7.23 (m, 1H), 7.21 (d, *J* = 1.3 Hz, 1H), 7.19 (d, *J* = 2.6 Hz, 1H), 7.03 (s, 1H), 4.12 – 3.99 (m, 1H), 3.99 – 3.88 (m, 1H), 3.32 – 3.21 (m, 1H), 3.13 – 3.01 (m, 1H), 2.39 (s, 3H), 2.10 – 1.97 (m, 1H), 1.97 – 1.89 (m, 1H), 1.89 – 1.82 (m, 1H), 1.82 – 1.71 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 196.34, 156.04, 153.55,

139.36, 139.16, 129.39, 129.26, 127.64, 127.59, 127.13, 124.43, 122.88, 121.24, 110.93, 104.17, 52.90, 52.46, 26.10, 24.42, 21.23. HRMS (ESI) m/z Calcd for $C_{20}H_{19}NOS$ ($M+H^+$): 322.1260, found: 322.1264.

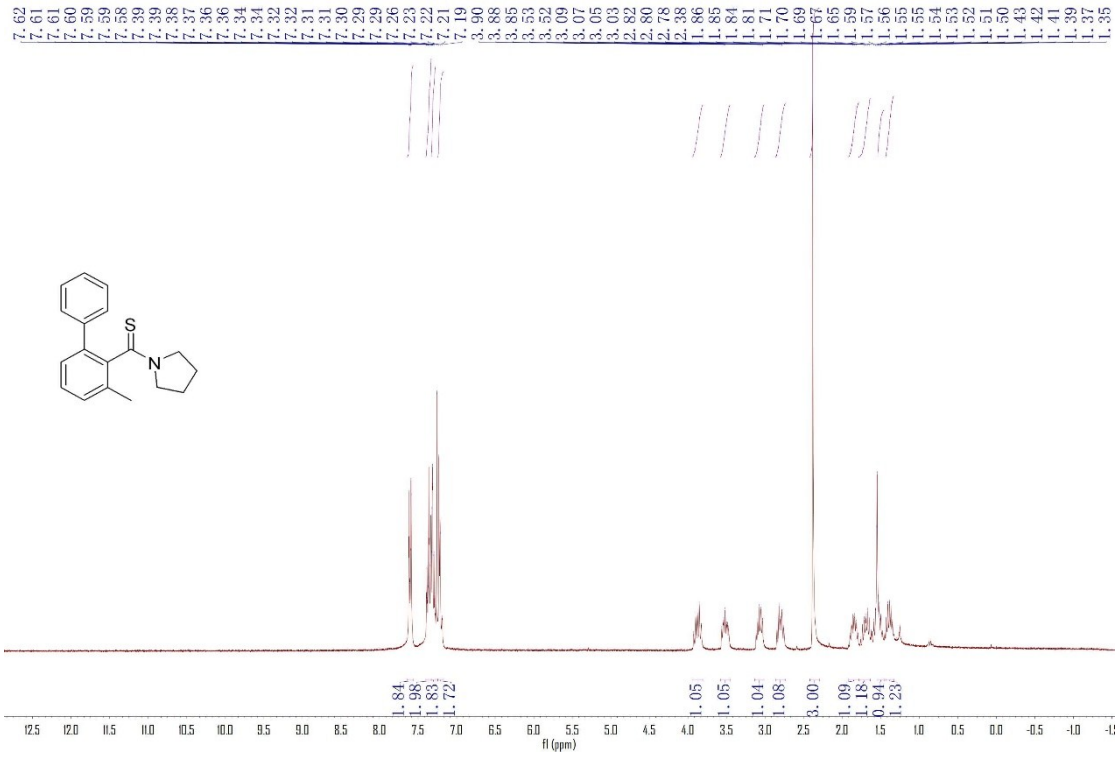
6. References

[1] L. Hie, N. F. Fine Nathel, T. K. Shah, E. L. Baker, X. Hong, Y.-F. Yang, P. Liu, K. N. Houk, N. K. Garg, *Nature.* **2015**, 524, 79-83.

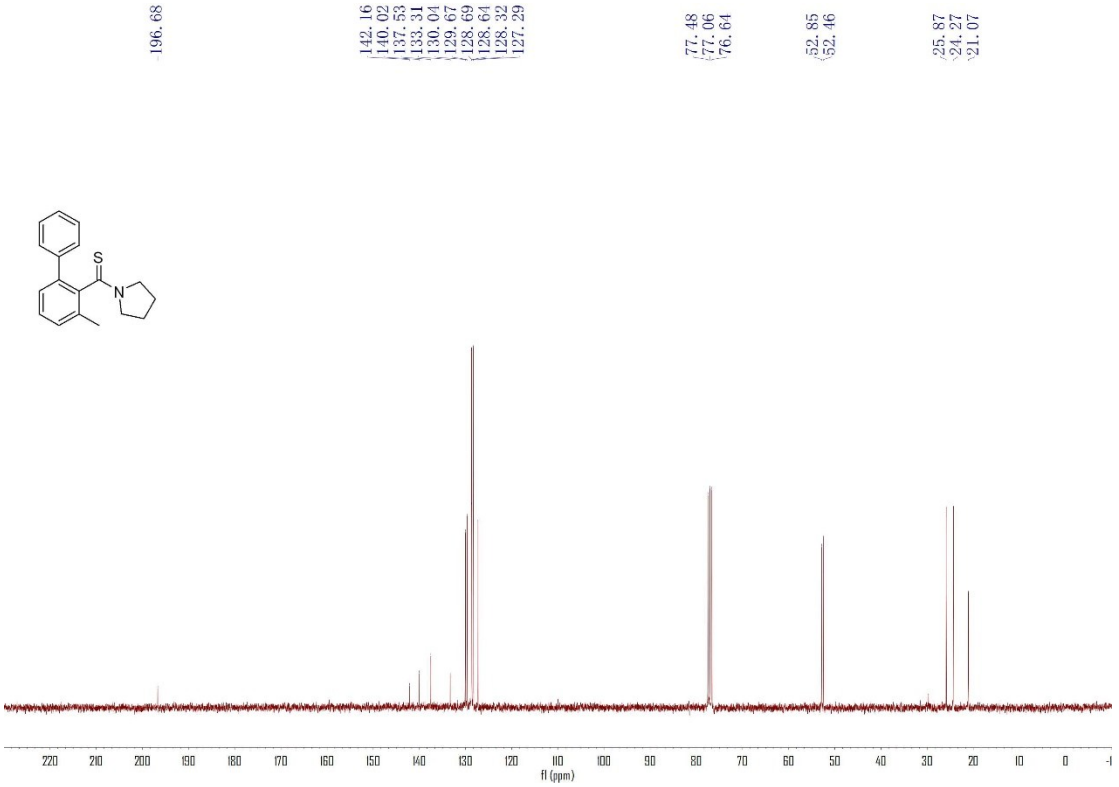
[2] J. E. Spangler, Y. Kobayashi, P. Verma, D.-H. Wang, J.-Q. Yu, *J. Am. Chem. Soc.* **2015**, 137, 11876-11879.

7. Copies of ^{1}H, ^{13}C NMR Spectra

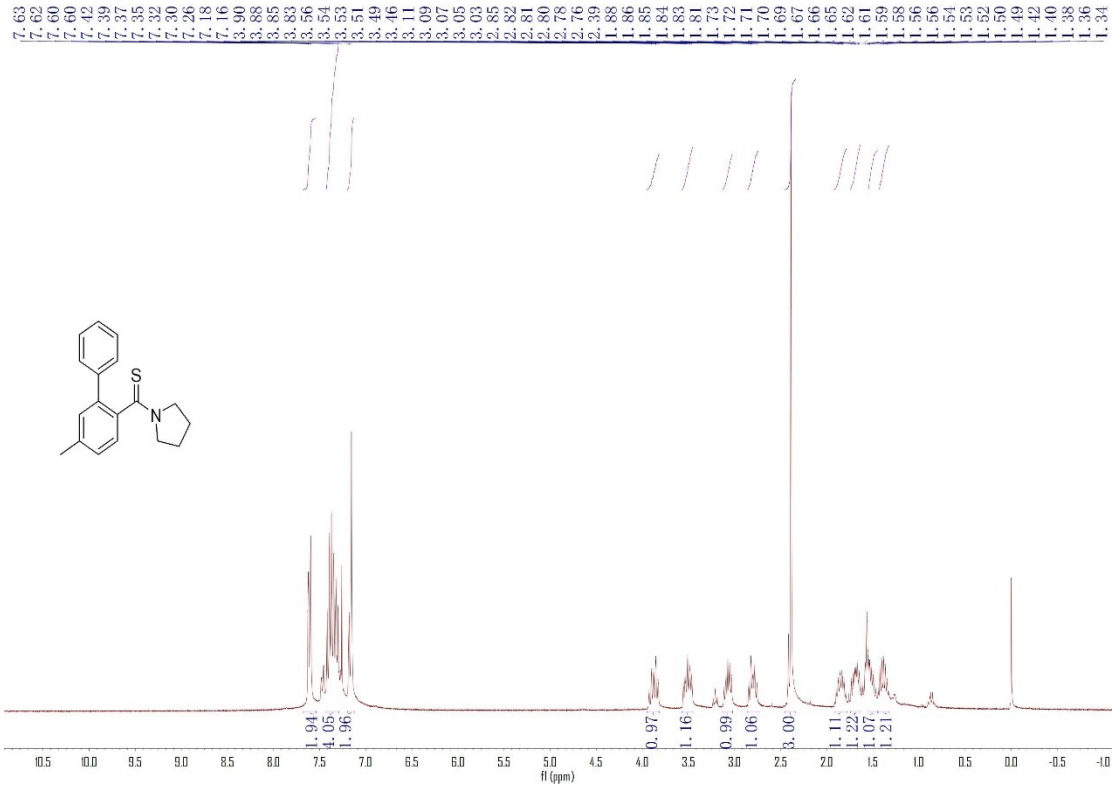
^{1}H-NMR Spectrum of Compound 3a



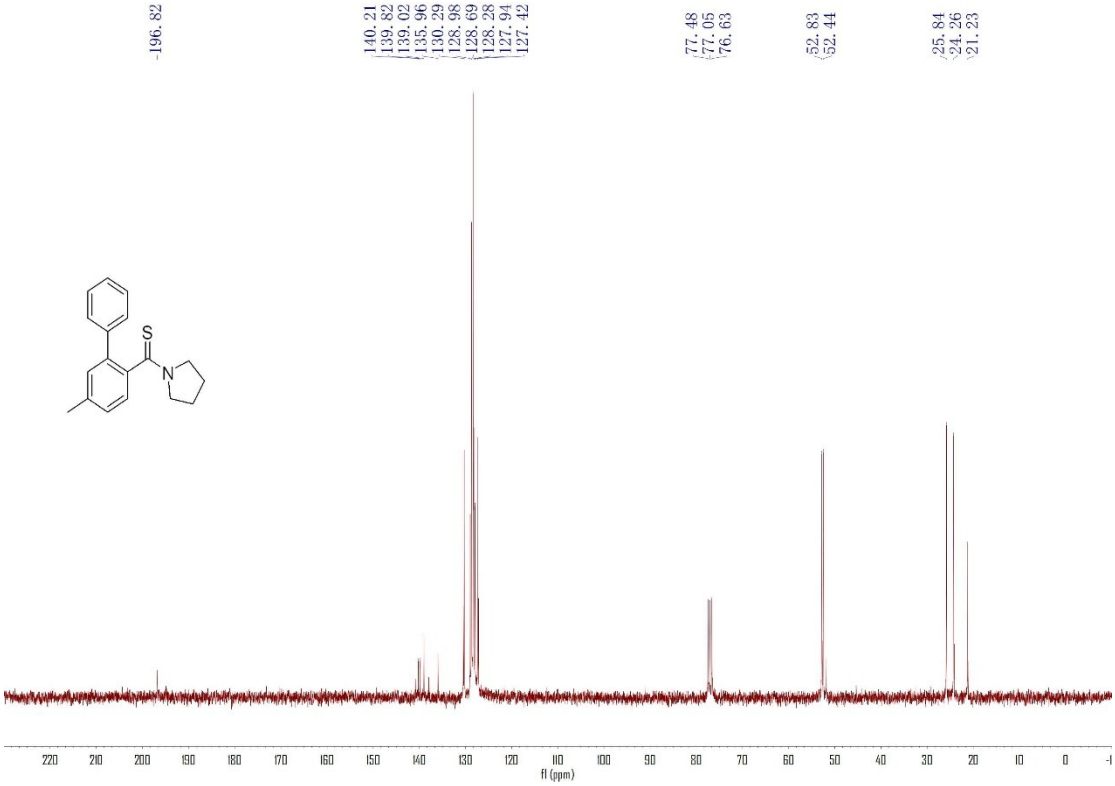
^{13}C-NMR Spectrum of Compound 3a



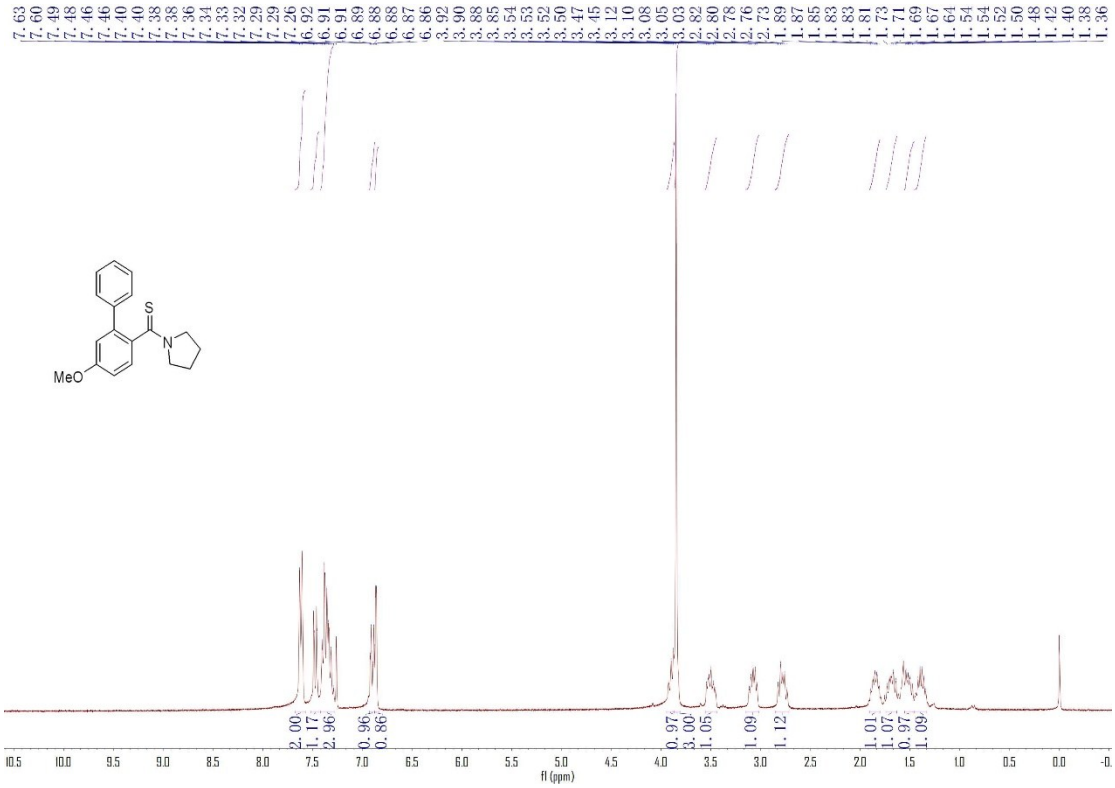
^{1}H-NMR Spectrum of Compound 3b



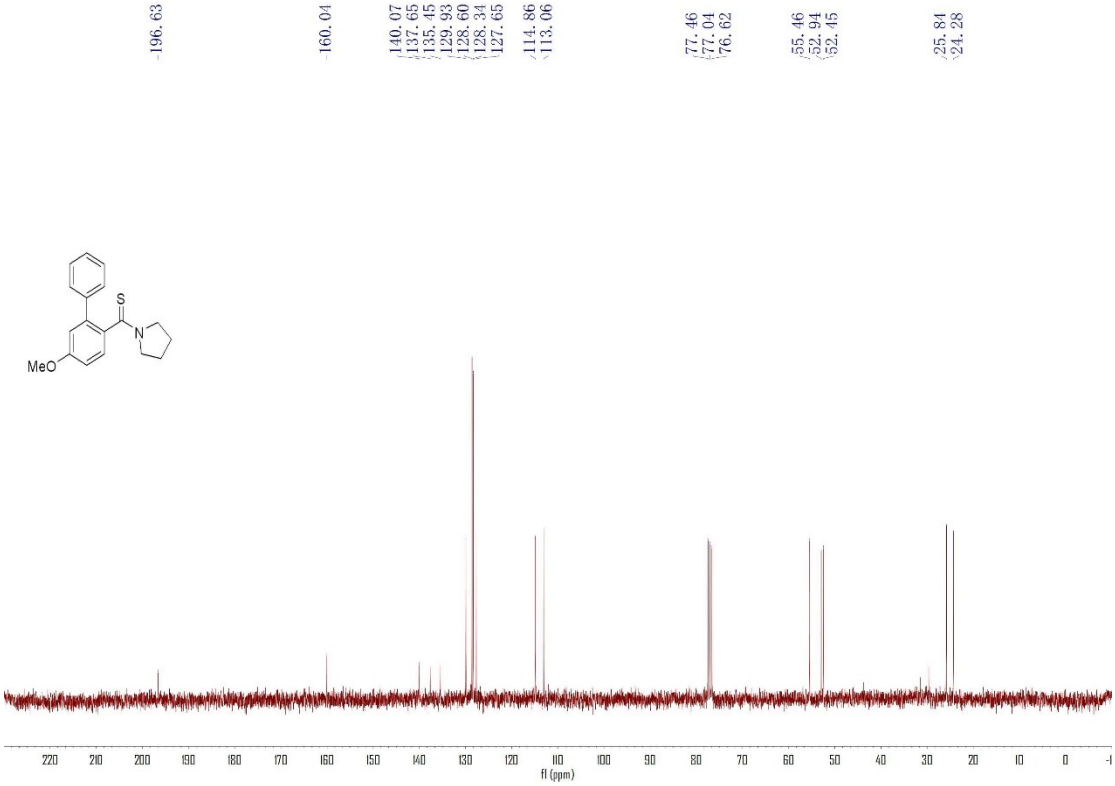
^{13}C-NMR Spectrum of Compound 3b



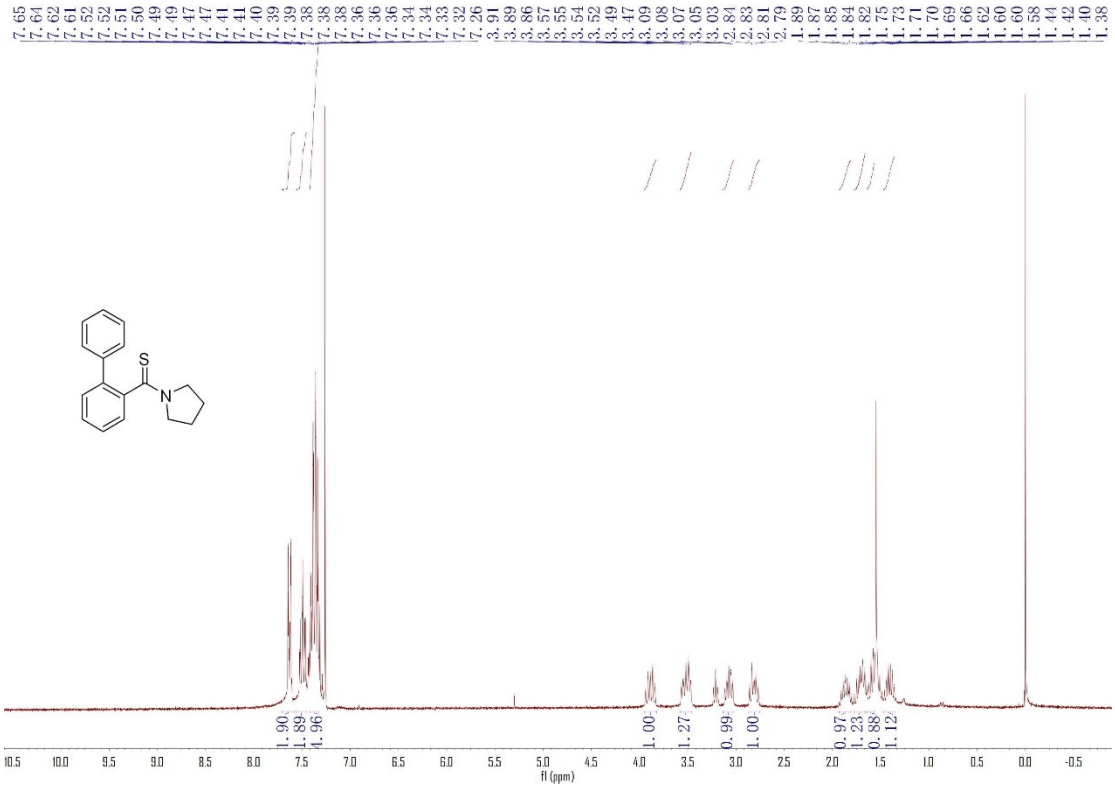
[1]H-NMR Spectrum of Compound 3c



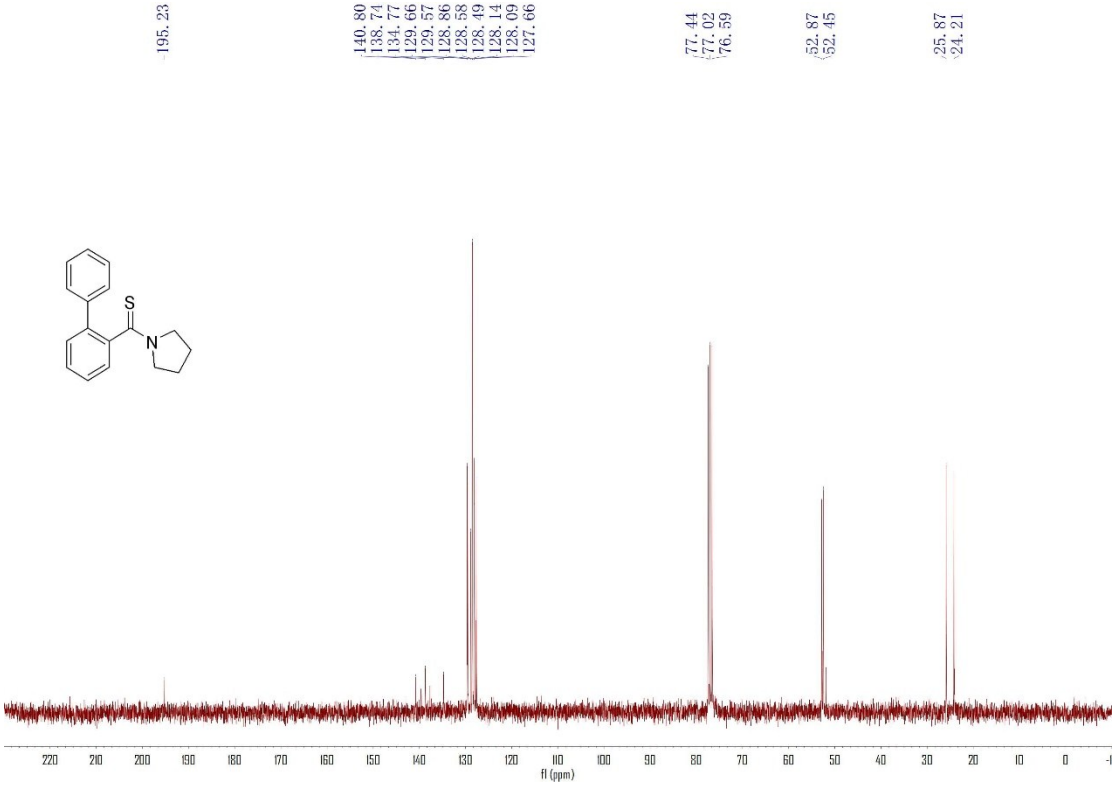
[13]C-NMR Spectrum of Compound 3c



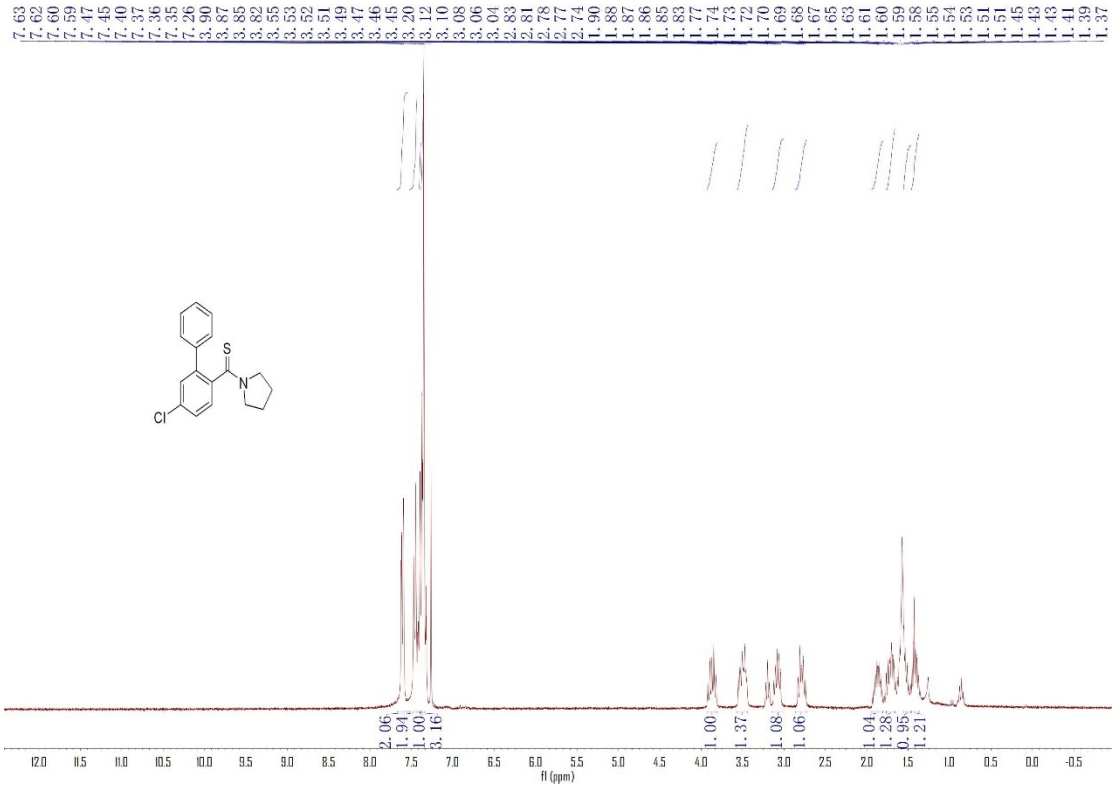
^{1}H-NMR Spectrum of Compound 3d



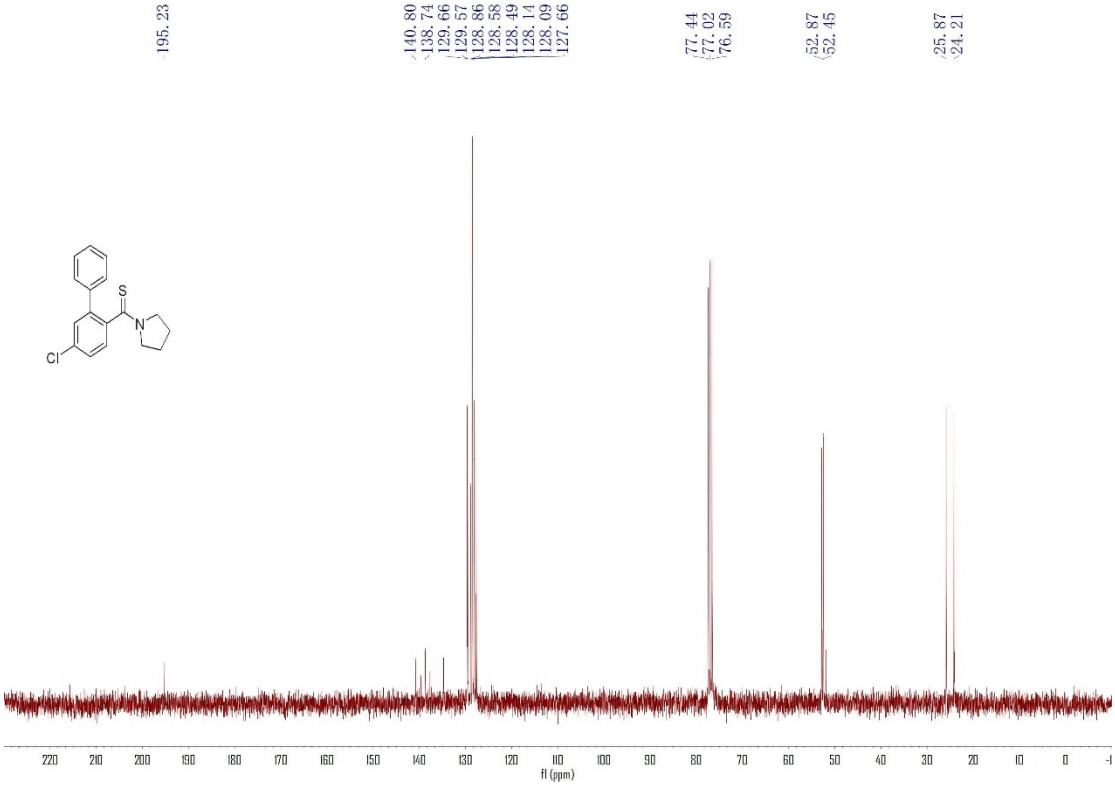
^{13}C-NMR Spectrum of Compound 3d



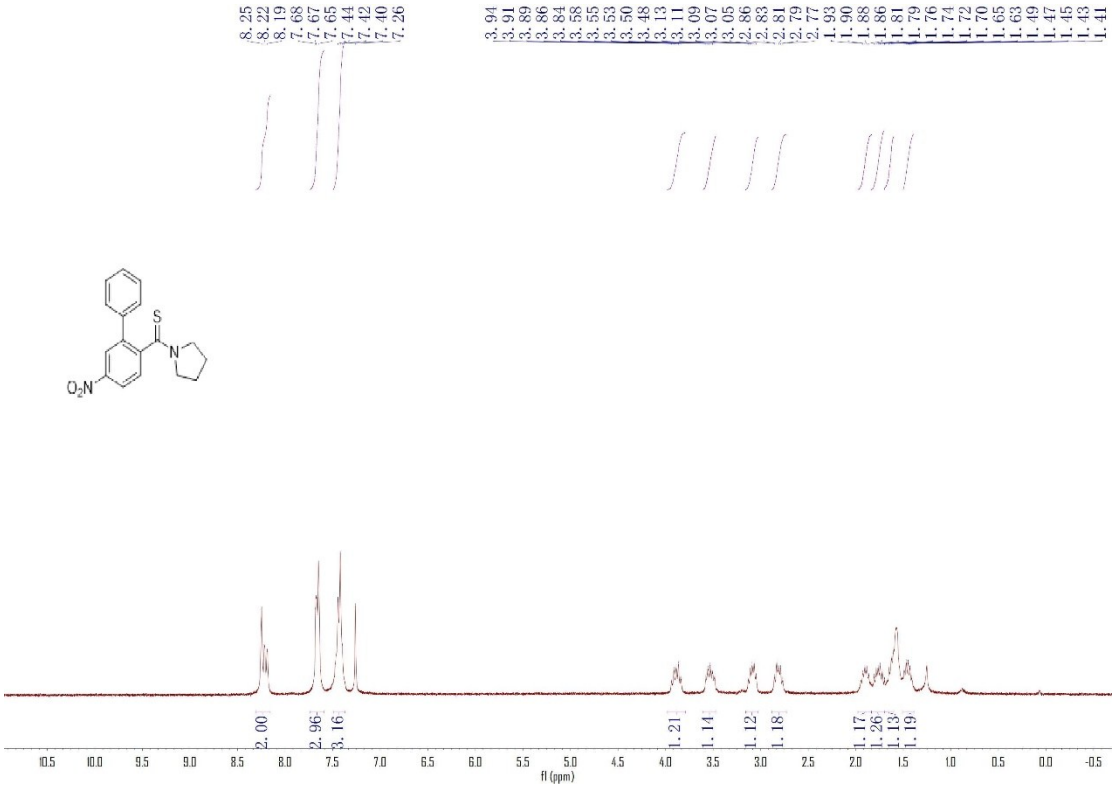
[1]H-NMR Spectrum of Compound 3e



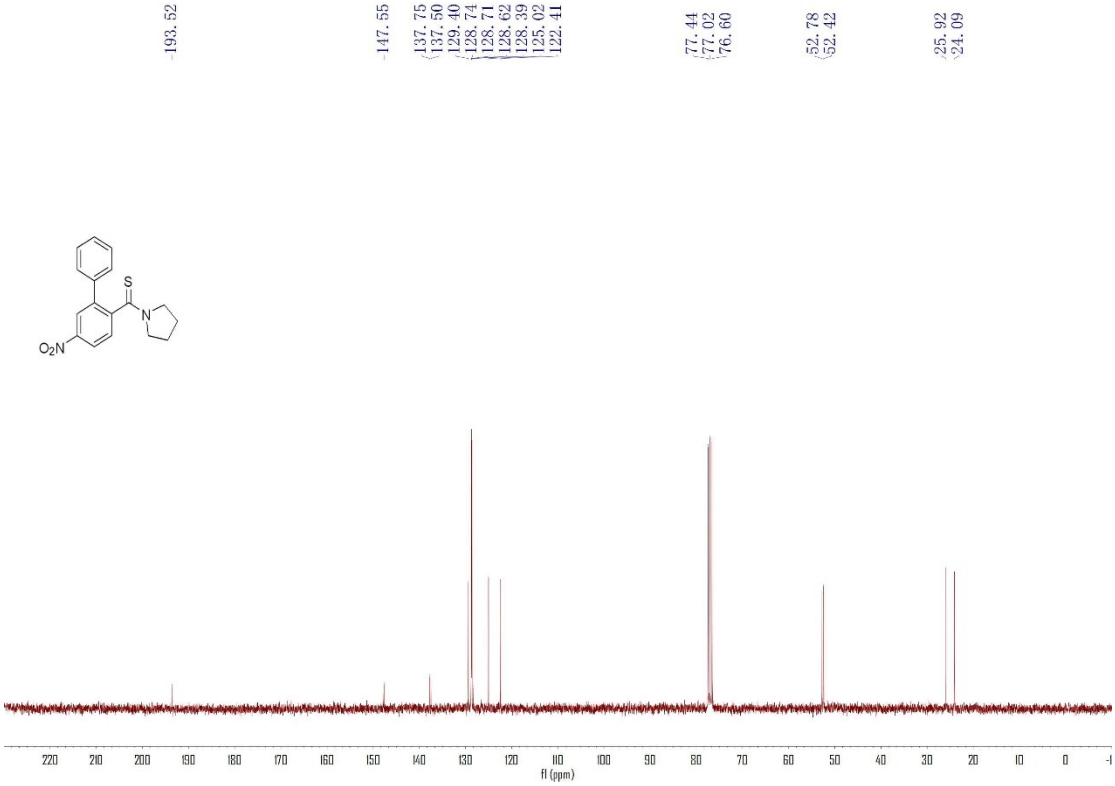
[13]C-NMR Spectrum of Compound 3e



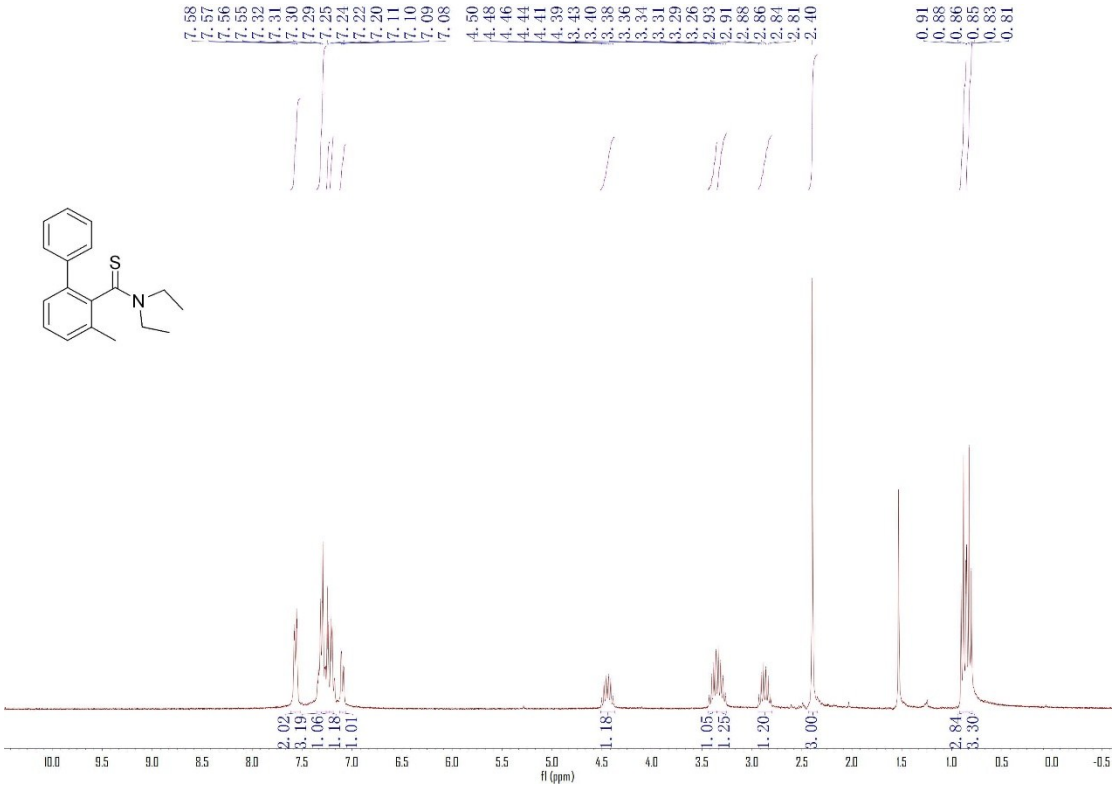
[1]H-NMR Spectrum of Compound 3f



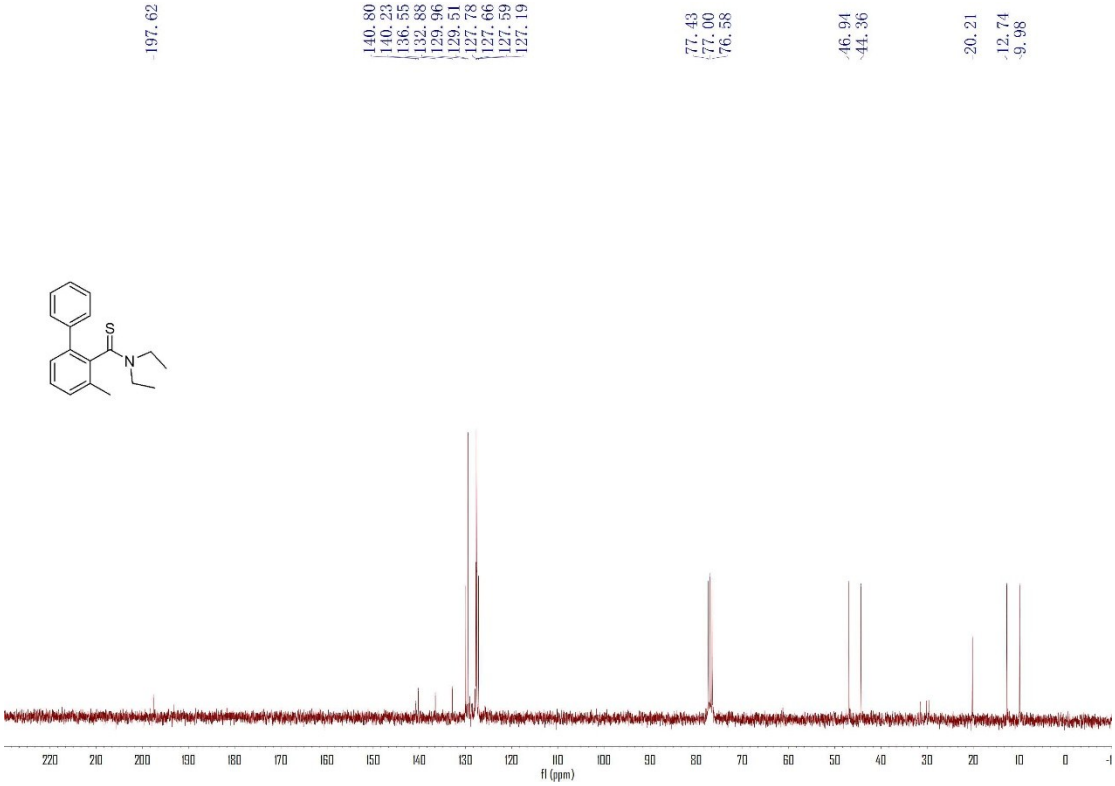
[13]C-NMR Spectrum of Compound 3f



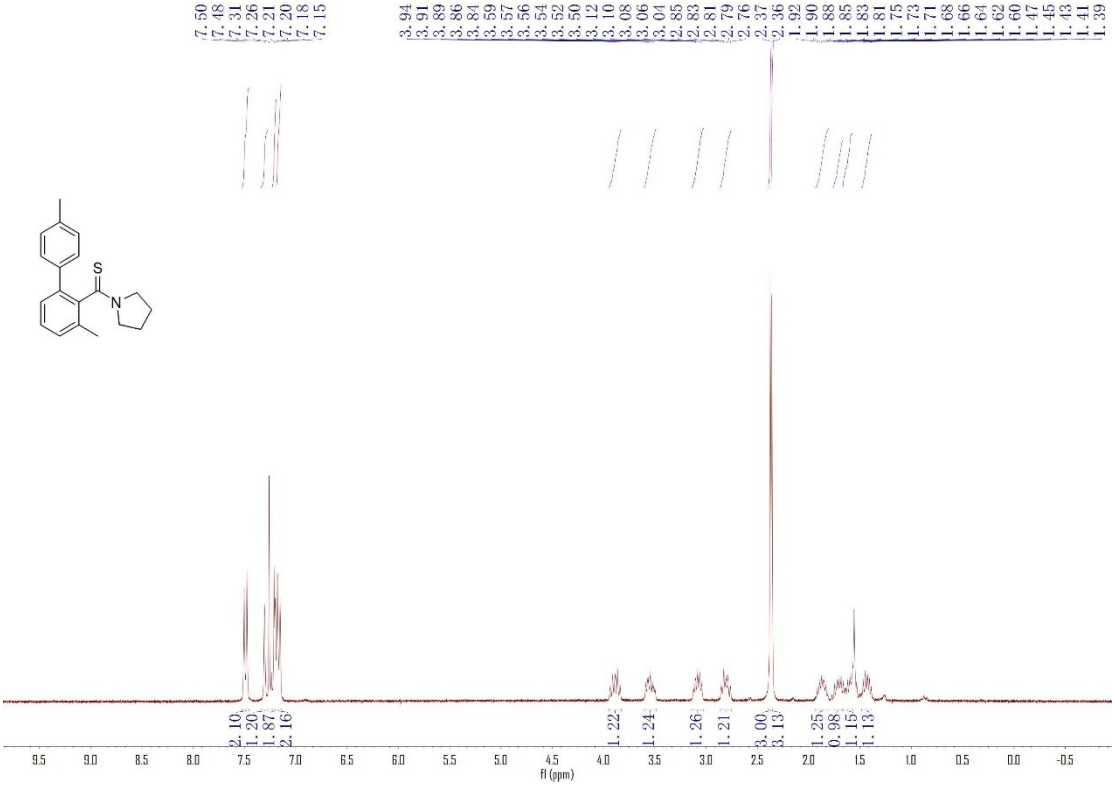
[1]H-NMR Spectrum of Compound 3h



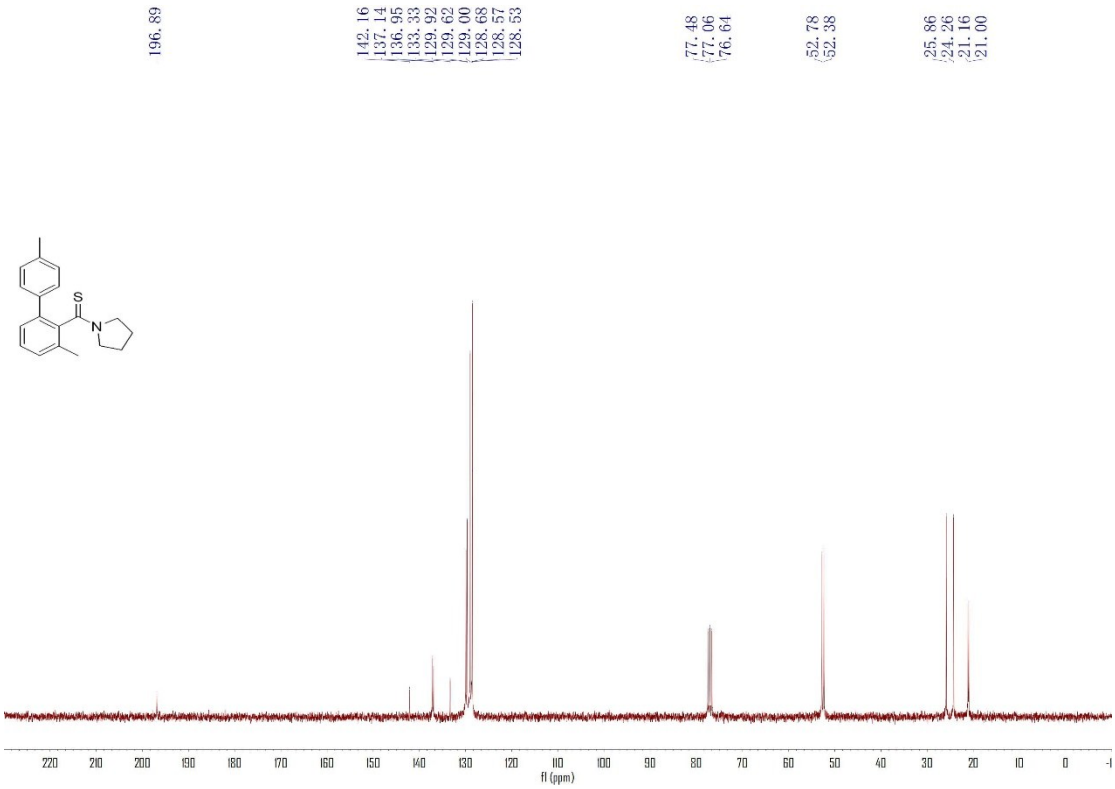
[13]C-NMR Spectrum of Compound 3h



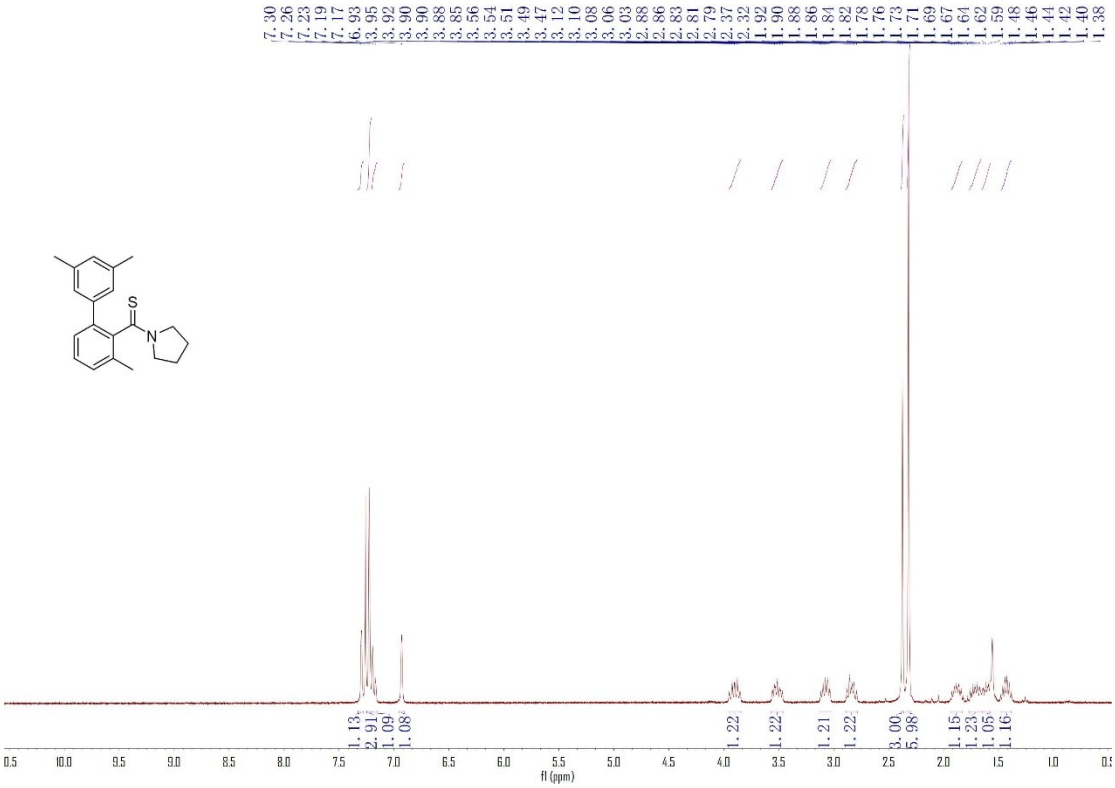
[1]H-NMR Spectrum of Compound 4a



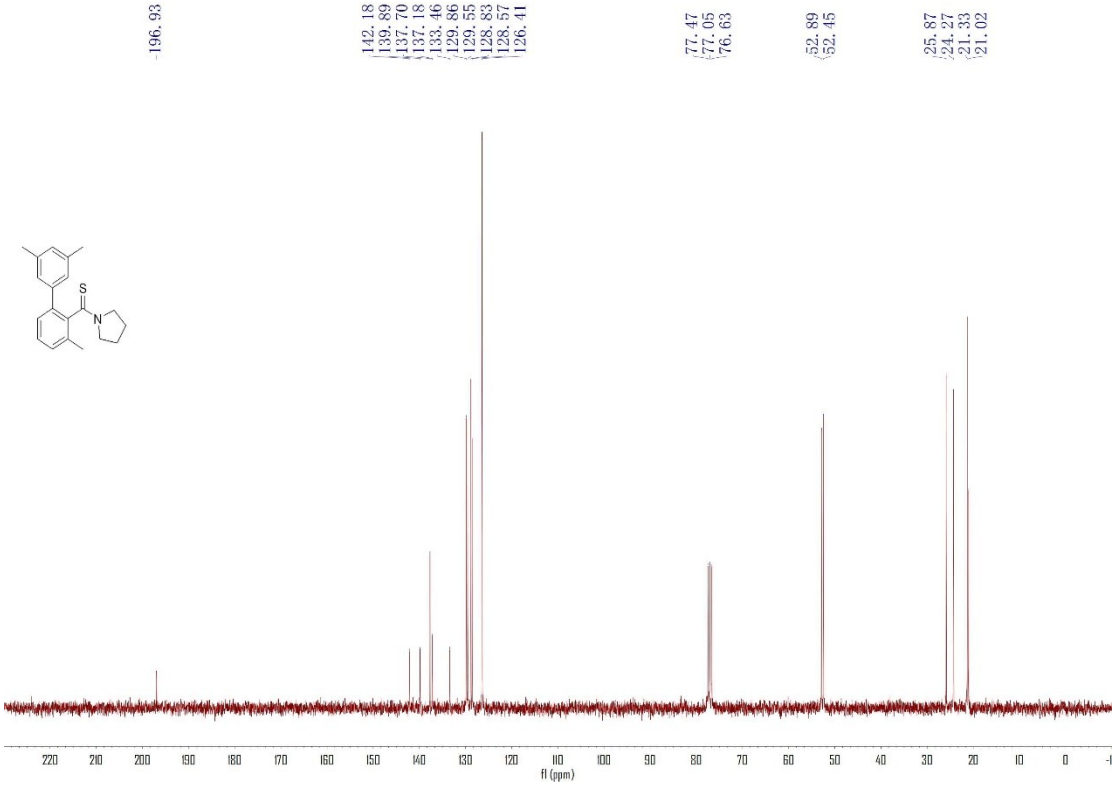
[13]C-NMR Spectrum of Compound 4a



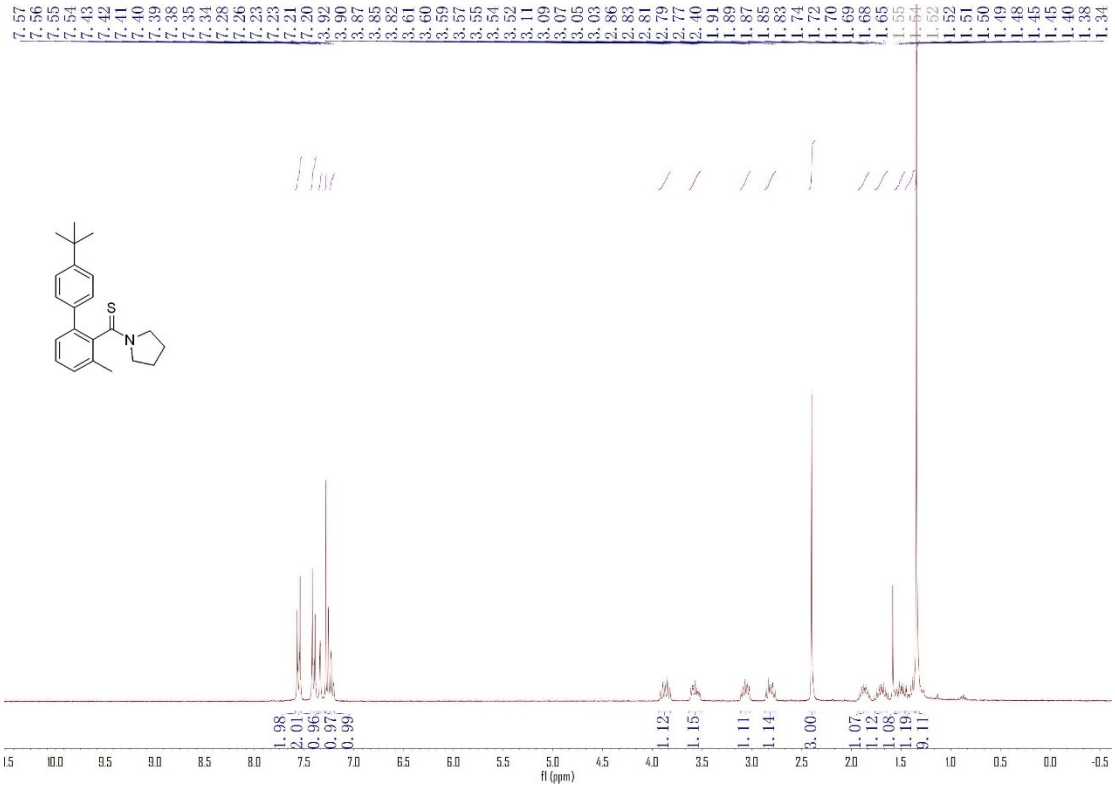
[1]H-NMR Spectrum of Compound 4b



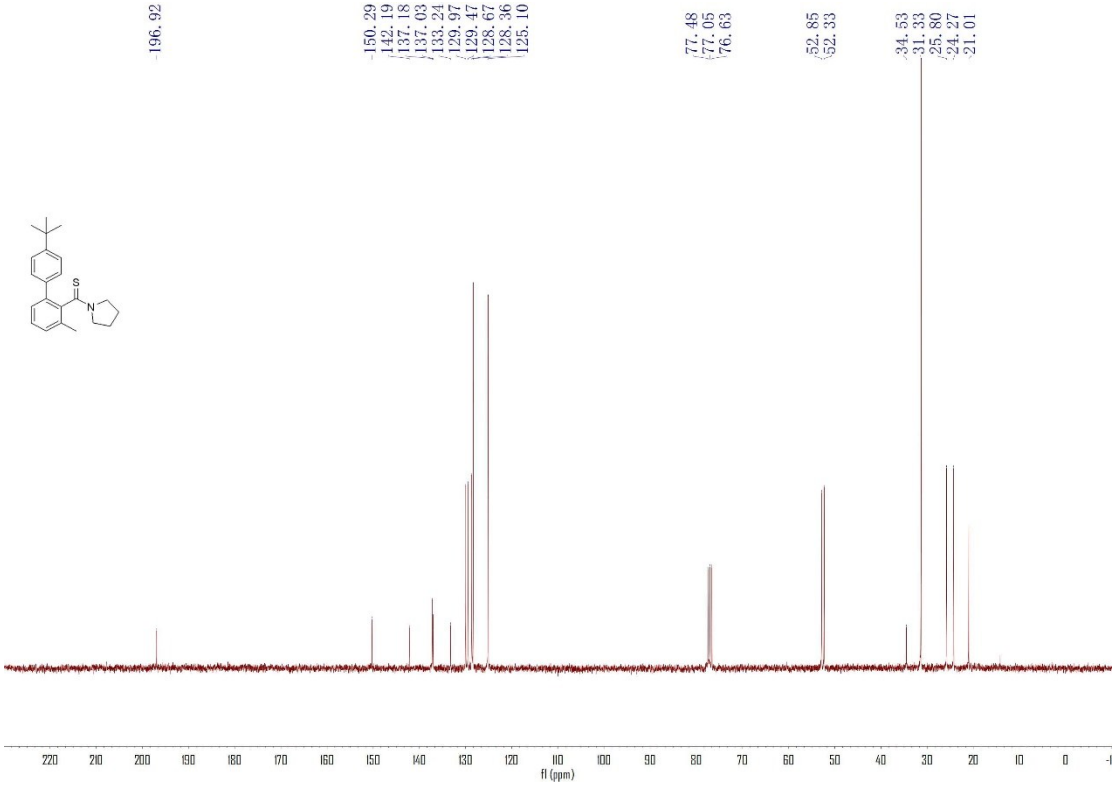
[13]C-NMR Spectrum of Compound 4b



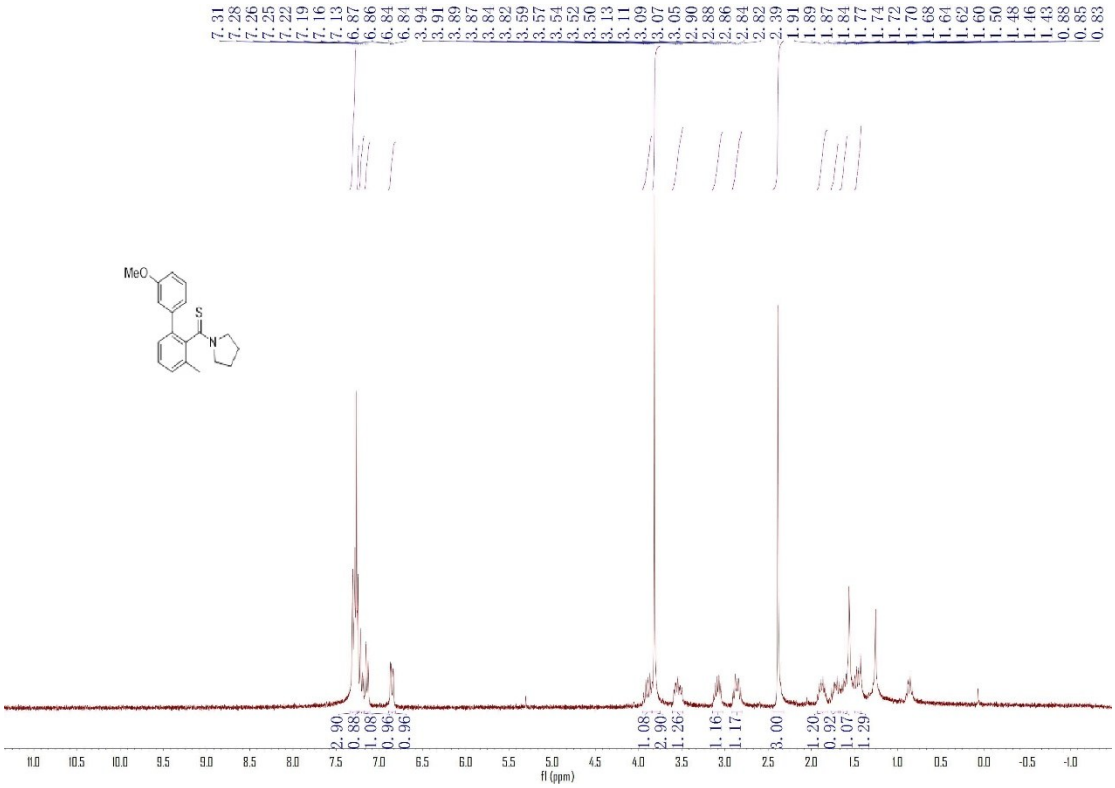
[1]H-NMR Spectrum of Compound 4c



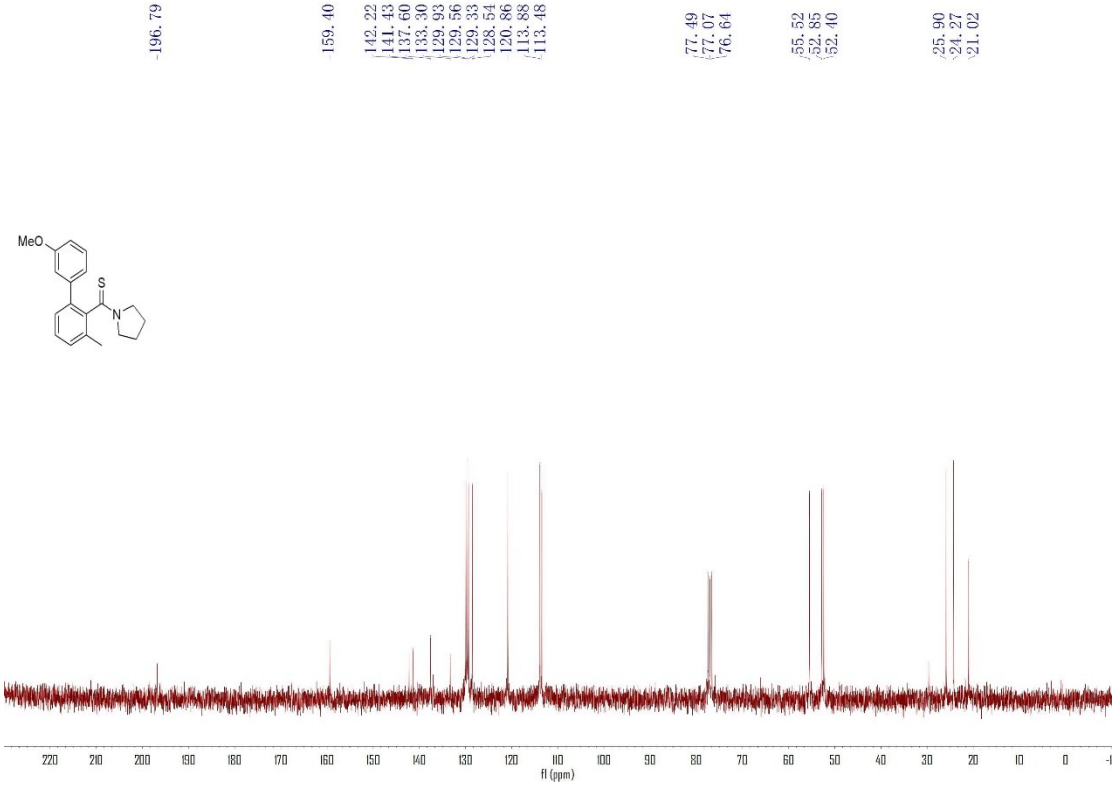
[13]C-NMR Spectrum of Compound 4c



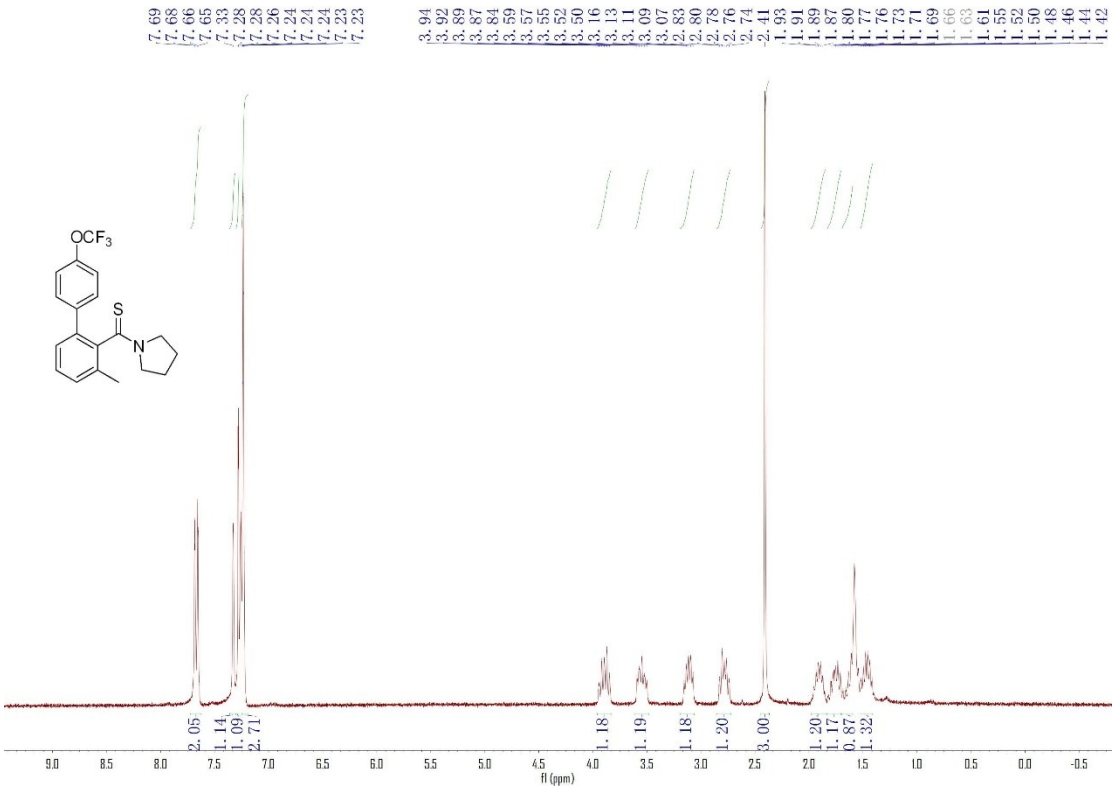
[1]H-NMR Spectrum of Compound 4d



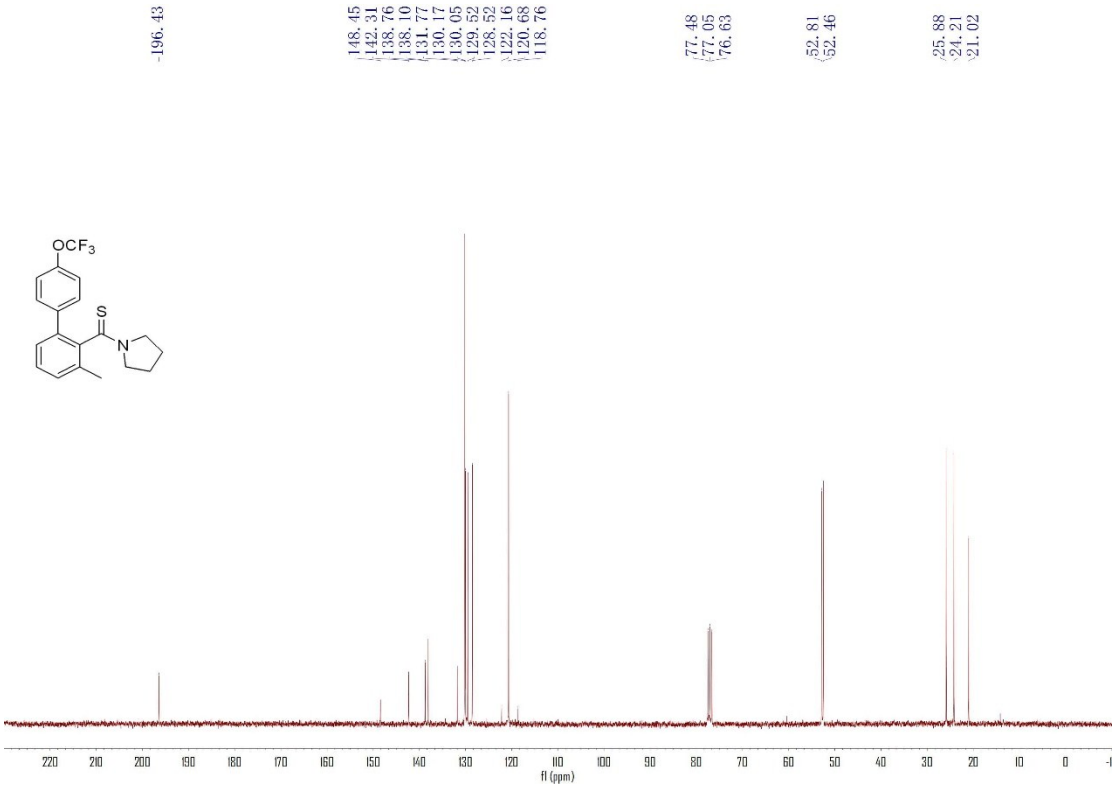
[13]C-NMR Spectrum of Compound 4d



^{1}H-NMR Spectrum of Compound 4e

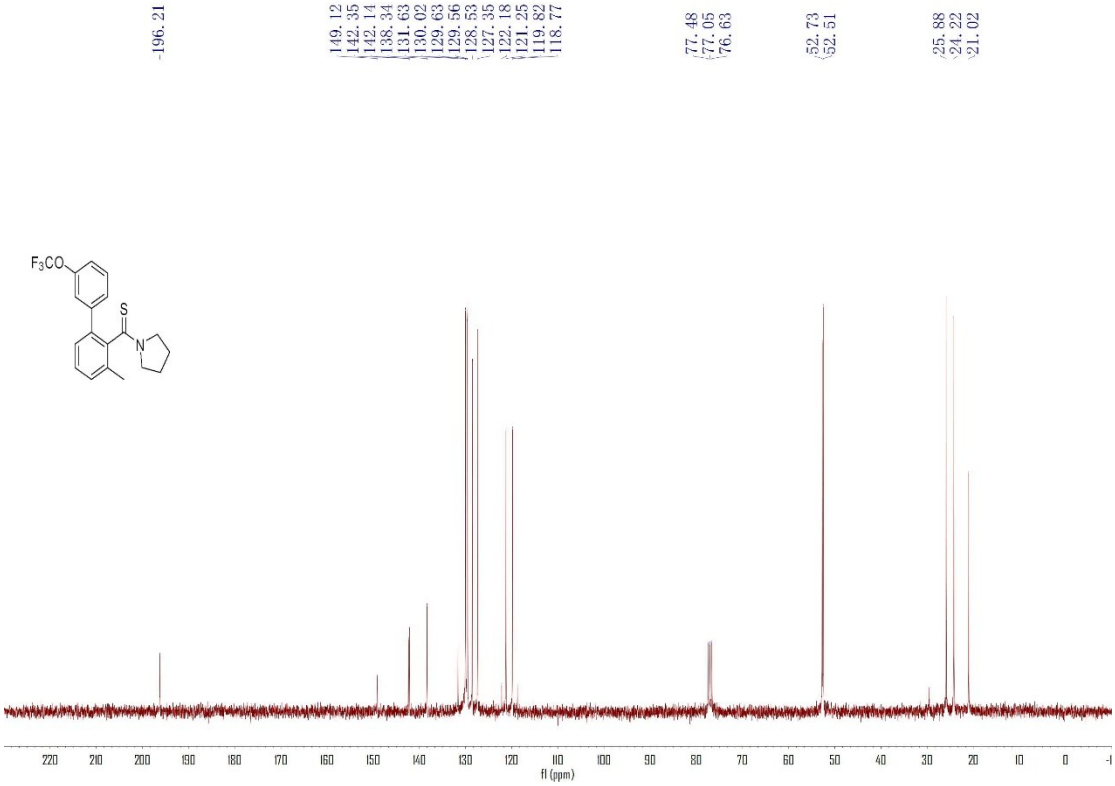


^{13}C-NMR Spectrum of Compound 4e

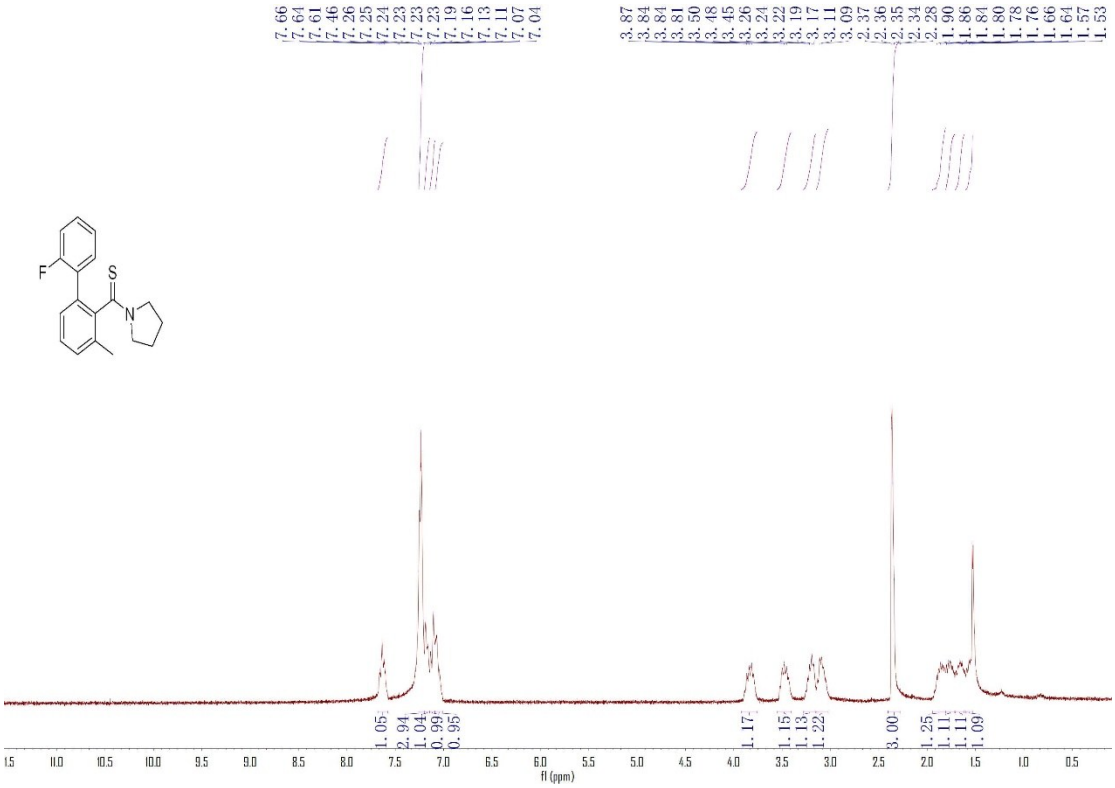


^{1}H-NMR Spectrum of Compound 4f

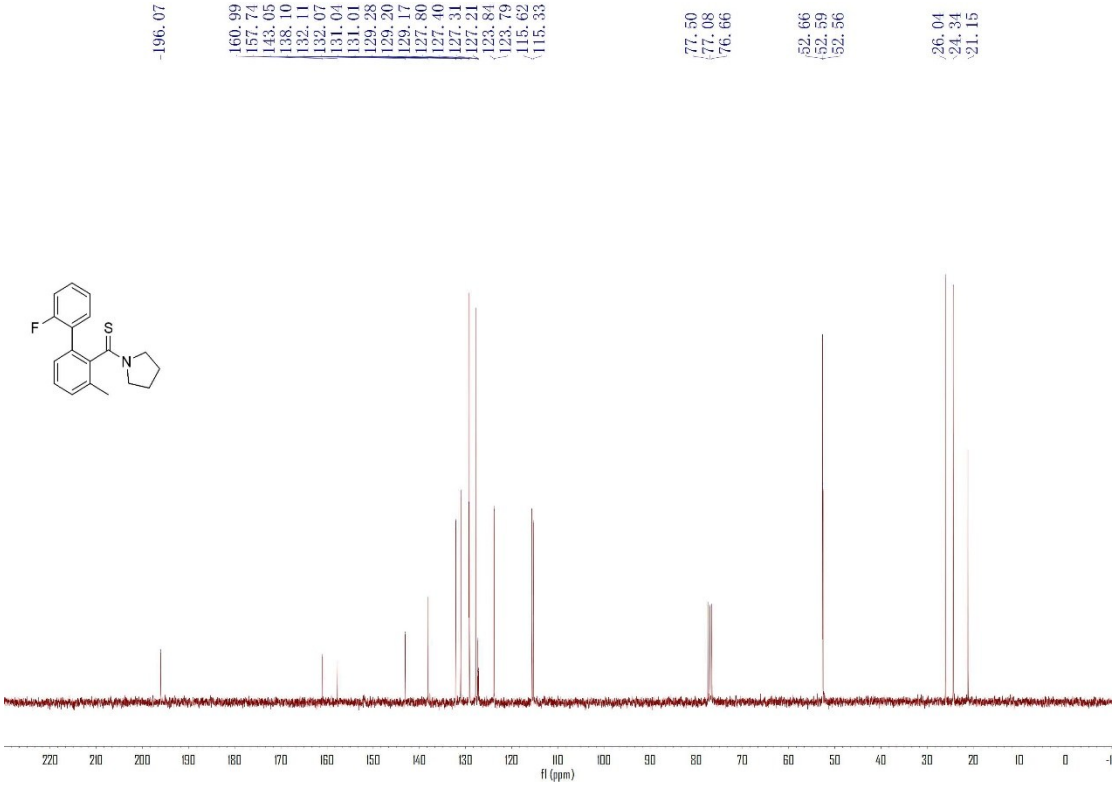
^{13}C-NMR Spectrum of Compound 4f



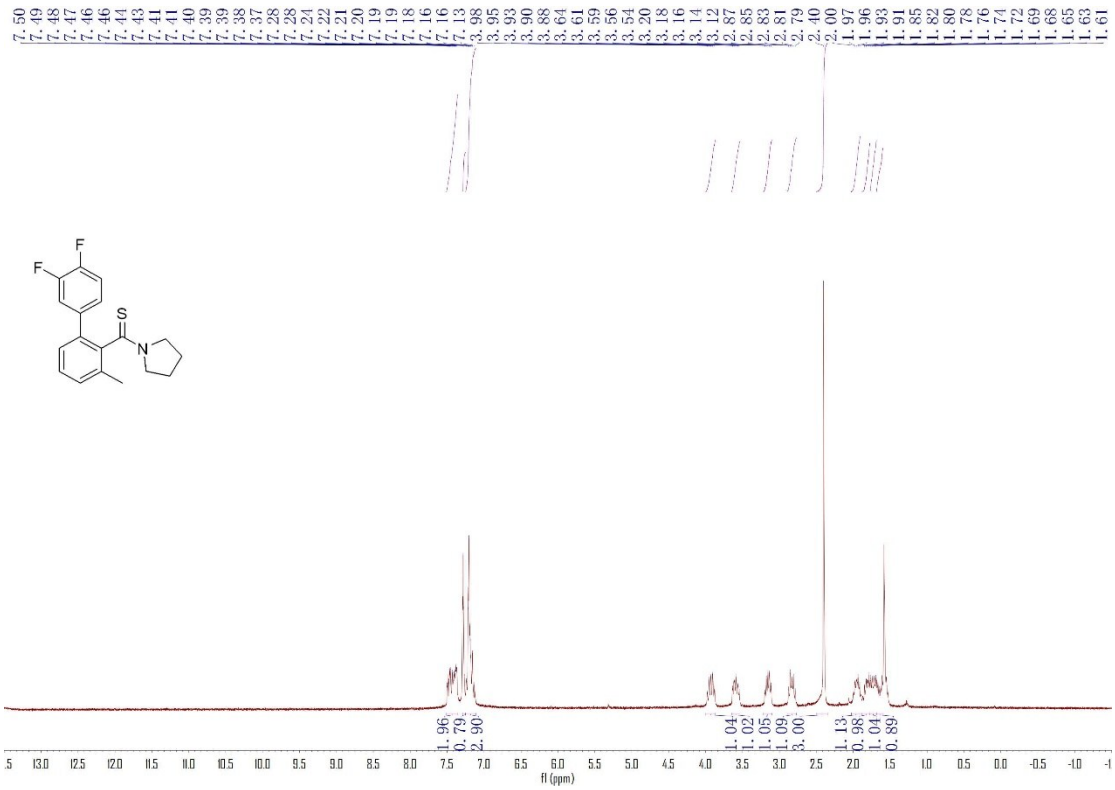
^{1}H-NMR Spectrum of Compound 4g



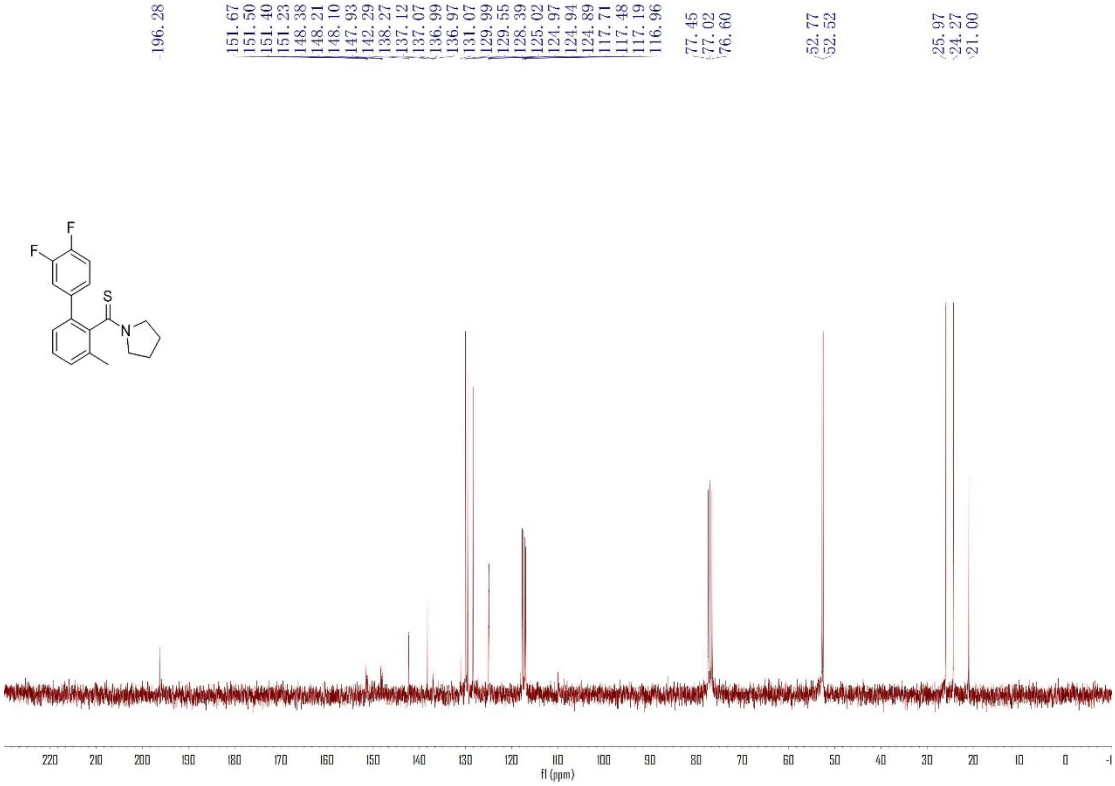
^{13}C-NMR Spectrum of Compound 4g



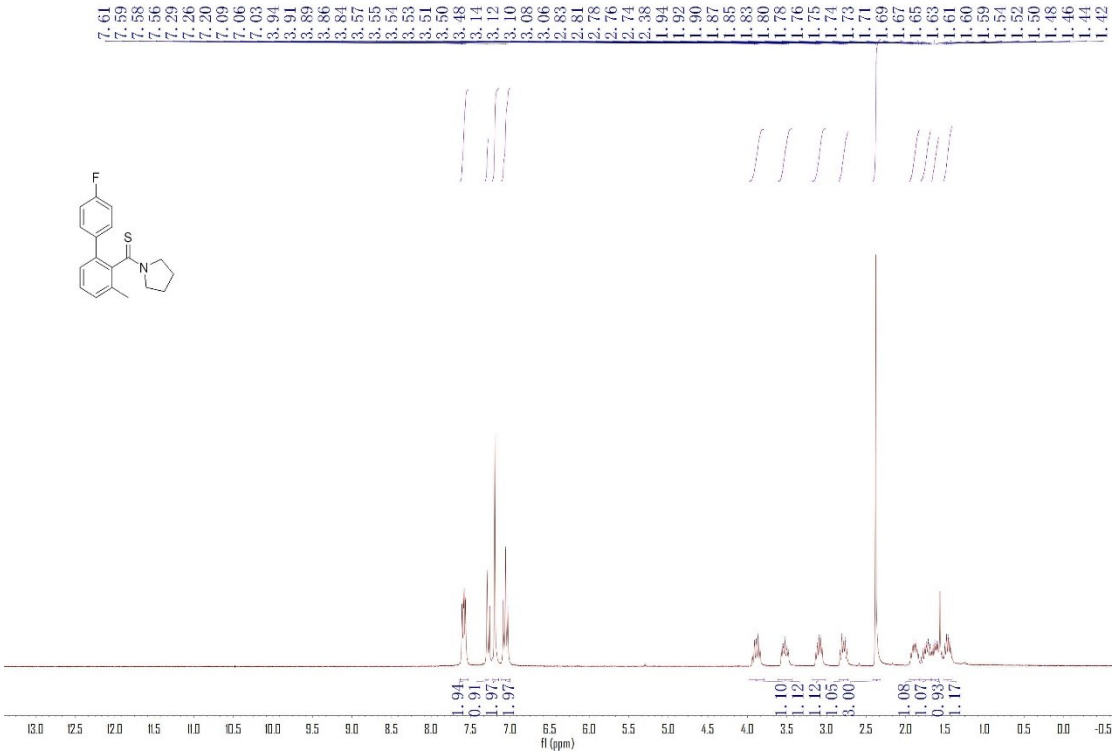
[1]H-NMR Spectrum of Compound 4h



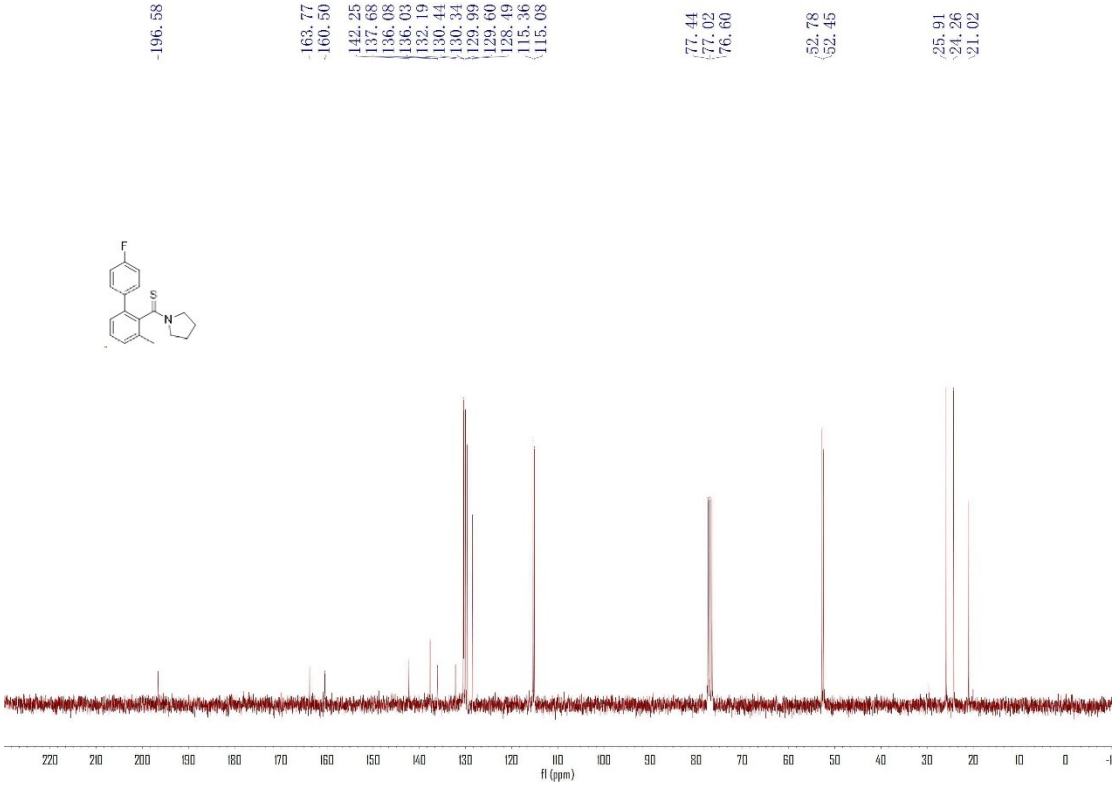
[13]C-NMR Spectrum of Compound 4h



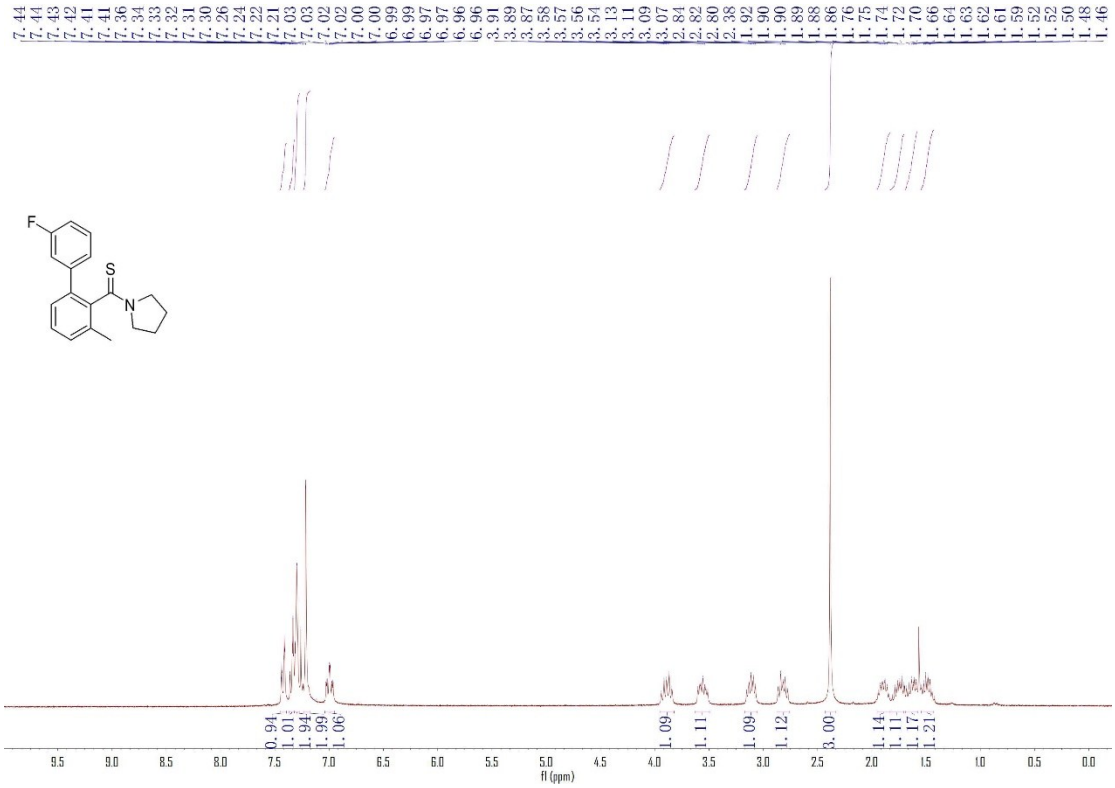
[1]H-NMR Spectrum of Compound 4i



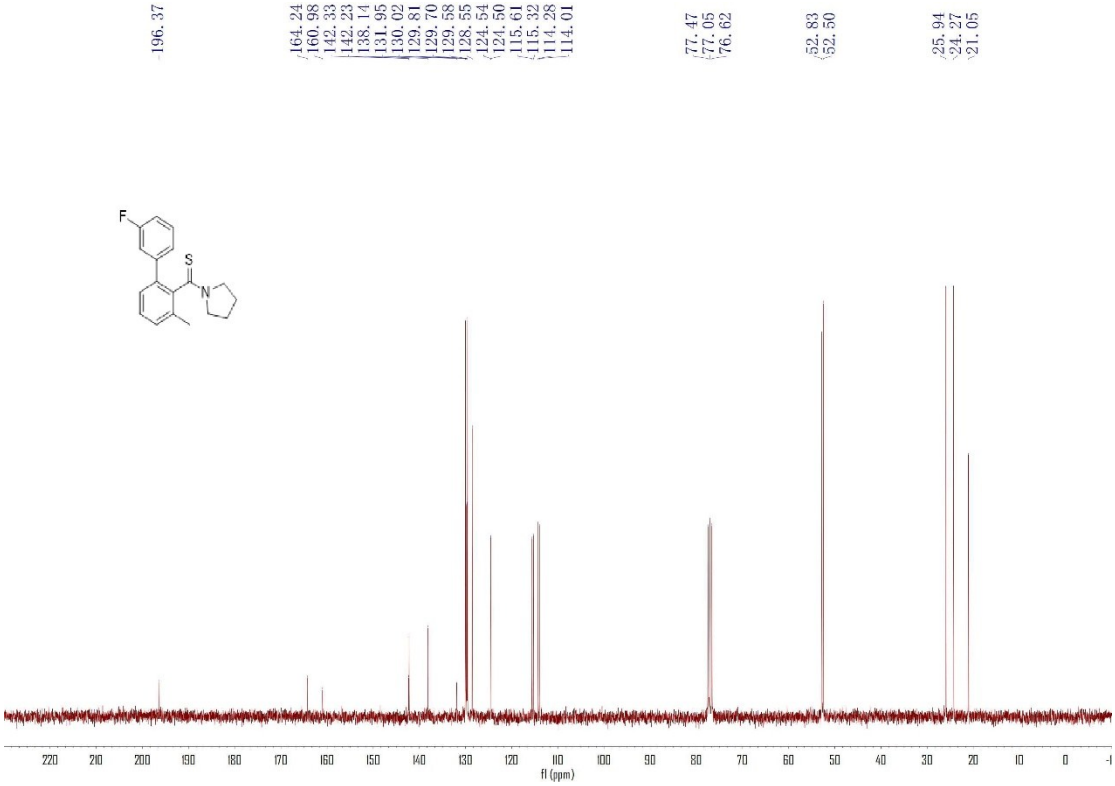
[13]C-NMR Spectrum of Compound 4i



[1]H-NMR Spectrum of Compound 4j

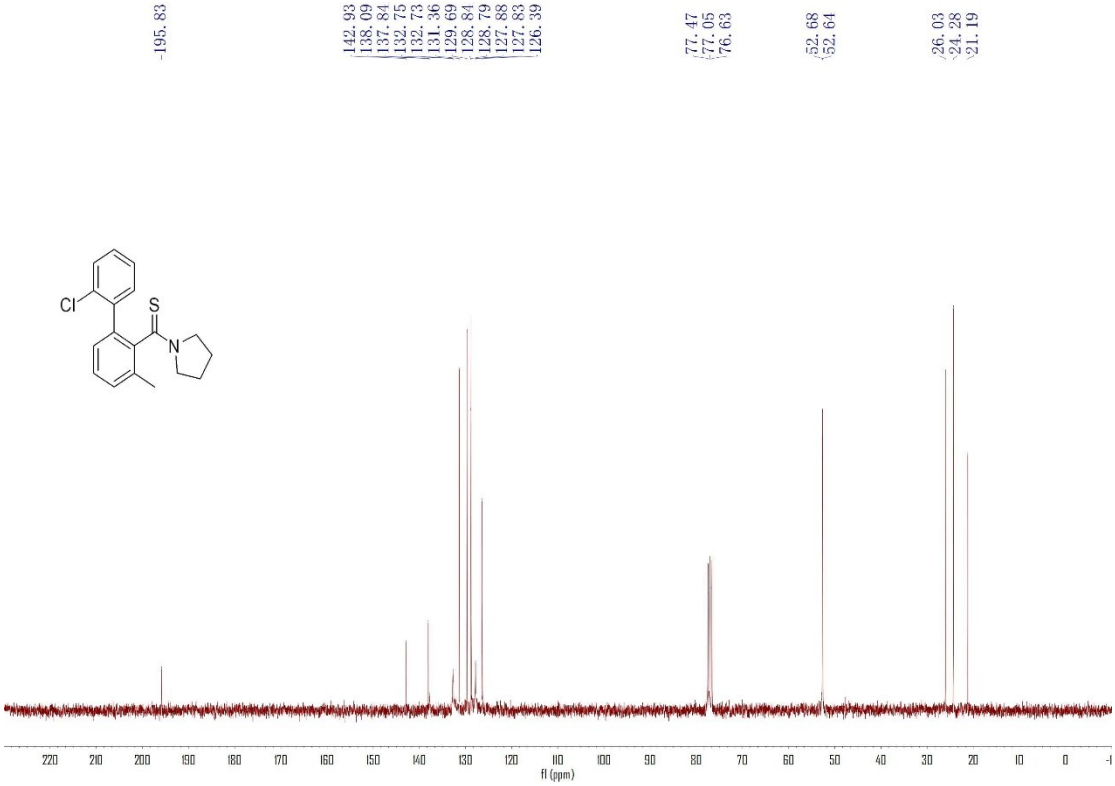


[13]C-NMR Spectrum of Compound 4j

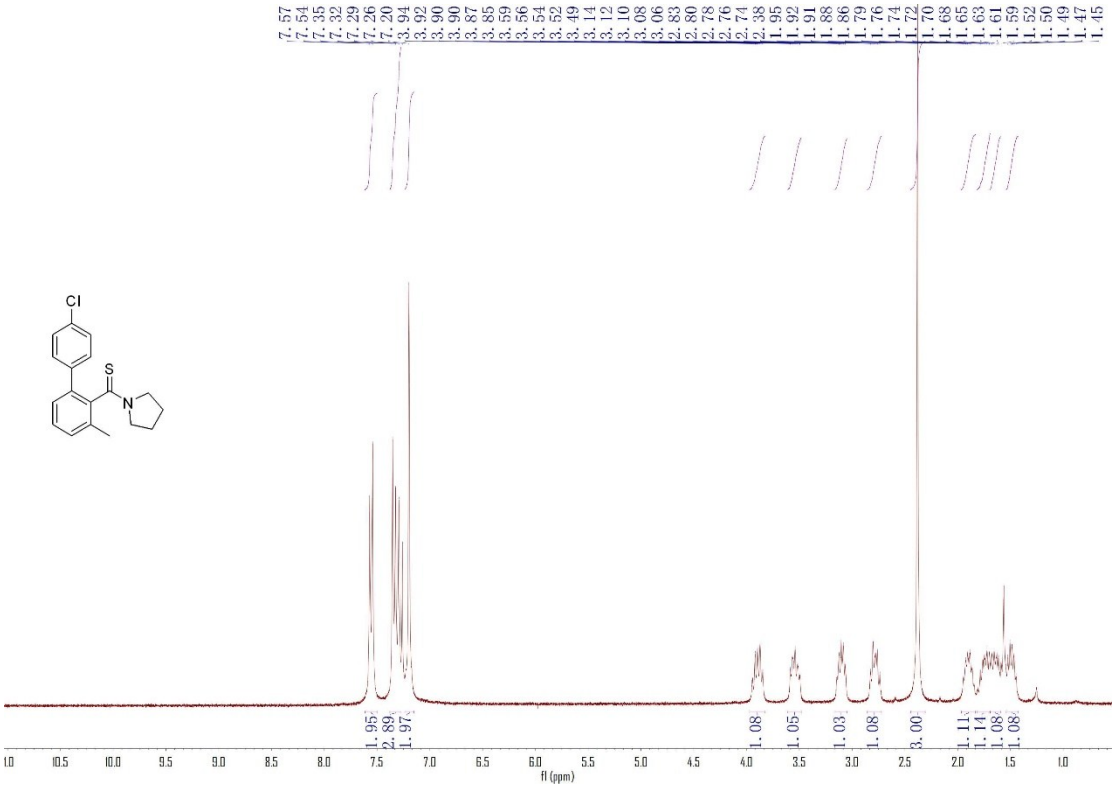


^{1}H-NMR Spectrum of Compound 4k

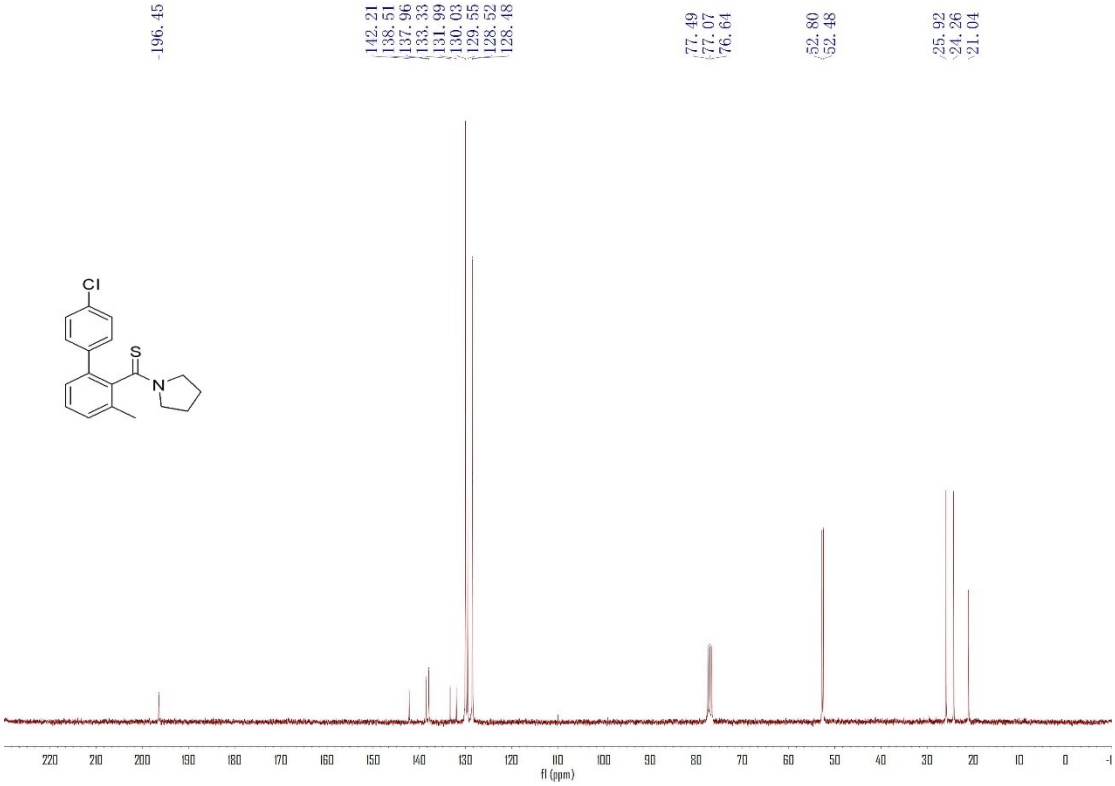
^{13}C-NMR Spectrum of Compound 4k



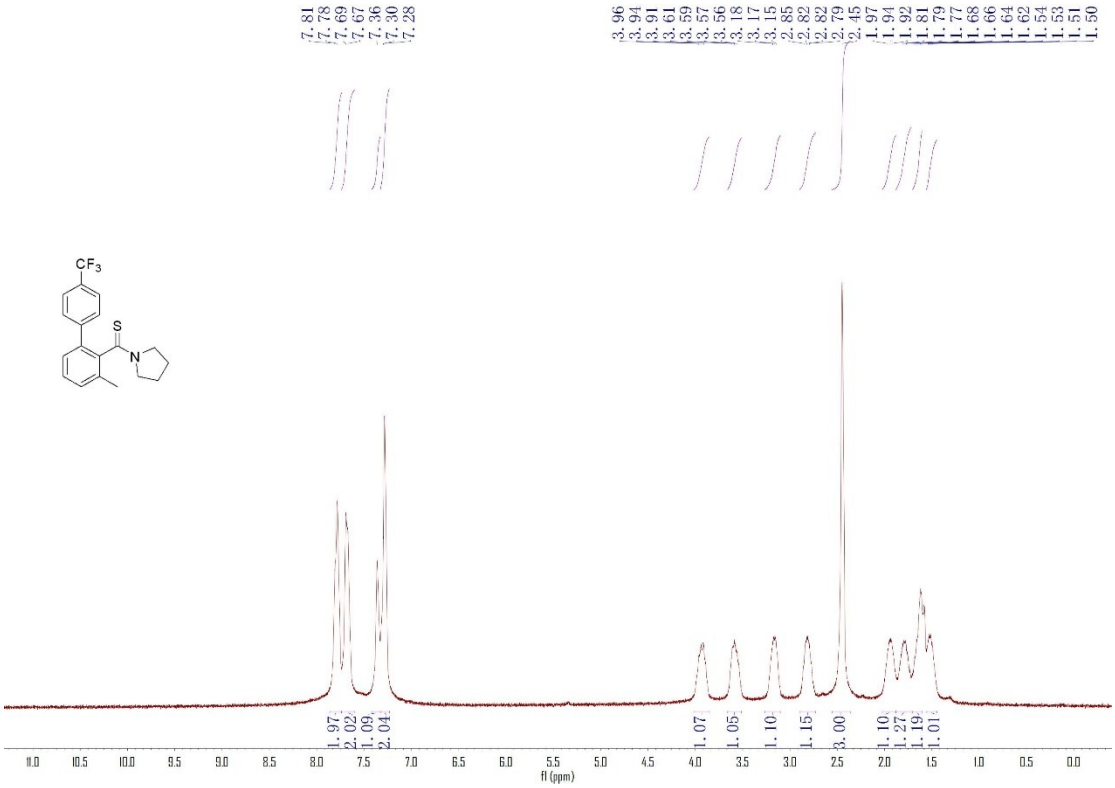
^{1}H-NMR Spectrum of Compound 4l



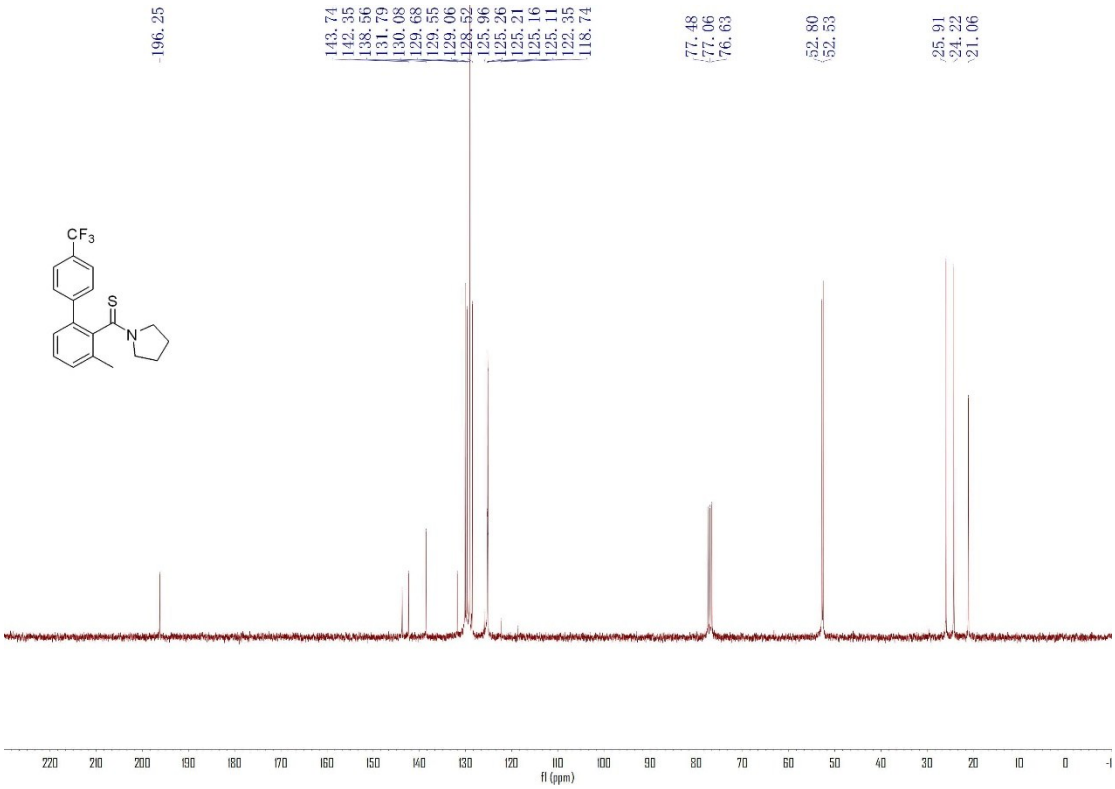
^{13}C-NMR Spectrum of Compound 4l



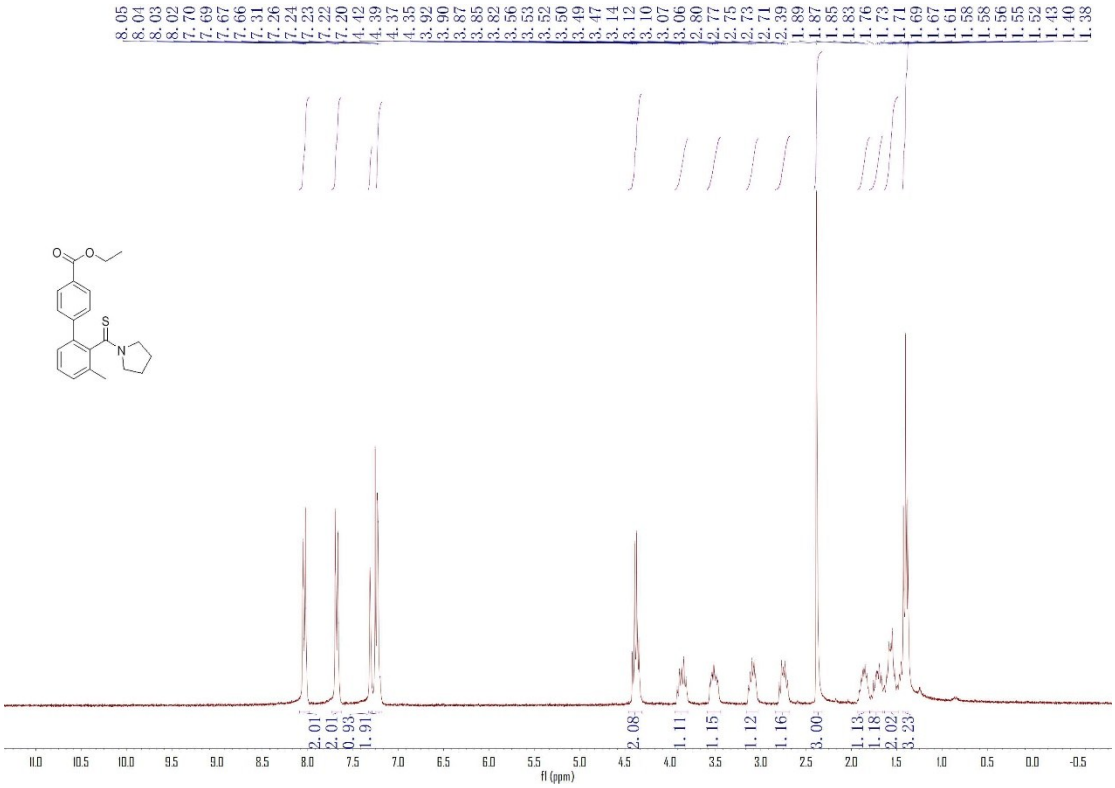
[1]H-NMR Spectrum of Compound 4m



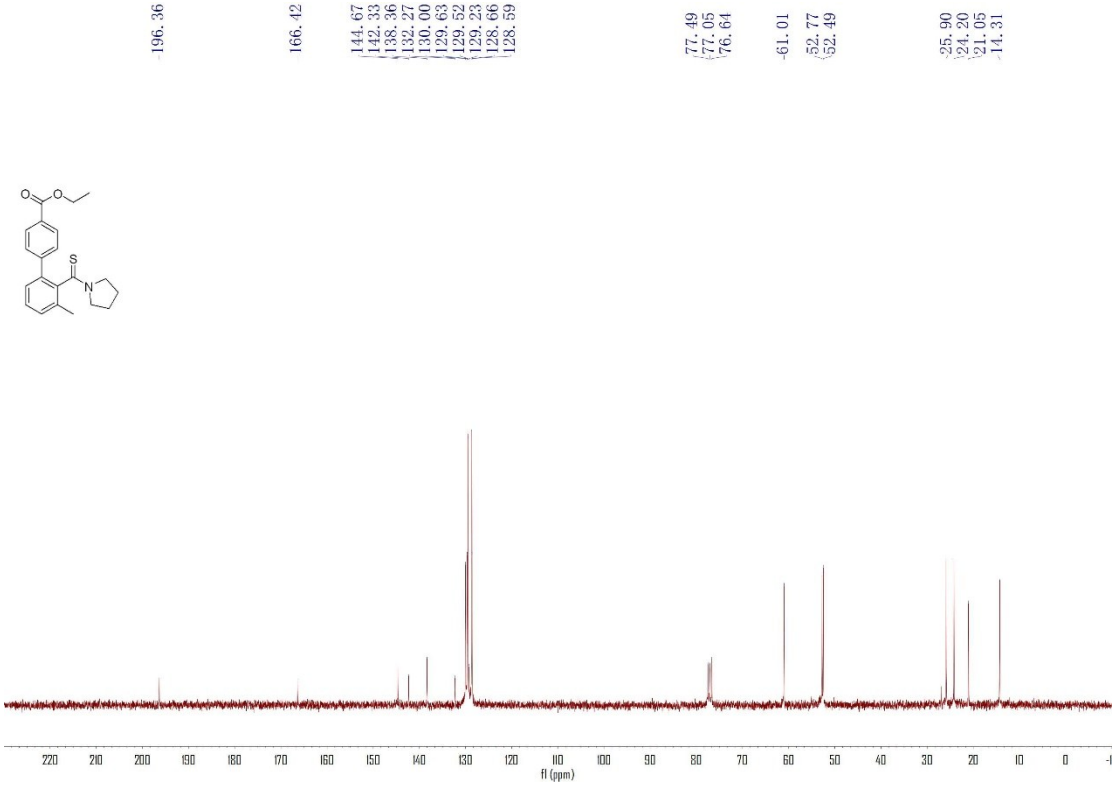
[13]C-NMR Spectrum of Compound 4m



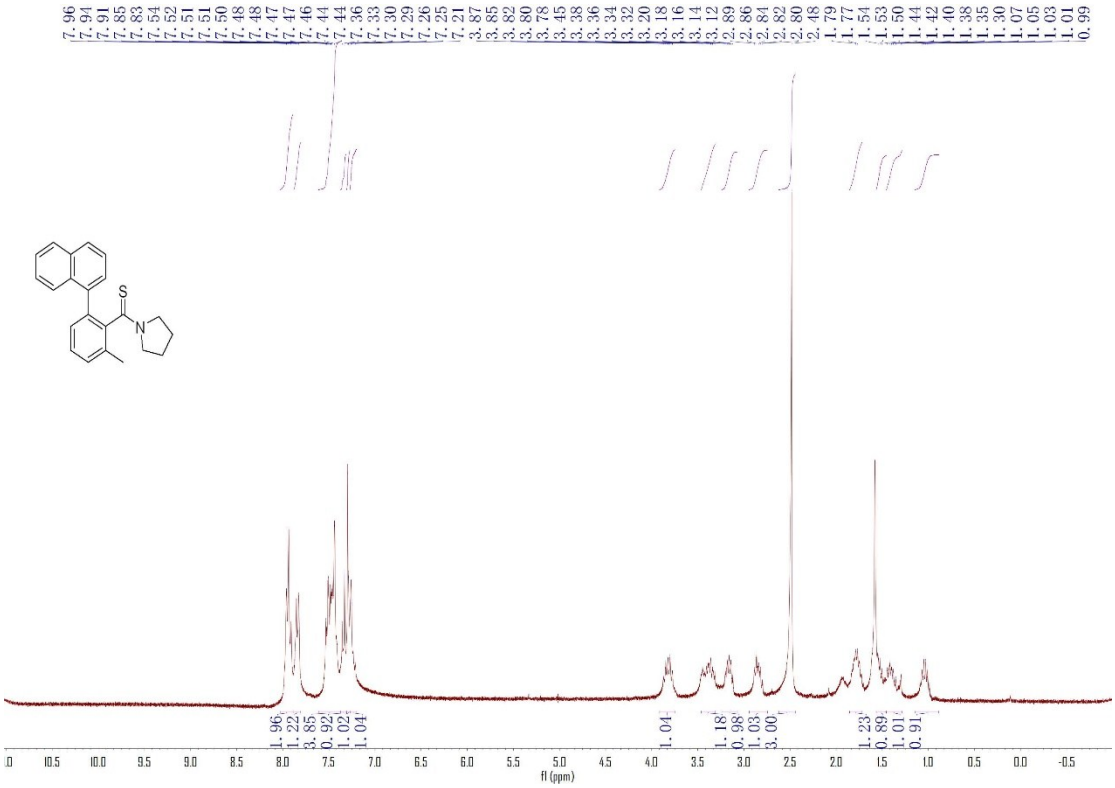
^{1}H-NMR Spectrum of Compound 4n



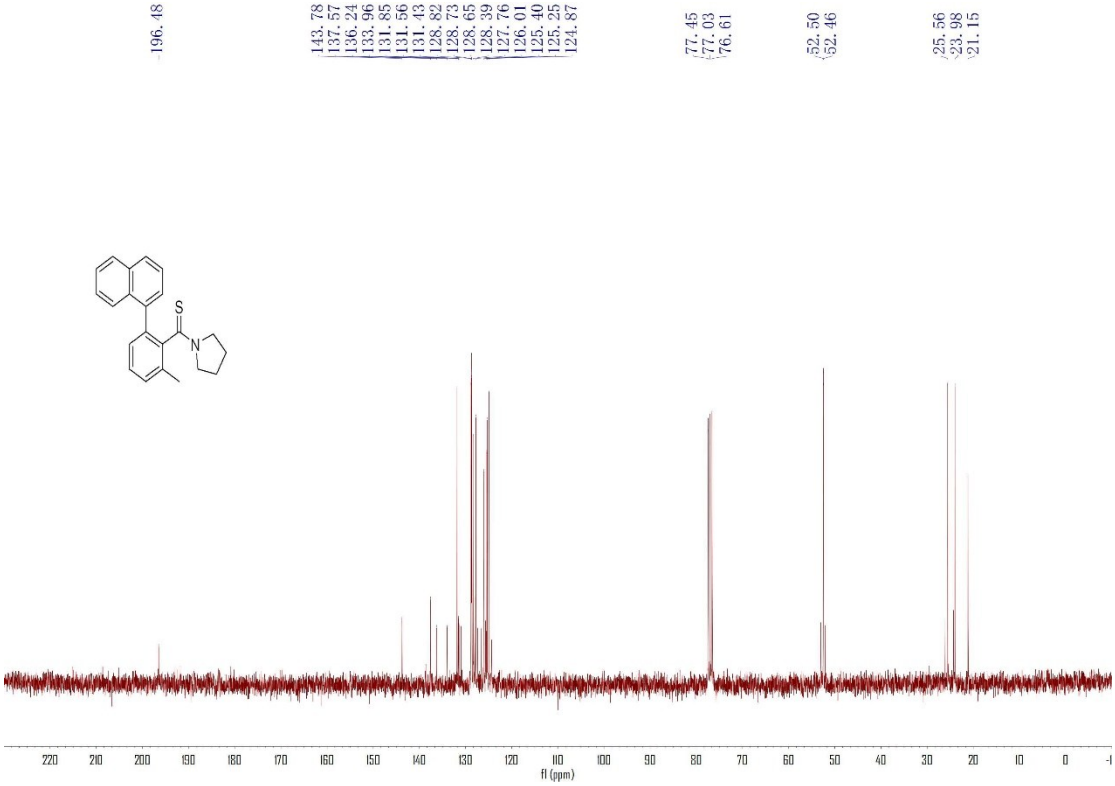
^{13}C-NMR Spectrum of Compound 4n



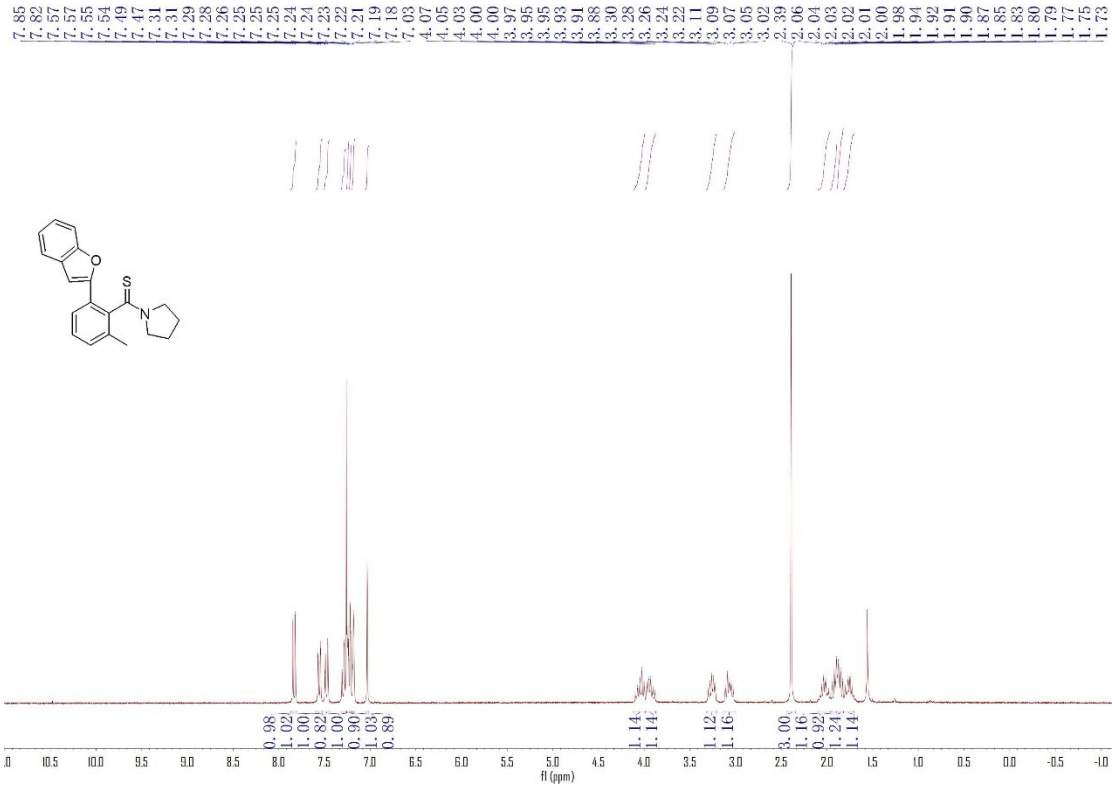
[1]H-NMR Spectrum of Compound 4o



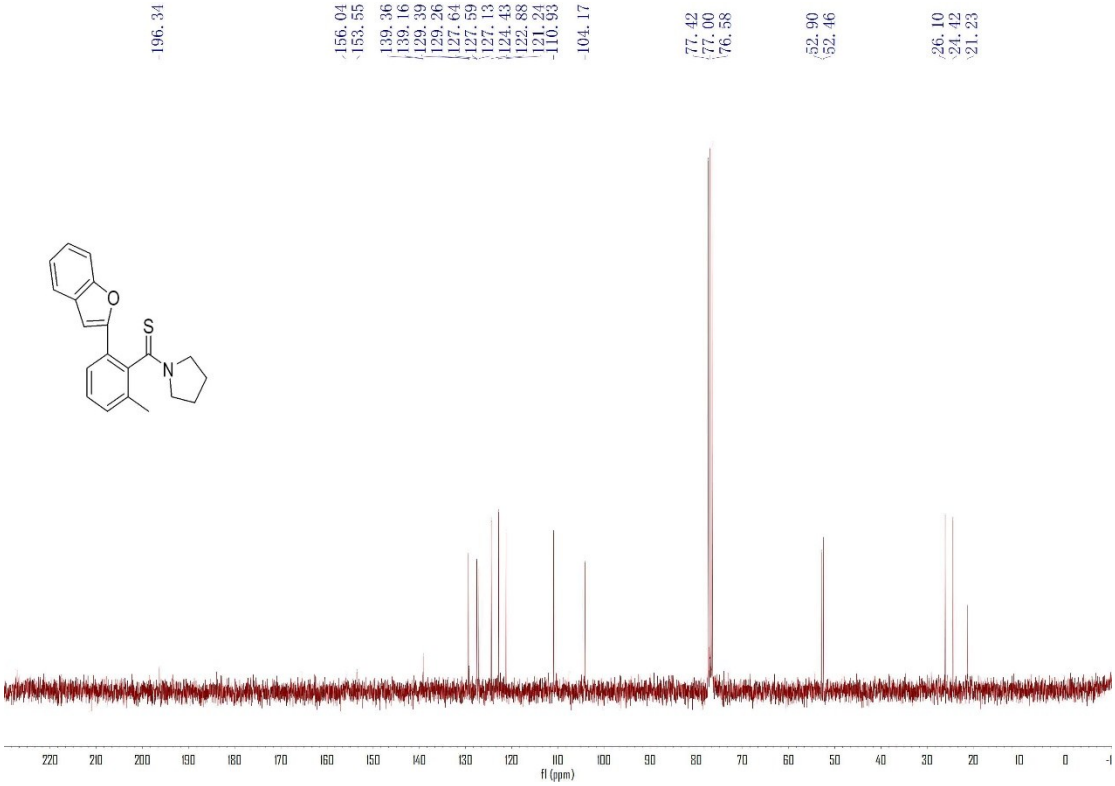
[13]C-NMR Spectrum of Compound 4o



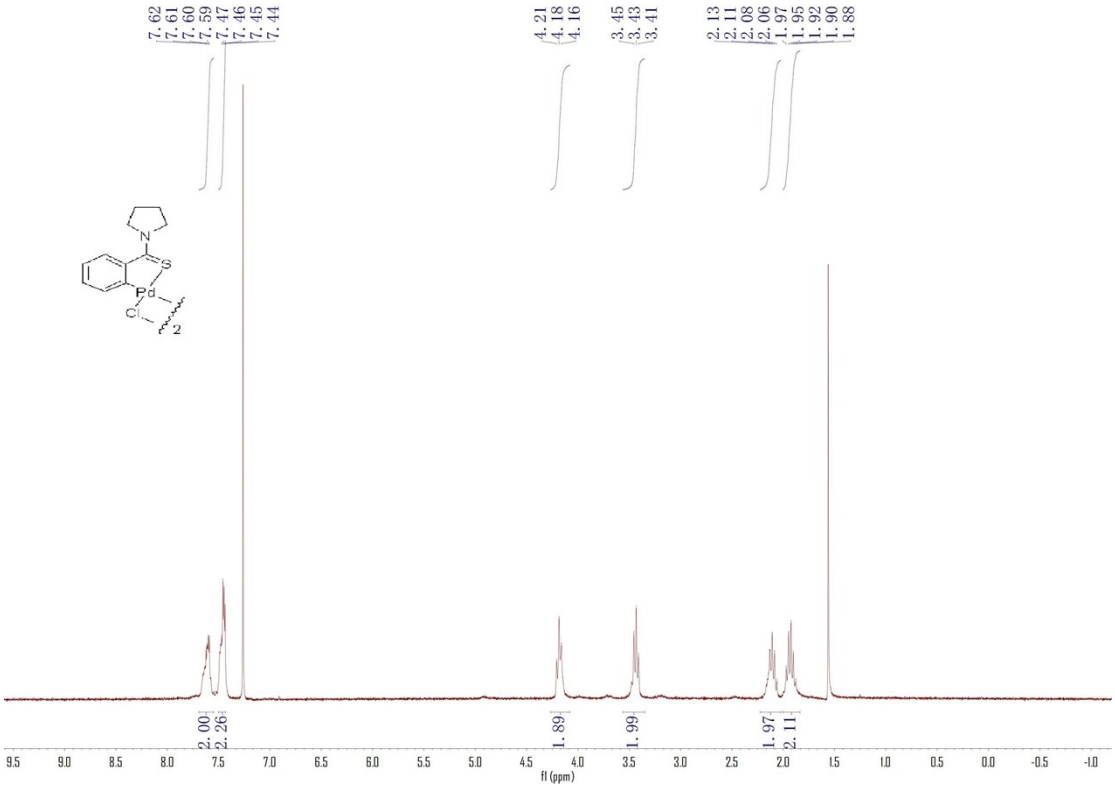
[1]H-NMR Spectrum of Compound 4p



[13]C-NMR Spectrum of Compound 4p



^{1}H-NMR Spectrum of Compound 5d



^{13}C-NMR Spectrum of Compound 5d