Supporting Information

Modular Multicomponent Cascade Synthesis of Benzo[*b*]thiophene-Fused N,O-Heterocycles from 1,2-Benzisothiazoles, Benzolactones and Aldehydes

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Table of Contents

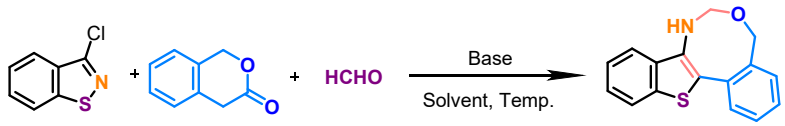
1. General Information 1
2. Optimization of Reaction Conditions.....1
3. Prerаration of Starting Materials 2
4. General Procedure for Synthesis of 1,2-Benzisothiazoles **1**, Benzofuran-2(3*H*)-ones **2,** 3-Isochromanones **5** and Aldehyde **3m**.....3
5. General Procedure for the Synthesis of **4** and **6**.....7
6. Mechanistic Studies 8
7. X-ray Diffraction Analysis of Compound **4k** 10
8. Characterization Data for Products 12
9. References 29
10. NMR Spectroscopic Data 30

1. General Information

^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz (100 MHz for ^{13}C NMR, 376 MHz for ^{19}F NMR) spectrometer. Chemical shift values are reported in ppm (parts per million) with tetramethylsilane (TMS) as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; td, triplet of doublets. The coupling constants (*J*) are reported in Hertz (Hz). Melting points were determined on a XT4A micromelting point apparatus and are uncorrected. High-resolution mass spectra (HRMS) were obtained on a Q-TOF Mass Spectrometer equipped with an electrospray ion source (ESI), and operated in the positive mode. The X-ray diffraction was measured on a Gmini E-type XRD. Column chromatography was performed over 200-300 mesh silica gel.

2. Optimization of Reaction Conditions

Table S1. Optimization of reaction conditions of eight-membered N,O-heterocycles **6**.[a]



1a **5a** **3a** **6a**

Entry	Solvent	Base	T(°C)	Yield(%)[b]
1	1,2-PG	K_2CO_3	r.t	36
2	1,2-PG	NaOH	r.t	30
3	1,2-PG	*t*-BuOK	r.t	28
4	1,2-PG	K_2CO_3	r.t	32
5	1,2-PG	DBU	r.t	34
6	1,2-PG	$NaHCO_3$	r.t	54
7	MeOH	$NaHCO_3$	r.t	47
8	EtOH	$NaHCO_3$	r.t	26
9	1,3-PG	$NaHCO_3$	r.t	20
10	EG	$NaHCO_3$	r.t	46
11	Isopropanol	$NaHCO_3$	r.t	0[c]
12	*n*-propanol	$NaHCO_3$	r.t	0[c]
13	*n*-BuOH	$NaHCO_3$	r.t	0[c]
14	*t*-BuOH	$NaHCO_3$	r.t	0[c]
15[d]	1,2-PG	$NaHCO_3$	60	58
16[e]	**1,2-PG**	**$NaHCO_3$**	**80**	**74**

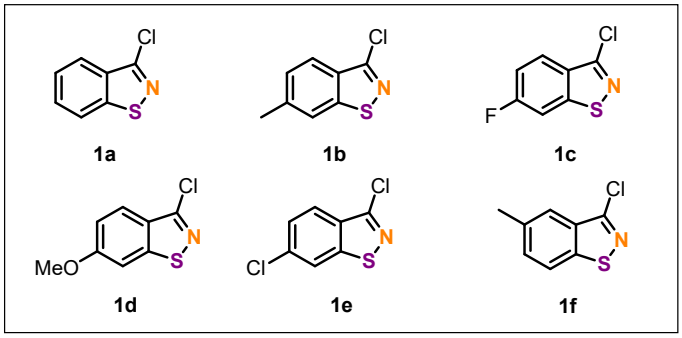
17[f]	1,2-PG	$NaHCO_3$	100	72

[a]Reaction conditions: Unless noted otherwise, **1a** (0.2 mmol), **5a** (0.24 mmol), HCHO (0.6 mmol), base (0.6 mmol) and solvent (2 mL) at room temperature for 10 h. [b]Isolated yields. [c]No Reaction. [d]at 60 °C for 8 h. [e]at 80 °C for 7 h. [f]at 100 °C for 5 h.

3. Prerаration of Starting Materials

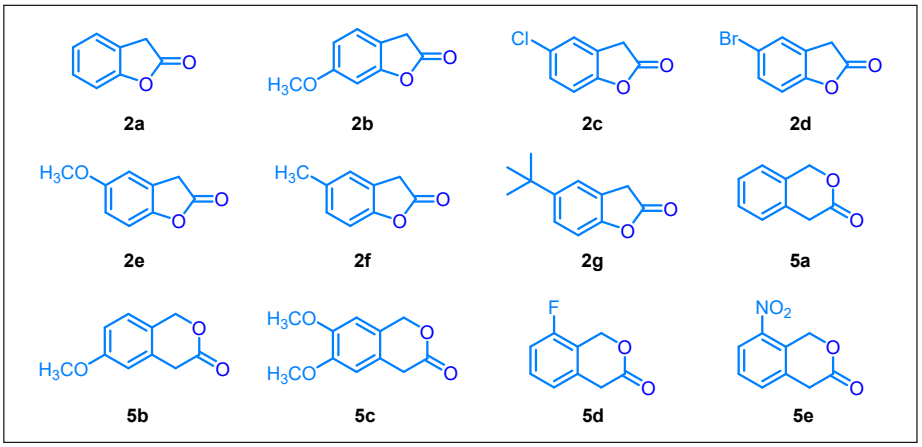
3.1 General Procedure for Prerаration of 1,2-Benzisothiazoles

3-Chlorobenzo[*d*]isothiazole **1a** was commercially purchased; 1,2-Benzisothiazoles **1b-1f** were prepared following previous literature procedures and obtained characterization data were in alignment with the literature reported data.[1]



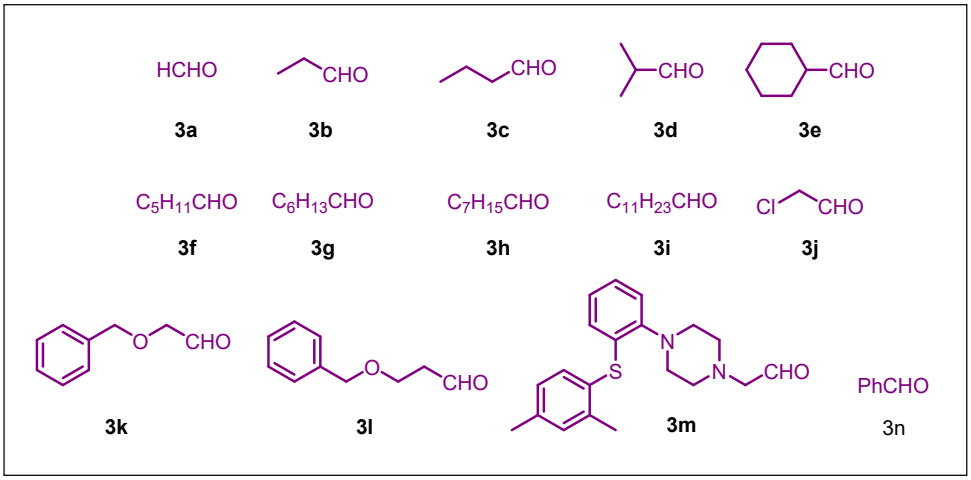
3.2 General Procedure for Prerаration of Benzofuran-2(3*H*)-ones and 3-Isochromanones

Benzofuran-2(3*H*)-ones **2a, 2b, 2c** and 3-Isochromanone **5a** were commercially purchased; Benzofuran-2(3*H*)-ones **2d-2g** and 3-Isochromanones **5b-5e** were prepared following previous literature procedures and obtained characterization data were in alignment with the literature reported data.[2-6]



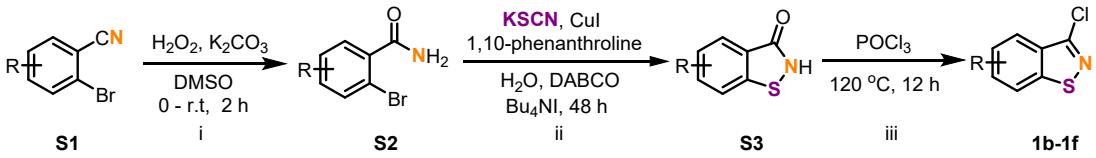
3.3 General Procedure for Prerаration of Aldehyde

Formaldehyde solution **3a** (contains 10-15% methanol as stabilizer, 37 wt. % in H_2O), **3b-3l and 3n** were commercially purchased; **3m** was prepared following previous literature procedures.[7-8]



4. General Procedure for Synthesis of 1,2-Benzisothiazoles 1, Benzofuran-2(3*H*)-ones 2, 3-Isochromanones 5 and Aldehyde 3m

4.1 General Procedure for Synthesis of 1,2-Benzisothiazoles 1[1]



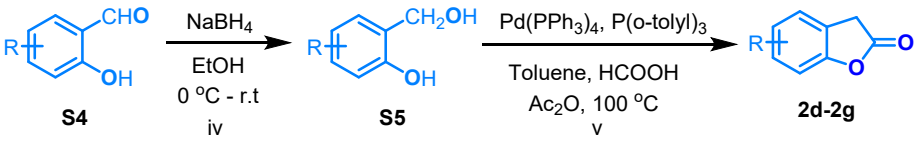
(i) To a dry 250 mL round-bottom flask was added 2-Bromobenzonitrile **S1** (10 mmol) and K_2CO_3 (30 mmol) in DMSO in an ice bath. Then, a solution of 30% H_2O_2 (4.5 g, 40 mmol) was added dropwise to the solution at 0 °C over a period of 30 min. The reaction mixture was stirred at room temperature for 0.5-2 h until substrate consumed as indicated by TLC. The reaction was quenched with H_2O (50 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were washed with brine (3 × 50 mL), then dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated *in vacuo* dried to afford *o*-halobenzamide **S2**. The crude products could be directly used for the next reaction without further purification.

(ii) To a sealed tube was added *o*-halobenzamide **S2** (1.1 g, 5 mmol), potassium thiocyanate (971.8 mg, 10 mmol), CuI (95.2 mg, 0.5 mmol), 1,10-phenanthroline (180.2 mg, 1.0 mmol), DABCO (1.1 g, 10 mmol), and Bu_4NI (369.4 mg, 1 mmol) and

H_2O (10 mL) in sequence, and then stirred at room temperature for 1.5 h. Then the reaction was heated to 140-160 °C in an oil bath and stirred for 48 h until it was judged to be complete by TLC. Then the reaction mixture was cooled to room temperature, quenched the reaction with H_2O (50 mL) and extracted with ethyl acetate (3 × 50 mL). The organic layer was dried over anhydrous Na_2SO_4, evaporated *in vacuo*, and purified by flash silica gel column chromatography (gradient eluent: 2:1~1:1 petroleum ether/ethyl acetate) to afford benzisothiazol-3(2*H*)-one **S3**.

(iii) To a sealed tube was added the corresponding benzisothiazol-3(2*H*)-one **S3** (82.6 mg, 0.5 mmol) and $POCl_3$ (2 mL) and then stirred at 120 °C for 12 h until it was judged to be complete by TLC. Then the reaction mixture was cooled to room temperature, quenched the reaction with H_2O (10 mL) and extracted with ethyl acetate (3 × 10 mL). The organic layer was dried over anhydrous Na_2SO_4, evaporated *in vacuo*, and purified by flash silica gel column chromatography (gradient eluent: 20:1~10:1 petroleum ether/ethyl acetate) to afford 1,2-benzisothiazoles **1b-1f**.

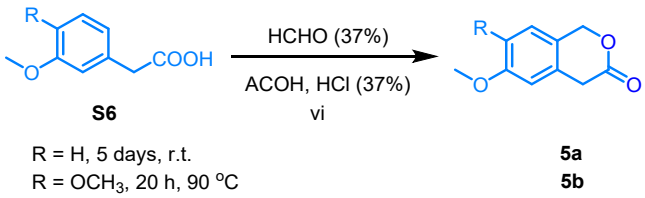
4.2 General Procedure for Synthesis of Benzofuran-2(3*H*)-ones 2



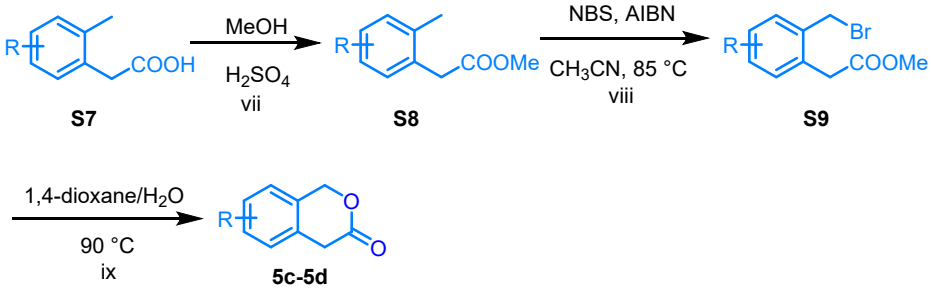
(iv) Sodium borohydride (136.2 mg, 3.6 mmol) was added in several portions to a stirring solution of salicylaldehyde (3 mmol) in ethanol (6 mL) at 0 °C. The reaction mixture was stirred at room temperature for 1 h. After the solvent was removed, H_2O (15 mL) and 1 N aqueous HCl solution (6 mL) were added to the residue and extracted with ethyl acetate (4 × 10 mL). The organic layers were combined, dried over Na_2SO_4 and filtered. The solution was evaporated *in vacuo* to afford the corresponding benzyl alcohol. The crude products could be directly used for the next reaction without further purification.[2]

(v) $Pd(PPh_3)_4$ (5 mol %) and P(*o*-tolyl) (20 mol %) were transferred into an oven-dried tube which was filled with nitrogen. Toluene (2 mL), 2-hydroxybenzyl alcohols (1 mmol) were added into the reaction tube. Then a mixture of formic acid (3.0 mmol) and acetic anhydride (3.0 mmol) was added to the reaction tube which was stirred for 1.5 h at 30 °C. The mixture was stirred for 2-3 h at 100 °C. After the reaction was complete, the reaction mixture was filtered and concentrated, column chromatography on silica gel (petroleum ether/ethyl acetate 20:1).[3]

4.3 General Procedure for Synthesis of 3-Isochromanones 5[4-6]



(vi) To a dry 100 mL round-bottom flask was added 3- Methoxyphenyl acetic acid (18.4 mmol), formaldehyde (37% aqueous) (4.5 mL), HCl (12 N) (1 mL) and glacial acetic acid (12 mL) in sequence, and then stirred until it was judged to be complete by TLC. Then the reaction mixture was quenched with $NaHCO_3$ and extracted with ethyl acetate (3 × 30 mL). The separated aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with brine (3 × 30 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated *in vacuo*. The crude residue was purified by column chromatography on silica gel (gradient eluent: 6:1~4:1 petroleum ether/ethyl acetate) to afford **5a** and **5b**.[4]

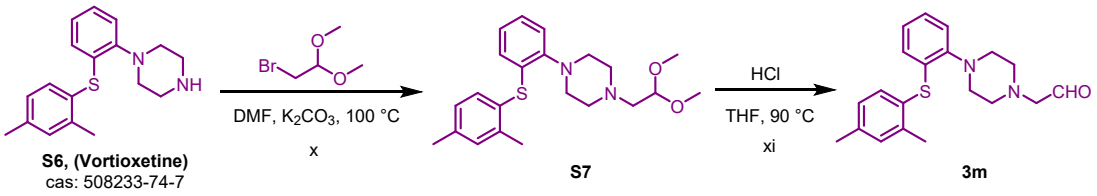


(vii) Concentrated H_2SO_4 (0.5 mL) was added to a solution of 2-(*o*-tolyl)acetic acid **S7** (5.35 mmol) in MeOH (15 mL) and the mixture was refluxed for overnight. The solvent was removed under reduced pressure, the crude rinsed up with ethyl acetate and washed twice with $NaHCO_3$ saturated solution and brine. The filtrate was evaporated *in vacuo*. The crude products could be directly used for the next reaction without further purification.

(viii) The obtained ester **S8** (4.95 mmol) was dissolved in CH_3CN (10 mL) and treated with *N*-bromosuccinimide (NBS, 968 mg, 5.94 mmol) and azaisobutyrronitrile (AIBN, 81 mg, 0.49 mmol) at 85°C in an oil bath for overnight. Then, the mixture was extracted by ether/water to remove succinimide and used for the next reaction without further purification.

(ix) the crude product **S9** (3.84 mmol) was dissolved in 1,4 dioxane/water (12 mL, 1/1) and refluxed at 90°C in an oil bath for overnight. Then, solvent was removed under reduced pressure and the crude was taken up with ethyl acetate. The crude residue was purified by column chromatography on silica gel (gradient eluent: 10:1~8:1 petroleum ether/ethyl acetate) to afford **5c** and **5d**.[5-6]

4.4 General Procedure for Synthesis of Aldehyde 3m



S6, (Vortioxetine)
cas: 508233-74-7

S7

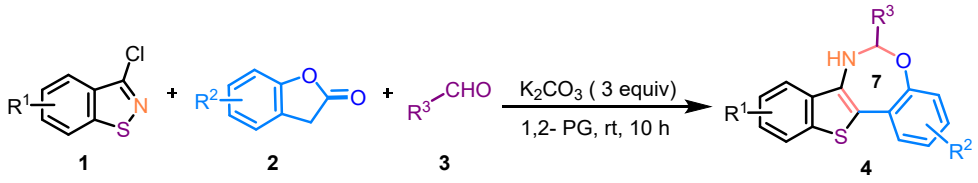
3m

(x) To a sealed tube was added the corresponding Vortioxetine **S6** (300 mg, 1.0 mmol), 2-bromo-1,1-dimethoxyethane (254 mg, 1.5 mmol), K_2CO_3 (276 mg, 2.0 mmol) and DMF (5 mL) in sequence, and then stirred at 100 °C for 6 h until it was judged to be complete by TLC. Then the reaction mixture was cooled to room temperature, quenched the reaction with H_2O (30 mL) and extracted with ethyl acetate (3 × 30 mL). The separated aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with brine (3 × 30 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated *in vacuo*. The crude residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (4:1) as eluent to afford product **S7** (336.3 mg, 87%) as a white solid.[7]

(xi) To a dry 50 mL round-bottom flask was added **S7** (300 mg, 0.78 mmol) and 4M HCl (2 mL) and THF in sequence, and then stirred at 90 °C for 2 h until it was judged to be complete by TLC. Then the reaction mixture was cooled to room temperature, quenched the reaction with $NaHCO_3$ (30 mL) and extracted with ethyl acetate (3 × 30 mL). The separated aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with brine (3 × 30 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated *in vacuo*. The crude products could be directly used for the next reaction without further purification.[8]

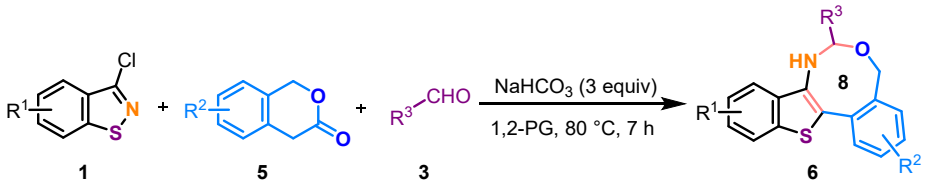
5. General Procedure for the Synthesis of 4 and 6

5.1 General Procedure for Synthesis of Benzo[*b*]thiophene-fused Seven-membered N,O-heterocycle Compounds 4



To a solution of 1,2-benzisothiazole **1** (0.2 mmol) in 1,2-PG (2 mL) was added benzofuran-2(3*H*)-one **2** (0.24 mmol) and K_2CO_3 (83 mg, 0.6 mmol), the resulting mixture was stirred at room temperature for 8 h. The reaction progress was monitored by TLC until completion. Then, aldehyde **3** (0.3 mmol) was added dropwise to the solution. The reaction mixture was stirred at room temperature for 2 h until substrate consumed as indicated by TLC. The mixture was partitioned between H_2O (15 mL) and EtOAc (15 mL). The separated aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine (3 × 15 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated *in vacuo*. The crude residue was purified by column chromatography on silica gel (gradient eluent: 15:1~8:1 petroleum ether/ethyl acetate) to afford typical product **4**.

5.2 General Procedure for Synthesis of Benzo[*b*]thiophene-fused Eight-membered N,O-heterocycle Compounds 6

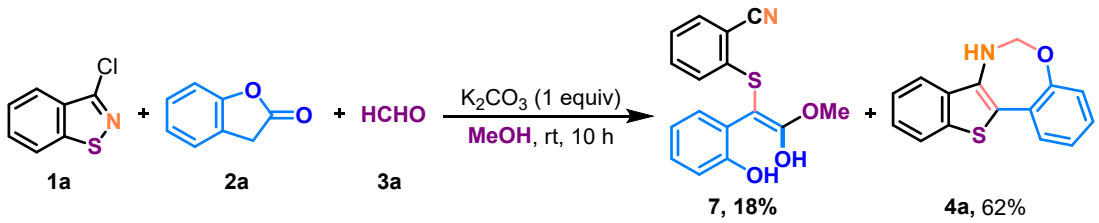


To a solution of 1,2-benzisothiazole **1** (0.2 mmol) in 1,2-PG (2 mL) was added 3-isochromanone **5** (0.24 mmol) and $NaHCO_3$ (50 mg, 0.6 mmol), the resulting mixture was stirred at 80 °C for 4 h. The reaction progress was monitored by TLC until completion. Then, aldehyde **3** (0.6 mmol) was added dropwise to the solution. The reaction mixture was stirred at 80 °C for 3 h until substrate consumed as indicated by TLC. The mixture was partitioned between H_2O (15 mL) and EtOAc (15 mL). The separated aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine (3 × 15 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated *in vacuo*. The crude residue was purified by column chromatography on silica gel (gradient eluent: 10:1~6:1 petroleum ether/ethyl acetate) to afford typical product **6**.

6. Mechanistic Studies

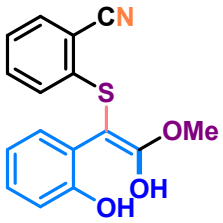
6.1 Control Experiments

6.1.1 Synthesis Step and Characterization Data of the Compound 7



General procedure: To a solution of 1,2-benzisothiazole **1a** (33.9 mg, 0.2 mmol) in MeOH (2 mL) was added benzofuran-2(3*H*)-one **2a** (32.2 mg, 0.24 mmol) and K_2CO_3 (27.6 mg, 0.2 mmol), the resulting mixture was stirred at room temperature for 8 h. The reaction progress was monitored by TLC until completion. Then, formaldehyde solution **3a** (contains 10-15% methanol as stabilizer, 37 wt. % in H_2O) **3a** (24.3 mg, 0.3 mmol) was added dropwise to the solution. The reaction mixture was stirred at room temperature for 2 h until substrate consumed as indicated by TLC. The mixture was partitioned between H_2O (15 mL) and EtOAc (15 mL). The separated aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine (3 × 15 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated *in vacuo*. The crude residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 10:1) to afford compound **7** (10.8 mg) in 18% yield as a white solid and **4a** (31.4 mg) in 62% yield as a white solid.

Characterization Data of Compound 7:

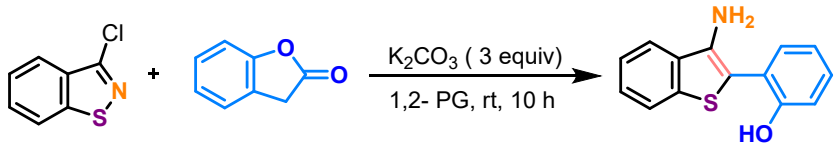


(Z)-2-((2-hydroxy-1-(2-hydroxyphenyl)-2-methoxyvinyl)thio)benzonitrile

Eluent (petroleum ether/ethyl acetate = 10:1); 10.8 mg; 18% yield; white solid; mp: 98-100 °C; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 10.19 (s, 1H), 8.76 (s, 1H), 7.92 (dd, J = 6.6, 2.2 Hz, 1H), 7.58 (dd, J = 6.6, 2.2 Hz, 1H), 7.41 (dd, J = 7.0, 1.6 Hz, 1H), 7.40 – 7.38 (m, 1H), 7.36 (dd, J = 7.0, 1.6 Hz, 1H), 7.26 (td, J = 8.3, 1.7 Hz, 1H), 7.00 (dd, J = 8.0, 0.7 Hz, 1H), 6.91 (td, J = 7.6, 0.7 Hz, 1H), 3.60 (s, 3H) ppm; **^{13}C NMR (101 MHz, DMSO-d_6)** δ 155.2, 154.7, 136.7, 136.4, 132.7, 131.1, 130.0, 126.4, 124.6,

124.1, 122.3, 121.9, 119.3, 119.2, 116.2, 51.9 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}NO_3S$: 300.0689, found: 300.0694.

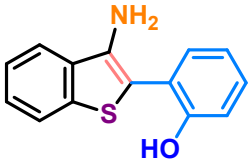
6.1.2 Synthesis Step and Characterization Data of the Compound 8



1a **2a** **8**

General procedure: To a solution of 1,2-benzisothiazole **1a** (33.9 mg, 0.2 mmol) in 1,2-PG (2 mL) was added benzofuran-2(3*H*)-one **2a** (32.2 mg, 0.24 mmol) and K_2CO_3 (27.6 mg, 0.6 mmol), the resulting mixture was stirred at room temperature for 8 h. The reaction progress was monitored by TLC until completion. The mixture was partitioned between H_2O (15 mL) and EtOAc (15 mL). The separated aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine (3 × 15 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated *in vacuo*. The crude residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 8:1) to afford compound **8** (45.4 mg) in 94% yield as a light yellow solid.

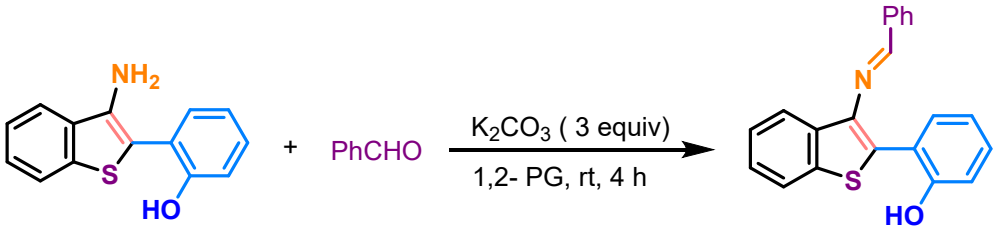
Characterization Data of Compound 8:



2-(3-Aminobenzo[*b*]thiophen-2-yl)phenol

Eluent (petroleum ether/ethyl acetate = 8:1); 45.3 mg; 94% yield; light yellow solid; mp: 158-160 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.80 (dd, J = 7.2, 1.4 Hz, 1H), 7.57 (dd, J = 7.2, 1.4 Hz, 1H), 7.47 (dd, J = 7.7, 1.7 Hz, 1H), 7.44 – 7.38 (td, J = 7.2, 1.3 Hz, 1H), 7.38 (dd, J = 7.6, 1.4 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.08 (dd, J = 8.2, 1.2 Hz, 1H), 7.01 (td, J = 7.5, 1.2 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 154.2, 138.6, 134.7, 131.3, 130.2, 130.1, 125.0, 124.4, 122.9, 122.2, 120.9, 120.3, 119.5, 118.9 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{14}H_{12}NOS$: 242.0635, found: 242.0637.

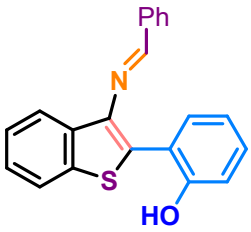
6.1.3 Synthesis Step and Characterization Data of the Compound 9



8 **3n** **9, 80%**

General procedure: To a solution of Compound **8** (48.2 mg, 0.2 mmol) in 1,2-PG (2 mL) was added benzaldehyde **3n** (31.8 mg, 0.3 mmol) and K_2CO_3 (27.6 mg, 0.6 mmol), the resulting mixture was stirred at room temperature for 4 h. The reaction progress was monitored by TLC until completion. The mixture was partitioned between H_2O (15 mL) and EtOAc (15 mL). The separated aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine (3 × 15 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated *in vacuo*. The crude residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 20:1) to afford compound **9** (52.7 mg) in 80% yield as a yellow oil liquid.

Characterization Data of Compound 9:



2-(3-(Benzylideneamino)benzo[*b*]thiophen-2-yl)phenol

Eluent (petroleum ether/ethyl acetate = 20:1); 52.7 mg; 80% yield; yellow oil liquid; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 11.38 (s, 1H), 8.75 (s, 1H), 7.95 (dd, J = 7.9, 1.7 Hz, 2H), 7.89 – 7.84 (m, 1H), 7.78 (dd, J = 6.8, 2.0 Hz, 1H), 7.61 – 7.52 (m, 4H), 7.43 – 7.37 (m, 2H), 7.34 – 7.30 (m, 1H), 7.15 – 7.12 (m, 1H), 6.98 (td, J = 7.6, 1.3 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 162.1, 154.9, 139.1, 136.2, 134.4, 134.2, 133.3, 132.9, 131.2, 130.4, 129.4, 129.3, 128.9, 126.6, 125.1, 125.1, 123.1, 121.3, 121.1, 120.5, 120.3 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{21}H_{16}NOS$: 330.0948, found: 330.0951.

7. X-ray Diffraction Analysis of Compound 4k

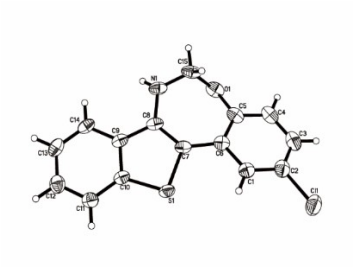


Figure S1. Single crystal structure of compound **4k**

Method for single crystals cultivation: The single crystal for compound **4k** was prepared from a mixture solvent of dichloromethane and hexane (*v*/*v* = 1:2).

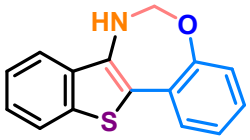
The structure of **4k** (containing little solvent) was determined by the X-ray diffraction. This crystal was deposited in the Cambridge Crystallographic Data and assigned as **CCDC: 2470543**.

Table S1. Crystal data and structure refinement for **4k**

Identification code	**4k**
Empirical formula	$C_{15}H_{10}ClNOS$
Formula weight	287.75
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	Pbca
a/Å	12.4025(2)
b/Å	8.06004(14)
c/Å	25.3975(6)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2538.85(9)
Z	8
ρcalcg/cm^3	1.506
μ/mm^{-1}	4.110
F(000)	1184.0

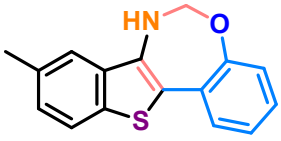
Crystal size/mm^3	0.18 × 0.11 × 0.04
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.96 to 134.104
Index ranges	-14 ≤ h ≤ 14, -9 ≤ k ≤ 7, -30 ≤ l ≤ 23
Reflections collected	8772
Independent reflections	2267 [R_{int} = 0.0437, Rsigma = 0.0362]
Data/restraints/parameters	2267/0/176
Goodness-of-fit on F^2	1.058
Final R indexes [I>=2σ (I)]	R1 = 0.0490, wR2 = 0.1364
Final R indexes [all data]	R1 = 0.0588, wR2 = 0.1480
Largest diff. peak/hole / e Å^{-3}	0.37/-0.21

8. Characterization Data for Products



6,7-Dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4a)

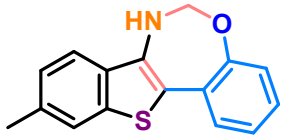
Eluent (petroleum ether/ethyl acetate = 10:1); 42 mg; 82% yield; white solid; mp: 128-130 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.74 (dd, J = 6.4, 1.7 Hz, 1H), 7.65 (dd, J = 7.7, 1.7 Hz, 1H), 7.49 (dd, J = 7.0, 2.1 Hz, 1H), 7.37 – 7.3 (m, 2H), 7.18 (td, J = 7.5, 1.7 Hz, 1H), 7.12 (td, J = 7.5, 1.6 Hz, 1H), 7.08 (dd, J = 7.8, 1.6 Hz, 1H), 5.26 (t, J = 8.0 Hz, 1H), 5.04 (d, J = 8.0 Hz, 2H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 159.1, 136.7, 135.9, 135.2, 128.4, 127.0, 125.5, 125.4, 124.2, 123.6, 122.4, 120.7, 120.3, 119.1, 79.6 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{15}H_{12}NOS$: 254.0635, found: 254.0638.



9-Methyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4b)

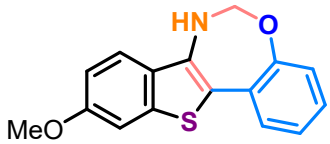
Eluent (petroleum ether/ethyl acetate = 8:1); 41.7 mg; 78% yield; white solid; mp: 125-127 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.63 (d, J = 1.2 Hz, 1H), 7.61 (d, J = 1.2 Hz, 1H), 7.35 (dd, J = 1.6, 0.9 Hz, 1H), 7.19 (dd, J = 8.1, 1.6 Hz, 1H), 7.15 (td, J = 7.4, 1.8

Hz, 1H), 7.10 (td, J = 7.4, 1.6 Hz, 1H), 7.04 (dd, J = 7.7, 1.6 Hz, 1H), 5.19 (brs, 1H), 5.08 (s, 2H), 2.47 (s, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 159.0, 135.6, 135.4, 134.1, 133.8, 128.3, 127.2, 126.9, 125.5, 123.5, 122.1, 120.6, 120.3, 119.5, 79.6, 21.5 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{16}H_{14}NOS$: 268.0791, found: 268.0794.



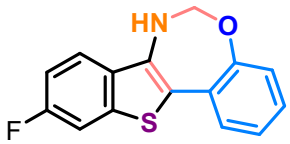
10-Methyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4c)

Eluent (petroleum ether/ethyl acetate = 15:1); 40.1 mg; 75% yield; white solid; mp: 146-148 ℃; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.61 (dd, J = 7.6, 1.6 Hz, 1H), 7.54 (s, 1H), 7.42 (d, J = 8.1 Hz, 1H), 7.17 (d, J = 7.5 Hz, 1H), 7.13 (dd, J = 7.5, 1.7 Hz, 1H), 7.10 (td, J = 7.4, 1.6 Hz, 1H), 7.04 (dd, J = 7.7, 1.5 Hz, 1H), 5.20 (brs, 1H), 5.06 (s, 2H), 2.47 (s, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 158.9, 136.9, 135.9, 135.6, 133.0, 128.2, 126.7, 125.9, 125.6, 123.5, 122.4, 120.6, 119.9, 118.0, 79.6, 21.7 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{16}H_{14}NOS$: 268.0791, found: 268.0792.



10-Methoxy-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4d)

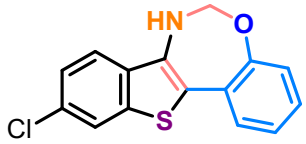
Eluent (petroleum ether/ethyl acetate = 8:1); 48.1 mg; 85% yield; white solid; mp: 194-196 ℃; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.57 (dd, J = 7.4, 1.9 Hz, 1H), 7.42 (d, J = 8.8 Hz, 1H), 7.22 (d, J = 2.3 Hz, 1H), 7.15 – 7.07 (m, 2H), 7.02 (dd, J = 7.5, 1.8 Hz, 1H), 6.97 (dd, J = 8.8, 2.3 Hz, 1H), 5.17 (brs, 1H), 5.06 (s, 2H), 3.88 (s, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 158.7, 158.4, 138.2, 135.7, 129.2, 128.0, 126.4, 125.6, 123.5, 121.1, 120.6, 116.8, 113.9, 105.2, 79.5, 55.6 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{16}H_{14}NO_2S$: 284.0740, found: 284.0739.



10-Fluoro-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4e)

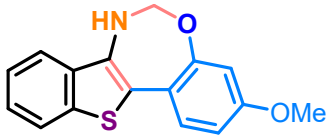
Eluent (petroleum ether/ethyl acetate = 10:1); 29.3 mg; 54% yield; yellow solid; mp:

143-145 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.57 (dd, J = 7.7, 1.7 Hz, 1H), 7.46 (dd, J = 8.8, 5.0 Hz, 1H), 7.42 (dd, J = 8.6, 2.3 Hz, 1H), 7.16 (td, J = 7.5, 1.7 Hz, 1H), 7.11 (dd, J = 6.7, 2.3 Hz, 1H), 7.08 (dd, J = 8.8, 2.3 Hz, 1H), 7.04 (dd, J = 7.8, 1.5 Hz, 1H), 5.18 (t, J = 6.9 Hz, 1H), 5.06 (d, J = 6.9 Hz, 2H) ppm; **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)** δ 161.4 (d, J = 245.7 Hz), 159.0, 137.9 (d, J = 10.3 Hz), 135.5, 131.9, 128.3, 127.1, 125.2, 123.8, 121.6 (d, J = 9.3 Hz), 120.8, 119.1 (d, J = 3.5 Hz), 113.2 (d, J = 24.3 Hz), 108.8 (d, J = 25.6 Hz), 79.6 ppm; **^{19}F NMR (376 MHz, $CDCl_3$)** δ = -115.86 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{15}H_{11}FNOS$: 272.0540, found: 272.0539.



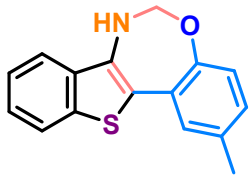
10-Chloro-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4f)

Eluent (petroleum ether/ethyl acetate = 10:1); 36.8 mg; 64% yield; yellow solid; mp: 152-154 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.71 (d, J = 1.9 Hz, 1H), 7.59 (dd, J = 7.8, 1.7 Hz, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.30 (dd, J = 8.5, 1.9 Hz, 1H), 7.17 (td, J = 7.5, 1.7 Hz, 1H), 7.10 (td, J = 7.5, 1.5 Hz, 1H), 7.04 (dd, J = 7.9, 1.5 Hz, 1H), 5.18 (brs, 1H), 5.06 (s, 2H) ppm; **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)** δ 159.2, 137.8, 135.5, 133.8, 131.7, 128.4, 127.3, 125.1, 125.0, 123.8, 122.1, 121.3, 120.9, 120.0, 79.6 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{15}H_{11}ClNOS$: 288.0245, found: 288.0241.



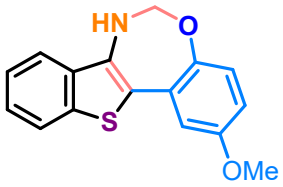
3-Methoxy-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4g)

Eluent (petroleum ether/ethyl acetate = 8:1); 36.8 mg; 65% yield; light yellow solid; mp: 150-152 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.75 – 7.71 (m, 1H), 7.54 – 7.52 (m, 1H), 7.52– 7.50 (m, 1H), 7.36 – 7.31 (m, 2H), 6.69 (dd, J = 8.7, 2.7 Hz, 1H), 6.61 (d, J = 2.7 Hz, 1H), 5.07 (s, 3H), 3.82 (s, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)** δ 160.2, 159.2, 136.4, 135.7, 134.2, 129.1, 125.1, 124.3, 122.4, 120.2, 120.1, 118.0, 110.1, 106.0, 79.7, 55.6 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}NO_2S$: 284.0740, found: 284.0742.



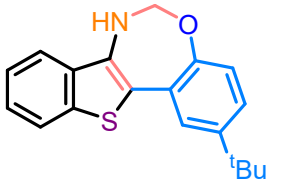
2-Methyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4h)

Eluent (petroleum ether/ethyl acetate = 15:1); 42.8 mg; 80% yield; white solid; mp: 153-155 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.74 (dd, J = 6.5, 1.8 Hz, 1H), 7.48 (dd, J = 6.9, 2.4 Hz, 1H), 7.45 (s, 1H), 7.34 (m, 2H), 6.98 (m, 2H), 5.24 (t, J = 7.8 Hz, 1H), 5.02 (d, J = 7.8 Hz, 2H), 2.39 (s, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 157.0, 136.6, 135.9, 135.2, 132.9, 128.7, 127.7, 125.4, 125.0, 124.2, 122.4, 120.5, 120.3, 119.0, 79.7, 20.9 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{16}H_{14}NOS$: 310.1261, found: 310.1267.



2-Methoxy-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4i)

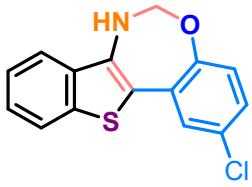
Eluent (petroleum ether/ethyl acetate = 10:1); 46.5 mg; 82% yield; light yellow solid; mp: 137-139 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.76 – 7.71 (m, 1H), 7.54 – 7.50 (m, 1H), 7.38 – 7.32 (m, 2H), 7.13 (d, J = 2.9 Hz, 1H), 6.96 (d, J = 8.8 Hz, 1H), 6.71 (dd, J = 8.8, 2.9 Hz, 1H), 5.25 (t, J = 7.5 Hz, 1H), 5.03 (d, J = 7.5 Hz, 2H), 3.85 (s, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 155.6, 153.4, 136.8, 136.3, 135.3, 126.3, 125.7, 124.3, 122.5, 121.3, 120.3, 118.6, 113.0, 112.5, 80.0, 55.9 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{16}H_{14}NO_2S$: 284.0740, found: 284.0743.



2-(Tert-butyl)-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4j)

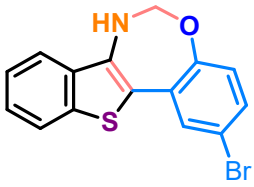
Eluent (petroleum ether/ethyl acetate = 10:1); 43.9 mg; 71% yield; white solid; mp: 168-170 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.77 – 7.72 (m, 1H), 7.64 (d, J = 2.3 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.38 – 7.32 (m, 2H), 7.19 (dd, J = 8.4, 2.3 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 5.21 (brs, 1H), 5.06 (s, 2H), 1.39 (s, 9H) ppm; **^{13}C{^{1}H} NMR (100**

MHz, $CDCl_3$) δ 157.0, 146.3, 136.7, 135.8, 135.4, 125.5, 125.3, 124.5, 124.3, 124.2, 122.4, 120.3, 120.2, 119.9, 79.7, 34.5, 31.6 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{19}H_{20}NOS$: 310.1261, found: 310.1267.



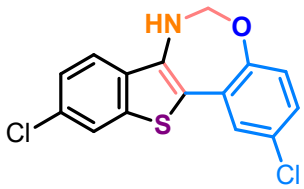
2-Chloro-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4k)

Eluent (petroleum ether/ethyl acetate = 8:1); 40.3 mg; 70% yield; white solid; mp: 154-156 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.77 – 7.72 (m, 1H), 7.57 (d, J = 2.4 Hz, 1H), 7.55 – 7.51 (m, 1H), 7.41 – 7.34 (m, 2H), 7.08 (dd, J = 8.6, 2.4 Hz, 1H), 6.95 (d, J = 8.6 Hz, 1H), 5.30 (t, J = 4.1 Hz, 1H), 5.05 (d, J = 4.1 Hz, 2H) ppm; **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)** δ 157.7, 136.9, 136.8, 134.9, 128.6, 127.7, 127.1, 126.6, 126.0, 124.5, 122.6, 121.9, 120.5, 117.5, 79.7 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{15}H_{11}ClNOS$: 288.0245, found: 288.0246.



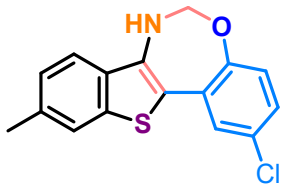
2-Bromo-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4l)

Eluent (petroleum ether/ethyl acetate = 15:1); 42.5 mg; 64% yield; white solid; mp: 174-176 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.78 – 7.73 (m, 1H), 7.71 (d, J = 2.3 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.40 – 7.35 (m, 2H), 7.22 (dd, J = 8.6, 2.3 Hz, 1H), 6.90 (d, J = 8.5 Hz, 1H), 5.31 (brs, 1H), 5.06 (s, 2H) ppm; **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)** δ 158.2, 136.9, 136.8, 134.9, 130.7, 129.5, 127.6, 126.1, 124.5, 122.6, 122.4, 120.5, 117.4, 116.2, 79.7 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{15}H_{11}BrNOS$: 331.9740, found: 331.9742.



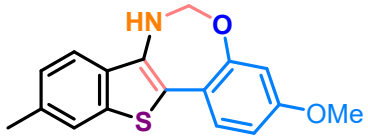
2,10-Dichloro-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4m)

Eluent (petroleum ether/ethyl acetate = 10:1); 34.8 mg; 54% yield; white solid; mp: 182-184 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.69 (dd, J = 1.9, 0.5 Hz, 1H), 7.50 (d, J = 2.4 Hz, 1H), 7.40 (dd, J = 8.5, 0.6 Hz, 1H), 7.29 (dd, J = 8.5, 1.9 Hz, 1H), 7.09 (dd, J = 8.6, 2.4 Hz, 1H), 6.95 (d, J = 8.6 Hz, 1H), 5.24 (t, J = 8.1 Hz, 1H), 5.01 (d, J = 8.1 Hz, 2H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 157.7, 137.8, 136.4, 133.5, 132.1, 128.7, 127.6, 126.8, 126.7, 125.3, 122.2, 122.0, 121.4, 118.1, 79.6 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{15}H_{10}Cl_2NOS$: 321.9855, found: 321.9858.



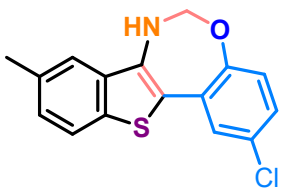
2-Chloro-10-methyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4n)

Eluent (petroleum ether/ethyl acetate = 10:1); 32.6 mg; 54% yield; white solid; mp: 145-147 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.54 (d, J = 2.3 Hz, 2H), 7.42 (d, J = 8.2 Hz, 1H), 7.18 (dd, J = 8.2, , 0.9 Hz, 1H), 7.06 (dd, J = 8.6, 2.4 Hz, 1H), 6.94 (d, J = 8.6 Hz, 1H), 5.28 (t, J = 7.9 Hz, 1H), 5.04 (d, J = 7.9 Hz, 2H), 2.47 (s, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 157.6, 137.1, 136.8, 136.3, 132.8, 128.6, 127.6, 127.3, 126.3, 126.2, 122.5, 121.9, 120.1, 116.3, 79.7, 21.8 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{16}H_{13}ClNOS$: 302.0401, found: 302.0402.



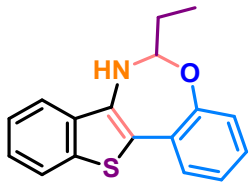
3-Methoxy-10-methyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4o)

Eluent (petroleum ether/ethyl acetate = 10:1); 29.7 mg; 50% yield; white solid; mp: 185-187 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.52 (s, 1H), 7.50 (d, J = 8.7 Hz, 1H), 7.40 (d, J = 8.1 Hz, 1H), 7.16 (d, J = 8.1 Hz, 1H), 6.68 (dd, J = 8.7, 2.6 Hz, 1H), 6.60 (d, J = 2.6 Hz, 1H), 5.06 (s, 3H), 3.81 (s, 3H), 2.46 (s, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 160.1, 159.0, 136.6, 135.2, 134.2, 133.5, 129.0, 126.0, 122.4, 119.8, 118.9, 118.2, 110.0, 106.0, 79.7, 55.6, 21.7 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{17}H_{16}NO_2S$: 298.0897, found: 298.0896.



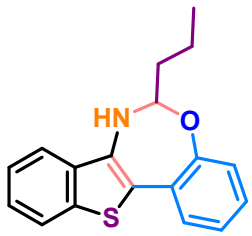
2-Chloro-9-methyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4p)

Eluent (petroleum ether/ethyl acetate = 10:1); 30.2 mg; 50% yield; white solid; mp: 144-146 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.61 (d, J = 8.2 Hz, 1H), 7.55 (d, J = 2.4 Hz, 1H), 7.32 (s, 1H), 7.20 (dd, J = 8.2, 1.6 Hz, 1H), 7.07 (dd, J = 8.6, 2.4 Hz, 1H), 6.95 (d, J = 8.6 Hz, 1H), 5.27 (t, J = 8.0 Hz, 1H), 5.04 (d, J = 8.0 Hz, 2H), 2.46 (s, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 157.6, 136.6, 135.2, 134.4, 134.0, 128.6, 127.7, 127.6, 127.2, 126.4, 122.3, 121.9, 120.5, 117.7, 79.7, 21.6 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{16}H_{13}ClNOS$: 302.0401, found: 302.0406.



6-Ethyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4q)

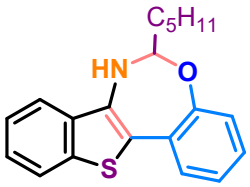
Eluent (petroleum ether/ethyl acetate = 8:1); 43.9 mg; 78% yield; white solid; mp: 111-113 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.74 (dd, J = 5.8, 3.0 Hz, 1H), 7.60 (dd, J = 7.4, 1.6 Hz, 1H), 7.53 (dd, J = 6.1, 3.3 Hz, 1H), 7.36 – 7.34 (m, 2H), 7.16 (dt, J = 7.6, 4.5 Hz, 1H), 7.10 (t, J = 7.3 Hz, 1H), 7.05 (d, J = 7.8 Hz, 1H), 4.89 (d, J = 9.0 Hz, 1H), 4.65 (dt, J = 9.0, 5.8 Hz, 1H), 2.11 (m, 2H), 1.21 (t, J = 7.4 Hz, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 158.3, 136.9, 135.2, 135.1, 128.2, 127.0, 126.2, 125.5, 124.2, 123.6, 122.5, 120.7, 120.2, 117.9, 91.3, 28.3, 10.2 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{17}H_{16}NOS$: 282.0948, found: 282.0947.



6-Propyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4r)

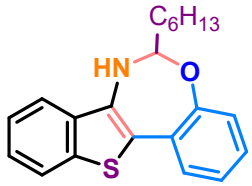
Eluent (petroleum ether/ethyl acetate = 8:1); 41.4 mg; 70% yield; white solid; mp: 138-140 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.77 – 7.72 (m, 1H), 7.61 (dd, J = 7.6, 1.7 Hz,

1H), 7.56 – 7.50 (m, 1H), 7.39 – 7.32 (m, 2H), 7.16 (td, *J* = 7.4, 1.8 Hz, 1H), 7.10 (td, *J* = 7.4, 1.6 Hz, 1H), 7.03 (dd, *J* = 7.8, 1.6 Hz, 1H), 4.90 (d, *J* = 9.4 Hz, 1H), 4.73 (m, 1H), 2.11 – 2.00 (m, 2H), 1.79 – 1.58 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** *δ* 158.4, 136.9, 135.2, 135.1, 128.2, 127.0, 126.2, 125.5, 124.2, 123.7, 122.5, 120.8, 120.2, 117.9, 89.9, 37.2, 19.0, 13.9 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{18}H_{18}NOS$: 296.1104, found: 296.1102.



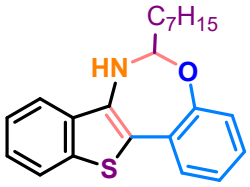
6-Pentyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4s)

Eluent (petroleum ether/ethyl acetate = 10:1); 39.9 mg; 68% yield; white solid; mp: 95-97 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** *δ* 7.77 – 7.71 (m, 1H), 7.60 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.39 – 7.32 (m, 2H), 7.16 (td, *J* = 7.5, 1.7 Hz, 1H), 7.10 (td, *J* = 7.4, 1.6 Hz, 1H), 7.03 (dd, *J* = 7.7, 1.6 Hz, 1H), 4.90 (d, *J* = 9.5 Hz, 1H), 4.71 (dt, *J* = 9.5, 6.0 Hz, 1H), 2.07 (td, *J* = 7.9, 6.0 Hz, 2H), 1.76 – 1.57 (m, 2H), 1.38 (m, *J* = 3.6 Hz, 4H), 0.94 (t, *J* = 6.9 Hz, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** *δ* 158.4, 136.9, 135.2, 135.1, 128.2, 127.0, 126.2, 125.5, 124.2, 123.7, 122.5, 120.8, 120.2, 117.9, 90.2, 35.1, 31.5, 25.4, 22.7, 14.2 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{20}H_{22}NOS$: 324.1417, found: 324.1413.



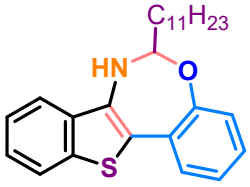
6-Hexyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4t)

Eluent (petroleum ether/ethyl acetate = 10:1); 42.5 mg; 63% yield; white solid; mp: 102-104 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** *δ* 7.77 – 7.71 (m, 1H), 7.60 (dd, *J* = 7.2, 1.7 Hz), 7.52 (dd, *J* = 6.0, 3.2 Hz, 1H), 7.35 (dd, *J* = 6.0, 3.2 Hz, 2H), 7.18 (td, *J* = 7.4, 1.6 Hz, 1H), 7.12 (td, *J* = 7.4, 1.6Hz, 1H), 7.06 (dd, *J* = 7.8, 1.6 Hz, 1H), 4.94 (d, *J* = 9.5 Hz, 1H), 4.69 (dt, *J* = 9.5, 5.9 Hz, 1H), 2.03 (td, *J* = 9.5, 5.9 Hz, 2H), 1.74 – 1.50 (m, 2H), 1.44 – 1.26 (m, 6H), 0.94 (t, *J* = 6.4 Hz, 3H)ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** *δ* 158.3, 136.8, 135.2, 135.1, 128.1, 126.9, 126.2, 125.4, 124.1, 123.6, 122.4, 120.7, 120.3, 117.8, 90.2, 35.0, 31.9, 29.0, 25.6, 22.7, 14.2ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{21}H_{24}NOS$: 338.1574, found: 338.1570.



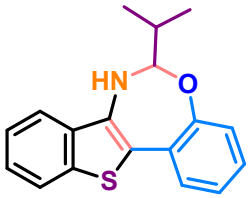
6-Heptyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4u)

Eluent (petroleum ether/ethyl acetate = 8:1); 42.1 mg; 60% yield; white solid; mp: 110-112 ℃; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.77 – 7.71 (m, 1H), 7.60 (dd, J = 7.7, 1.7 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.39 – 7.32 (m, 2H), 7.16 (td, J = 7.4, 1.8 Hz, 1H), 7.10 (td, J = 7.4, 1.6 Hz, 1H), 7.03 (dd, J = 7.8, 1.6 Hz, 1H), 4.90 (d, J = 9.5 Hz, 1H), 4.71 (dt, J = 9.5, 6.0 Hz, 1H), 2.06 (td, J = 7.9, 6.0 Hz, 2H), 1.76 – 1.57 (m, 2H), 1.43 – 1.26 (m, 8H), 0.91 (t, J = 6.7 Hz, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 158.4, 136.9, 135.2, 135.1, 128.2, 127.0, 126.2, 125.5, 124.2, 123.6, 122.5, 120.8, 120.2, 117.9, 90.2, 35.1, 31.9, 29.4, 25.7, 22.8, 14.3 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{22}H_{26}NOS$: 352.1730, found: 352.1724.



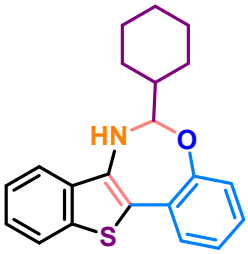
6-Undecyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4v)

Eluent (petroleum ether/ethyl acetate = 15:1); 45.7 mg; 56% yield; white solid; mp: 74-76 ℃; **^{1}H NMR (400 MHz, CDCl$_3$)** δ7.77 – 7.71 (m, 1H), 7.60 (dd, J = 7.8, 1.7 Hz, 1H), 7.55 – 7.52 (m, 1H), 7.38 – 7.32 (m, 2H), 7.15 (td, J = 7.5, 1.6 Hz, 1H), 7.10 (td, J = 7.5, 1.6 Hz, 1H), 7.03 (dd, J = 7.8, 1.6 Hz, 1H), 4.89 (d, J = 9.1 Hz, 1H), 4.71 (dt, J = 9.1, 5.9 Hz, 1H), 2.07 (td, J = 7.8, 5.9 Hz, 2H), 1.65 (m, 2H), 1.43 – 1.26 (m, 16H), 0.89 (t, J = 6.7 Hz, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 158.4, 135.2, 135.1, 128.2, 127.0, 126.3, 125.5, 124.2, 123.7, 122.6, 120.8, 120.2, 90.2, 35.2, 32.1, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 25.7, 22.8, 14.3ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{26}H_{34}NOS$: 408.2356, found: 408.2352.



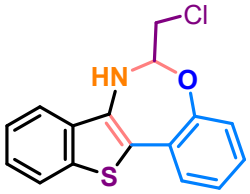
6-Isopropyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4w)

Eluent (petroleum ether/ethyl acetate = 15:1); 47.3 mg; 80% yield; white solid; mp: 92-94 ℃; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.78 – 7.73 (m, 1H), 7.63 (dd, J = 7.7, 1.7 Hz, 1H), 7.58 – 7.52 (m, 1H), 7.38 – 7.34 (m, 2H), 7.18 (td, J = 7.5, 1.7 Hz, 1H), 7.12 (td, J = 7.5, 1.6 Hz, 1H), 7.07 (dd, J = 7.7, 1.6 Hz, 1H), 4.89 (d, J = 9.8 Hz, 1H), 4.48 (dd, J = 9.8, 5.9 Hz, 1H), 2.35 – 2.25 (m, 1H), 1.25 (dd, J = 15.4, 6.8 Hz, 6H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 158.6, 136.9, 135.3, 135.2, 128.1, 127.0, 126.3, 125.4, 124.1, 123.5, 122.5, 120.6, 120.2, 117.8, 94.0, 32.8, 19.1, 17.9 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{18}H_{18}NOS$: 296.1104, found: 296.1102.



6-Cyclohexyl-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4x)

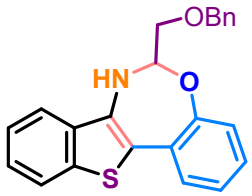
Eluent (petroleum ether/ethyl acetate = 8:1); 55.0 mg; 82% yield; white solid; mp: 178-180 ℃; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.78 – 7.71 (m, 1H), 7.60 (dd, J = 7.6, 1.7 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.38 – 7.32 (m, 2H), 7.15 (td, J = 7.5, 1.8 Hz, 1H), 7.09 (td, J = 7.5, 1.6 Hz, 1H), 7.04 (dd, J = 7.7, 1.6 Hz, 1H), 4.91 (d, J = 9.8 Hz, 1H), 4.45 (dd, J = 9.8, 6.3 Hz, 1H), 2.24 – 2.17 (m, 1H), 2.03 – 1.92 (m, 2H), 1.90 – 1.81 (m, 2H), 1.78 – 1.70 (m, 1H), 1.44 – 1.23 (m, 5H) ppm; **^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$)** δ 158.7, 136.9, 135.4, 135.3, 128.1, 127.0, 126.4, 125.5, 124.2, 123.6, 122.5, 120.6, 120.3, 117.8, 93.6, 42.3, 29.6, 28.4, 26.4, 26.0, 25.9 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{21}H_{21}NOS$: 336.1417, found: 336.1418.



6-(Chloromethyl)-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4y)

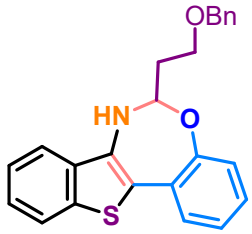
Eluent (petroleum ether/ethyl acetate = 10:1); 38.0 mg; 63% yield; yellow solid; mp: 116-118 ℃; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.77 – 7.70 (m, 1H), 7.61 (dd, J = 7.6, 1.8 Hz, 1H), 7.59 – 7.56 (m, 1H), 7.40 – 7.34 (m, 2H), 7.17 (td, J = 7.5, 1.8 Hz, 1H), 7.12 (td, J = 7.4, 1.7 Hz, 1H), 7.08 (dd, J = 7.7, 1.7 Hz, 1H), 5.25 (d, J = 9.6 Hz, 1H), 4.98

(dt, J = 9.6, 4.0 Hz, 1H), 4.07 (d, J = 4.0 Hz, 2H) ppm; **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)** δ 157.5, 136.8, 135.2, 134.3, 128.3, 127.3, 125.7, 125.5, 124.4, 124.1, 122.5, 120.9, 120.4, 119.1, 86.9, 45.7 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{16}H_{13}ClNOS$: 302.0401, found: 302.0403.



6-((Benzyloxy)methyl)-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4z)

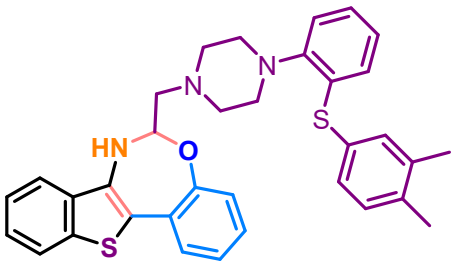
Eluent (petroleum ether/ethyl acetate = 10:1); 38.8 mg; 52% yield; white solid; mp: 102-104 °C; **^1H NMR (400 MHz, $CDCl_3$)** δ 7.76 – 7.72 (m, 1H), 7.61 (dd, J = 7.5, 1.9 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.47 – 7.39 (m, 4H), 7.38 – 7.33 (m, 3H), 7.15 (td, J = 7.4, 1.7 Hz, 1H), 7.10 (td, J = 7.4, 1.7 Hz, 1H), 7.05 (dd, J = 7.6, 1.8 Hz, 1H), 5.55 (d, J = 8.9 Hz, 1H), 4.92 (dt, J = 8.9, 3.7 Hz, 1H), 4.82 (d, J = 12.0 Hz, 1H), 4.73 (d, J = 12.0 Hz, 1H), 4.05 (d, J = 3.7 Hz, 2H) ppm; **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)** δ 158.1, 137.7, 136.9, 135.2, 135.2, 128.7, 128.3, 128.2, 128.1, 126.9, 125.8, 125.6, 124.2, 123.8, 122.5, 120.9, 120.4, 87.5, 73.9, 70.6 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{23}H_{20}NO_2S$: 374.1210, found: 374.1204.



6-(2-(Benzyloxy)ethyl)-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepane (4aa)

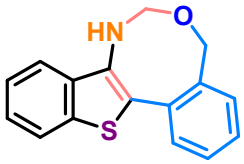
Eluent (petroleum ether/ethyl acetate = 8:1); 35.6 mg; 46% yield; white solid; mp: 90-92 °C; **^1H NMR (400 MHz, $CDCl_3$)** δ 7.71 (d, J = 8.0 Hz, 1H), 7.60 (dd, J = 7.5, 2.0 Hz, 1H), 7.38 – 7.32 (m, 5H), 7.30 (dd, J = 8.0, 1.5 Hz, 1H), 7.25 (dd, J = 8.0, 1.5 Hz, 1H), 7.20 (td, J = 6.8, 1.1 Hz, 1H), 7.12 (td, J = 7.2, 1.9 Hz, 1H), 7.09 (td, J = 7.4, 1.8 Hz, 1H), 6.98 (dd, J = 7.4, 1.8 Hz, 1H), 6.06 (d, J = 8.1 Hz, 1H), 4.96 (dt, J = 7.9, 5.1 Hz, 1H), 4.58 (d, J = 11.4 Hz, 1H), 4.52 (d, J = 11.4 Hz, 1H), 4.01 (m, 1H), 3.80 (m, 1H), 2.38 (m, 2H) ppm; **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)** δ 158.1, 137.9, 136.8,

135.7, 134.9, 128.6, 128.0, 127.9, 126.6, 126.3, 125.4, 124.0, 123.6, 122.3, 120.7, 120.3, 116.0, 88.3, 73.5, 66.6, 34.3 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{24}H_{22}NO_2S$: 388.1366, found: 388.1362.



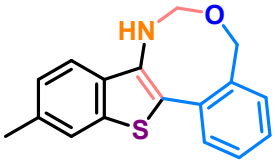
6-((4-(2-((3,4-Dimethylphenyl)thio)phenyl)piperazin-1-yl)methyl)-6,7-dihydrobenzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazepine (4ab)

Eluent (petroleum ether/ethyl acetate = 10:1); 45.1 mg; 62% yield; white solid; mp: 122-124 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79 (dd, J = 7.3, 1.4 Hz, 1H), 7.68 – 7.61 (m, 2H), 7.44 (td, J = 7.9, 3.2 Hz, 2H),7.40 (td, J = 7.4, 1.2 Hz, 1H), 7.20 (d, J = 2.0 Hz, 1H), 7.19 – 7.11 (m, 4H), 7.09 (m, 2H), 6.92 (m, 1H), 6.58 (d, J = 7.9 Hz, 1H), 6.44 (d, J = 6.9 Hz, 1H), 4.96 (dt, J = 6.9, 4.6 Hz, 1H), 3.21 (s, 4H), 3.14 (d, J = 4.6 Hz, 2H), 3.02 (s, 2H), 2.88 (dd, J = 10.6, 5.1 Hz, 2H), 2.41 (s, 3H), 2.38 (s, 3H) ppm; **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)** δ 157.8, 149.1, 142.6, 139.3, 137.0, 136.4, 135.5, 134.7, 134.6, 131.8, 128.1, 127.9, 127.9, 126.6, 126.2, 126.1, 125.5, 125.4, 124.5, 124.2, 123.7, 122.6, 121.0, 120.1, 119.8, 115.4, 86.5, 60.3, 54.3, 51.9, 21.3, 20.7 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{34}H_{34}N_3OS_2$: 564.2138, found: 564.2140.



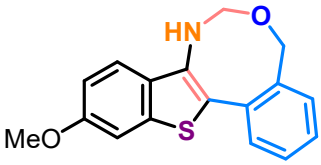
7,8-Dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6a)

Eluent (petroleum ether/ethyl acetate = 10:1); 39.6 mg; 74% yield; white solid; mp: 163-165 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.80 – 7.74 (m, 1H), 7.56 (dd, J = 7.6, 1.4 Hz, 1H), 7.54 – 7.51 (m, 1H), 7.45 (dd, J = 7.2, 1.8 Hz, 1H), 7.43 – 7.36 (m, 4H), 5.02 (s, 2H), 4.97 (d, J = 7.8 Hz, 2H), 4.71 (t, J = 7.8 Hz, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.2, 136.5, 135.6, 134.2, 132.3, 132.1, 129.6, 129.5, 128.4, 125.1, 124.1, 122.6, 119.9, 71.1, 68.2 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}NOS$: 268.0791, found: 268.0782.



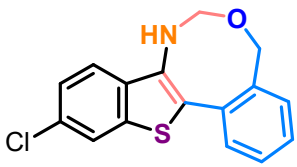
11-Methyl-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6b)

Eluent (petroleum ether/ethyl acetate = 8:1); 42.8 mg; 76% yield; white solid; mp: 213-215 ℃; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 7.77 (d, J = 8.2 Hz, 1H), 7.61 (dt, J = 1.6, 0.7 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.38 (dd, J = 7.2, 1.3 Hz, 1H), 7.32 (m, 1H), 7.20 (dd, J = 8.2, 0.9 Hz, 1H), 7.01 (t, J = 7.4 Hz, 1H), 4.93 (s, 2H), 4.83 (d, J = 7.4 Hz, 2H), 2.41 (s, 3H) ppm; **^{13}C NMR (101 MHz, DMSO-d_6)** δ 137.4, 137.2, 137.0, 134.8, 132.3, 131.8, 131.5, 129.5, 128.4, 127.7, 125.5, 122.0, 121.0, 106.7, 69.8, 66.6, 21.1 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{17}H_{16}NOS$:282.0948, found: 282.0942.



11-Methoxy-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6c)

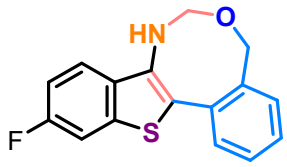
Eluent (petroleum ether/ethyl acetate = 8:1); 47.6 mg; 80% yield; white solid; mp: 198-200 ℃; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 7.77 (d, J = 8.9 Hz, 1H), 7.42 (dd, J = 7.6, 1.3 Hz, 1H), 7.39 (d, J = 2.7 Hz, 2H), 7.36 (d, J = 6.3 Hz, 1H), 7.29 (td, J = 7.1, 1.8 Hz, 1H), 7.01 (d, J = 2.4 Hz, 1H), 7.00 – 6.97 (m, 1H), 4.92 (s, 2H), 4.82 (d, J = 7.3 Hz, 2H), 3.81 (s, 3H) ppm; **^{13}C NMR (101 MHz, DMSO-d_6)** δ 157.7, 138.8, 137.1, 132.3, 131.4, 129.5, 128.3, 127.9, 127.5, 122.1, 113.6, 105.3, 105.1, 69.9, 66.6, 55.5 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{17}H_{16}NO_2S$:298.0897, found: 298.0888.



11-Chloro-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6d)

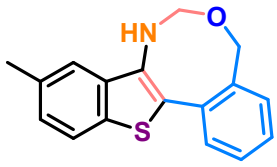
Eluent (petroleum ether/ethyl acetate = 10:1); 41.0 mg; 68% yield; white solid; mp: 224-226 ℃; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 7.99 (d, J = 1.9 Hz, 1H), 7.88 (d, J = 8.7 Hz, 1H), 7.45 (dd, J = 7.4, 1.6 Hz, 1H), 7.43 (d, J = 2.1 Hz, 2H), 7.40 (dd, J = 7.2, 1.6 Hz, 1H), 7.34 (m, 1H), 7.12 (t, J = 7.3 Hz, 1H), 4.92 (s, 2H), 4.83 (d, J = 7.3 Hz,

2H) ppm; **^{13}C NMR (101 MHz, DMSO-d_6)** δ 138.5, 137.0, 136.4, 132.5, 132.4, 131.5, 130.1, 129.7, 128.5, 128.2, 124.5, 122.7, 121.9, 108.8, 69.7, 66.5 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{16}H_{13}ClNOS$:302.0401, found: 302.0408.



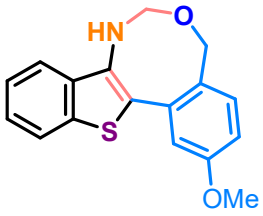
11-Fluoro-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6e)

Eluent (petroleum ether/ethyl acetate = 10:1); 32.0 mg; 56% yield; white solid; mp: 208-210 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.50 (dd, J = 7.5, 1.4 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.45 (d, J = 1.8 Hz, 1H), 7.43 (d, J = 2.1 Hz, 1H), 7.40 (dd, J = 7.6, 1.9 Hz, 1H), 7.36 (td, J = 7.4, 1.3 Hz, 1H), 7.13 (td, J = 8.8, 2.4 Hz, 1H), 4.99 (s, 2H), 4.93 (d, J = 7.4 Hz, 2H), 4.59 (s, 1H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 161.1 (d, J = 245.5 Hz), 139.2 (d, J = 10.2 Hz), 136.2, 135.2, 132.4, 132.1, 131.0, 129.7, 129.5, 128.6, 121.2 (d, J = 9.2 Hz), 113.1 (d, J = 24.4 Hz), 108.8 (d, J = 25.3 Hz), 71.2, 68.3 ppm; **^{19}F NMR (376 MHz, $CDCl_3$)** δ = -116.48 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{16}H_{13}FNOS$: 286.0697, found: 286.0694.



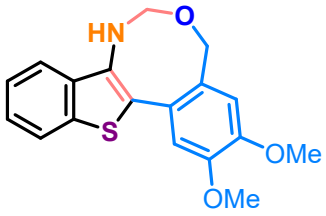
10-Methyl-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6f)

Eluent (petroleum ether/ethyl acetate = 10:1); 36.0 mg; 64% yield; white solid; mp: 199-201 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.64 (d, J = 8.1 Hz, 1H), 7.54 (dd, J = 7.3, 0.7 Hz, 1H), 7.43 (dd, J = 7.2, 1.6 Hz, 1H), 7.41 – 7.38 (m, 1H), 7.36 (dd, J = 7.2, 1.3 Hz, 1H), 7.33 (s, 1H), 7.20 (dd, J = 8.2, 1.6 Hz, 1H), 5.00 (s, 2H), 4.95 (d, J = 4.0 Hz, 2H), 4.59 (s, 1H), 2.50 (s, 3H) ppm; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 136.7, 135.4, 135.3, 134.6, 134.0, 132.3, 132.2, 129.6, 129.5, 128.4, 126.9, 122.3, 120.0, 71.3, 68.3, 21.7 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{17}H_{16}NOS$: 282.0948, found: 282.0940.



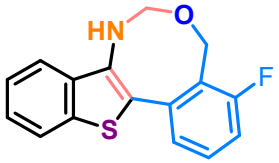
2-Methoxy-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6g)

Eluent (petroleum ether/ethyl acetate = 6:1); 41.6 mg; 70% yield; white solid; mp: 102-104 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.76 (dd, J = 6.6, 2.1 Hz, 1H), 7.52 (dd, J = 7.0, 2.1 Hz, 1H), 7.40 (td, J = 7.2, 1.6 Hz, 1H), 7.36 (td, J = 7.2, 1.6 Hz, 1H), 7.32 (d, J = 8.3 Hz, 1H), 7.08 (d, J = 2.6 Hz, 1H), 6.89 (dd, J = 8.3, 2.6 Hz, 1H), 4.96 (s, 4H), 4.65 (s, 1H), 3.88 (s, 3H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)** δ 160.4, 138.1, 137.9, 135.8, 134.2, 133.6, 125.2, 124.4, 124.2, 122.6, 119.9, 115.1, 113.6, 70.9, 67.6, 55.5 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{17}H_{16}NO_2S$: 298.0897, found: 298.0900.



2,3-Dimethoxy-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6h)

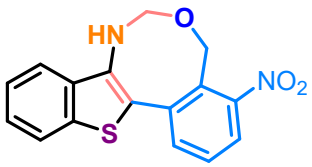
Eluent (petroleum ether/ethyl acetate = 6:1); 39.3 mg; 60% yield; white solid; mp: 190-192 °C; **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 7.87 (d, J = 7.9 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.35 – 7.31 (m, 1H), 7.02 (s, 1H), 6.97 (s, 1H), 6.90 (t, J = 7.4 Hz, 1H), 4.90 (s, 2H), 4.84 (d, J = 7.4 Hz, 2H), 3.82 (s, 3H), 3.80 (s, 3H) ppm; **^{13}C NMR (101 MHz, DMSO-*d*$_6$)** δ 149.2, 148.4, 136.9, 136.5, 134.0, 129.2, 124.9, 123.9, 123.7, 122.2, 121.1, 115.6, 112.0, 108.4, 69.6, 66.4, 55.7, 55.6 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{18}H_{18}NO_3S$: 328.1002, found: 328.1005.



4-Fluoro-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6i)

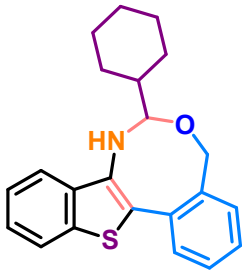
Eluent (petroleum ether/ethyl acetate = 10:1); 29.7 mg; 52% yield; white solid; mp: 143-145 °C; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.77 – 7.74 (m, 1H), 7.54 – 7.49 (m, 1H), 7.42 – 7.40 (m, 1H), 7.39 (d, J = 3.4 Hz, 1H), 7.38 – 7.35 (m, 1H), 7.32 (dd, J = 7.8,

1.3 Hz, 1H), 7.08 (td, J = 7.8, 1.3 Hz, 1H), 5.17 (s, 2H), 5.01 (s, 2H), 4.80 (s, 1H) ppm; **^{13}C NMR (100 MHz, CDCl$_3$)** δ 162.0 (d, J = 248.2 Hz), 138.9 (d, J =10.5 Hz), 138.1, 136.3, 133.9, 130.8 (d, J = 9.5 Hz), 125.4, 125.1 (d, J = 3.0 Hz), 124.2, 122.6, 120.0, 119.4 (d, J = 16.7 Hz), 114.9 (d, J = 23.3 Hz), 71.2, 59.7 (d, J = 5.8 Hz) ppm; **^{19}F NMR (376 MHz, CDCl$_3$)** δ = -116.58 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{16}H_{13}FNOS$: 286.0697, found: 286.0699.



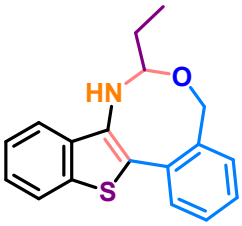
4-Nitro-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6j)

Eluent (petroleum ether/ethyl acetate = 8:1); 28.7 mg; 46% yield; yellow solid; mp: 220-222 °C; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 7.97 – 7.92 (m, 1H), 7.88 – 7.86 (m, 1H), 7.85 – 7.83 (m, 1H), 7.76 (dd, J = 7.8, 1.3 Hz, 1H), 7.68 (t, J = 7.9 Hz, 1H), 7.43 – 7.41(m, 2H), 7.39 – 7.36 (m, 1H), 5.07 (s, 2H), 4.91 (s, 2H) ppm; **^{13}C NMR (101 MHz, DMSO-d_6)** δ 152.0, 139.5, 138.9, 137.4, 133.3, 132.9, 130.8, 125.9, 124.4, 124.2, 122.6, 122.4, 121.6, 105.7, 70.2, 70.0 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{16}H_{13}N_2O_3S$: 313.0642, found: 313.0644.



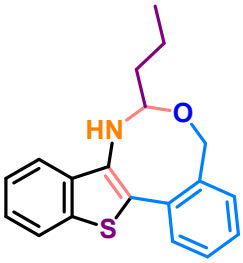
7-Cyclohexyl-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6k)

Eluent (petroleum ether/ethyl acetate = 10:1); 53.1 mg; 76% yield; white solid; mp: 136-138 °C; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 8.01 (d, J = 7.5 Hz, 1H), 7.76 (d, J = 7.4 Hz, 1H), 7.35 (m, 6H), 6.20 (d, J = 10.1 Hz, 1H), 5.29 (d, J = 11.4 Hz, 1H), 4.84 (t, J = 8.8 Hz, 1H), 4.57 (d, J = 11.4 Hz, 1H), 1.82 (t, J = 10.7 Hz, 2H), 1.57 (m, 4H), 1.13 (m, 2H), 0.99 (m, 1H), 0.78 (m, 2H) ppm; **^{13}C NMR (101 MHz, DMSO-d_6)** δ 137.5, 136.9, 136.6, 134.4, 132.4, 132.0, 129.3, 128.2, 127.8, 125.1, 123.7, 122.1, 121.9, 108.5, 83.6, 66.7, 41.7, 28.7, 25.9, 25.5, 25.3 ppm; **ESI-HRMS**: *m/z* [M + H]$^+$ calcd for $C_{22}H_{24}NOS$: 350.1574, found: 350.1573.



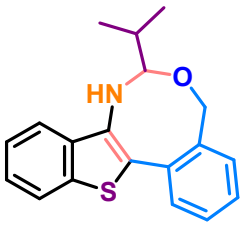
7-Ethyl-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6l)

Eluent (petroleum ether/ethyl acetate = 10:1); 42.5 mg; 72% yield; white solid; mp: 113-115 °C; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 8.03 (d, J = 7.7 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H), 7.48 – 7.25 (m, 6H), 6.38 (d, J = 9.9 Hz, 1H), 5.30 (d, J = 11.5 Hz, 1H), 5.08 (m, 1H), 4.58 (d, J = 11.5 Hz, 1H), 1.77 – 1.54 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H) ppm; **^{13}C NMR (101 MHz, DMSO-d_6)** δ 137.3, 137.0, 136.6, 134.2, 132.3, 132.1, 129.3, 128.3, 127.8, 125.2, 123.8, 122.2, 121.8, 108.3, 81.3, 66.7, 28.0, 10.1 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{18}H_{18}NOS$: 296.1104, found: 296.1107.



7-Propyl-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6m)

Eluent (petroleum ether/ethyl acetate = 10:1); 46.4 mg; 75% yield; white solid; mp: 98-100 °C; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 8.02 (d, J = 7.2 Hz, 1H), 7.77 (dd, J = 7.2, 1.4 Hz, 1H), 7.49 – 7.22 (m, 6H), 6.40 (d, J = 9.9 Hz, 1H), 5.29 (d, J = 11.4 Hz, 1H), 5.18 (m, 1H), 4.57 (d, J = 11.4 Hz, 1H), 1.72 – 1.53 (m, 2H), 1.34 – 1.15 (m, 2H), 0.73 (t, J = 7.4 Hz, 3H) ppm; **^{13}C NMR (101 MHz, DMSO-d_6)** δ 137.2, 137.0, 136.6, 134.2, 132.3, 132.0, 129.3, 128.3, 127.8, 125.1, 123.7, 122.2, 121.8, 108.2, 79.5, 66.7, 36.8, 18.4, 13.6 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{19}H_{20}NOS$: 310.1261, found: 310.1263.



7-Isopropyl-7,8-dihydro-5*H*-benzo[*f*]benzo[4,5]thieno[3,2-*d*][1,3]oxazocine (6n)

Eluent (petroleum ether/ethyl acetate = 10:1); 48.3 mg; 78% yield; white solid; mp: 152-154 ℃; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 8.08 – 7.98 (m, 1H), 7.80 (dd, J = 6.7, 1.9 Hz, 1H), 7.49 – 7.28 (m, 6H), 6.16 (d, J = 10.2 Hz, 1H), 5.29 (d, J = 11.5 Hz, 1H), 4.79 (dd, J = 10.2, 7.4 Hz, 1H), 4.60 (d, J = 11.5 Hz, 1H), 1.93 (m, 1H), 0.86 (dd, J = 17.6, 6.8 Hz, 6H) ppm; **^{13}C NMR (101 MHz, DMSO-d_6)** δ 137.4, 136.9, 136.5, 134.4, 132.4, 132.0, 129.3, 128.2, 127.8, 125.2, 123.8, 122.2, 121.9, 108.9, 84.7, 66.7, 32.5, 18.9, 18.7 ppm; **ESI-HRMS**: *m/z* $[M + H]^+$ calcd for $C_{19}H_{20}NOS$: 310.1261, found: 310.1263.

9. References

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6. M. S. Mousavi, A. Di Mola, G. Pierri and A. Massa, Isochroman-3,4-dione and Tandem Aerobic Oxidation of 4-Bromoisochroman-3-one in the Highly Regio- and Diastereoselective Diels-Alder Reaction for the Construction of Bridged Polycyclic Lactones, *J. Org. Chem.*, 2024, **89**, 18602-18611.

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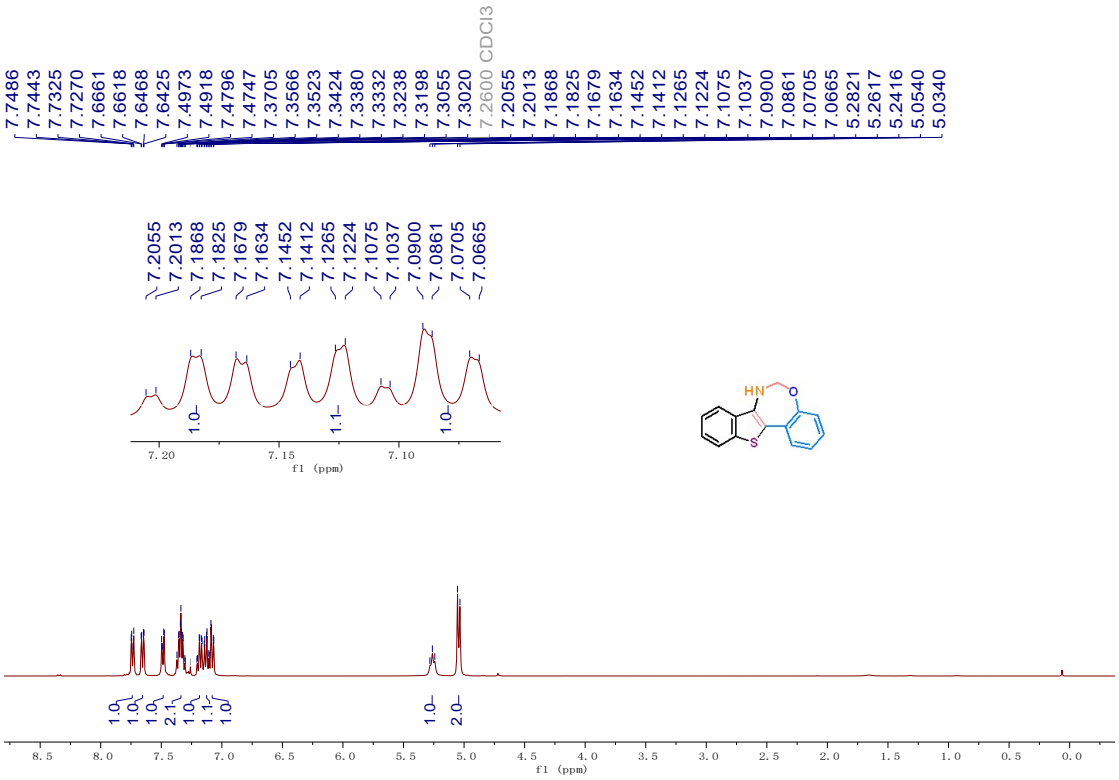
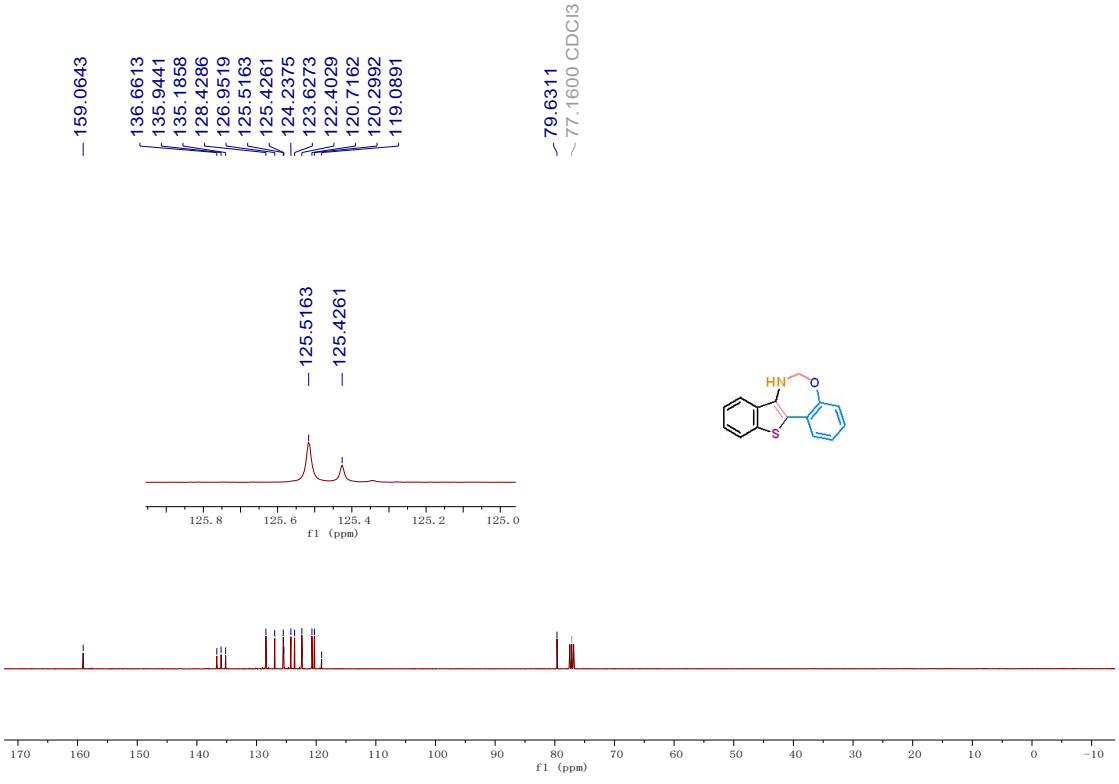
10. NMR Spectroscopic Data



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



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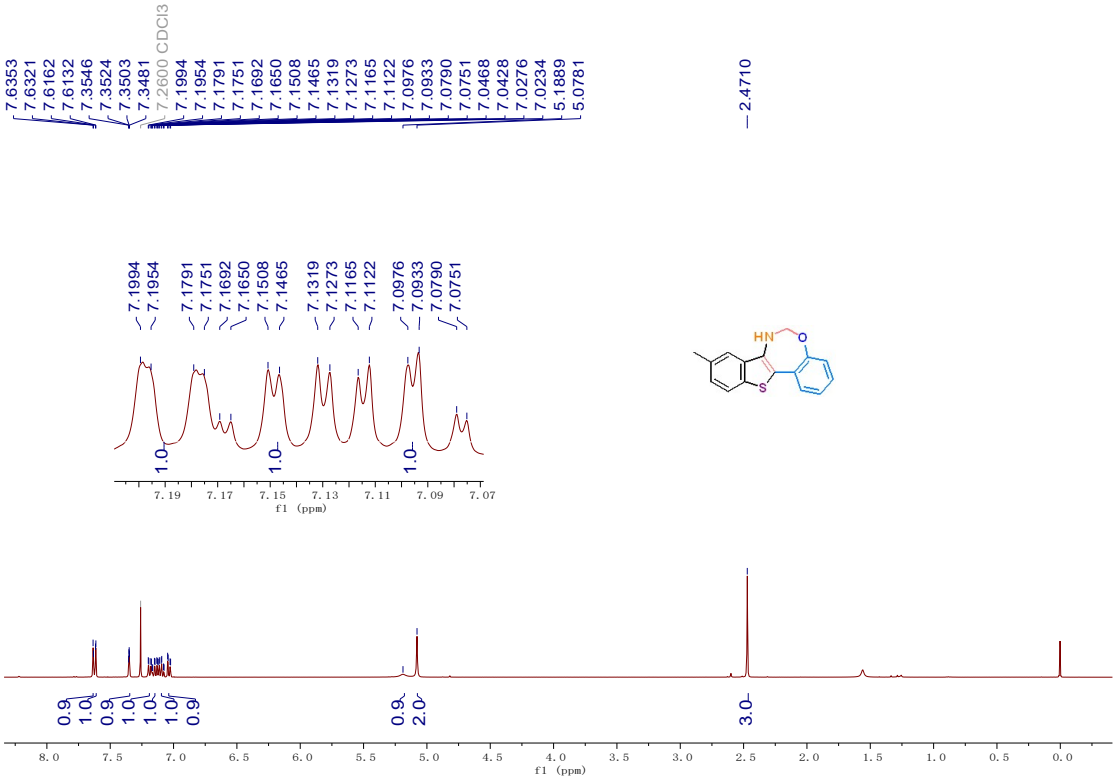
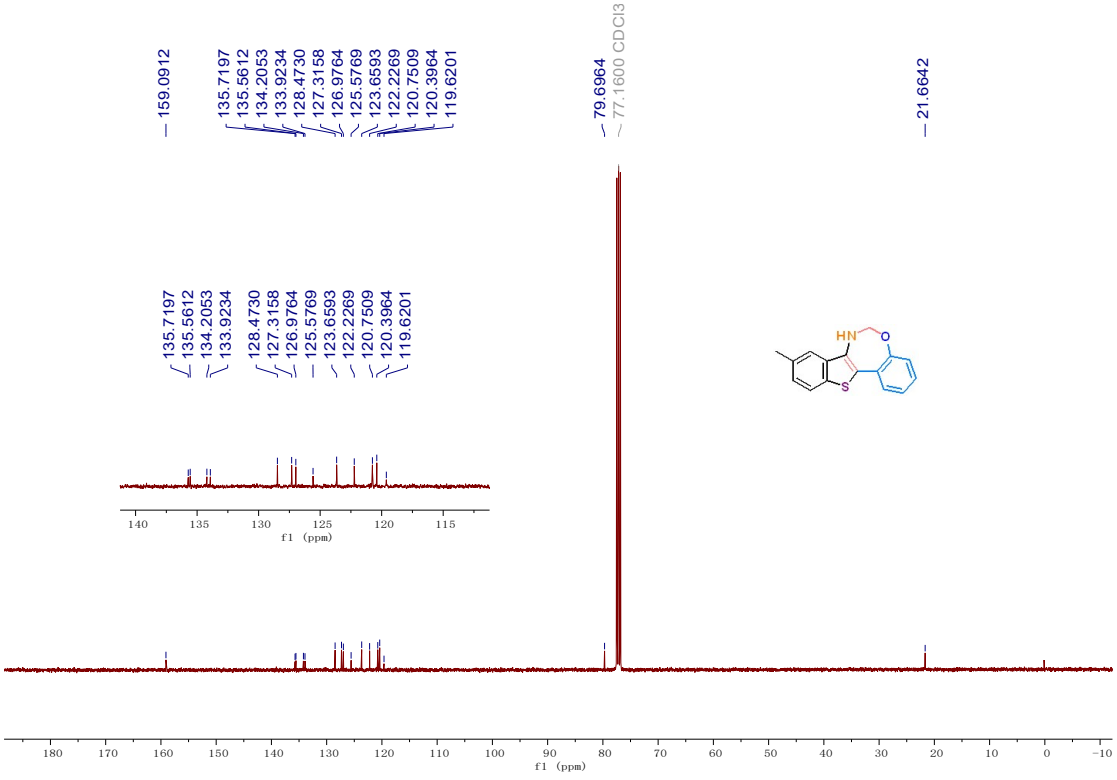
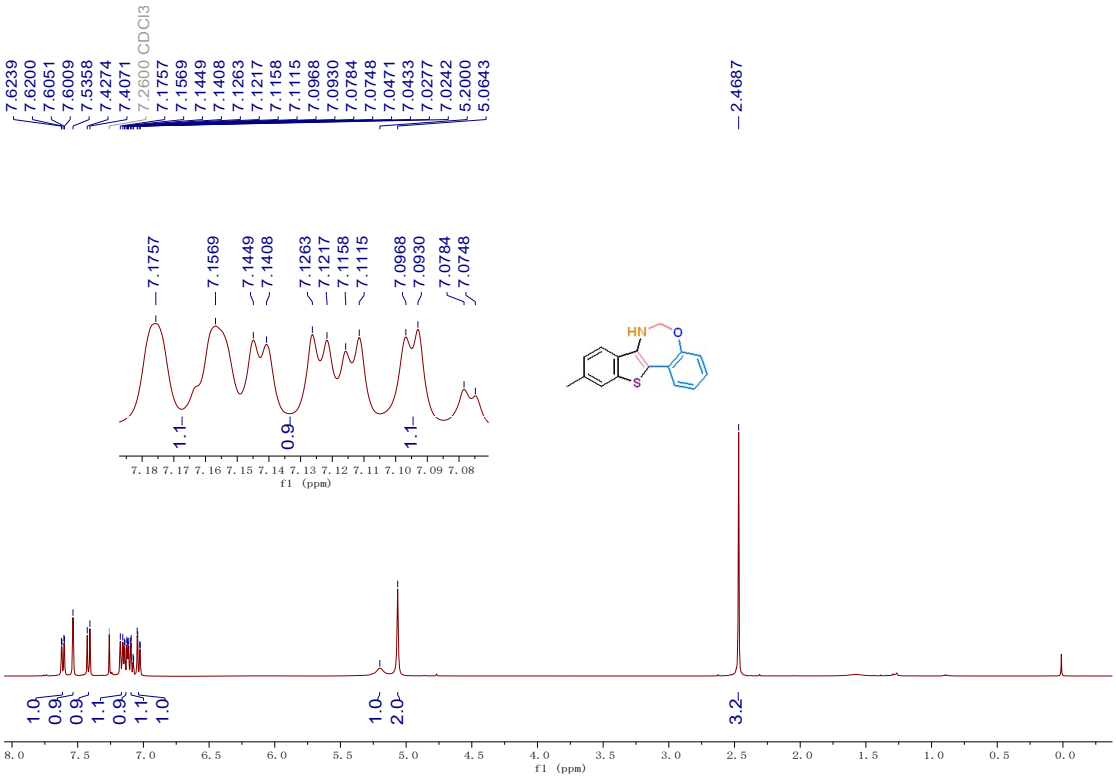


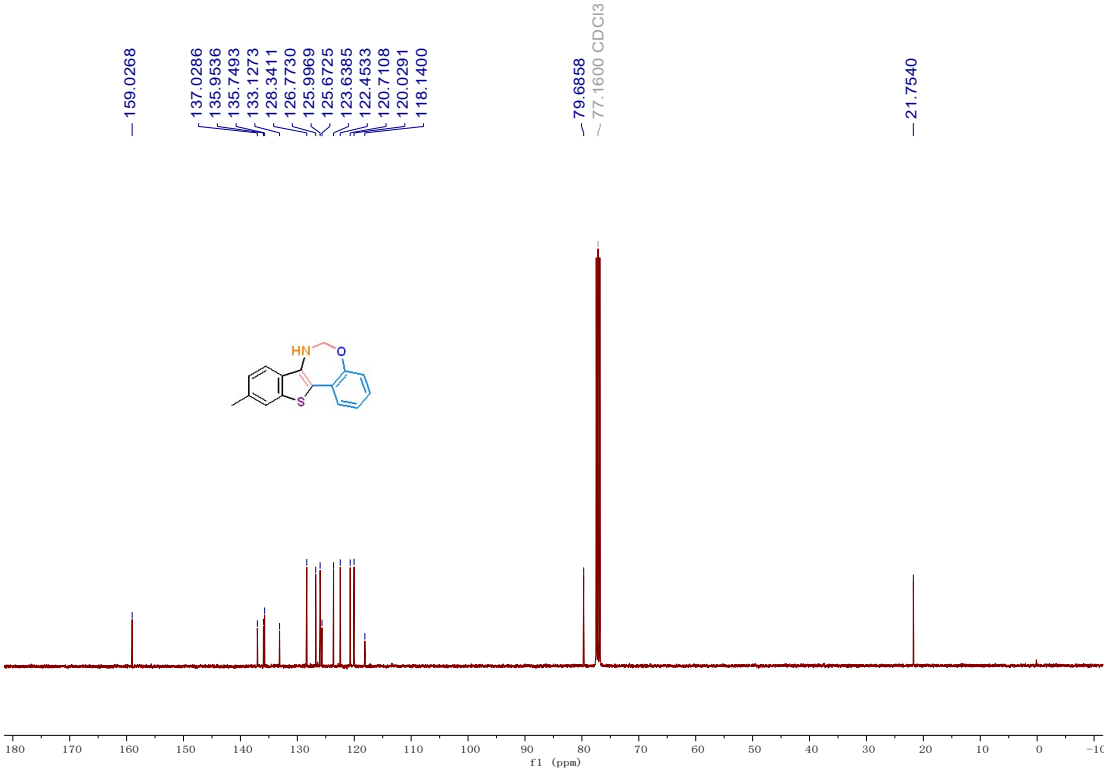
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4b



^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4b



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



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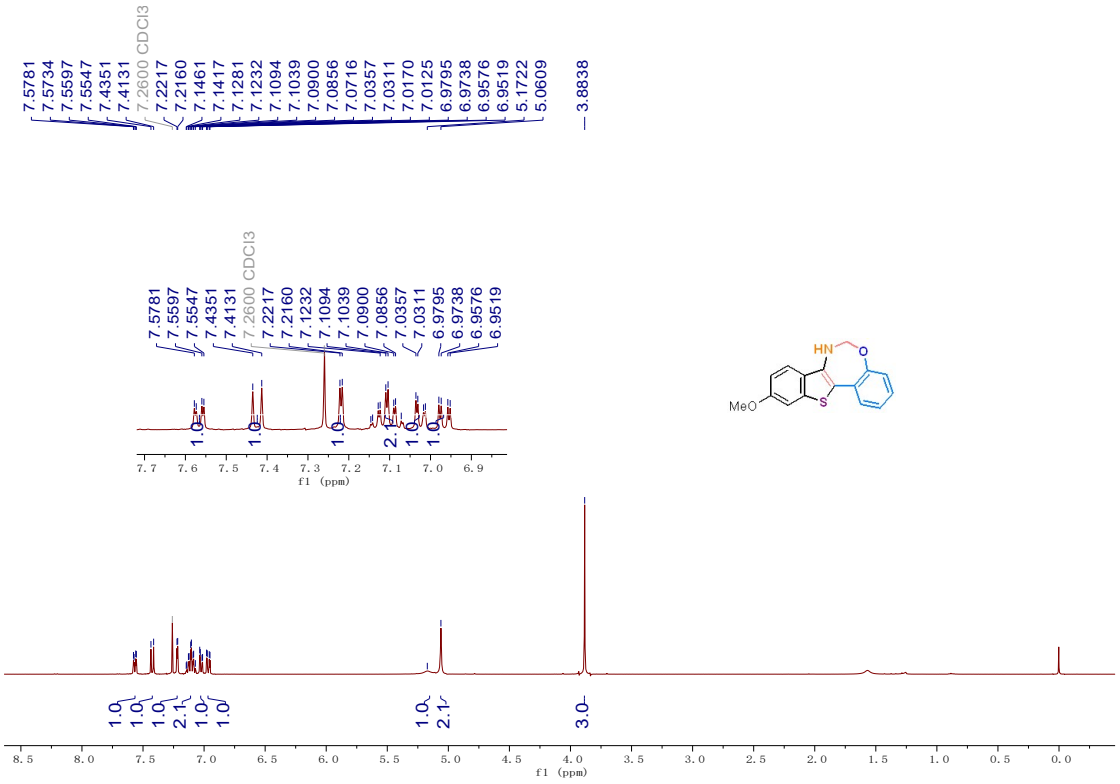
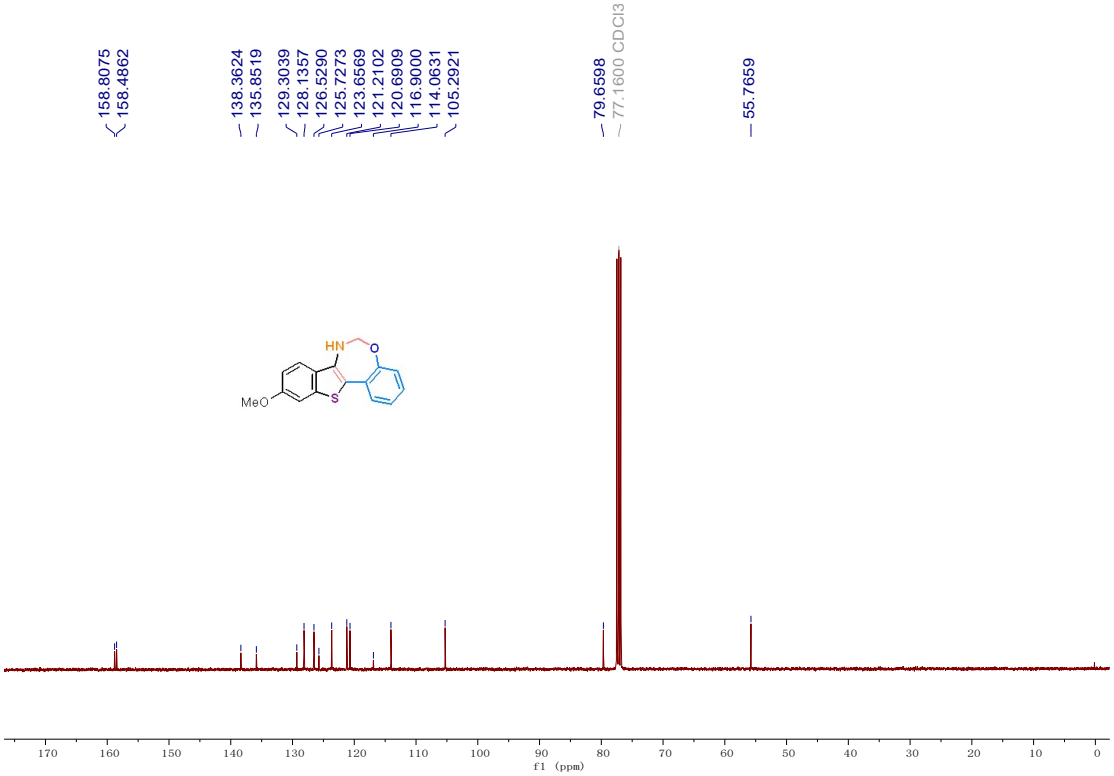
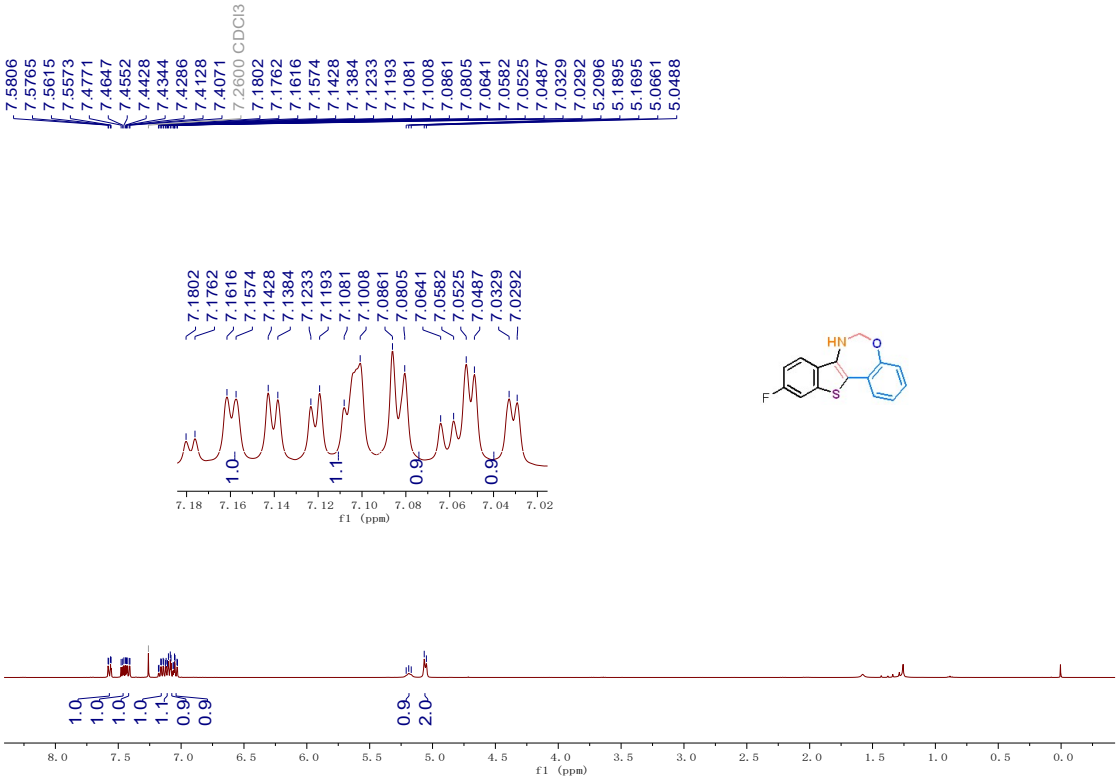


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4d



^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4d



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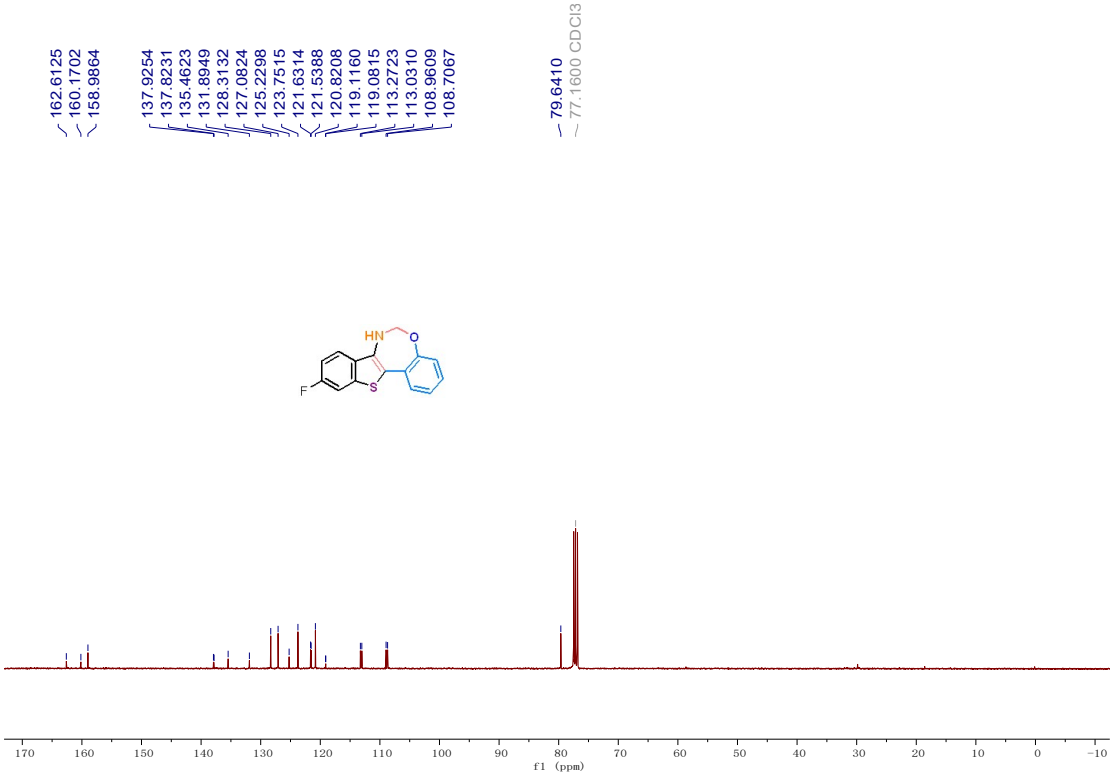

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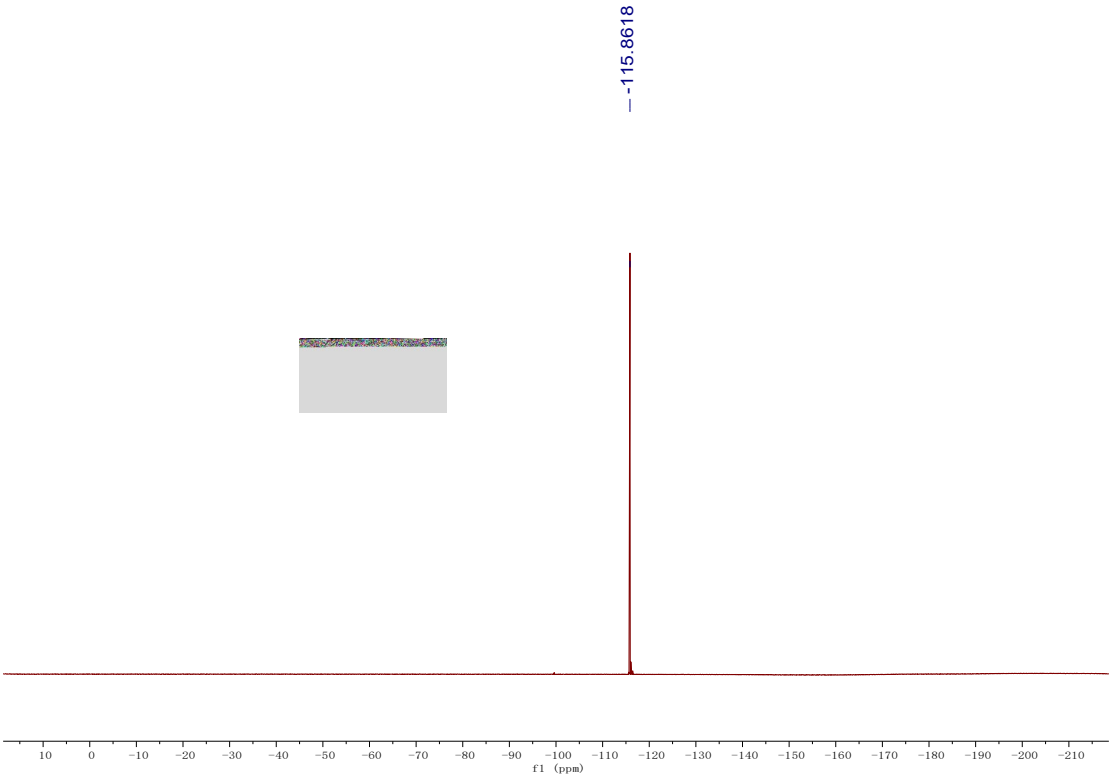
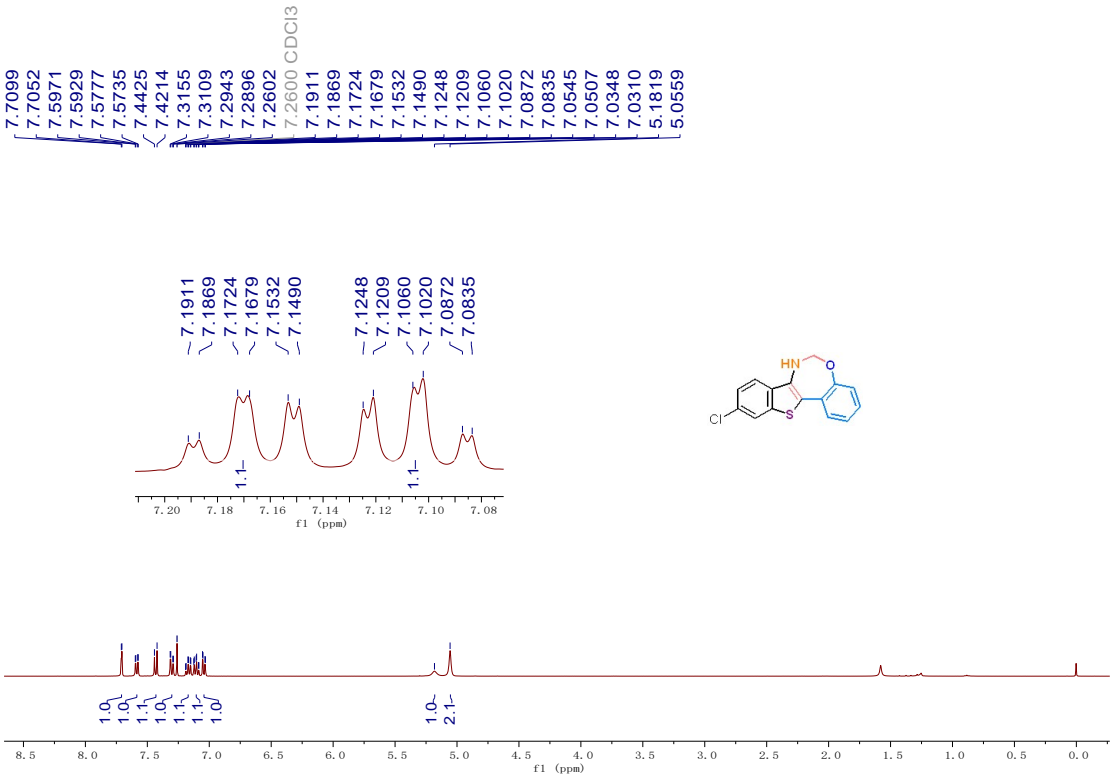
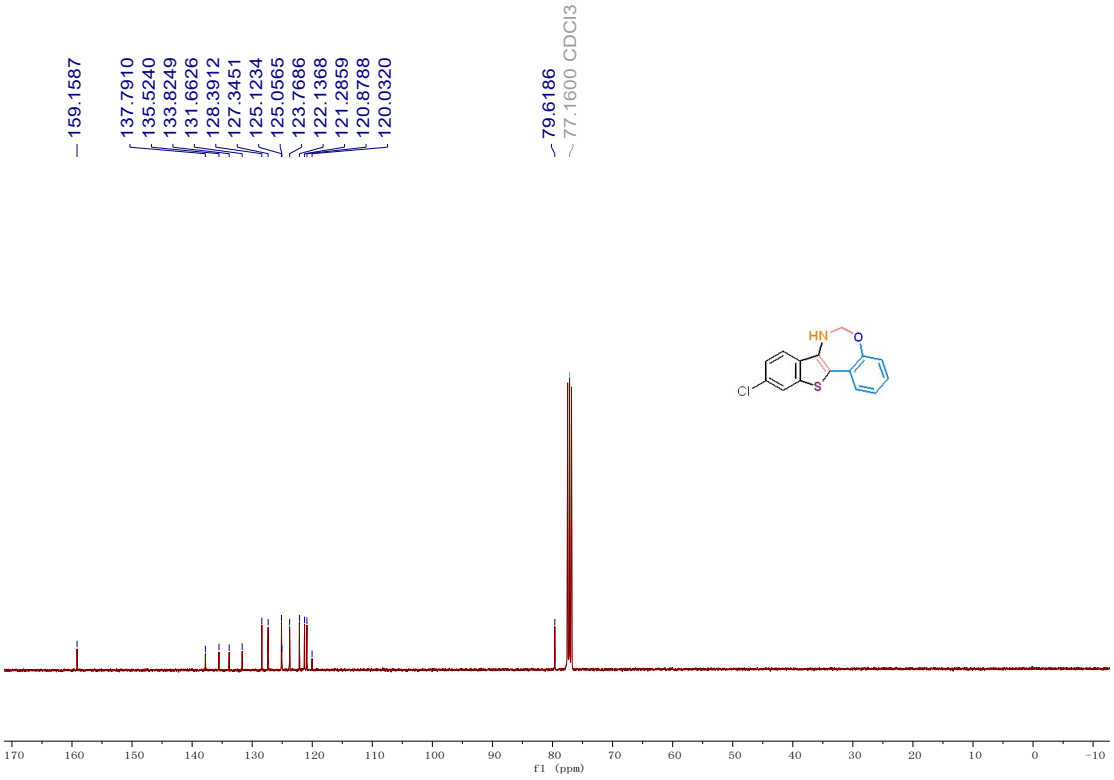


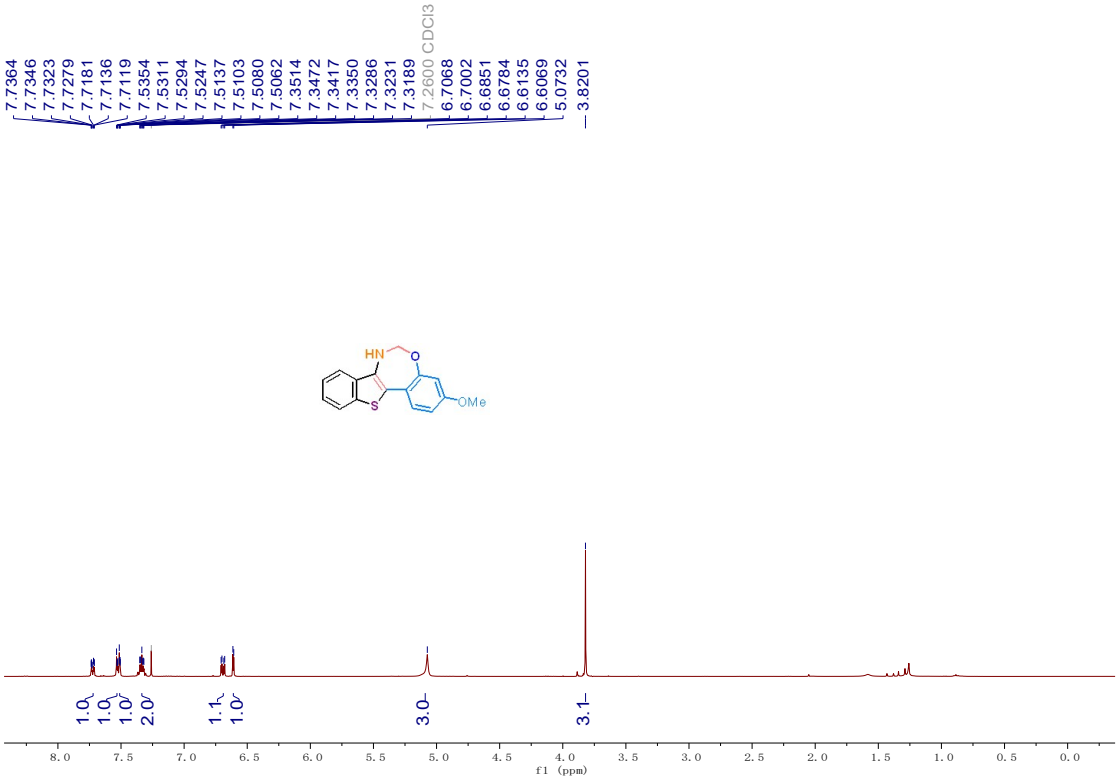
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of compound 4e



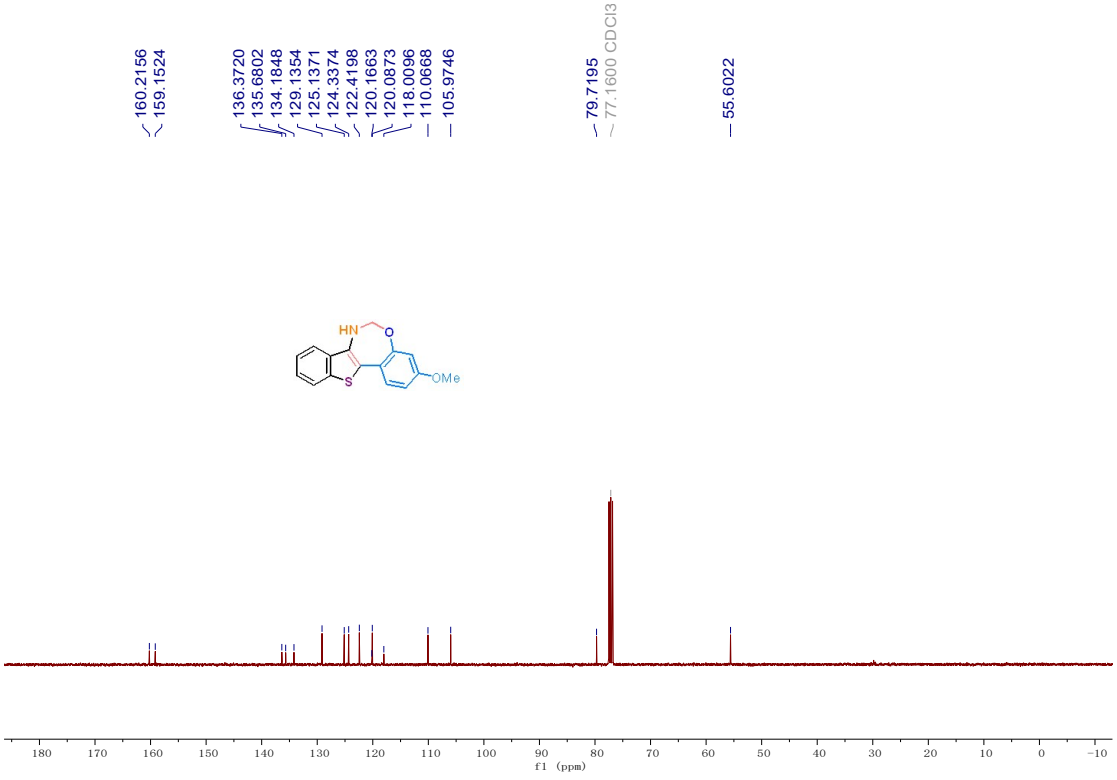
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4f



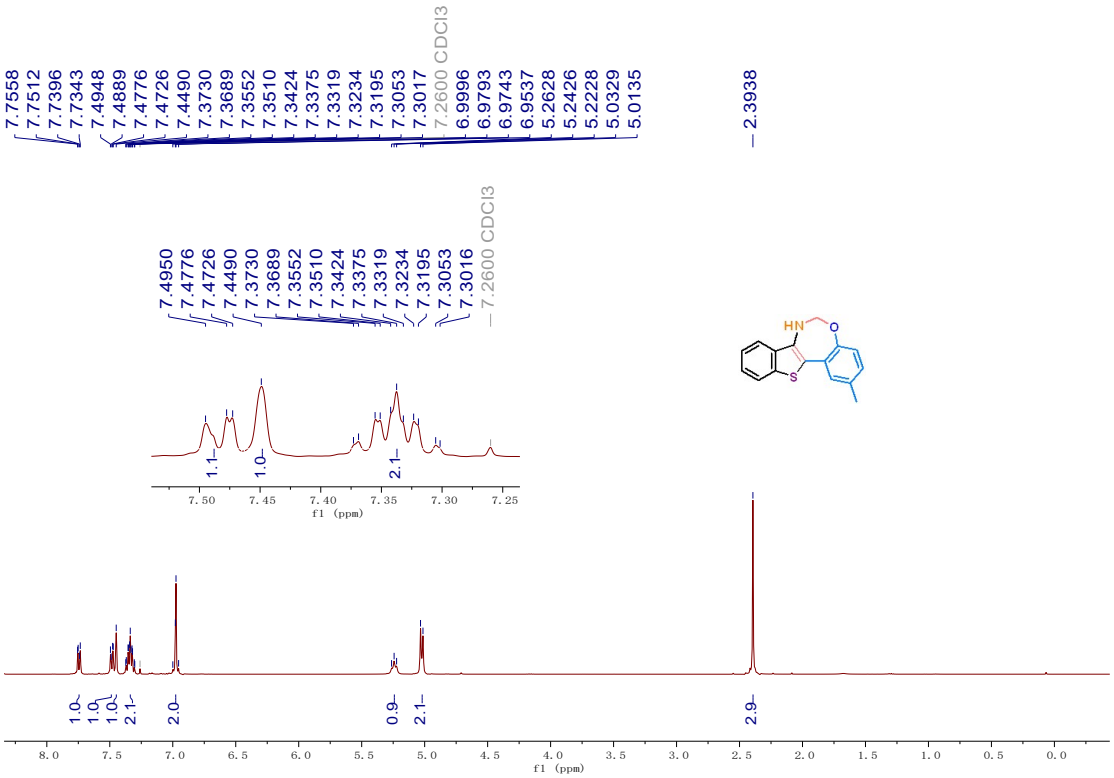
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4f



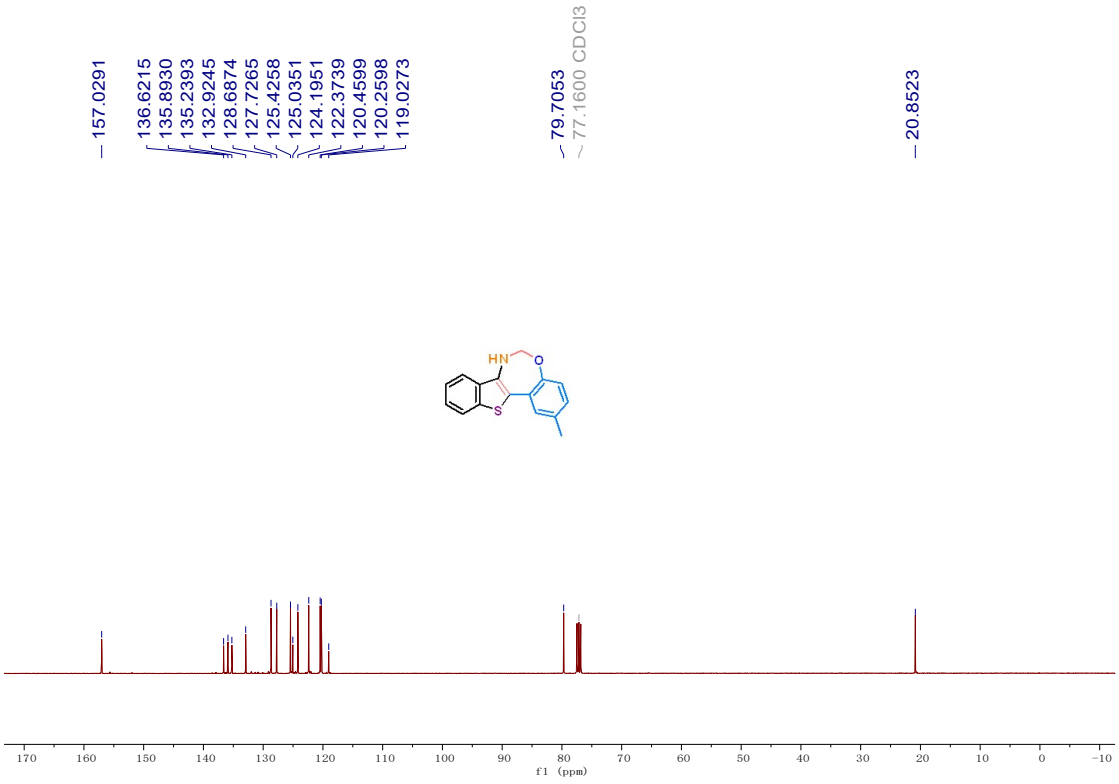
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4g



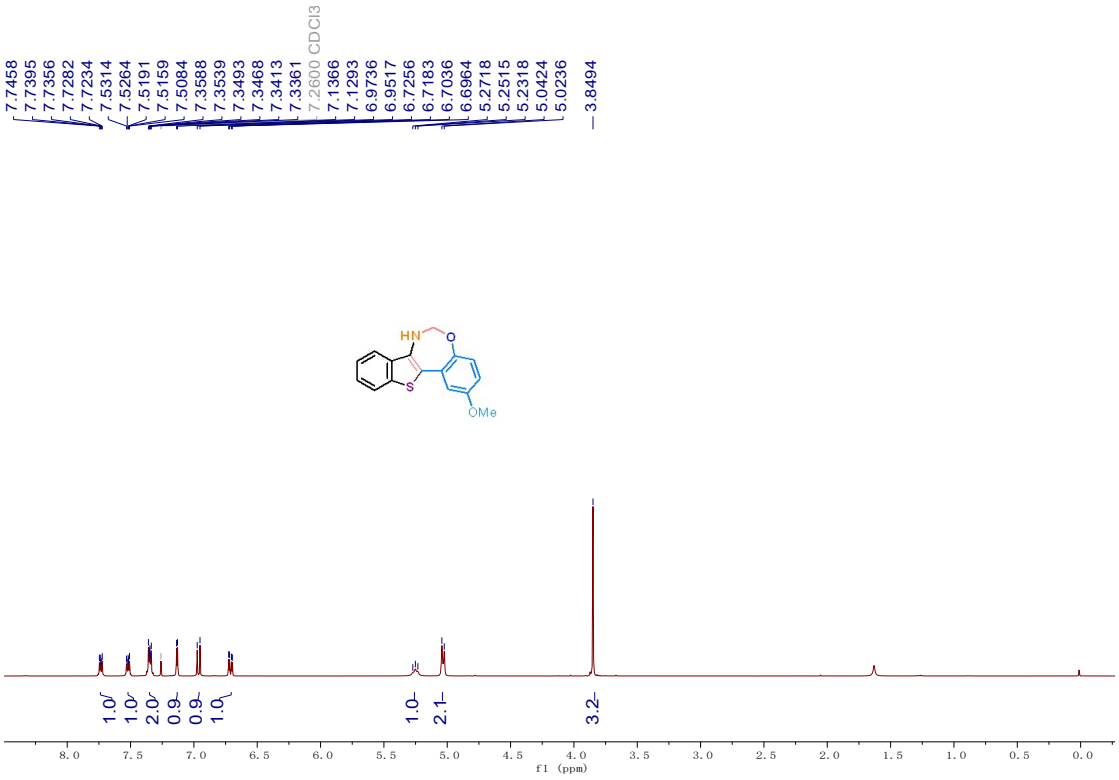
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4g



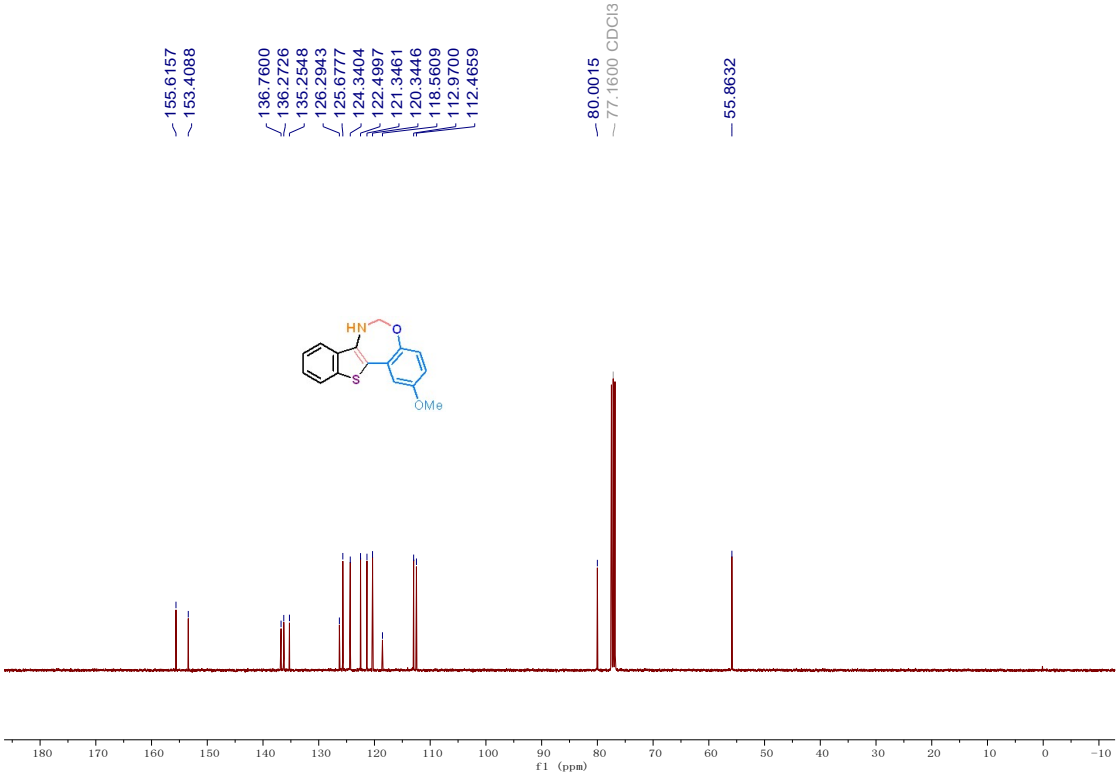
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4h



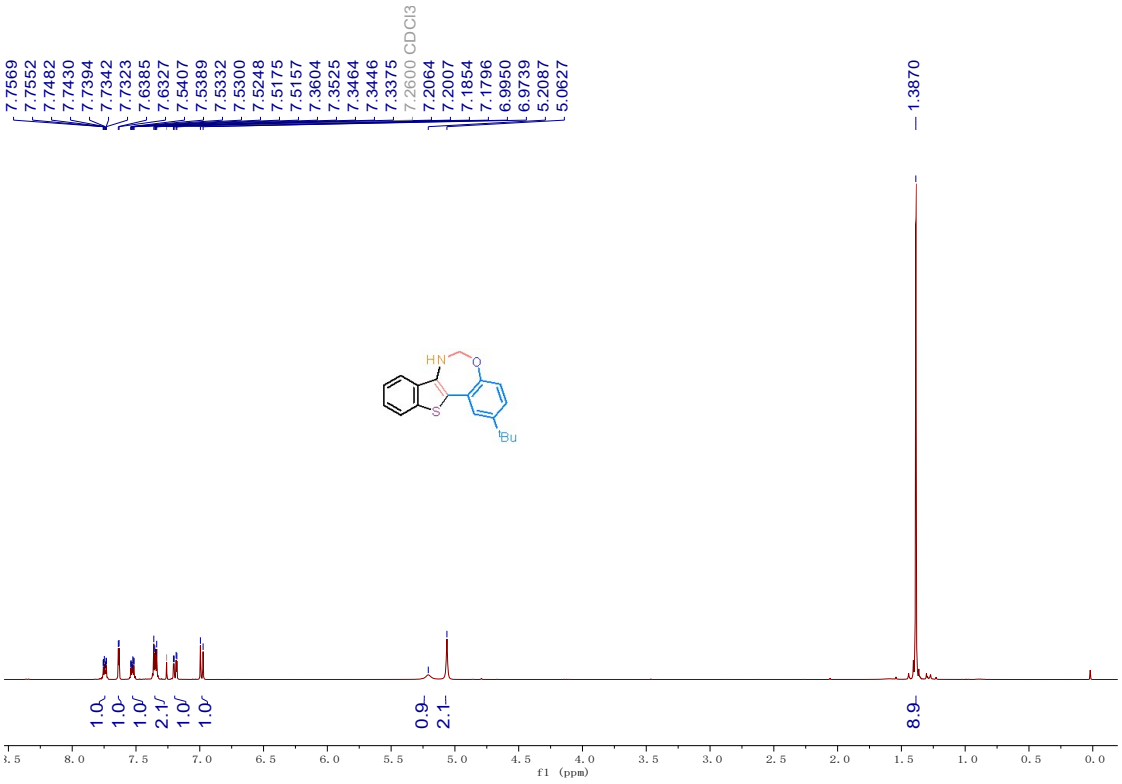
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4h



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



^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4i



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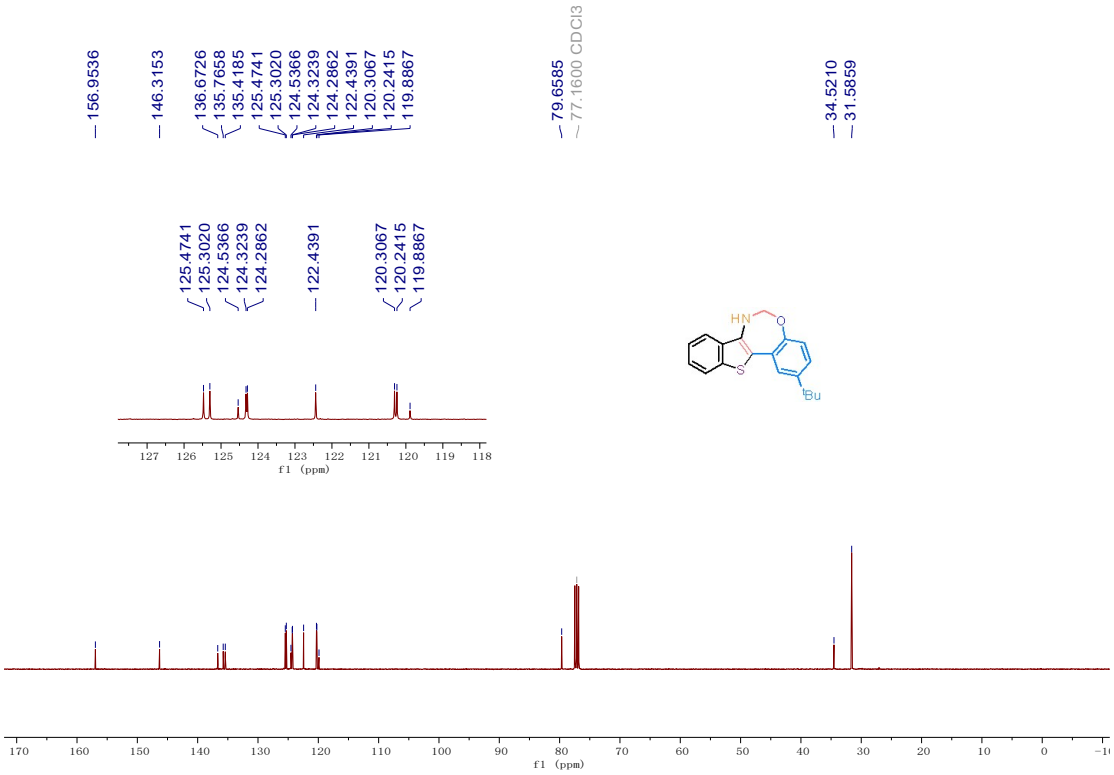

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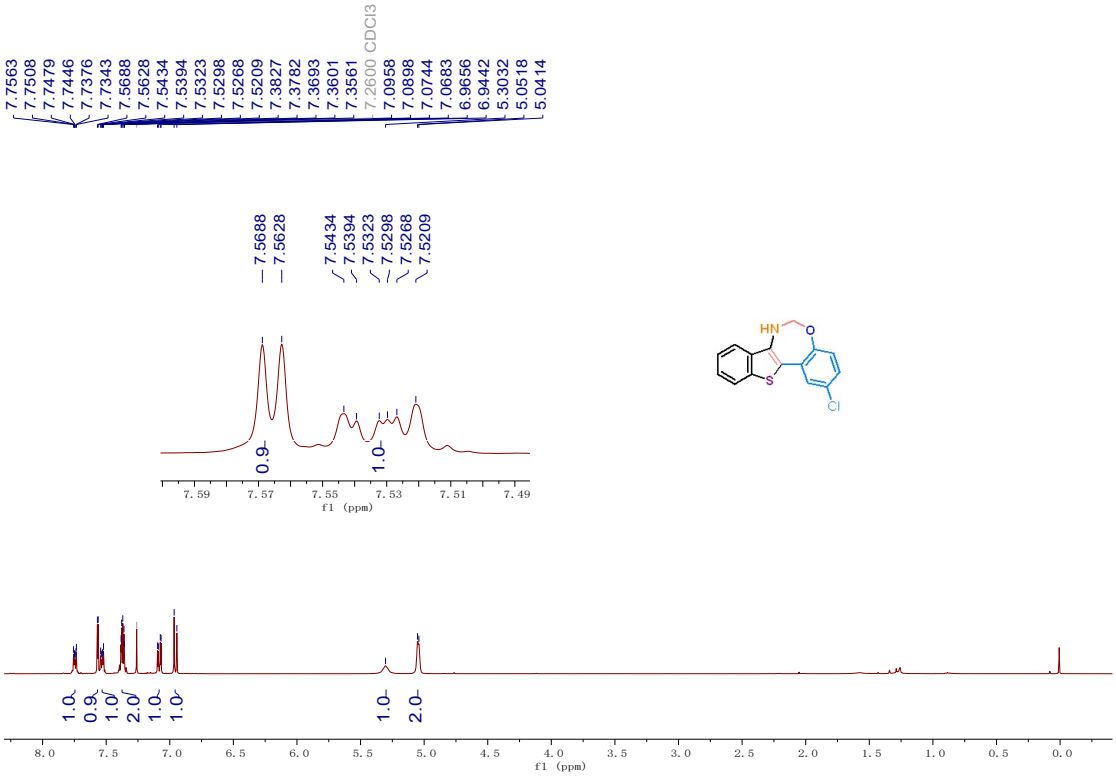

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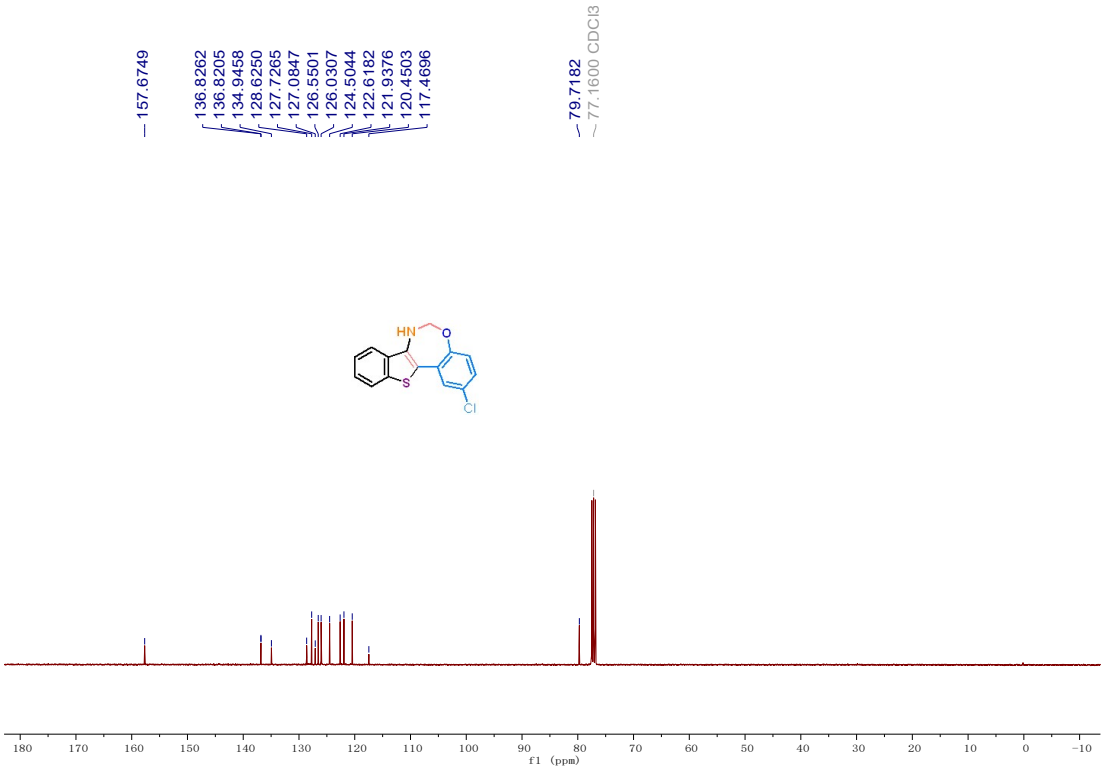

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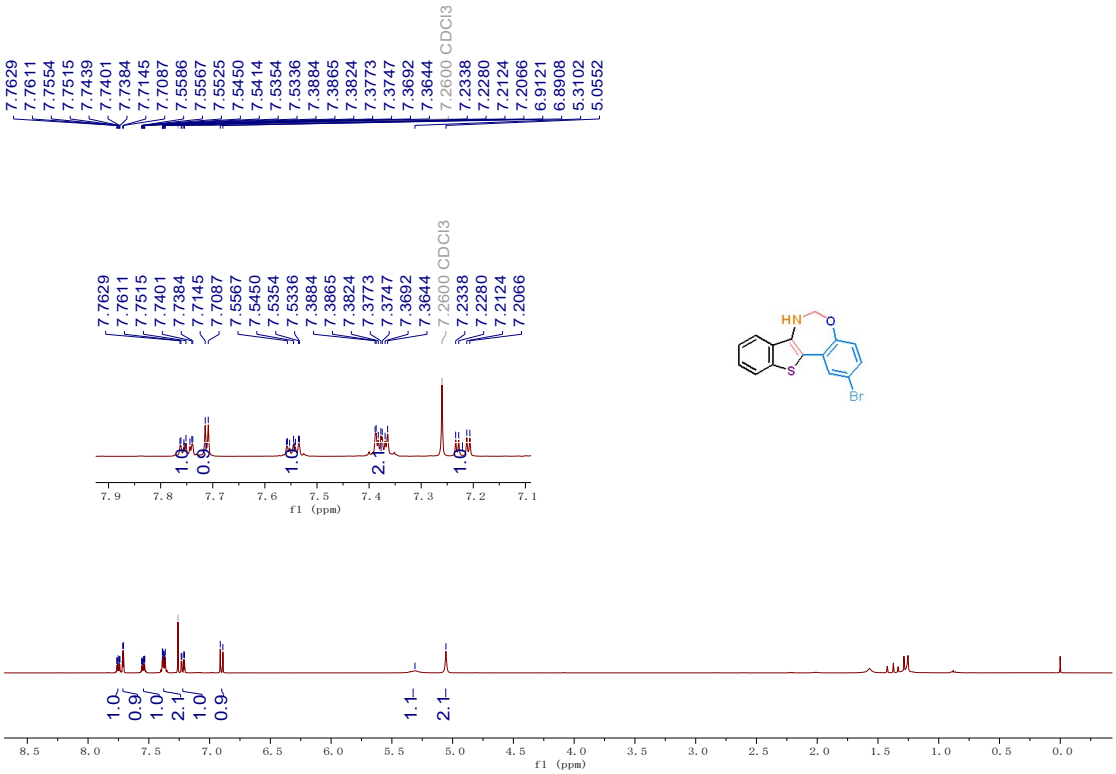

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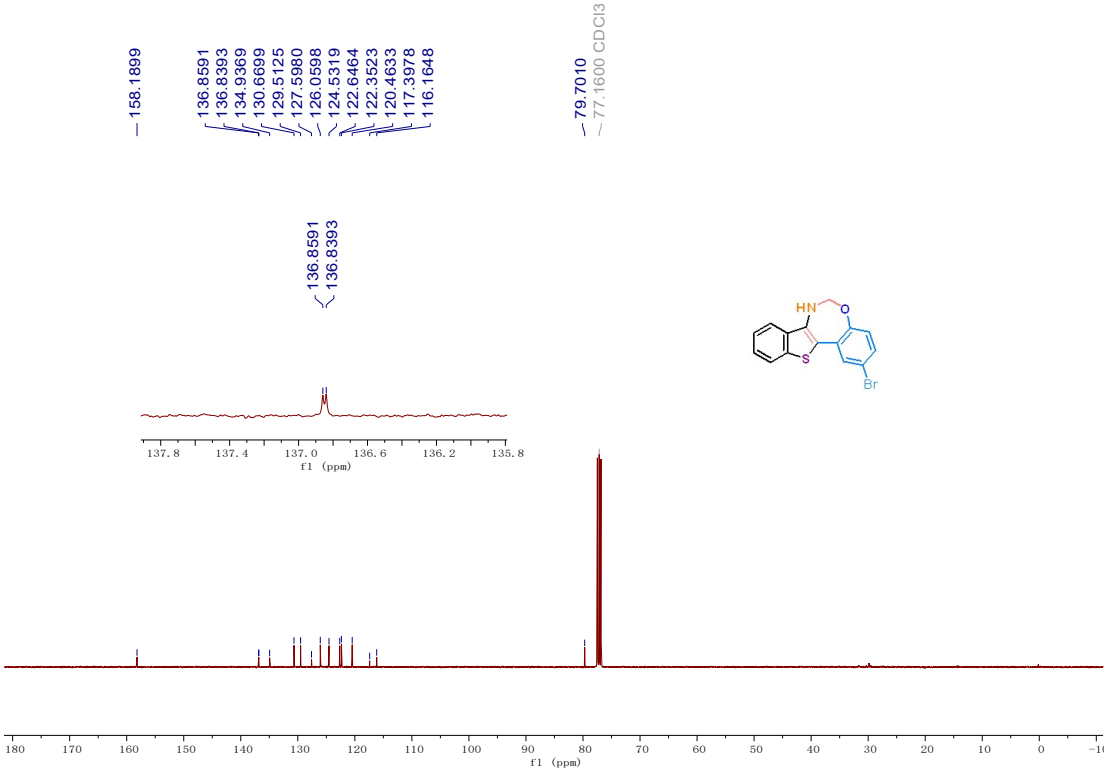
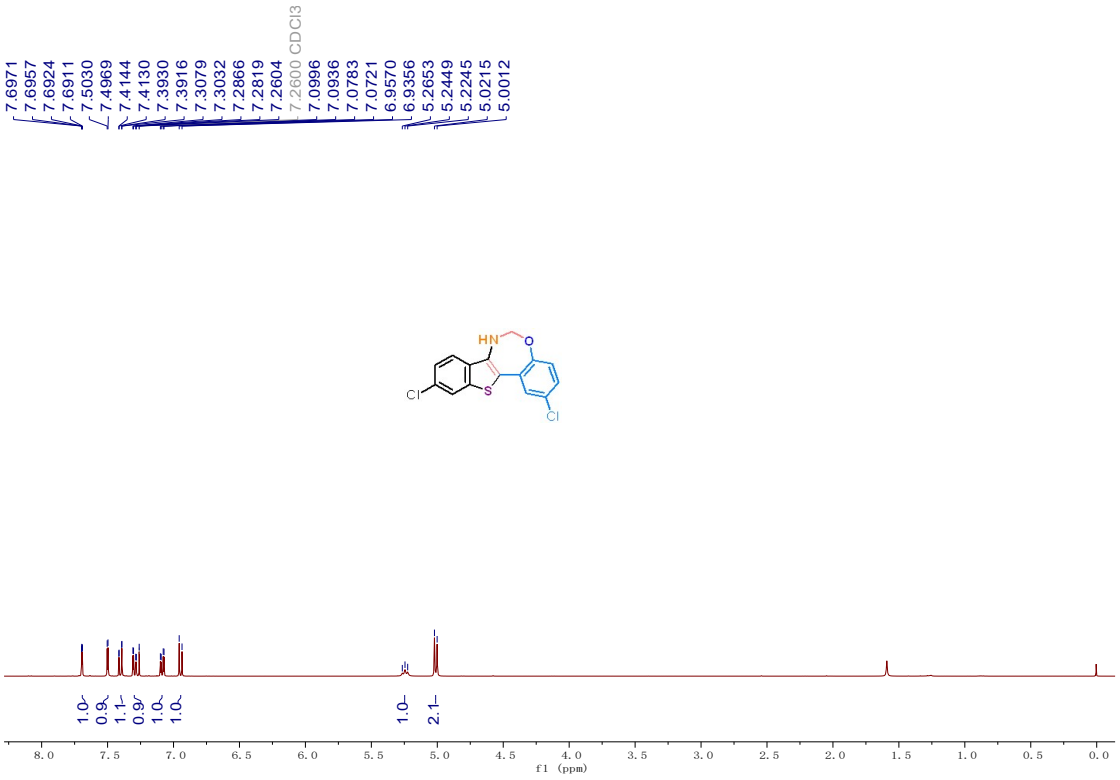
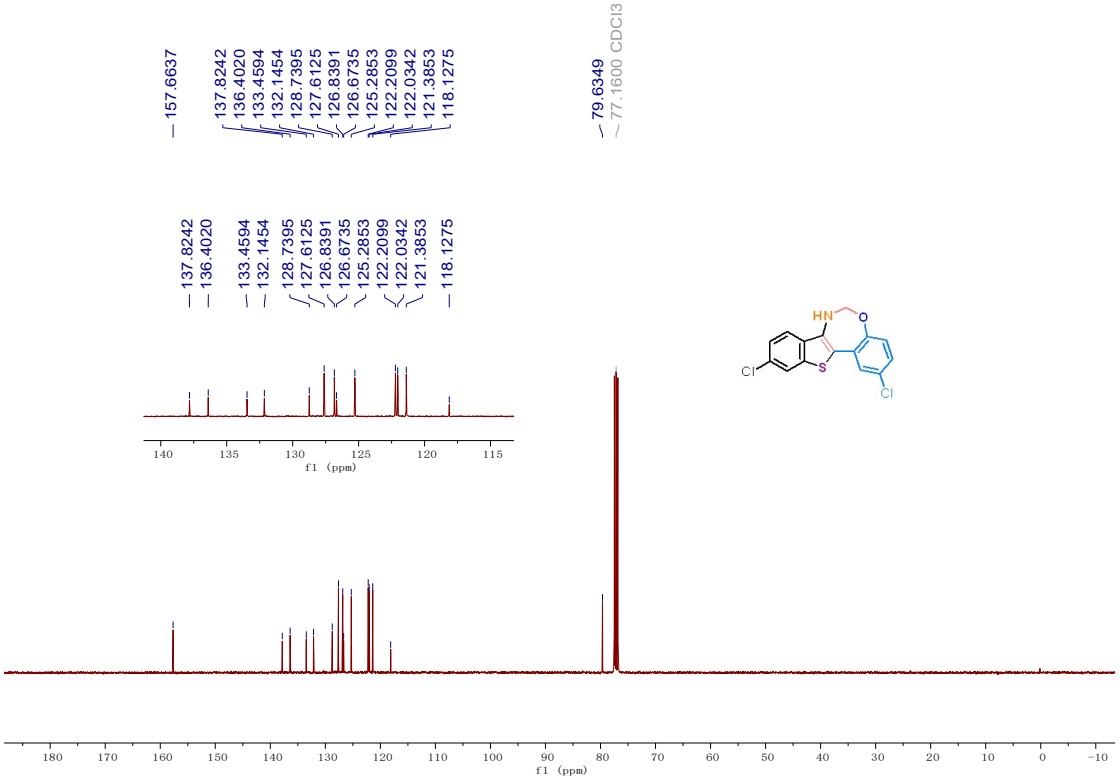


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4l



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4m



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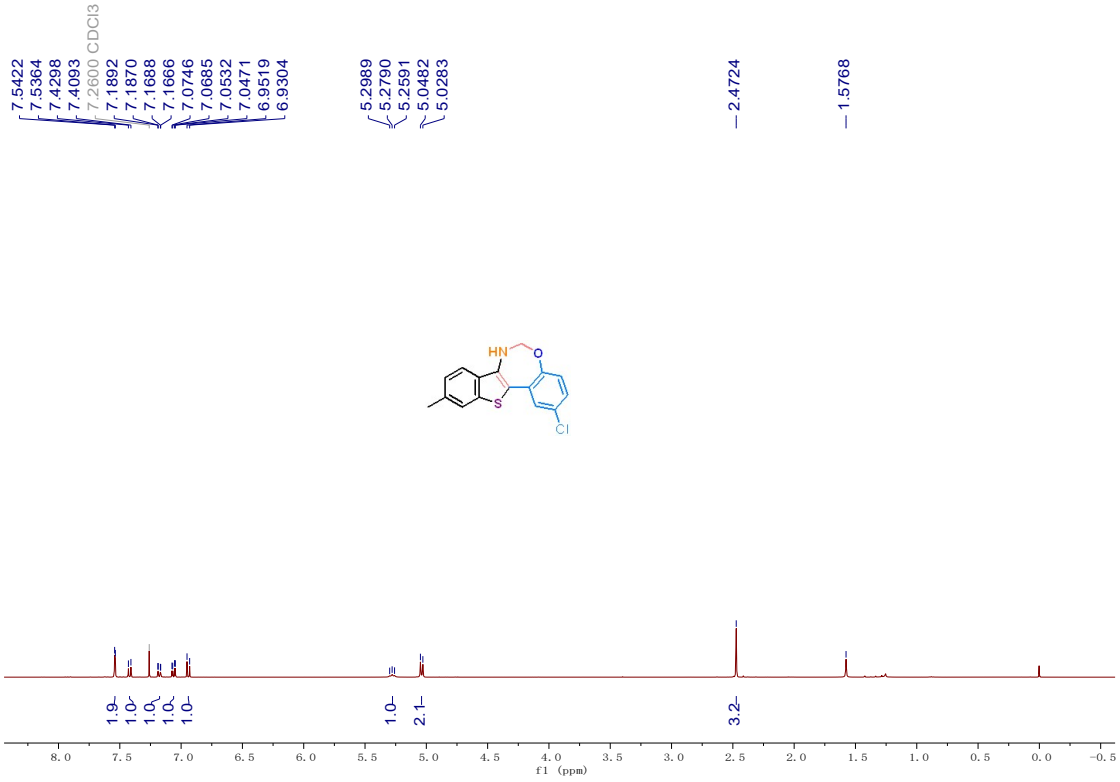

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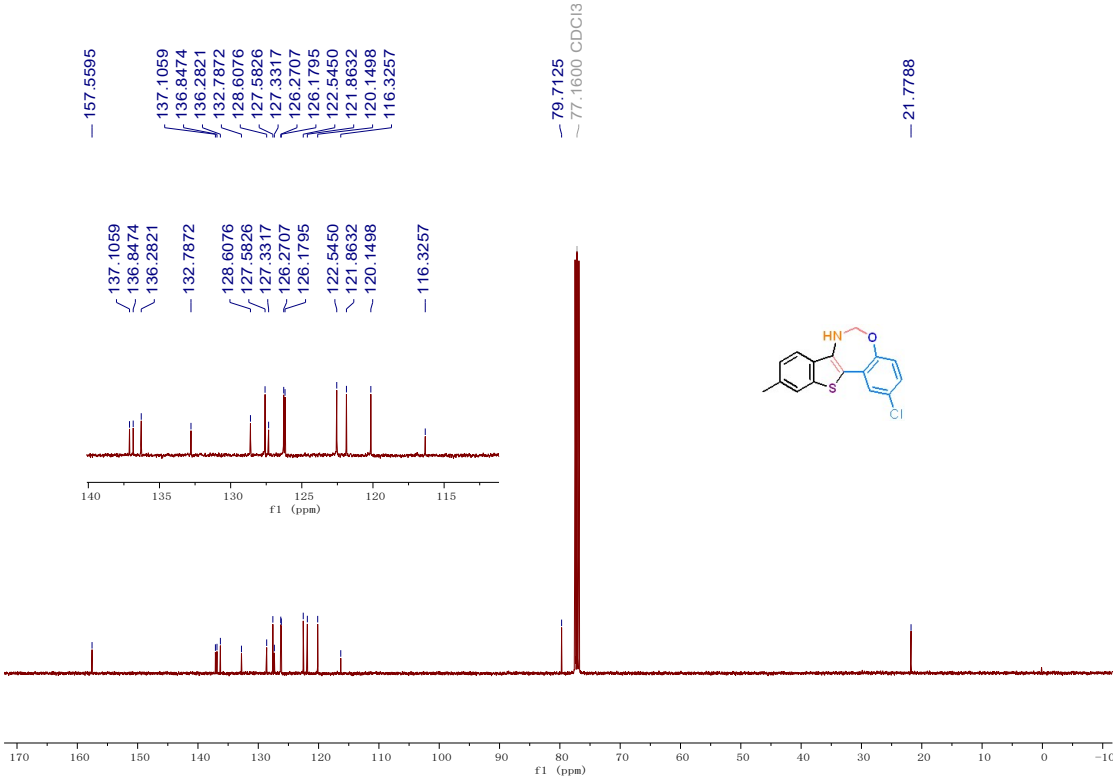

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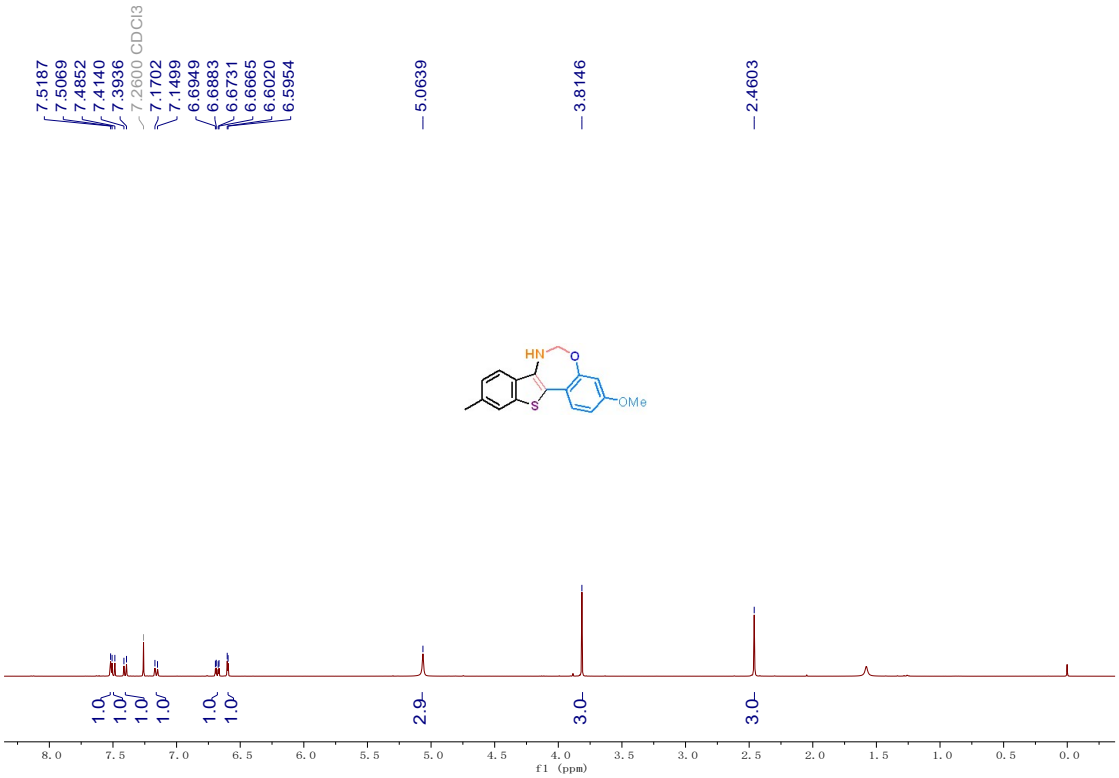

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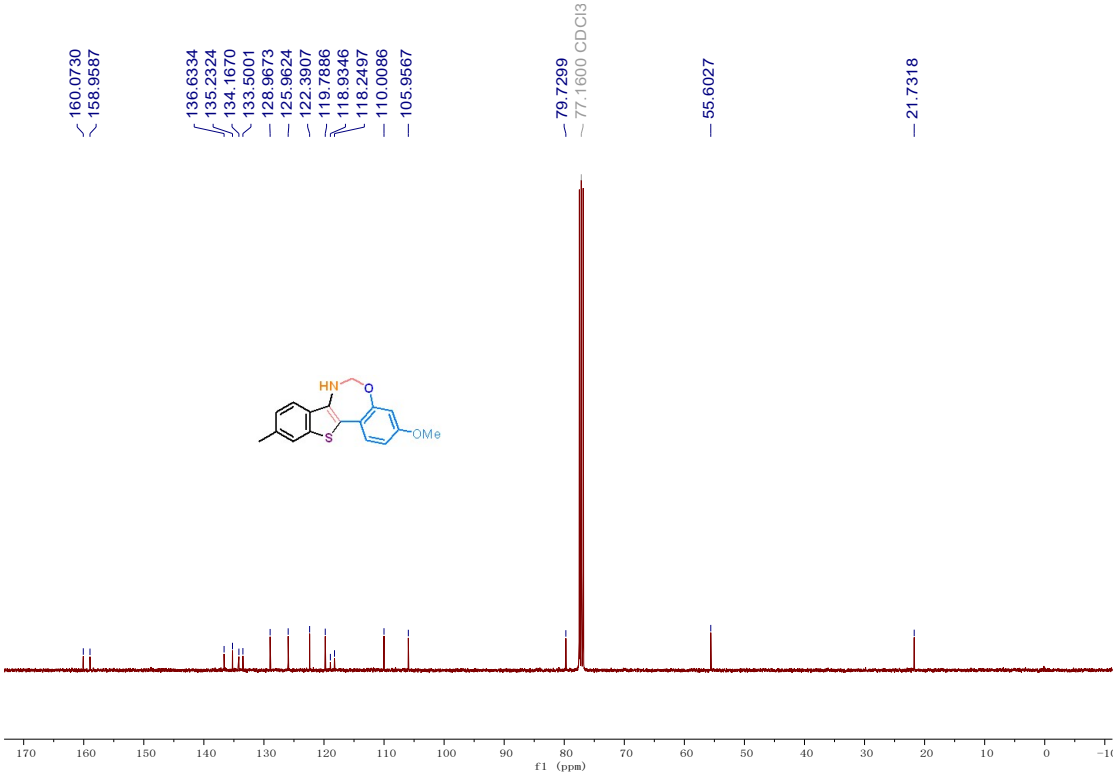

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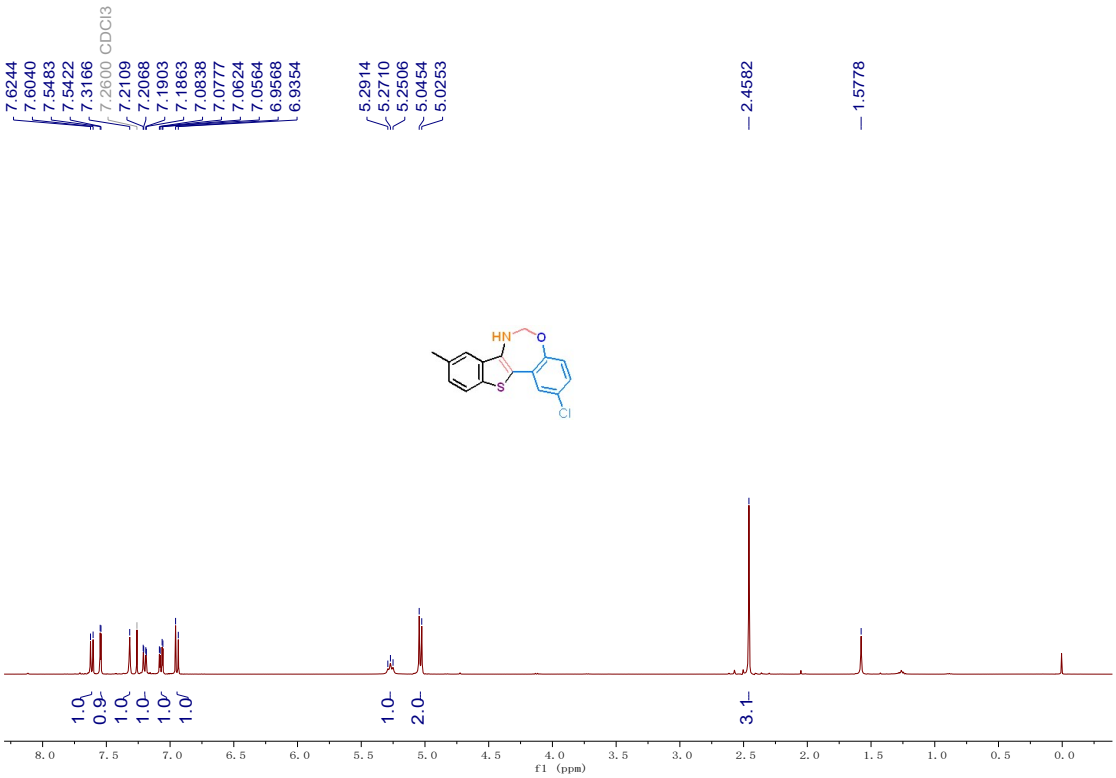

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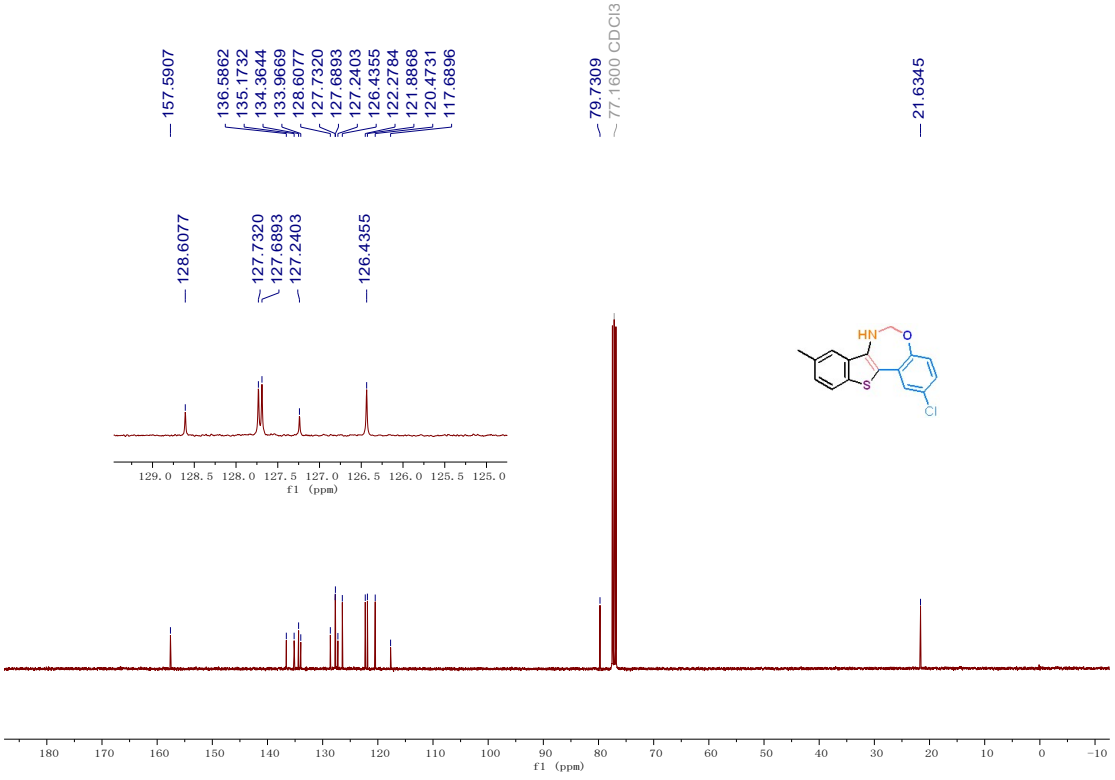

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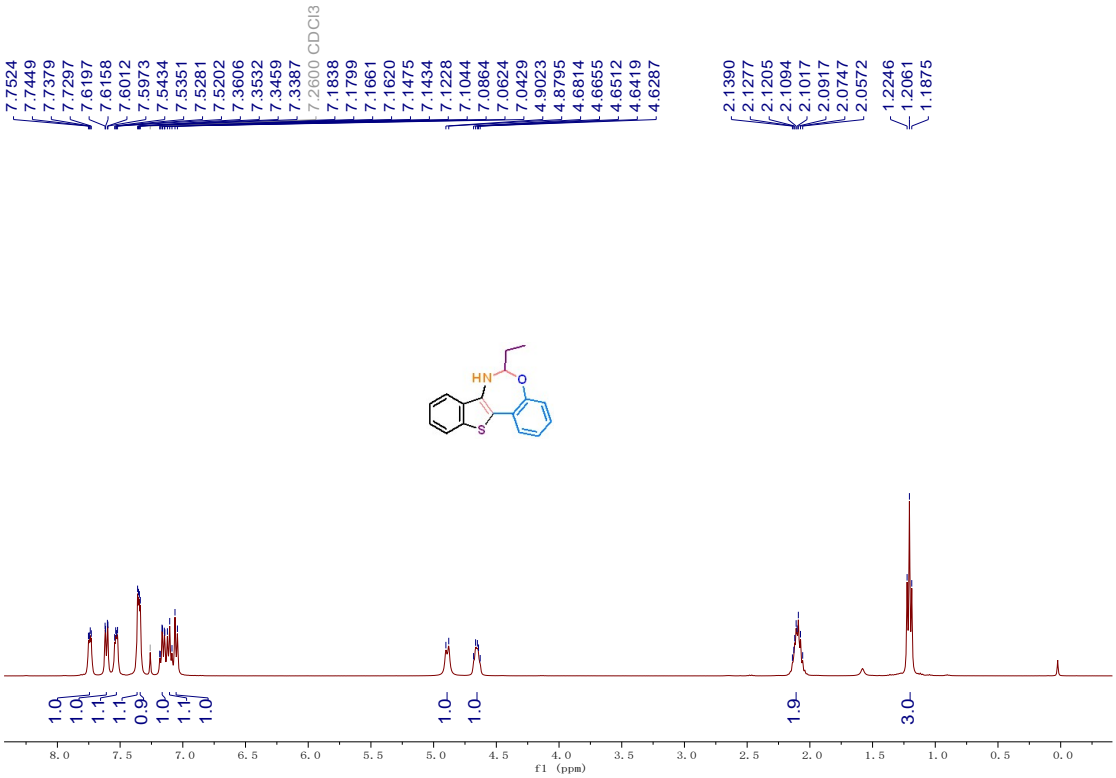

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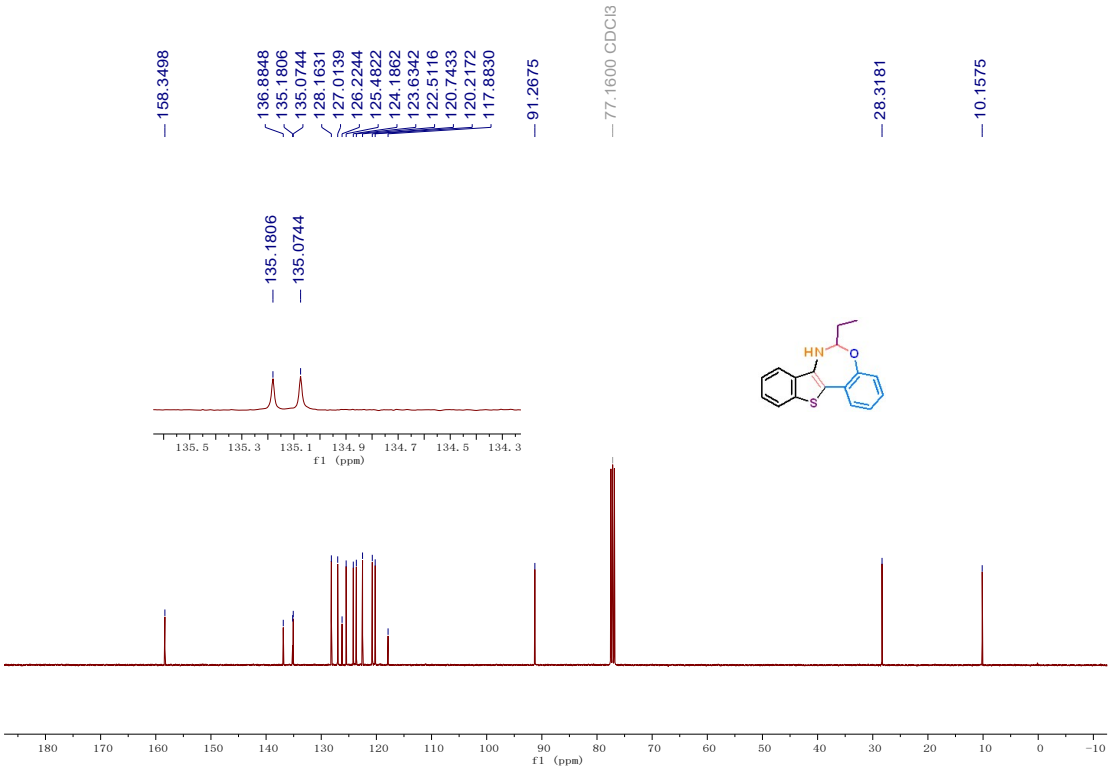
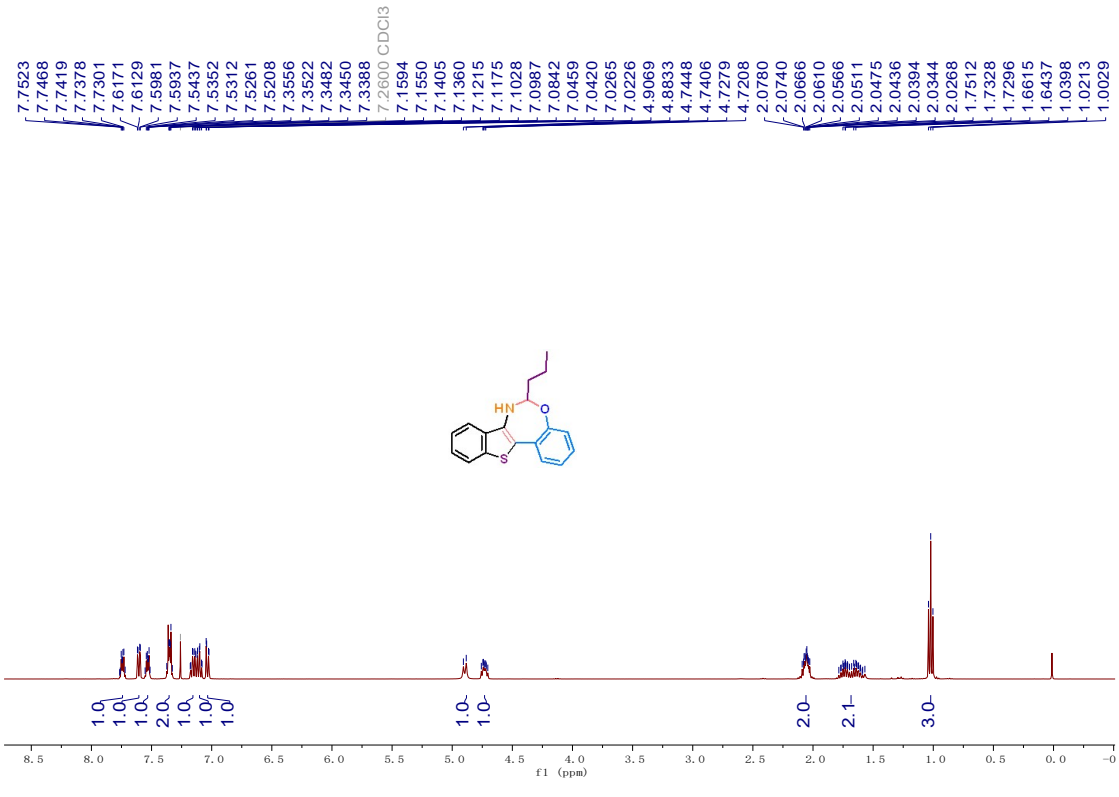


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4q



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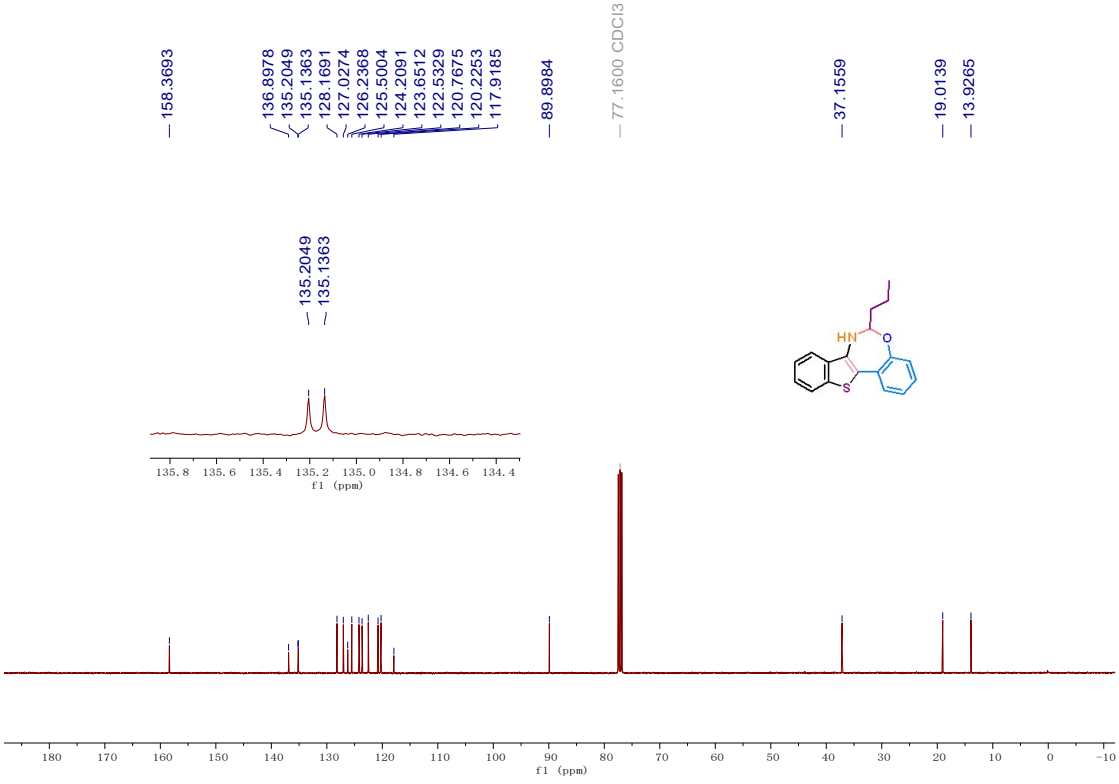

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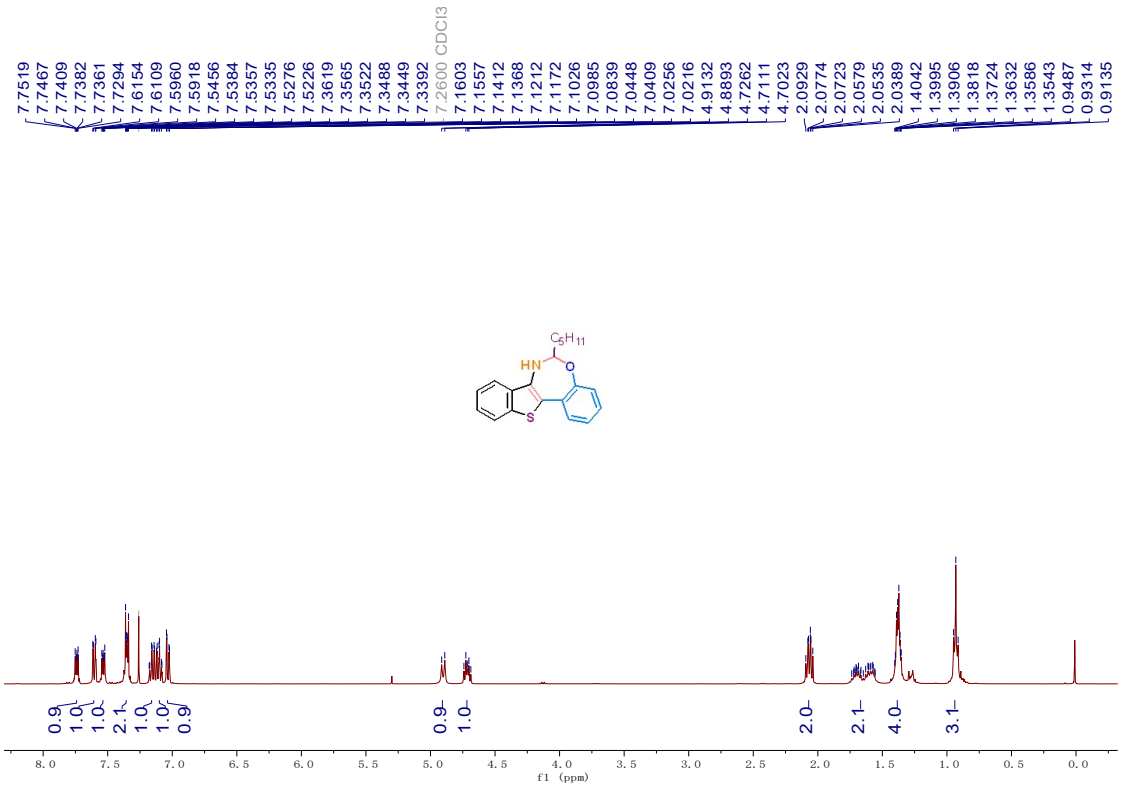

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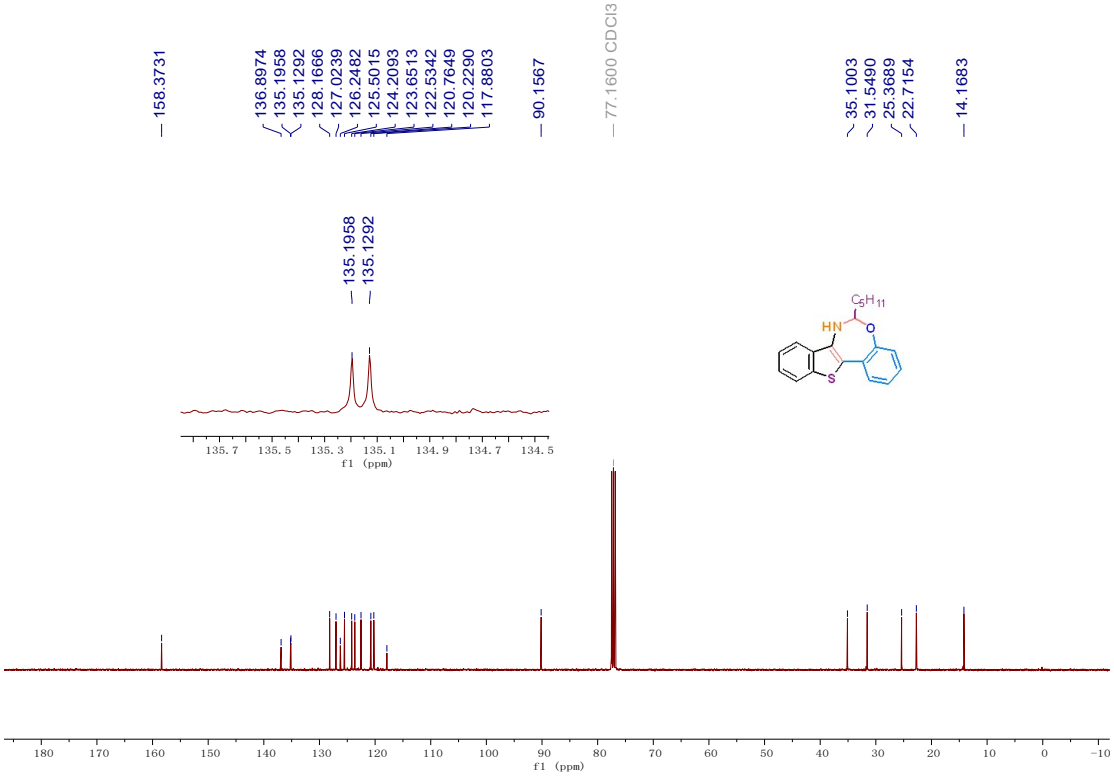

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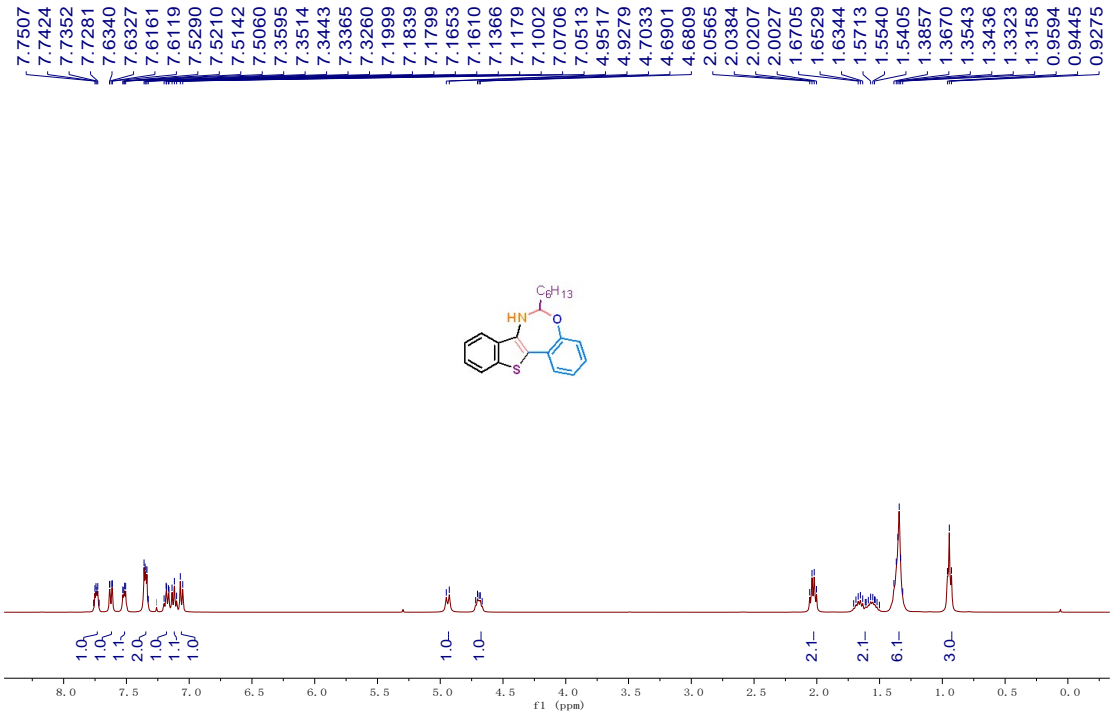

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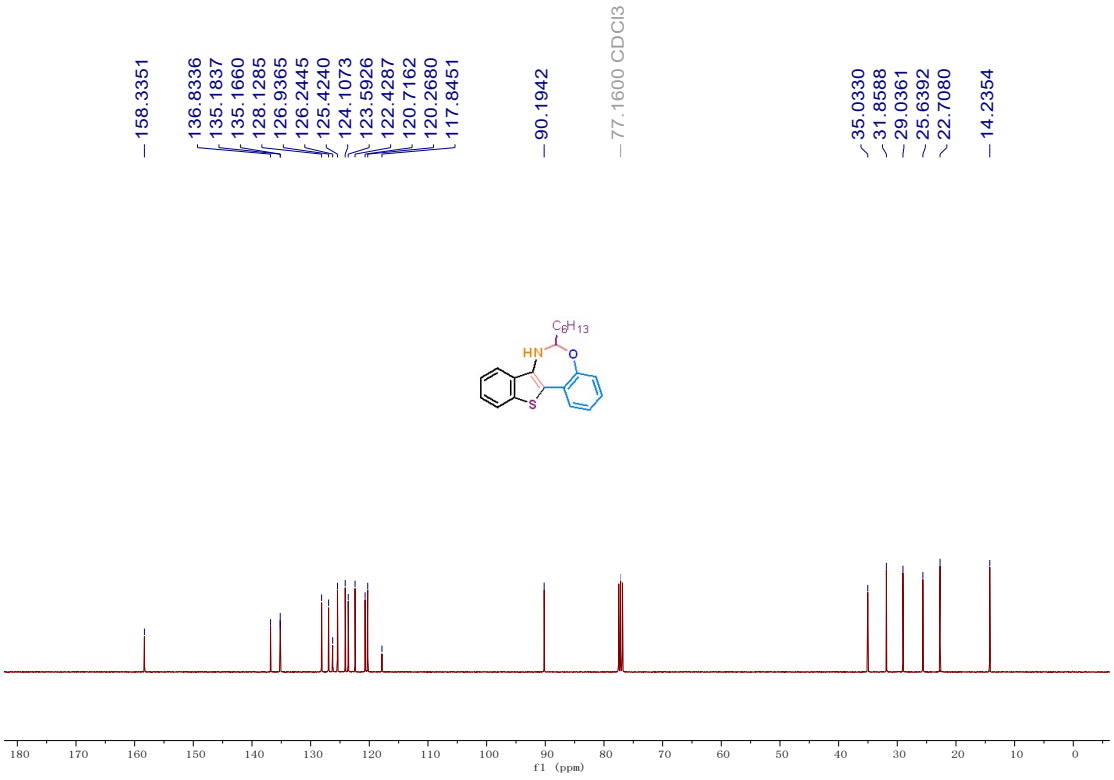
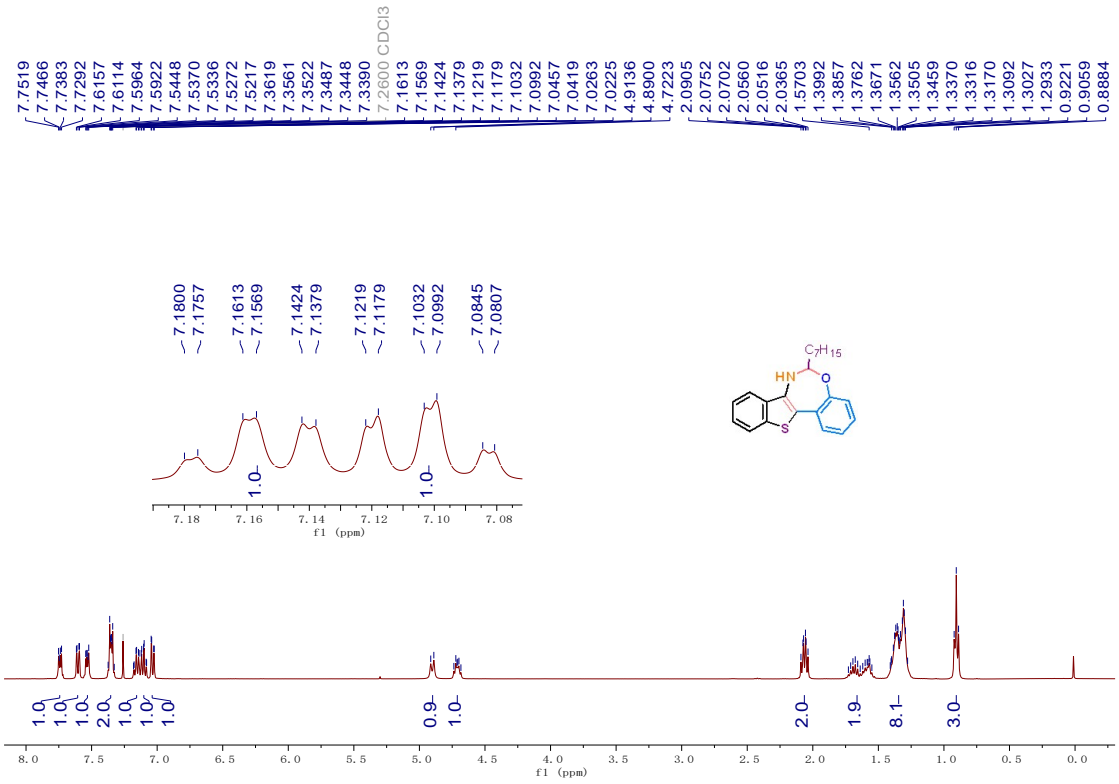
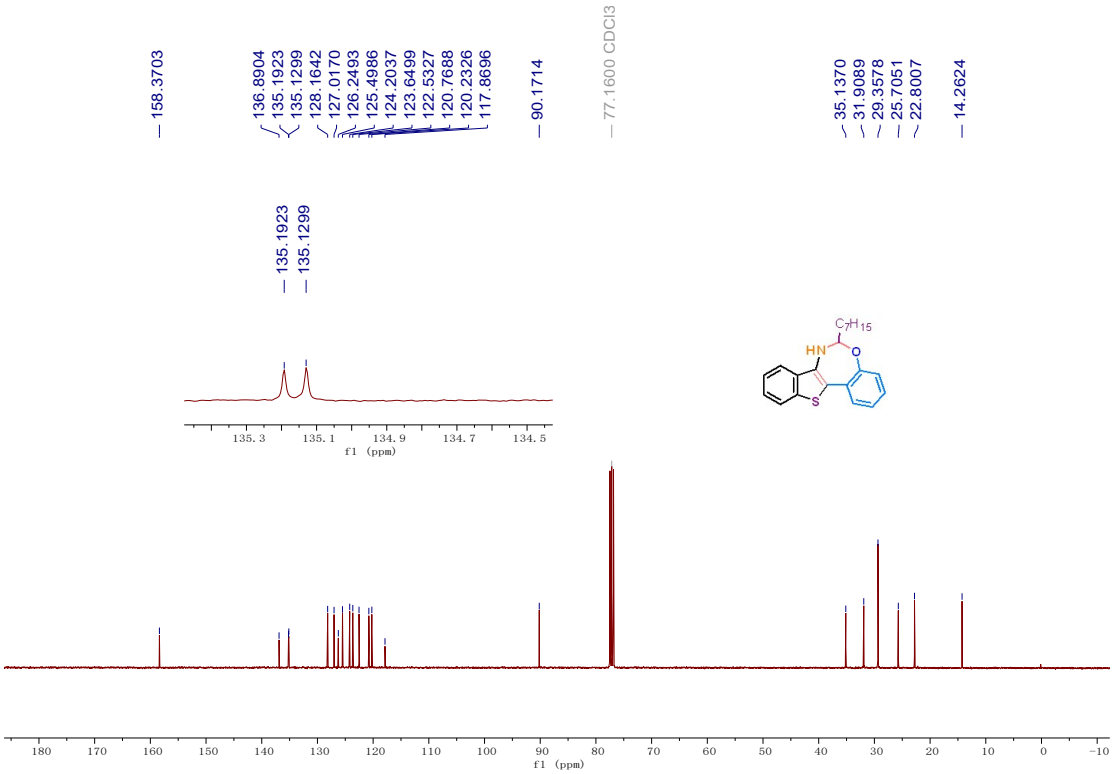


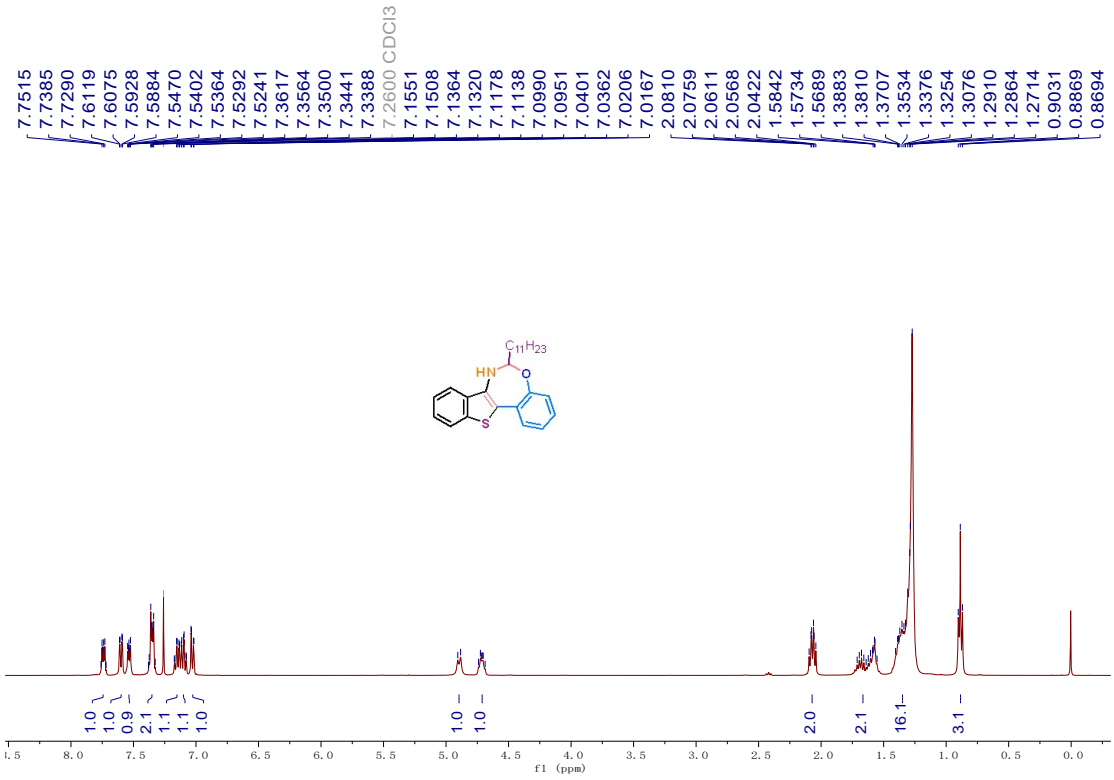
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4t



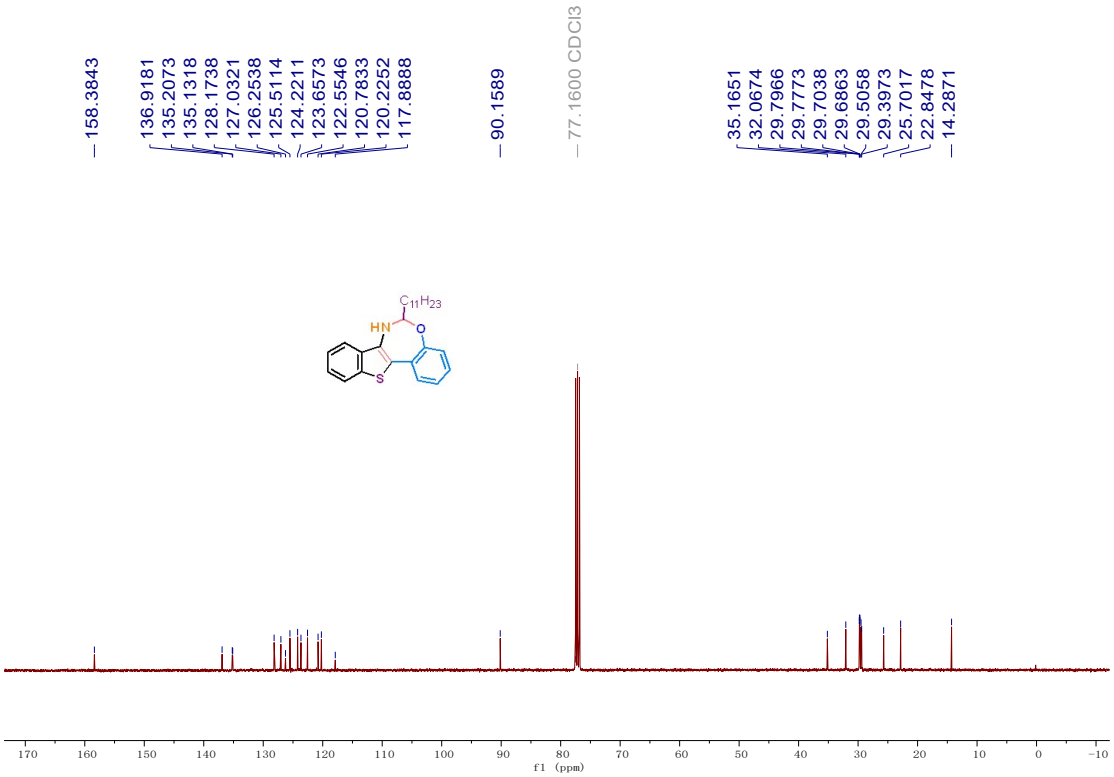
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4u



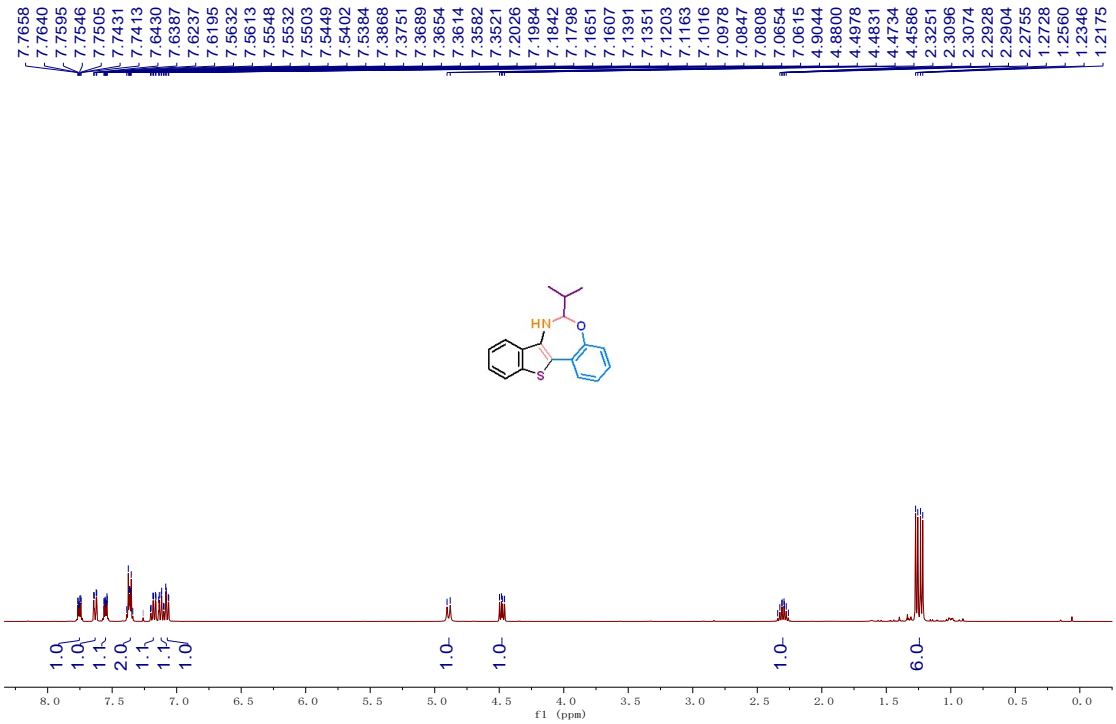
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4u



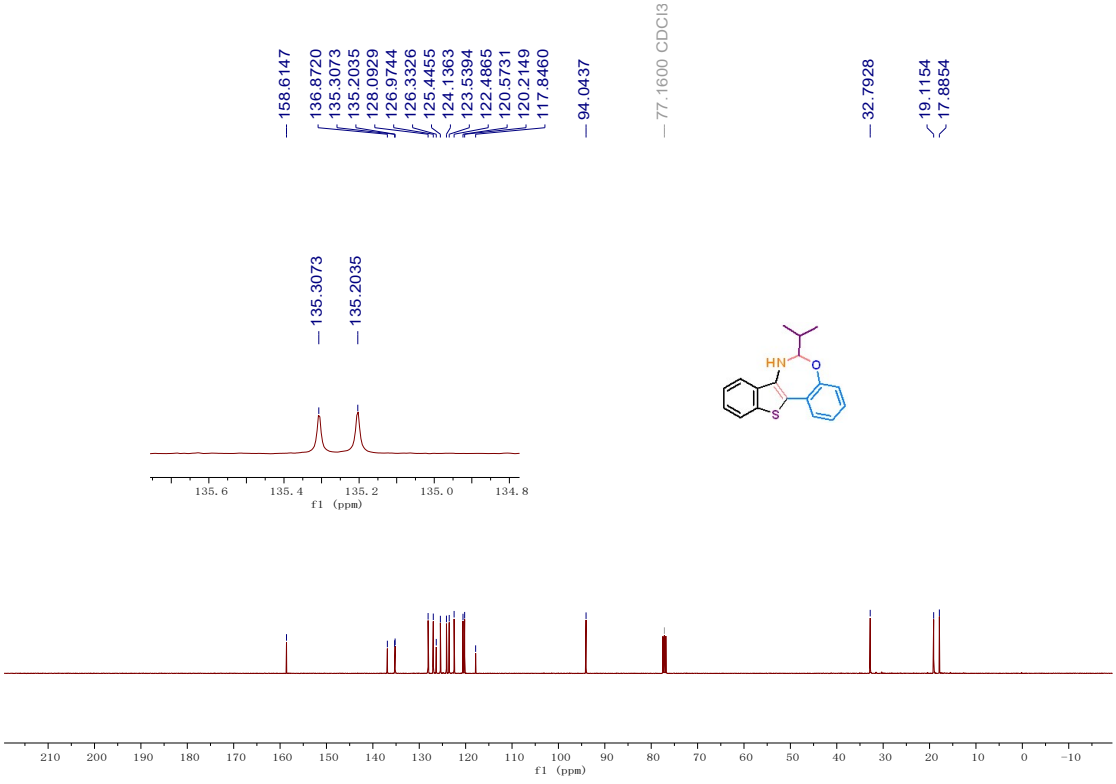
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4v



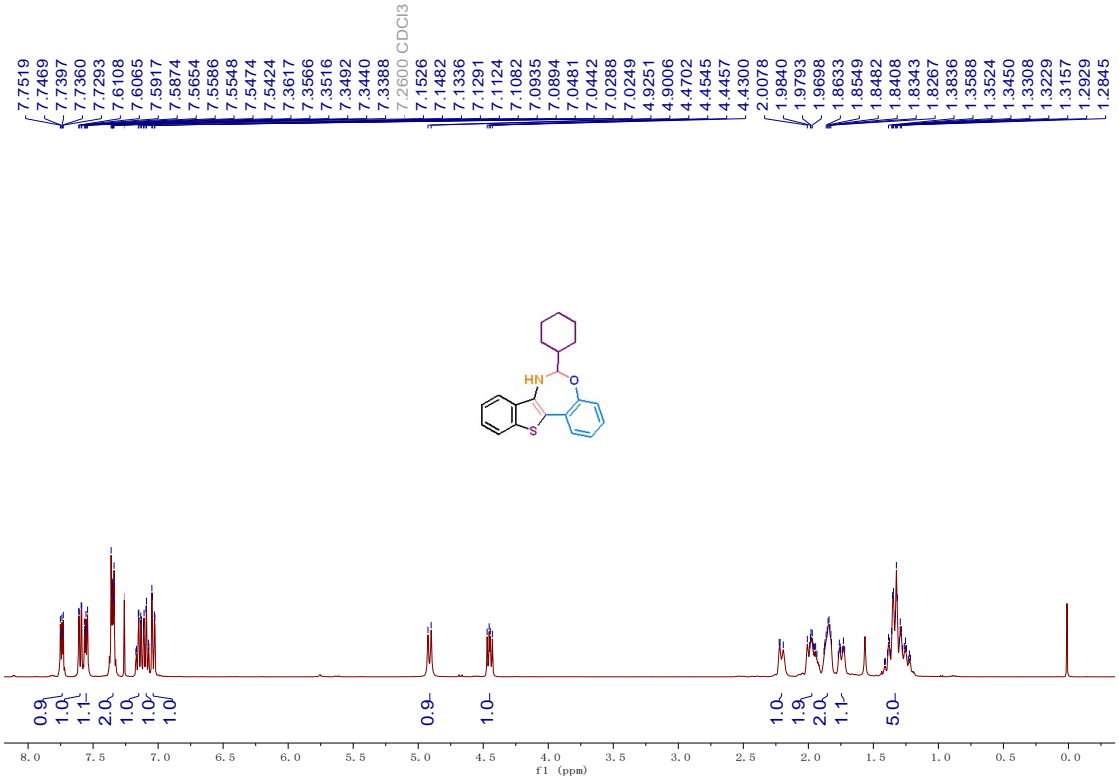
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4v



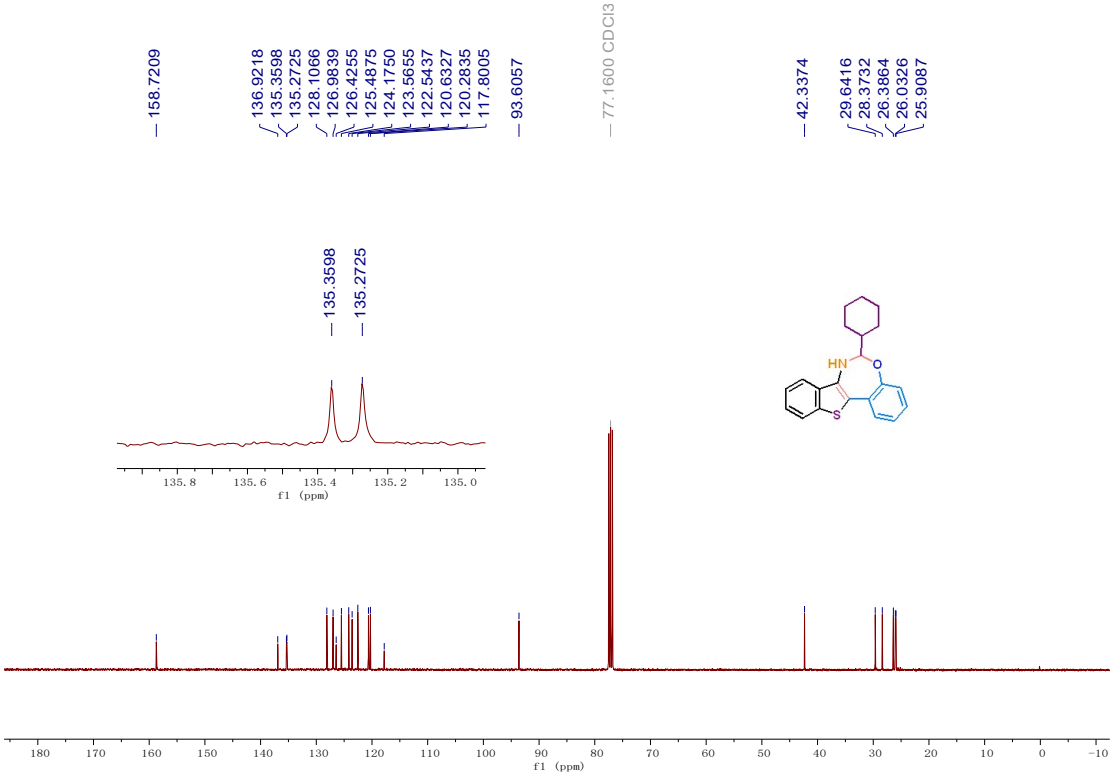
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4w



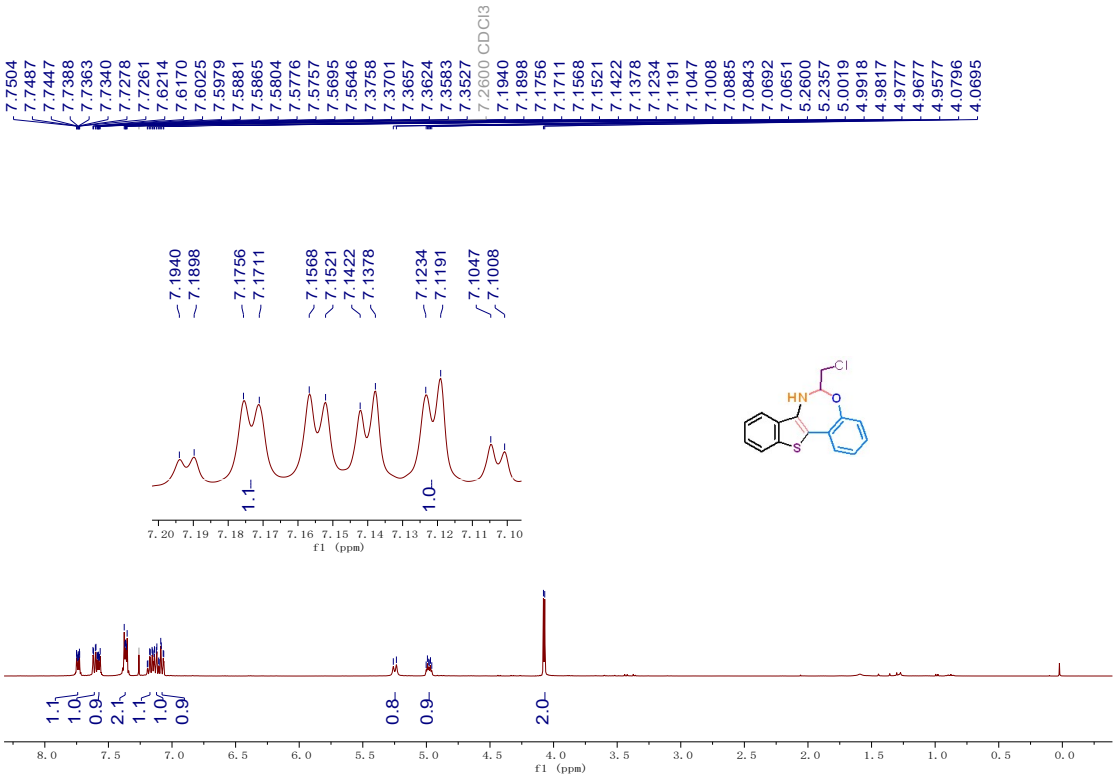
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4w



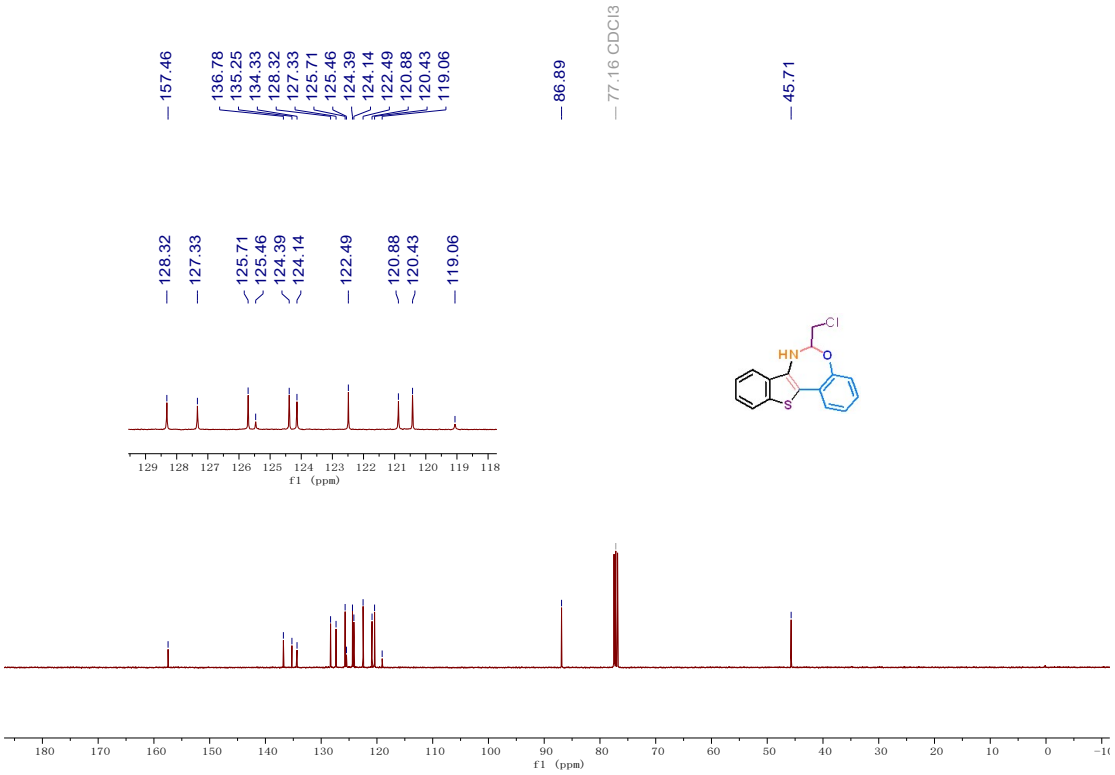
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4x



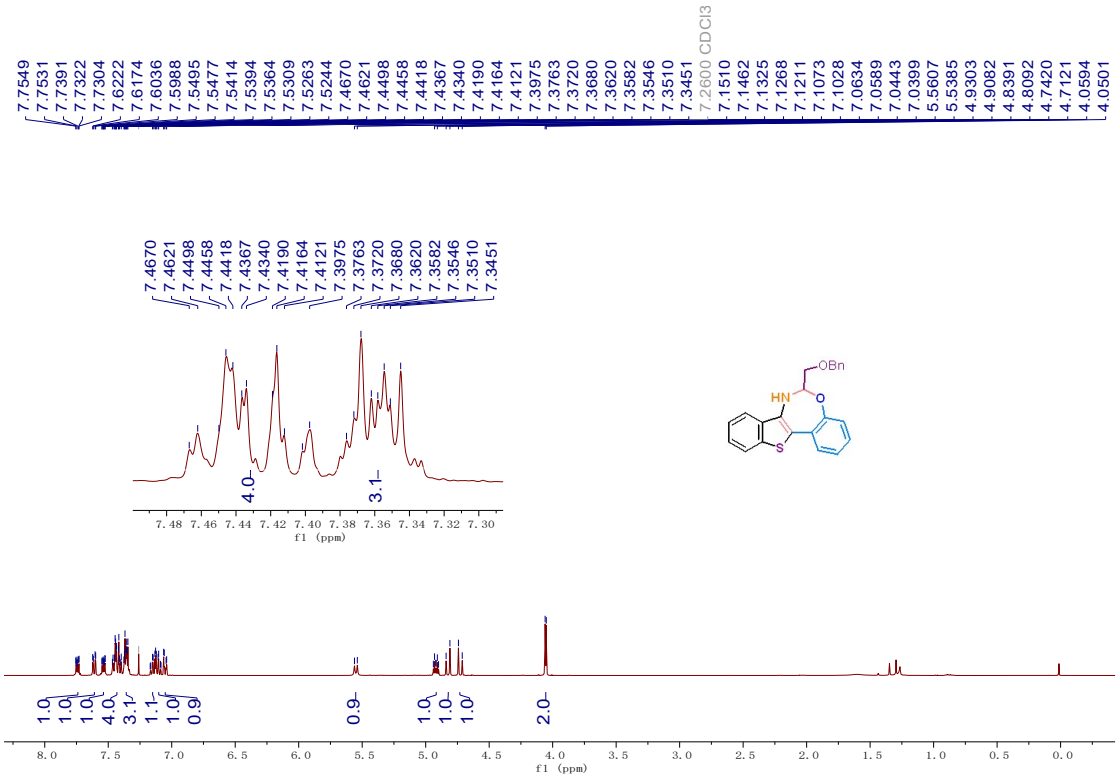
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4x



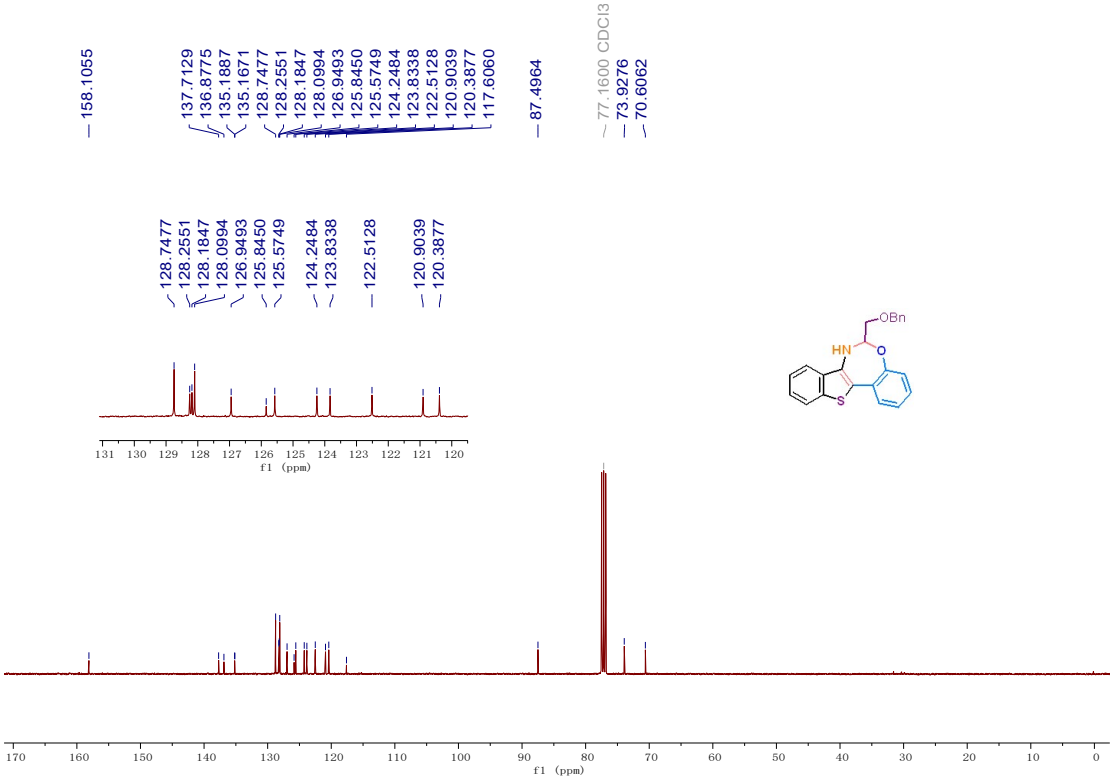
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4y



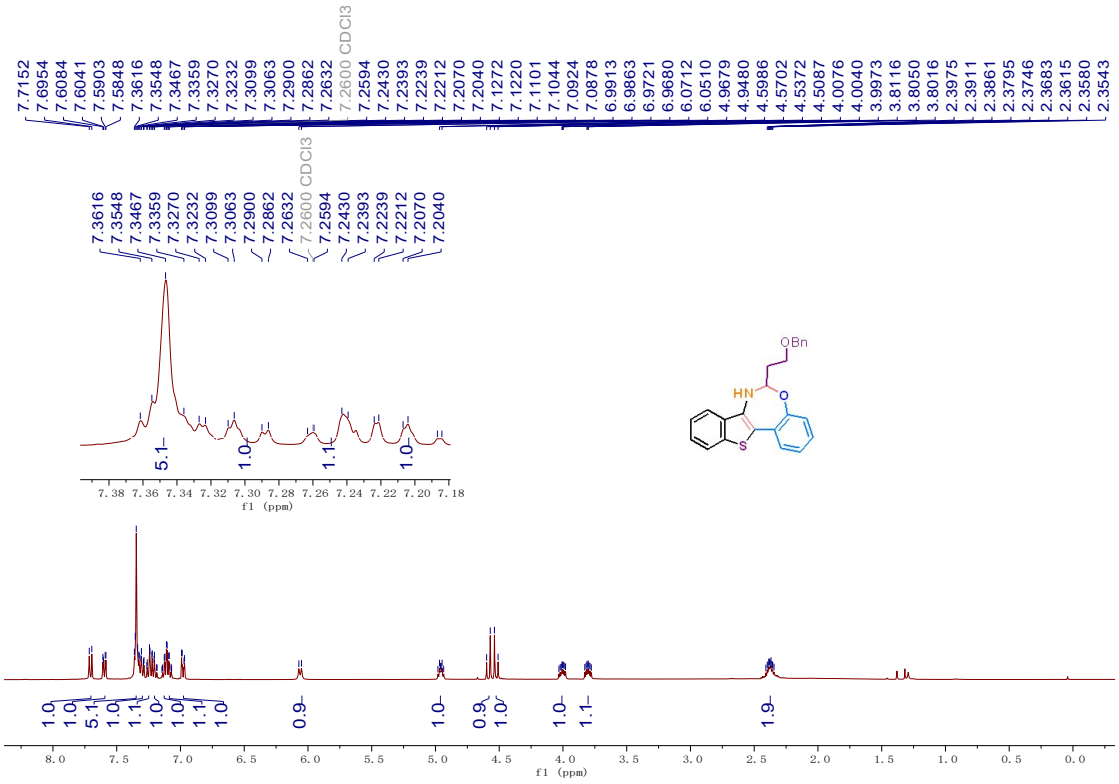
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4y



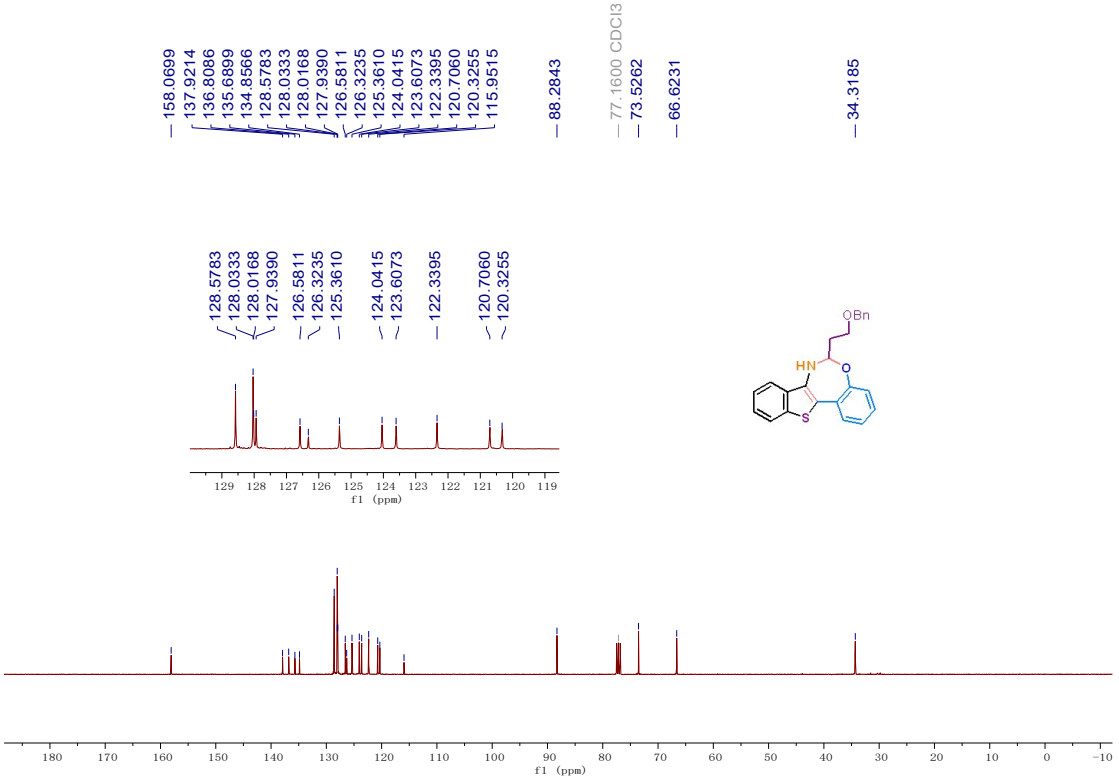
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4z



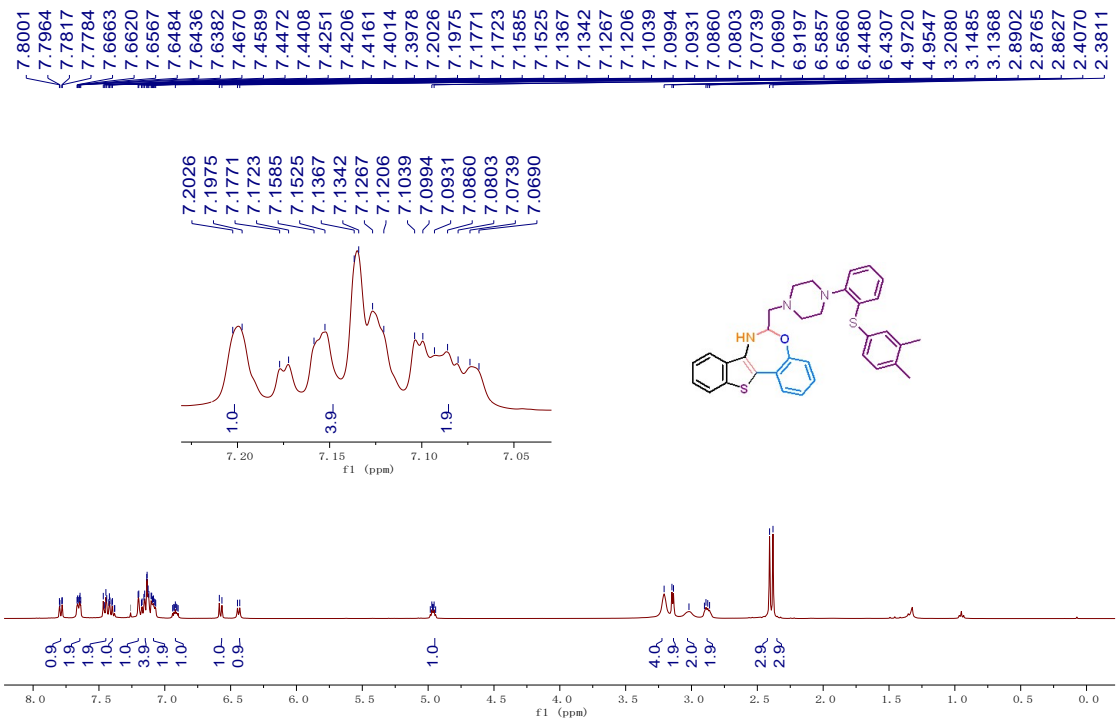
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4z



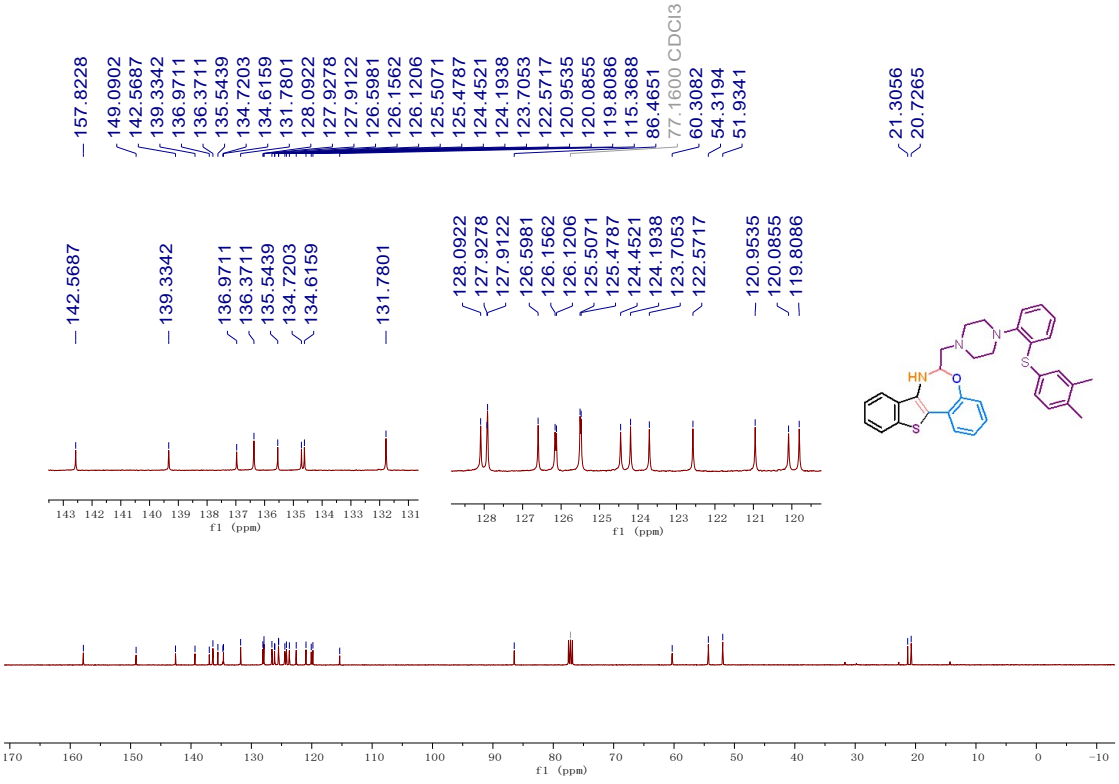
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4aa



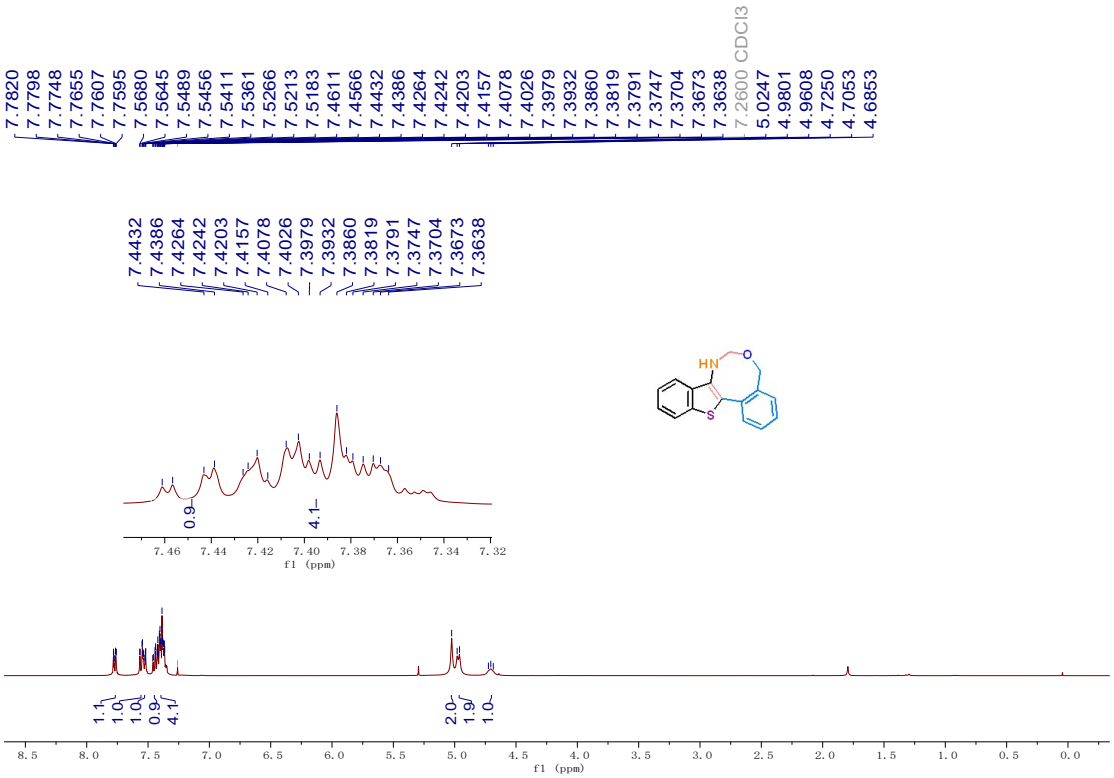
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4aa



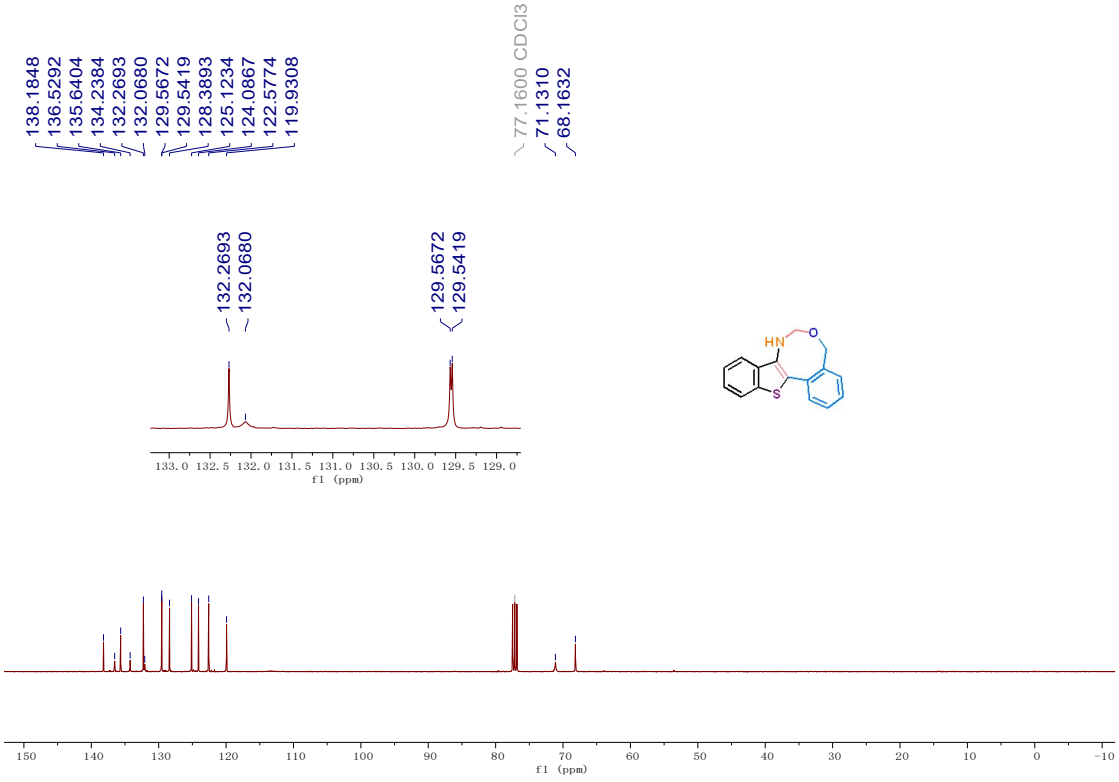
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 4ab



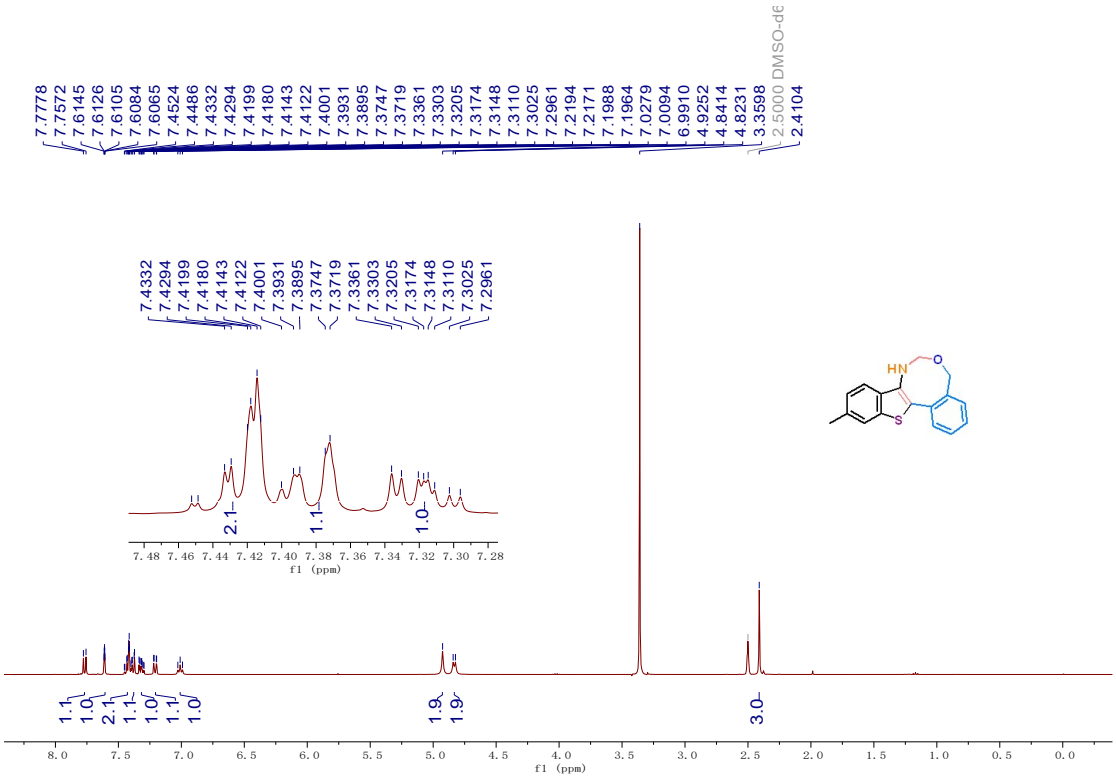
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 4ab



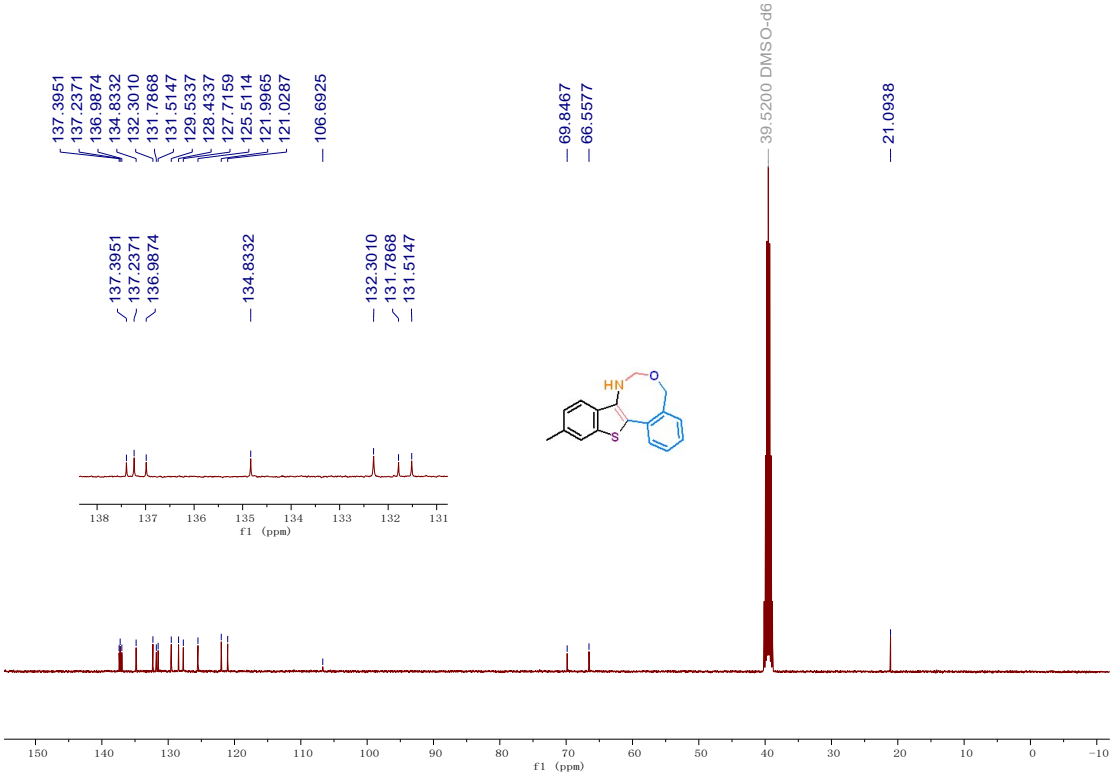
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 6a



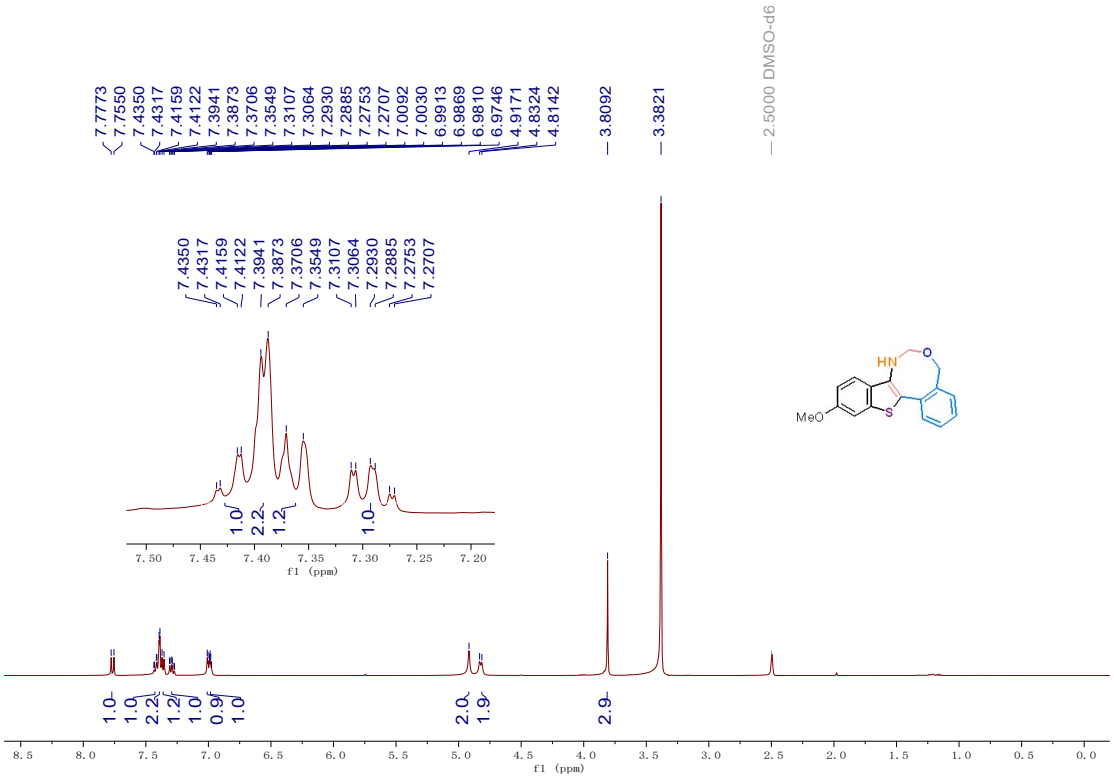
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 6a



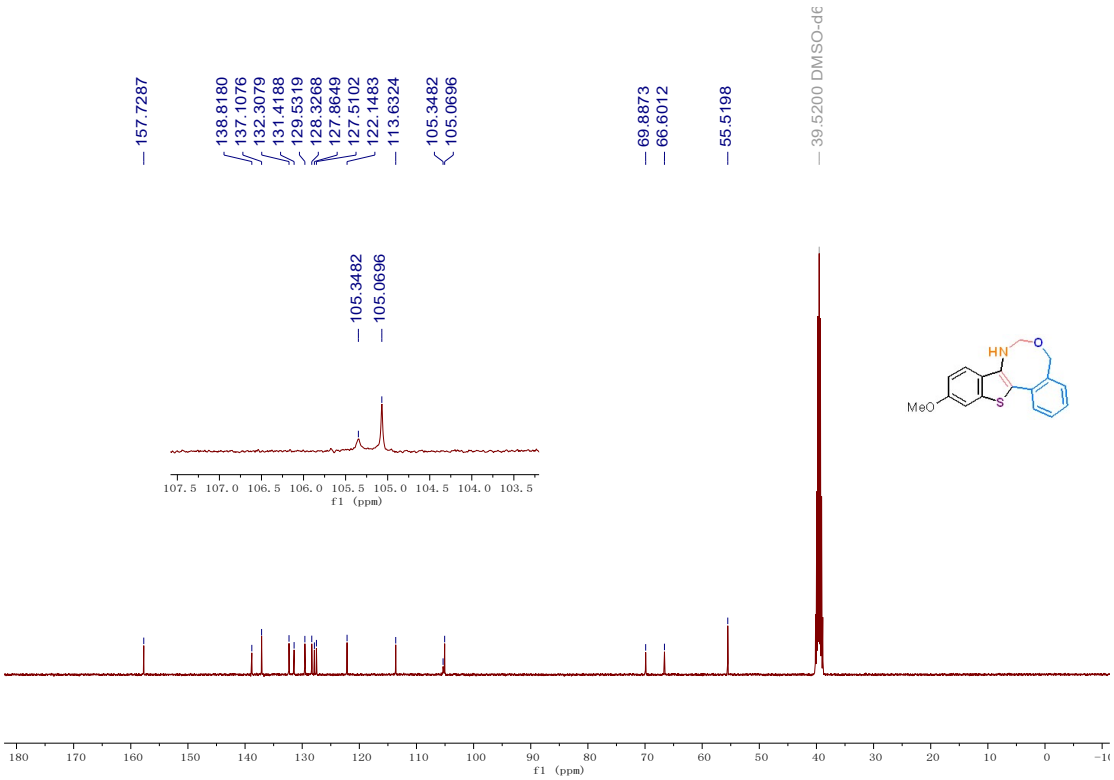
^{1}H NMR (400 MHz, DMSO) spectrum of compound 6b



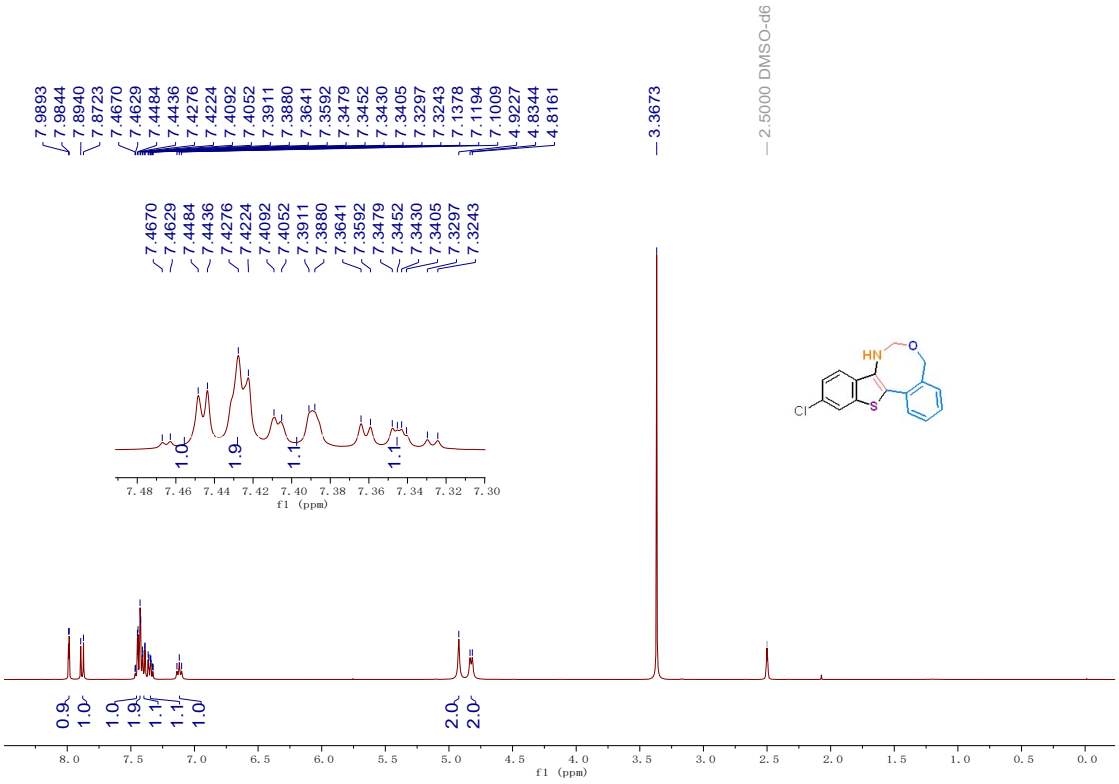
^{13}C NMR (100 MHz, DMSO) spectrum of compound 6b



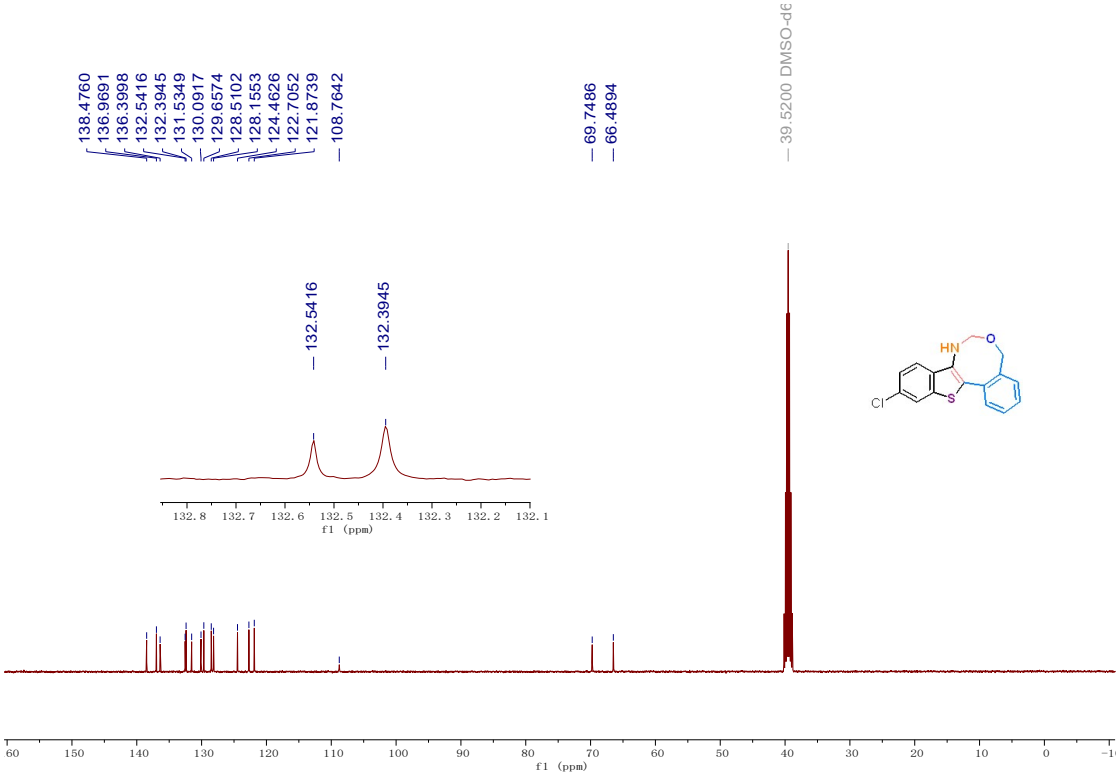
^{1}H NMR (400 MHz, DMSO) spectrum of compound 6c



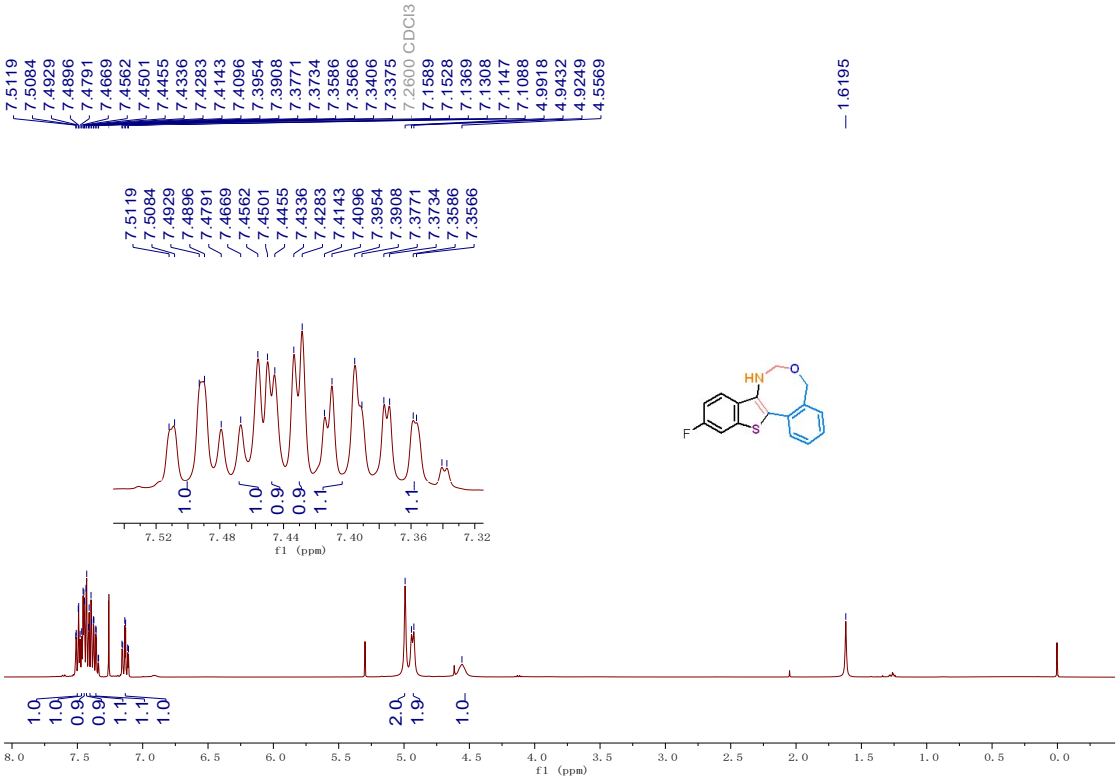
^{13}C NMR (100 MHz, DMSO) spectrum of compound 6c



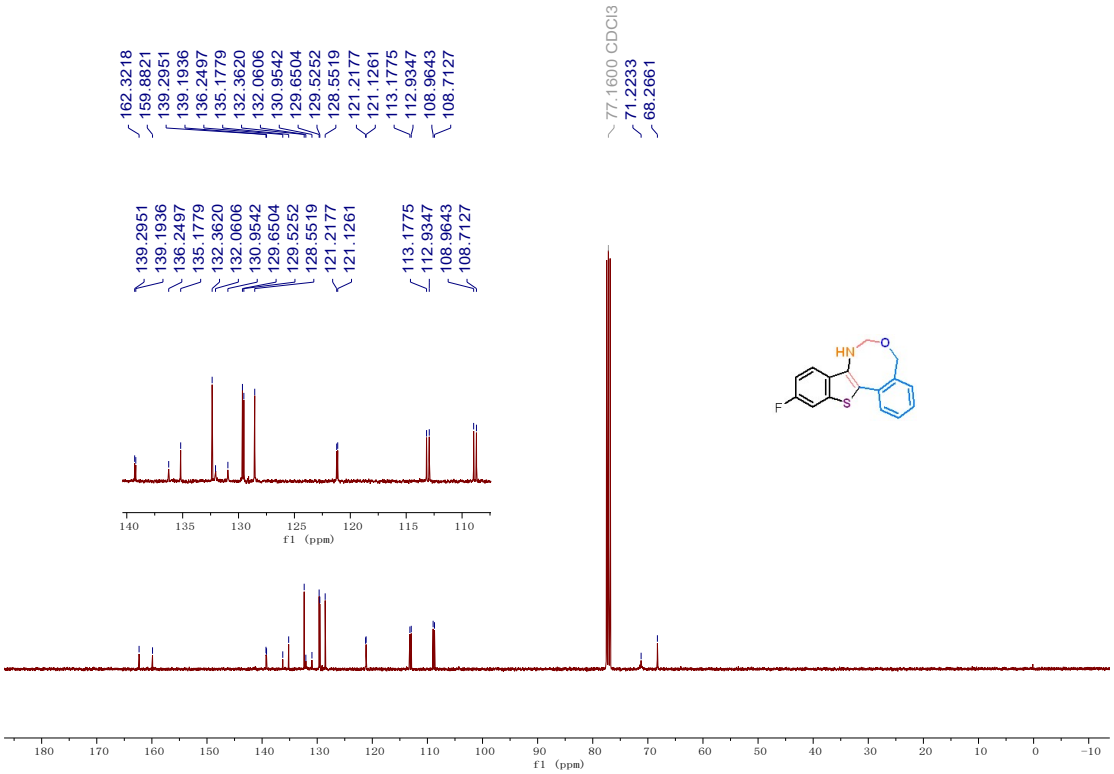
^{1}H NMR (400 MHz, DMSO) spectrum of compound 6d



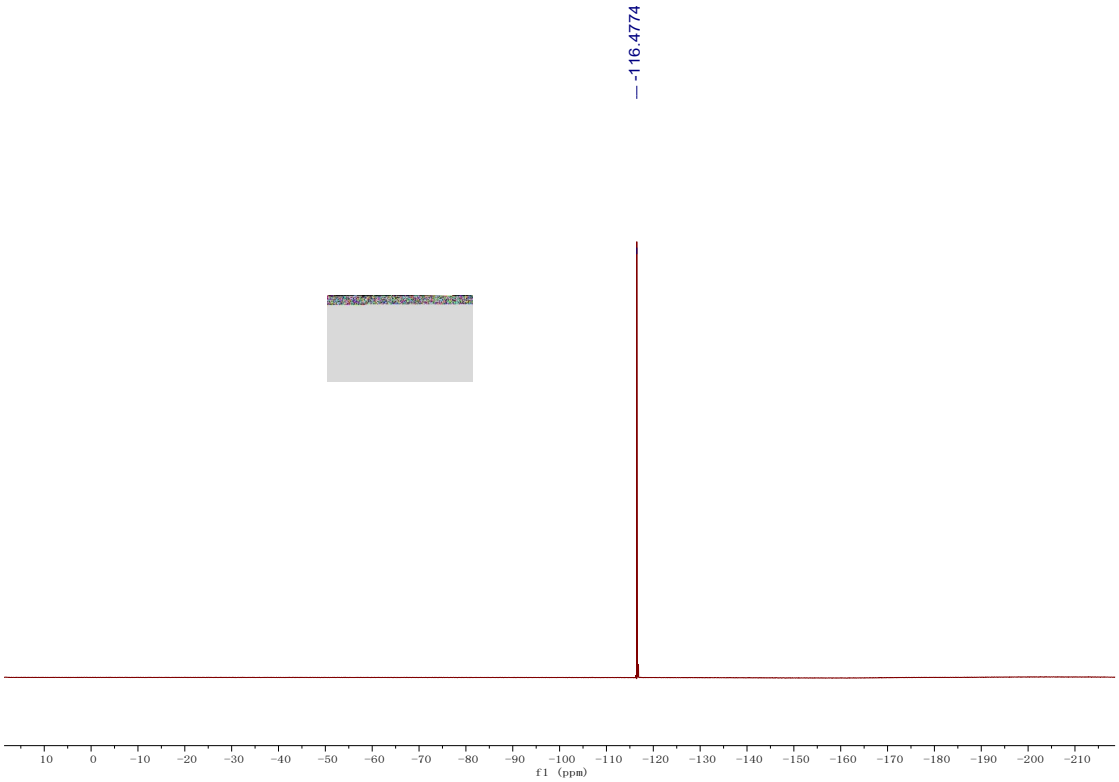
^{13}C NMR (100 MHz, DMSO) spectrum of compound 6d



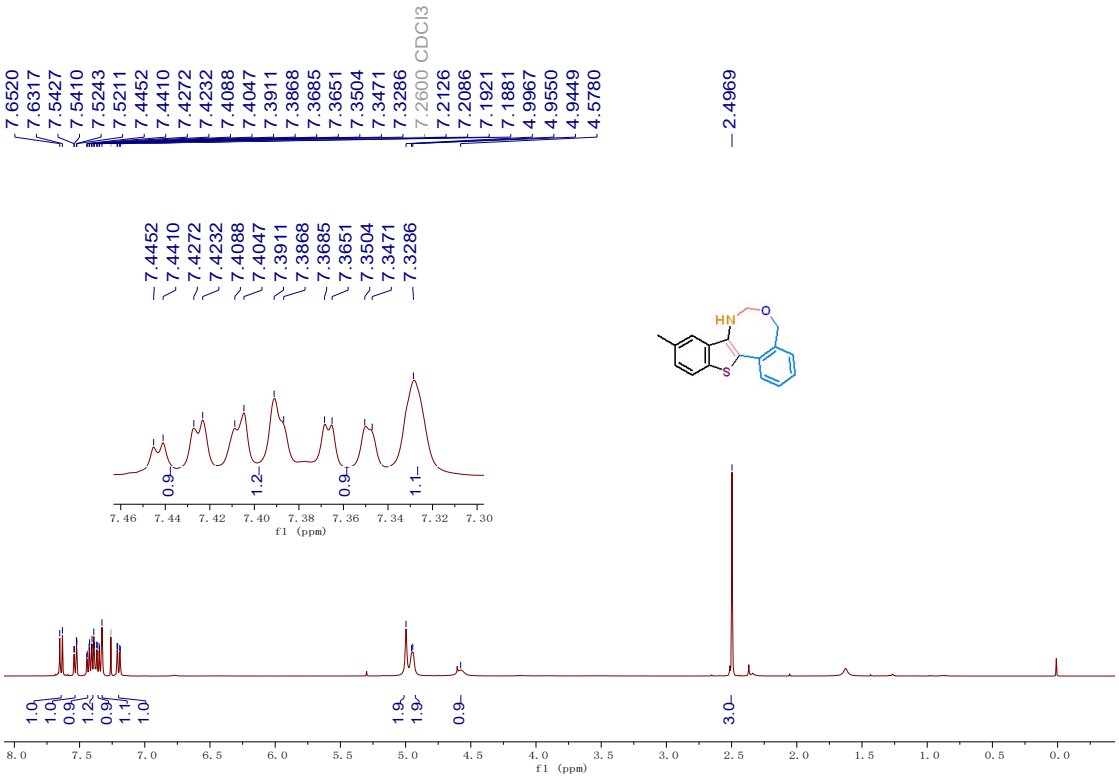
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 6e



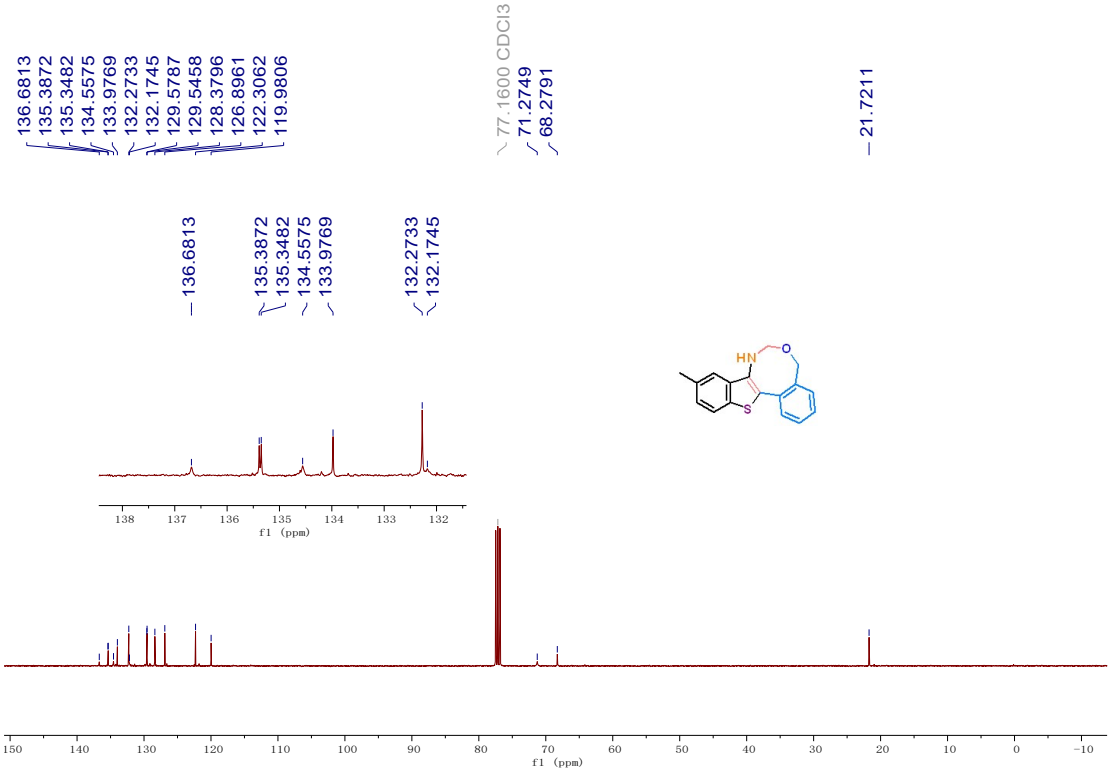
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 6e



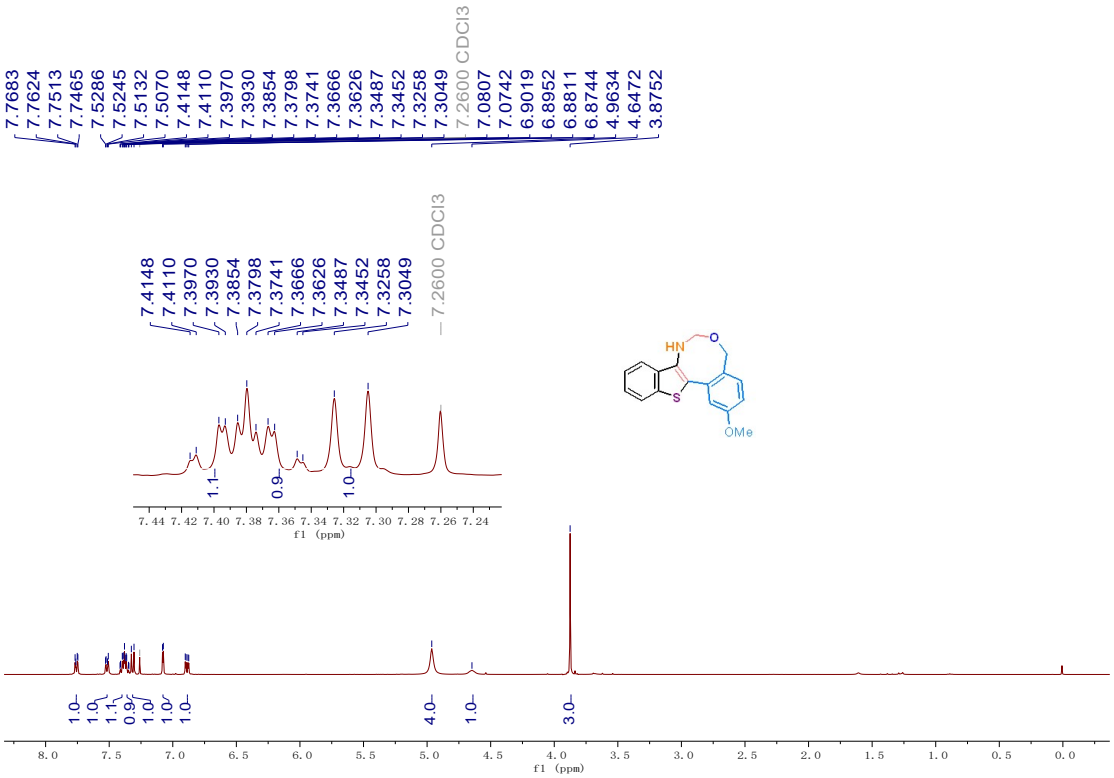
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of compound 6e



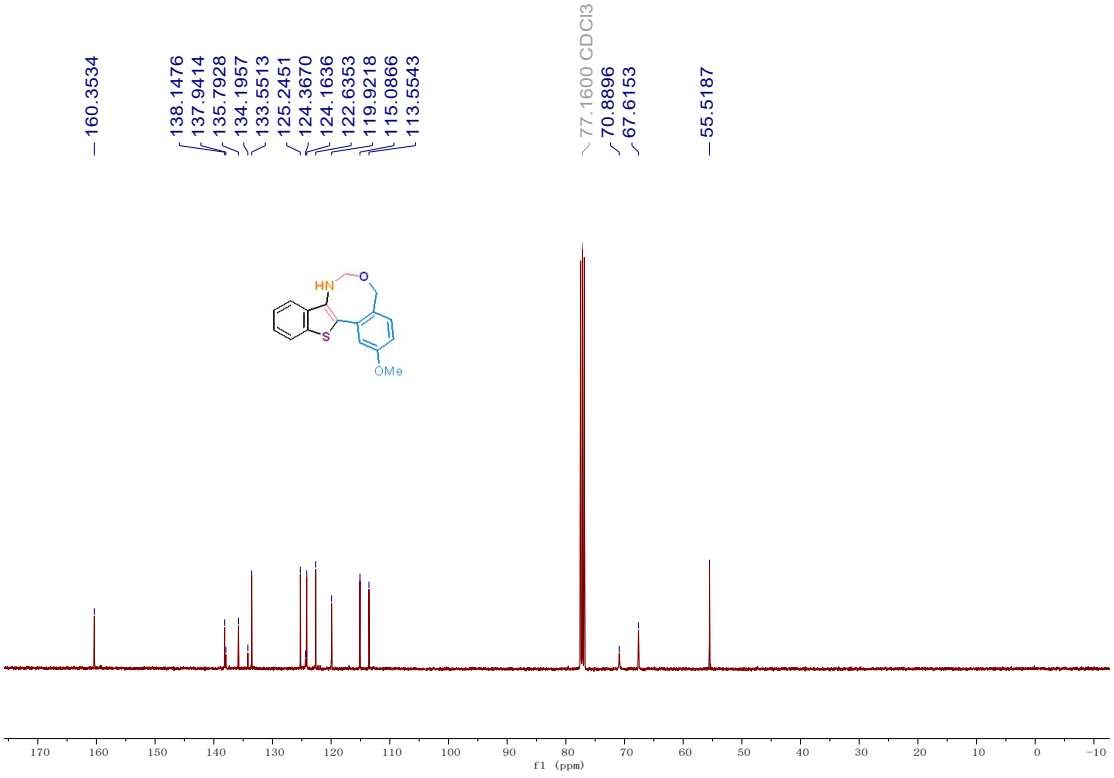
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 6f



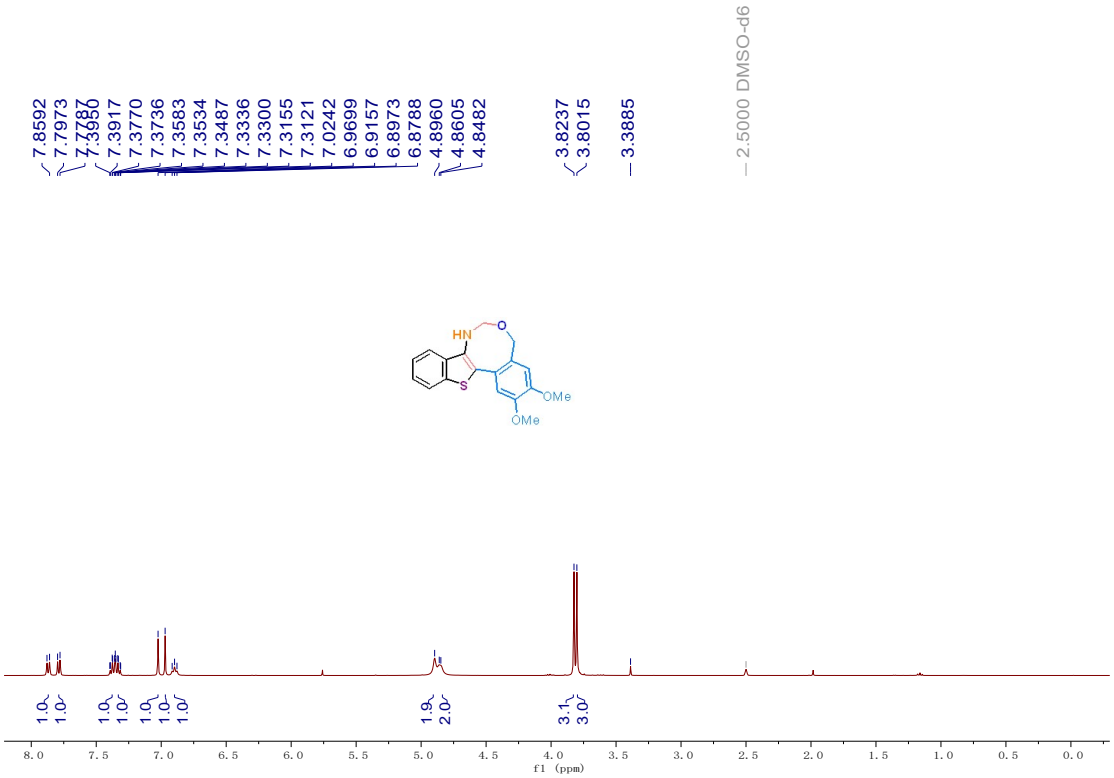
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 6f



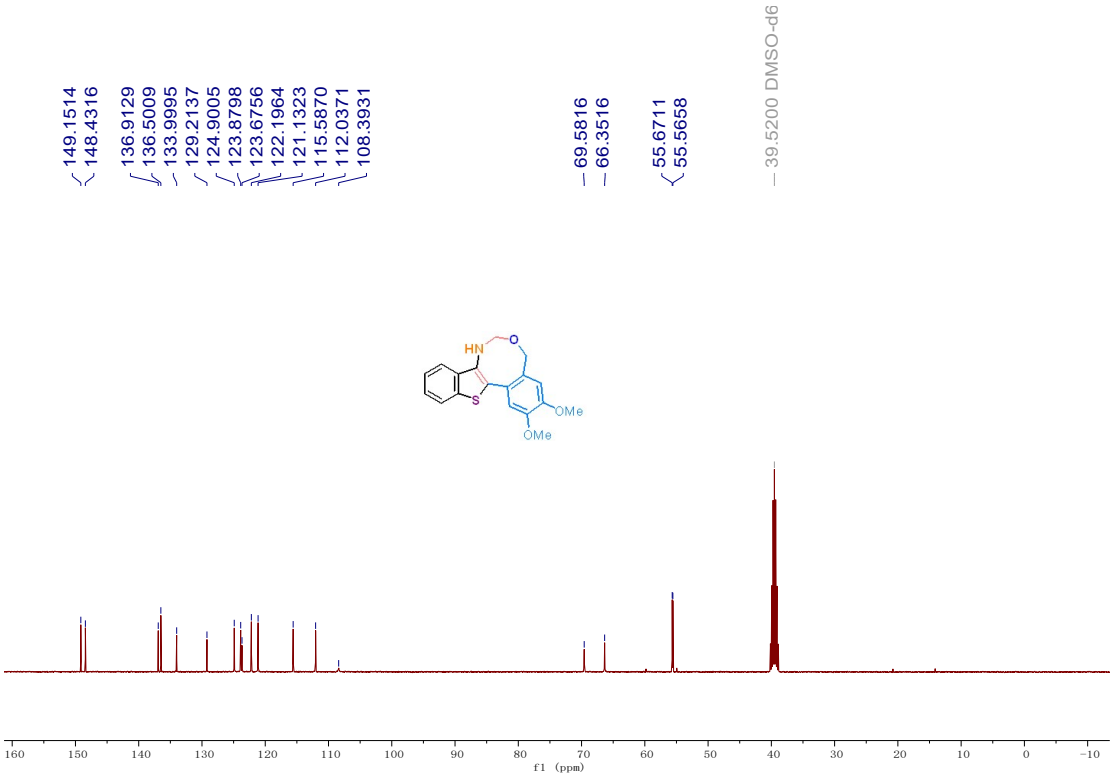
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 6g



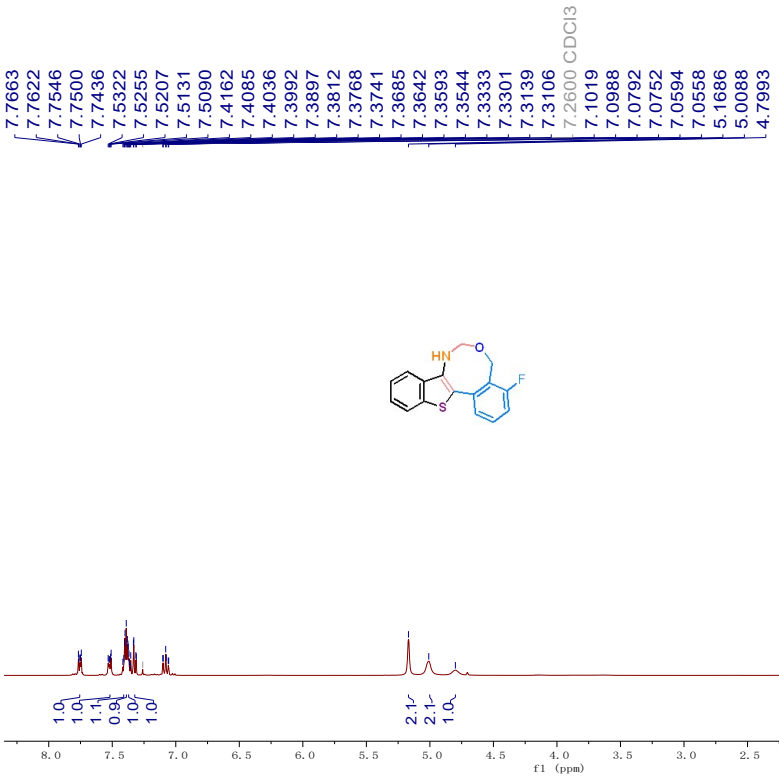
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 6g



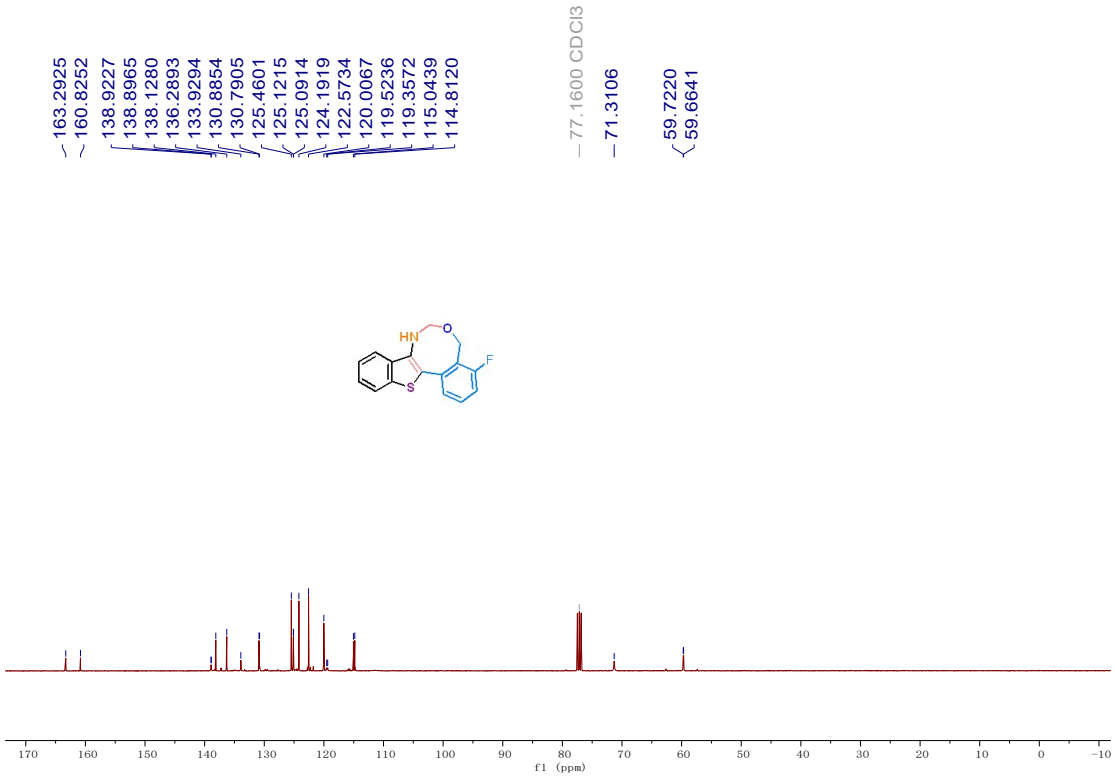
^{1}H NMR (400 MHz, DMSO) spectrum of compound 6h



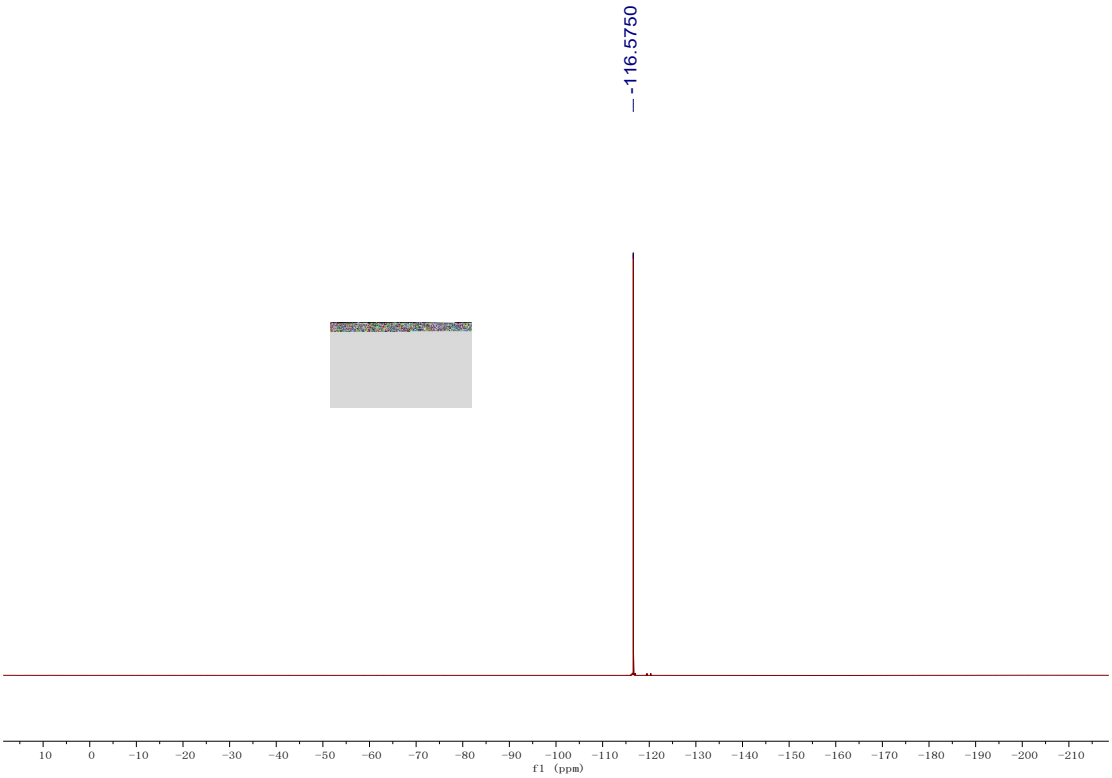
^{13}C NMR (100 MHz, DMSO) spectrum of compound 6h



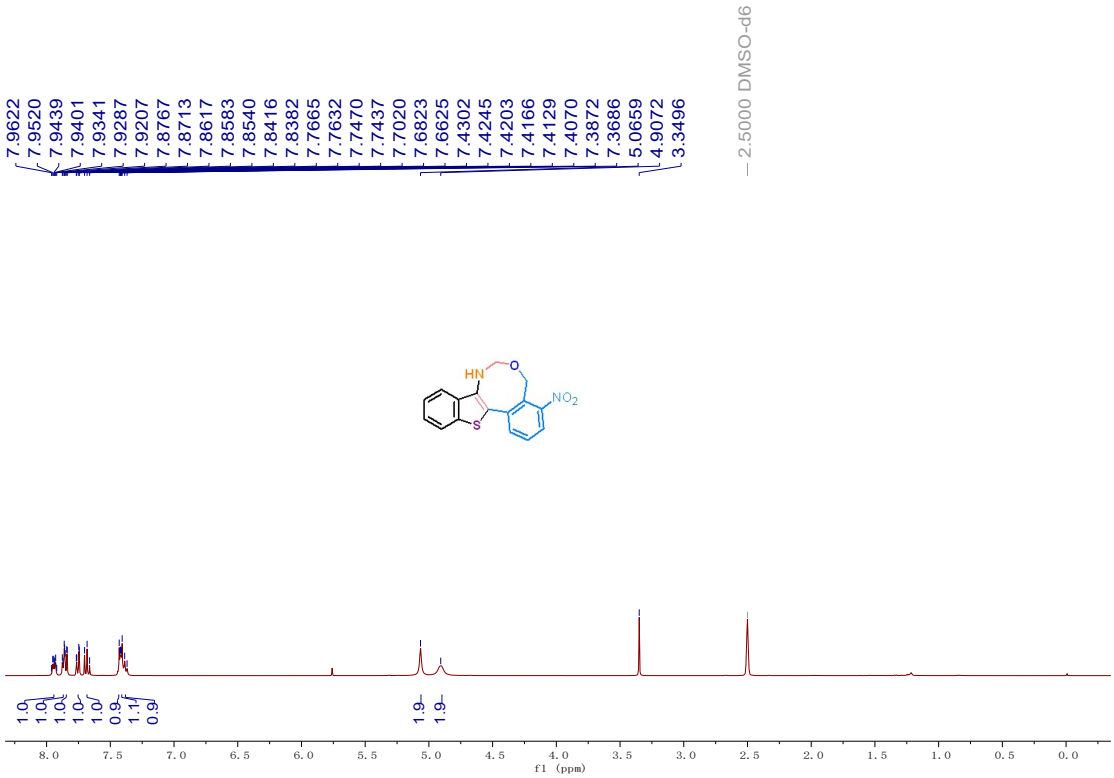
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 6i



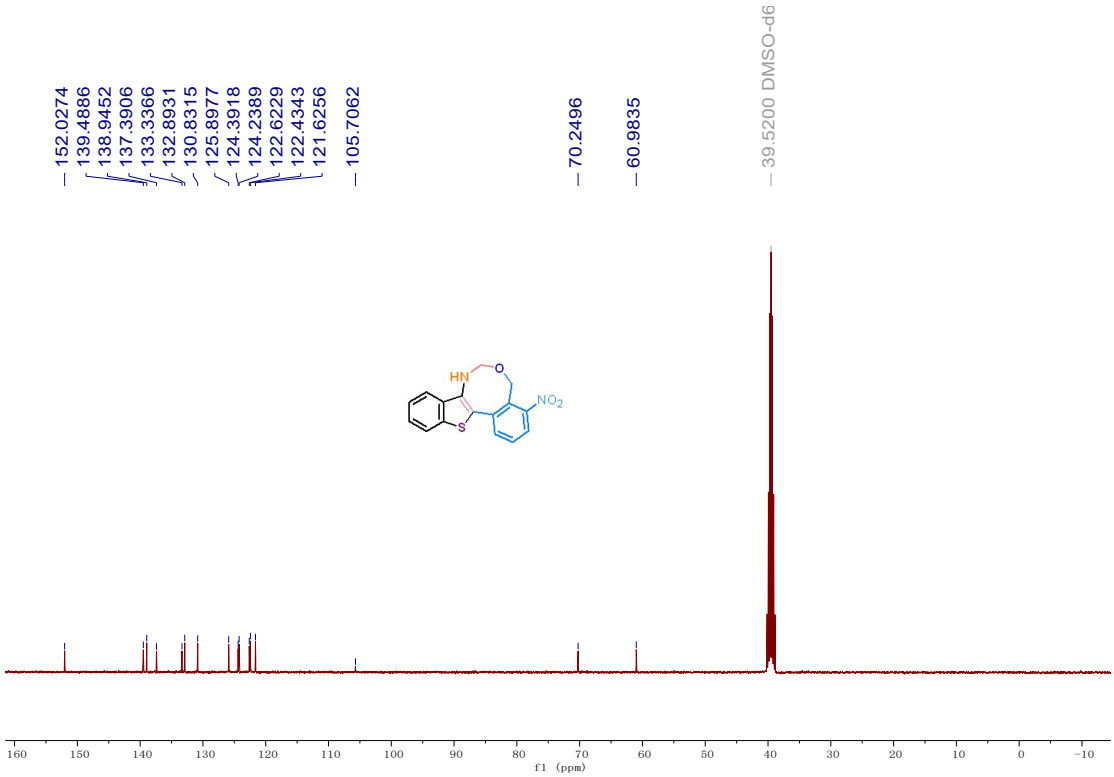
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 6i



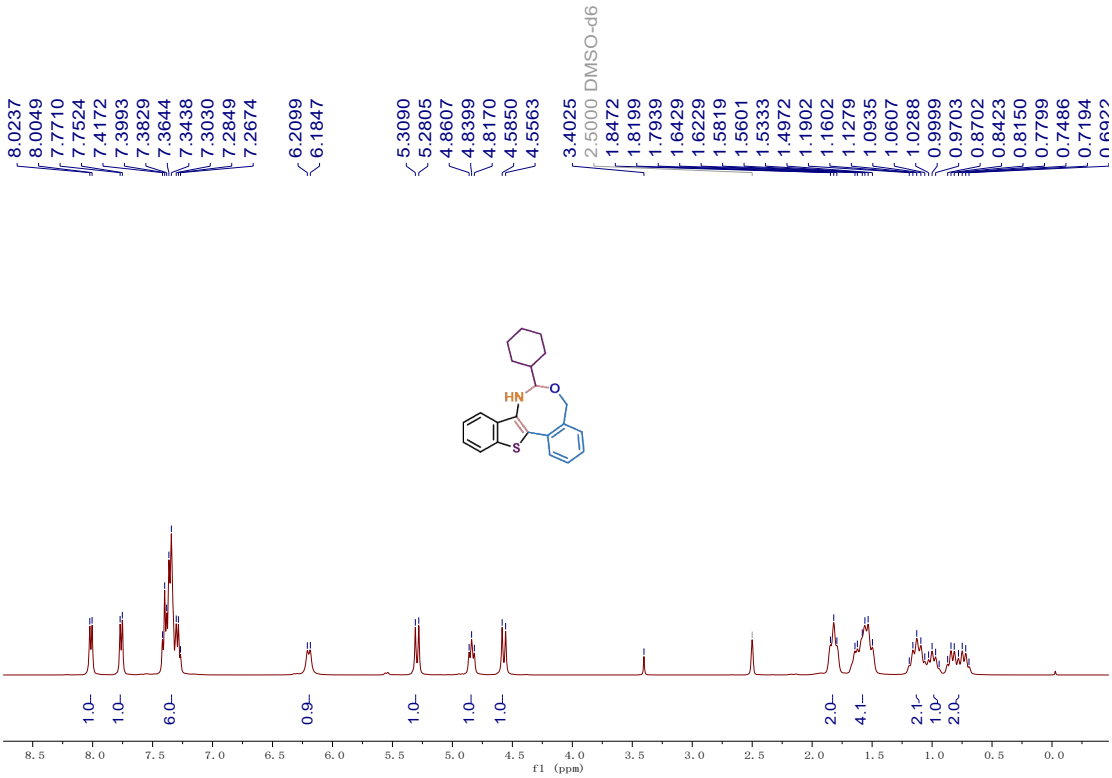
^{19}F NMR (376 MHz, $CDCl_3$) spectrum of compound 6i



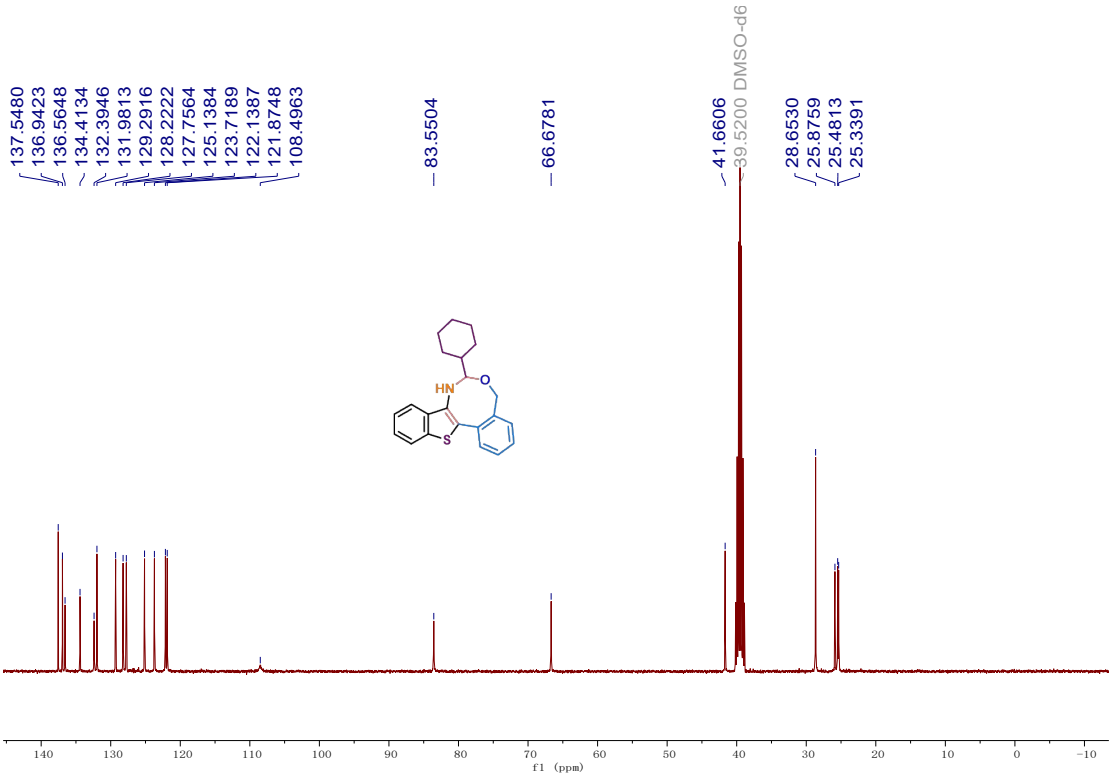
^{1}H NMR (400 MHz, DMSO) spectrum of compound 6j



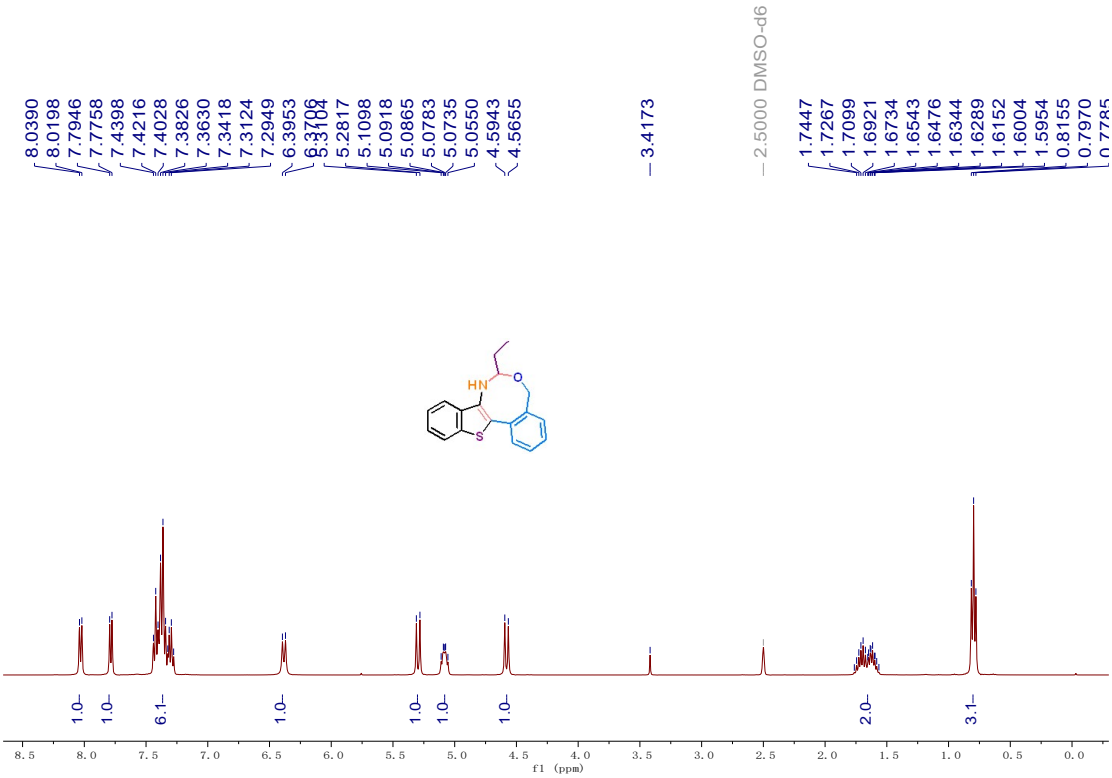
^{13}C NMR (100 MHz, DMSO) spectrum of compound 6j



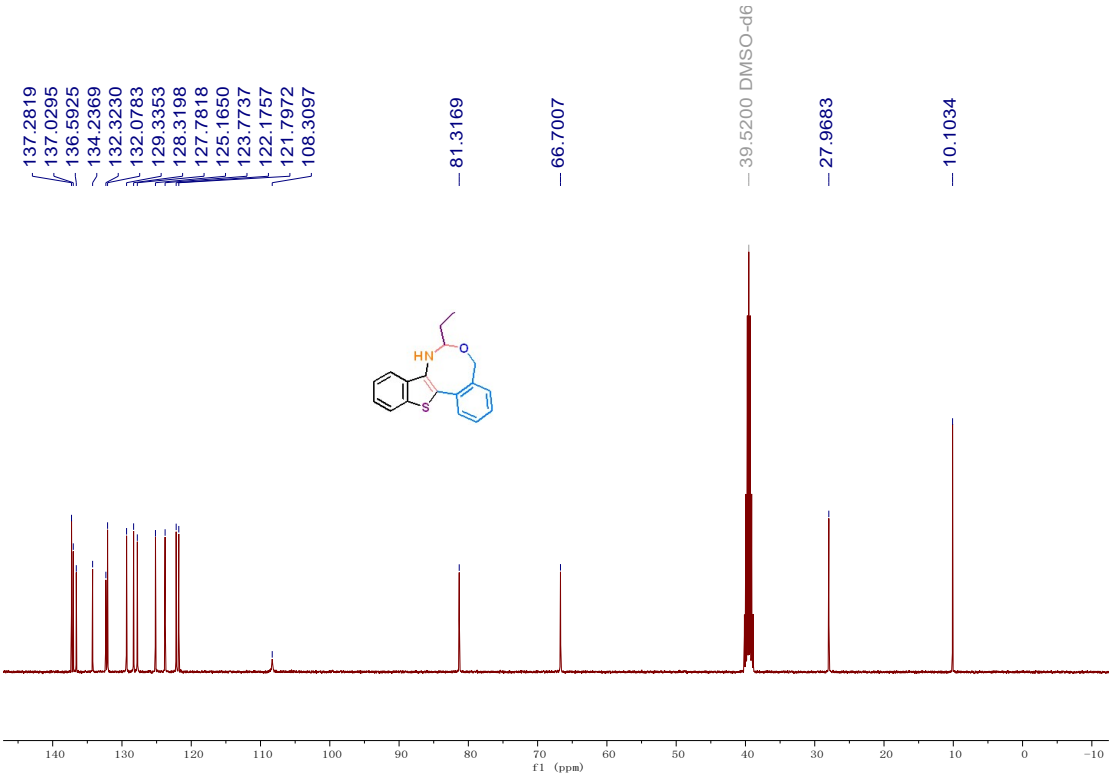
^{1}H NMR (400 MHz, DMSO) spectrum of compound 6k



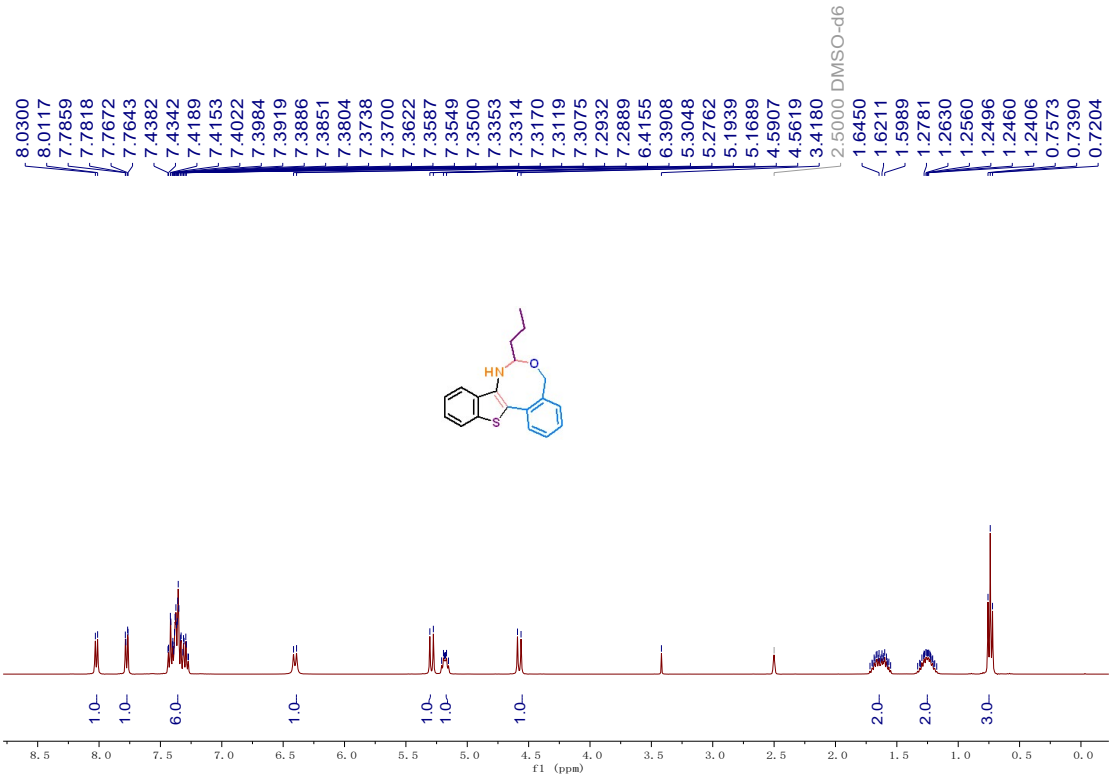
^{13}C NMR (100 MHz, DMSO) spectrum of compound 6k



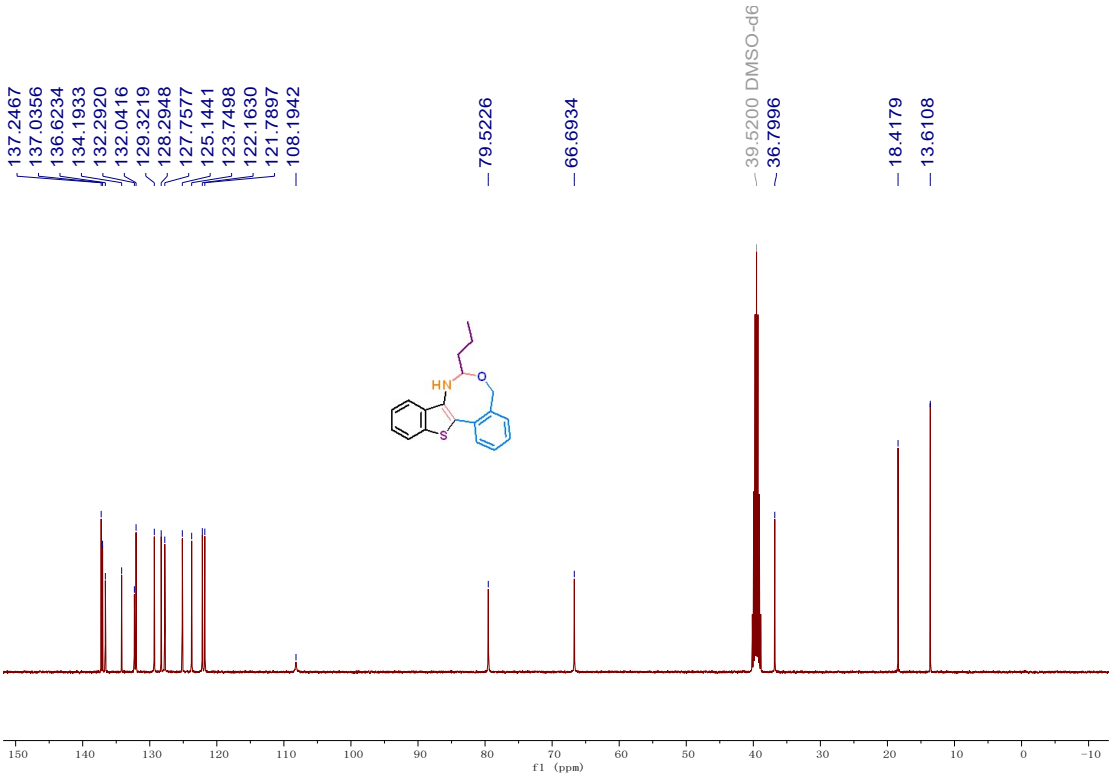
^{1}H NMR (400 MHz, DMSO) spectrum of compound 6l



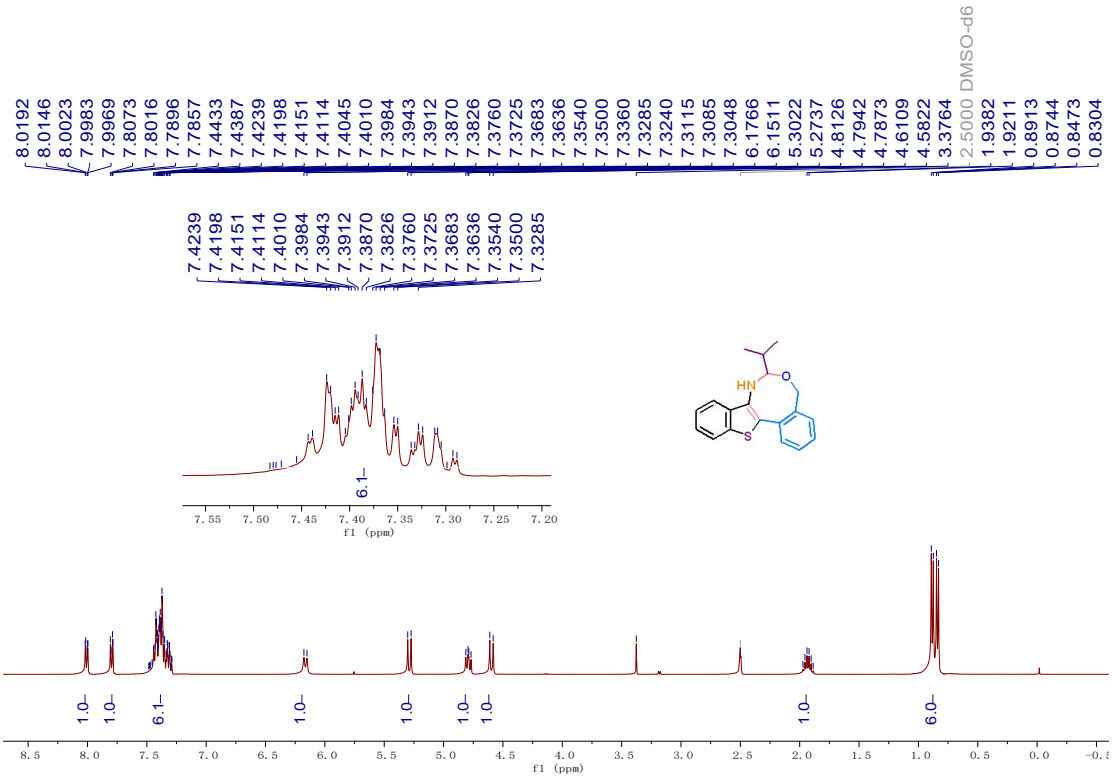
^{13}C NMR (100 MHz, DMSO) spectrum of compound 6l



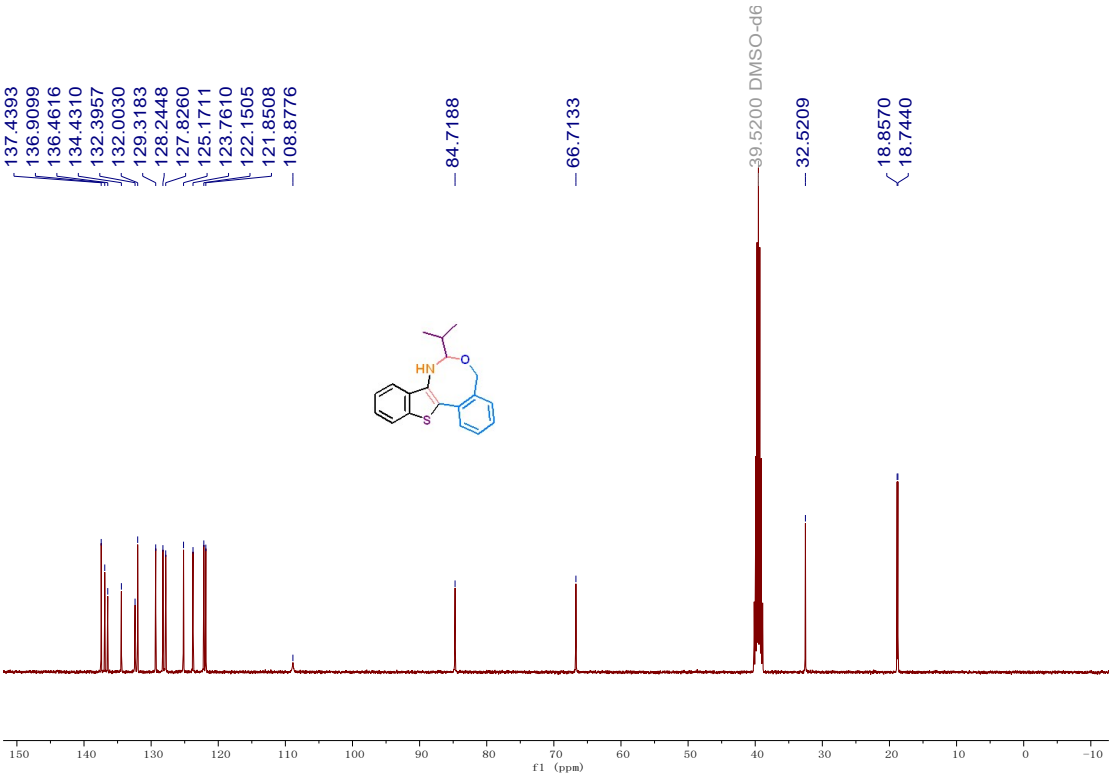
^{1}H NMR (400 MHz, DMSO) spectrum of compound 6m



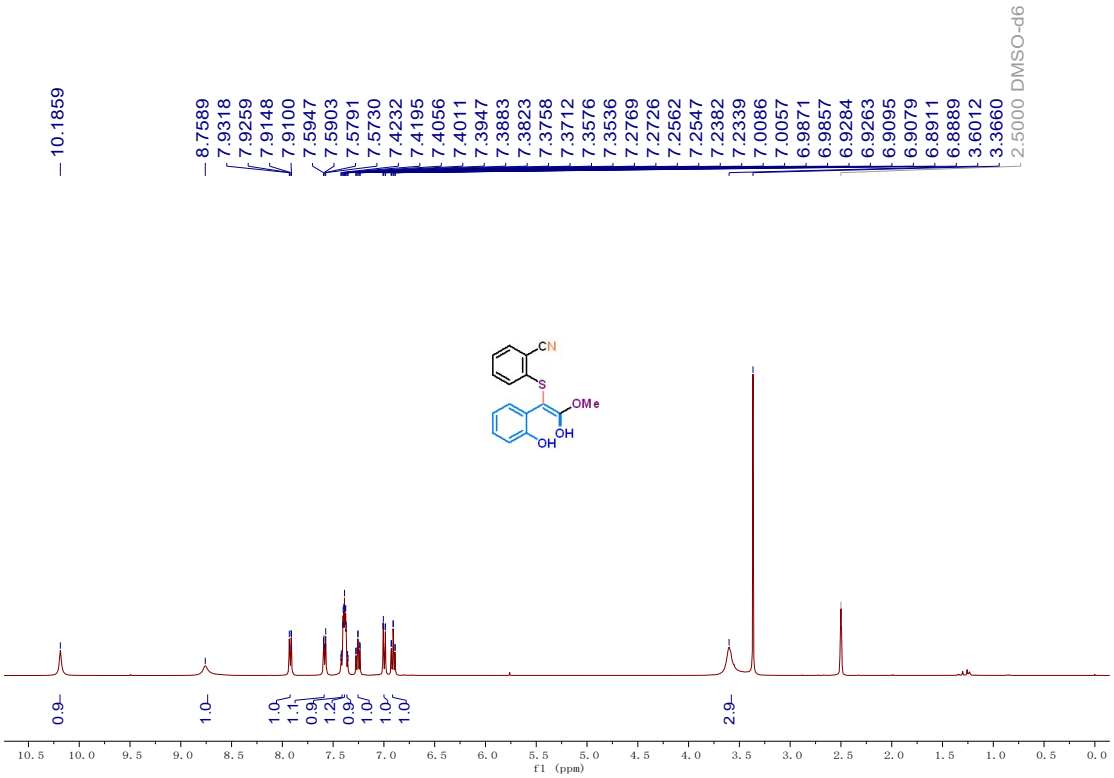
^{13}C NMR (100 MHz, DMSO) spectrum of compound 6m



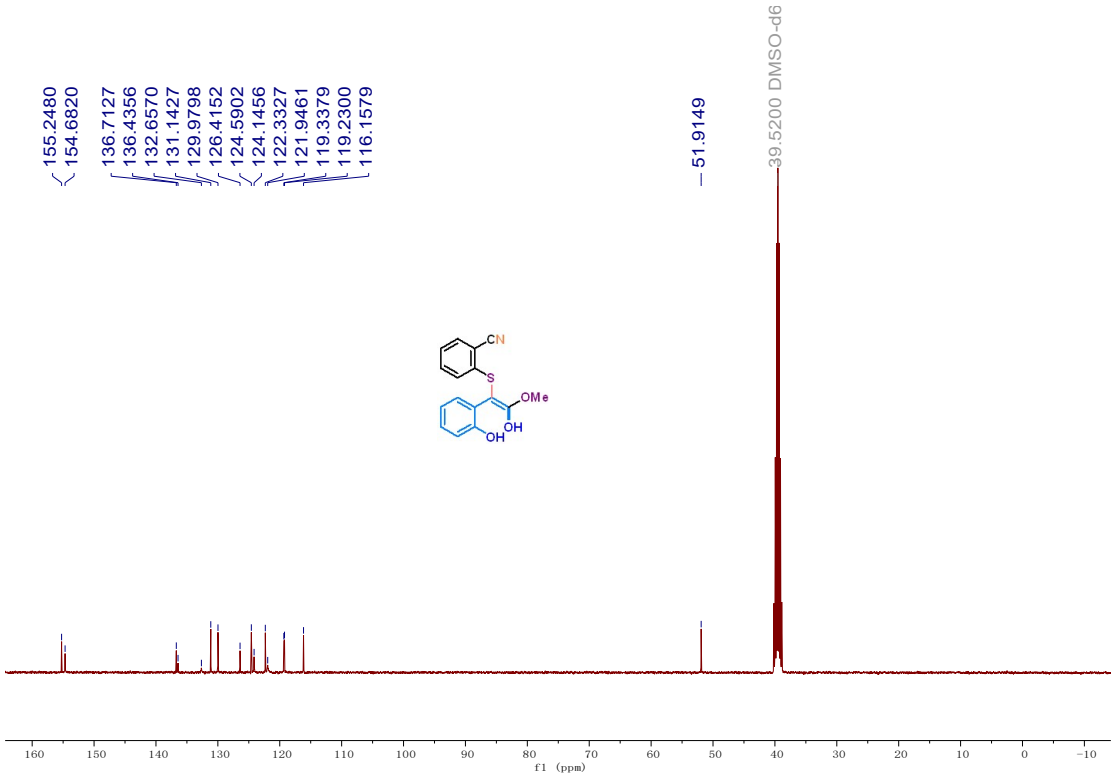
^{1}H NMR (400 MHz, DMSO) spectrum of compound 6n



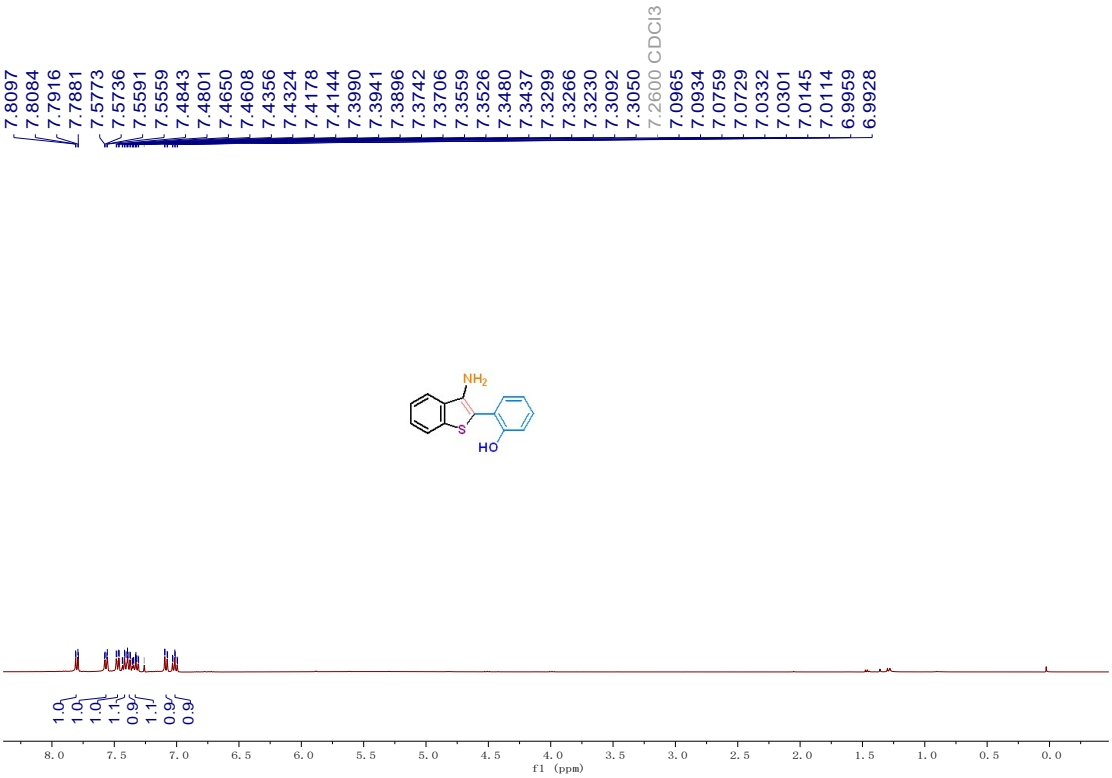
^{13}C NMR (100 MHz, DMSO) spectrum of compound 6n



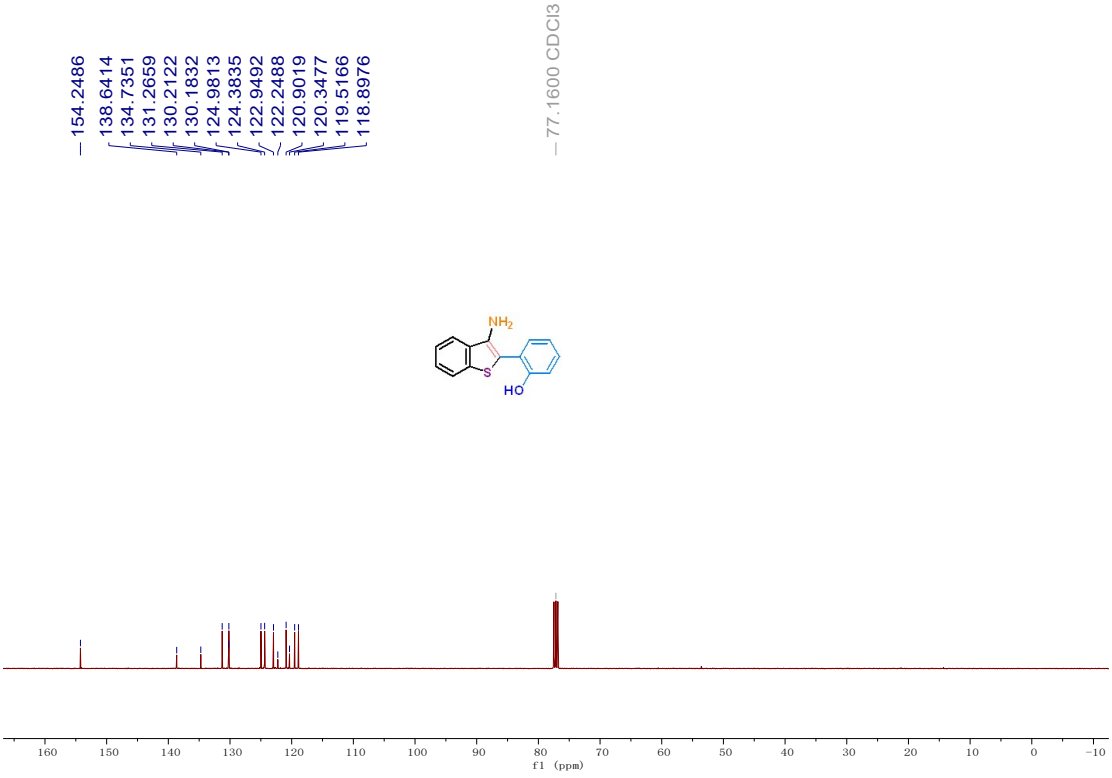
^{1}H NMR (400 MHz, DMSO) spectrum of compound 7



^{13}C NMR (100 MHz, DMSO) spectrum of compound 7



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 8



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