Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Metal-free, thiolation of sulfonyl hydrazone with thiophenol: synthesis of 4-thio-chroman and diarylmethyl thioethers

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SUPPORTING INFORMATION

Contents

General Experimental

All the starting materials were obtained from commercial sources and used as such. NMR spectrum were recorded on 300, 400 or 500 MHz spectrometer for ^{1}H NMR, 75 or 100 or 125 MHz for ^{13}C NMR spectroscopy. Chemical shifts are reported relative to the residual signals of either tetramethylsilane in $CDCl_3$ or deuterated DMSO for ^{1}H and ^{13}C NMR spectroscopy. Multiplicities are reported as follows: singlet (s), broad singlet (bs), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m). HRMS were recorded by using Q-TOF mass spectrometer. Column chromatography was performed with silica gel (100-200 mesh) as the stationary phase. All reactions were monitored by using TLC. The purity and characterization of compounds were further established by using HRMS. Melting points are uncorrected and were determined in capillary tubes on SMP 10 melting point apparatus.

General Procedures:

General Procedure A: For the preparation of sulfonyl hydrazones

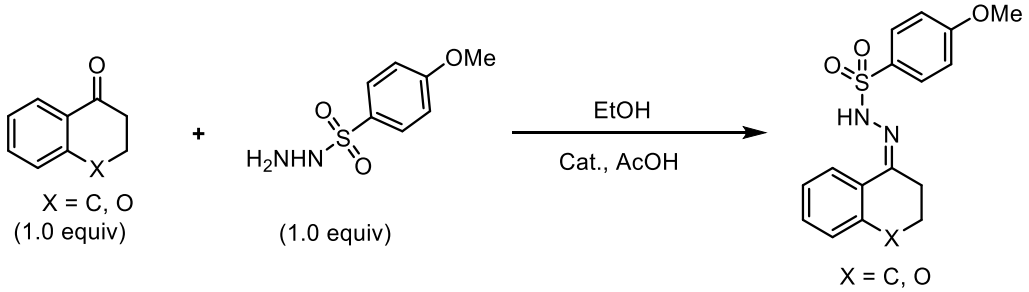


Figure 1: Synthesis of sulfonyl hydrazones.

Sulfonyl hydrazones were prepared according to the previously reported procedure.[1] To the (1.0 equiv.) of ketone in a 50 ml RB flask, was added (1.0 equiv.) of corresponding sulfonyl hydrazide followed by a catalytic amount of AcOH (2 mol%) in ethanol (0.2 M). The solution was stirred at 80 ^{o}C for 16-20 hours over which time the white solid precipitated out, and TLC showed the complete consumption of both starting materials. The solid was filtered and dried to give the desired sulfonyl hydrazones and further used in the next steps without purification.

General Procedure B: Coupling of sulfonyl hydrazones with thiophenol

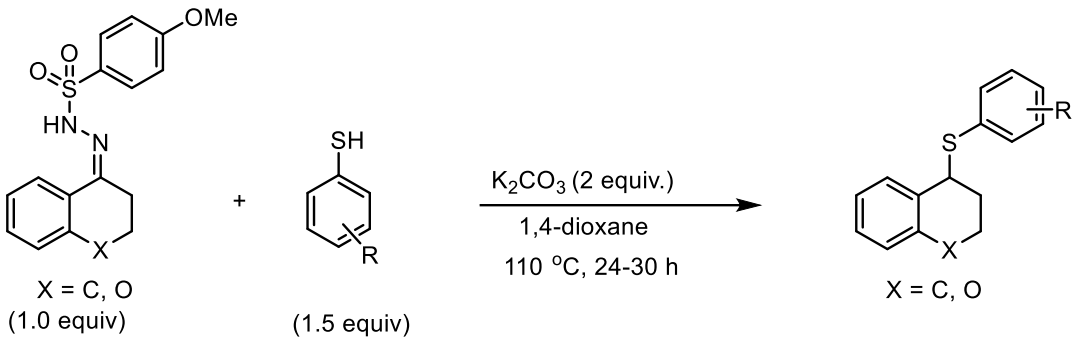


Figure 2: Cross-Coupling between sulfonyl hydrazones and thiophenol.

A screw-capped vial was charged with sulfonyl hydrazones (1.0 equiv.), thiophenol (1.2 equiv.) and potassium carbonate (2 equiv.). The tube was evacuated and backfilled with nitrogen three times, followed by the addition of 1,4-dioxane (2 ml) *via* a syringe. The reaction mixture was stirred for 24-30 hours at 110 ^{o}C. Then, the vial was cooled to room temperature, quenched with H_2O and diluted with EtOAc. The layers were separated and the aqueous phase was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel to afford the title compound.

General Procedure C: Gram-scale Coupling of sulfonyl hydrazones with naphthalene-2-thiol

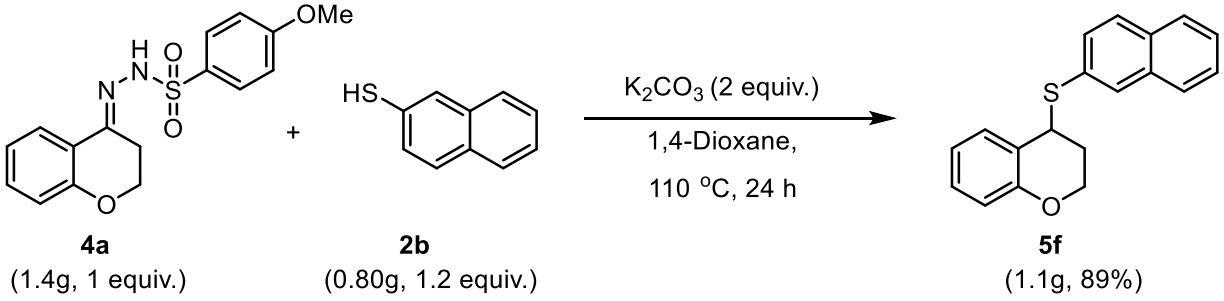
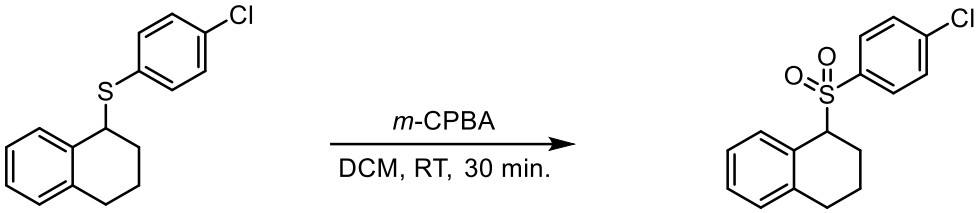


Figure 3: Gram-scale Cross-Coupling of sulfonyl hydrazones with naphthalene-2-thiol.

A round bottom flask charged with sulfonyl hydrazones (derived from chroman-4-one, 1.4 g, 4.21 mmol, 1.0 equiv.), naphthalene-2-thiol (0.80 g, 5.06 mmol, 1.2 equiv.) and potassium carbonate (1.17 g, 8.43 mmol, 2 equiv.), was evacuated and backfilled with nitrogen for three times. 1,4-dioxane (15 ml) was added, and the suspended solution was stirred at 110 °C for 24 hours. After completion of the reaction, the reaction mixture was cooled to room temperature,

quenched with H_2O and diluted with EtOAc. The layers were separated and the aqueous phase was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel to afford the product as a colourless oil (1.1 g, 89.48%).

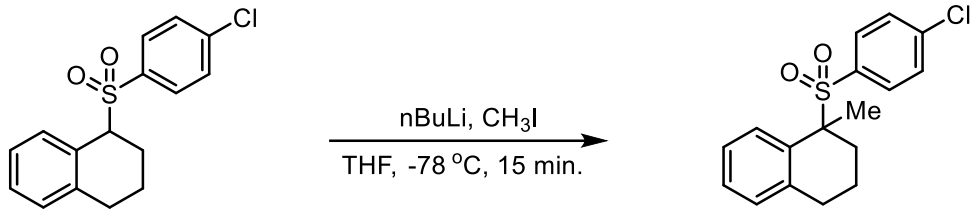
General Procedure D: Oxidation of compounds (5k)



5k **6**

Compound **5k** (350 mg, 1.28 mmole) was dissolved in 5 ml DCM and *meta*-Chloroperbenzoic acid (*m*CPBA) (75%, 878 mg, 5.10 mmole) was added. The reaction was stirred at room temperature for 30 minutes. The reaction mixture was quenched with 0.4g sodium thiosulfate in 40 ml water and extracted with EtOAc. Then the organic layer was washed with IN NaOH solution (40 ml) and brine (40 ml), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel to afford product **6** as a white solid (340 mg, 86.95%).

General Procedure E: Synthesis of tetra substituted compounds

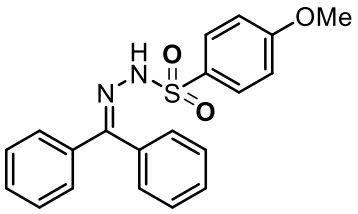


6 **7**

To a solution of compound **6** (100 mg, 0.32 mmol) in THF (3 ml) at -78 °C was added *n*-BuLi (2 N in hexanes) (0.81 ml, 1.63 mmol) followed, 5 minutes later by iodomethane (0.16 ml, 2.62 mmol) and the reaction mixture was allowed to warm to RT. After 15 minutes, the reaction mixture was poured into saturated NH_4CI, extracted with DCM, dried over $MgSO_4$, filtered and

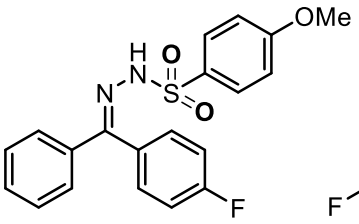
concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel to afford product **7** as a colourless oil (85 mg, 83.00%).

Following sulfonyl hydrazones (1a to 1c and 4a to 4f) were used to synthesised diarylmethyl thioethers and thio-chroman:



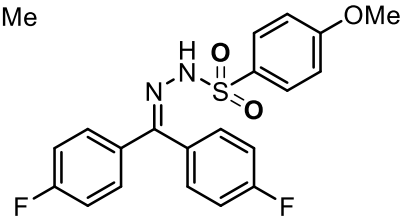
1a

HRMS (ESI) m/z for
$C_{20}H_{18}N_2O_3S$
[M+H]+: 367.1111,
found: 367.1116



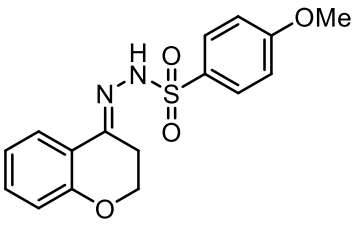
1b

HRMS (ESI) m/z for
$C_{20}H_{17}FN_2O_3S$
[M+H]+: 385.1017,
found: 385.1019



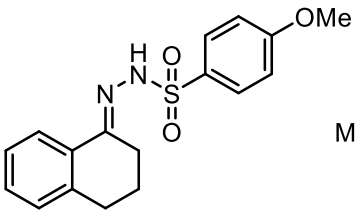
1c

HRMS (ESI) m/z for
$C_{20}H_{16}F_2N_2O_3S$
[M+H]+: 403.0923,
found: 403.0931



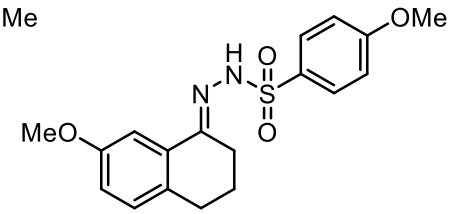
4a

HRMS (ESI) m/z for
$C_{16}H_{16}N_2O_4S$
[M+H]+: 333.0904,
found: 333.0910



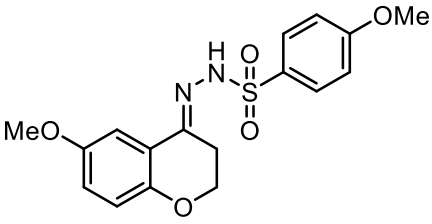
4b

HRMS (ESI) m/z for
$C_{17}H_{18}N_2O_3S$
[M+H]+: 331.1111,
found: 331.1114



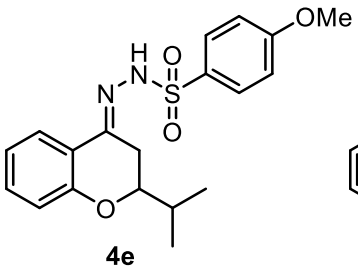
4c

HRMS (ESI) m/z for
$C_{18}H_{20}N_2O_4S$
[M+H]+: 361.1217,
found: 361.1223



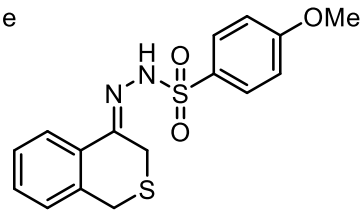
4d

HRMS (ESI) m/z for
$C_{17}H_{18}N_2O_5S$
[M+H]+: 363.1010,
found: 363.1017



4e

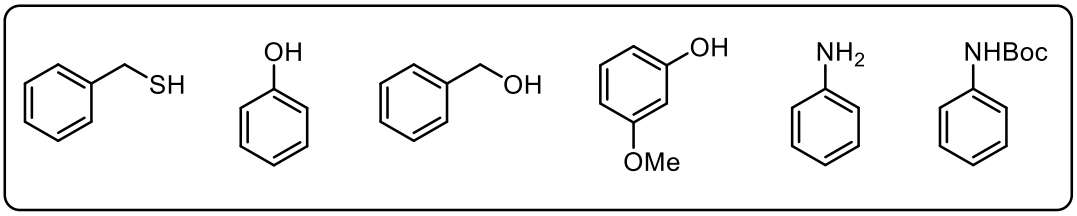
HRMS (ESI) m/z for
$C_{19}H_{22}N_2O_4S$
[M+H]+: 375.1374,
found: 375.1376



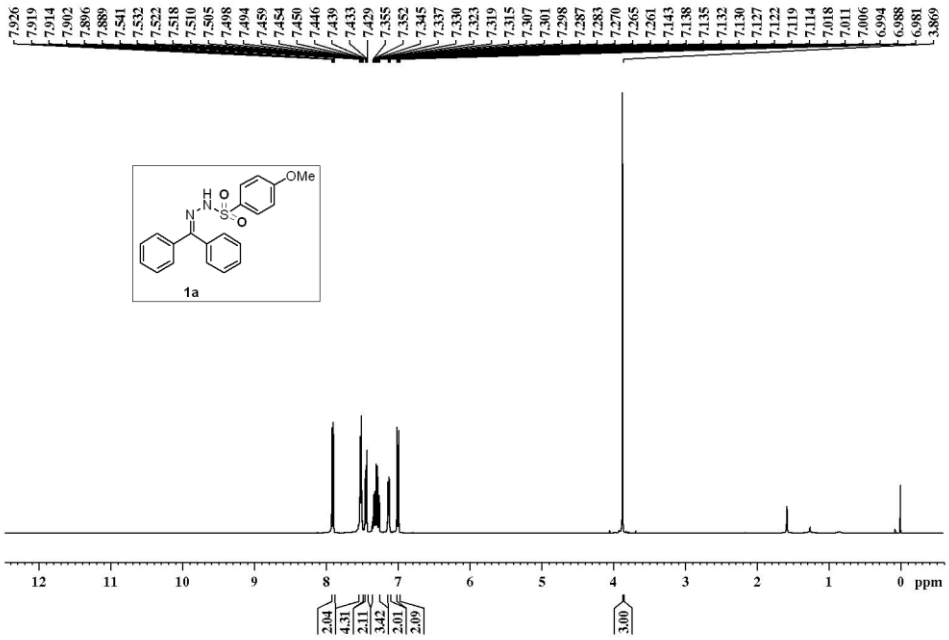
4f

HRMS (ESI) m/z for
$C_{16}H_{16}N_2O_3S_2$
[M+H]+: 349.0676,
found: 349.0677

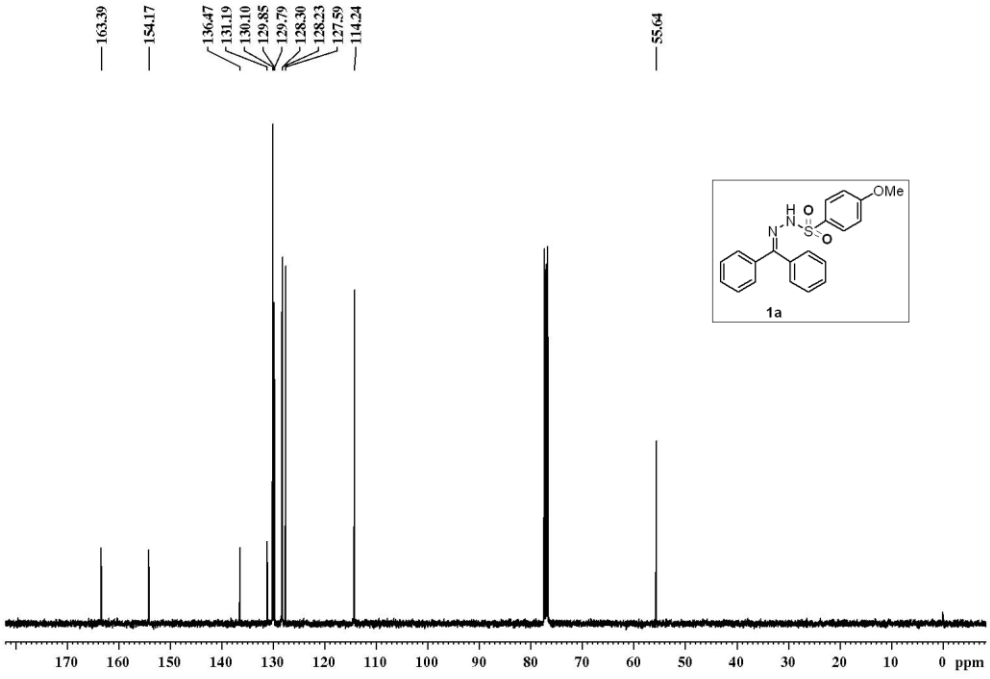
Unsuccessfull substrates



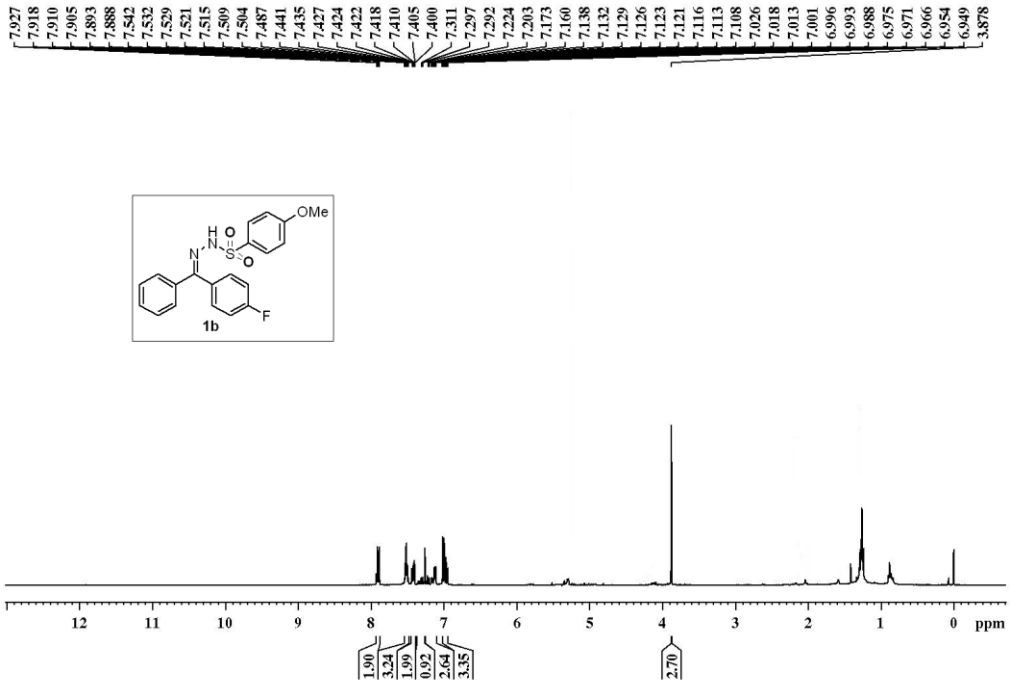
NMR spectra of the synthesized compounds



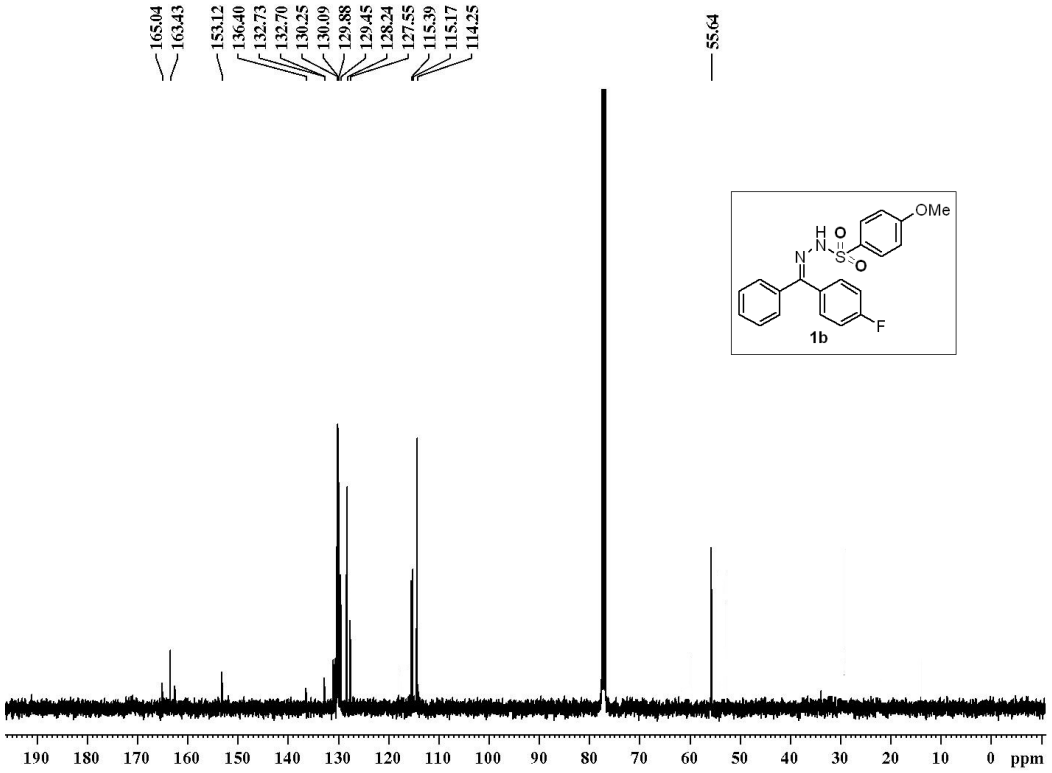
^{1}H NMR spectrum of compound **1a** (400 MHz, $CDCl_3$)



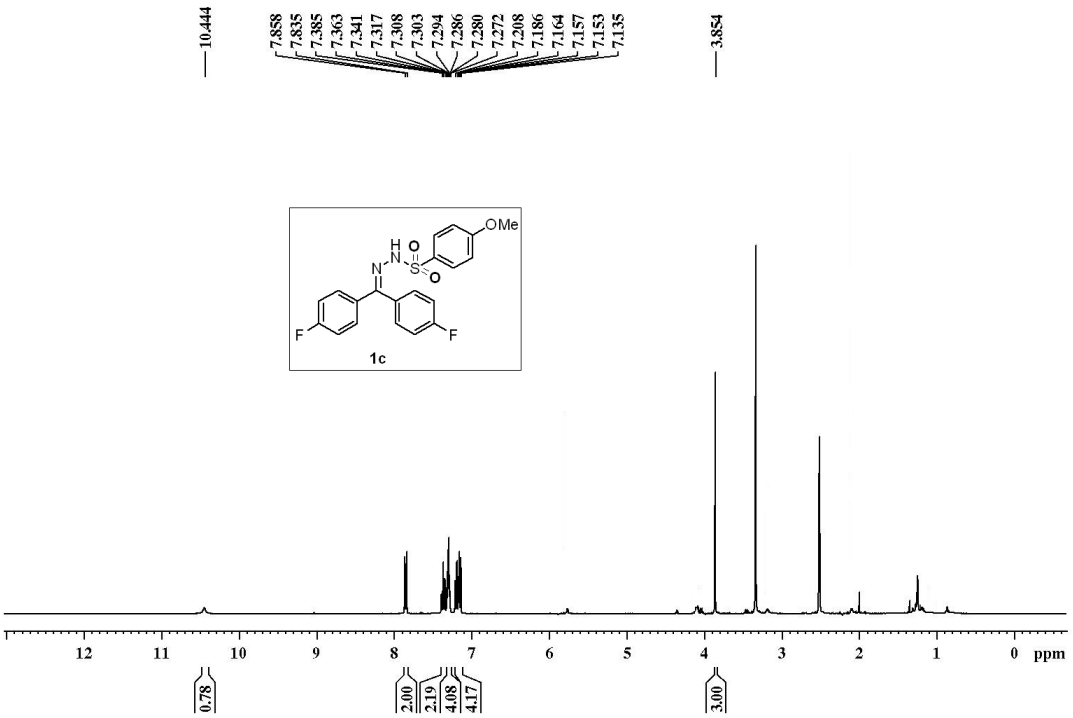
^{13}C NMR spectrum of compound **1a** (100 MHz, $CDCl_3$)



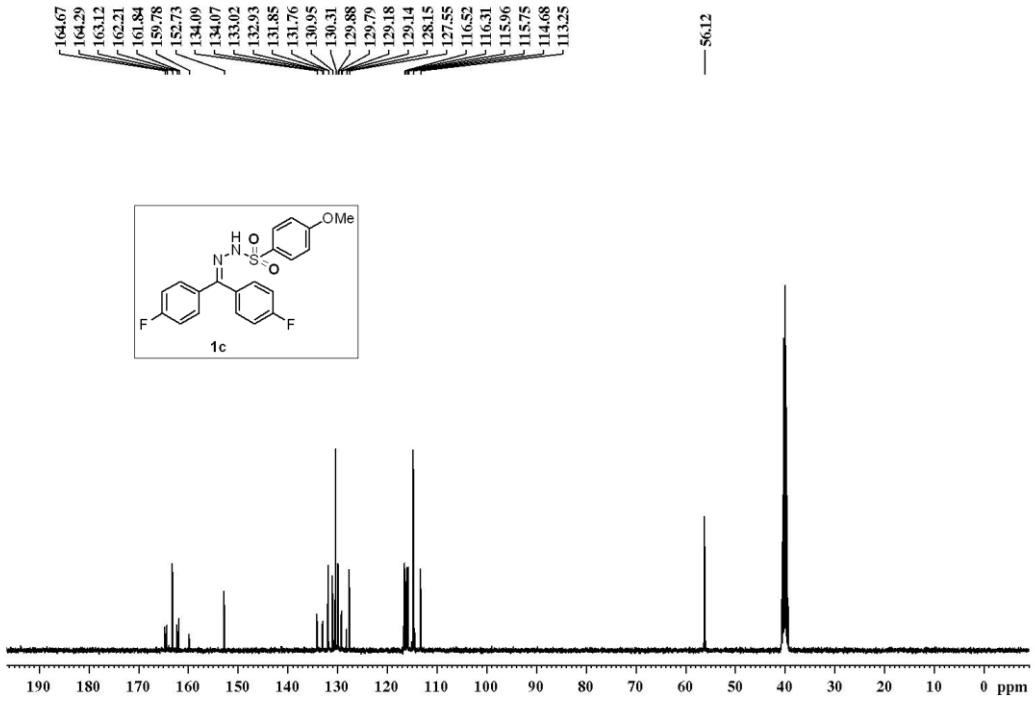
^{1}H NMR spectrum of compound **1b** (400 MHz, $CDCl_3$)



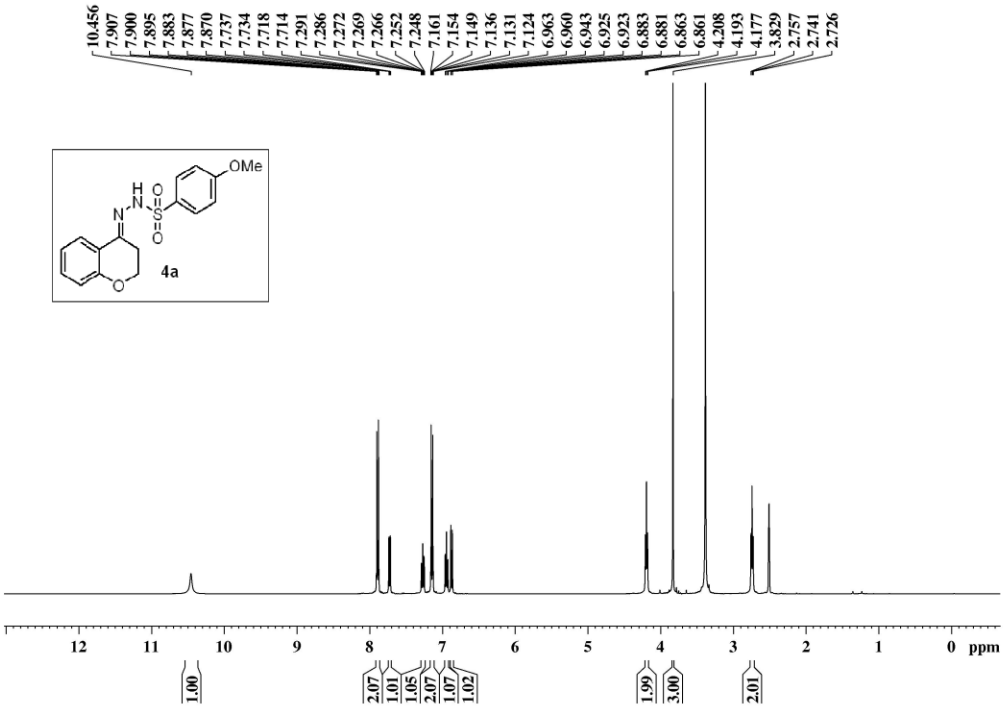
^{13}C NMR spectrum of compound **1b** (100 MHz, $CDCl_3$)



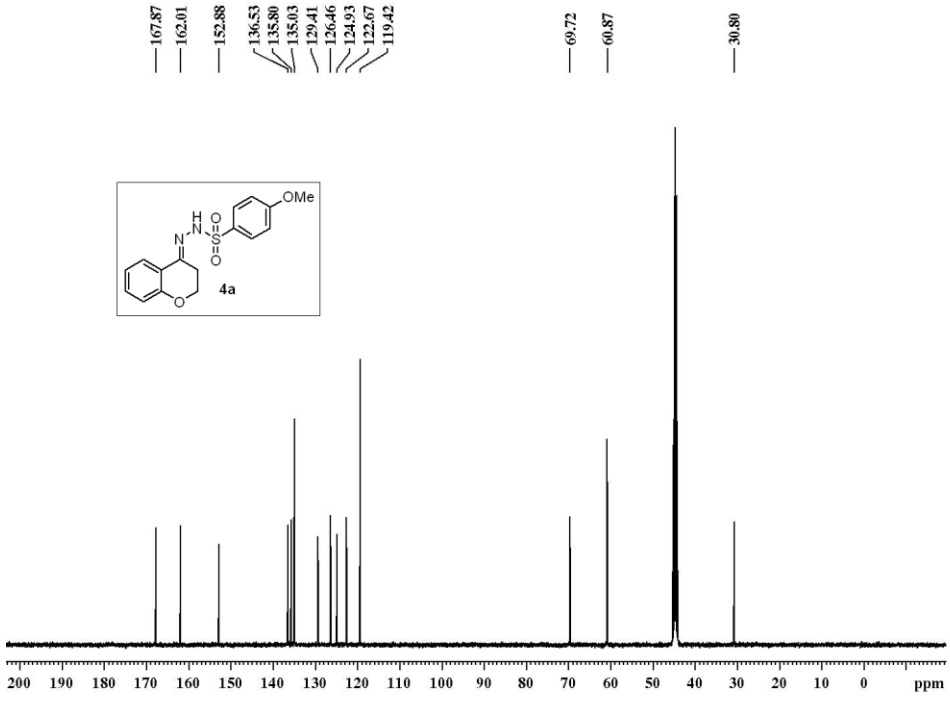
^{1}H NMR spectrum of compound **1c** (400 MHz, DMSO d6)



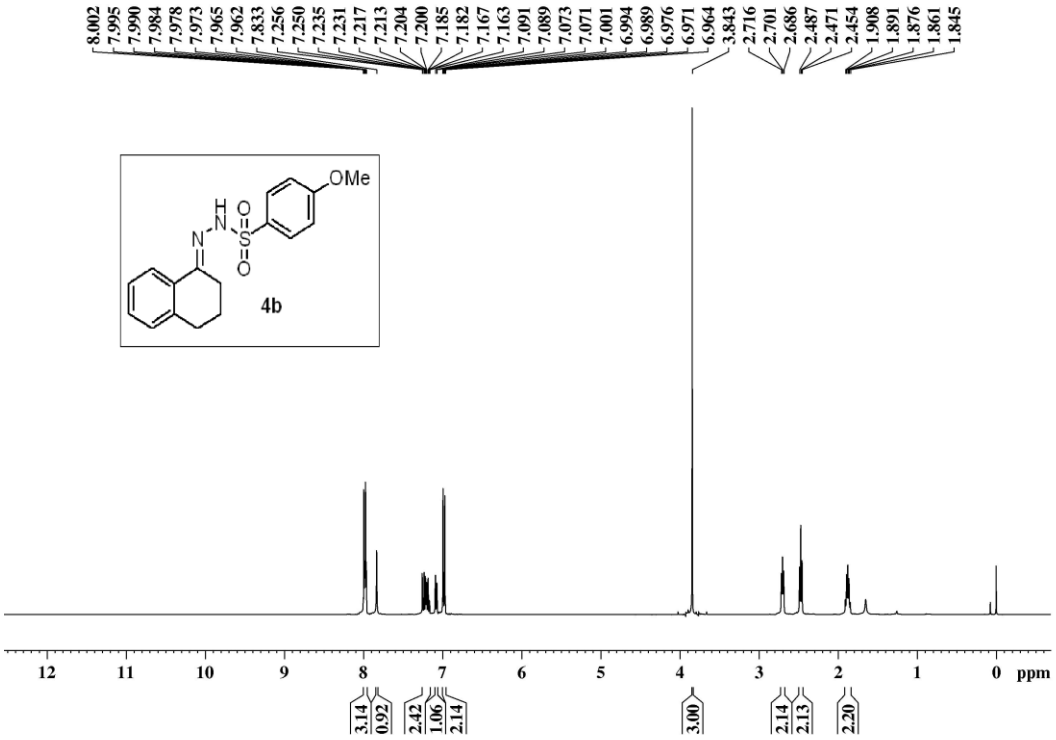
^{13}C NMR spectrum of compound **1c** (100 MHz, DMSO d6)



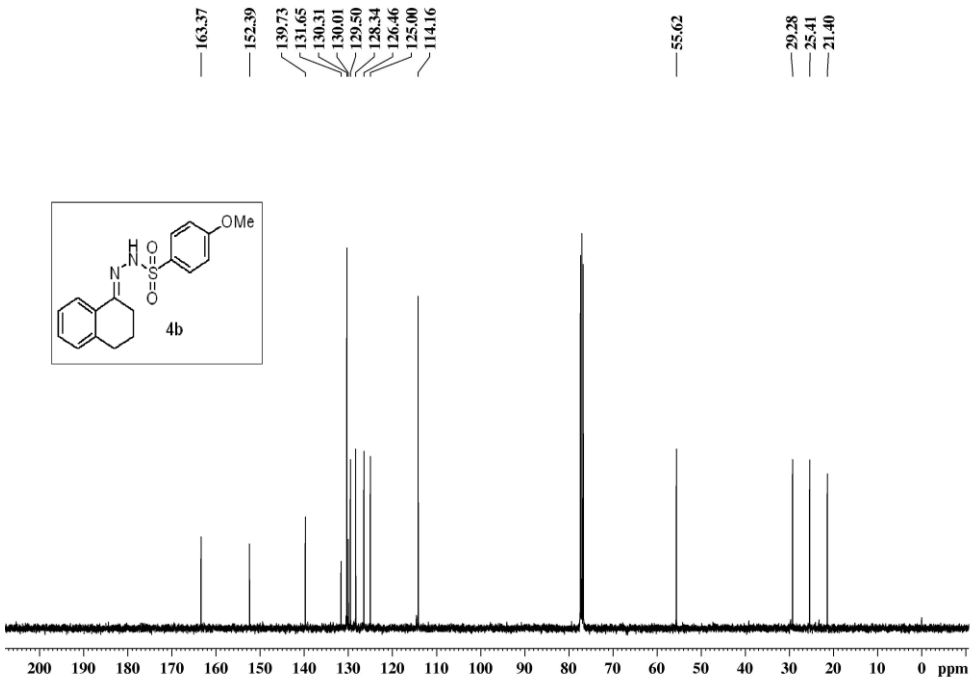
^{1}H NMR spectrum of compound **4a** (400 MHz, DMSO d6)



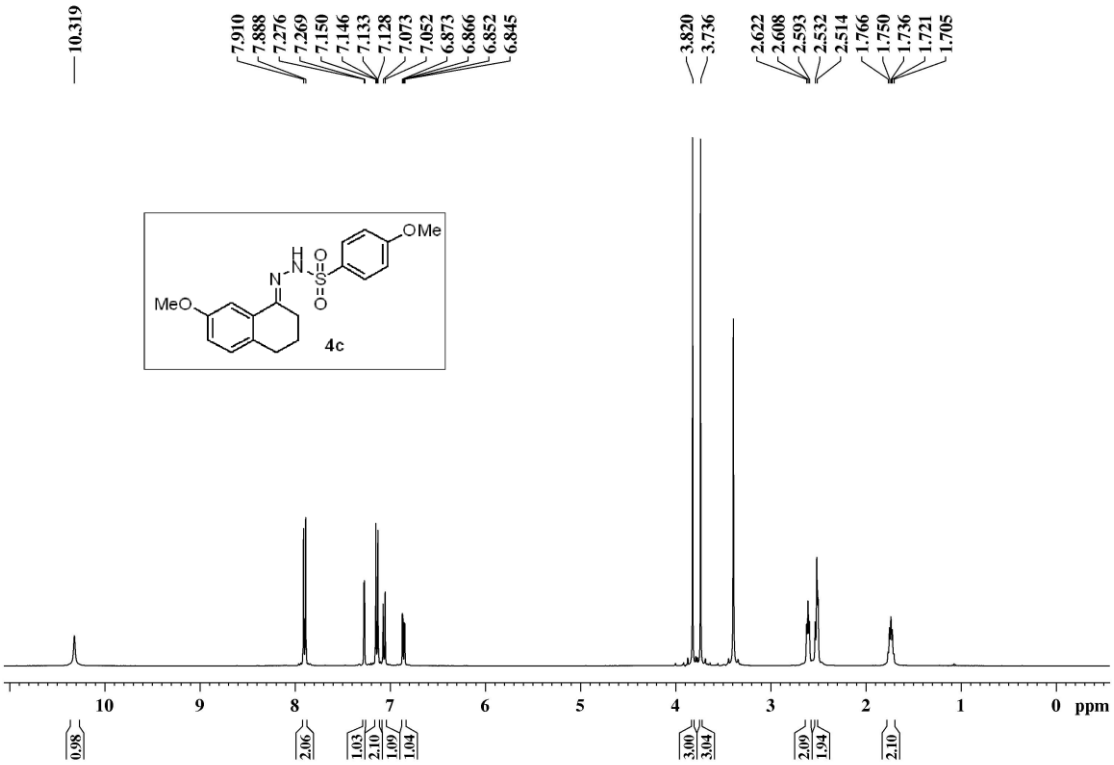
^{13}C NMR spectrum of compound **4a** (100 MHz, DMSO d6)



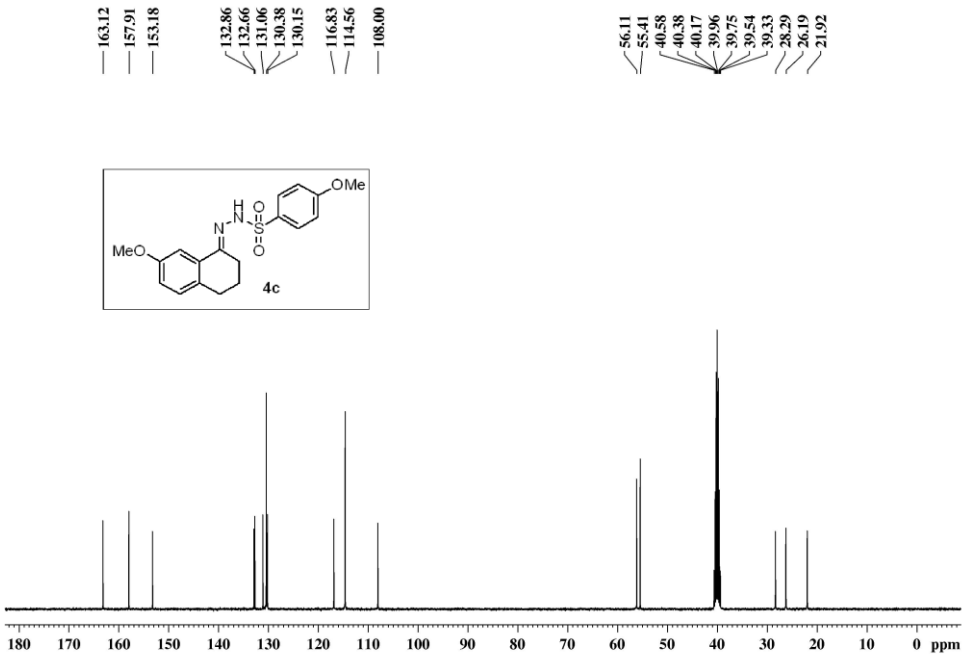
^{1}H NMR spectrum of compound **4b** (400 MHz, $CDCl_3$)



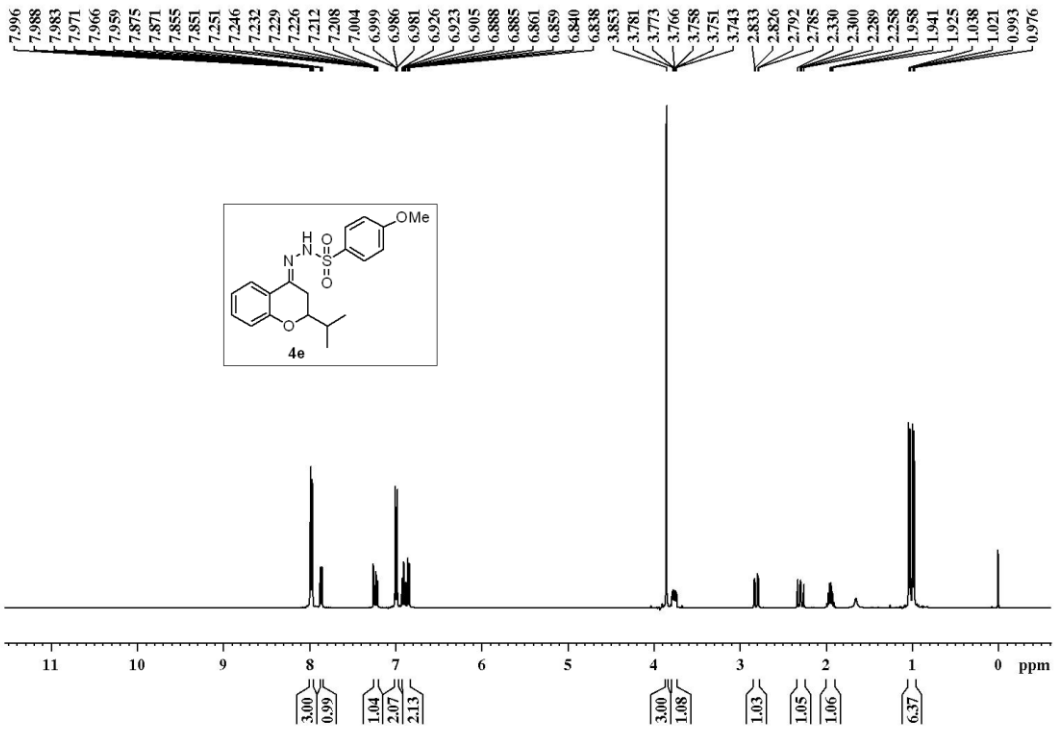
^{13}C NMR spectrum of compound **4b** (100 MHz, $CDCl_3$)



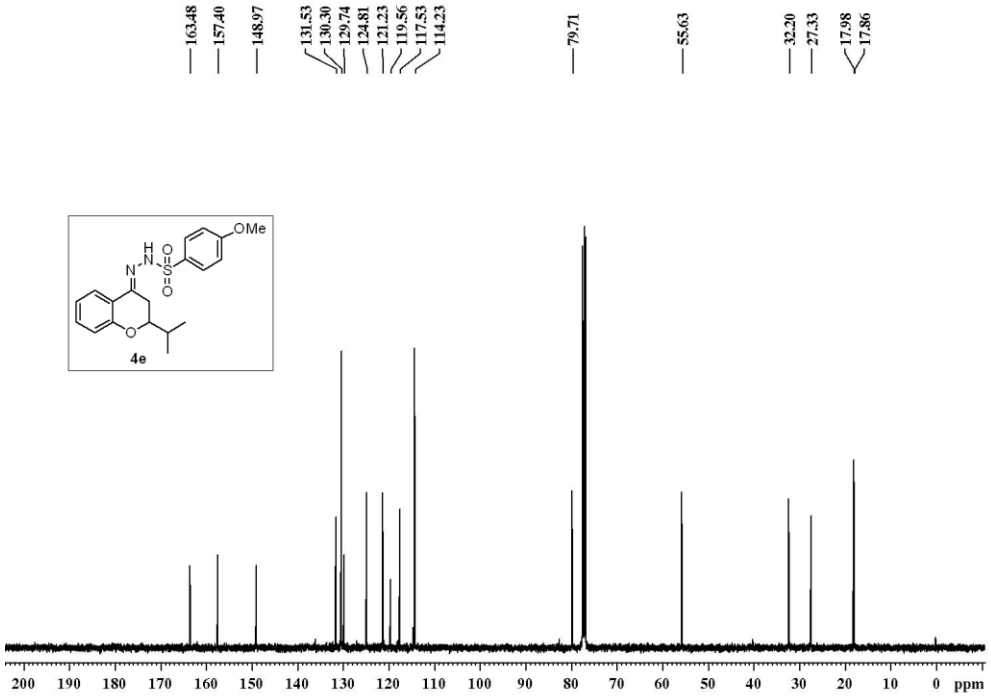
^{1}H NMR spectrum of compound **4c** (400 MHz, DMSO d6)



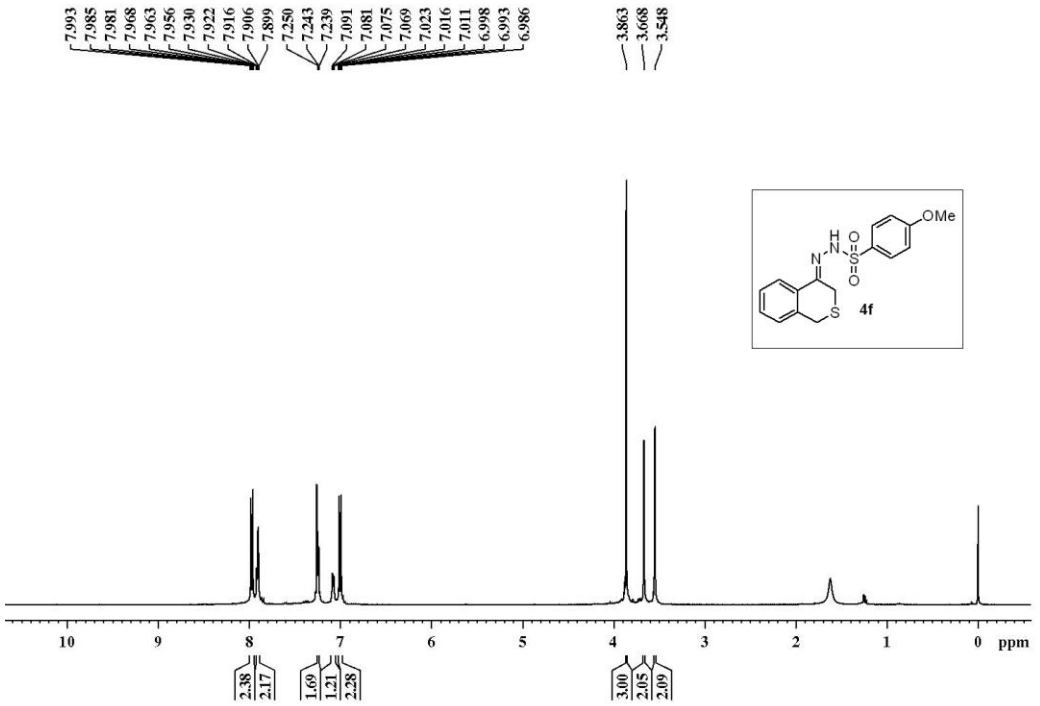
^{13}C NMR spectrum of compound **4c** (100 MHz, DMSO d6)



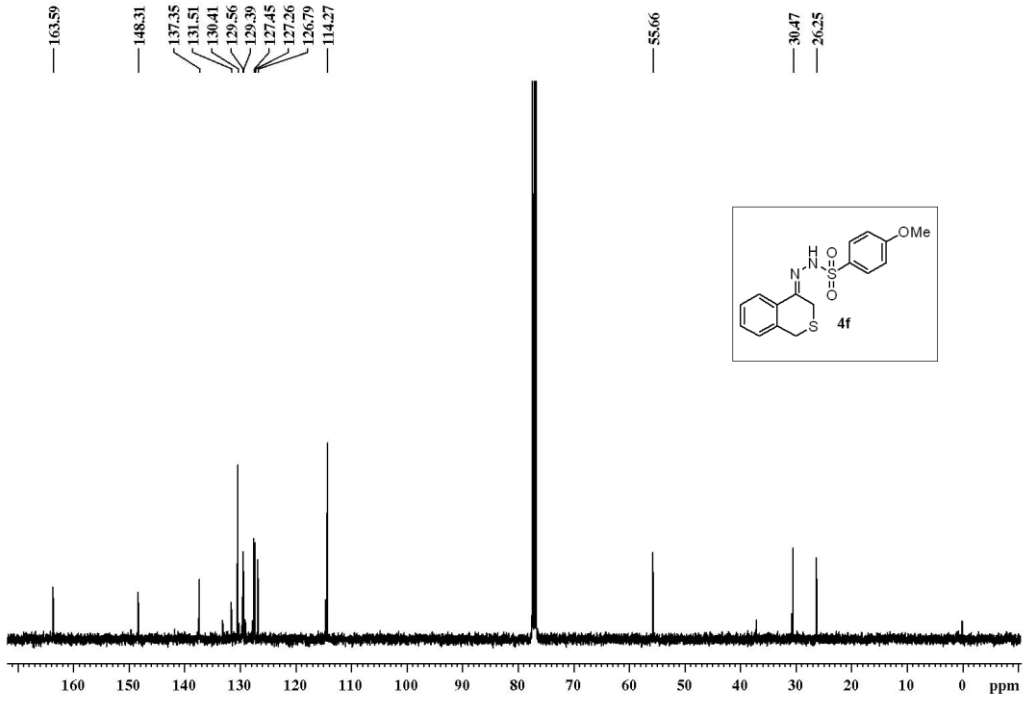
^{1}H NMR spectrum of compound **4e** (400 MHz, $CDCl_3$)



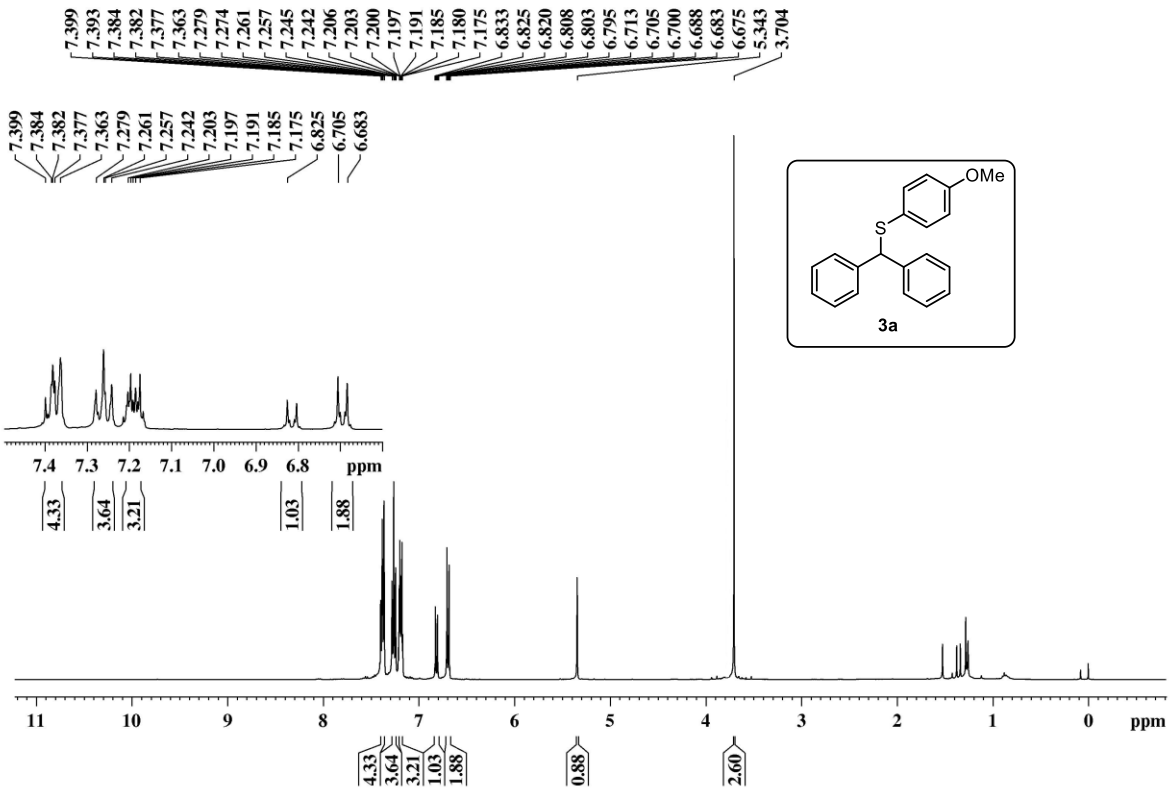
^{13}C NMR spectrum of compound **4e** (100 MHz, $CDCl_3$)



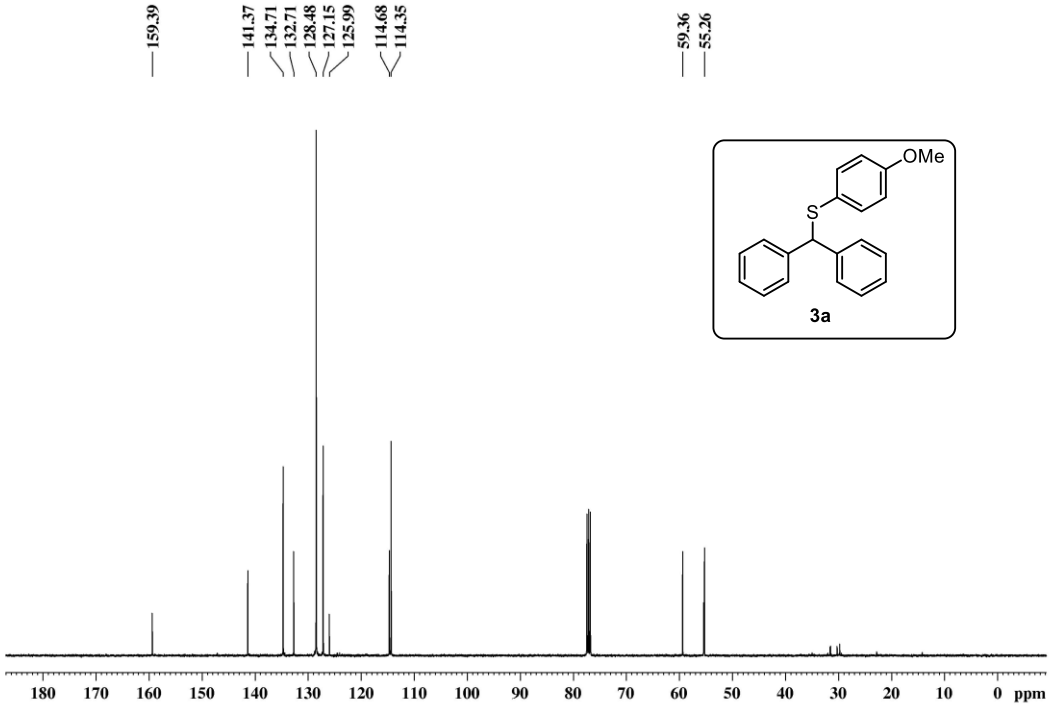
^{1}H NMR spectrum of compound **4f** (400 MHz, $CDCl_3$)



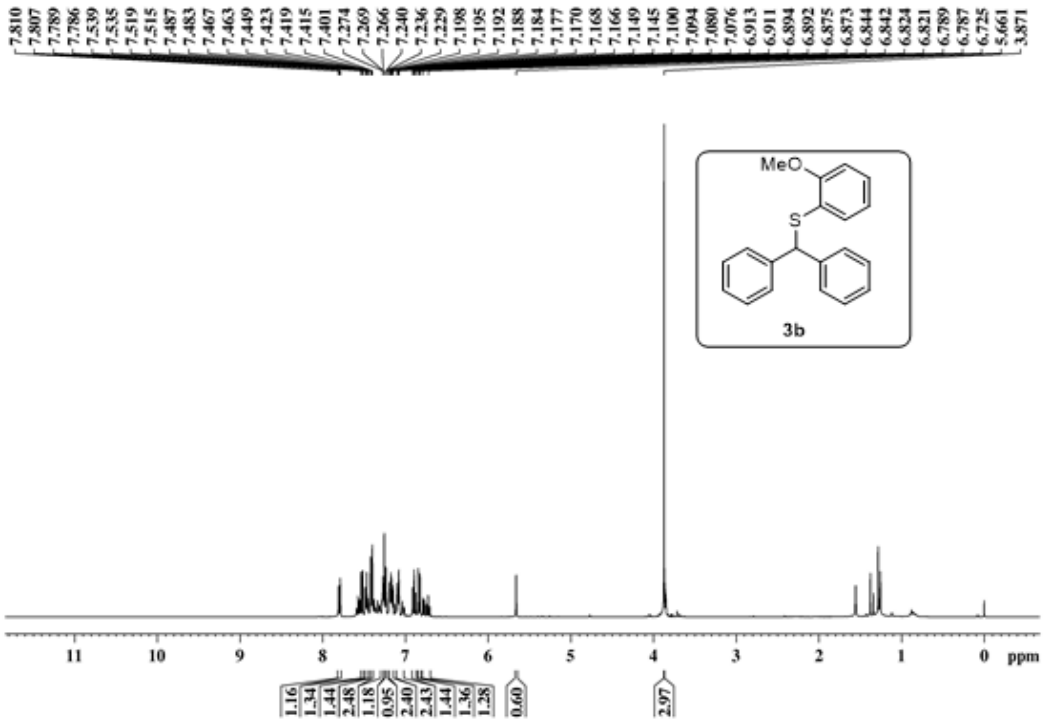
^{13}C NMR spectrum of compound **4f** (100 MHz, $CDCl_3$)



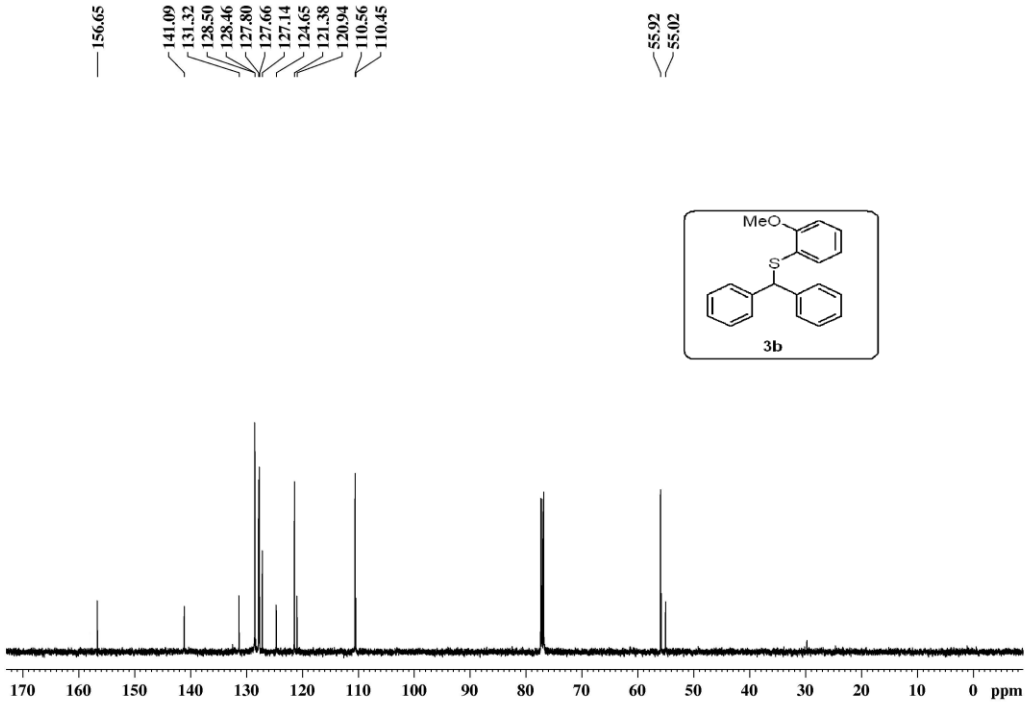
^{1}H NMR spectrum of compound **3a** (400 MHz, $CDCl_3$)



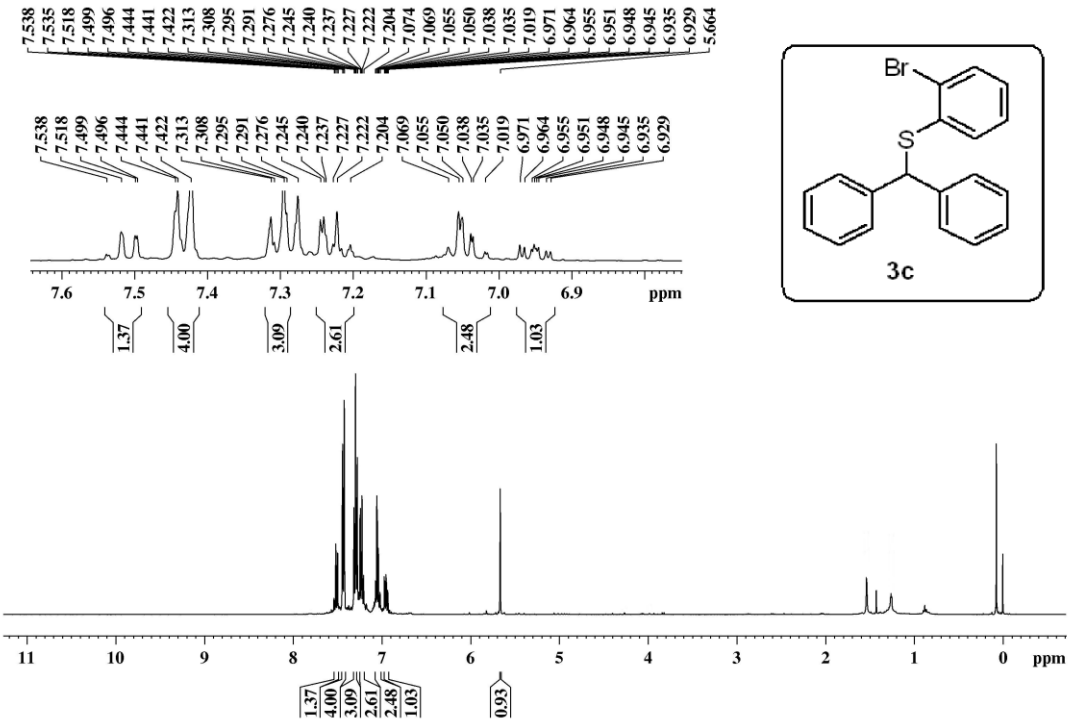
^{13}C NMR spectrum of compound **3a** (100 MHz, $CDCl_3$)



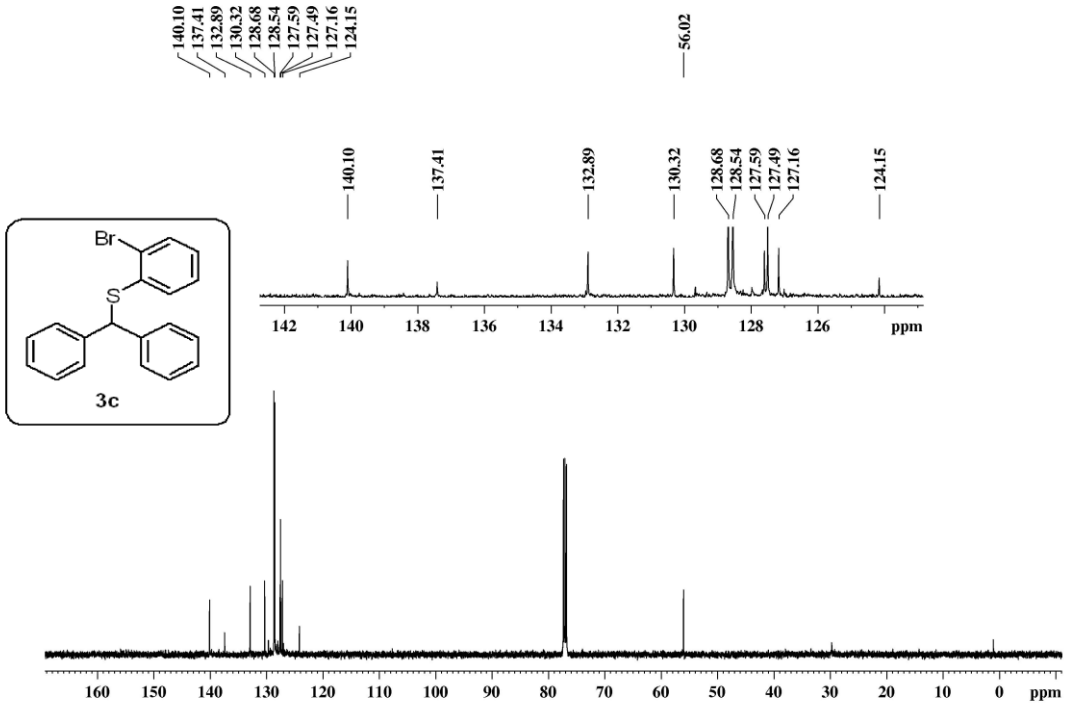
^{1}H NMR spectrum of compound **3b** (400 MHz, $CDCl_3$)



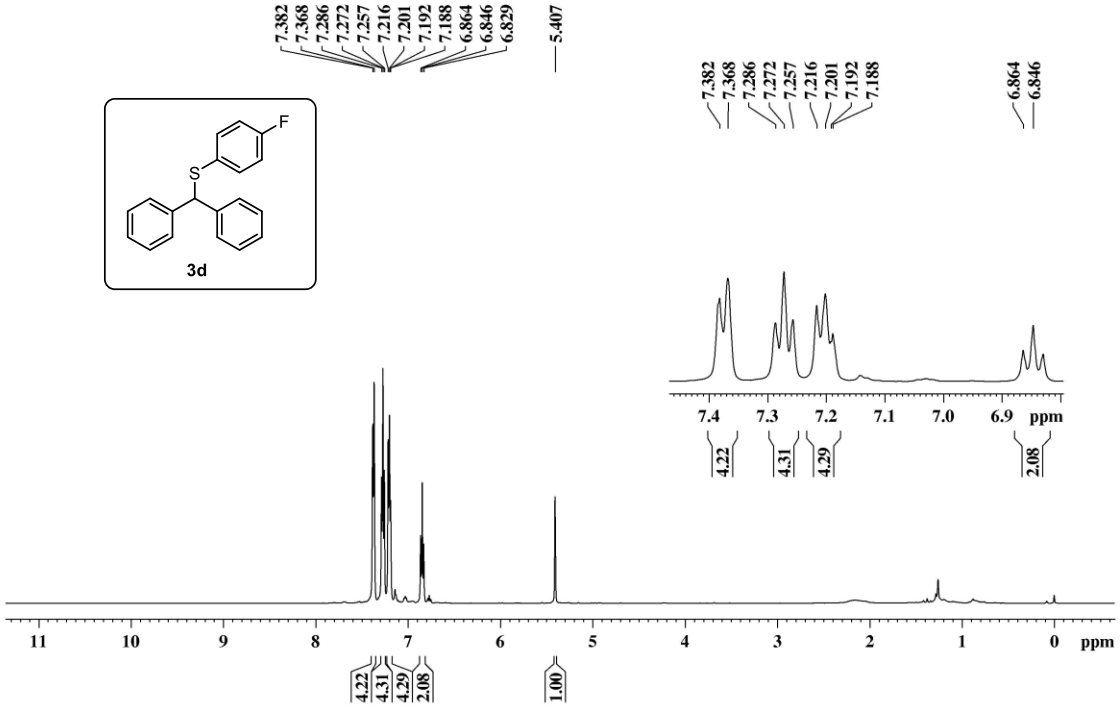
^{13}C NMR spectrum of compound **3b** (100 MHz, $CDCl_3$)



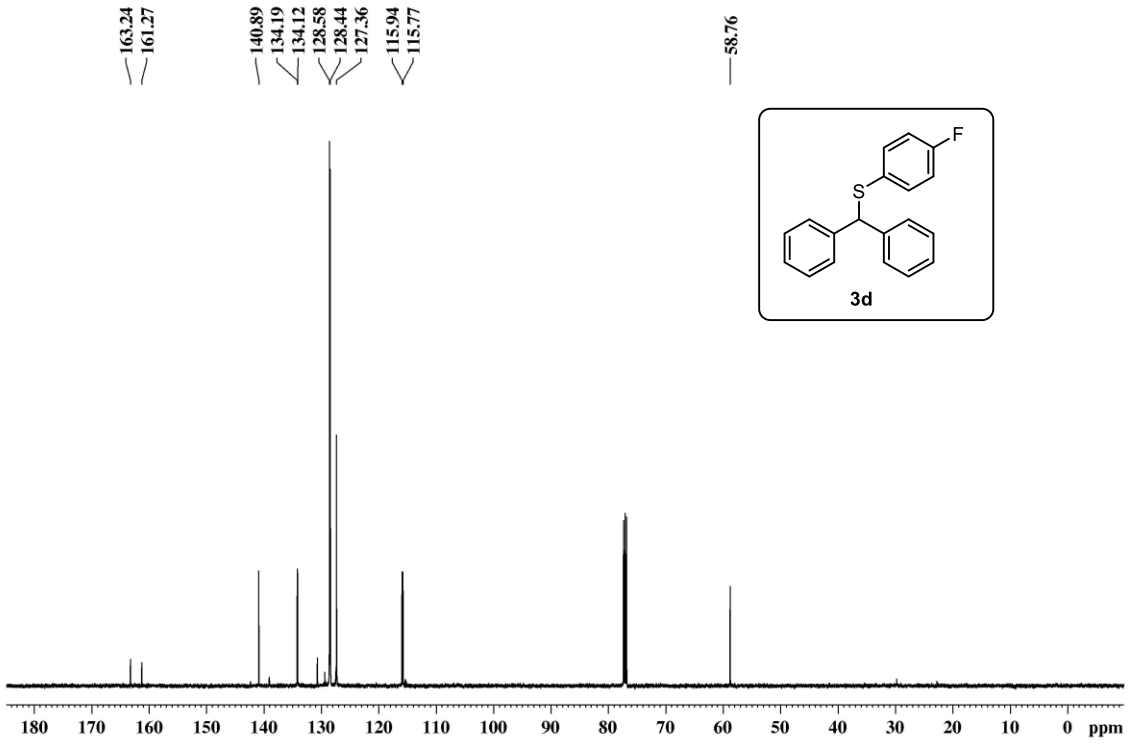
^{1}H NMR spectrum of compound **3c** (400 MHz, $CDCl_3$)



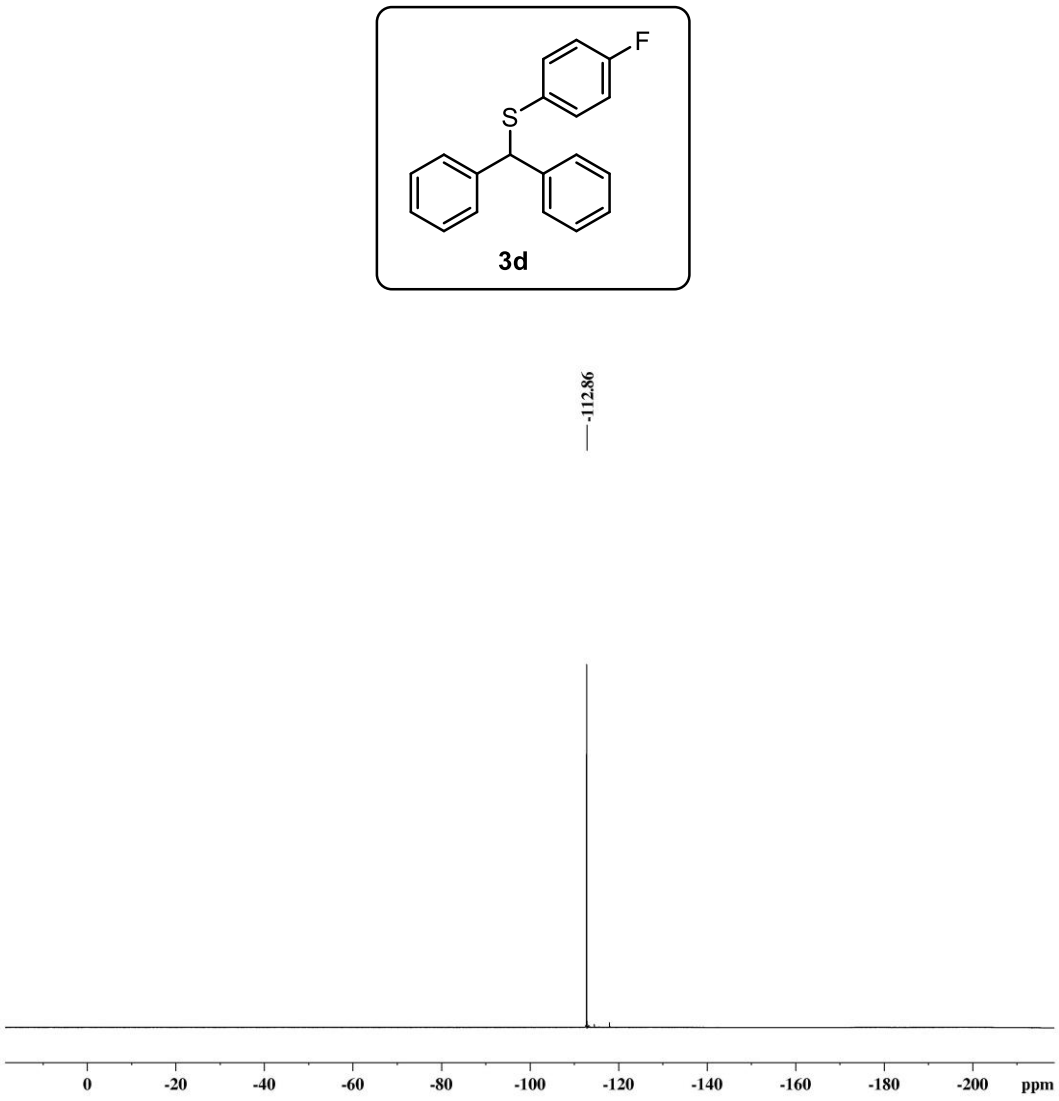
^{13}C NMR spectrum of compound **3c** (100 MHz, $CDCl_3$)



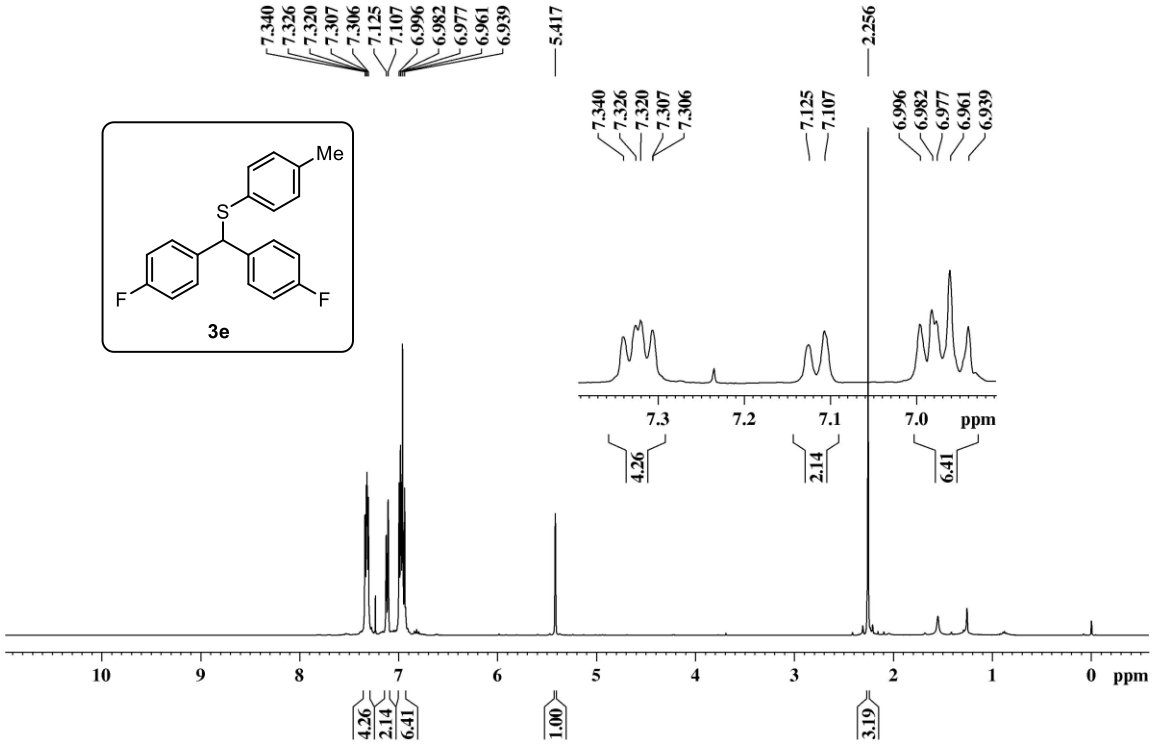
^{1}H NMR spectrum of compound **3d** (400 MHz, $CDCl_3$)



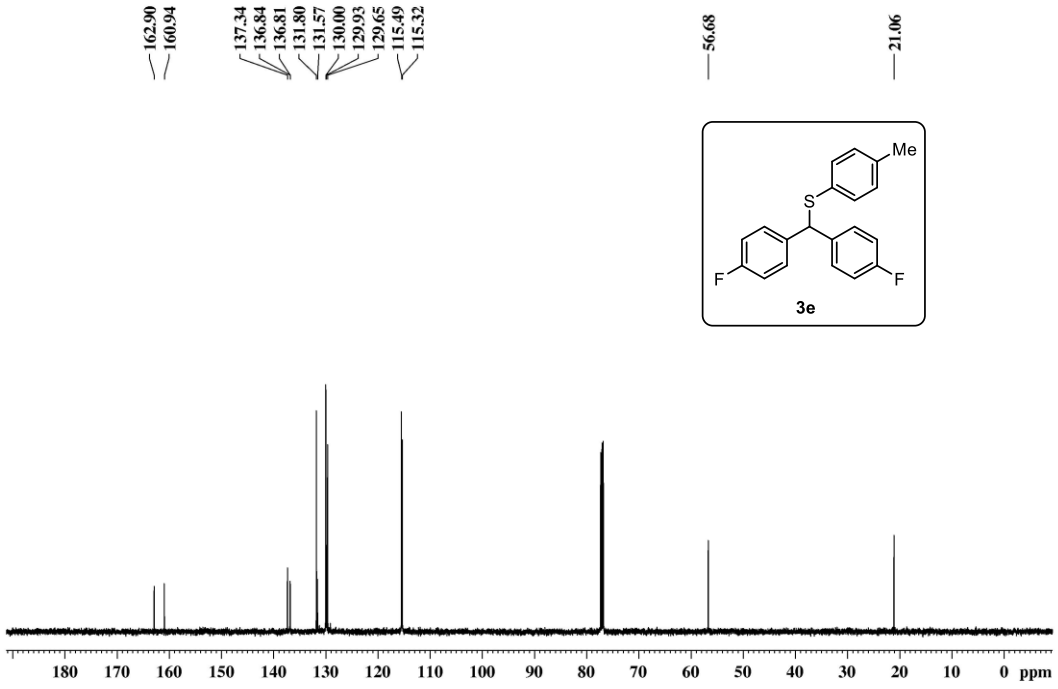
^{13}C NMR spectrum of compound **3d** (100 MHz, $CDCl_3$)



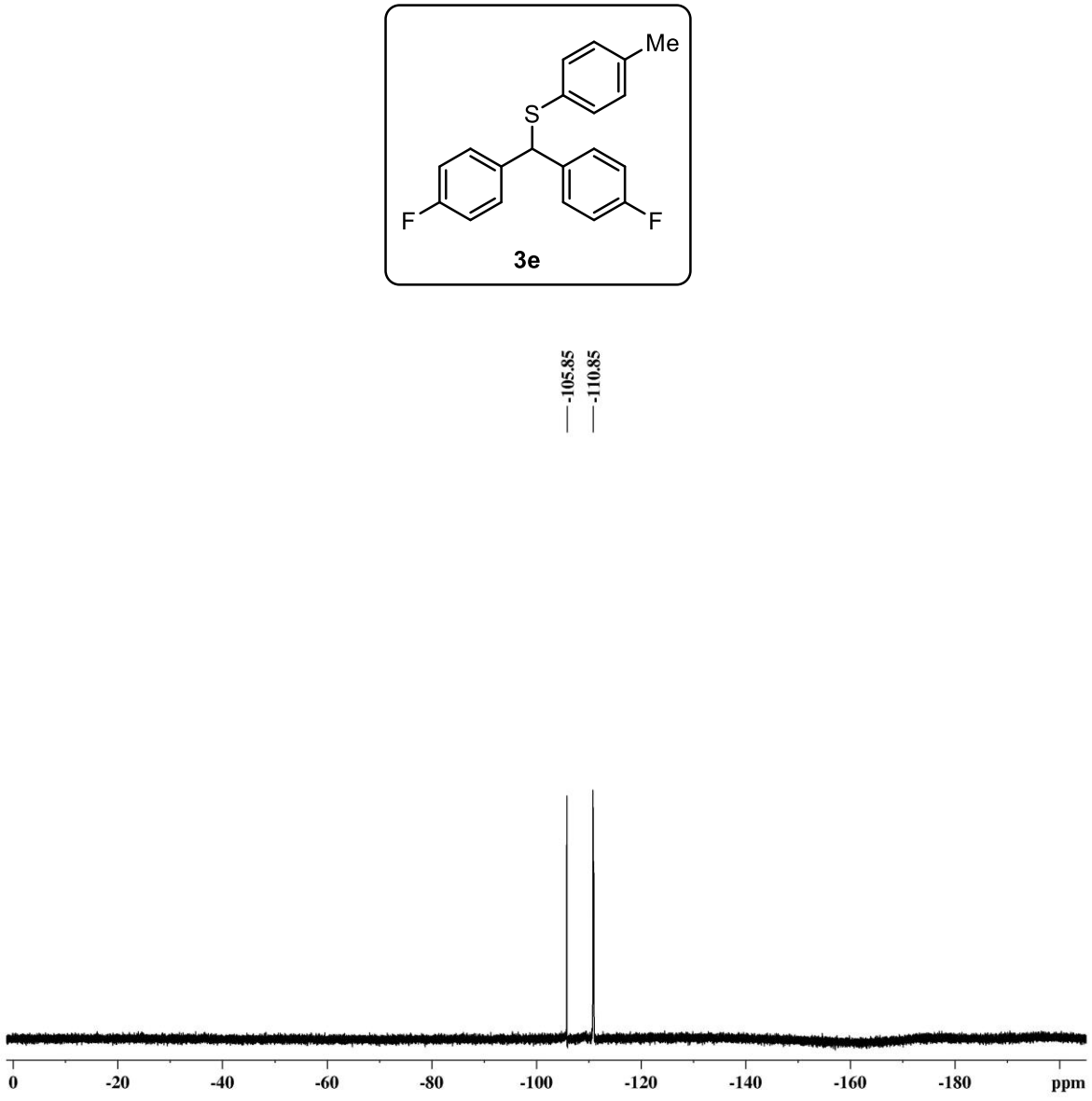
^{19}F NMR spectrum of compound **3d** (376 MHz, $CDCl_3$)



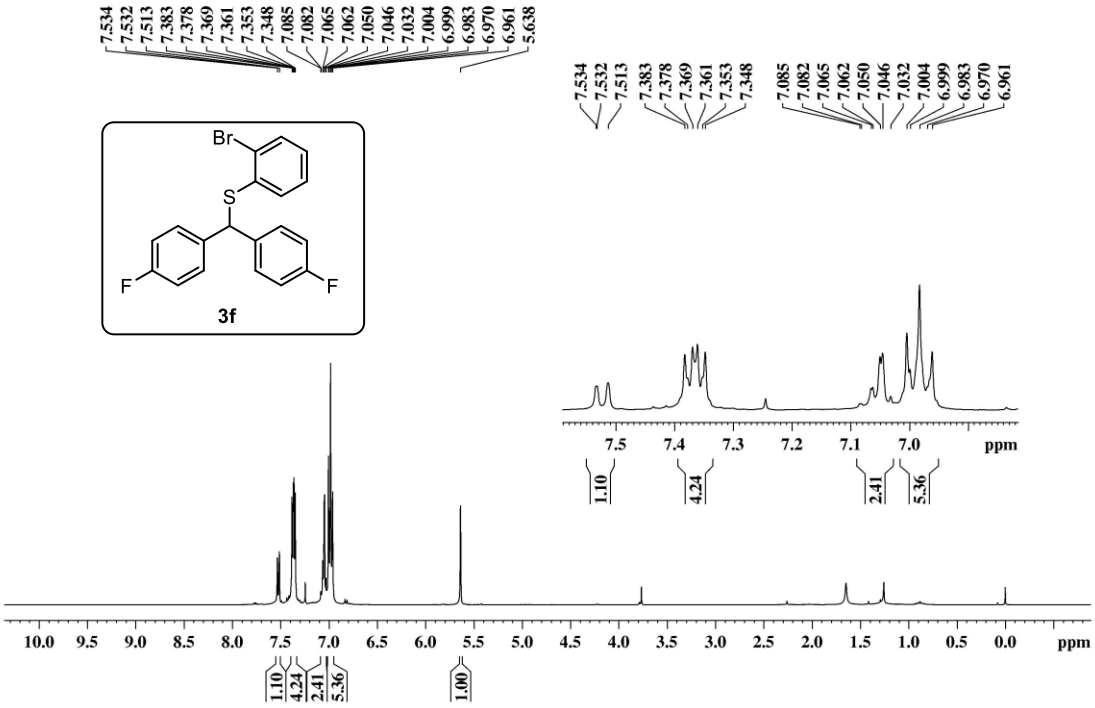
^{1}H NMR spectrum of compound **3e** (400 MHz, $CDCl_3$)



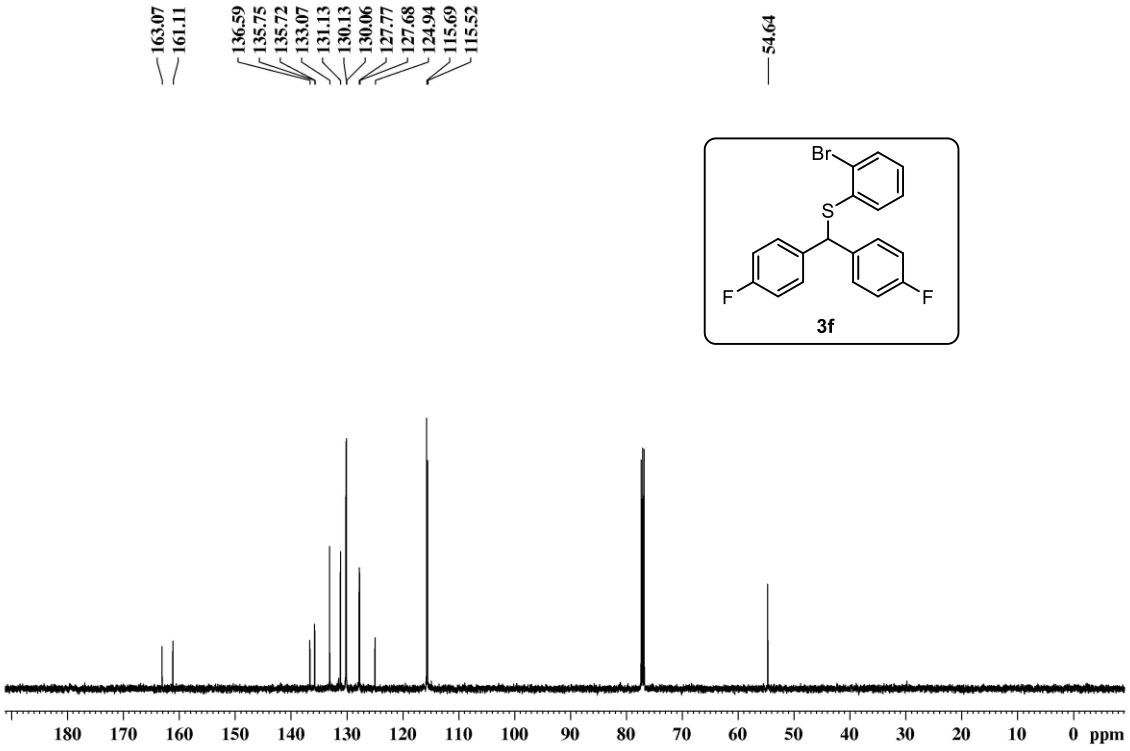
^{13}C NMR spectrum of compound **3e** (100 MHz, $CDCl_3$)



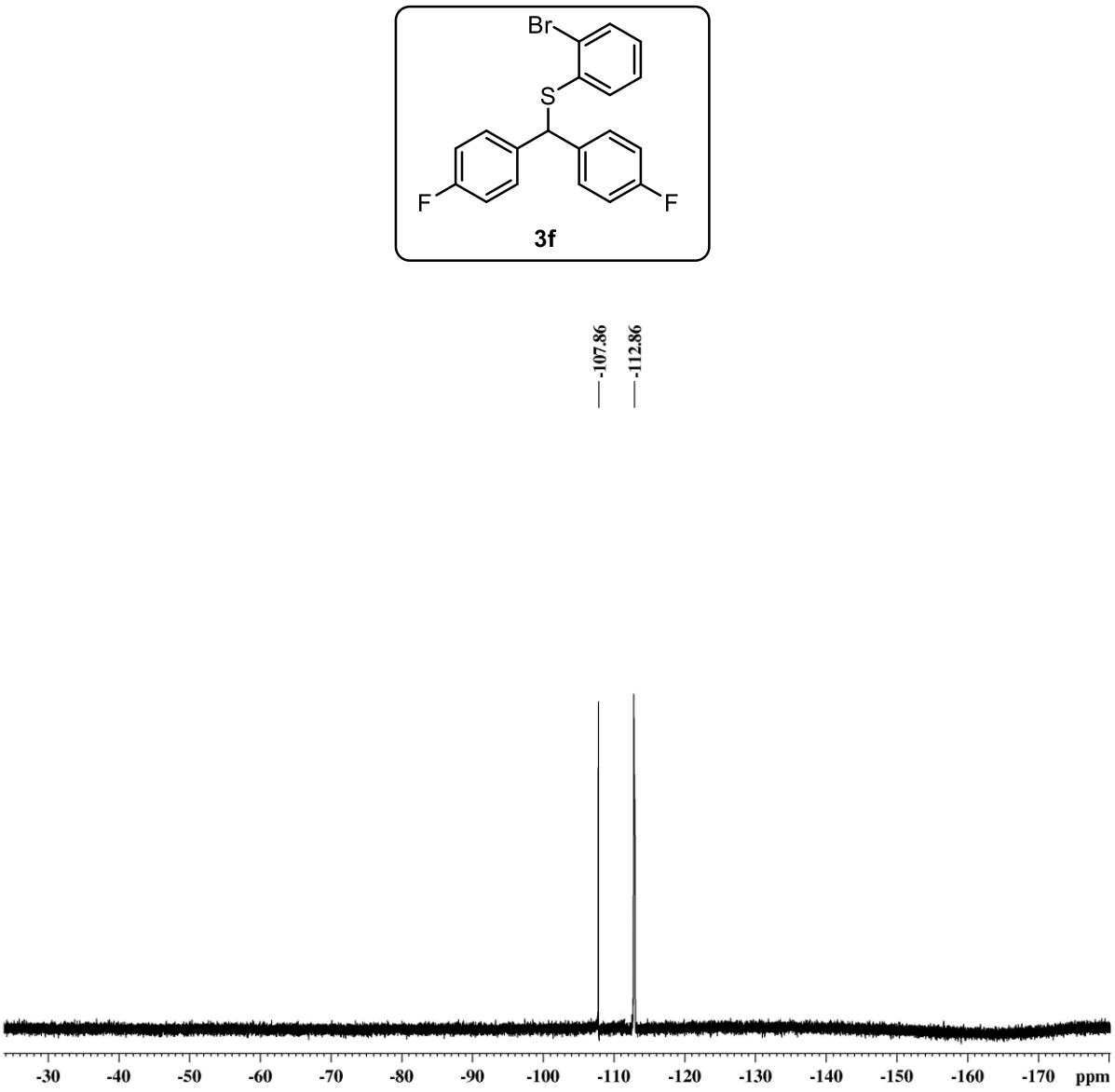
^{19}F NMR spectrum of compound **3e** (376 MHz, $CDCl_3$)



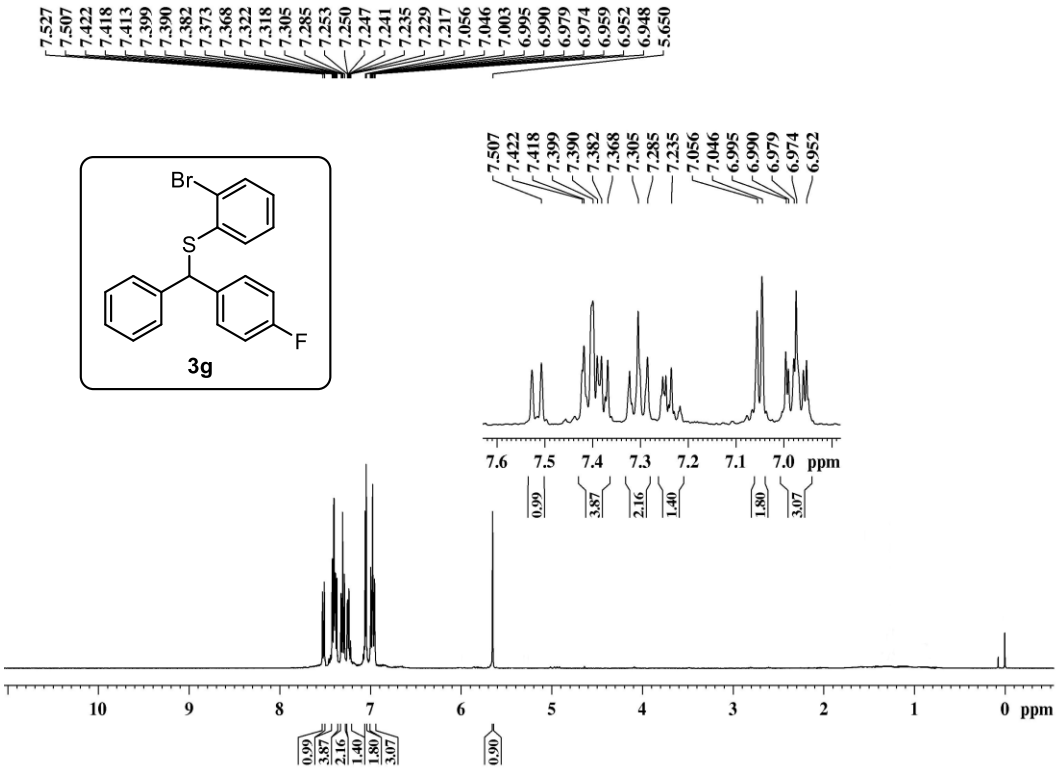
^{1}H NMR spectrum of compound **3f** (400 MHz, $CDCl_3$)



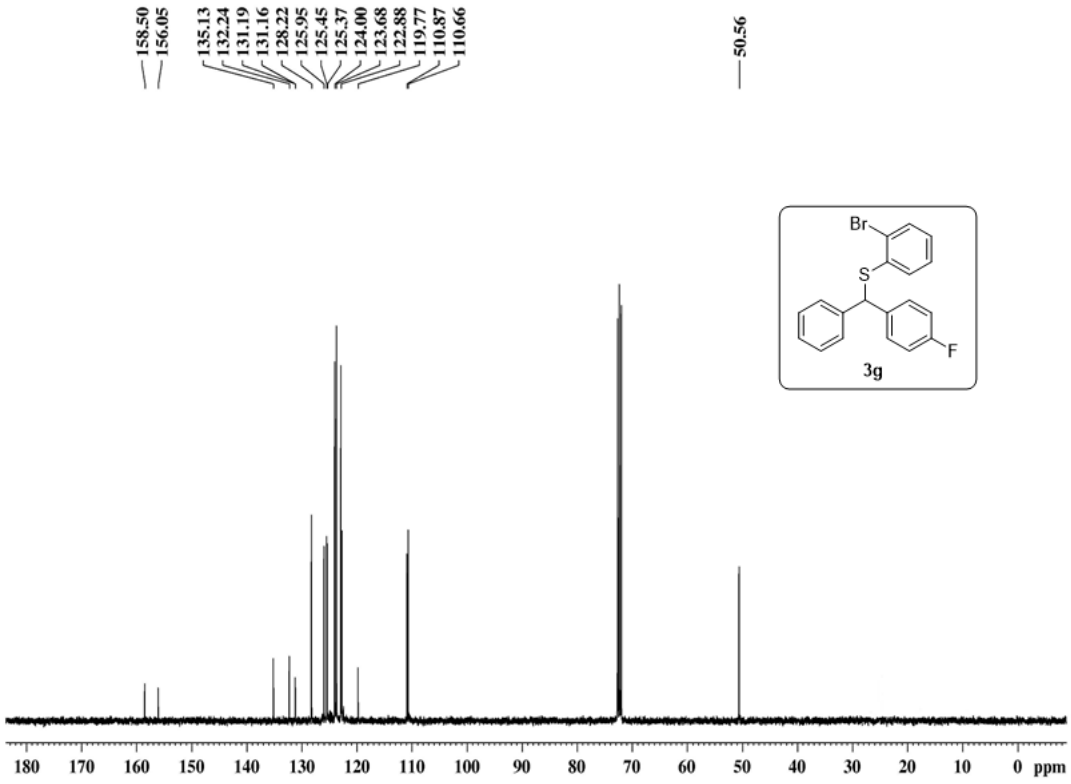
^{13}C NMR spectrum of compound **3f** (100 MHz, $CDCl_3$)



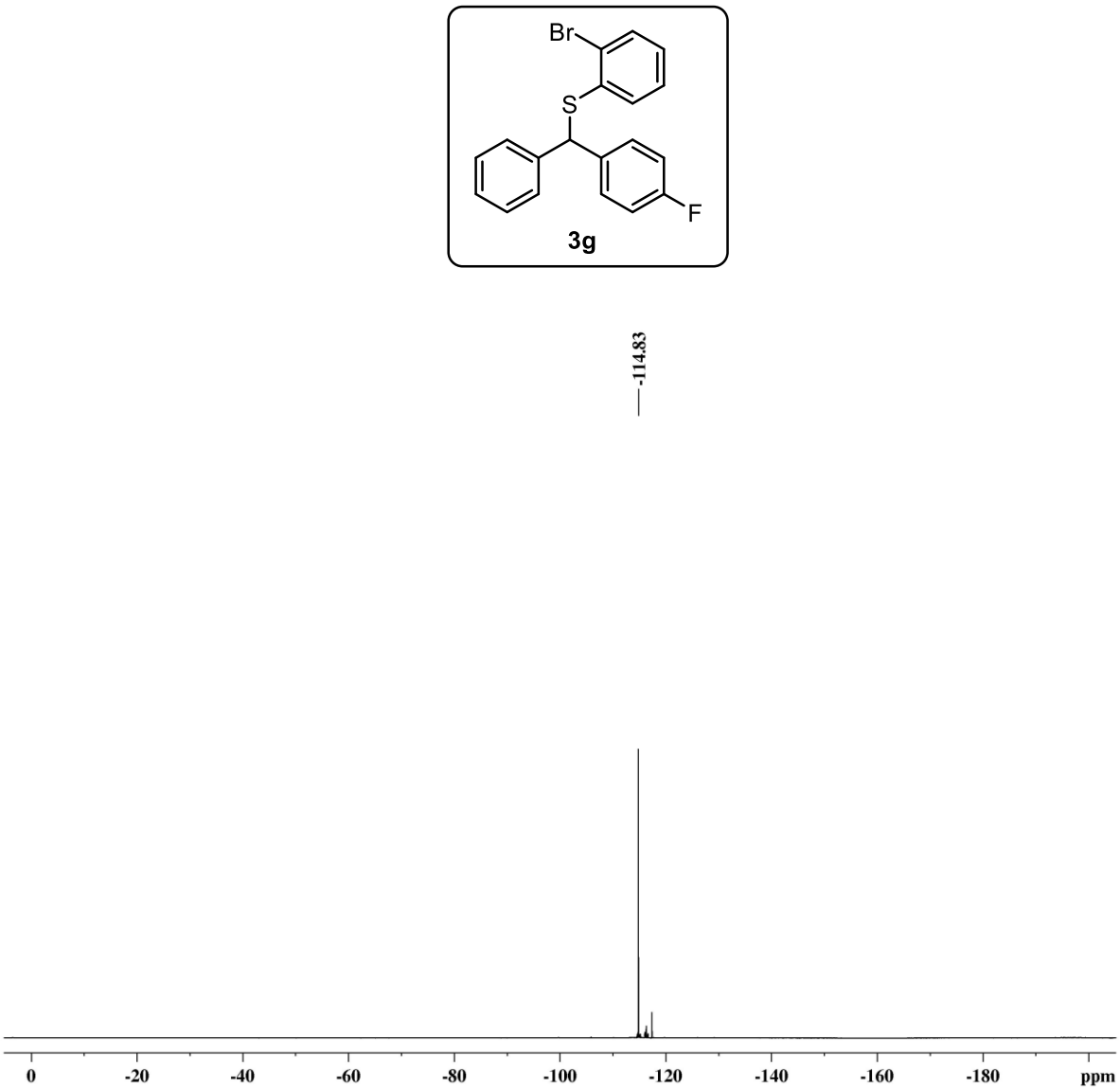
^{19}F NMR spectrum of compound **3f** (376 MHz, $CDCl_3$)



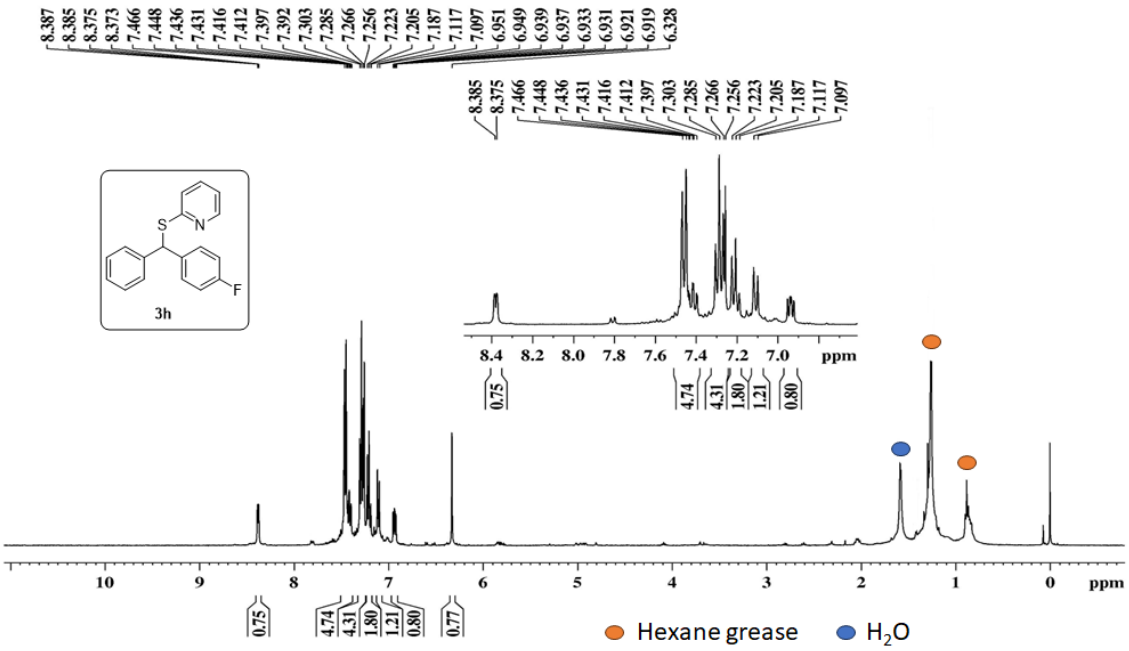
^{1}H NMR spectrum of compound **3g** (400 MHz, $CDCl_3$)



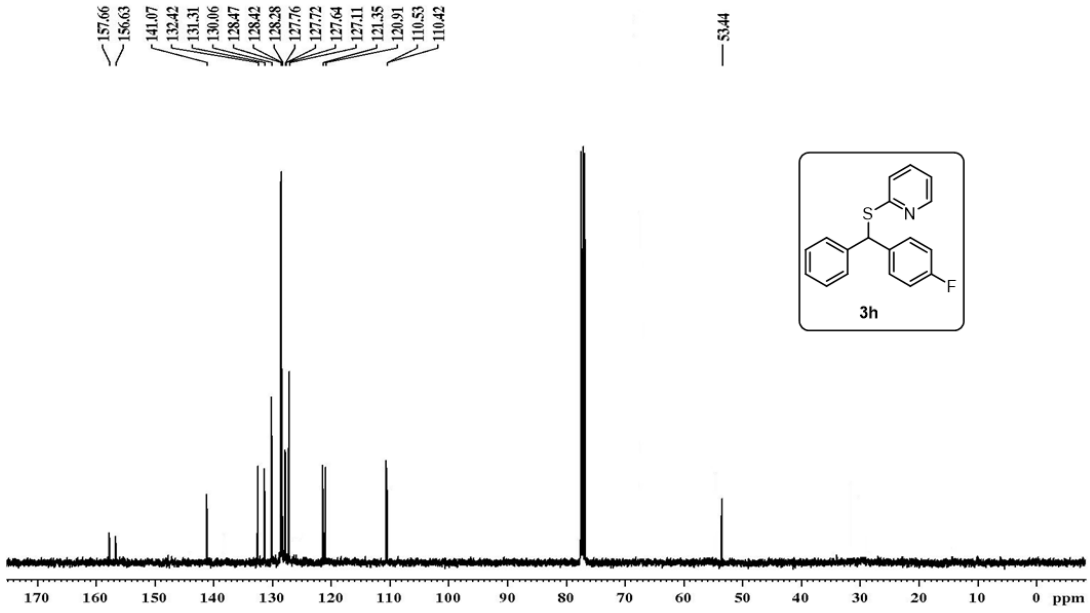
^{13}C NMR spectrum of compound **3g** (100 MHz, $CDCl_3$)



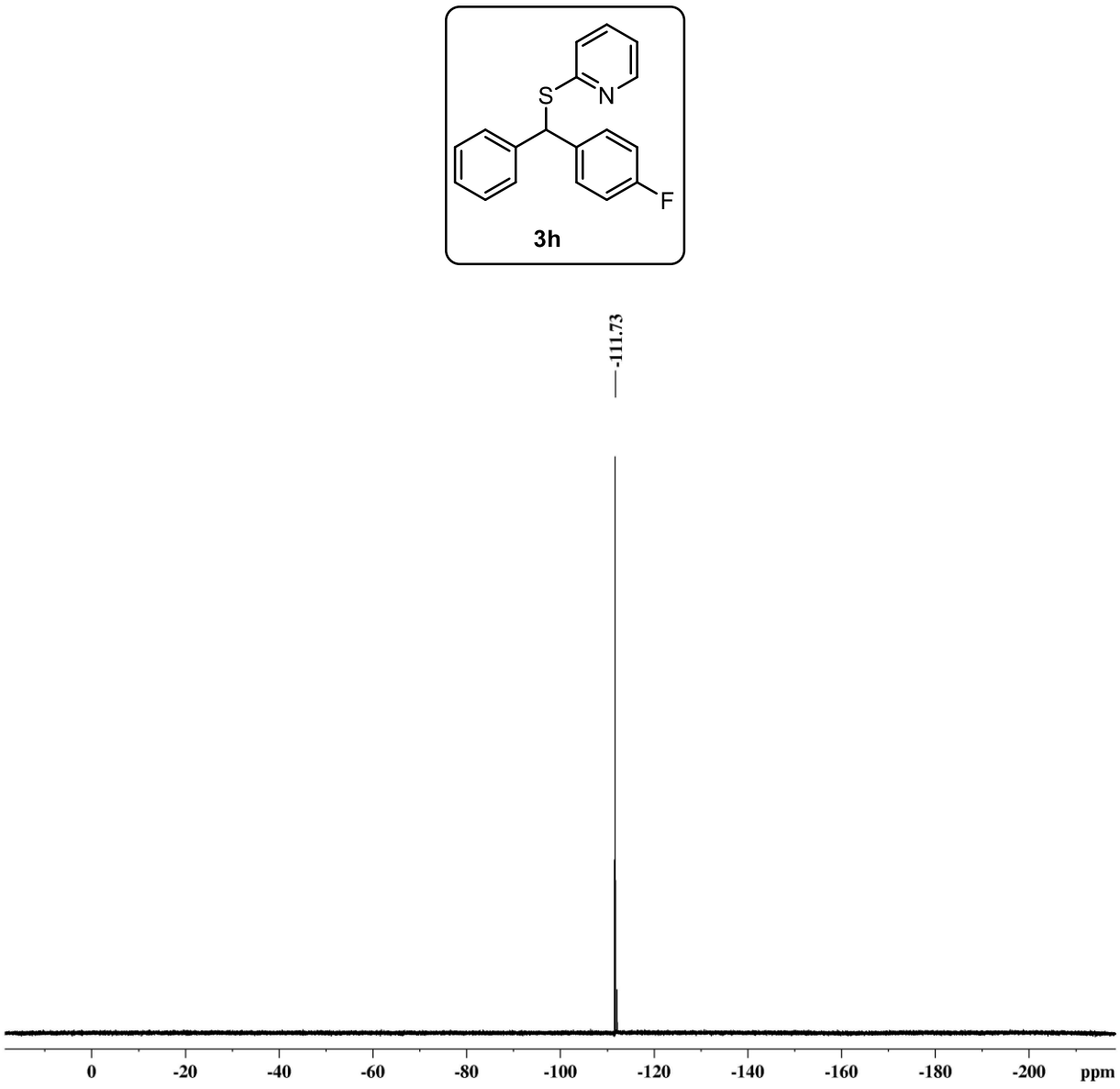
^{19}F NMR spectrum of compound **3g** (376 MHz, $CDCl_3$)



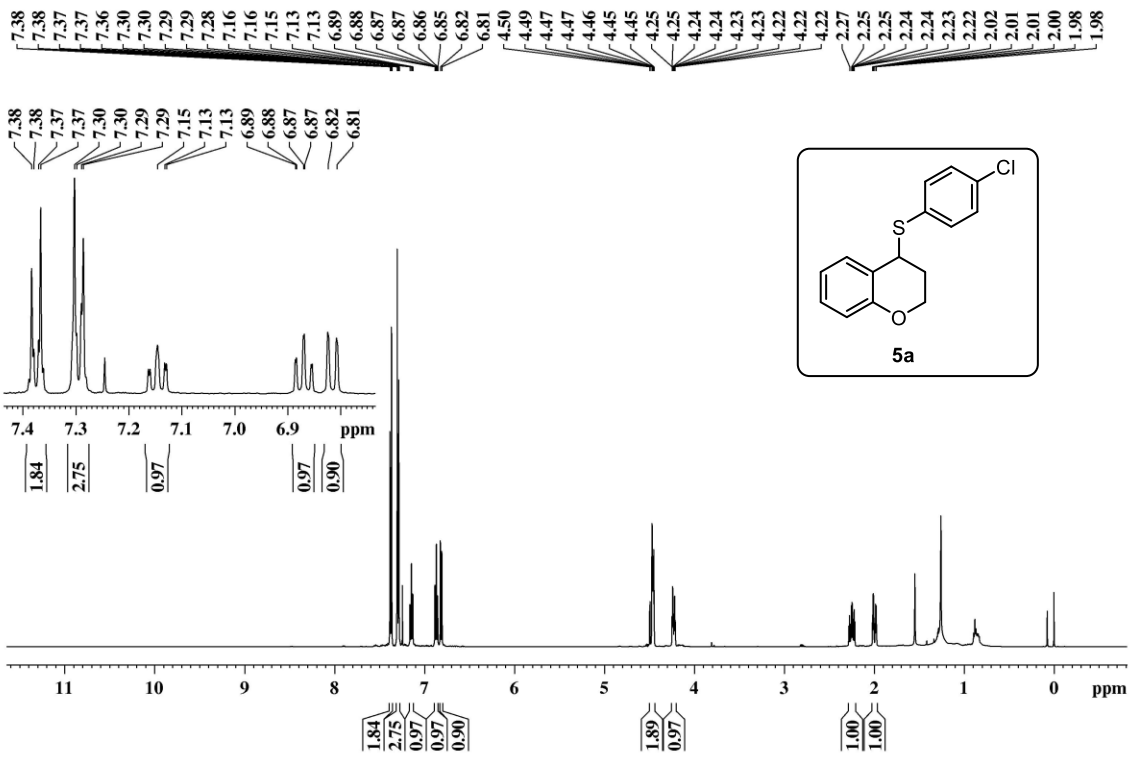
^{1}H NMR spectrum of compound **3h** (400 MHz, $CDCl_3$)



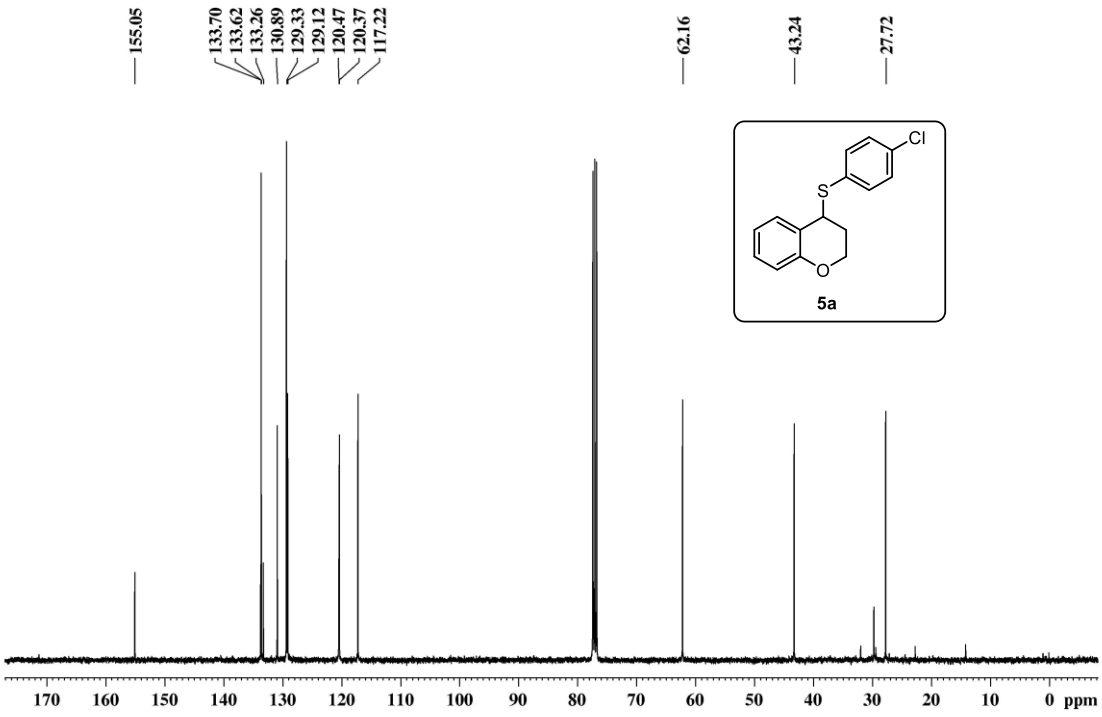
^{13}C NMR spectrum of compound **3h** (100 MHz, $CDCl_3$)



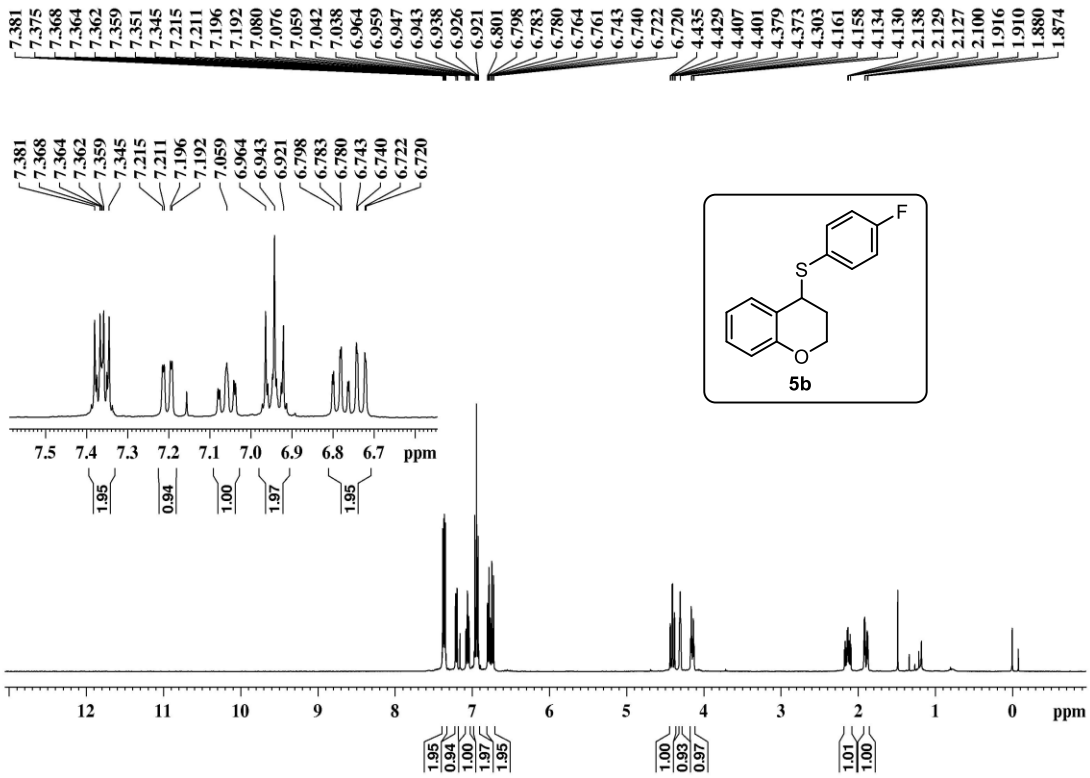
^{19}F NMR spectrum of compound **3h** (376 MHz, $CDCl_3$)



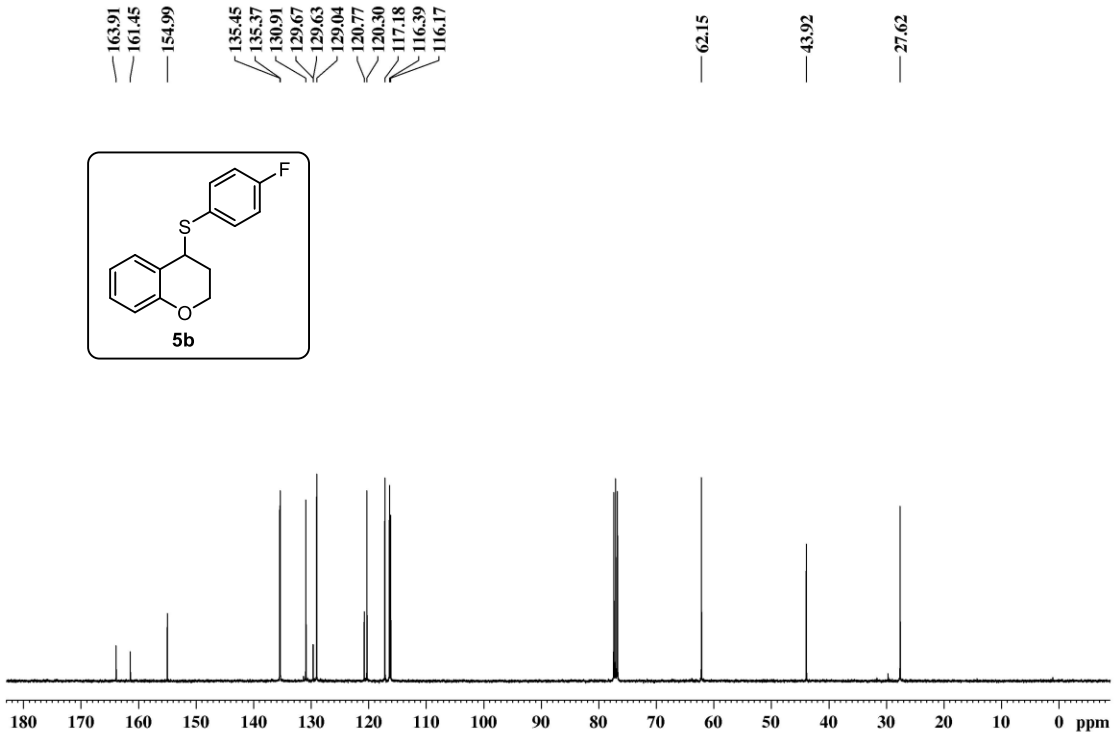
^{1}H NMR spectrum of compound **5a** (400 MHz, $CDCl_3$)



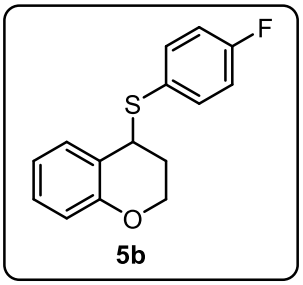
^{13}C NMR spectrum of compound **5a** (100 MHz, $CDCl_3$)

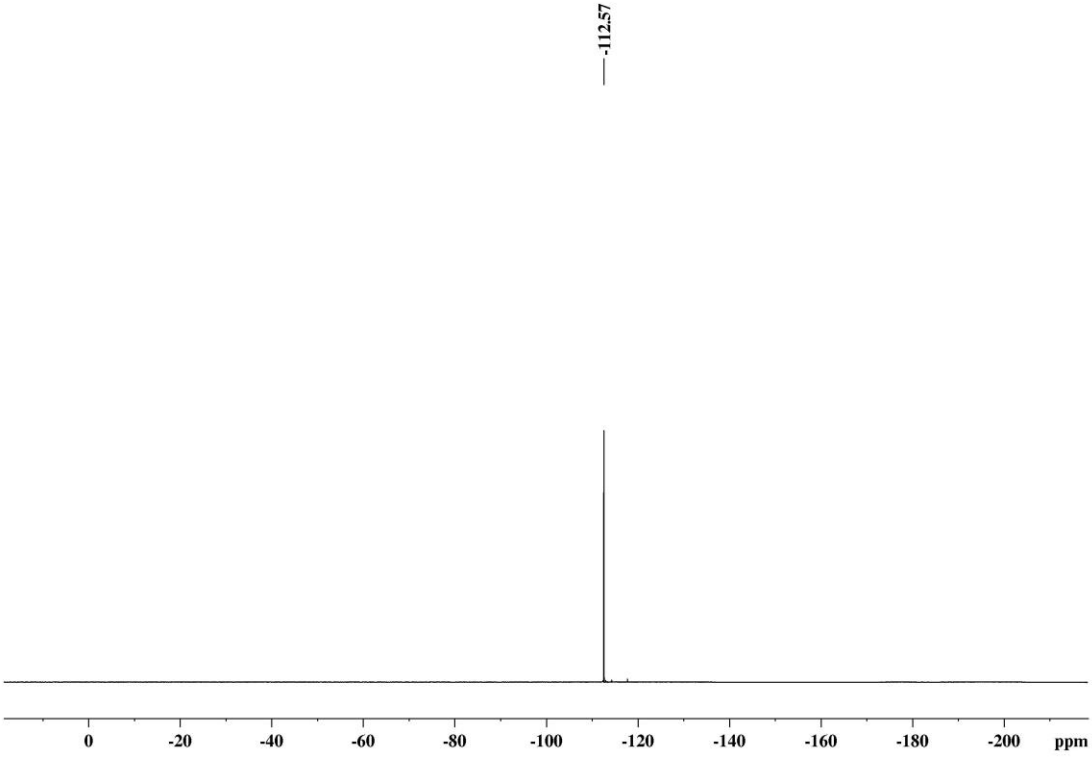


^{1}H NMR spectrum of compound **5b** (400 MHz, $CDCl_3$)

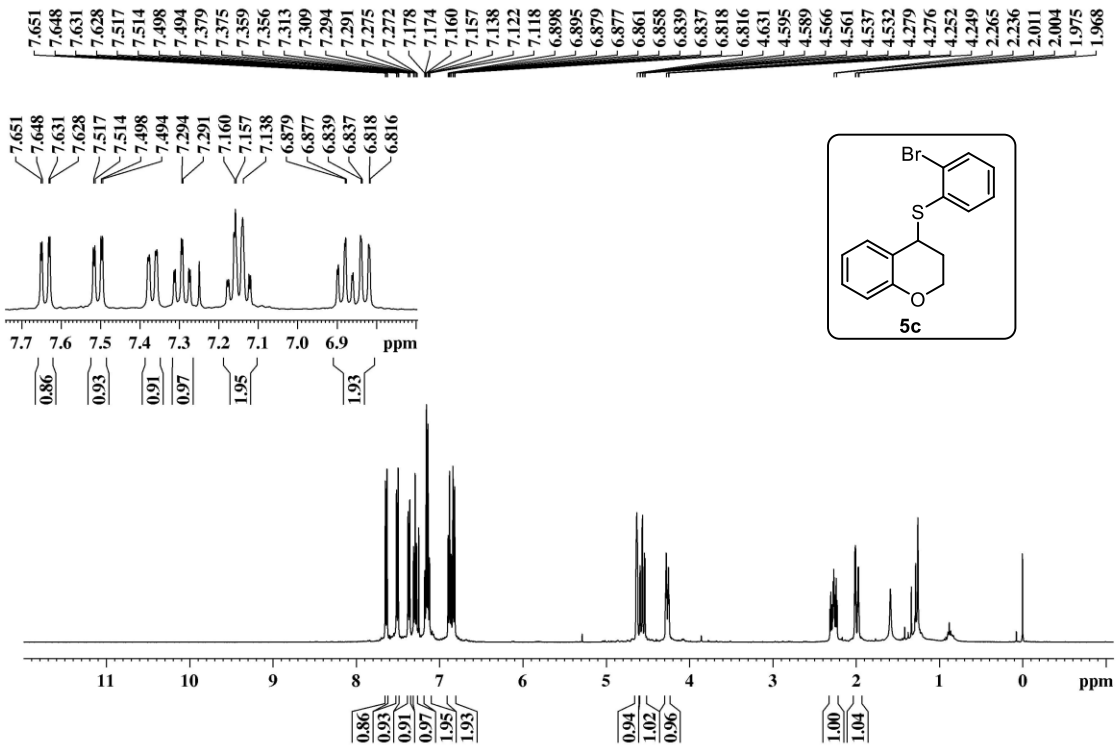


^{13}C NMR spectrum of compound **5b** (100 MHz, $CDCl_3$)

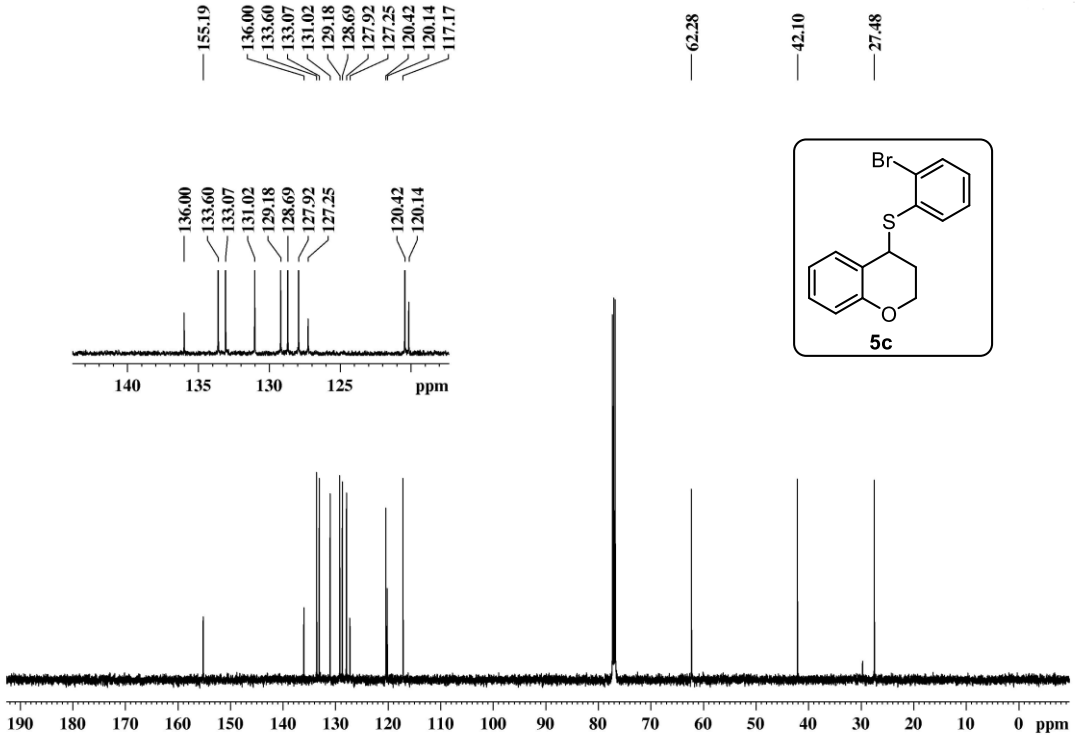




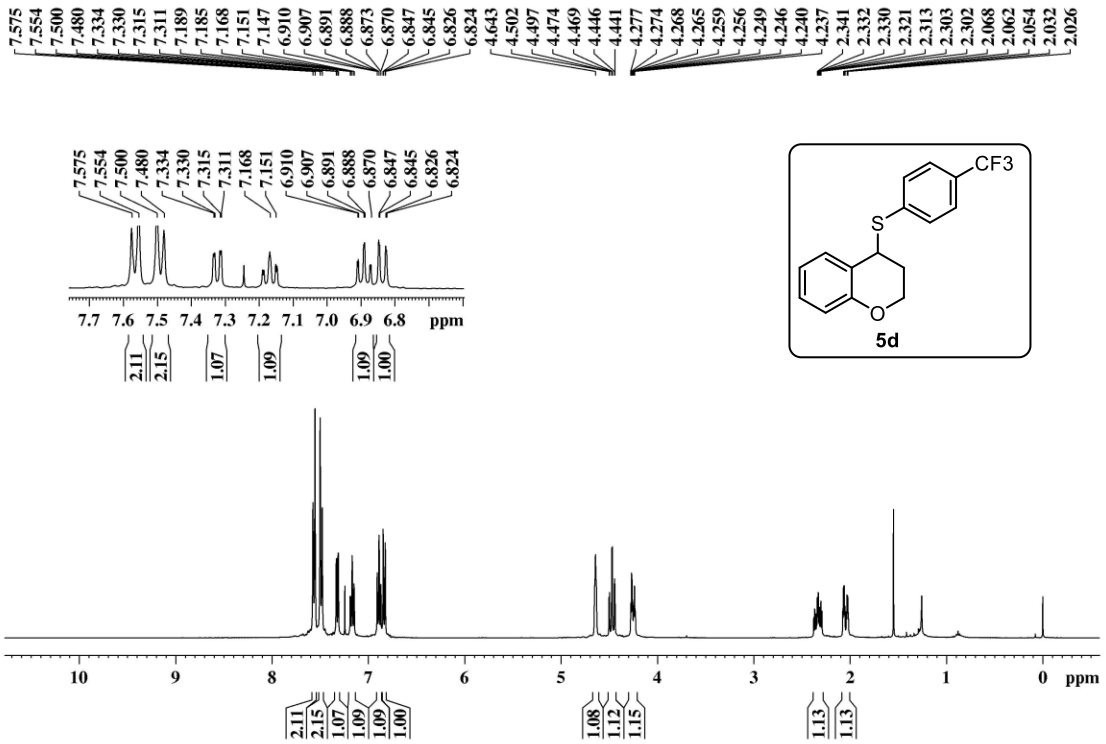
^{19}F NMR spectrum of compound **5b** (376 MHz, $CDCl_3$)



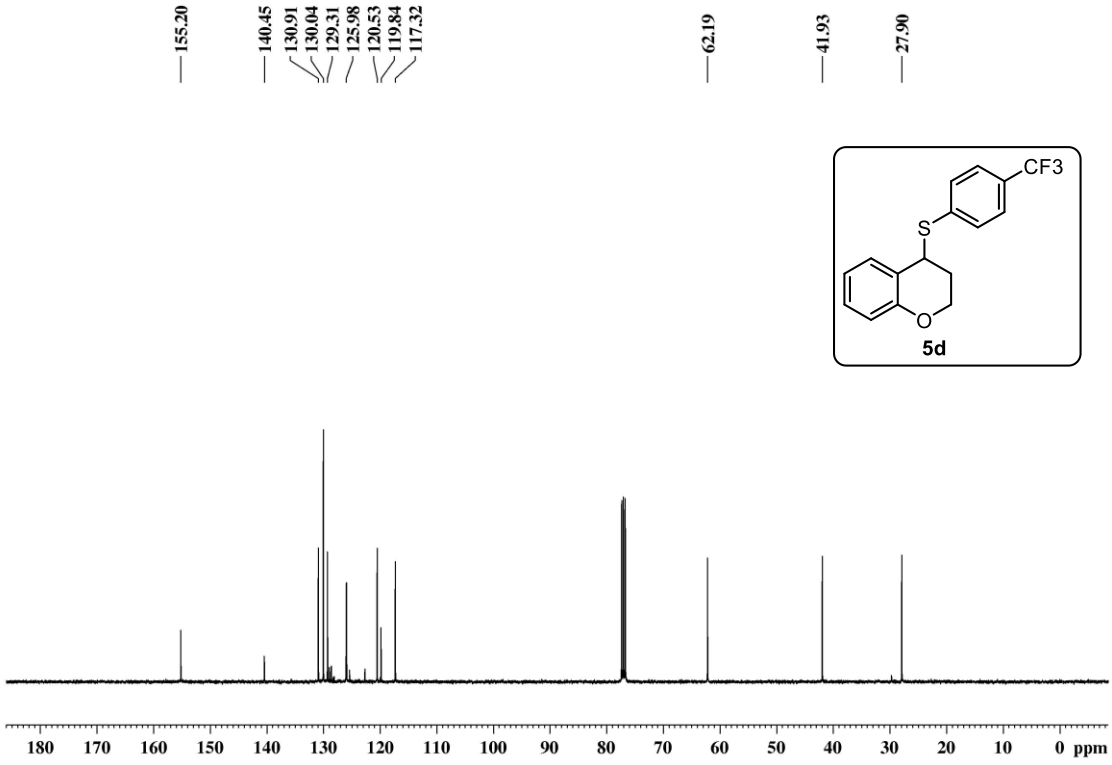
^{1}H NMR spectrum of compound **5c** (400 MHz, $CDCl_3$)



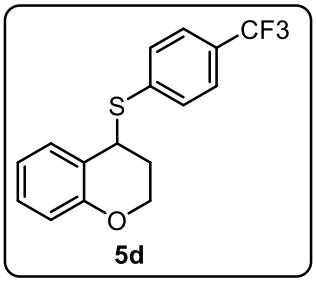
^{13}C NMR spectrum of compound **5c** (100 MHz, $CDCl_3$)

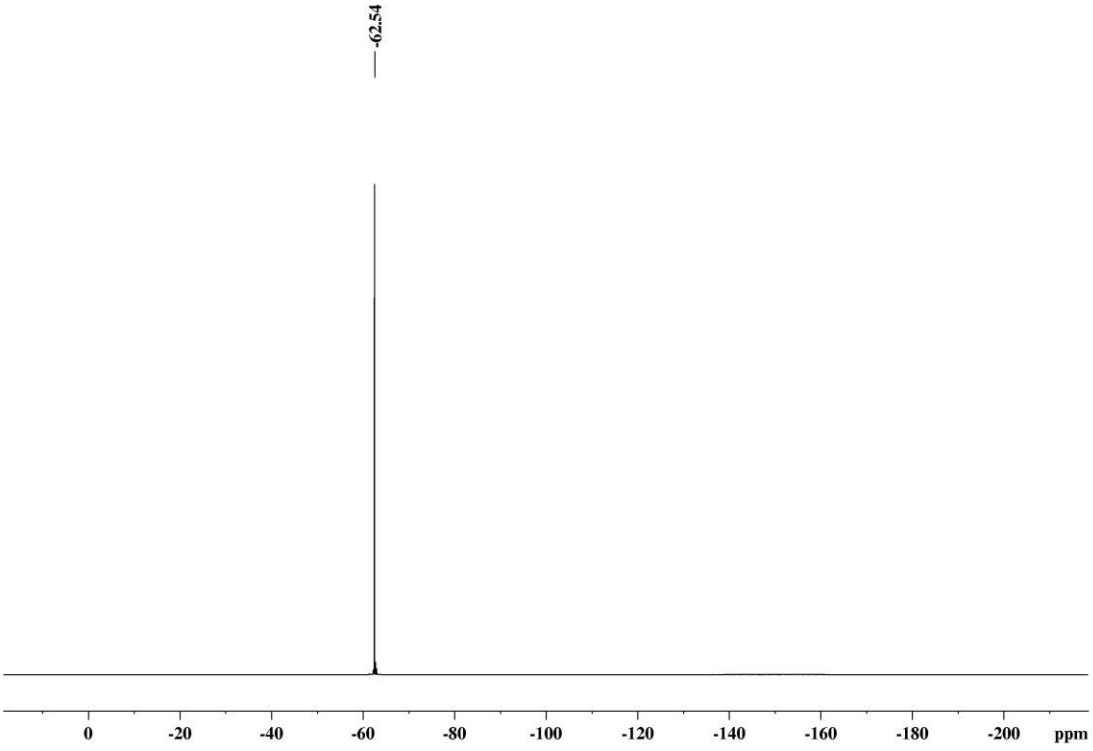


^{1}H NMR spectrum of compound **5d** (400 MHz, $CDCl_3$)

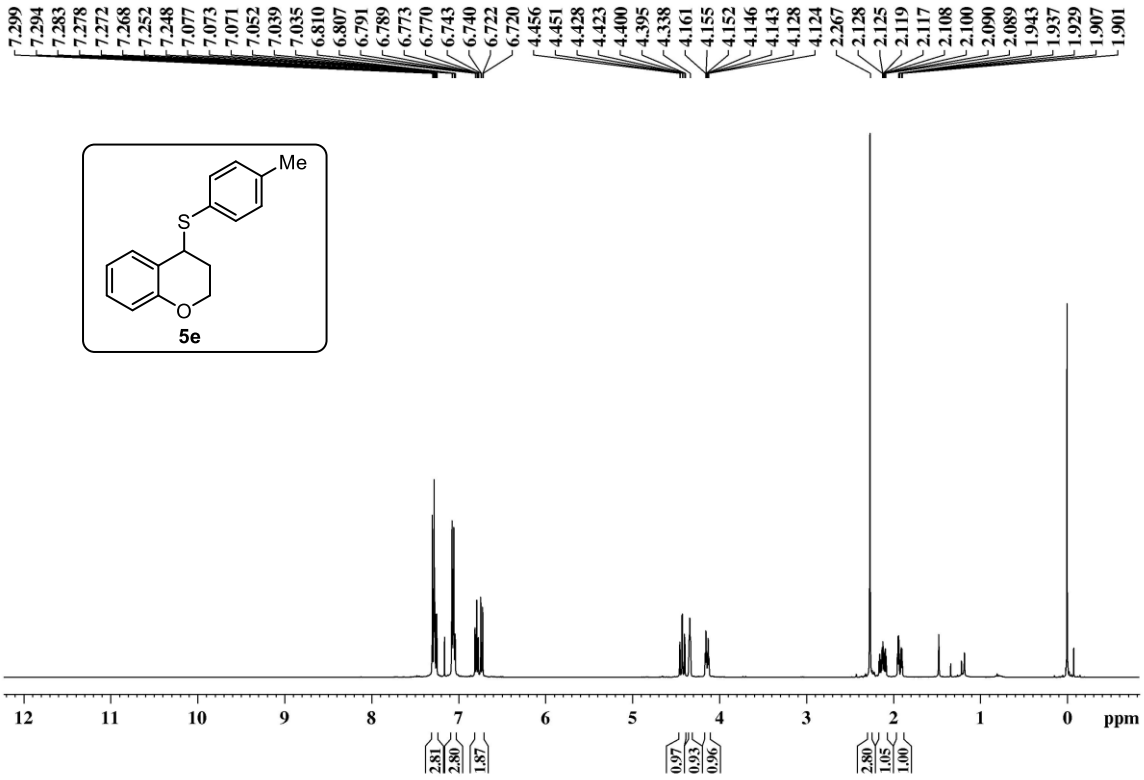


^{13}C NMR spectrum of compound **5d** (100 MHz, $CDCl_3$)

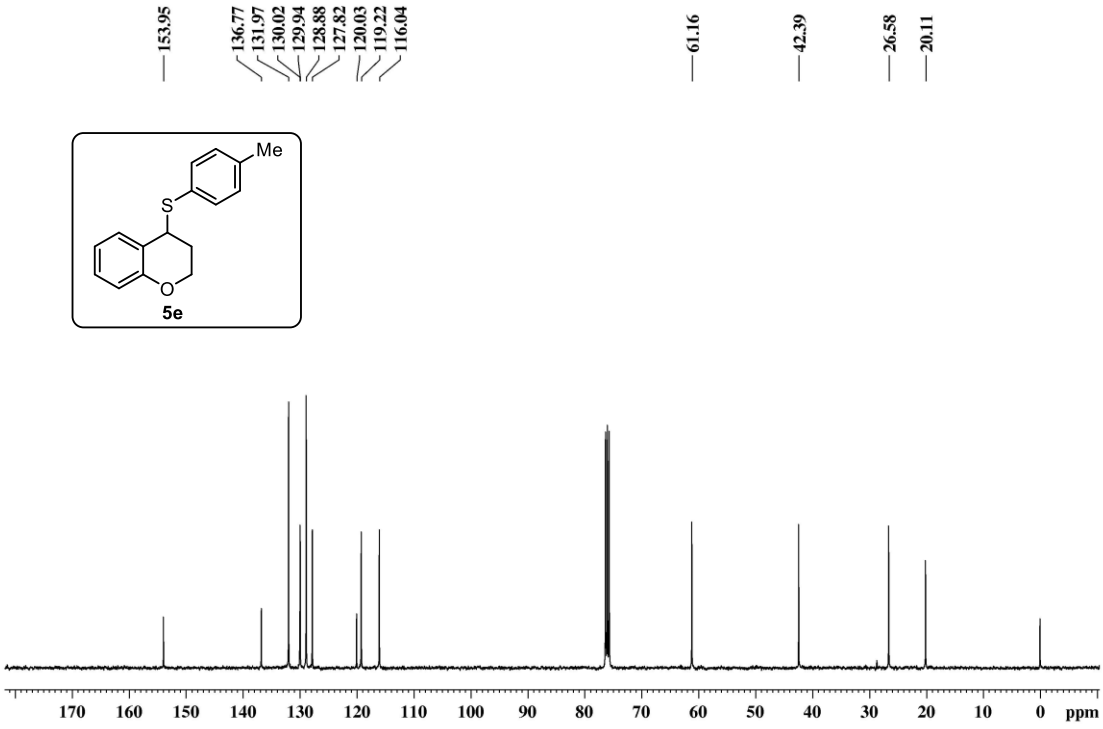




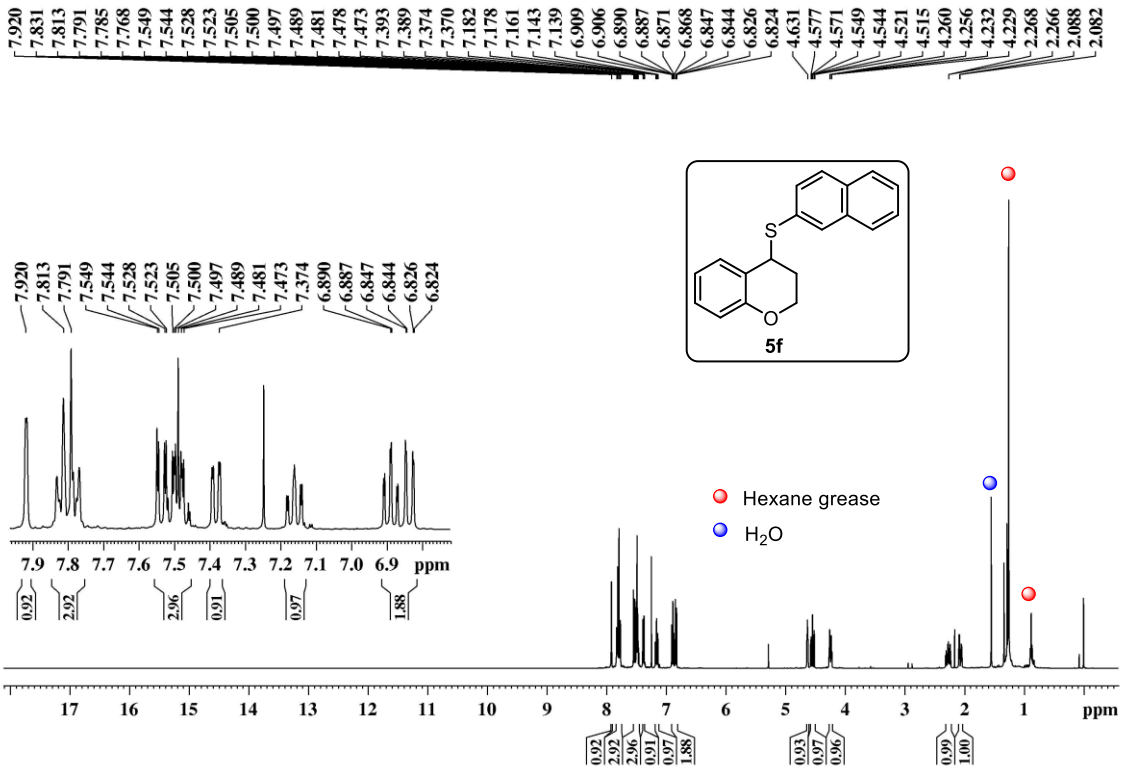
^{19}F NMR spectrum of compound **5d** (376 MHz, $CDCl_3$)



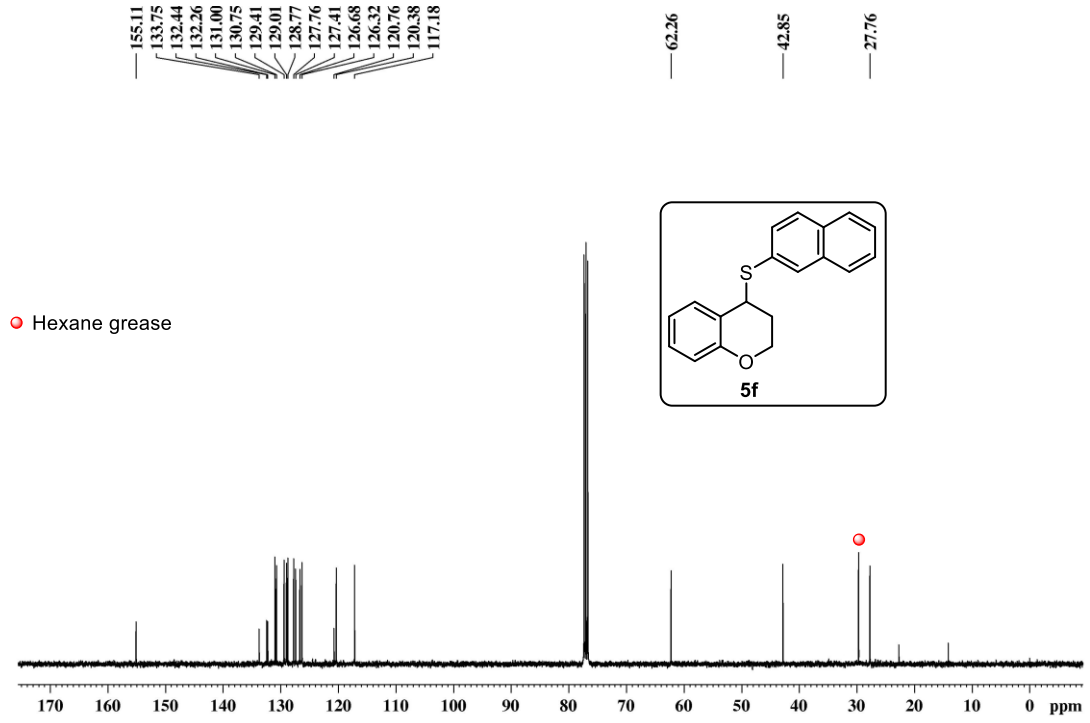
^{1}H NMR spectrum of compound **5e** (400 MHz, $CDCl_3$)



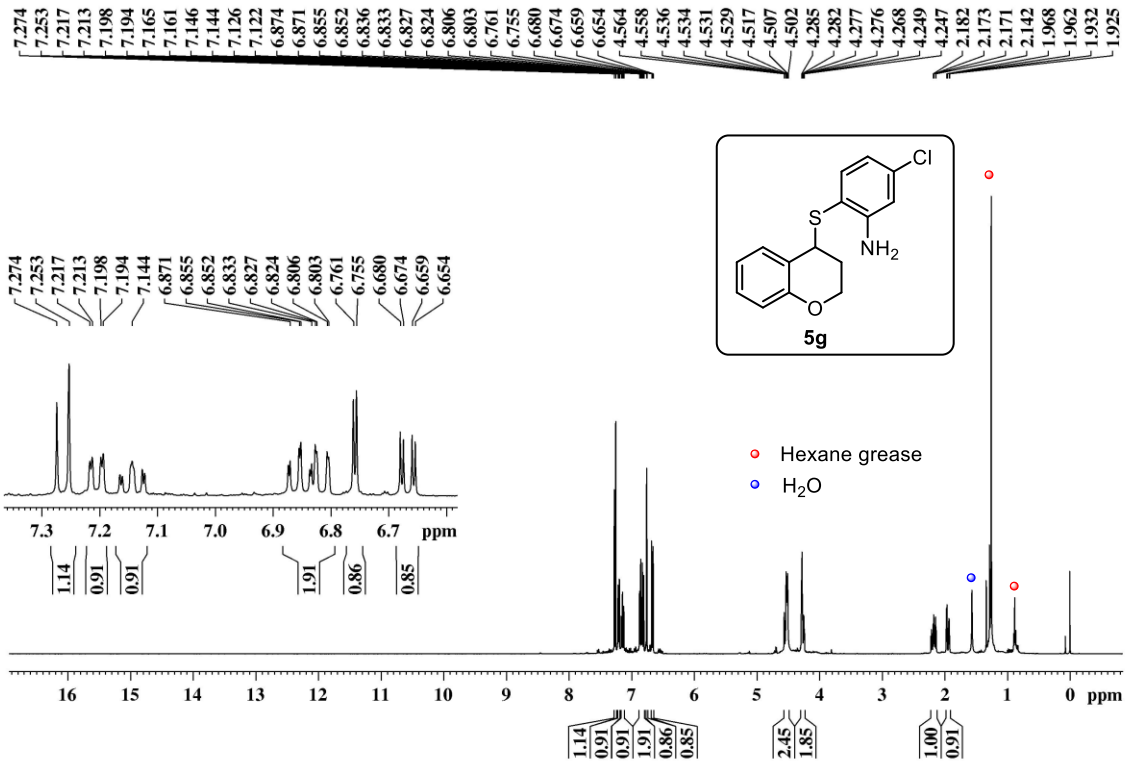
^{13}C NMR spectrum of compound **5e** (100 MHz, $CDCl_3$)



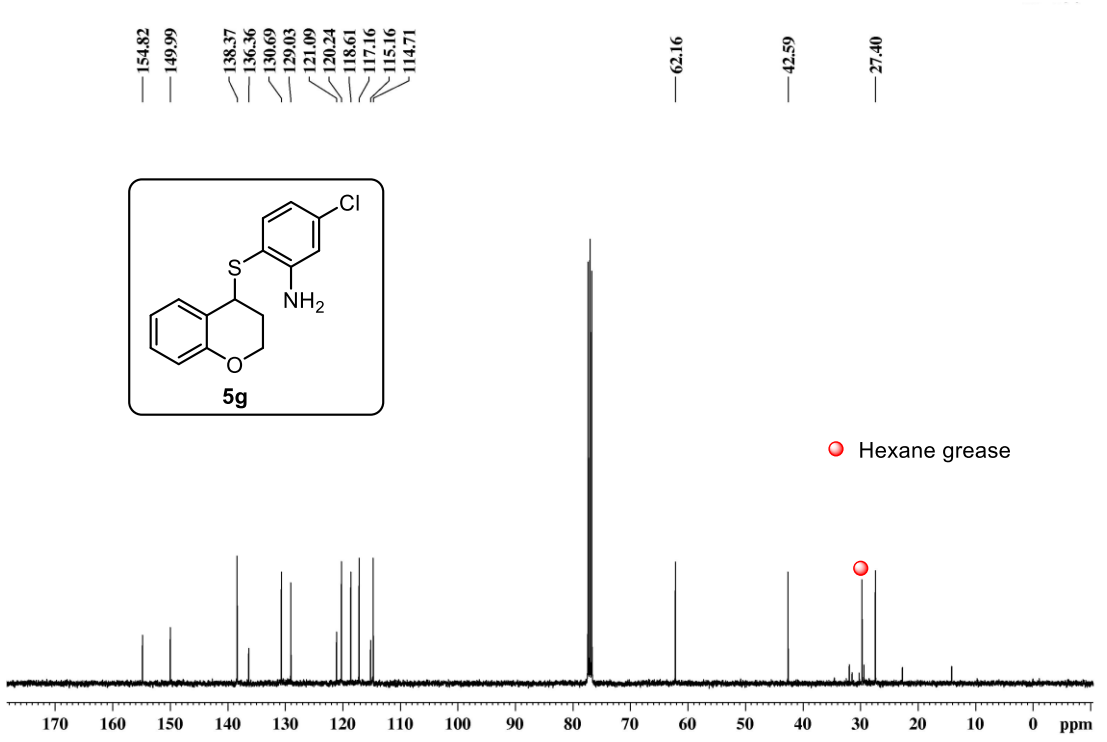
^{1}H NMR spectrum of compound **5f** (400 MHz, $CDCl_3$)



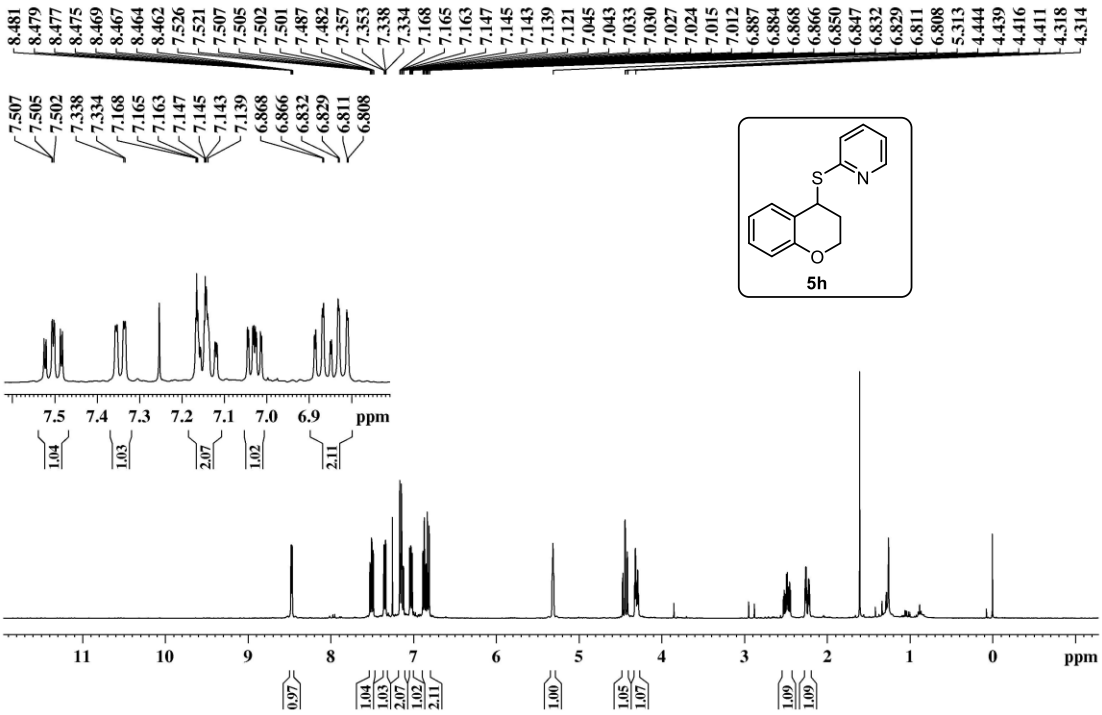
^{13}C NMR spectrum of compound **5f** (100 MHz, $CDCl_3$)



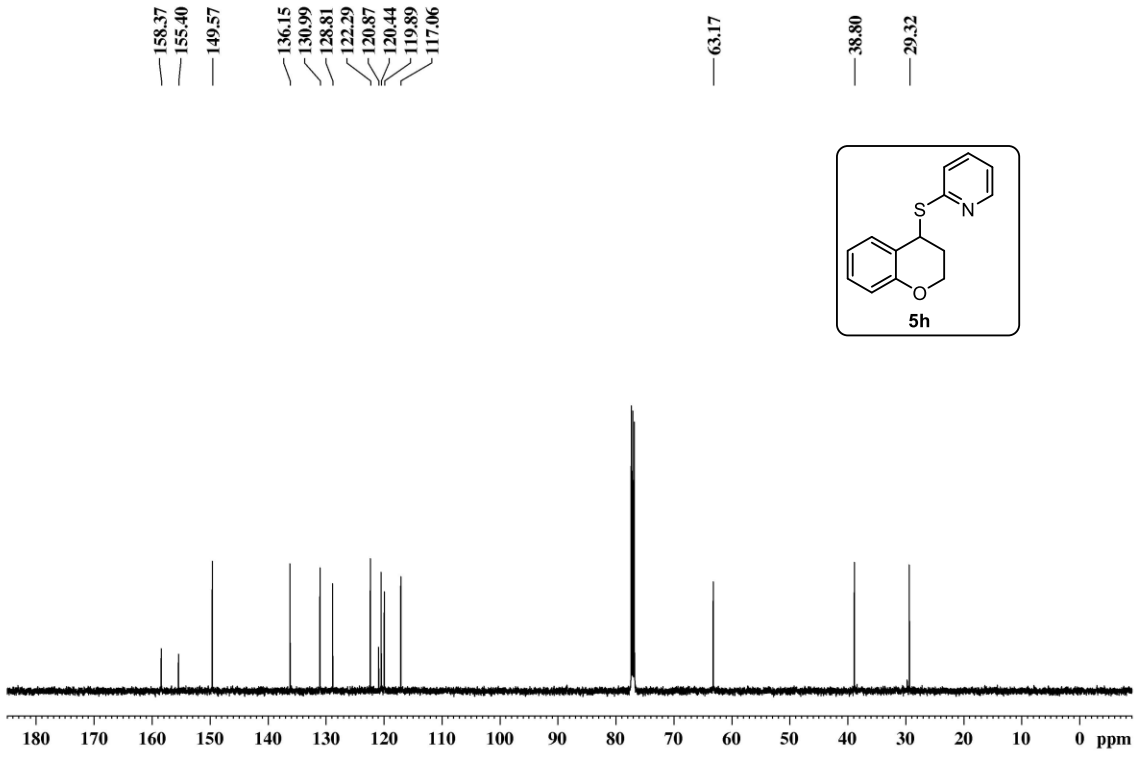
^{1}H NMR spectrum of compound **5g** (400 MHz, $CDCl_3$)



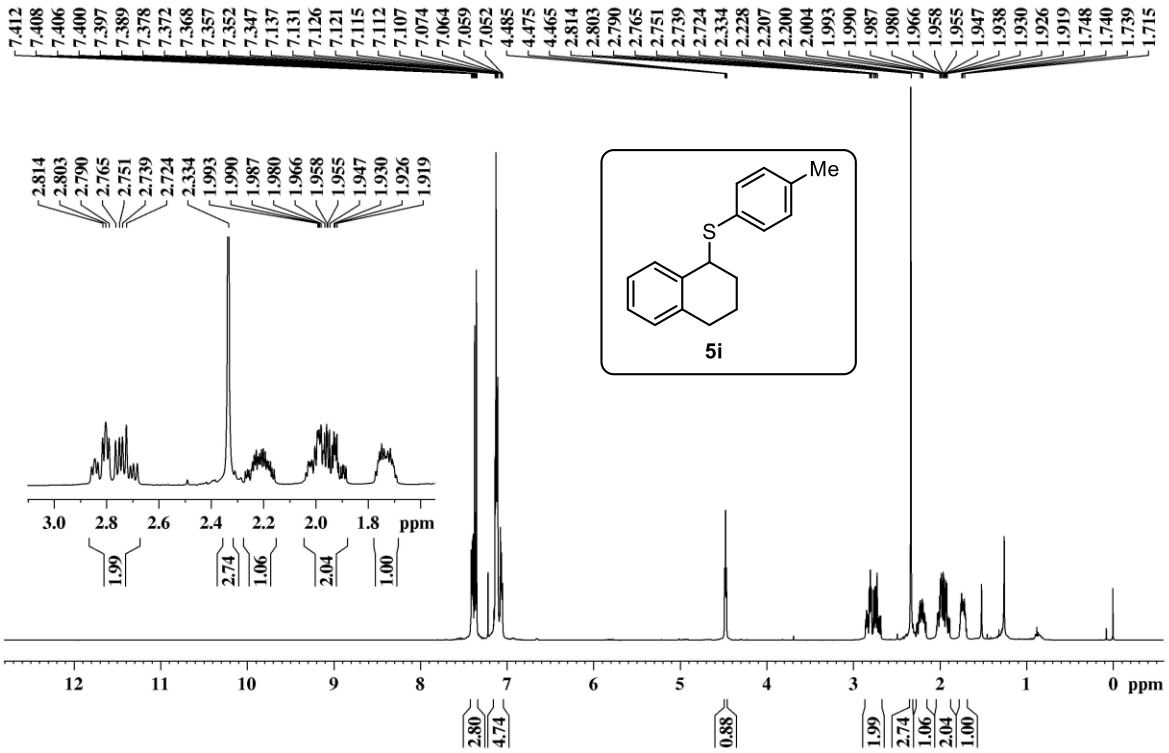
^{13}C NMR spectrum of compound **5g** (100 MHz, $CDCl_3$)



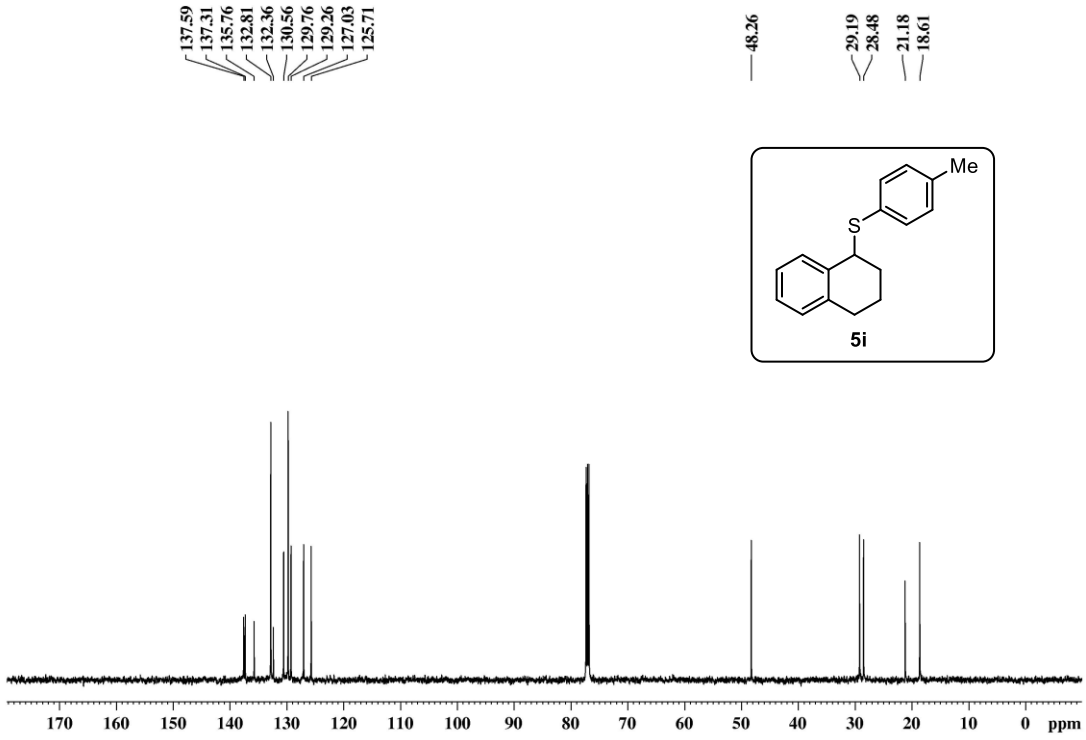
^{1}H NMR spectrum of compound **5h** (400 MHz, $CDCl_3$)



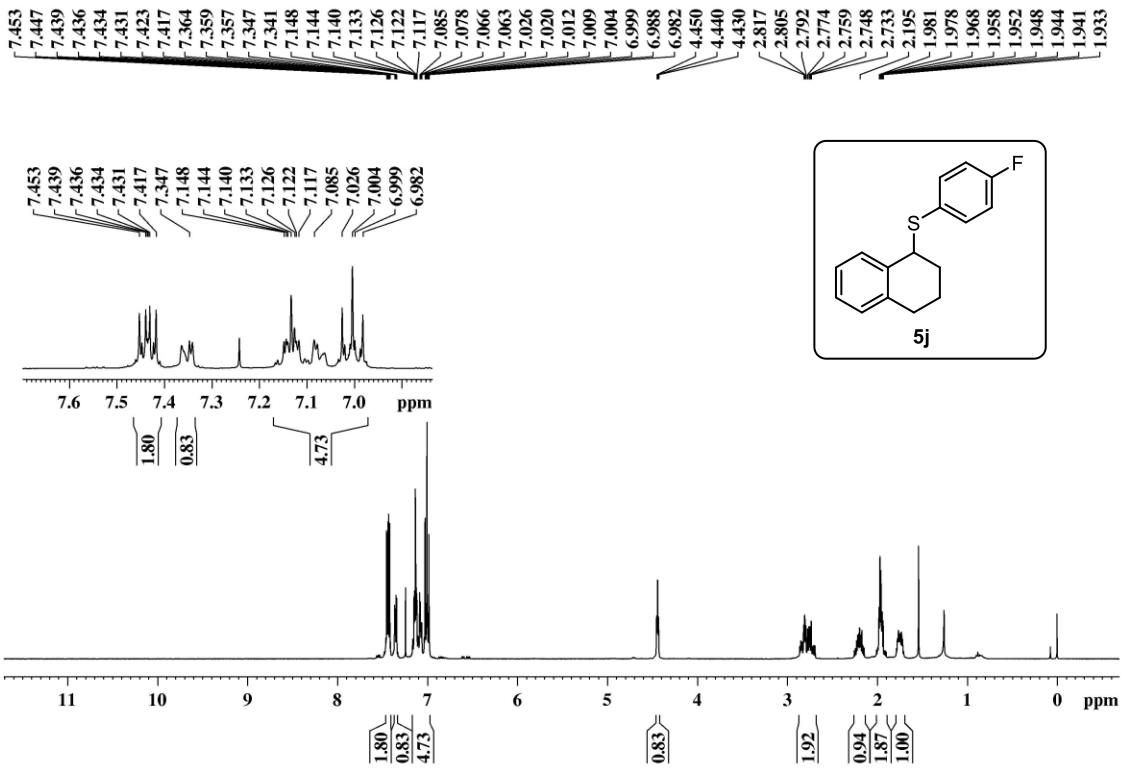
^{13}C NMR spectrum of compound **5h** (100 MHz, $CDCl_3$)



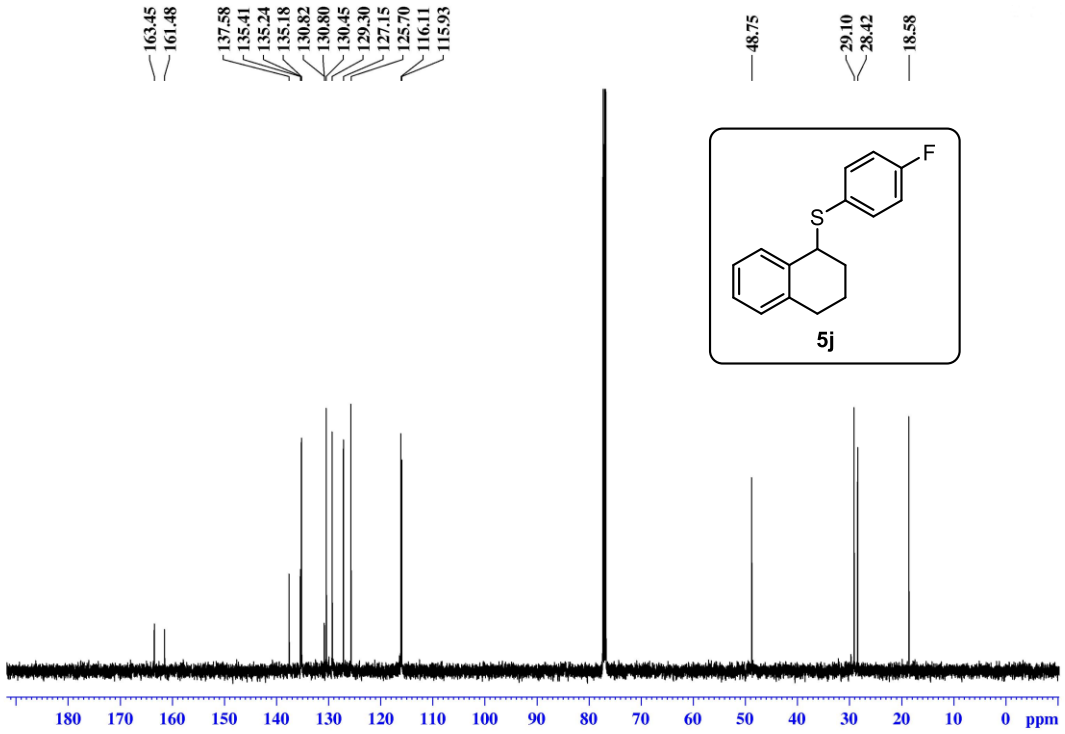
^{1}H NMR spectrum of compound **5i** (400 MHz, $CDCl_3$)



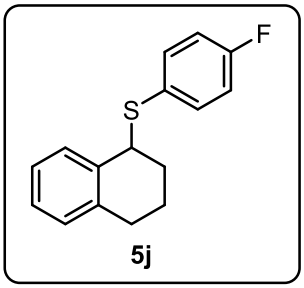
^{13}C NMR spectrum of compound **5i** (100 MHz, $CDCl_3$)

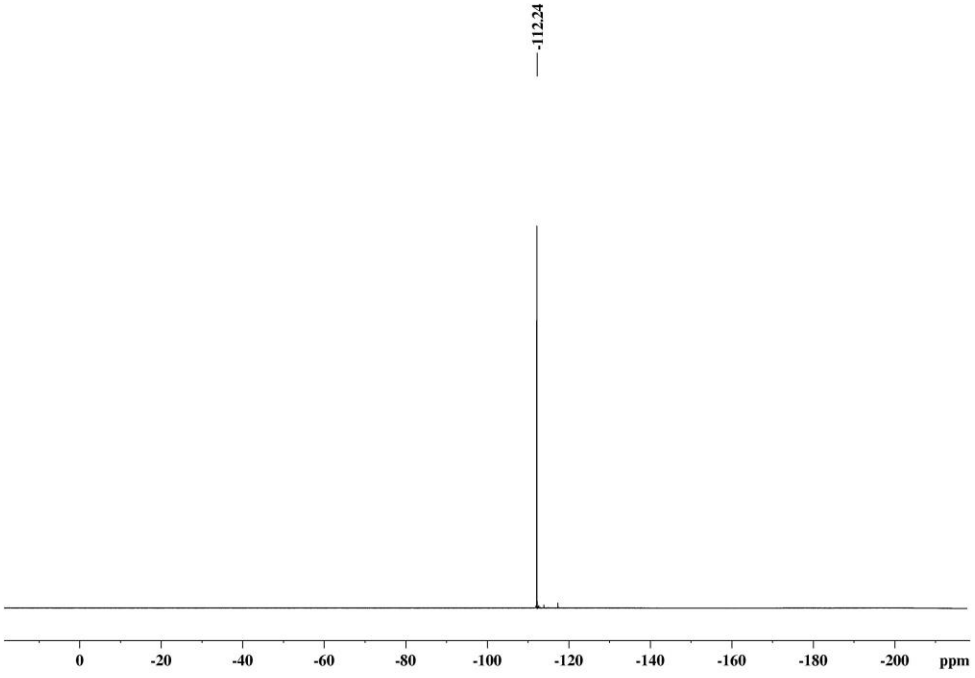


^{1}H NMR spectrum of compound **5j** (400 MHz, $CDCl_3$)

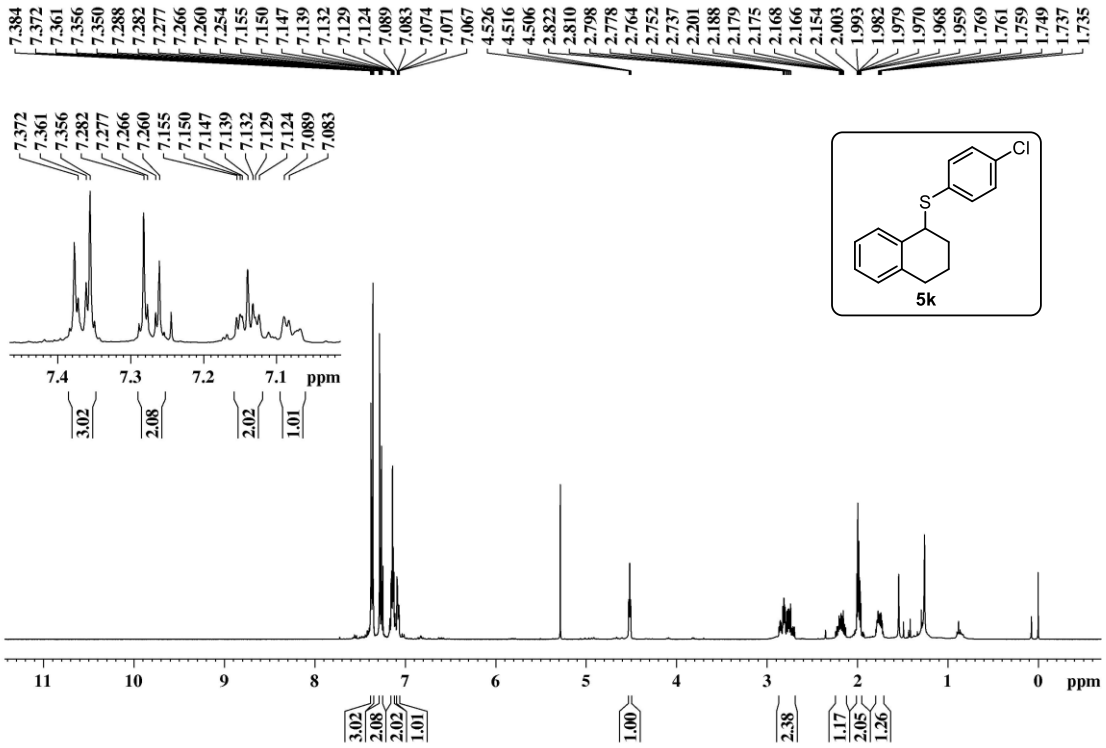


^{13}C NMR spectrum of compound **5j** (100 MHz, $CDCl_3$)

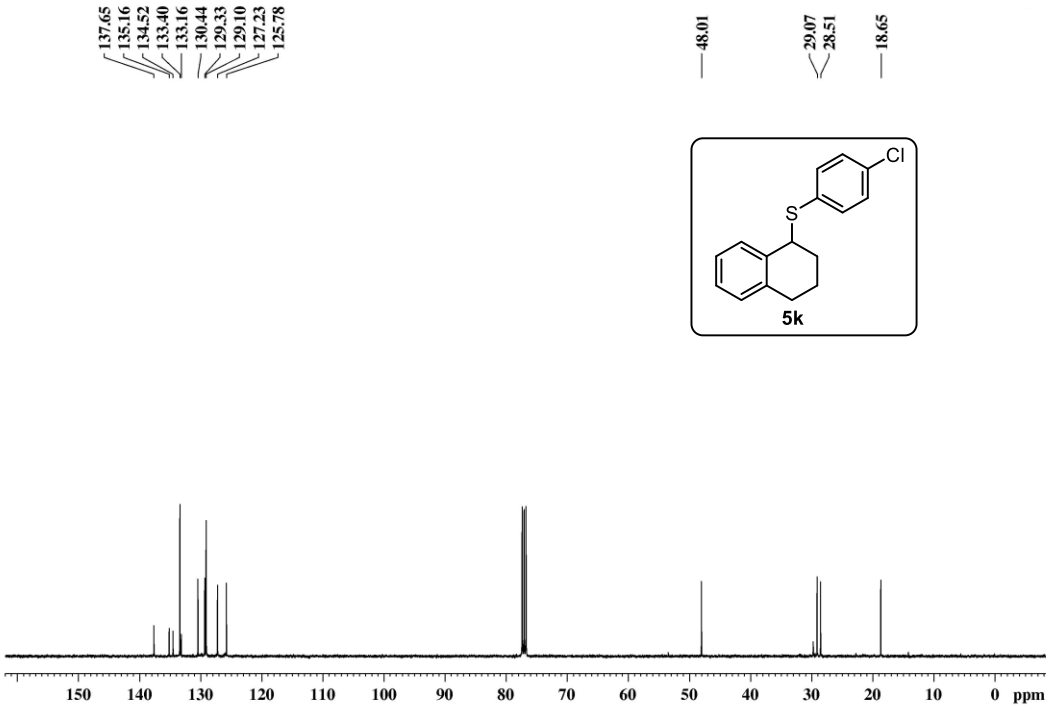




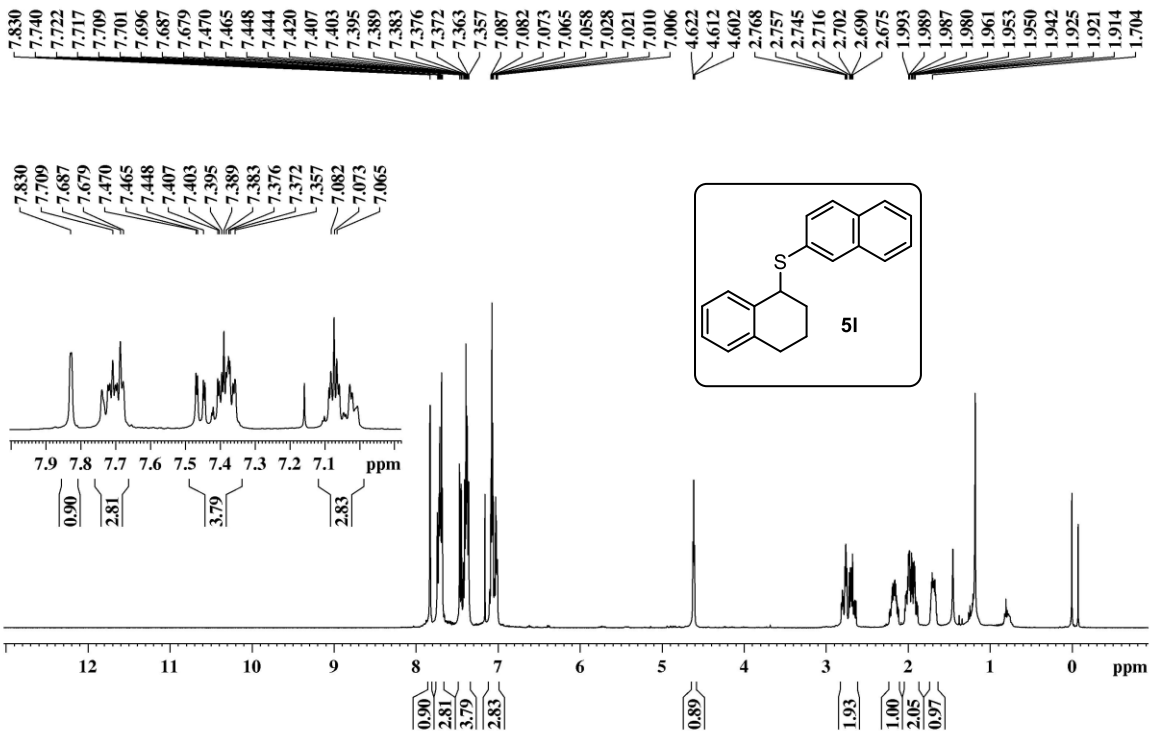
^{19}F NMR spectrum of compound **5j** (376 MHz, $CDCl_3$)



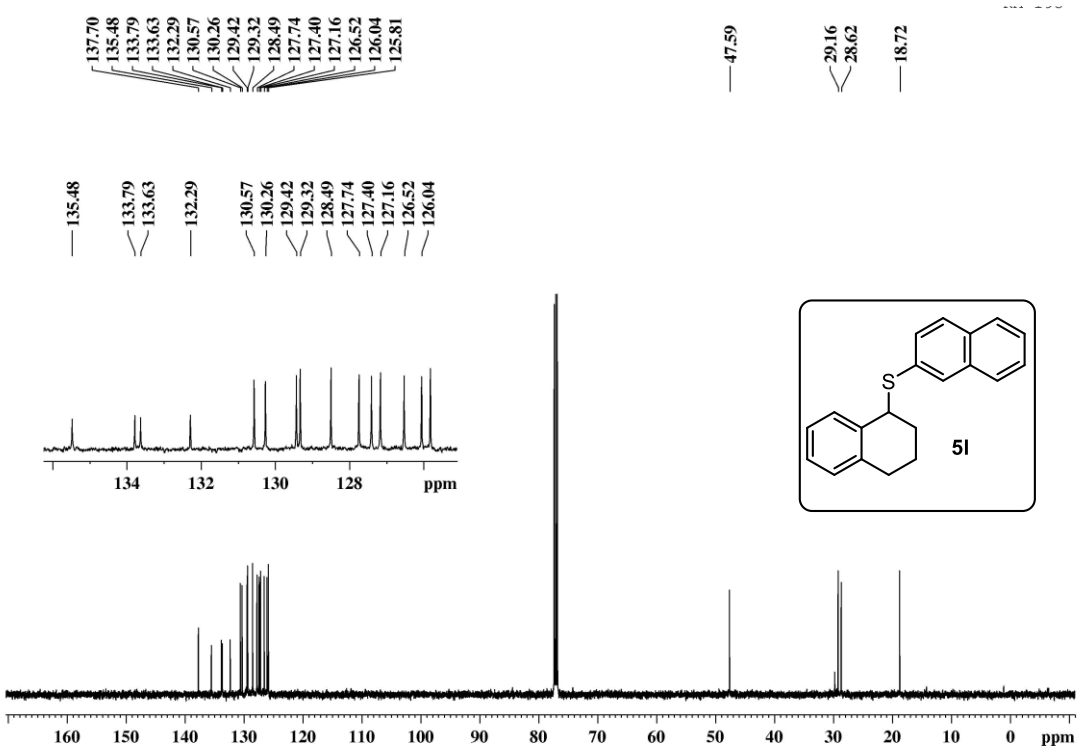
^{1}H NMR spectrum of compound **5k** (400 MHz, $CDCl_3$)



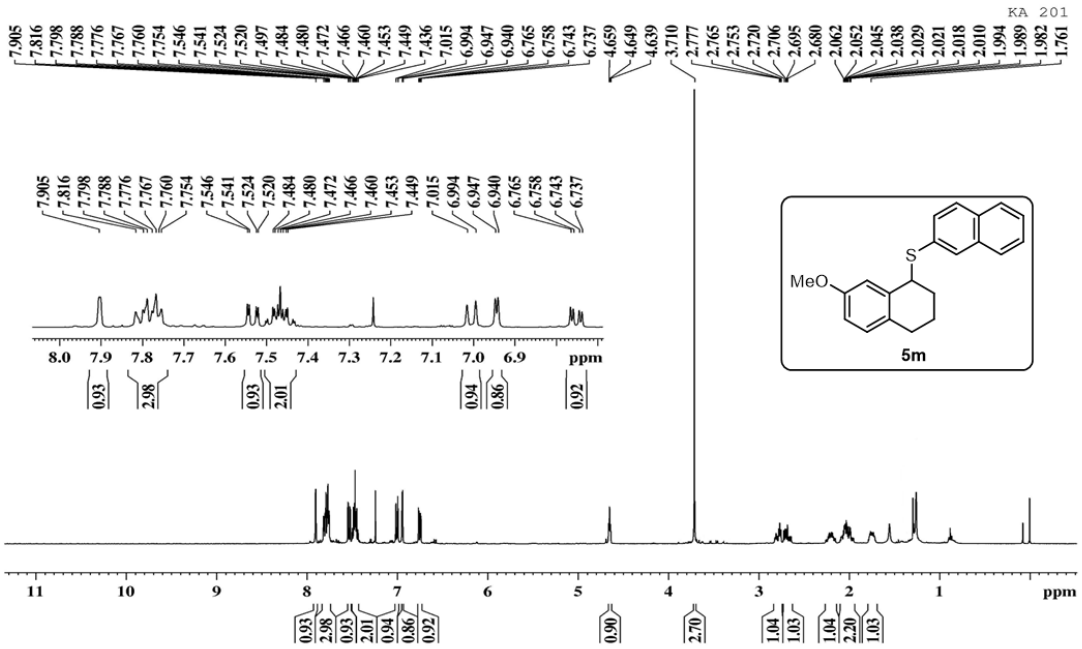
^{13}C NMR spectrum of compound **5k** (100 MHz, $CDCl_3$)



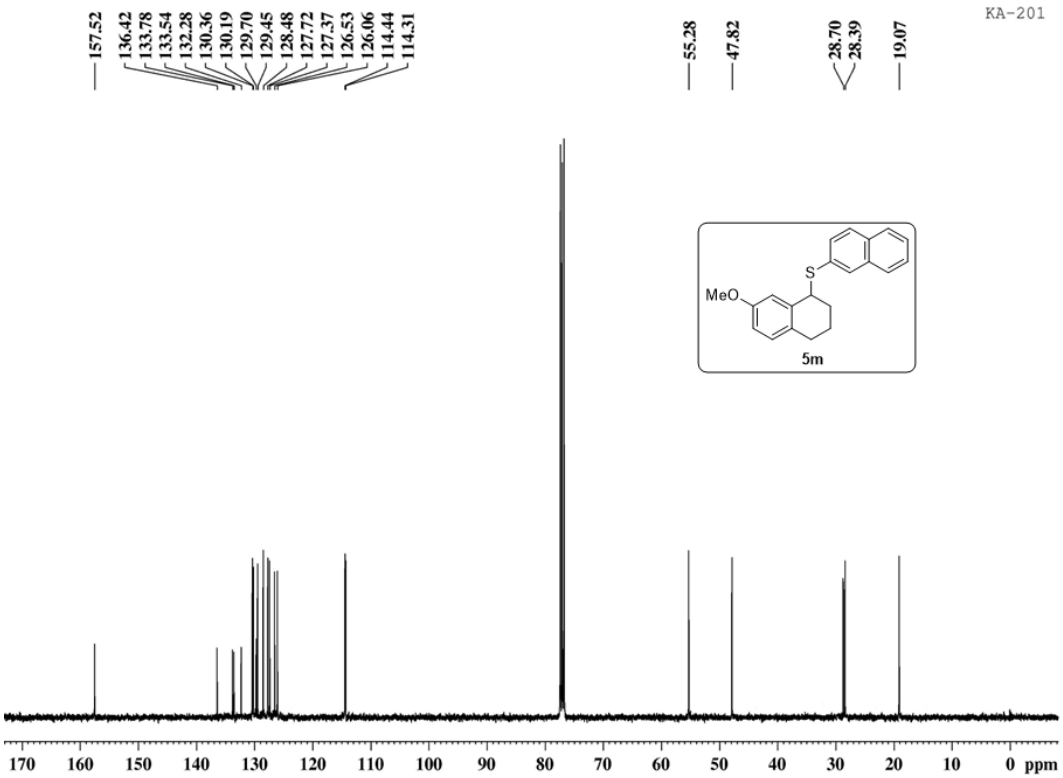
^{1}H NMR spectrum of compound **5l** (400 MHz, $CDCl_3$)



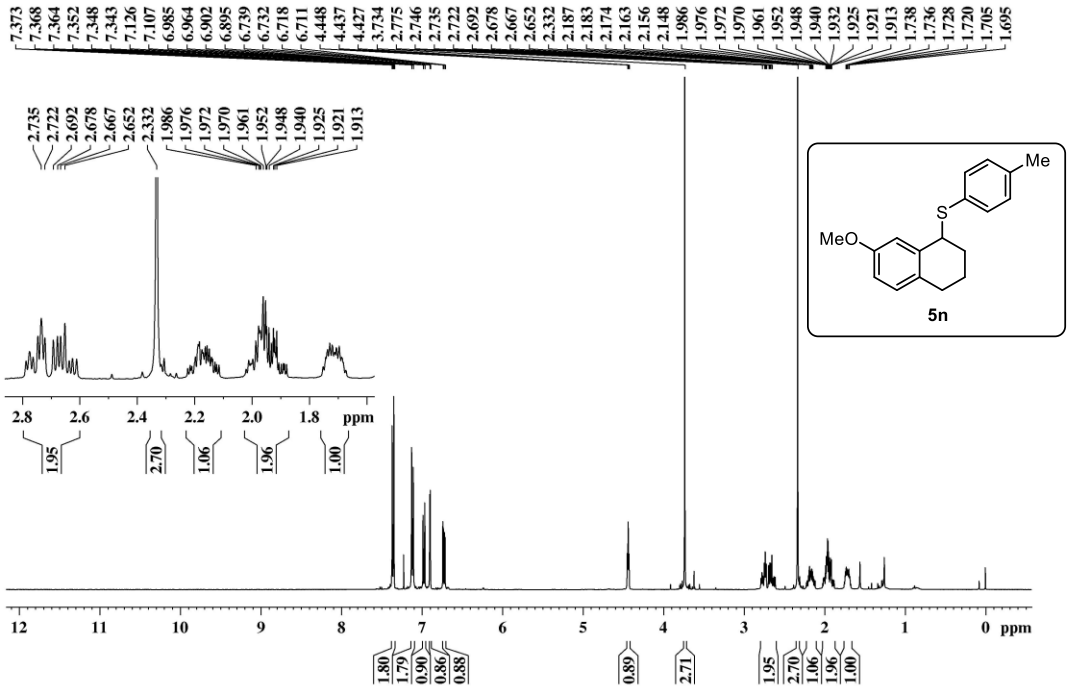
^{13}C NMR spectrum of compound **5l** (100 MHz, $CDCl_3$)



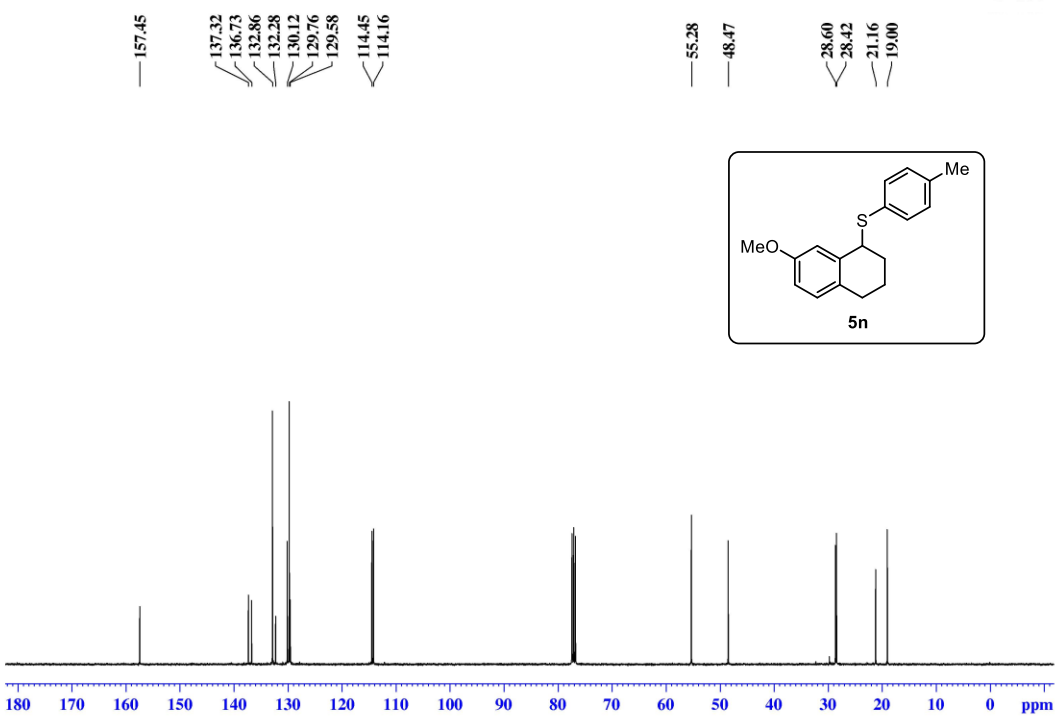
^{1}H NMR spectrum of compound **5m** (400 MHz, $CDCl_3$)



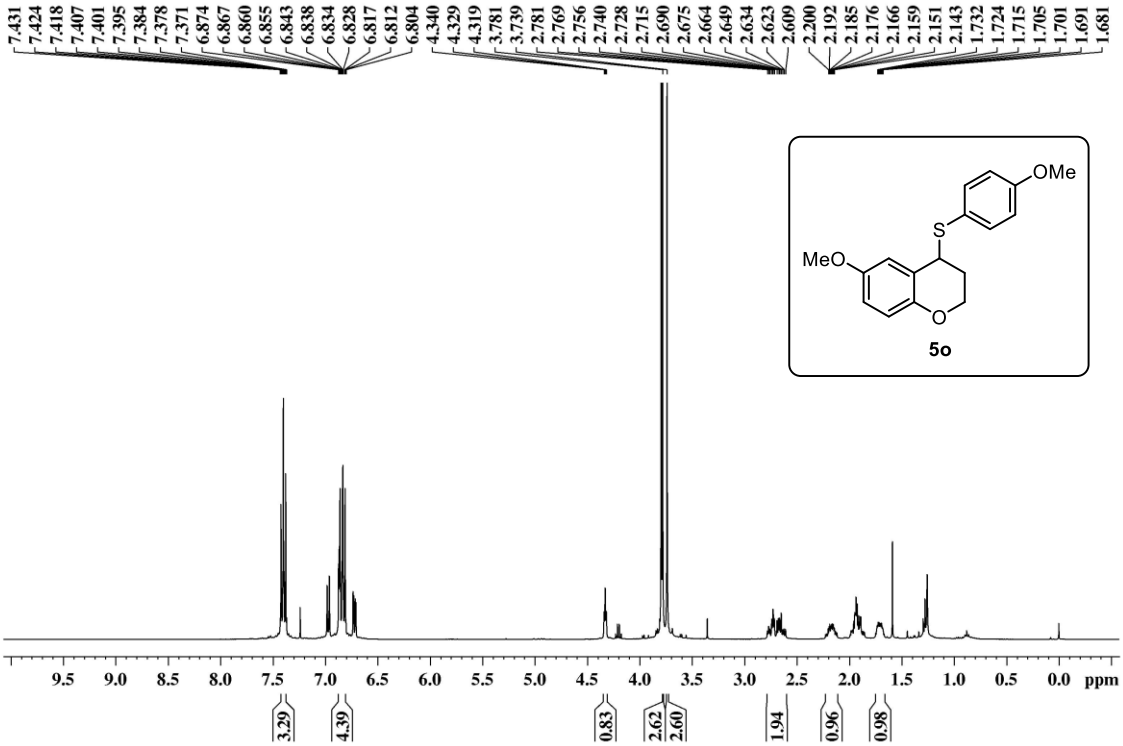
^{13}C NMR spectrum of compound **5m** (100 MHz, $CDCl_3$)



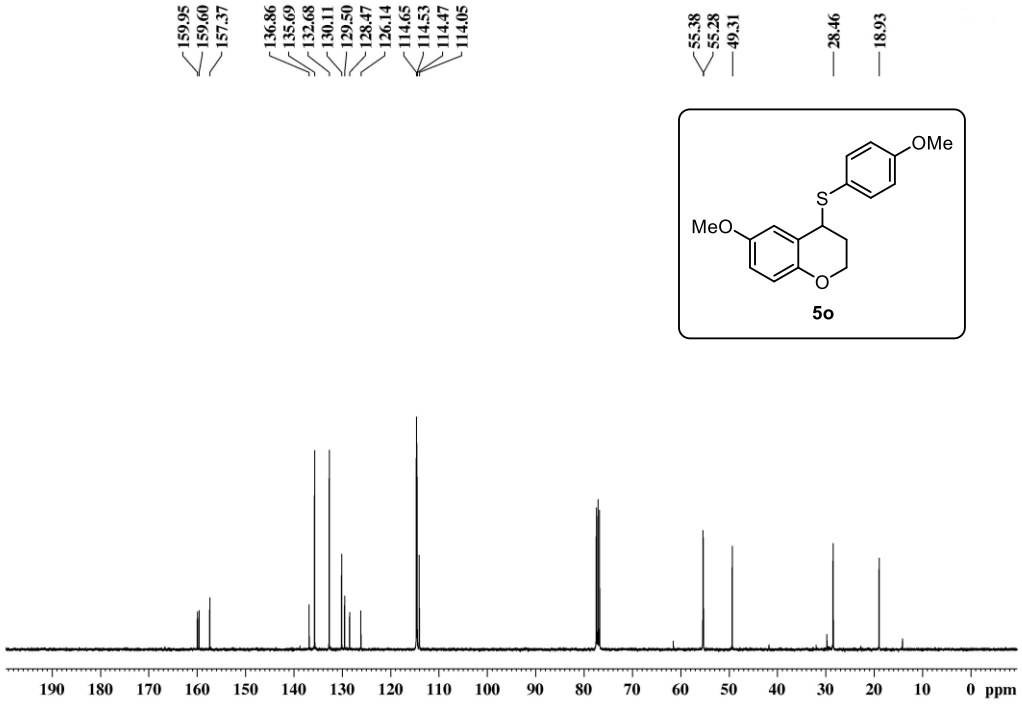
^{1}H NMR spectrum of compound **5n** (400 MHz, $CDCl_3$)



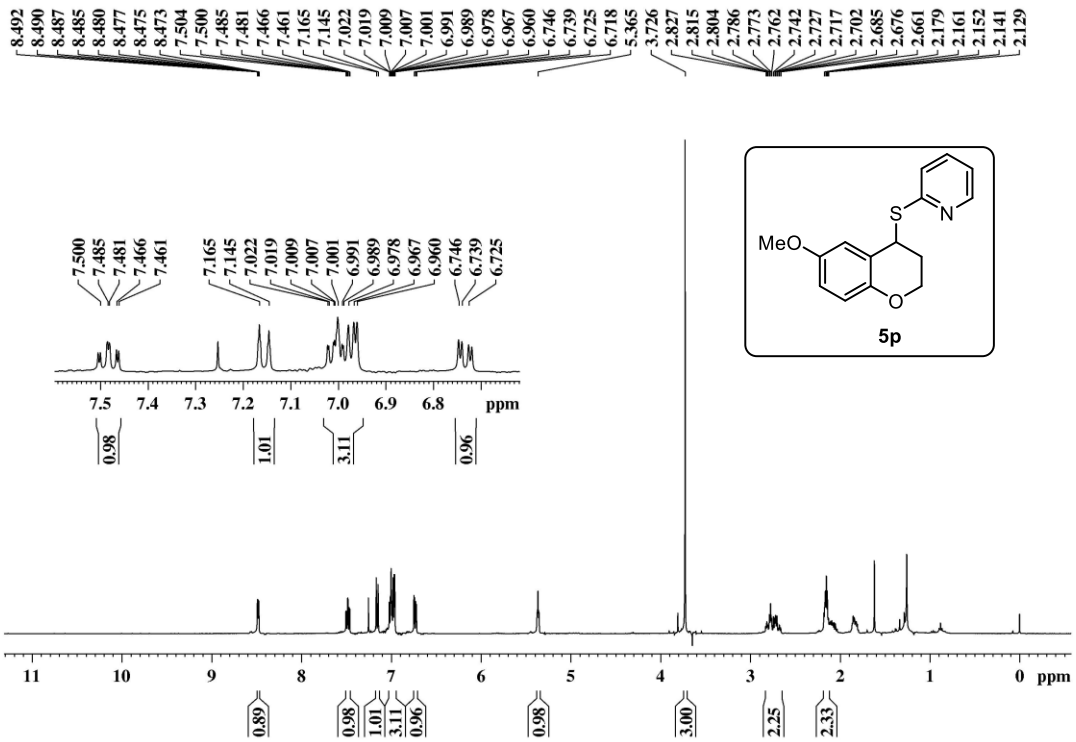
^{13}C NMR spectrum of compound **5n** (100 MHz, $CDCl_3$)



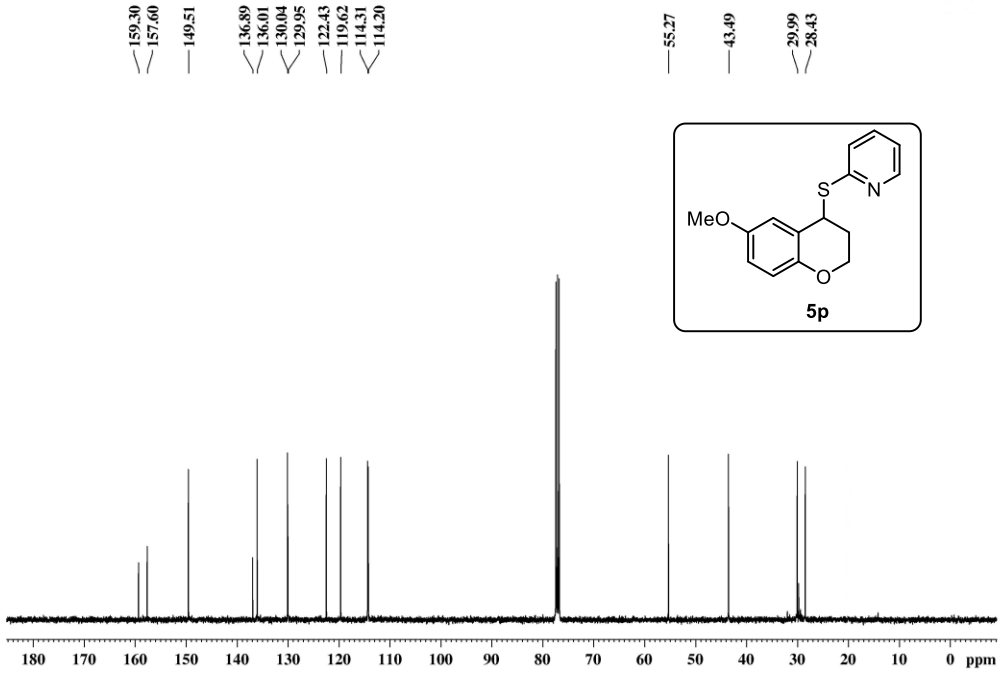
^{1}H NMR spectrum of compound **5o** (400 MHz, $CDCl_3$)



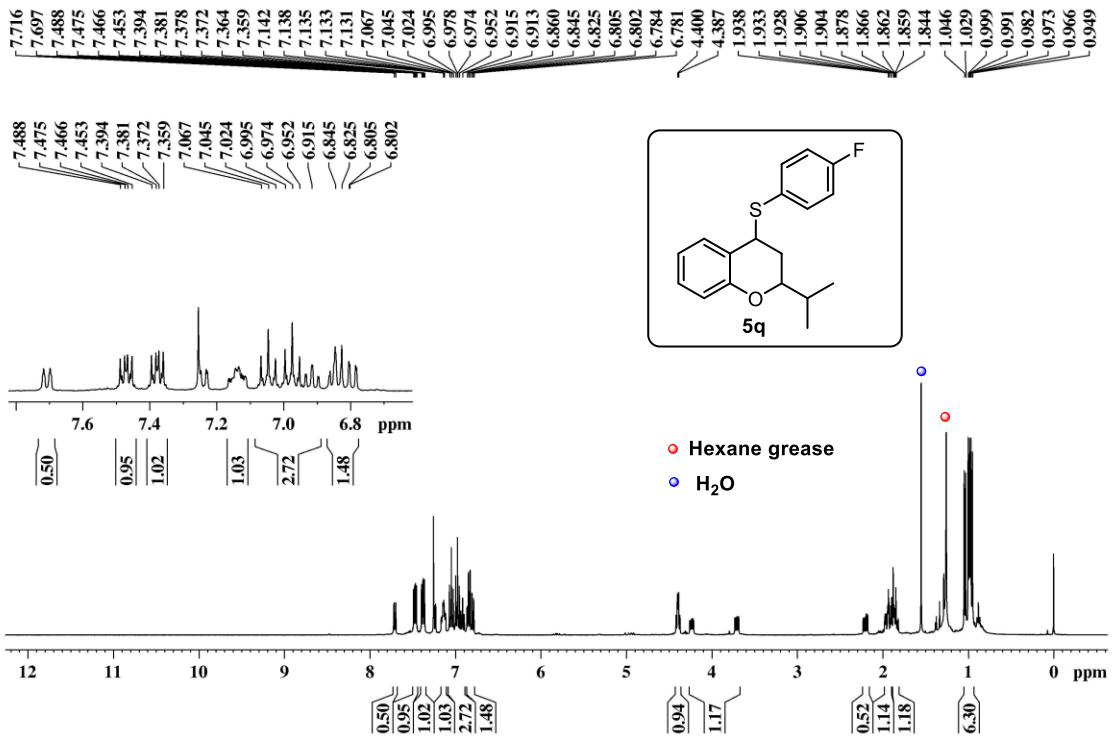
^{13}C NMR spectrum of compound **5o** (100 MHz, $CDCl_3$)



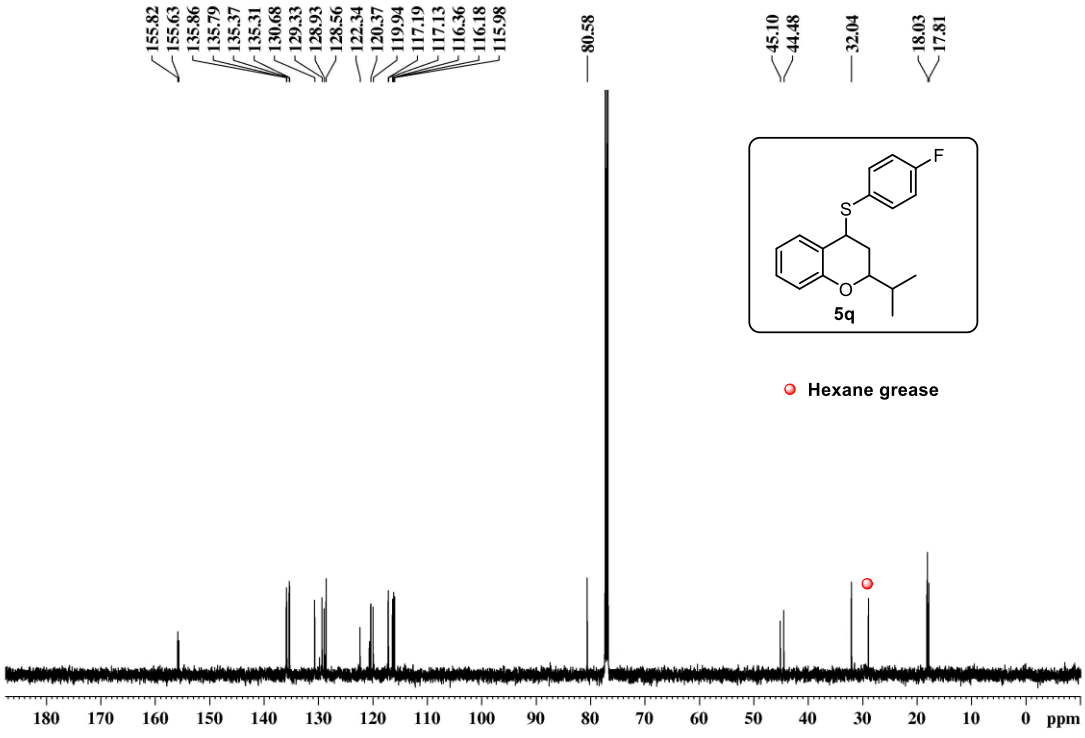
^{1}H NMR spectrum of compound **5p** (400 MHz, $CDCl_3$)



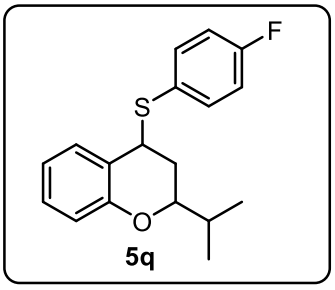
^{13}C NMR spectrum of compound **5p** (100 MHz, $CDCl_3$)

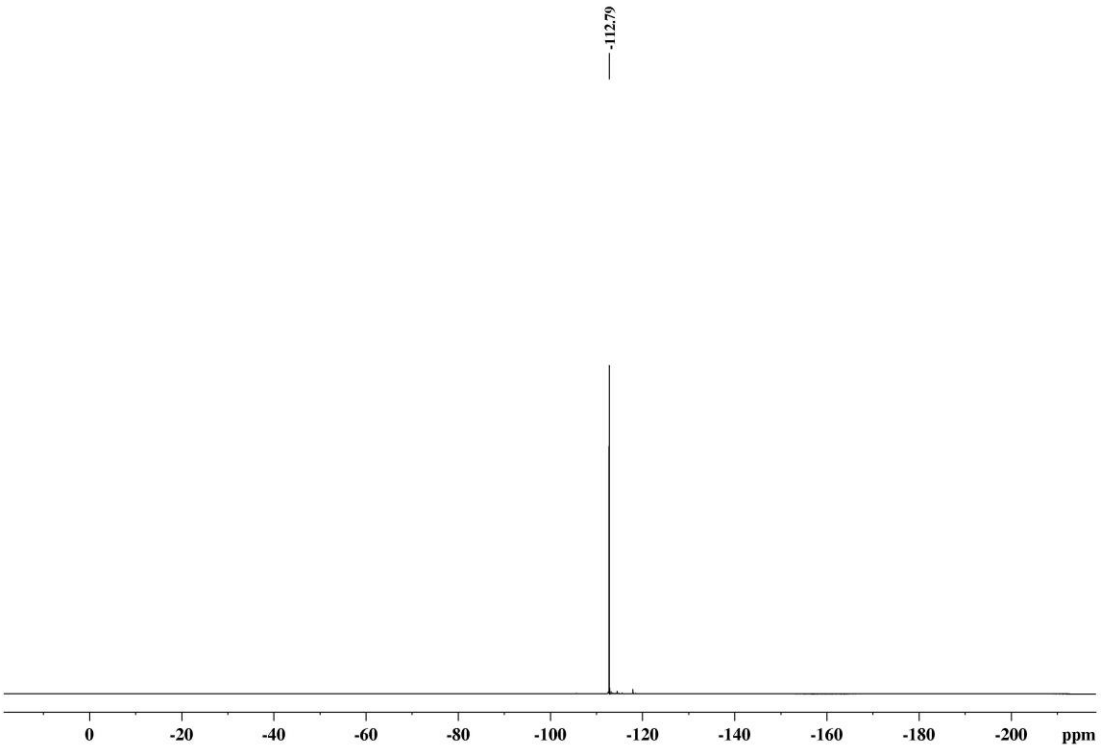


^{1}H NMR spectrum of compound **5q** (400 MHz, $CDCl_3$)

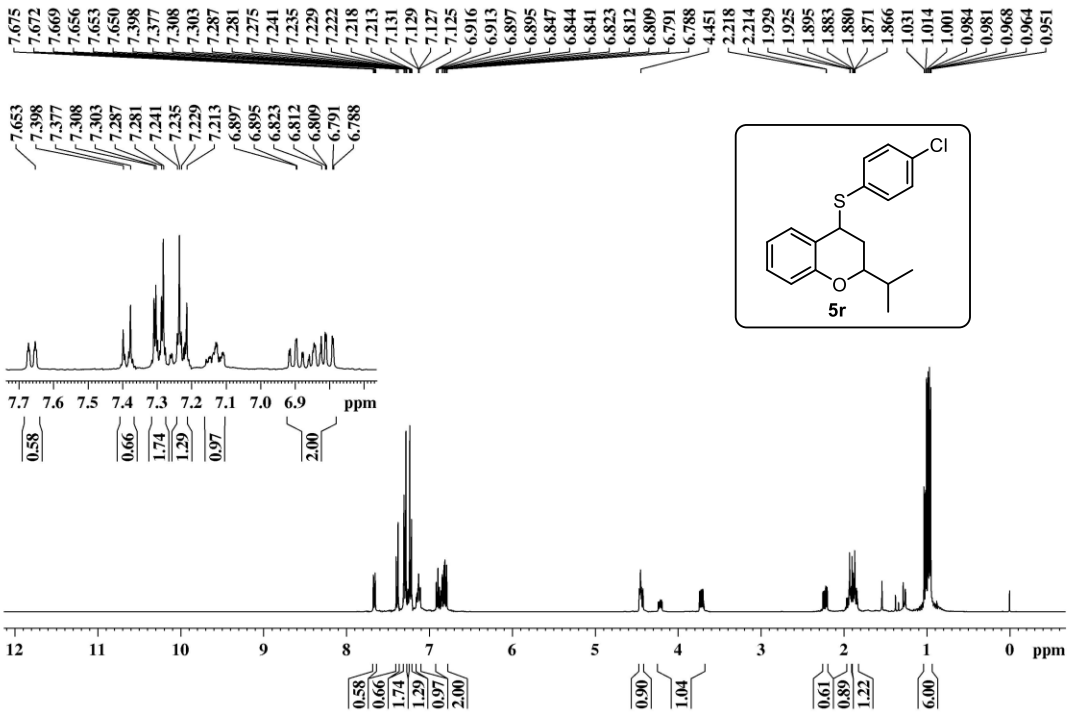


^{13}C NMR spectrum of compound **5q** (100 MHz, $CDCl_3$)

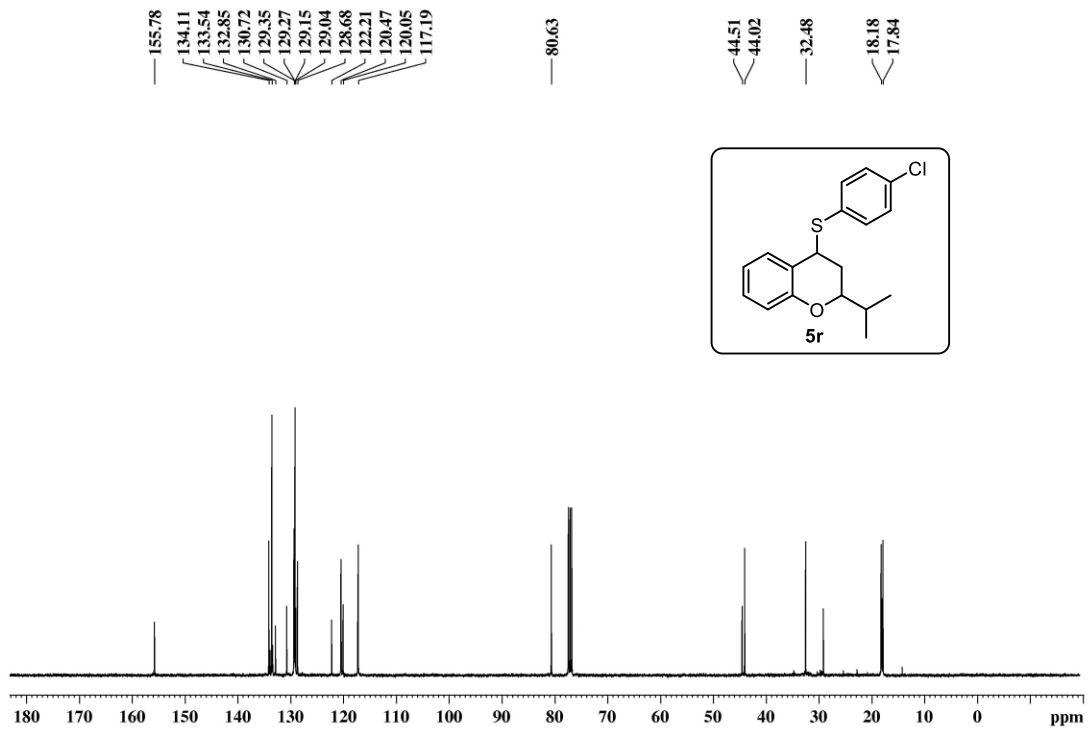




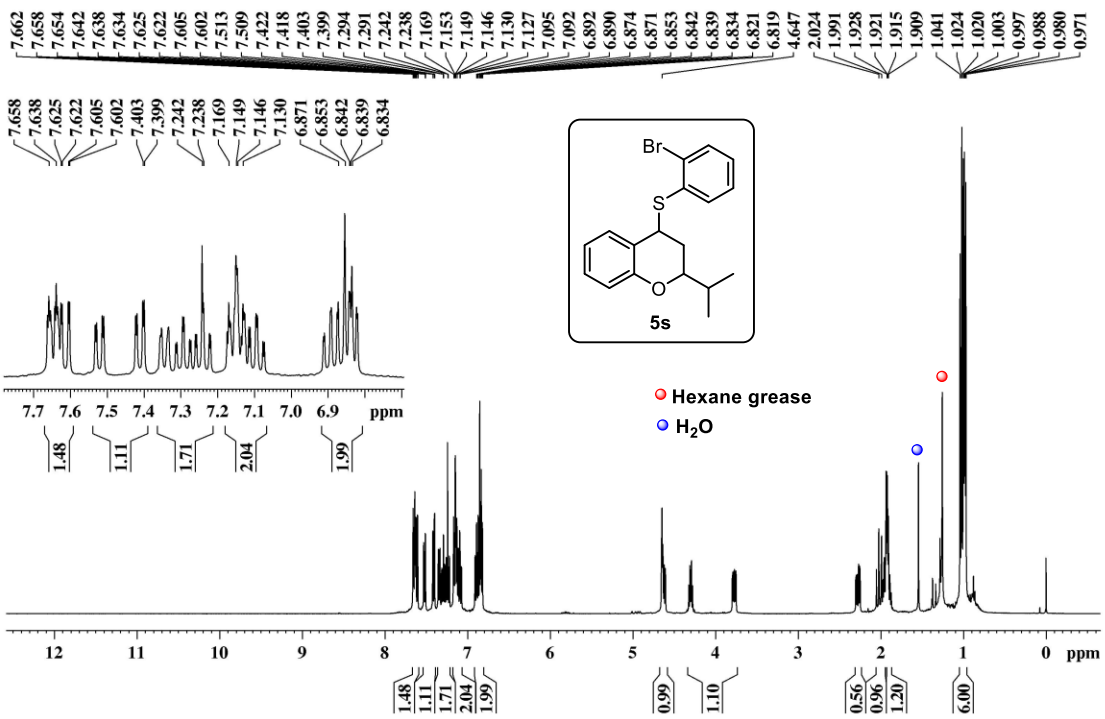
^{19}F NMR spectrum of compound **5q** (376 MHz, $CDCl_3$)



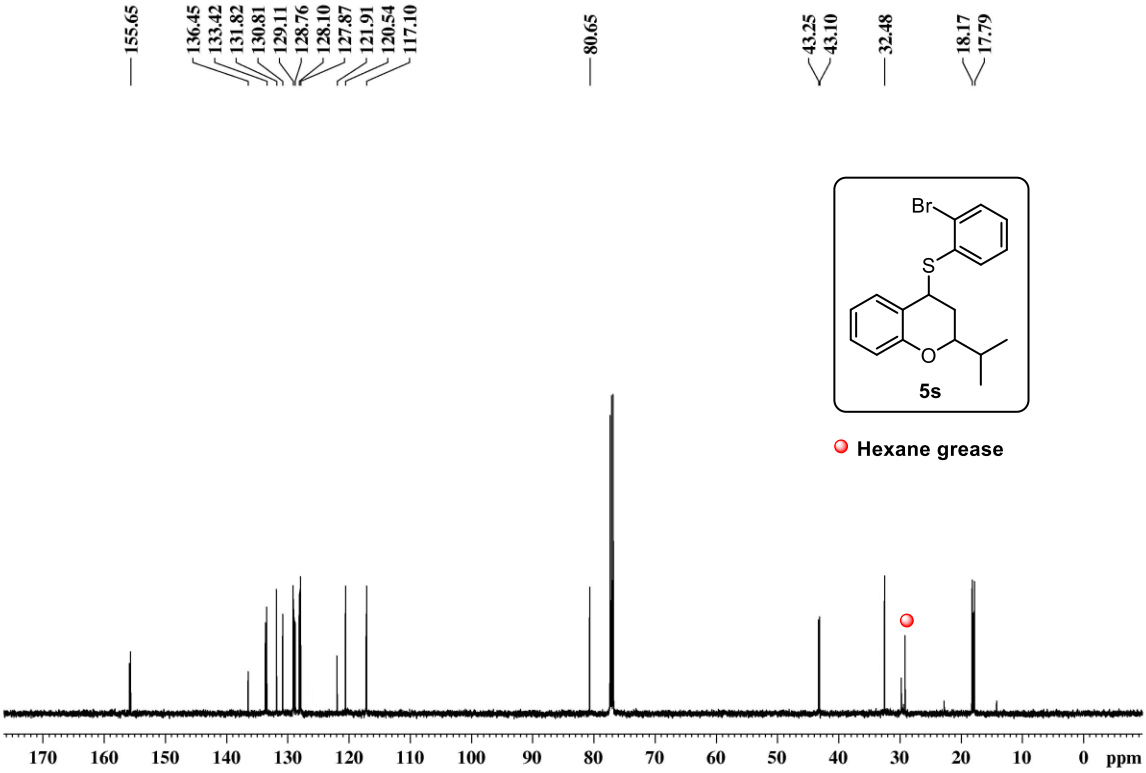
^{1}H NMR spectrum of compound **5r** (400 MHz, $CDCl_3$)



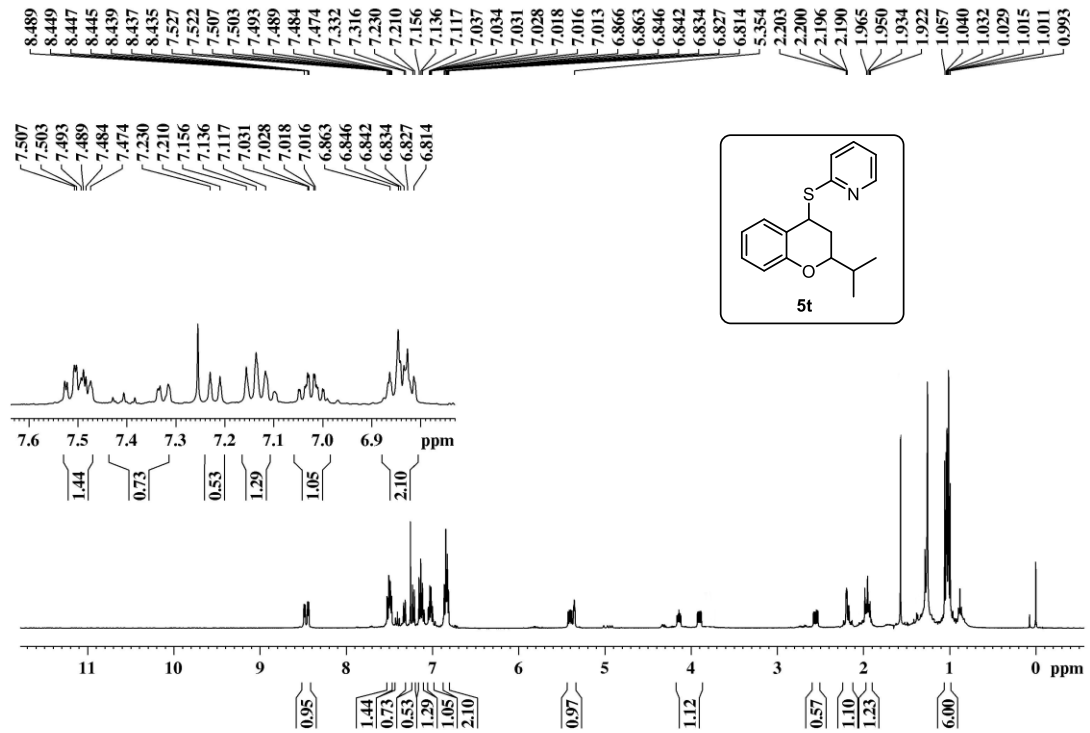
^{13}C NMR spectrum of compound **5r** (100 MHz, $CDCl_3$)



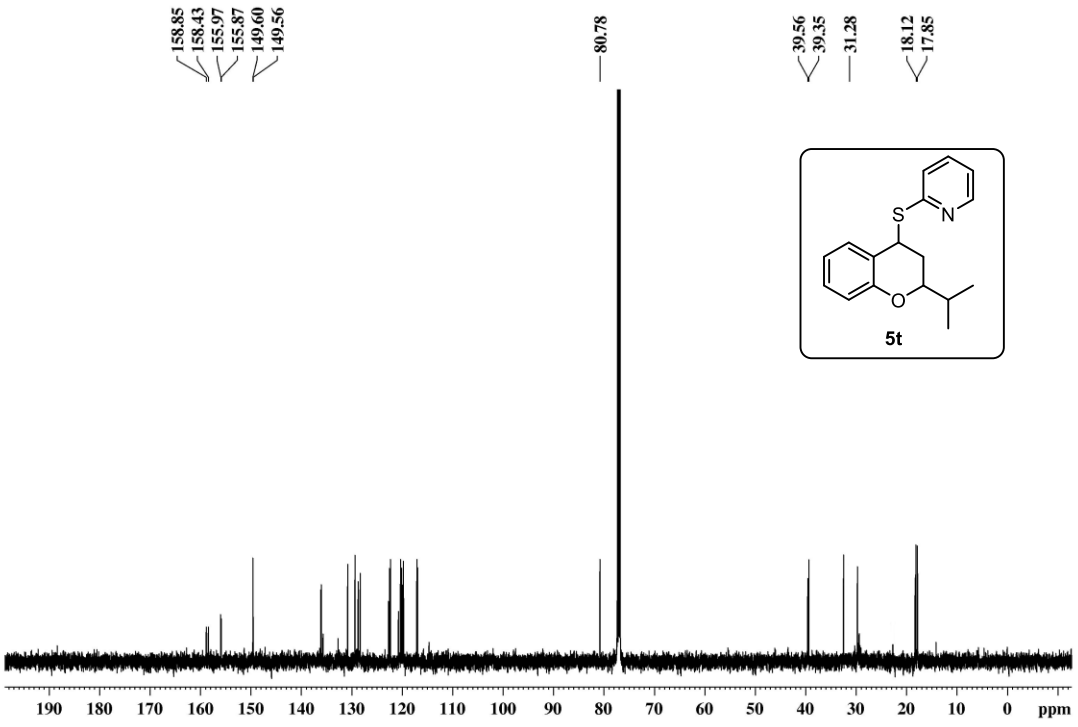
^{1}H NMR spectrum of compound **5s** (400 MHz, $CDCl_3$)



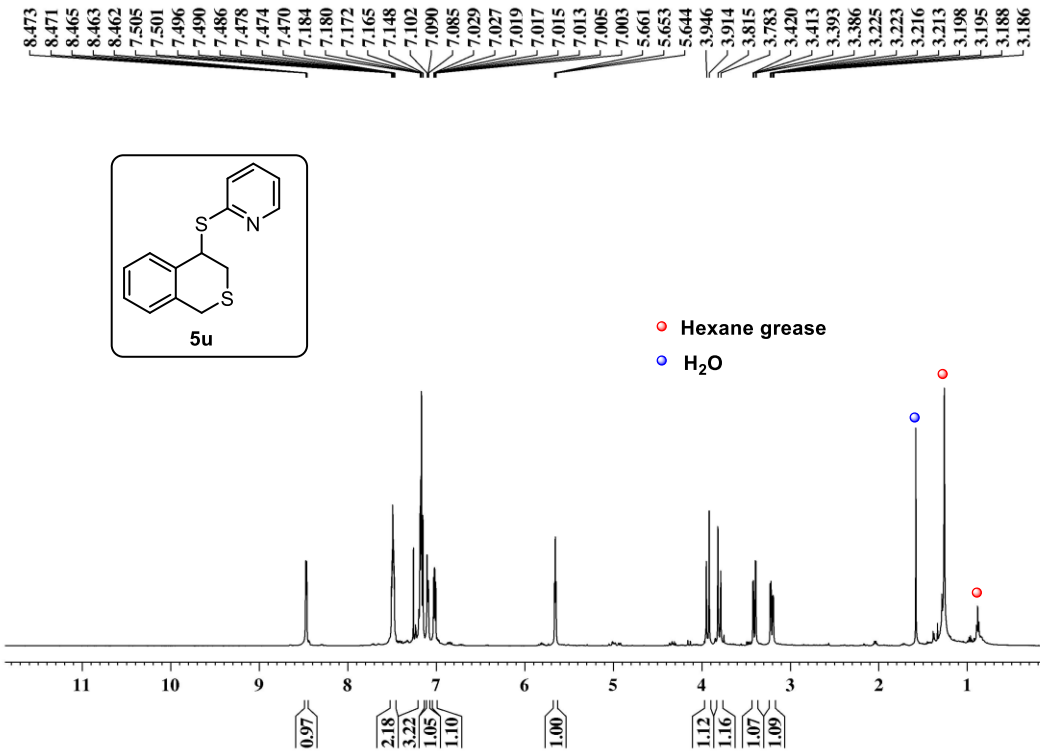
^{13}C NMR spectrum of compound **5s** (100 MHz, $CDCl_3$)



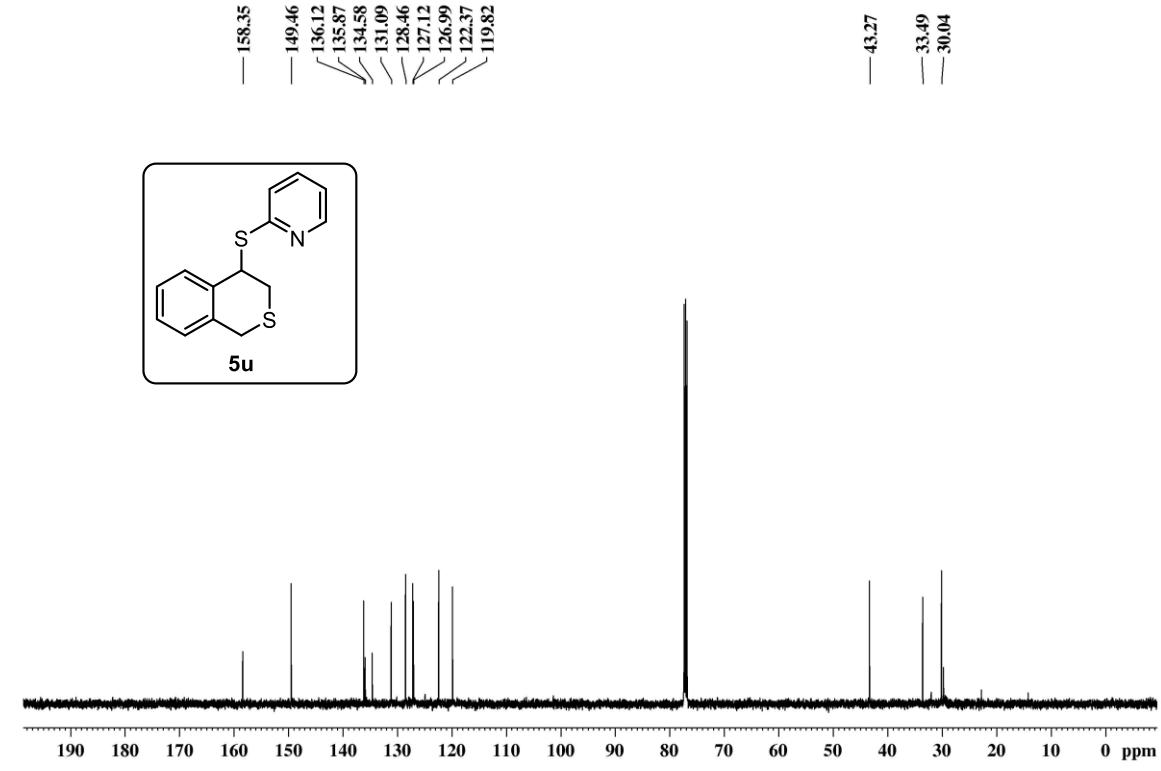
^{1}H NMR spectrum of compound **5t** (400 MHz, $CDCl_3$)



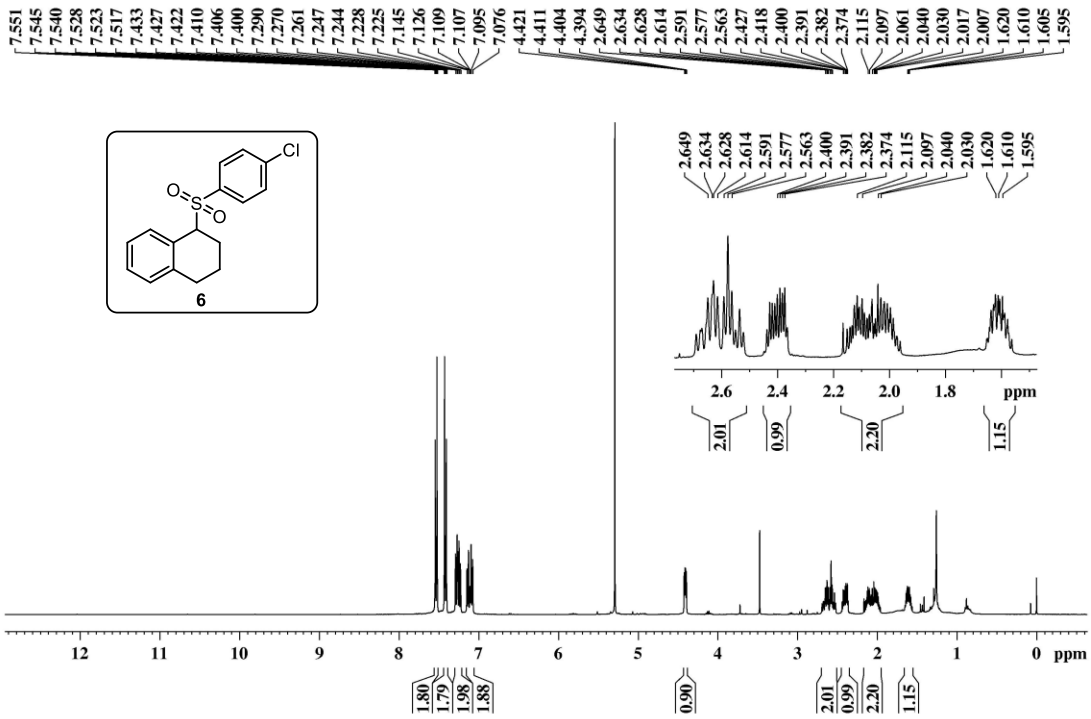
^{13}C NMR spectrum of compound **5t** (100 MHz, $CDCl_3$)



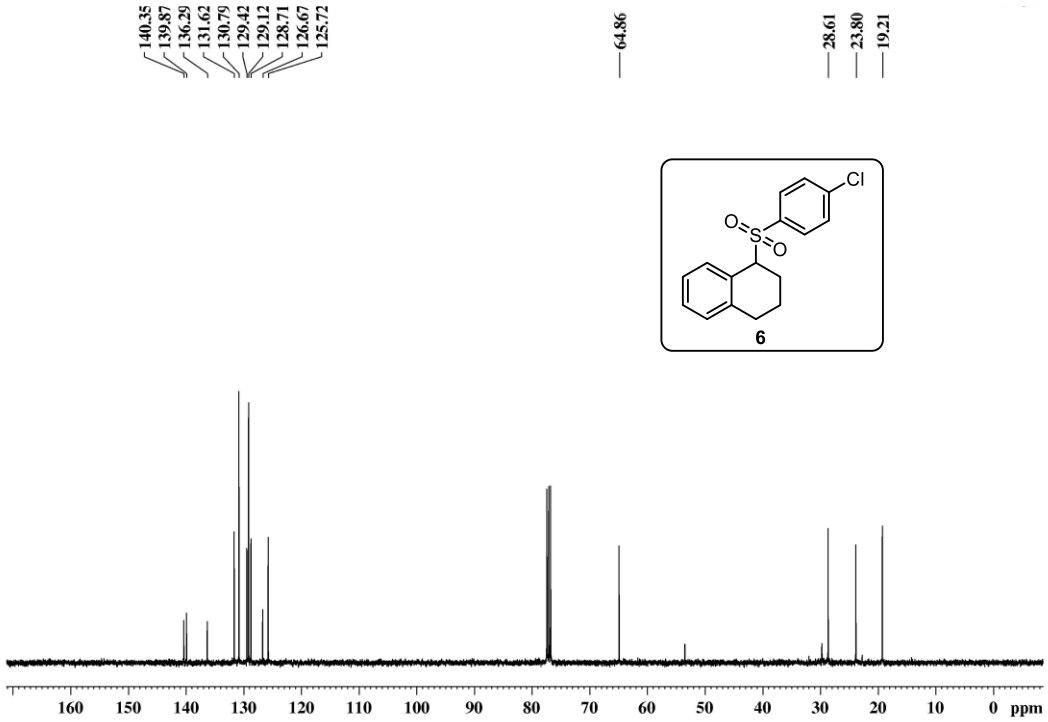
^{1}H NMR spectrum of compound **5u** (400 MHz, $CDCl_3$)



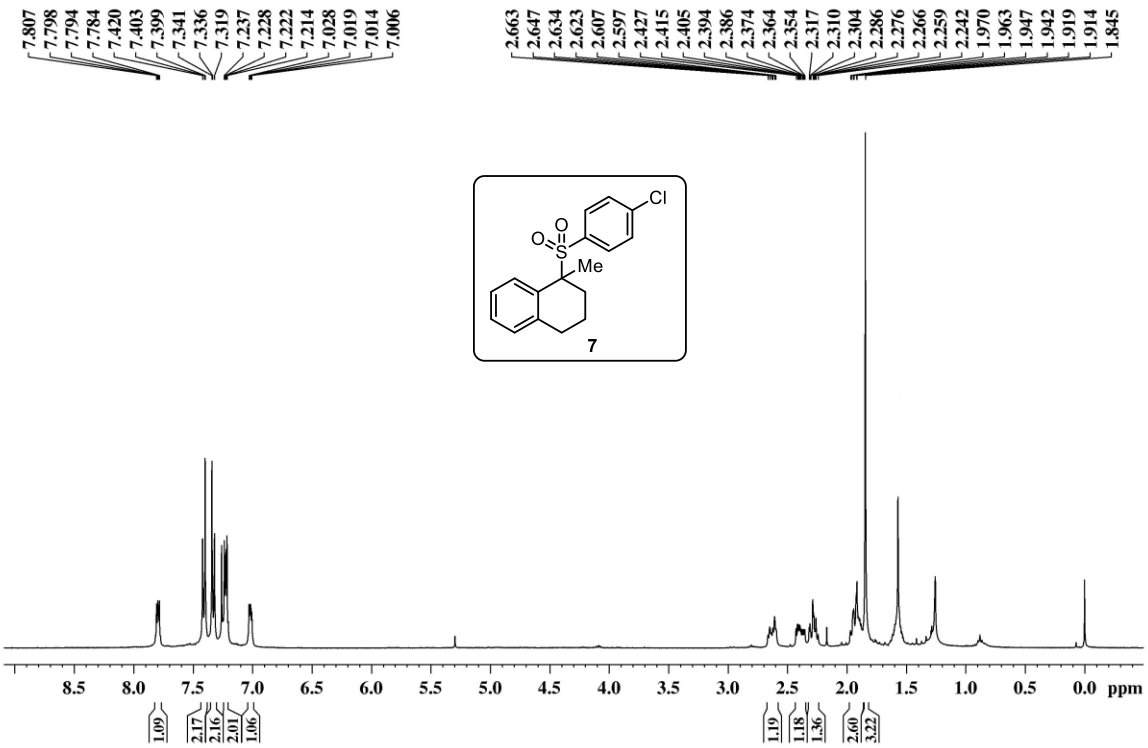
^{13}C NMR spectrum of compound **5u** (100 MHz, $CDCl_3$)



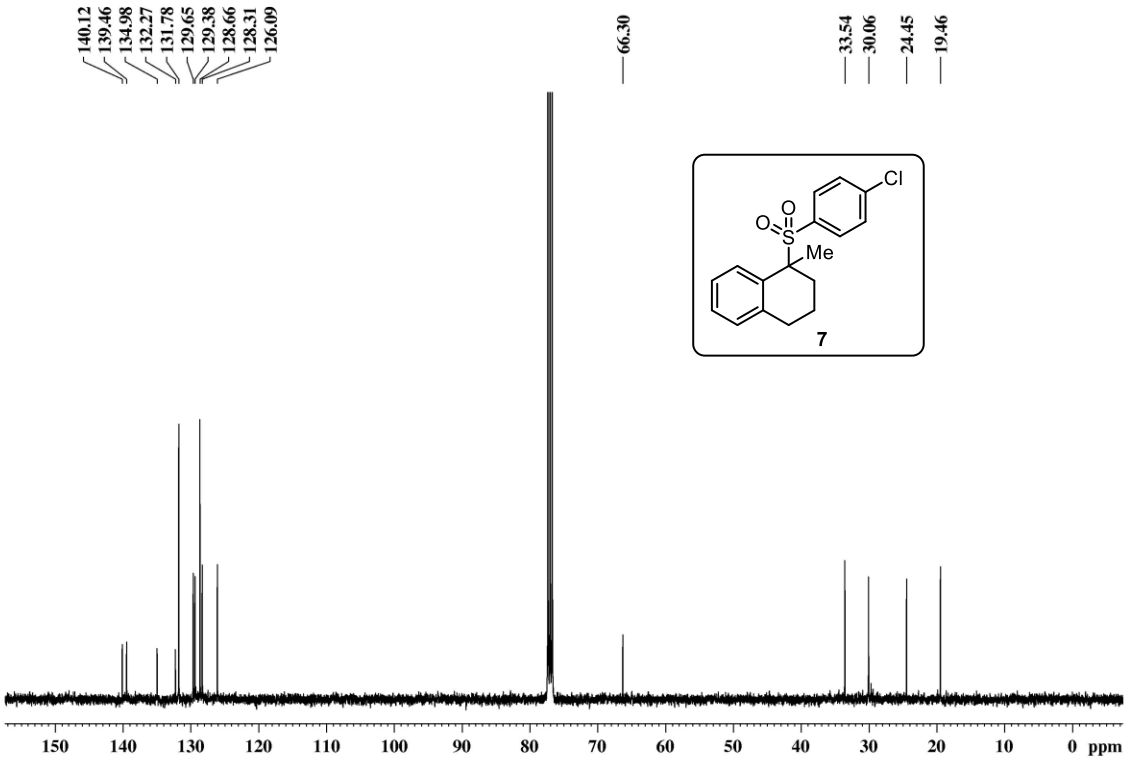
^{1}H NMR spectrum of compound **6** (400 MHz, $CDCl_3$)



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



^{1}H NMR spectrum of compound **7** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of compound **7** (100 MHz, $CDCl_3$)

Reference

(1) S. H. Bertz and G. Dabbagh, *J. Org. Chem*., 1983, **48,** 116-119.