Electronic Supplementary Material (ESI) for Green Chemistry.

Electronic Supplementary Information

$Na_2S_2O_8$-mediated efficient synthesis of isothiocyanates from primary amines in water

Zhicheng Fu, [a] Wenhao Yuan, [a] Ning Chen, [a] Zhanhui Yang*[a] and Jiaxi Xu*[a]

State Key Laboratory of Chemical Resource Engineering, Department of Organic Chemistry, College of Science, Beijing University of Chemical Technology, Beijing 100029, China

Corresponding authors:

Zhanhui Yang: zhyang@mail.buct.edu.cn;

Jiaxi Xu: jxxu@mail.buct.edu.cn.

Contents

1. General Information

All reagents and solvents were used as commercially received, without further purification, unless otherwise noted. ^{1}H (400 MHz), ^{13}C (100 MHz) and ^{19}F NMR (376 MHz) spectra were recorded on Bruker AMX 400 spectrometer with TMS as an interal standard in $CDCl_3$ solution. Chemical shifts for ^{1} H NMR are reported as follows: chemical shift in reference to residual $CHCl_3$ at 7.26 ppm (δ ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet), coupling constant (Hz), and integration. Chemical shifts for ^{13}C NMR are reported in terms of chemical shift in reference to the $CDCl_3$ solvent signal (77.16 ppm). Chemical shifts for ^{19}F-NMR are reported in terms of chemical shift in reference to an internal standard (1-(4-(trifluoromethyl)phenyl)ethan-1-one set to δ −63.60 ppm). IR spectra （ν/cm^{-1}） were taken on a Nicolet 5700 FT-IR spectrometer (neat or KBr pellets). Melting points were obtained on a melting point apparatus and were uncorrected. High resolution mass spectra were obtained via an Agilent LC/MSD TOF mass spectrometer. The specific rotation analysis was measured by Anton Paar MCP200 Polarimeter. HPLC data were measured using the Agilent Technologies. Products were purified on column chromatography with silica gel (200-300 mesh). Thin-layer chromatography (TLC) separations was performed on silica gel GF_{254} plates with petroleum ether (PE) and ethyl acetate (EA), and the plates were visualized with UV light. The pH values were tested by PHS-25 pH meter, which was calibrated with buffer solutions every day.

Dithiocarbamate salts 1 were prepared according to reported procedure by replacing THF with PE and EA (2:1, *v/v*) for green-chemistry purpose.[1]

[1] R. Wong and S. J. Dolman, *J. Org. Chem.*, 2007, **72**, 3969.

2. Procedure for the condition optimization

To a 10-mL vial were added dithiocarbamate **1a** (72 mg, 0.25 mmol), oxidant, base and water (3 mL), then the contents were stirred at room temperature. The progress of the reaction was monitored by TLC. After indicated time in Table 1, 2 mL of brine was added, and the mixture was extracted with ethyl acetate (2 mL x 3). Then internal standard (1-(4-(trifluoromethyl)phenyl)ethan-1-one (15.6 mg, 0.083 mmol) was added, followed by drying over anhydrous sodium sulfate. Then 0.5 mL of the organic phase was concentrated and the crude mixture was submitted to ^{19}F NMR analyses to determine the total yield (in DMSO-d_6).

3. Mechanistic studies and pH test.

3.1 Radical probing experiments

To a 10-mL vial were added dithiocarbamate **1a** (288 mg, 1.0 mmol), sodium persulfate (238 mg, 1.0 mmol), TEMPO (469 mg, 3.0 mmol), potassium carbonate (138 mg, 1.0 mmol) and water (3 mL). The mixture was stirred at room temperature for 1 h. After addition of 2 mL of brine, the mixture was extracted with dichloromethane (2 mL x 3), and dried over anhydrous sodium sulfate. Concentration of the organic phase under vacuum and purification by column chromatography on silica gel (eluent: hexanes/EA) afforded radical trapping product **4**.

***O*-(2,2,6,6-tetramethylpiperidin-1-yl) (4-fluorophenyl)carbamothioate (4)**

White solid. ^1H NMR (400 MHz, $CDCl_3$): 8.88 (s, 1H), 7.54 – 7.28 (m, 2 H), 7.18 – 6.88 (m, 2 H), 1.73 – 1.38 (m, 6 H), 1.24 (s, 6 H), 1.15 (s, 6 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.28 (d, J_{C-F} = 242.8 Hz), 155.43, 133.25 (d, J_{C-F} = 2.6 Hz), 121.02 (d, J_{C-F} = 7.9 Hz), 115.69 (d, J_{C-F} = 22.6 Hz), 61.06, 39.78, 31.66, 20.65, 16.69. ^{19}F NMR (376 MHz, $CDCl_3$) 118.96. IR (KBr, cm^{-1}): 3260, 2949, 1713, 1518, 1407. 1249, 1173, 1010, 830. HRMS (ESI) calcd. for $C_{16}H_{23}FN_2S_2O$ ($M + H^+$) 311.1582, found 311.1588.

3.2 pH tests

The procedures were identical with those described in Section 2. pH tests were performed with a pH meter every 5 min for optimal conditions or every 10 min for other conditions. The pH of the solution of 1a in 3 mL of water is 8.9.

Table S1. 1a (0.25 mmol), H_2O_2 (1.0 eq.), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	9.01	27.4
10	9.06	25.5
20	9.08	25.3
30	9.10	24.9
40	9.07	25.2
50	9.11	25.1
60	9.09	25.6

Table S2. 1a (0.25 mmol), H_2O_2 (4.0 eq.), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	7.53	29.5
10	7.38	26.2
20	7.37	25.7
30	7.43	25.1
40	7.47	25.4
50	7.53	25.2
60	7.52	25.5

Table S3. 1a (0.25 mmol), $Na_2S_2O_5$ (1.0 eq.), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	5.57	25.8
10	5.96	25.6
20	6.06	25.5
30	6.15	25.6
40	6.17	25.9
50	6.21	25.9
60	6.24	25.6

Table S4. 1a (0.25 mmol) , $Na_2S_2O_4$ (1.0 eq.), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	5.69	26.9
10	5.91	26.3
20	6.03	26.0

30	6.14	25.8
40	6.25	26.1
50	6.32	26.0
60	6.36	26.1

Table S5. 1a (0.25 mmol), Oxone (0.27.0 eq.) (1.0 eq.), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	4.80	27.3
10	5.29	26.8
20	5.49	26.2
30	5.61	26.0
40	5.70	26.1
50	5.81	26.2
60	5.88	26.3

Table S6. 1a (0.25 mmol), Oxone (1.0 eq.), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	1.47	29.8
10	1.51	27.6
20	1.38	27.0
30	1.38	26.9
40	1.36	27.0
50	1.38	27.2
60	1.36	27.0

Table S7. 1a (0.25 mmol), $K_2S_2O_8$ (1.0 eq.), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	4.84	28.1
10	3.46	26.9
20	3.20	26.6
30	3.04	26.3
40	2.89	26.4
50	2.88	26.4
60	2.83	26.6

Table S8. 1a (0.25 mmol), $Na_2S_2O_8$ (1.0 eq.), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	3.32	28.1
10	3.20	26.5
20	3.05	26.1
30	2.91	26.0
40	2.84	25.7

50	2.78	25.6
60	2.80	25.7

Table S9. 1a (0.25 mmol) , $Na_2S_2O_8$ (1.5 eq.), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （^oC）
0	4.90	28.8
10	3.14	27.4
20	2.96	27.0
30	2.80	27.0
40	2.74	27.1
50	2.66	27.3
60	2.63	27.2

Table S10. 1a (0.25 mmol), $Na_2S_2O_8$ (1.0 eq.), K_2CO_3 (1.0 eq), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （^oC）
0	6.85	28.2
5	7.01	24.6
10	7.40	23.8
15	7.54	23.8
20	7.64	23.3
25	7.81	23.8
30	7.97	22.8
35	8.14	22.6
40	8.25	22.6
45	8.28	22.6
50	8.32	22.1
55	8.43	21.7
60	8.41	22.4

Table S11. 1a (0.25 mmol), $Na_2S_2O_8$ (1.0 eq.), AcOK (1.0 eq), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （^oC）
0	4.12	28.8
10	4.07	26.0
20	4.01	25.5
30	3.99	25.7
40	3.96	25.6
50	3.94	25.4
60	3.92	25.9

Table S12.

1a (0.25 mmol), $Na_2S_2O_8$ (1.0 eq.), AcONa (1.0 eq), water (3 mL), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	4.16	28.7
10	4.05	26.5
20	4.02	25.9
30	3.98	25.7
40	3.96	25.8
50	3.94	25.8
60	3.90	26.2

Table S13

1a (0.25 mmol), $Na_2S_2O_8$ (1.0 eq.), NaOH (1.0 eq), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	9.52	30.2
10	8.85	27
20	8.81	26.6
30	8.77	26.5
40	8.69	26.2
50	8.63	26.5
60	8.01	26.7

Table S14

1a (0.25 mmol), $Na_2S_2O_8$ (1.0 eq.), Cs_2CO_3 (1.0 eq), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	6.90	23.2
10	7.54	25.6
20	7.85	22.9
30	8.17	22.3
40	8.34	22.2
50	8.42	21.8
60	8.48	21.8

Table S15. 1a (0.25 mmol), $Na_2S_2O_8$ (1.0 eq.), $NaHCO_3$ (1.0 eq), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （°C）
0	5.62	26.7
10	6.01	24.1
20	6.52	22.7
30	6.96	21.8
40	7.27	21.8
50	7.58	22.9
60	7.74	23.1

Table S16. 1a (0.25 mmol) , $Na_2S_2O_8$ (1.0 eq.), K_2CO_3(1.5 eq), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （ºC）
0	8.91	28.6
10	8.74	25.0
20	8.79	24.2
30	8.78	23.6
40	8.76	23.8
50	8.84	24.0
60	8.85	24.6

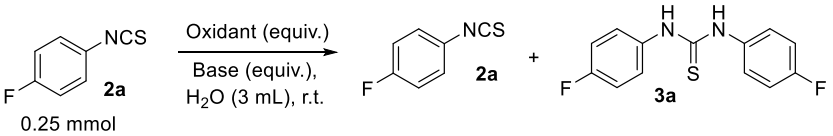
Table S17. 1a (0.25 mmol) , $Na_2S_2O_8$ (1.0 eq.), K_2CO_3(2.0 eq), water (3 mL), 1.0 h

Time (min)	pH values	Temperature （ºC）
0	9.34	29.9
10	9.19	27.6
20	9.15	26.5
30	9.09	26.0
40	9.05	26.0
50	9.12	25.5
60	9.08	25.6

3.3 Role of isothiocyanate in the reactions

Isothiocyanate **2a** (38 mg, 0.25 mmol) was added to a flask charged with oxidant (0.25 mmol) and base (0.25 mmol), if needed, at room temperature. The mixture was allowed to stir for 1 h. After extraction with petroleum ether (5 ml x 2) and drying over Na_2SO_4, the mixture was filtrated through a short column of silica gel. Removal of the solvent afforded recovered **2a**.

Table S18. Conversion or erosion of isothiocyanate exposed to different oxidants and conditions



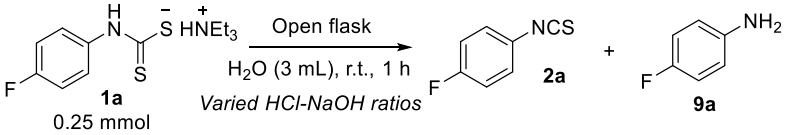
entry	Oxidant (equiv.)	Base (equiv.)	Time (h)	Isolated yield (%)	
				2a	**3a**
1	$Na_2S_2O_5$ (1.0)		1	67	-
2	$Na_2S_2O_4$ (1.0)		1	67	-
3	Oxone (0.27)		1	73	-
4	Oxone (1.0)		1	63	-

5	$K_2S_2O_8$ (1.0)		1	76	-
6	$Na_2S_2O_8$ (1.0)		1	71	-
7	$Na_2S_2O_8$ (1.0)	K_2CO_3 (1.0)	1	67	-

3.3 Base effect studies

N-(4-Fluorophenyl) dithiocarbamate **1a** (72 mg, 0.25 mmol) was added to a flask charged with a 3 ml of a solution with different HCl-NaOH ratios (different pH). The mixture was allowed to stir for 1 h. After extraction with ethyl acetate (5 ml x 2) and drying over Na_2SO_4, the mixture was submitted a short column chromatography on silica gel to purify all possible products. For entries 6 and 7, the solvent water is necessary to refrigeration deoxygenation under N_2 atmosphere.

Table S19. pH effect on the reaction of 1a with air as oxidant



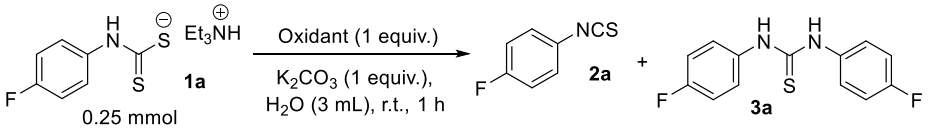
entry	pH	Isolated yield (%)	
		9a	**2a**
1	1 (0.98)	44	-
2	3 (2.92)	7	-
3	5 (5.05)	trace	-
4	7 (6.86)	trace	11
5	9 (9.18)	trace	35
6[a]	7 (7.02)	trace	trace
7[a]	9 (9.19)	trace	trace

[a] The reactions proceed under N_2 atmosphere in degassed water.

Different oxidants. was added to a flask charged with 3 ml of an aqueous solution of *N*-(4-fluorophenyl) dithiocarbamate **1a** (72 mg, 0.25 mmol) and K_2CO_3 (34.5 mg, 0.25 mmol). The mixture was allowed to stir for 1 h. After extraction with

dichloromethane (5 ml x 2), 4-(trifluoromethyl)acetophenone (15.6 mg, 0.08 mmol) was added. Part of the solution was concentrated and submitted to ^{19}F NMR to determine the yields of **2a** and **3a**.

Table S20. The effect of K_2CO_3 on the chemoselectivity with different oxidants



entry	Oxidant (1 equiv.)	Base (1 equiv.)	Time (h)	Yield (%)[a]	
				2a	**3a**
1	$Na_2S_2O_5$	K_2CO_3	1	42	-
2	$Na_2S_2O_4$	K_2CO_3	1	32	4
3	Oxone	K_2CO_3	1	27	trace
4	$K_2S_2O_8$	K_2CO_3	1	89	-

[a]Yields based on ^{19}F NMR of crude reaction mixtures with 4-(trifluoromethyl)acetophenone as internal standard.

4. General procedure of conditions A and conditions B

4.1 Procedure for *Conditions A*

To a 10-mL vial were added dithiocarbamate **1** (0.25 mmol), potassium carbonate (34.5 mg, 0.25 mmol), sodium persulfate (59.5 mg, 0.25 mmol), and water (3 mL). The mixture was stirred at room temperature for 1 h. After addition of 2 mL of brine, the mixture was extracted with petroleum ether (2 mL x 3), and dried over anhydrous sodium sulfate. In most cases, filtration through a short column of silica gel with petroleum ether followed by concentration afforded **2**. In some cases, purification by column chromatography on silica gel (eluent: PE/EA) was necessary.

4.2 Procedure for *Conditions B*

To a 10-mL vial were added primary amines **9** (1.0 mmol), CS_2 (0.18 mL, 2.5 mmol), potassium carbonate (138 mg, 1.0 mmol) and water (3 mL). Then the mixture was stirred at room temperature overnight, followed by addition of sodium persulfate (238

mg, 1.0 mmol), potassium carbonate (138 mg, 1.0 mmol) and water (2 mL). The mixture was further stirred at room temperature for another 1 h. Similar workup as described in Procedure for *Conditions A* afforded isothiocyanates **2**.

4.3 Preparation of 4-methylbenzenesulfonyl isothiocyanate (TsNCS)

To a 25-mL flask were added 4-methylbenzenesulfonamide **9al** (10 mmol), KOH (560 mg, 10 mmol), PE-EA (10 mL, *v/v* = 2:1) to form a suspension. Then a solution of CS_2 (1.8 mL, 25 mmol) in PE-EA (6 mL, *v/v* = 2:1) was slowly added during 5 minutes. Upon addition, the mixture was stirred at room temperature for overnight. The precipitation was filtered, washed with PE (3 x 2 mL), and recrystallized from PE and acetone to give tosylcarbamodithioate in 85% yield.

To a 10-mL vial were added tosylcarbamodithioate (71 mg, 0.25 mmol), sodium persulfate (71.4 mg, 0.3 mmol), and water (3 mL), and stirred at room temperature for 1 h. After addition of 2 mL of brine, the mixture was extracted with ethyl acetate (2 mL x 3), and dried over anhydrous sodium sulfate. Concentration of the organic phase under vacuum and purification by column chromatography on silica gel (eluent: hexanes/EA) afforded **2al.**

5. Characterization Data for Products 3a, 2a-2al[2]

1,3-Bis(4-fluorophenyl)thiourea (**3a**) Yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6): 9.77 (s, 2H), 7.46 (q, J = 8.8 Hz, 5.1 Hz, 4H), 7.16 (t, J = 8.8 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ: 180.4, 159.18 (d, J_{C-F} = 241.5 Hz), 135.7 (d, J_{C-F} = 2.7 Hz), 126.3 (d, J_{C-F} = 8.3 Hz), 115.1 (d, J_{C-F} = 22.5 Hz).^{19}F NMR (376 MHz, DMSO-d_6) 117.9. HRMS (ESI) calcd. for $C_{13}H_{10}F_2N_2S$ (M + H^+) 265.0606, found 265.0609.

[2] (a) R. Yella, H. Ghosh, S. Murru, K. S. Sahoo and B. K. Patel. *Syn. Comm.*, 2010, **40**, 2083. (b) J. Nath, L. Jamir and B. K. Patel, *Green Chem. Lett. Rev.*, 2011, **4**, 1. (c) T. Scattolin, A. Klein, and F. Schoenebeck, *Org. Lett.*, 2017, **19**, 1831. (d) J. Nath, H. Ghosh, R. Yella and B. K. Patel, *Eur. J. Org. Chem.*, 2009, 1849.

1-Fluoro-4-isothiocyanatobenzene (**2a**) Colorless oil. Yield (Conditions A: 34 mg, 90 %; Conditions B: 125 mg, 82 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.24 – 7.17 (m, 2H), 7.02 – 7.07 (m, 2H). ^{13}C NMR (101 MHz, CDCl3) δ 161.26 (d, J_{C-F} = 249.0 Hz), 136.1, 127.50 (d, J_{C-F} = 8.6 Hz), 116.80 (d, J_{C-F} = 23.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) 112.1.

1-Isothiocyanato-4-methoxybenzene (**2b**) Colorless liquid. Yield (Conditions A: 25 mg, 61 %; Conditions B: 158 mg, 96 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.16 (d, *J* = 9.0 Hz, 2H), 6.85 (d, *J* = 9.0 Hz, 2H), 3.80 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 158.7, 134.1, 127.1, 123.7, 114.9, 55.7.

(4-Isothiocyanatophenyl)(methyl)sulfane (**2c**) White solid. Yield (Conditions A: 25 mg, 55 %; Conditions B: 129 mg, 71 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.17 (d, *J* = 8.6 Hz 2H), 7.11 (d, *J* = 8.5 Hz 2H,), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 138.5, 135.2, 127.7, 127.0, 126.0, 15.7.

2-Isothiocyanato-1,3,5-trimethylbenzene (**2d**) White solid. Yield (Conditions A: 44 mg, 99 %; Conditions B: 176 mg, 99 %). ^{1}H NMR (400 MHz, $CDCl_3$): 6.85 (s, 2H), 2.33 (s, 6H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 137.1, 135.0, 134.9, 128.8, 126.9, 21.2, 18.7.

1-Isothiocyanato-2,4-dimethylbenzene (**2e**) White solid. Yield (Conditions A: 39 mg, 96 %; Conditions B: 137 mg, 84 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.08 (d, *J* = 8.0 Hz, 1H), 7.01 (s, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 2.34 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 137.6, 134.8, 134.6, 131.4, 127.6, 125.8, 21.3, 18.4.

1-Isopropyl-4-isothiocyanatobenzene (**2f**) Colorless oil liquid. Yield (Conditions A: 40 mg, 90 %, Conditions B: 121 mg, 73 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.21-7.14 (m, 4H), 2.91 (hept, *J* = 6.9 Hz, 1H), 1.24 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR(101 MHz, $CDCl_3$): 148.6, 134.5, 128.7, 127.7, 125.8, 34.0, 23.9.

1-Isothiocyanato-2-methylbenzene (**2g**) Colorless liquid. Yield (Conditions A: 21 mg, 56 %; Conditions B: 127 mg, 85 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.19 – 7.08 (m, 4H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 135.4, 135.1, 130.8, 130.4, 127.5, 127.0, 126.0, 18.5.

1-Isothiocyanato-4-methylbenzene (**2h**) Colorless liquid. Yield (Conditions A: 33 mg,

89 %; Conditions B: 142 mg, 95 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.17 – 7.09 (m, 4H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 137.7, 134.5, 130.3, 128.5, 125.7, 21.3.

1-(*tert*-Butyl)-4-isothiocyanatobenzene (**2i**) White solid. Yield (Conditions A: 40 mg, 84 %; Conditions B: 122 mg, 64 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.38 – 7.34 (m, 2H), 7.18 – 7.14 (m, 2H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): 150.9, 134.5, 128.4, 126.6, 125.5, 34.9, 31.3.

1,3-Di-*tert*-butyl-5-isothiocyanatobenzene (**2j**) White solid. M.p. 97-98 ^{o}C. Yield (Conditions A: 50 mg, 81 %; Conditions B: 156 mg, 63 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.34 (t, J = 1.6 Hz, 1H), 7.07 (d, J = 1.6 Hz, 2H), 1.31 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$): 152.7, 133.5, 130.7, 121.8, 120.2, 35.1, 31.4. IR (KBr, cm^{-1}): 2955, 2924, 2146, 1595, 1455. 1394, 1361, 1247, 1203, 866, 737, 698. HRMS (ESI) calcd. for $C_{15}H_{21}NS$ ($M + H^{+}$) 248.1467, found 248.1470.

Isothiocyanatobenzene (**2k**) Colorless oil. Yield (Conditions A: 28 mg, 81 %; Conditions B: 117 mg, 87 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.38 – 7.19 (m, 5 H). ^{13}C NMR (101 MHz, $CDCl_3$): 135.5, 131.4, 129.7, 127.4, 125.8.

1-Fluoro-2-isothiocyanatobenzene (**2l**) Colorless liquid. Yield (Conditions A: 31 mg, 82 %; Conditions B: 21 mg, 14 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.26 – 6.97 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.66 (d, J_{C-F} = 253.9 Hz), 141.07 (d, J_{C-F} = 7.7 Hz), 128.46 (d, J_{C-F} = 7.3 Hz), 126.58, 124.81 (d, J_{C-F} = 3.8 Hz), 120.50 (d, J_{C-F} = 14.2 Hz), 116.53 (d, J_{C-F} = 18.6 Hz).

1-Chloro-4-isothiocyanatobenzene (**2m**) White solid. Yield (Conditions A: 36 mg, 85 %; Conditions B: 100 mg, 59 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.35 – 7.29 (m, 2H), 7.19 – 7.13 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 137.0, 133.1, 130.2, 129.9, 127.0.

1-Chloro-3-isothiocyanatobenzene (**2n**) Colorless oil liquid. Yield (Conditions A: 36 mg, 85 %; Conditions B: 74 mg, 44 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.25 – 7.16 (m, 3H), 7.10 – 7.04 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 137.6, 135.3, 132.8, 130.6, 127.7, 126.0, 124.1.

1-Bromo-4-isothiocyanatobenzene (**2o**). White solid. Yield (Conditions A: 45 mg, 85 %; Conditions B: 183 mg, 86 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.51 – 7.43 (m, 2H),

7.13 – 7.05 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 137.1, 132.9, 130.7, 127.3, 120.9.

1-Isothiocyanato-3-nitrobenzene (**2p**). White solid. Yield (Conditions A: 33 mg, 73 %; Conditions B: trace). ^{1}H NMR (400 MHz, $CDCl_3$): 8.13 (d, *J* = 7.1 Hz, 1H), 8.06 (s, 1H), 7.59 – 7.51 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 148.9, 139.9, 133.4, 131.6, 130.6, 121.9, 120.8.

Ethyl 4-isothiocyanatobenzoate (**2q**). White solid. Yield (Conditions A: 40 mg, 78 %; Conditions B: trace). ^{1}H NMR (400 MHz, $CDCl_3$): 7.98 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 165.3, 137.9, 135.5, 131.0, 129.0, 125.6, 61.3, 14.3.

1-Isothiocyanatonaphthalene (**2r**). White solid. Yield (Conditions A: 40 mg, 87 %; Conditions B: 131 mg, 71 %). ^{1}H NMR (400 MHz, $CDCl_3$): 8.11 (d, *J* = 8.3 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.78 – 7.76 (m, 2H), 7.64 – 7.54 (m, 2H), 7.44 – 7.38 (2 H, m). ^{13}C NMR (101 MHz, $CDCl_3$): 136.2, 134.1, 129.4, 128.5, 127.8, 127.6, 127.48, 127.2, 125.5, 123.6, 122.8.

(2-Isothiocyanatoethyl)benzene (**2s**). Yellow oil liquid. Yield (Conditions A: 34 mg, 83 %; Conditions B: 108 mg, 66 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.29 – 7.11 (m, 5H), 3.64 (t, *J* = 7.0 Hz, 2H), 2.91 (t, *J* = 7.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 137.1, 130.9, 128.9 (2C), 127.3, 46.5, 36.6.

(Isothiocyanatomethyl)benzene (**2t**). White solid. Yield (Conditions A: 36 mg, 97 %; Conditions B: 109 mg, 73 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.35 – 7.16 (m, 5H), 4.63 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 134.3, 132.3, 129.1, 128.5, 126.9, 48.8.

1-(Isothiocyanatomethyl)-4-methoxybenzene (**2u**). Colorless liquid. Yield (Conditions A: 32 mg, 72 %; Conditions B: 72 mg, 40 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.16 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 4.55 (s, 2H), 3.73 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 159.7, 132.1, 128.5, 126.4, 114.4, 55.5, 48.4.

1-Chloro-4-(isothiocyanatomethyl)benzene (**2v**). Colorless liquid. Yield (Conditions A: 40 mg, 87 %; Conditions B: 112 mg, 61 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.29 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 4.61 (s, 2H), ^{13}C NMR (101 MHz, $CDCl_3$): 133.4, 132.3, 131.9, 128.3, 127.4, 47.2. IR (KBr, cm^{-1}): 3047, 2922, 2178, 2094, 1591,

1492, 1439, 1340, 1091, 1015, 807, 726, 672. HRMS (ESI) calcd. for C_8H_6ClNS (M + H^+) 183.9982, found 183.9991.

1-Chloro-2-(isothiocyanatomethyl)benzene (**2w**). Yellow oil liquid. Yield (Conditions A: 42 mg, 92 %; Conditions B: 112 mg, 61 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.43 – 7.17 (m, 4H), 4.75 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 133.4, 132.8, 132.1, 129.9, 129.9, 128.8, 127.5, 46.8. IR (KBr, cm^{-1}): 3066, 2924, 2090, 1583, 1438, 1341, 1047, 745, 683. HRMS (ESI) calcd. for C_8H_6ClNS (M + H^+) 183.9982, found 183.9982.

2-(Isothiocyanatomethyl)furan (**2x**). Yellow oil liquid. Yield (Conditions A: 25 mg, 81 %; Conditions B: 114 mg, 82 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.42 (d, *J* = 1.0 Hz, 1H), 6.37 (dd, *J* = 3.2 Hz, 1.9 Hz, 1H), 6.34 (d, *J* = 3.2 Hz, 1H), 4.65 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 147.4, 143.4, 135.0, 110.8, 108.9, 42.0.

2-(Isothiocyanatomethyl)thiophene (**2y**). Colorless oil. Yield (Conditions A: 30 mg, 77 %; Conditions B: 107 mg, 69 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.31 (dd, *J* = 5.2 Hz, 1.2 Hz, 1H), 7.05 (d, *J* = 2.6 Hz, 1H), 6.99 (dd, *J* = 5.0 Hz, 3.6 Hz, 1H), 4.84 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 136.6, 134.4, 127.1, 126.7, 126.2, 43.9.

3-Isothiocyanatoprop-1-ene (**2z**). White solid. Yield (Conditions A: 70 mg, 71 %; Conditions B: 74 mg, 37 %). ^{1}H NMR (400 MHz, $CDCl_3$): 5.83 (ddt, *J* = 16.8 Hz, 10.0 Hz, 4.8 Hz, 1H), 5.38 (d, *J* = 16.9 Hz,1 H), 5.27 (d, *J* = 10.2 Hz, 1H), 4.13 (dt, *J* = 4.7 Hz, 1.6 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$): 132.3, 130.4, 117.8, 47.2.

(1-Isothiocyanatoethyl)benzene (**2aa**). Yellow oil. Yield (Conditions A: 35 mg, 88 %; Conditions B: 140 mg, 88 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.41-7.32 (m, 5H), 4.92 (q, *J* = 6.8 Hz, 1H), 1.68 (d, *J* = 6.8 Hz, 3H). 4.65 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 140.3, 132.4, 129.0, 128.3, 125.5, 57.1, 25.1.

(Isothiocyanatomethylene)dibenzene (**2ab**). White solid. Yield (Conditions A: 44 mg, 78 %; Conditions B: 187 mg, 83 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.48 – 7.35 (m, 10 H), 6.04 (s, 1H).^{13}C NMR (101 MHz, $CDCl_3$): 139.2, 134.5, 128.9, 128.3, 126.6, 64.6.

Isothiocyanatocyclohexane (**2ac**). Colorless oil. Yield (Conditions A: 29 mg, 82 %; Conditions B: 109 mg, 77 %). ^{1}H NMR (400 MHz, $CDCl_3$): 3.68 (tt, *J* = 7.5 Hz, 3.6 Hz, 1H), 1.88 (dt, *J* = 9.0 Hz, 6.3 Hz, 2H), 1.79 – 1.58 (m, 4H), 1.53 – 1.32 (m, 4H) ^{13}C

NMR (101 MHz, $CDCl_3$): 129.9, 55.5, 33.3, 25.2, 23.4.

2-Isothiocyanato-2-methylpropane (**2ad**). White solid. Yield (Conditions A: 113 mg, 98 %; Conditions B: 94 mg, 41 %). ^{1}H NMR (400 MHz, $CDCl_3$): 1.37 (s, 9H).^{13}C NMR (101 MHz, $CDCl_3$): 130.0, 58.4, 30.8.

1-Isothiocyanatoadamantane (**2ae**). White solid. M.p. 74-75 ^{o}C. Yield (Conditions A: 40 mg, 83 %; Conditions B: 141 mg, 73 %). ^{1}H NMR (400 MHz, $CDCl_3$): 2.09 (s, 1H), 1.96 (d, *J* = 2.7 Hz, 2H), 1.69 – 1.58 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 129.7, 58.5, 43.8, 35.6, 29.3. IR (KBr, cm^{-1}): 2917, 2854, 2123, 2092, 2062, 1491, 1449, 1305, 1090, 803, 763, 705. HRMS (ESI) calcd. for $C_{11}H_{15}NS$ ($M + H^+$) 194.0998, found 194.0998.

1,2-Diisothiocyanatocyclohexane (**2af**). Yellow oil. Yield (Conditions A: 46 mg, 93 %; Conditions B: 149 mg, 75 %). ^{1}H NMR (400 MHz, $CDCl_3$): 3.69 (dd, *J* = 10.1 Hz, 5.9 Hz, 2H), 2.14 (d, *J* = 13.4 Hz, 2H), 1.73 (d, *J* = 5.7 Hz, 2H), 1.64 – 1.50 (m, 2H), 1.43 – 1.20 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 135.0, 60.0, 31.5, 22.9.

6-Isothiocyanatohexan-1-ol (**2ag**). Colorless oil. Yield: (Conditions A: 27 mg, 68 %; Conditions B: 119 mg, 75 %). ^{1}H NMR (400 MHz, $CDCl_3$): 3.62 (t, *J* = 6.5 Hz, 2H), 3.50 (t, *J* = 6.6 Hz, 2H), 1.72 (s, 1H), 1.72-1.65 (m, 2H), 1.61 – 1.51 (m, 2H), 1.49 – 1.33 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): 129.6, 62.7, 45.1, 32.5, 30.0, 26.4, 25.1. IR (KBr, cm^{-1}): 3345, 2934, 2859, 2106, 1453, 1347, 1053. HRMS (ESI) calcd. for $C_7H_{13}NOS$ ($M + H^+$) 160.0791, found 160.0790.

4-Isothiocyanatophenol (**2ah**). Yellow oil liquid. Yield (Conditions A: 36 mg, 94 %; Conditions B: 143 mg, 95 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.08 (d, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 5.72 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 154.6, 133.8, 127.2, 123.8, 116.4.

1-Ethynyl-3-isothiocyanatobenzene (**2ai**) Yellow oil liquid. Yield: (Conditions A: 35 mg, 88 %; Conditions B: 62 mg, 39 %). ^{1}H NMR (400 MHz, $CDCl_3$): 7.40 – 7.17 (m, 4H), 3.13 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 137.1, 131.8, 131.0, 129.8, 129.2, 126.2, 124.0, 82.0, 79.0. IR (KBr, cm^{-1}): 3295, 2255, 2143 2101, 2062, 1592, 1573, 1482, 1474, 1264, 1085, 999, 883, 789, 680, 661, 629. HRMS (ESI) calcd. for

$C_8H_{13}NO_2S$ (M + H^+) 160.0213 found 160.0213.

4-Isothiocyanato-1*H*-indole (**2aj**) Yellow oil. Yield (Conditions A: 36 mg, 83 %; Conditions B: 54 mg, 31 %). ^{1}H NMR (400 MHz, $CDCl_3$): 8.29 (s, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.21 (t, *J* = 2.8 Hz, 1H), 7.08 (t, *J* = 7.9 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.72 – 6.64 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 136.6, 135.9, 125.4, 125.3, 122.7, 122.2, 116.7, 111.0, 100.2. IR (KBr, cm^{-1}): 3416, 2922, 2048, 1573, 1497, 1435, 1346, 1117, 786, 743. HRMS (ESI) calcd. for $C_9H_6N_2S$ (M + H^+) 175.0324, found 175.0318.

3-Isothiocyanatopyridine (**2ak**) Yellow oil liquid. Yield (Conditions A: 195 mg, 72 %; Conditions B: 27 mg, 20 %). ^{1}H NMR (400 MHz, $CDCl_3$): 8.29 (s, 1H), 7.29 (d, J = 8.2 Hz, 1H), 7.21 (t, J = 2.8 Hz, 1H), 7.08 (t, J = 7.9 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 6.72 – 6.64 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 136.6, 135.9, 125.4, 125.3, 122.7, 122.2, 116.7, 111.0, 100.2.

4-Methylbenzenesulfonyl isothiocyanate. Colorless liquid. 20 mg, 38%. ^{1}H NMR (400 MHz, $CDCl_3$): 7.87 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 8.2 Hz, 2H), 2.48 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 156.1, 146.3, 136.6, 130.3, 127.5, 21.9.

6. Preparation of Chiral Isothiocyantes

Procedure for *Conditions A*: To a 25 mL flask were added chiral amino ester **10a** (908 mg, 5.0 mmol), Et_3N (1.40 mL, 10 mmol), and a solution of CS_2 (0.9 mL, 12.5 mmol) in PE/EA (32 mL, *v/v* = 2:1). Then the mixture was stirred at room temperature overnight. The solvent was removed, followed by addition of water (15 mL), potassium carbonate (690 mg, 5.0 mmol), and sodium persulfate (1.19 g, 5.0 mmol). The mixture was stirred at room temperature for 1 h. After addition of 5 mL of brine, the mixture was extracted with ethyl acetate (10 mL x 3), and dried over anhydrous sodium sulfate. Concentration of the organic phase under vacuum and purification by column chromatography on silica gel (eluent: hexane/ethyl acetate) to afford **11a** and *epi*-**11a.**

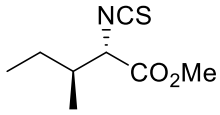
Colorless oil. Yield (615 mg, 66 %, *dr* = 1:1).

Procedure for *Conditions B*: To a 25 mL flask were sequentially added chiral amino ester **10** (5.0 mmol), water (5 mL), CS_2 (0.9 mL, 12.5 mmol), and potassium carbonate (1.38 g, 10 mmol). The mixture was stirred at room temperature overnight, followed by sodium persulfate (1.19 g, 5.0 mmol), potassium carbonate (690 mg, 5.0 mmol), and water (5 mL). The mixture was stirred at room temperature for 1 h. The same workup as described above afforded chiral isothiocyanates **11**.

The racemic isothiocyanates were prepared from the corresponding racemic amino esters under *Conditions B*.

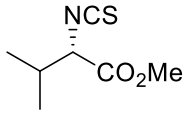
7. Characterization Data for Chiral Isothiocyantes

Methyl (2*S*,3*S*)-2-isothiocyanato-3-methylpentanoate (**11a**)



Colorless oil. Yield: 615 mg, 66 %. ^{1}H NMR (400 MHz, $CDCl_3$): 4.18 (d, *J* = 4.4 Hz, 1H), 3.77 (s, 3H), 2.11 – 1.98 (m, 1H), 1.49 – 1.18 (m, 2H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) 168.6, 136.7, 64.9, 53.0, 39.1, 24.6, 16.3, 11.4. IR (KBr, cm^{-1}): 2967, 2074, 1458, 1209. HRMS (ESI) calcd. for $C_8H_{13}NO_2S$ ($M + H^+$) 188.0740, found 188.0736.$[\alpha]_D$ = +15.3 (0.01 g/mL, EtOH, 589 nm, 20 °C). HPLC Analysis: Chiralpak: OD-H (Hex/IPA = 95/5, 1.0 mL/min, 280 nm, 20 °C) 4.151 min (minor), 4.546 min (major), 99% ee.

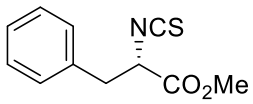
Methyl (*S*)-2-isothiocyanato-3-methylbutanoate (11b)



Yellow oil. Yield: 485 mg, 56 %. ^{1}H NMR (400 MHz, $CDCl_3$): 4.15 (d, *J* = 4.2 Hz, 1H), 3.76 (s, 3H), 2.35 – 2.23 (m, 1H), 1.03 (d, *J* = 6.8Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 168.5, 136.8, 65.5, 53.0, 32.7, 19.7, 17.1. IR (KBr, cm^{-1}): 2923, 2073, 1750, 1262, 792. HRMS (ESI) calcd. for $C_7H_{11}NO_2S$ ($M + H^+$) 174.0583,

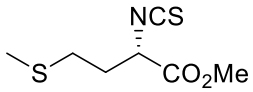
found 174.0585. $[\alpha]_D$ = + 4.10 (0.01 g/mL, EtOH, 589 nm, 20 °C). HPLC Analysis: Chiralpak: OD-H (Hex/IPA = 95/5, 1.0 mL/min, 280 nm, 22 °C) 4.593 min (minor), 4.888 min (major), 98% ee.

Methyl (*S*)-2-isothiocyanato-3-phenylpropanoate (**11c**)



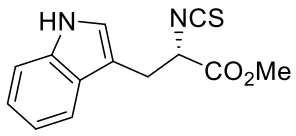
Yellow oil. Yield: 811 mg, 77 %. ^{1}H NMR (400 MHz, $CDCl_3$): 7.42 – 7.23 (m, 5H), 4.52 (dd, *J* = 8.1 Hz, 4.8 Hz, 1H), 3.79 (d, *J* = 2.7 Hz, 3H), 3.27 (dd, *J* = 13.8 Hz, 4.6 Hz, 1H), 3.15 (dd, *J* = 13.8 Hz, 8.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 168.1, 137.6, 135.0, 129.2, 128.6, 127.5, 60.6, 53.0, 39.5. IR (KBr, cm^{-1}): 3031, 3006, 2072, 1751, 1604, 1459, 1437, 1340, 1216, 748, 700. HRMS (ESI) calcd. for $C_{11}H_{11}NO_2S$ ($M + H^+$) 222.0583, found 222.0578. $[\alpha]_D$ = - 6.3 (0.01 g/mL, EtOH, 589 nm, 20 °C). HPLC Analysis: Chiralpak: AS-H (Hex/IPA = 99/1, 1.0 mL/min, 280 nm, 22 °C) 9.045 min (minor), 9.689 min (major), 99% ee.

Methyl (*S*)-2-isothiocyanato-4-(methylthio)butanoate (11d)



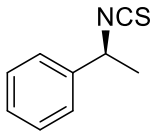
Yellow oil. Yield: 524 mg, 51 %. ^{1}H NMR (400 MHz, $CDCl_3$): 4.54 (dd, *J* = 8.2 Hz, 4.8 Hz, 1H), 3.80 (s, 3H), 2.71 – 2.55 (m, 2H), 2.23 – 2.11 (m, 2H), 2.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 168.9, 138.2, 58.1, 53.4, 32.6, 30.1, 15.5. IR (KBr, cm^{-1}): 2920, 2064, 1748, 1435, 1212. HRMS (ESI) calcd. for $C_7H_{11}NO_2S_2$ ($M + H^+$) 206.0304, found 206.0294. $[\alpha]_D$ = - 1.89 (0.01 g/mL, EtOH, 589 nm, 20 °C). HPLC Analysis: Chiralpak: AS-H (Hex/IPA = 99/1, 1.0 mL/min, 280 nm, 22 °C), 21.063 min (minor), 21.935 min (major), 94% ee.

Methyl (*S*)-3-(1H-indol-3-yl)-2-isothiocyanatopropanoate (**11e**)



Colorless oil liquid. Yield: 700 mg, 54 %. ^{1}H NMR (400 MHz, $CDCl_3$): 8.14 (s, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.18 (m, 1H), 7.17 – 7.12 (m, 2H), 4.57 (dd, *J* = 7.9 Hz, 4.6 Hz, 1H), 3.74 (s, 3H), 3.45 (ddd, *J* = 14.6 Hz, 4.6 Hz, 0.5 Hz), 3.34 (dd, *J* = 14.6 Hz, 7.8 Hz,1H). ^{13}C NMR (101 MHz, $CDCl_3$): 168.9, 137.5, 136.2, 127.0, 124.1, 122.5, 120.0, 118.4, 111.6, 109.3, 60.4, 53.3, 30.2. IR (KBr, cm^{-1}): 3417, 3057, 2953, 2842, 2081, 1740, 1490, 1435, 1340, 1211, 1096, 1011, 744. HRMS (ESI) calcd. for $C_{13}H_{12}N_2O_2S$ ($M + H^+$) 261.0692, found261.0693. $[\alpha]_D$ = + 9.13 (0.01 g/mL, EtOH, 589 nm, 20 ^{o}C). HPLC Analysis: Chiralpak: OD-H (Hex/IPA = 80/20, 1.0 mL /min, 280 nm, 18 ^{o}C) 13.237 min (minor), 14.953 min (major), 98% ee.

(S)-(1-Isothiocyanatoethyl)benzene (**11f**)



Colorless oil.[3] Yield: 481 mg, 59 %. ^{1}H NMR (400 MHz, $CDCl_3$): 7.36 – 7.22 (m, 5H), 4.81 (q, *J* = 6.8 Hz, 1H), 1.57 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 140.0, 132.2, 128.8, 128.1, 125.3, 56.9, 24.8. IR (KBr, cm^{-1}): 2984, 2090, 1454, 1376, 1308, 1067, 698. HRMS (ESI) calcd. for C_9H_9NS ($M + H^+$) 164.0528, found 164.0533. $[\alpha]_D$ = +12.7 (0.01 g/mL, $CHCl_3$, 589 nm, 20 ^{o}C).

8. Large-scale Preparation of Isothiocyanates by One-pot Procedure

2-Isothiocyanato-1,3,5-trimethylbenzene (2d)

To a 100-mL flask were sequentially added water (20 mL), potassium carbonate

[3] A. Kotynski, K. Lesiak and W. J. Stec. *Polish J. Chem.* 1979, **53**, 2403.

(6.9 g, 50 mmol), 2,4,6-trimethylaniline **4d** (6.75 g, 50 mmol), and CS_2 (9 mL, 125 mmol). Then the mixture was stirred at room temperature overnight, followed by slow addition of water (20 mL), potassium carbonate (50 mmol, 6.9 g), and sodium persulfate (11.9 g, 50 mmol) in ice-water bath. The mixture was stirred at room temperature for 1 h. After addition of 30 mL of brine, the mixture was extracted with PE (30 mL x 3), and dried over anhydrous sodium sulfate. The obtained yellow solution was filtrated through a pad of silica gel under reduced pressure to give a colorless solution. Removal of the solvent afforded the title product **2d** as white solid (8.70g, 99% yield).

(Isothiocyanatomethyl)benzene (2t)

To a 100-mL flask containing 30 mL of water were added potassium carbonate (6.9 g, 50 mmol), benzylamine **4t** (5.35 g, 50 mmol), and CS_2 (9 mL, 125 mmol). The mixture was stirred at room temperature overnight, followed by slow addition of water (20 mL), potassium carbonate (6.9 g, 50 mmol), sodium persulfate (11.9 g, 50 mmol) in ice-water bath. The mixture was stirred at room temperature for 1 h. After addition of 30 mL of brine, the mixture was extracted with PE (30 mL x 3), and dried over anhydrous sodium sulfate. The obtained yellow solution was filtrated through a pad of silica gel under reduced pressure to give a colorless solution. Removal of the solvent gave the title product **2t** as yellowish oil (5.21g, 70% yield).

3-Ethyl-5-methyl-4-(2-chlorophenyl)-2-((2-isothiocyanatoethoxy)methyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate (13)

To a 50-mL flask containing 10 mL of water were sequentially added potassium carbonate (1.38 g, 10 mmol), CS_2 (1.8 mL, 25 mmol), and Amlodipine benzenesulfonic acid salt **7** (5.67 g, 10 mmol). Then the mixture was stirred at room temperature overnight, followed by slow addition of water (5 mL), potassium carbonate (1.38 g, 10 mmol), and sodium persulfate (2.38 g, 10 mmol) in ice-water bath. The resultant mixture was stirred at room temperature for 1 h. After addition of 10 mL of brine, the mixture was extracted with ethyl acetate (10 mL x 3), and dried over anhydrous sodium sulfate. Concentration of the organic phase under vacuum and recrystallization from EtOH three times afforded the title product **13** as yellowish solid (3.83g, 84% yield).

3-Ethyl-5-methyl-4-(2-chlorophenyl)-2-((2-isothiocyanatoethoxy)methyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate (**13**)

Yellowish solid. Mp. 169-170 ^{o}C. Yield: 3.84 g, 85 %. ^{1}H NMR (400 MHz, $CDCl_3$): 7.39 (dd, *J* = 7.8 Hz, 1.5 Hz, 1H), 7.23 (dd, *J* = 7.9 Hz, 1.0 Hz, 1H), 7.17 – 7.11 (m, 1H), 7.04 (td, *J* = 7.8 Hz, 1.6 Hz, 1H), 7.00 (s, 1H), 5.41 (s, 1H), 4.79 (q, *J* = 15.7 Hz, 2H), 4.16 – 3.94 (m, 2H), 3.85 – 3.68 (m, 4H), 3.61 (s, 3H), 2.39 (s, 3H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 168.0, 167.3, 145.7, 144.4, 144.1, 135.4, 132.4, 131.6, 129.7, 127.5, 127.0, 104.2, 102.0, 69.2, 68.0, 60.0, 50.9, 45.4, 37.2, 19.7,

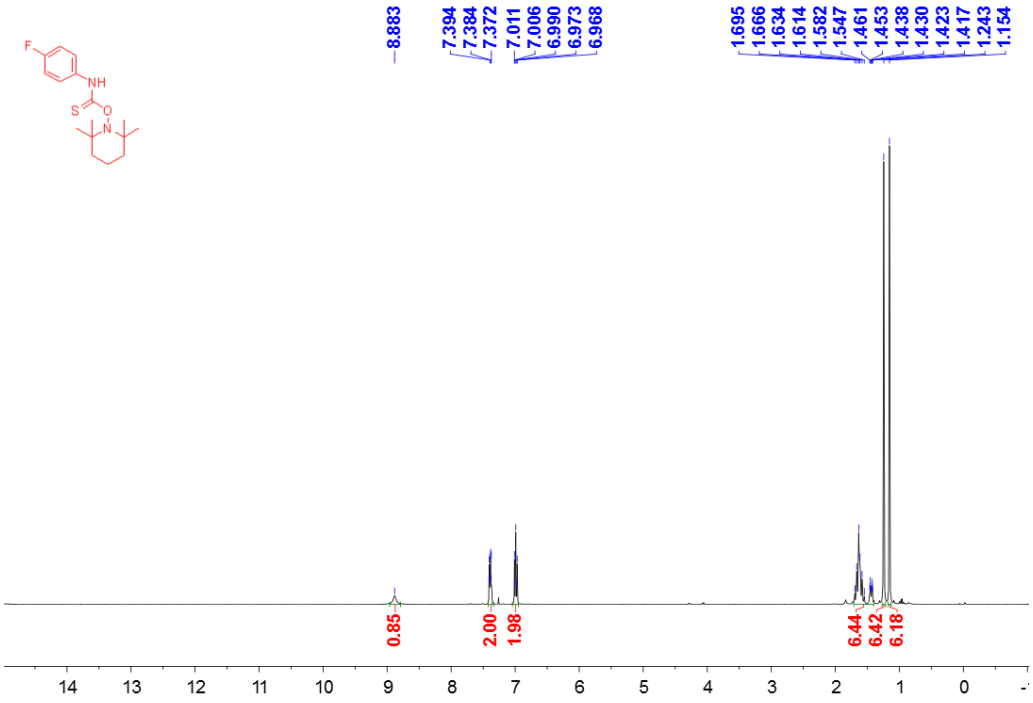
14.4, 1.1. IR (KBr, cm^{-1}): 3396, 2986, 2952, 2900, 2212, 2095, 1697, 1645, 1602, 1475, 1432, 1282, 1205, 1099, 1033, 763. HRMS (ESI) calcd. for $C_{21}H_{23}ClN_2O_5S$ ($M + H^+$) 451.1089, found 451.1087.

tert-Butyl isothiocyanate (**2ad**)

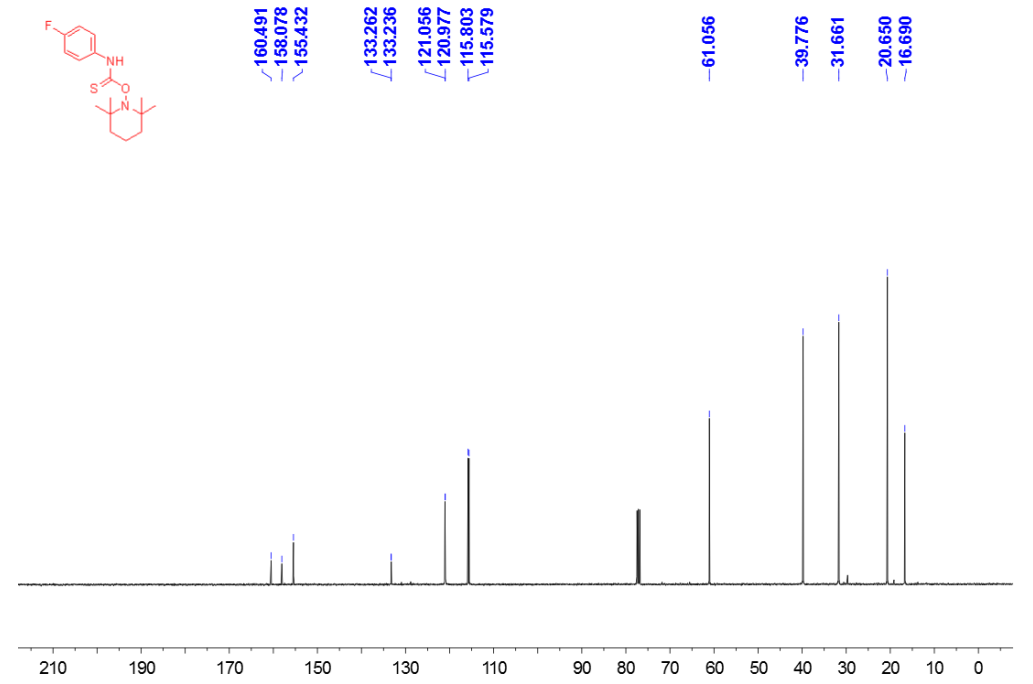
To a 100-mL flask containing 10 mL of water were sequentially added potassium carbonate (1.38 g, 10 mmol), *tert*-butyl amine **1ad** (0.73 g, 10 mmol), and CS_2 (1.8 mL, 25 mmol). The mixture was stirred at room temperature overnight, followed by slow addition of water (5 mL), potassium carbonate (1.38 g, 10 mmol), and sodium persulfate (2.38 g, 10 mmol) in an ice-water bath. The mixture was stirred at room temperature for 1 h. After addition of 5 mL of brine, the mixture was extracted with PE (5 mL x 3), and dried over anhydrous sodium sulfate. The obtained yellow solution was filtrated through a pad of silica gel under reduced pressure to give a colorless solution. Removal of the solvent under vacuum in low temperature gave the title product **2ad** as a yellowish oil (0.98g, 86% yield).

9. Copies of Spectra

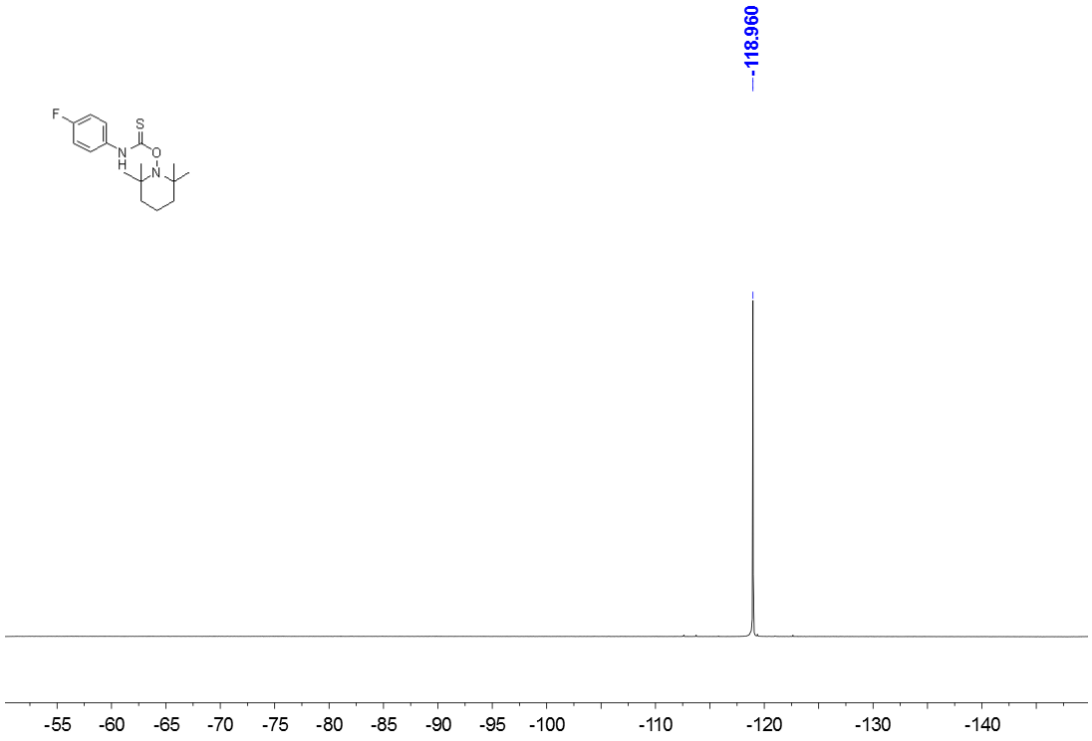
9.1. Copies of ^{1}H and ^{13}C spectra of products



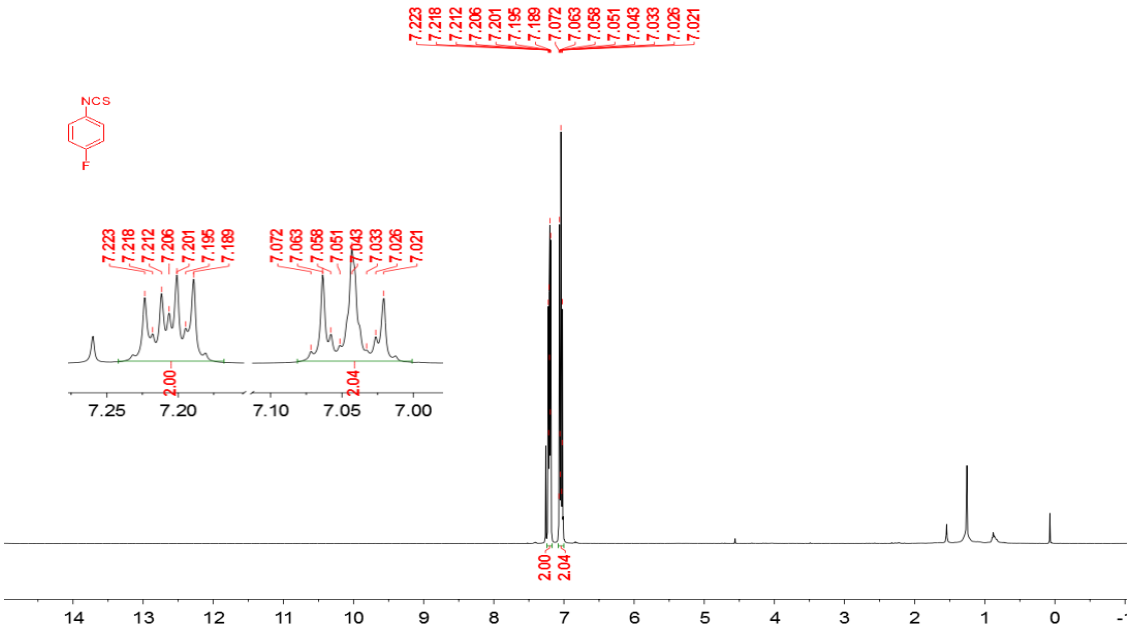
^{1}H NMR of Compound **4**



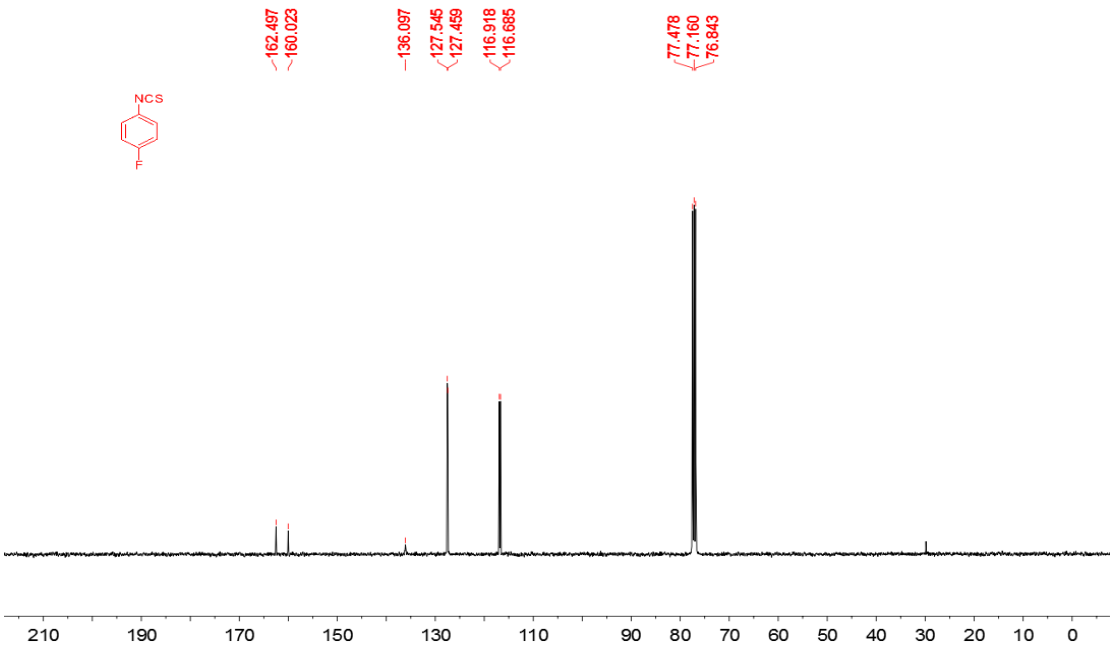
^{13}C NMR of Compound **4**



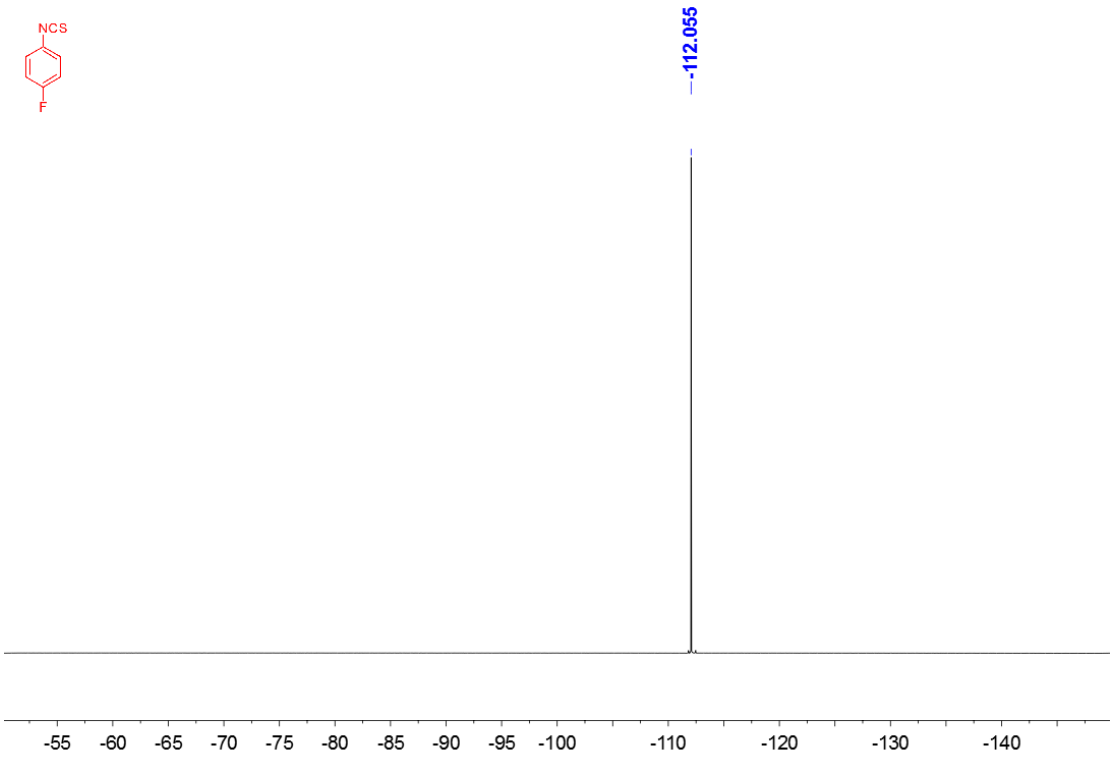
^{19}F NMR of Compound **4**



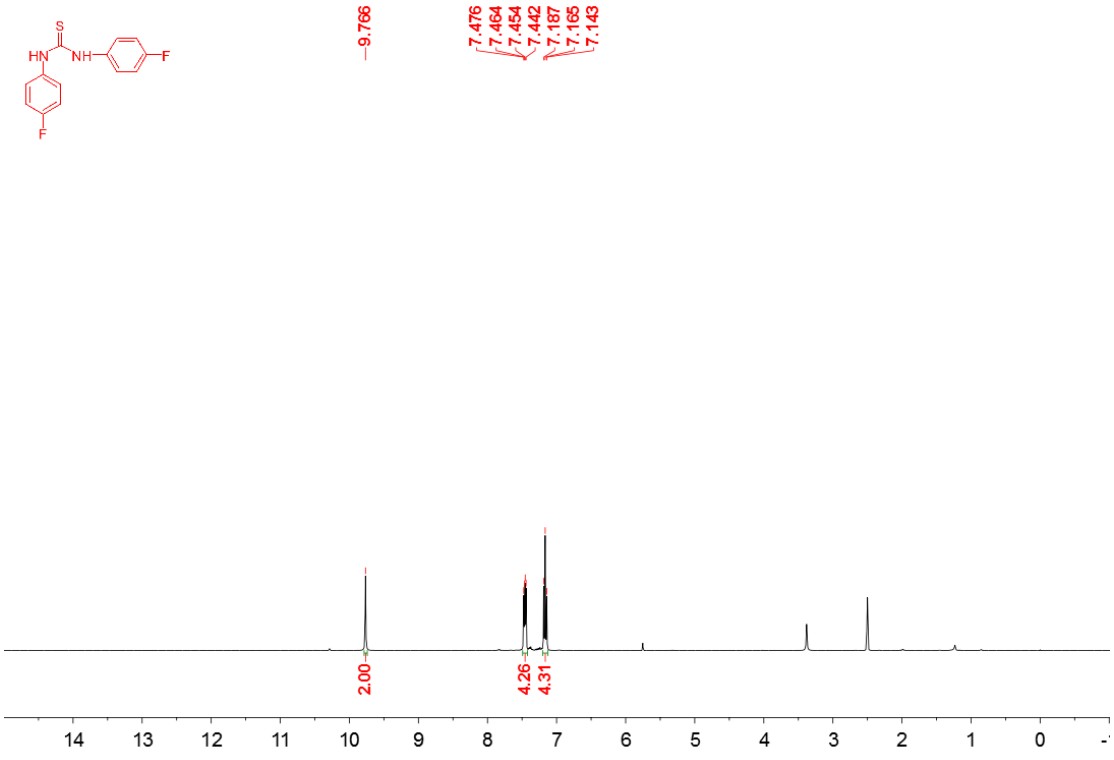
^{1}H NMR of Compound **2a**



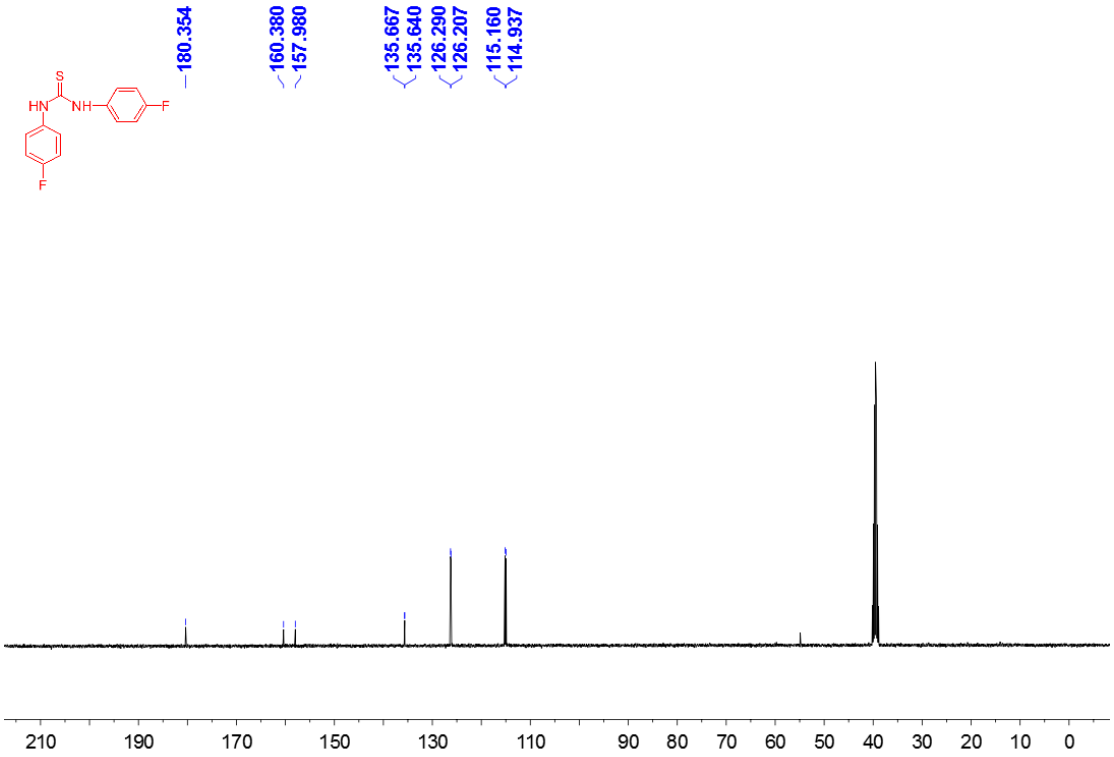
^{13}C NMR of Compound **2a**



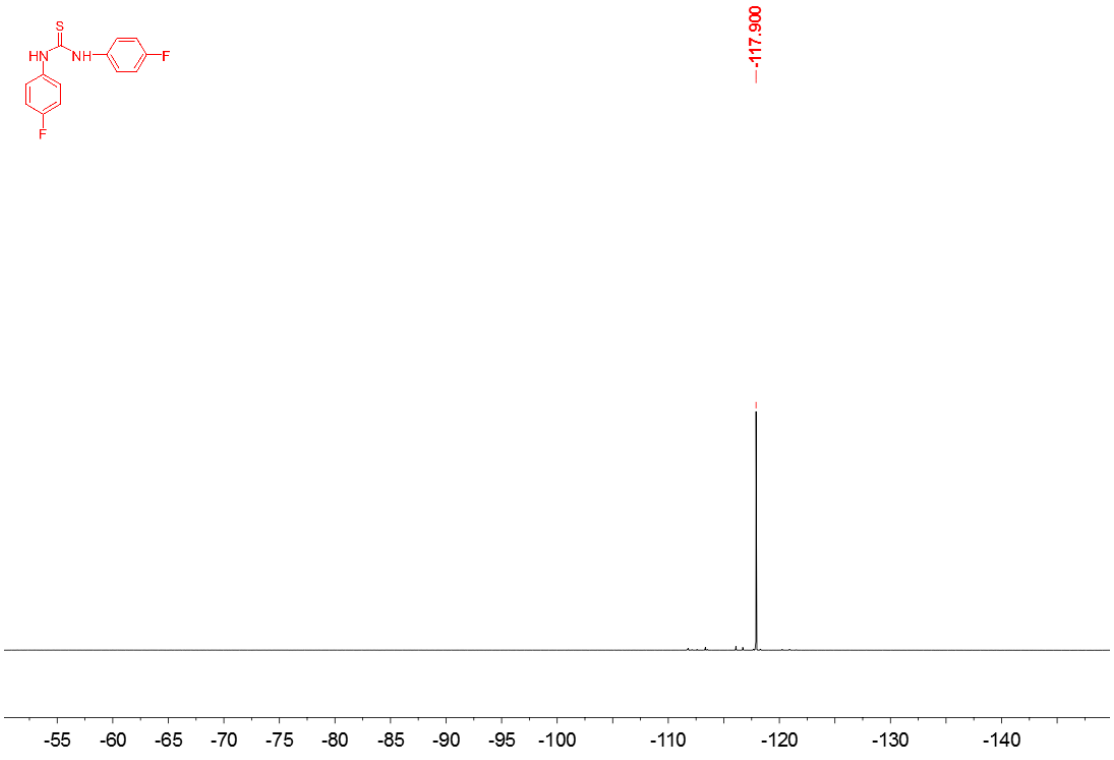
^{19}F NMR of Compound **2a**



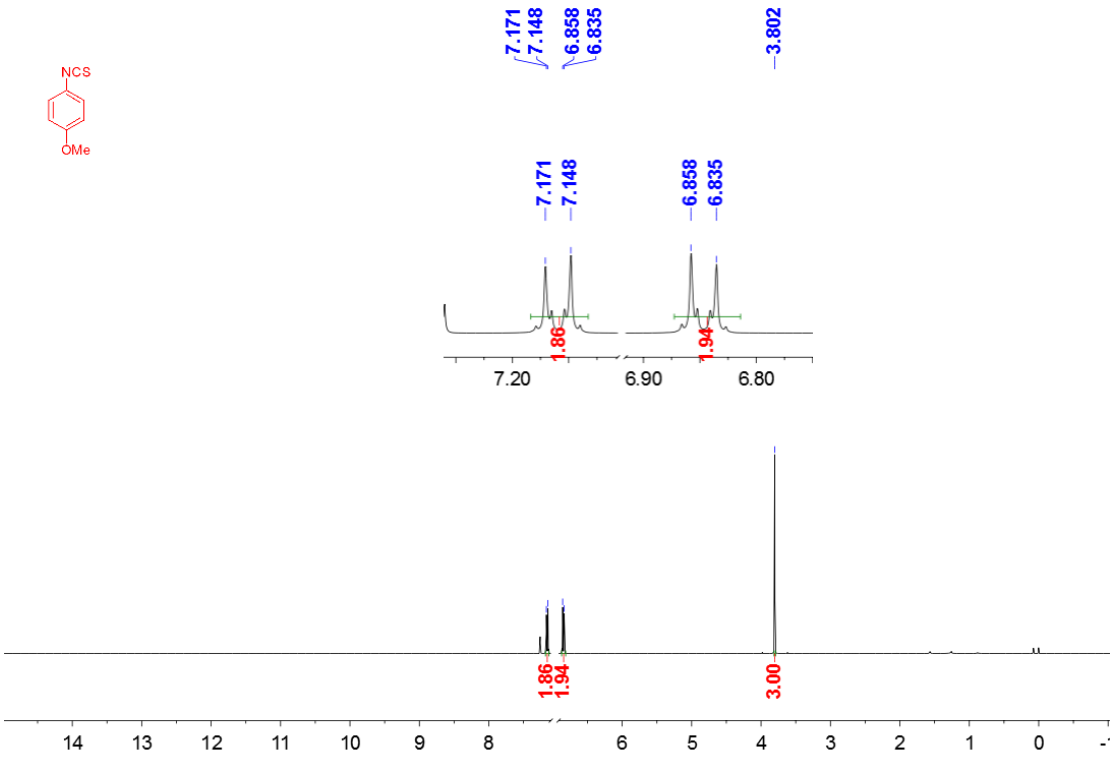
^{1}H NMR of Compound **3a**



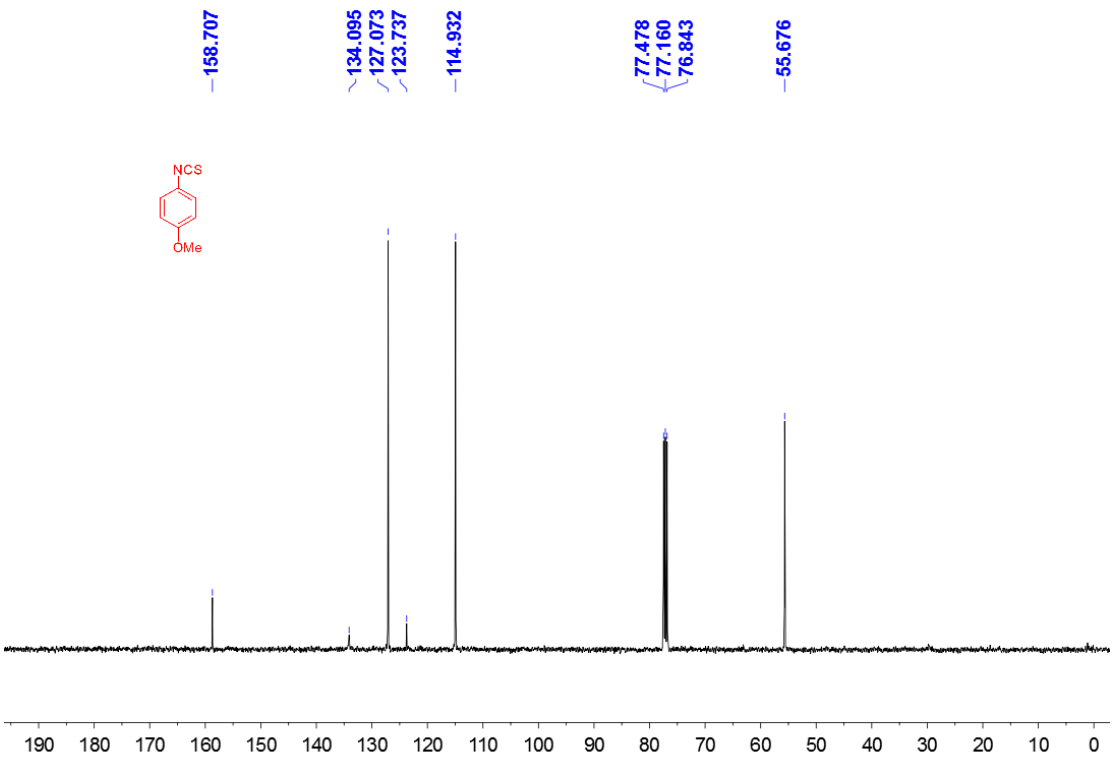
^{13}C NMR of Compound **3a**



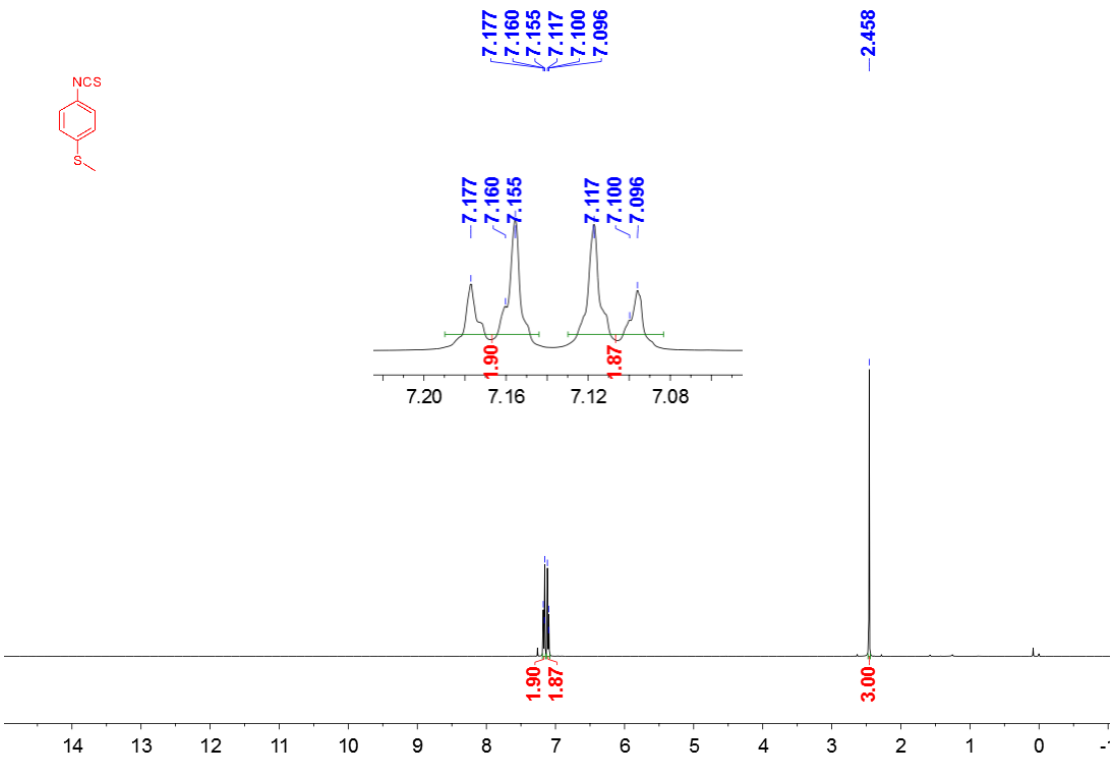
^{19}F NMR of Compound **3a**



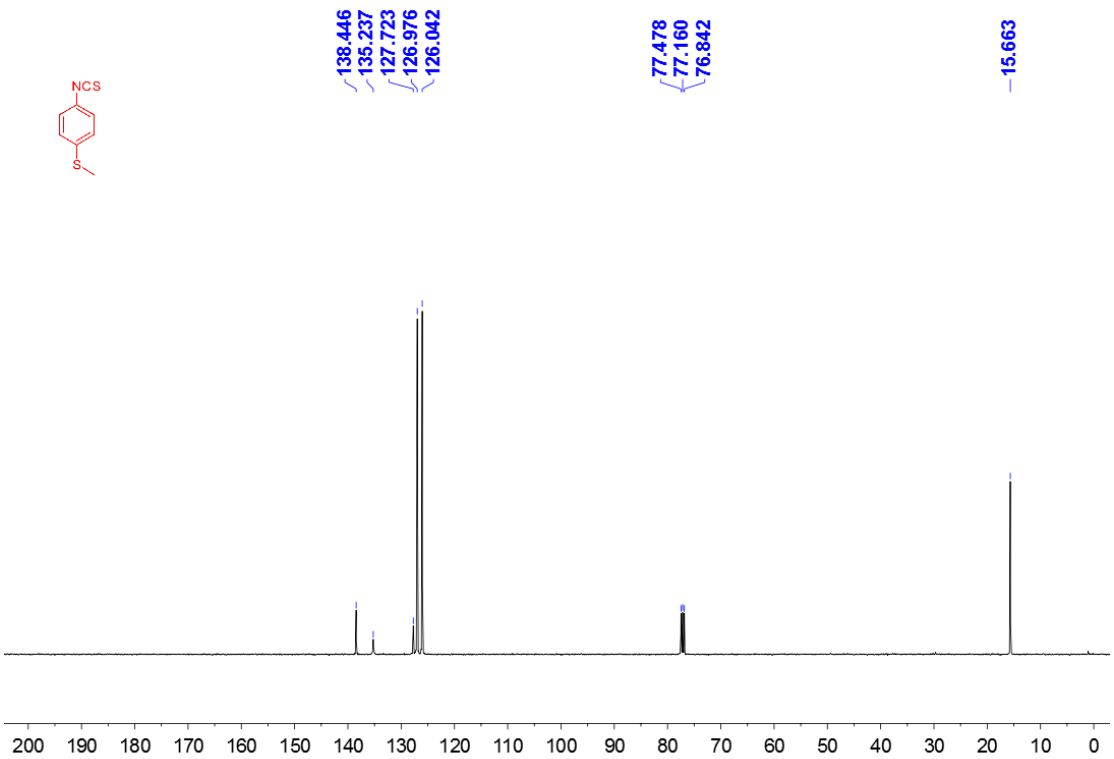
^{1}H NMR of Compound **2b**



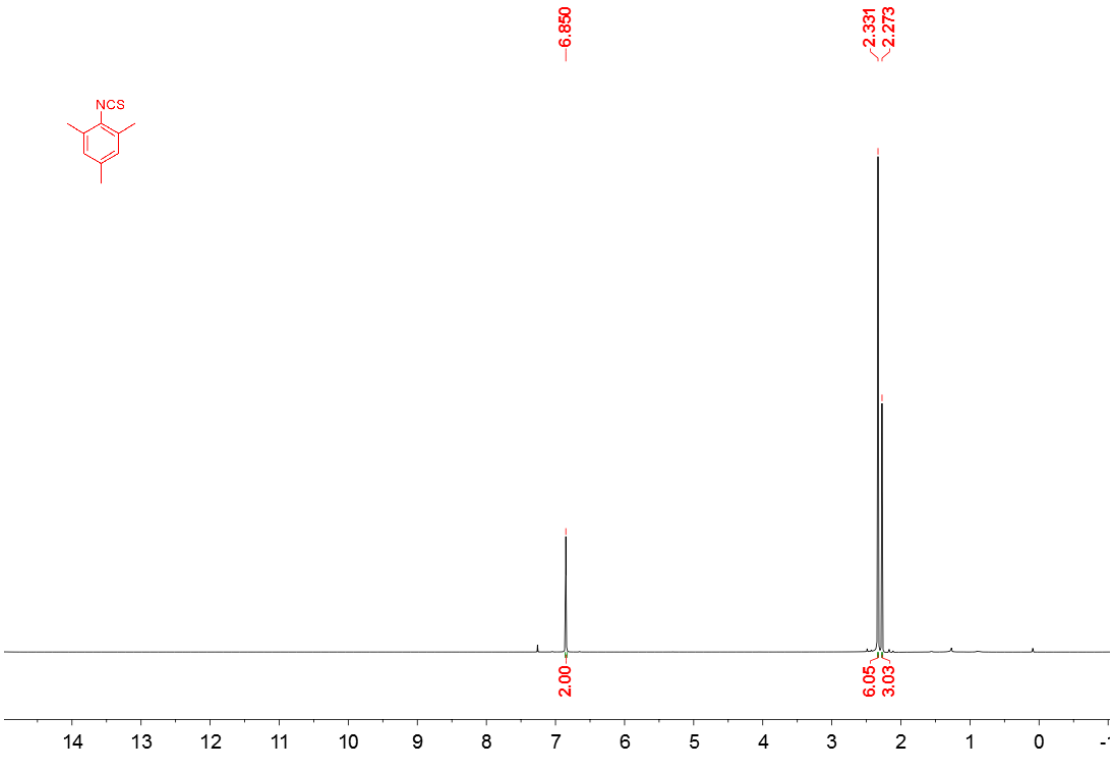
^{13}C NMR of Compound **2b**



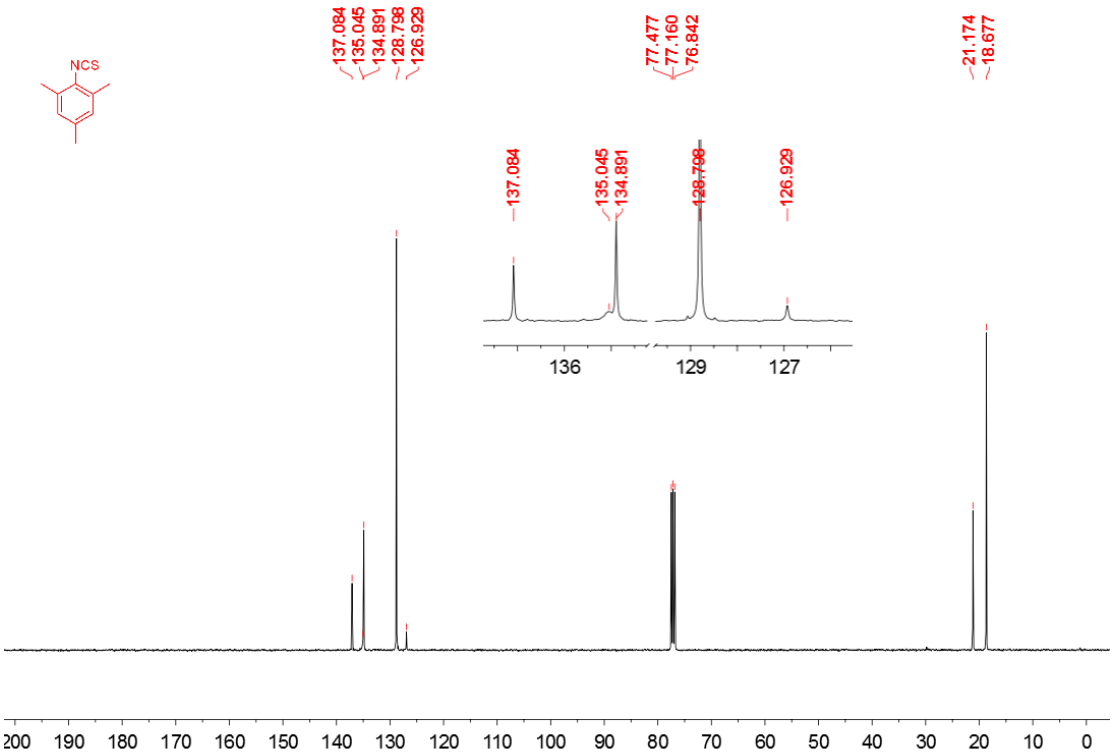
^{1}H NMR of Compound **2c**



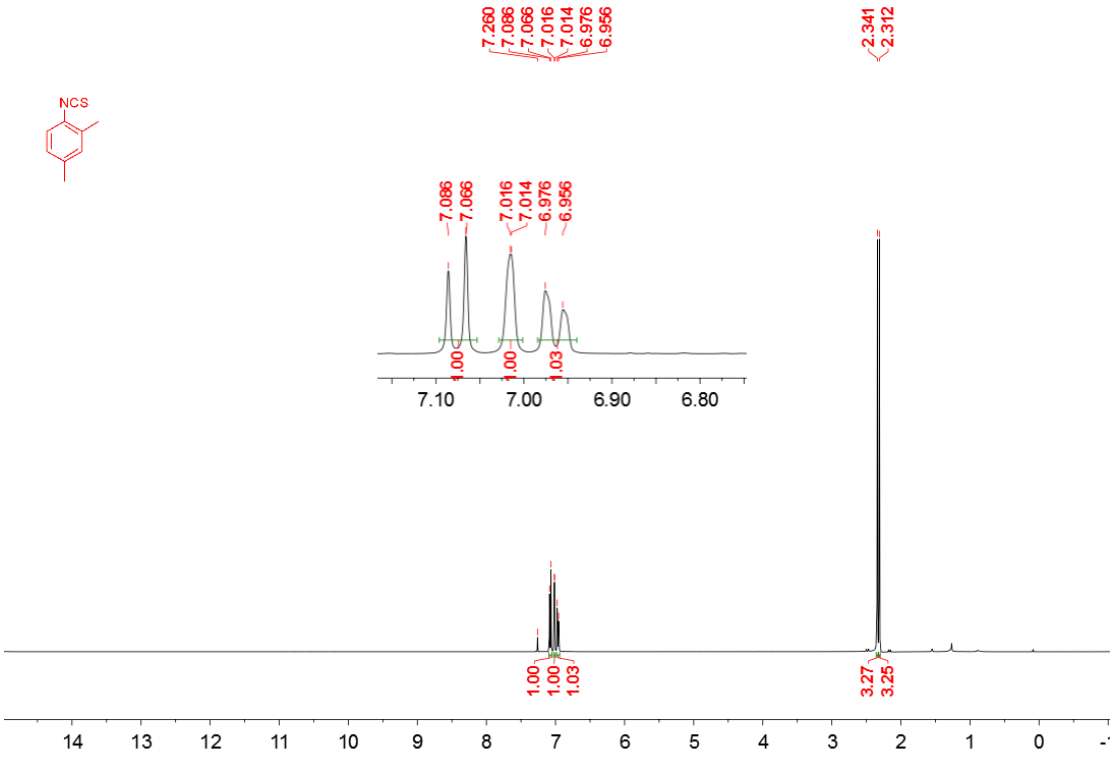
^{13}C NMR of Compound **2c**



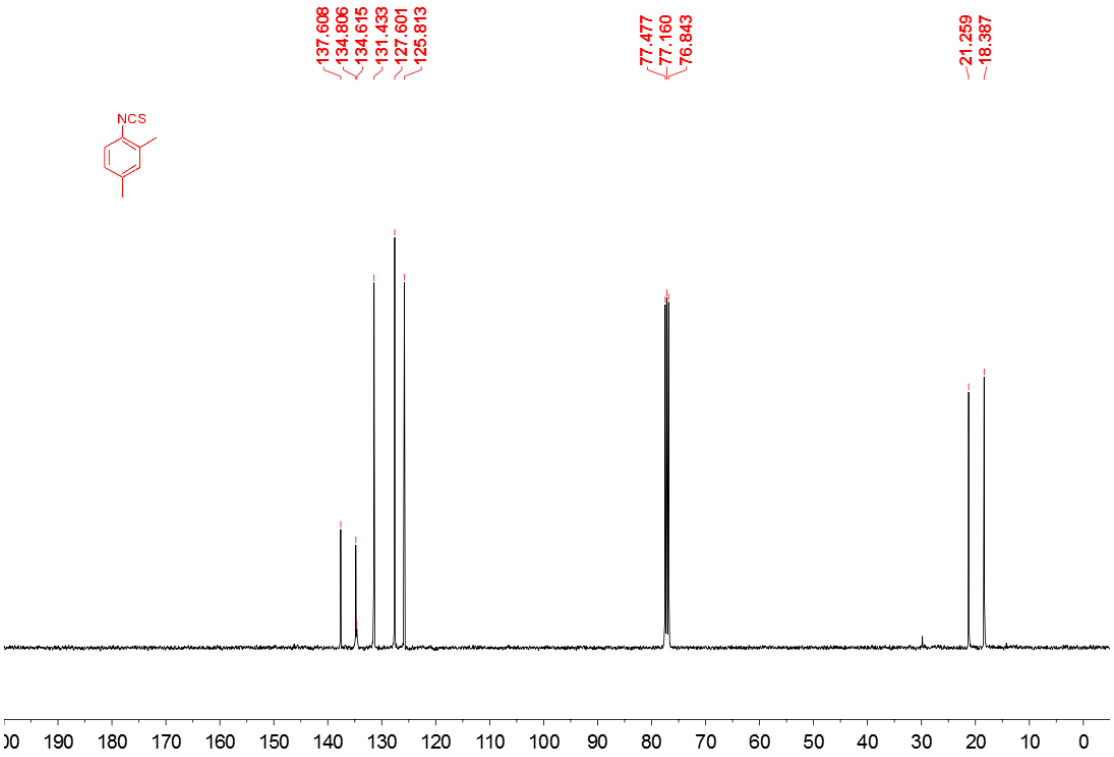
^{1}H NMR of Compound **2d**



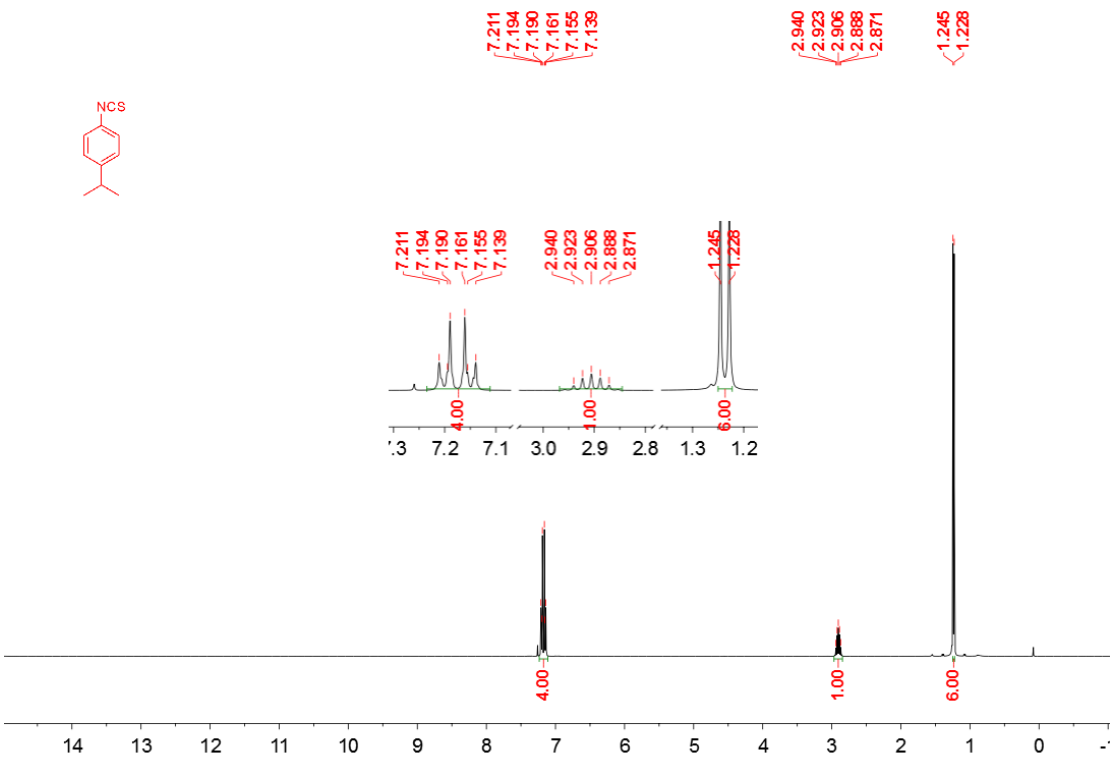
^{13}C NMR of Compound **2d**



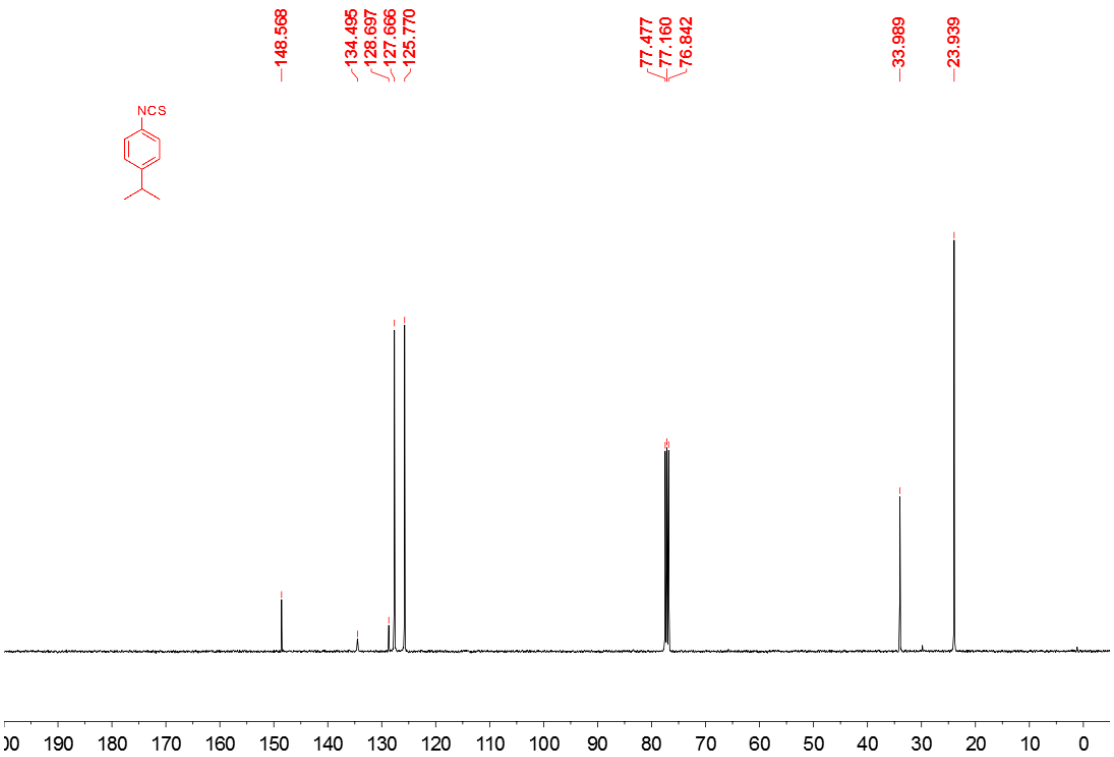
^{1}H NMR of Compound **2e**



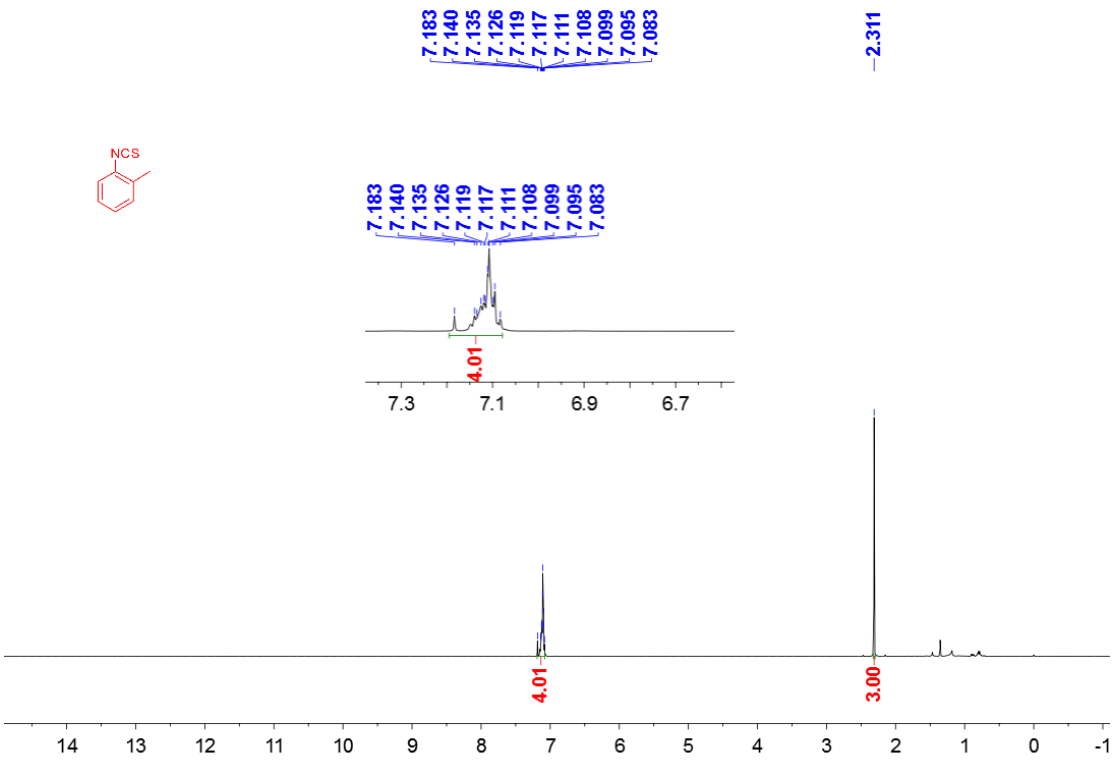
^{13}C NMR of Compound **2e**



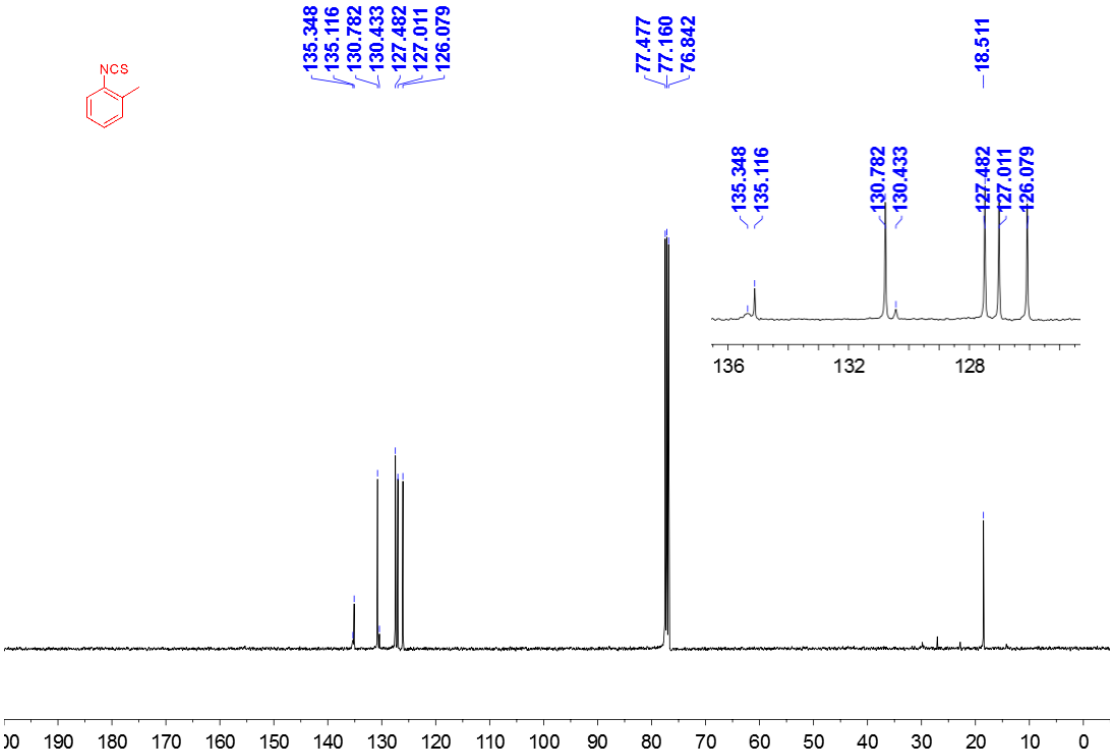
^{1}H NMR of Compound **2f**



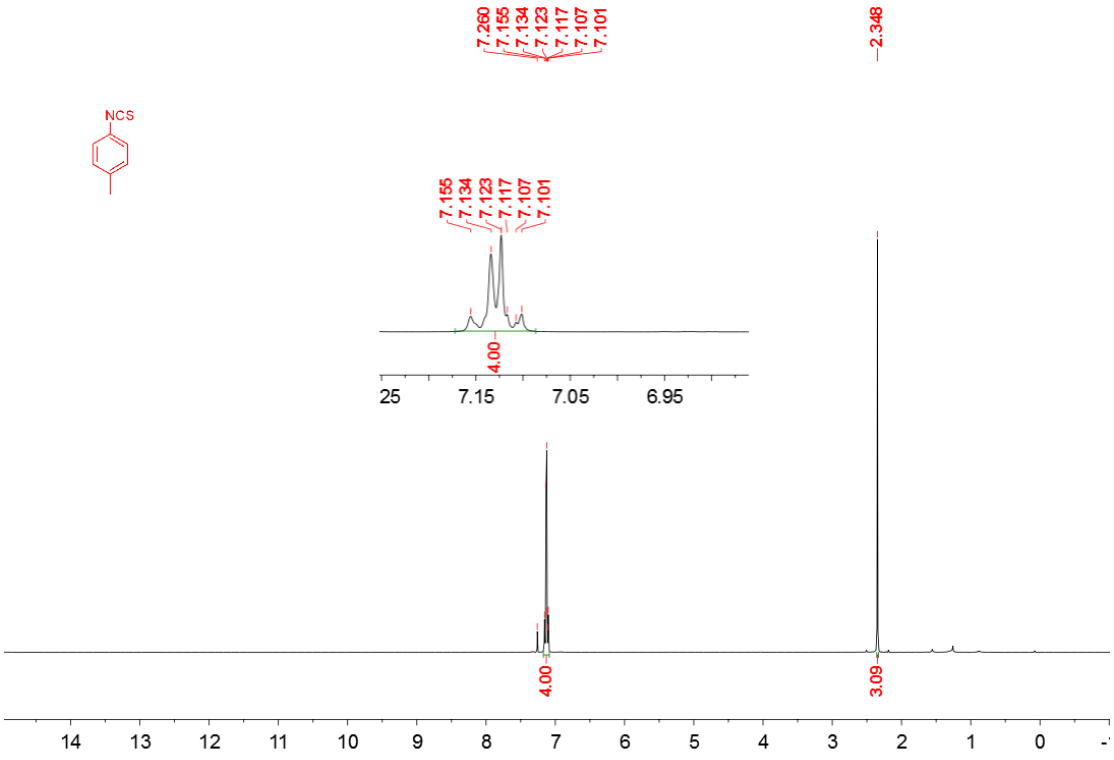
^{13}C NMR of Compound **2f**



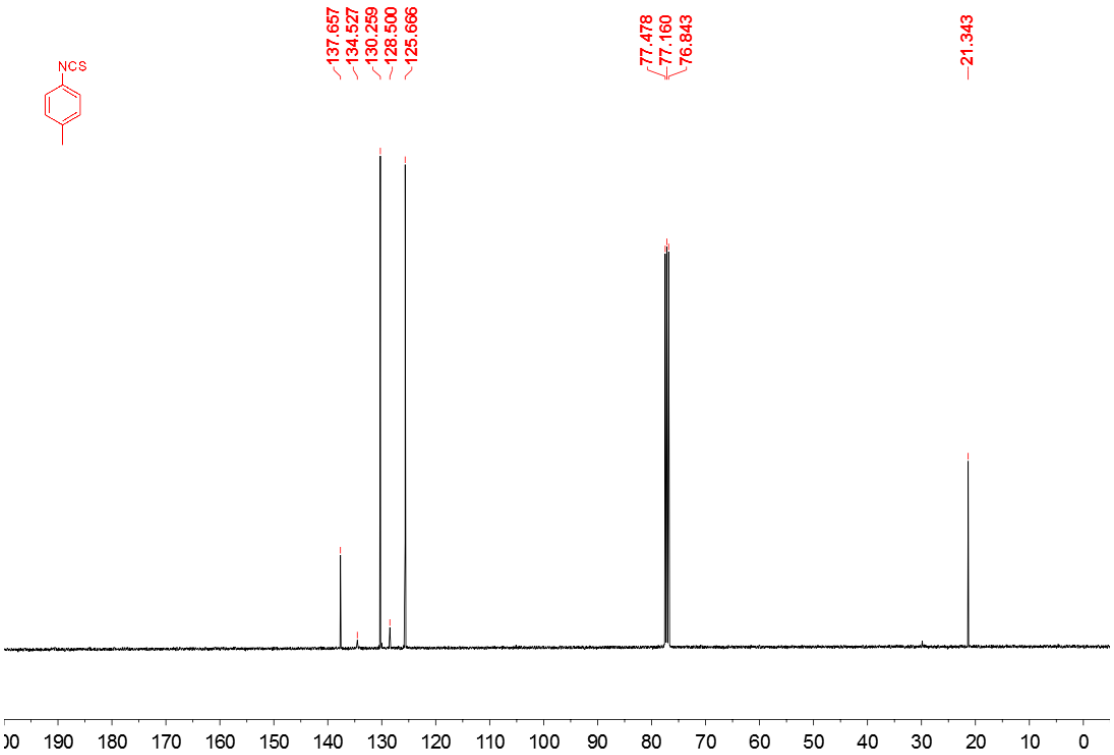
^{1}H NMR of Compound **2g**



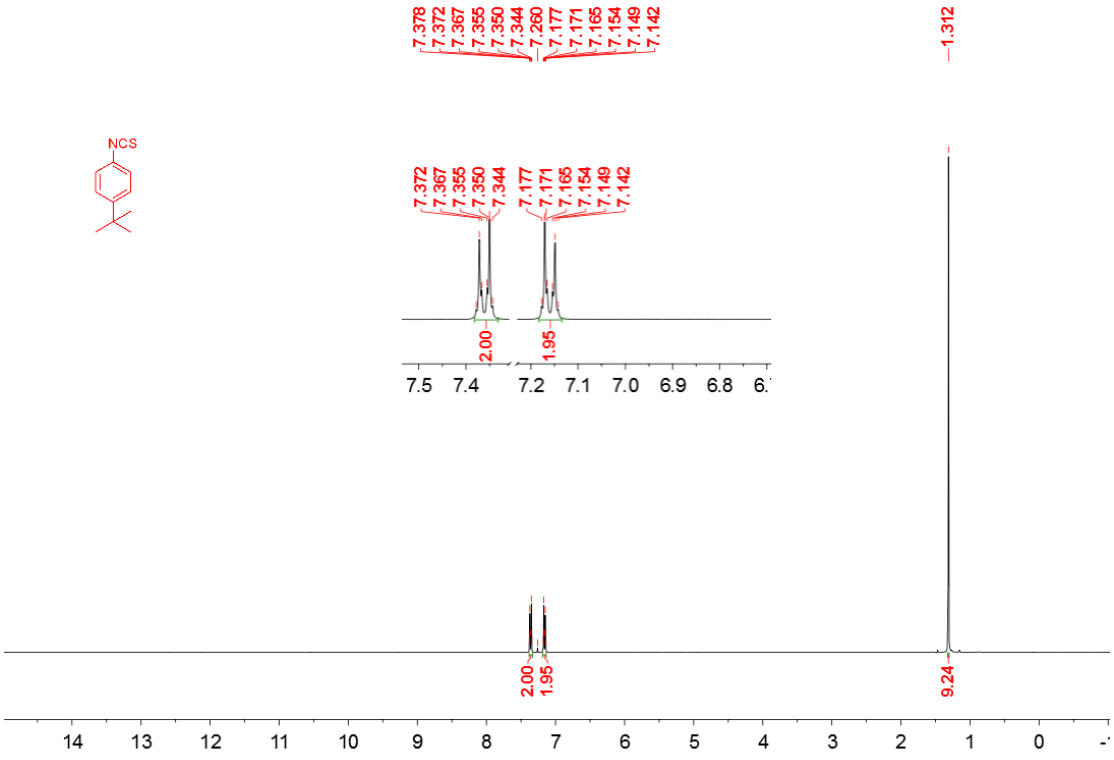
^{13}C NMR of Compound **2g**



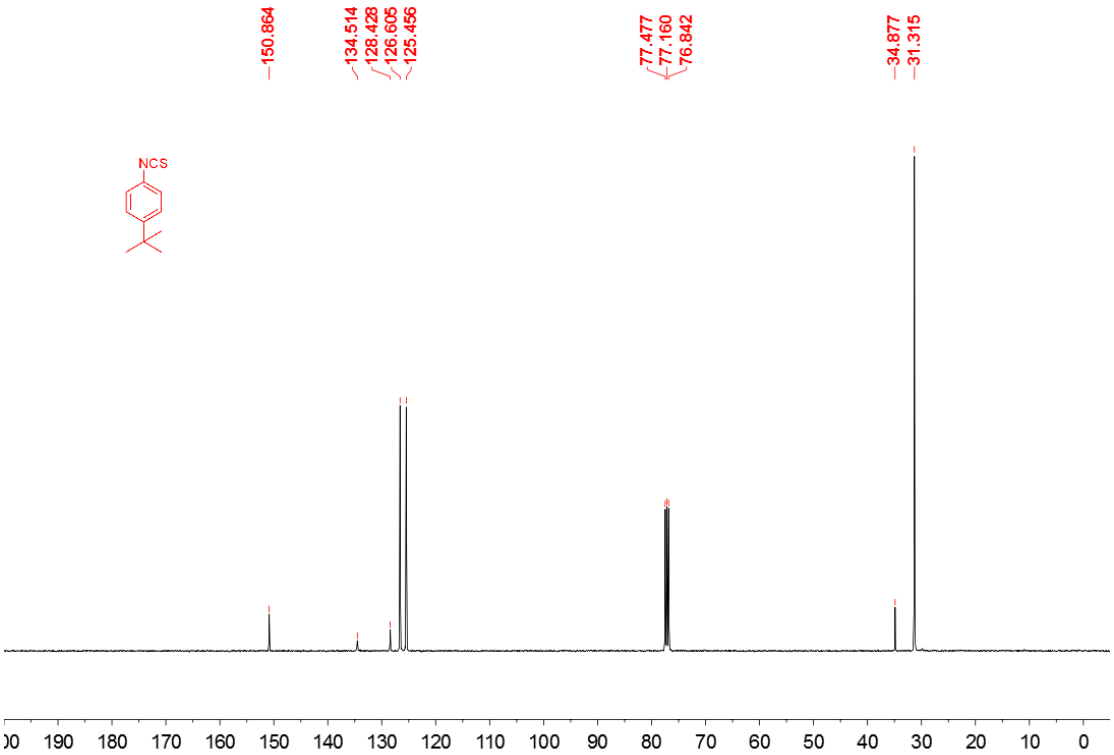
^{1}H NMR of Compound **2h**



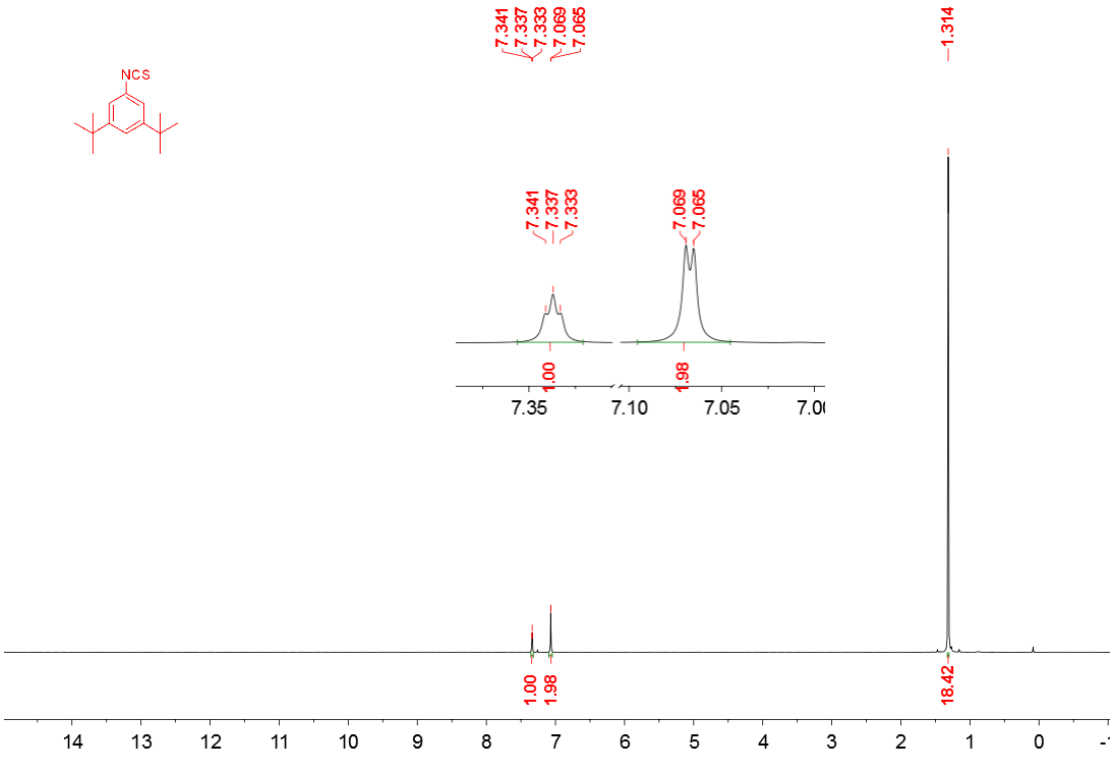
^{13}C NMR of Compound **2h**



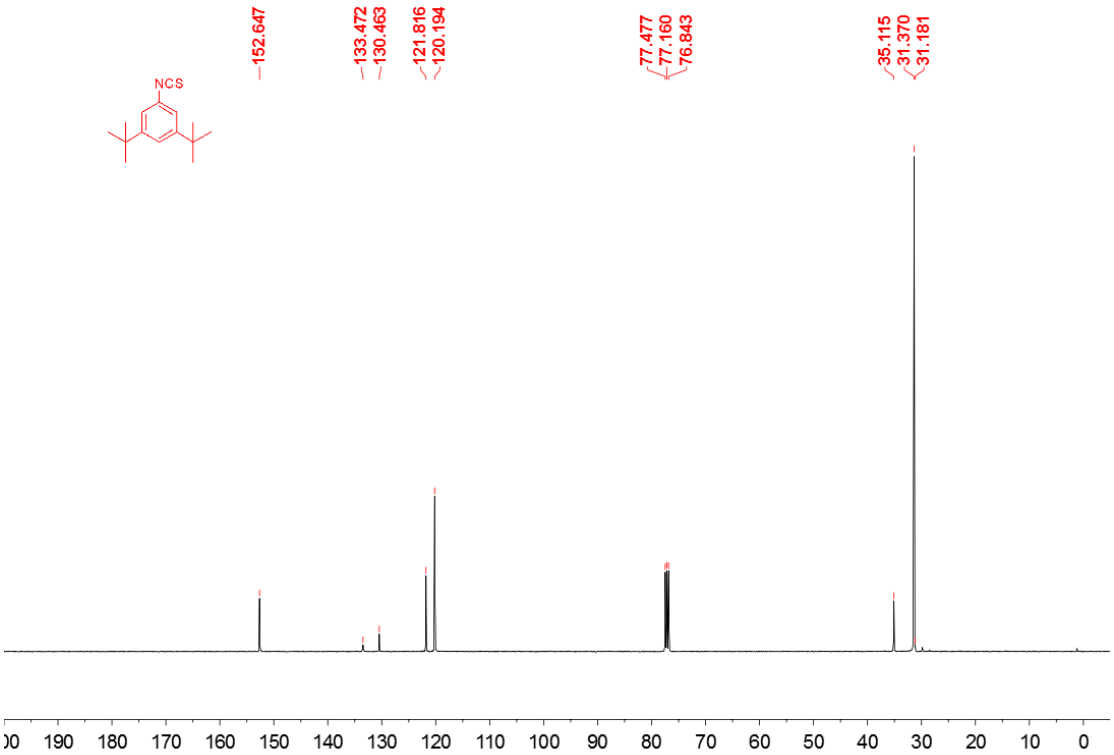
^{1}H NMR of Compound **2i**



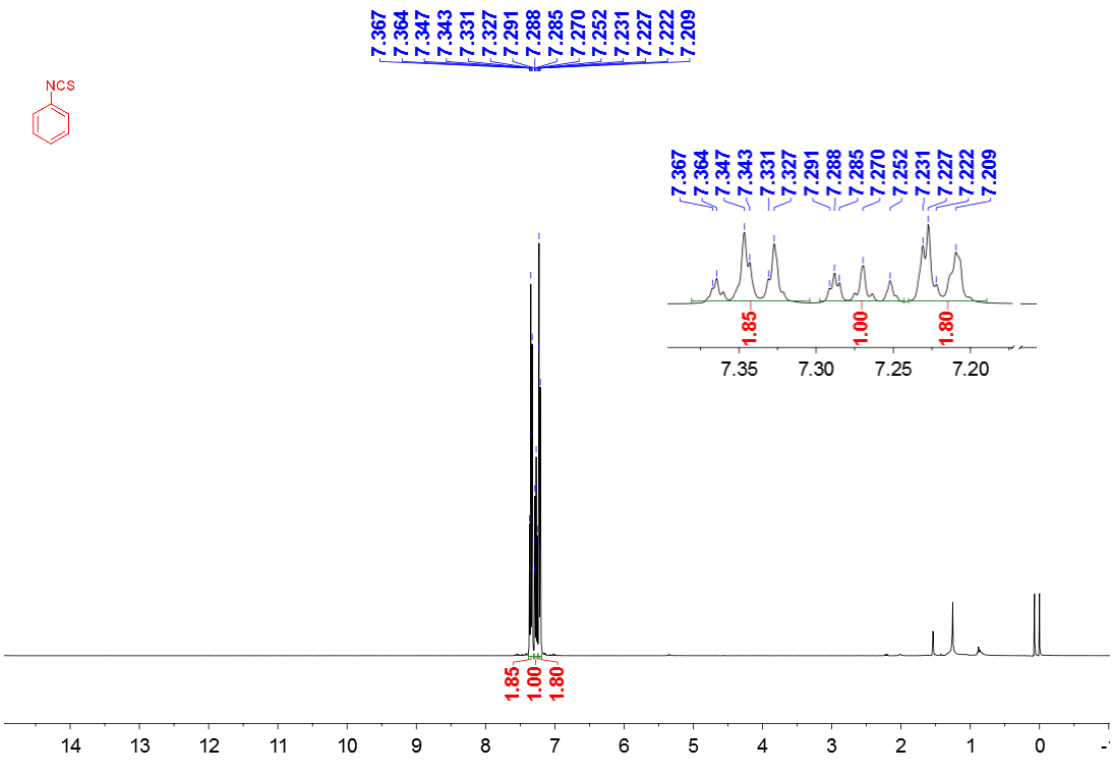
^{13}C NMR of Compound **2i**



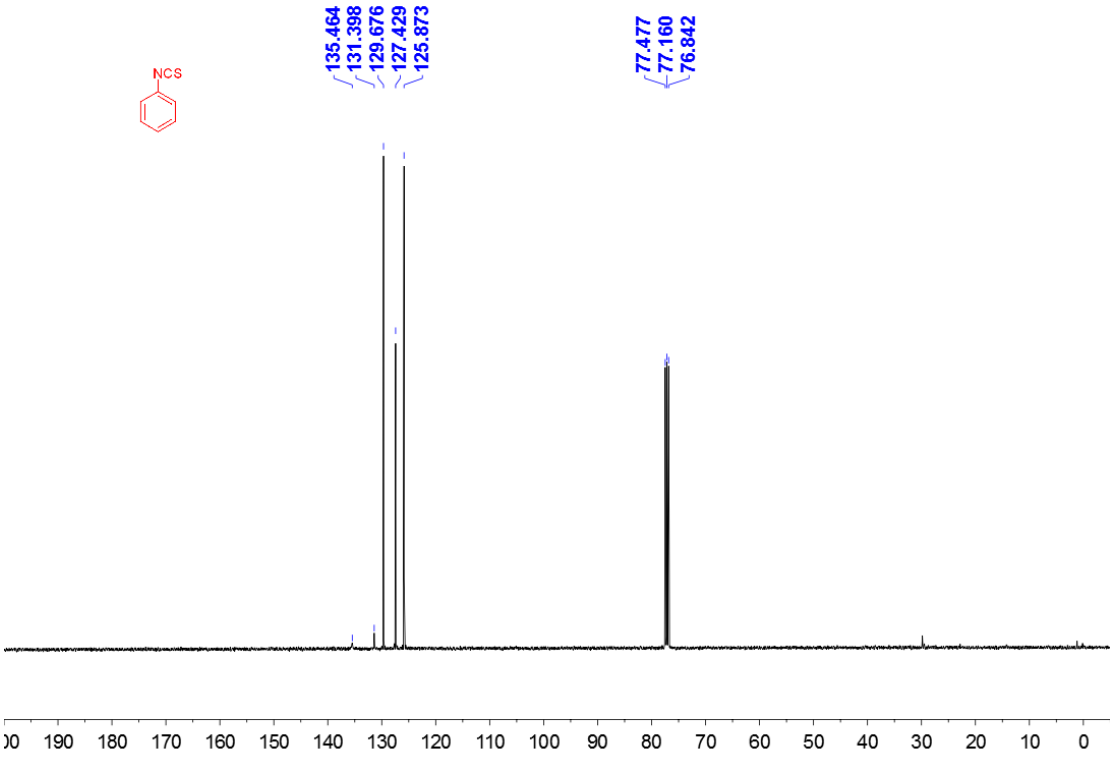
^{1}H NMR of Compound **2j**



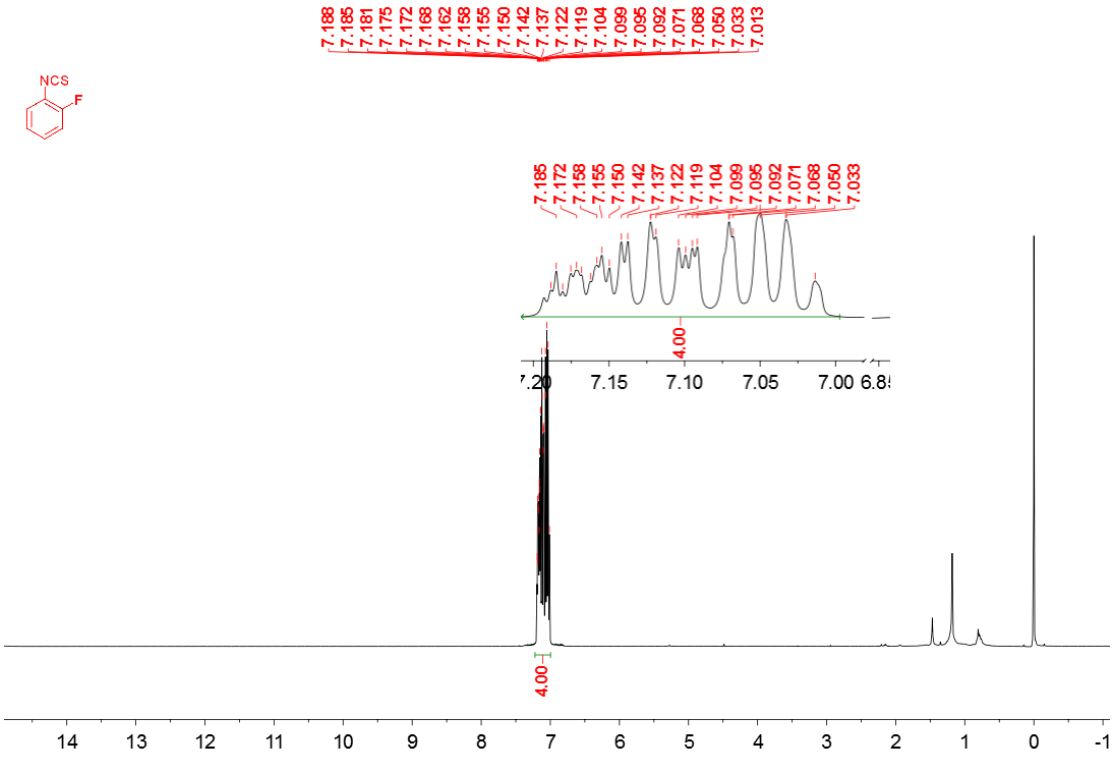
^{13}C NMR of Compound **2j**



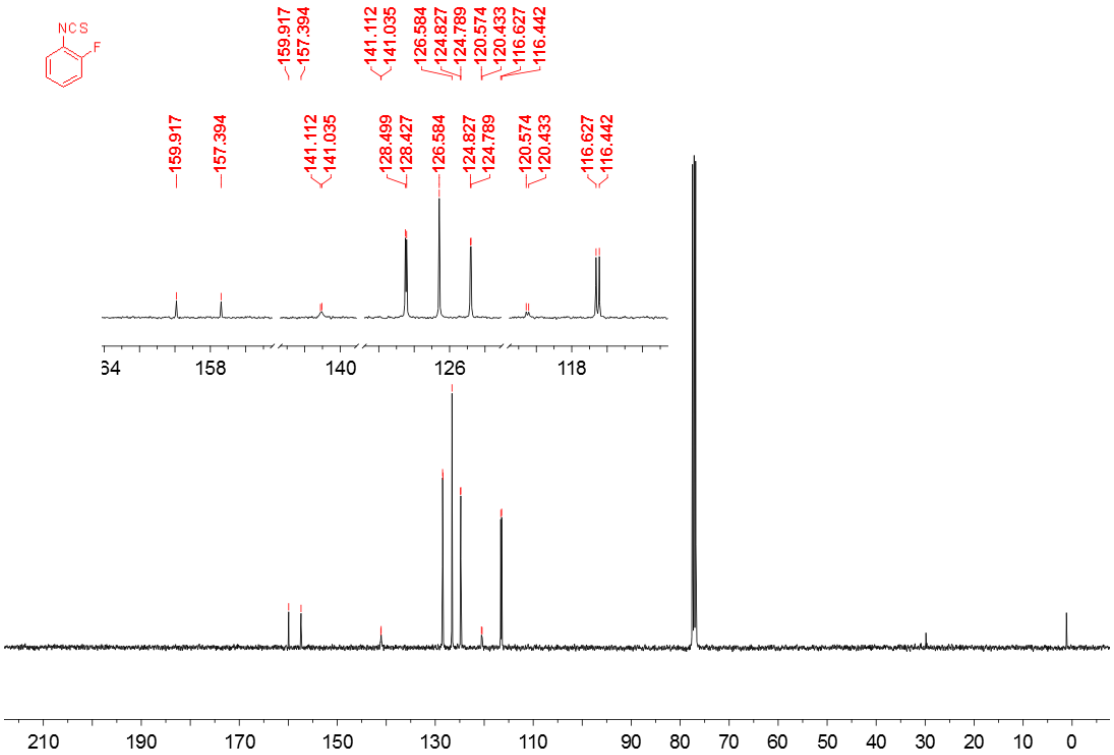
^{1}H NMR of Compound **2k**



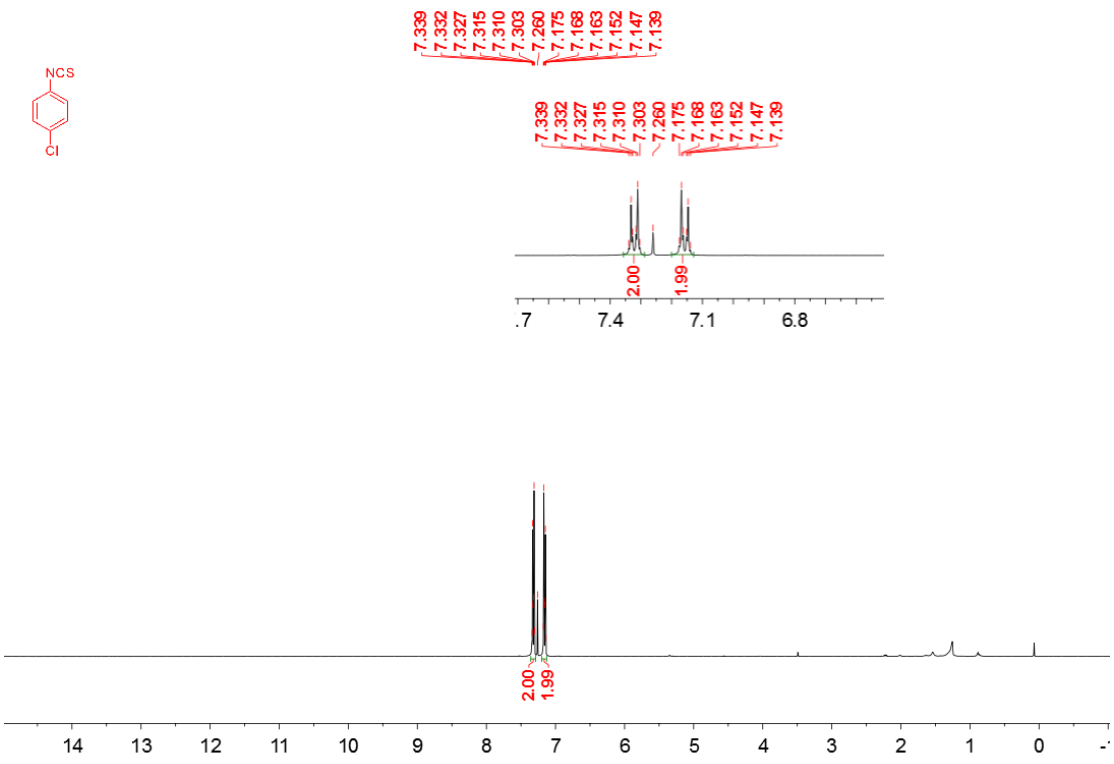
^{13}C NMR of Compound **2k**



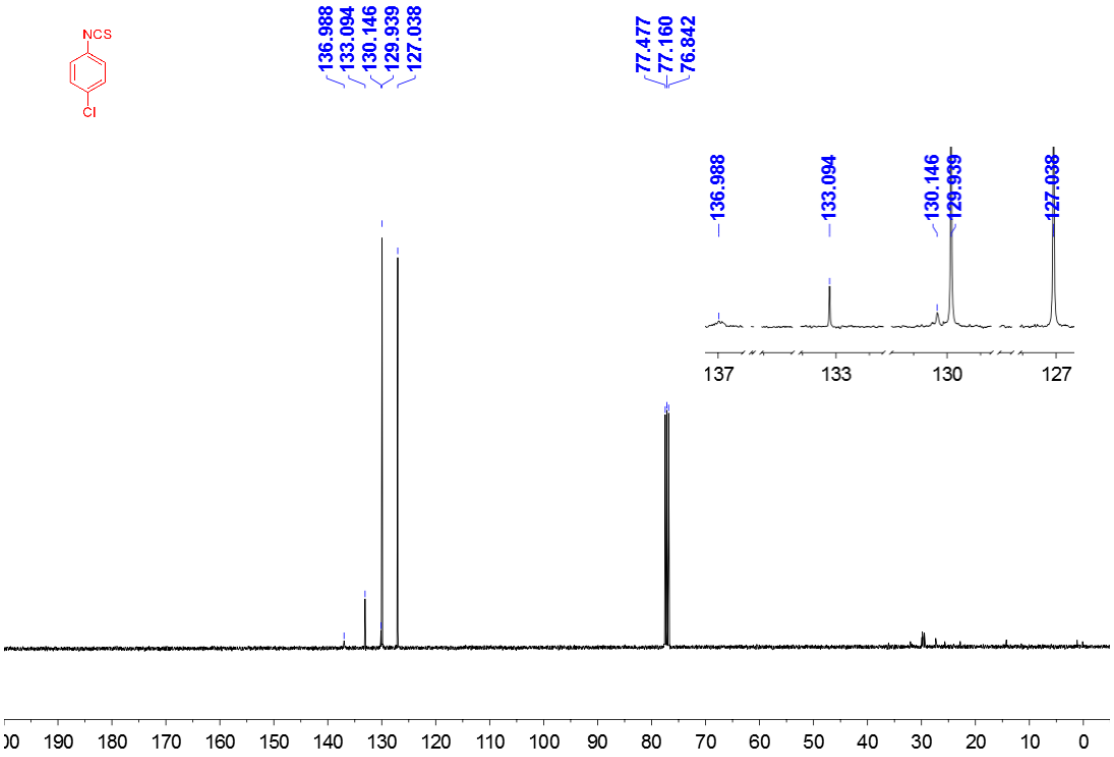
^{1}H NMR of Compound **2l**



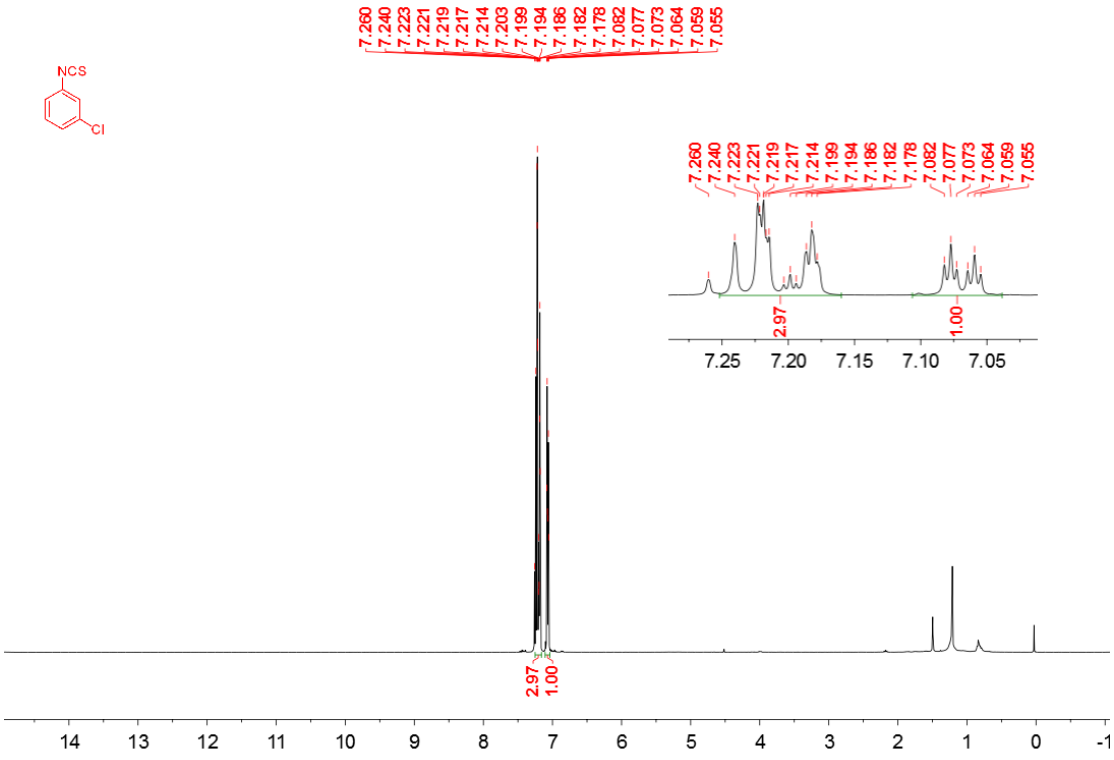
^{13}C NMR of Compound **2l**



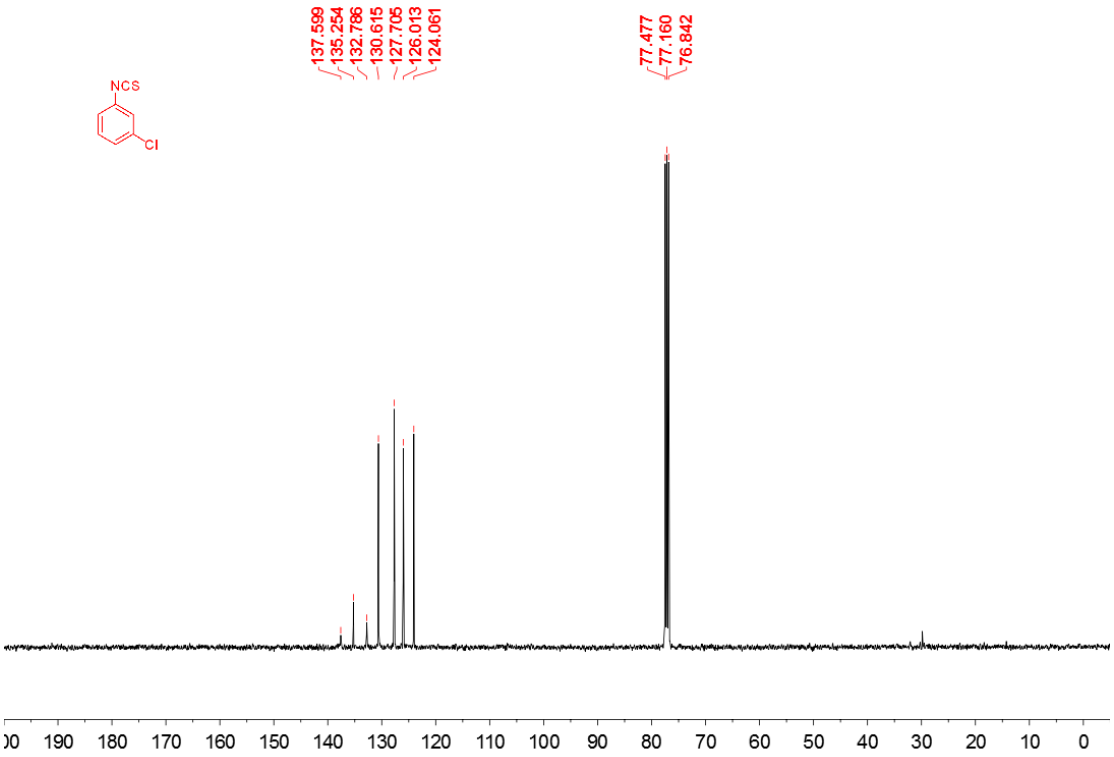
^{1}H NMR of Compound **2m**



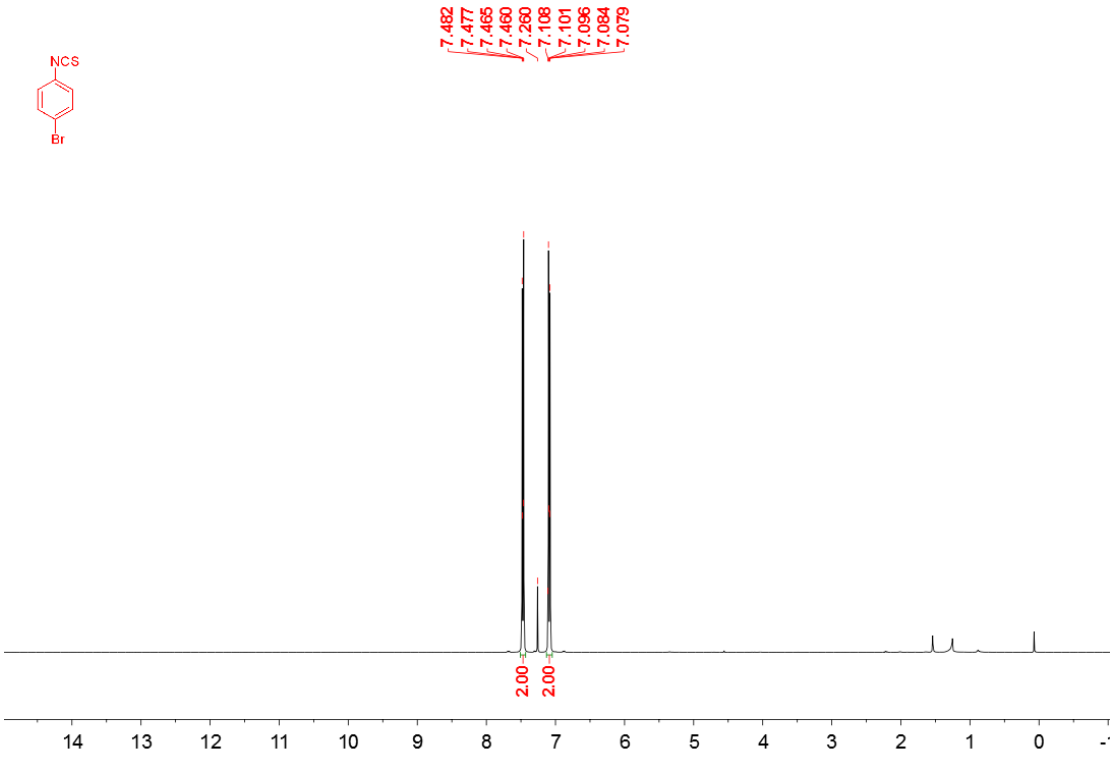
^{13}C NMR of Compound **2m**



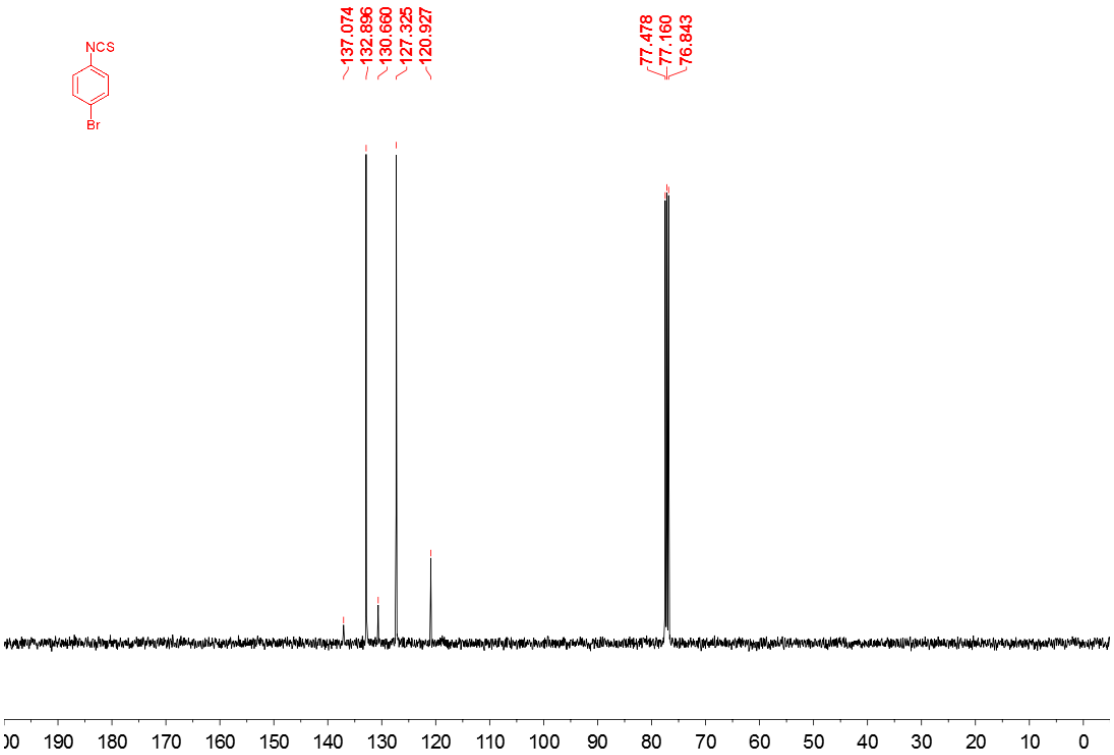
^{1}H NMR of Compound **2n**



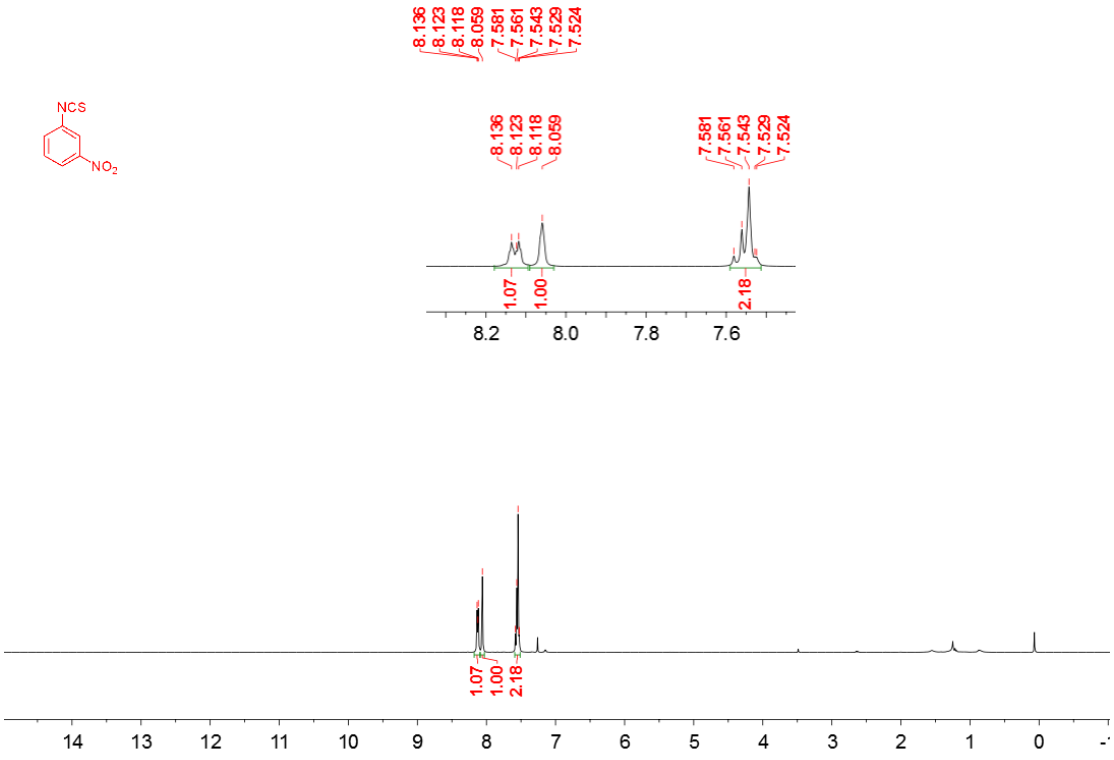
^{13}C NMR of Compound **2n**



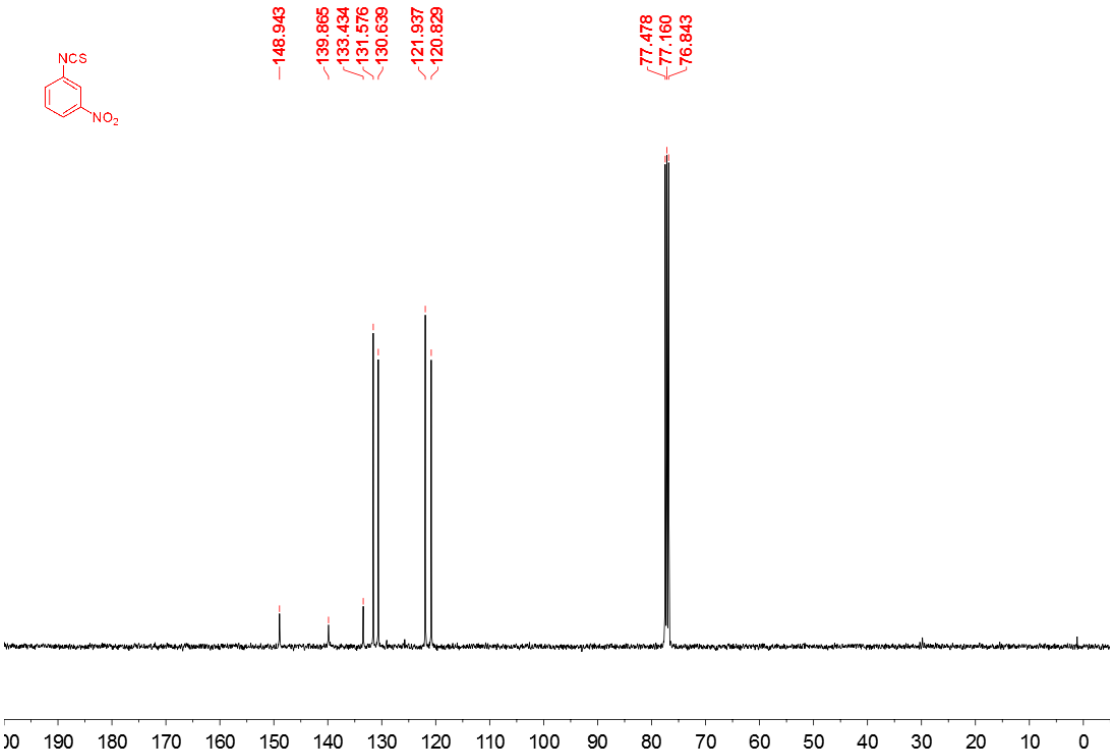
^{1}H NMR of Compound **2o**



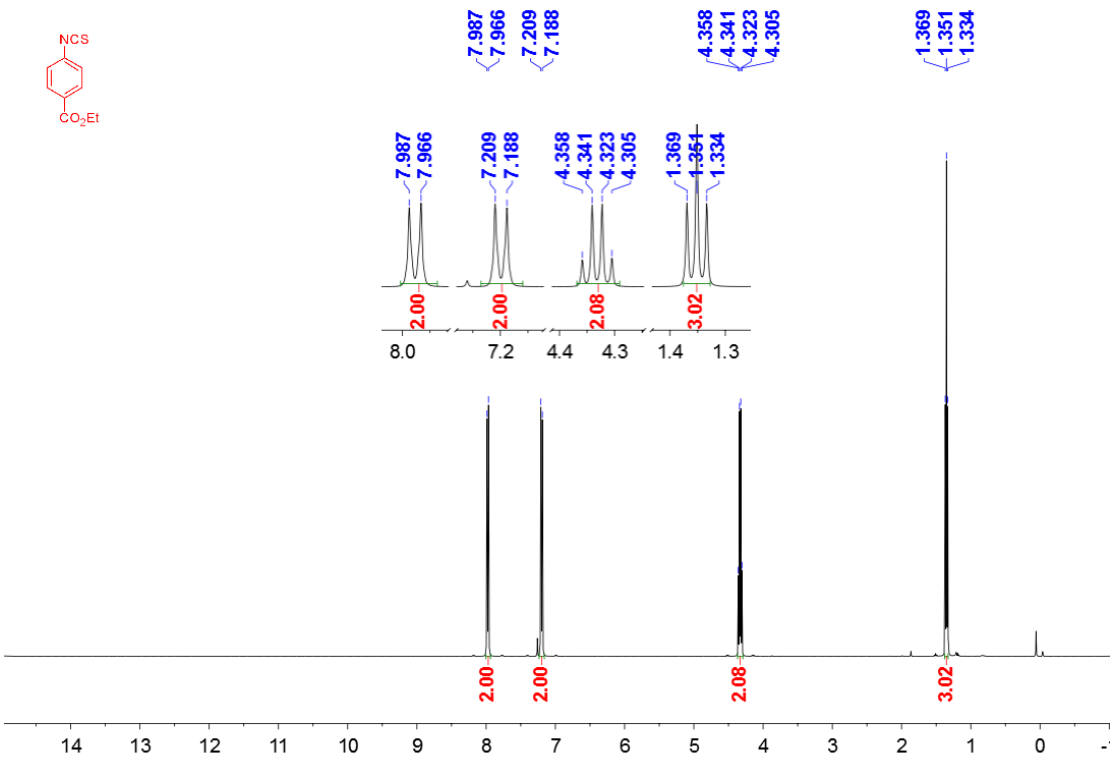
^{13}C NMR of Compound **2o**



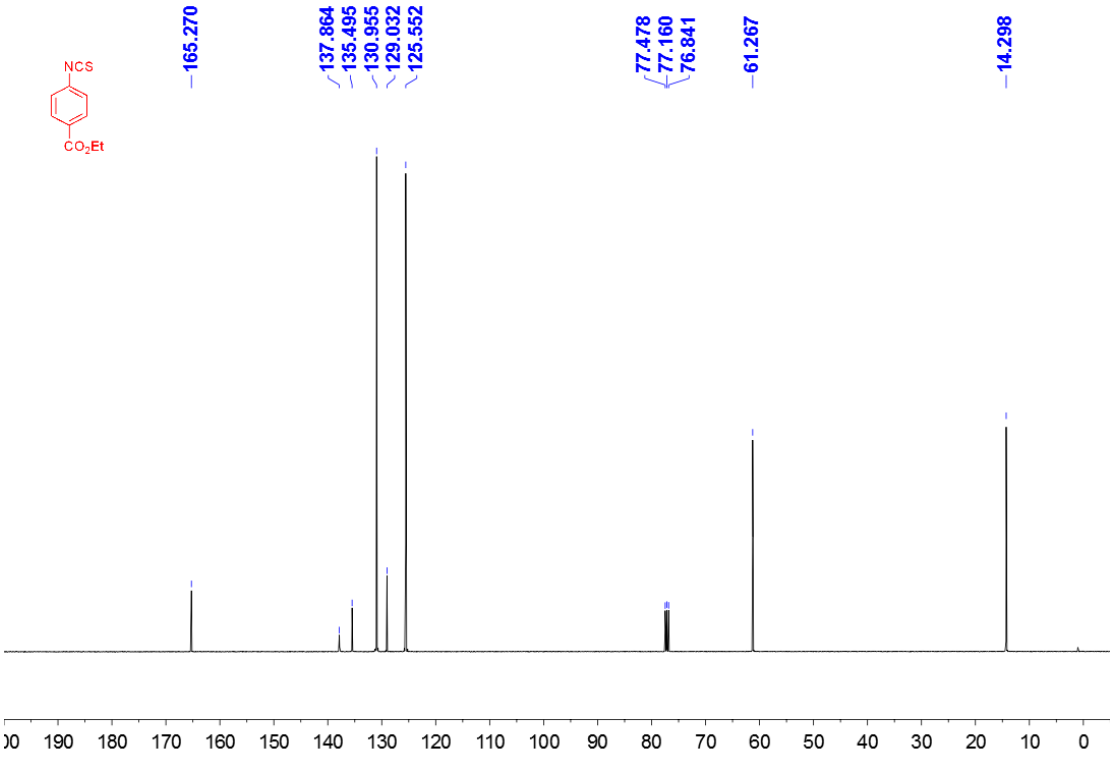
^{1}H NMR of Compound **2p**



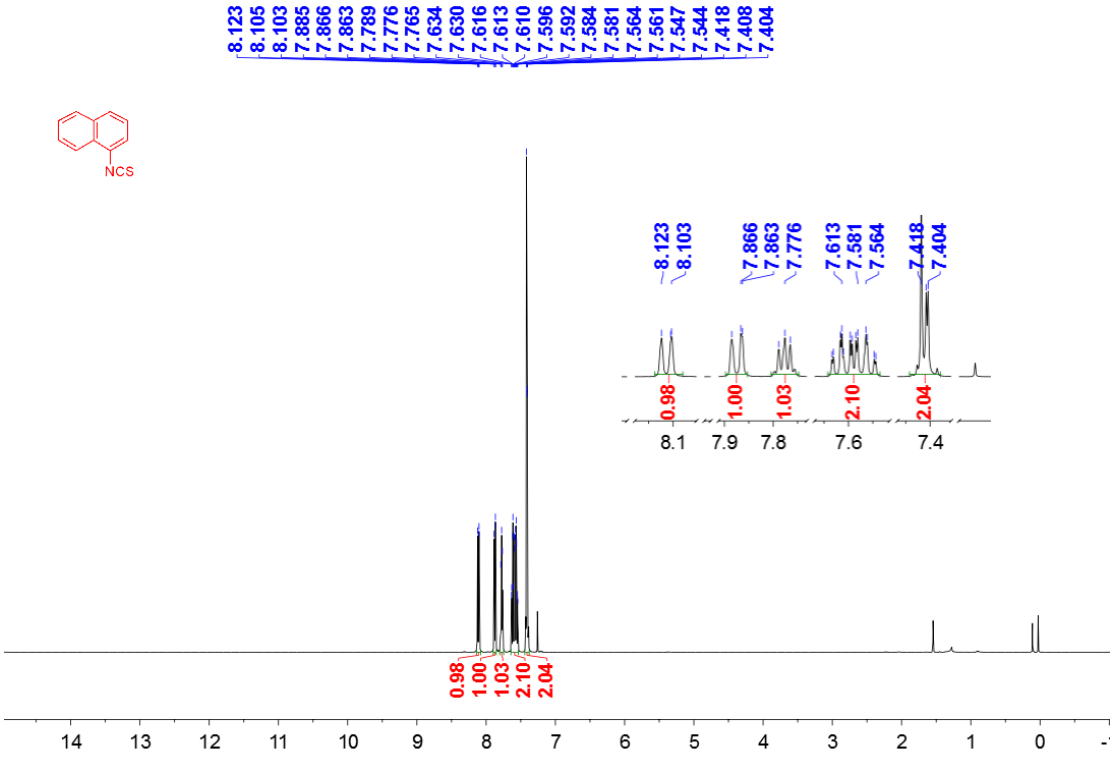
^{13}C NMR of Compound **2p**



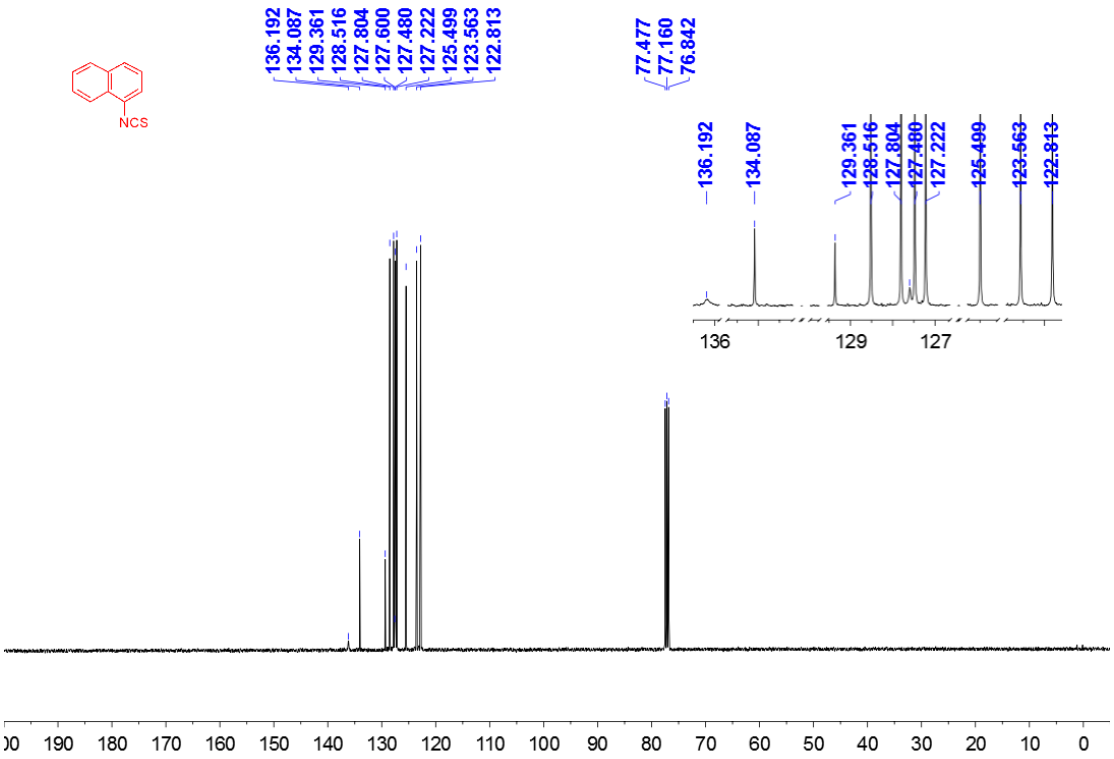
^{1}H NMR of Compound **2q**



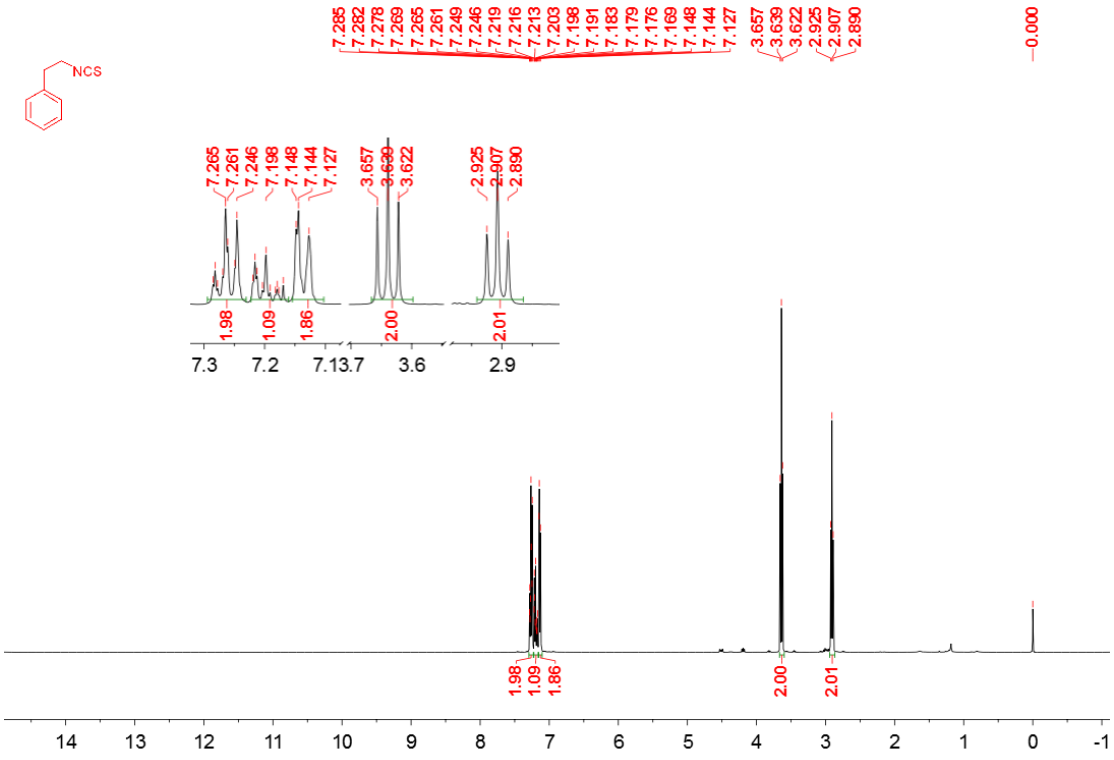
^{13}C NMR of Compound **2q**



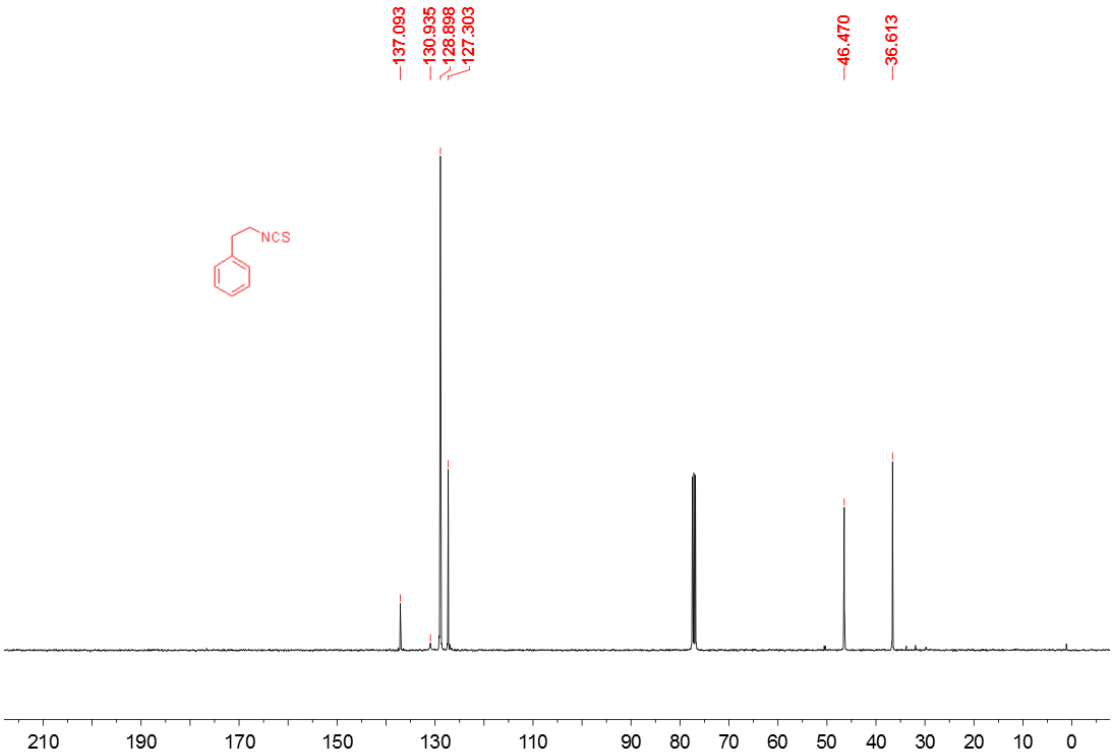
^{1}H NMR of Compound **2r**



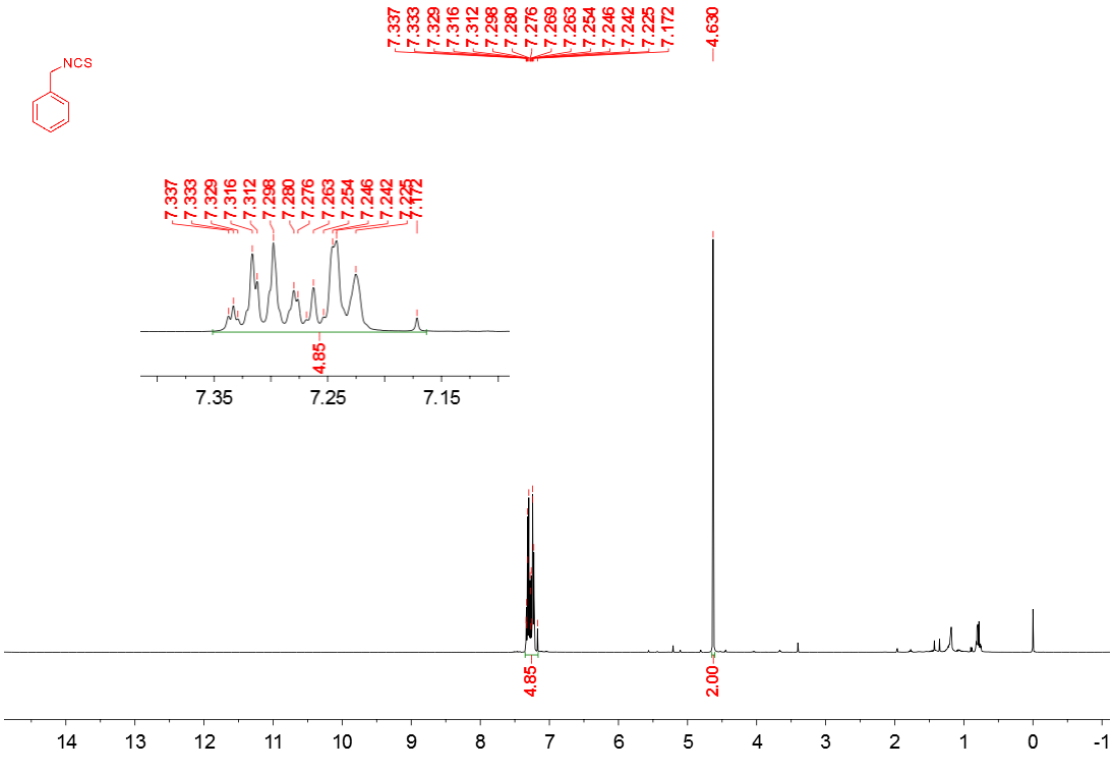
^{13}C NMR of Compound **2r**



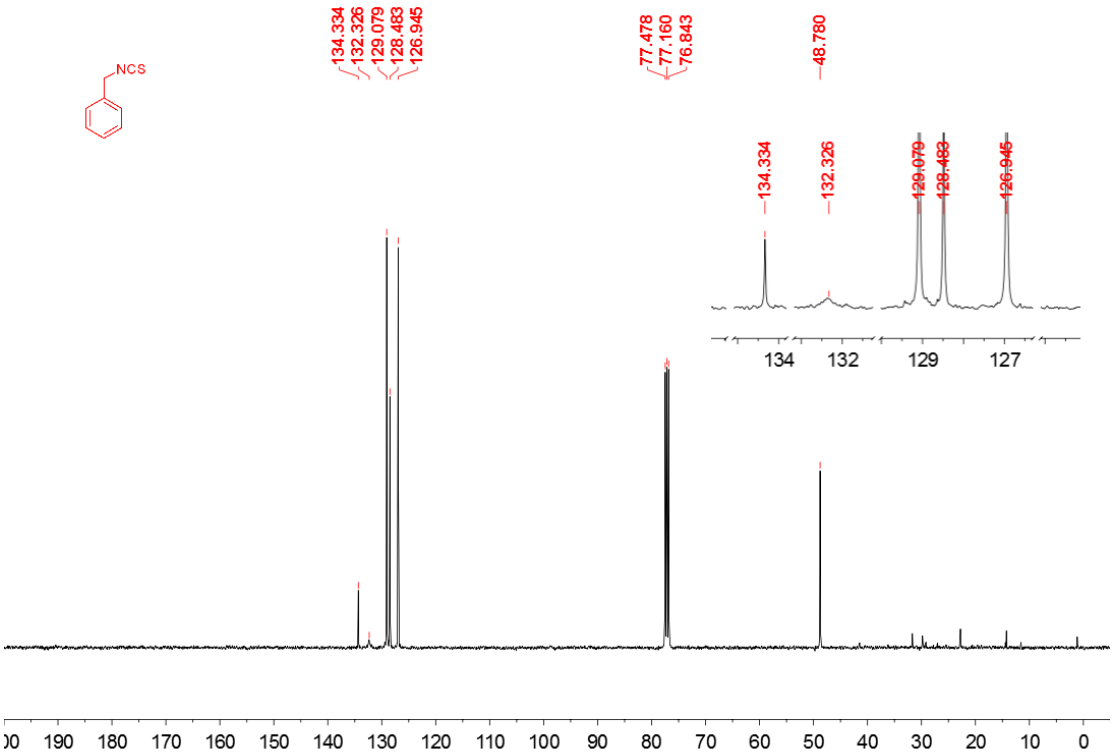
^{1}H NMR of Compound **2s**



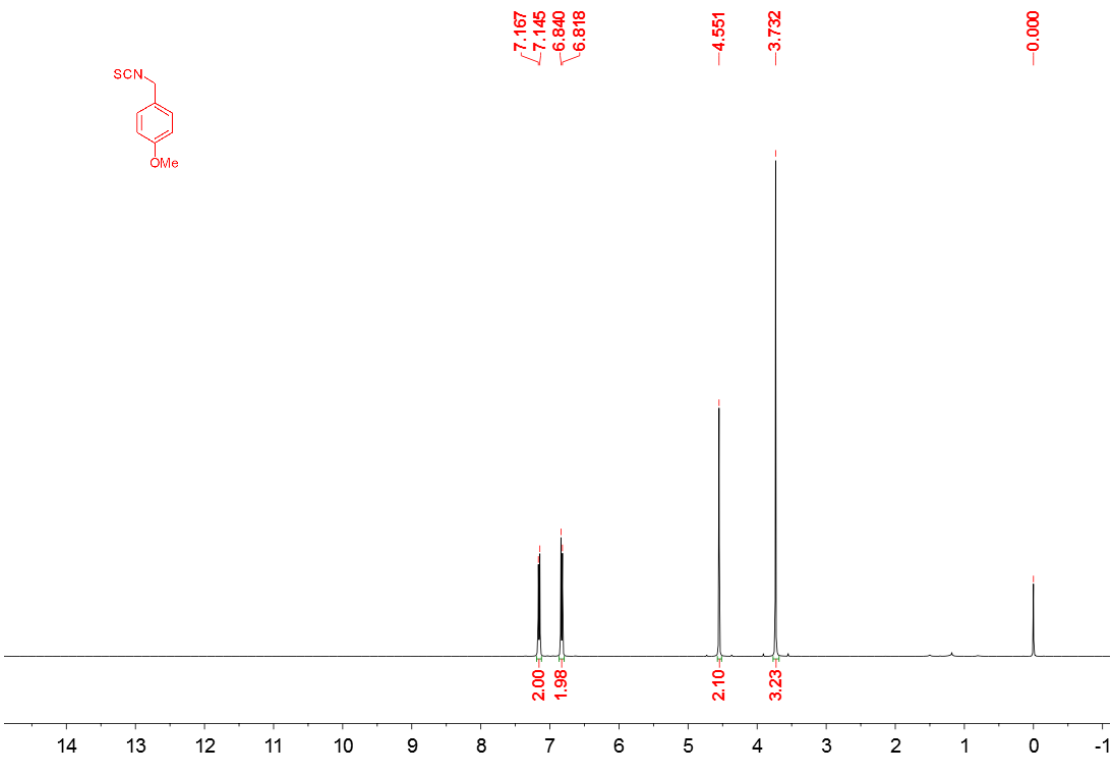
^{13}C NMR of Compound **2s**



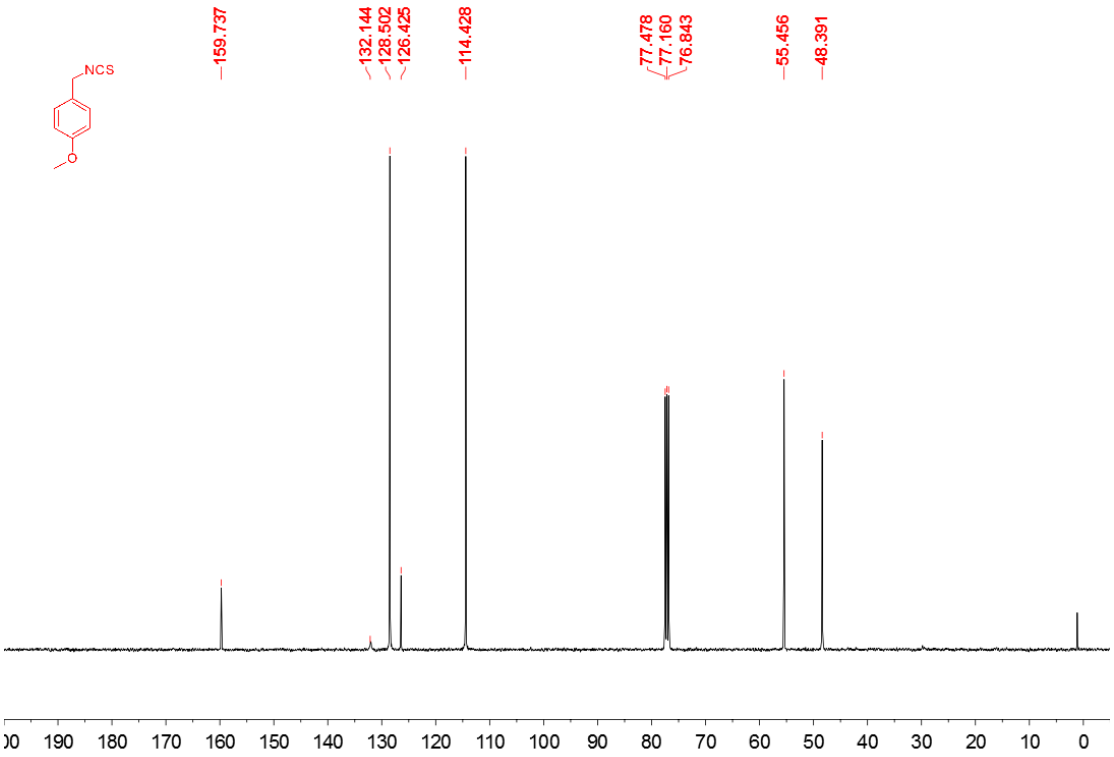
^{1}H NMR of Compound **2t**



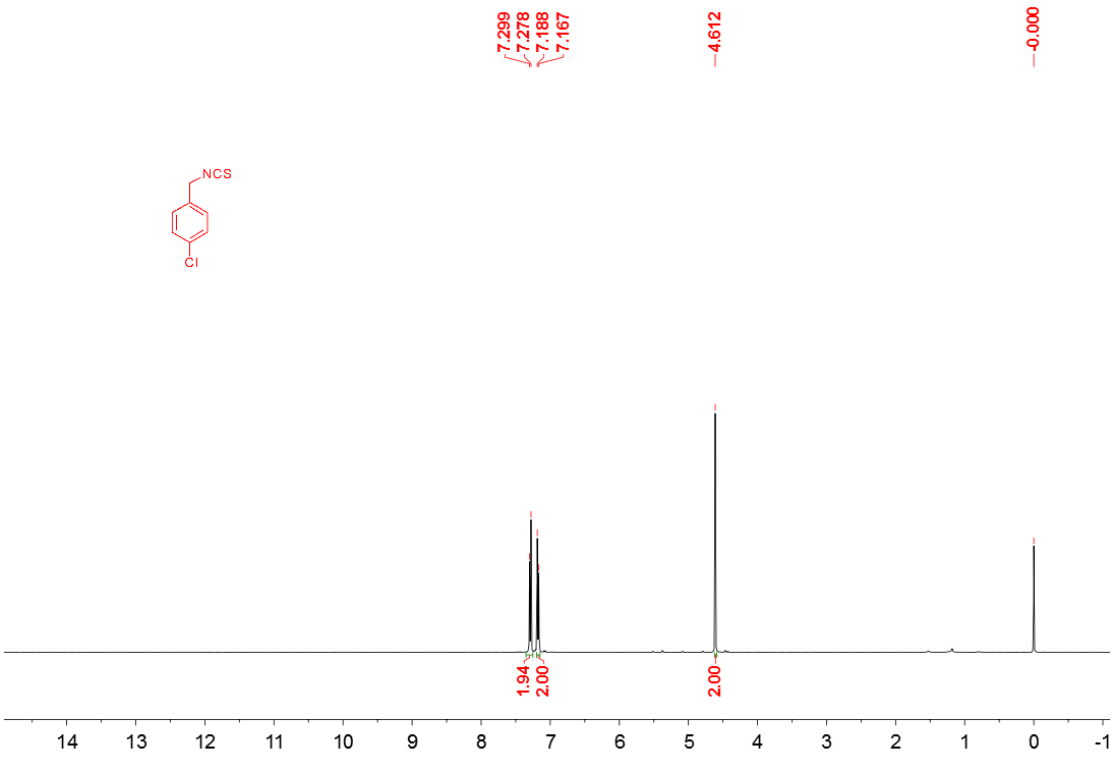
^{13}C NMR of Compound **2t**



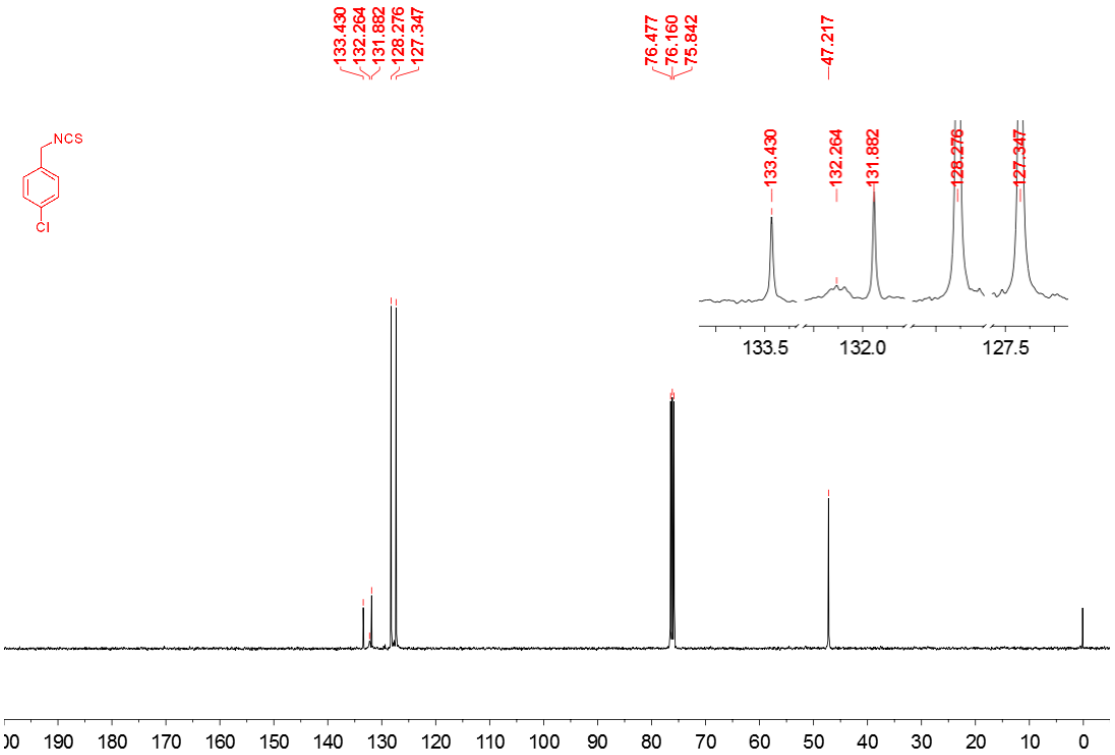
^{1}H NMR of Compound **2u**



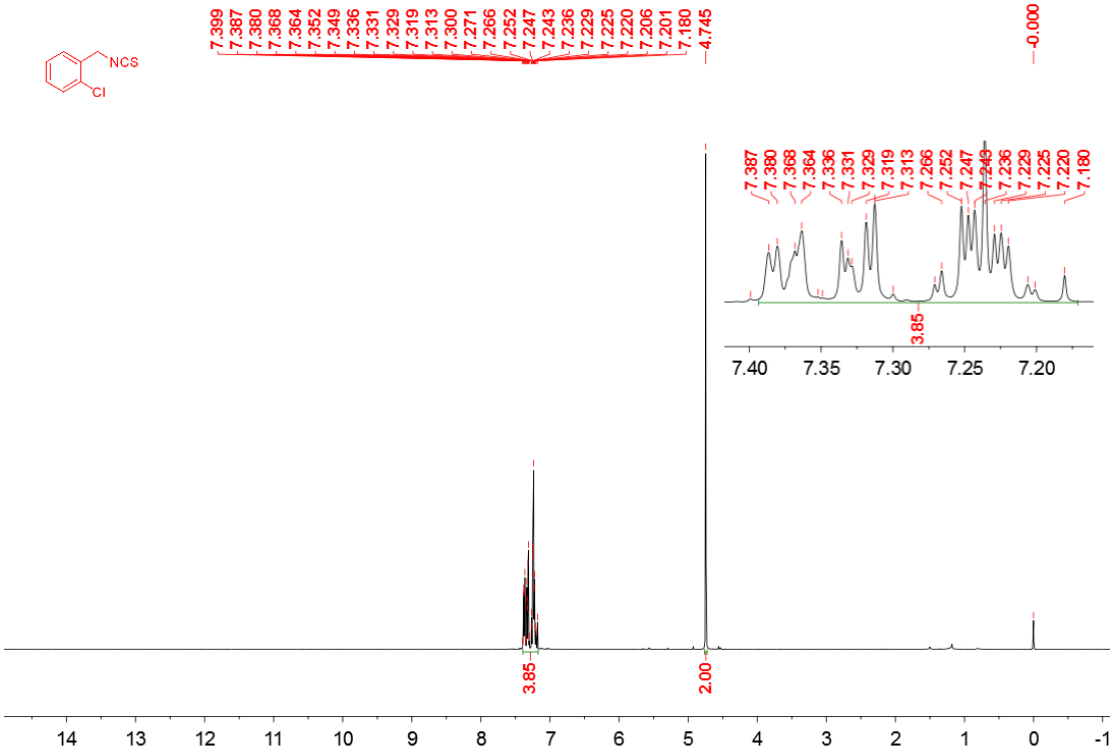
^{13}C NMR of Compound **2u**



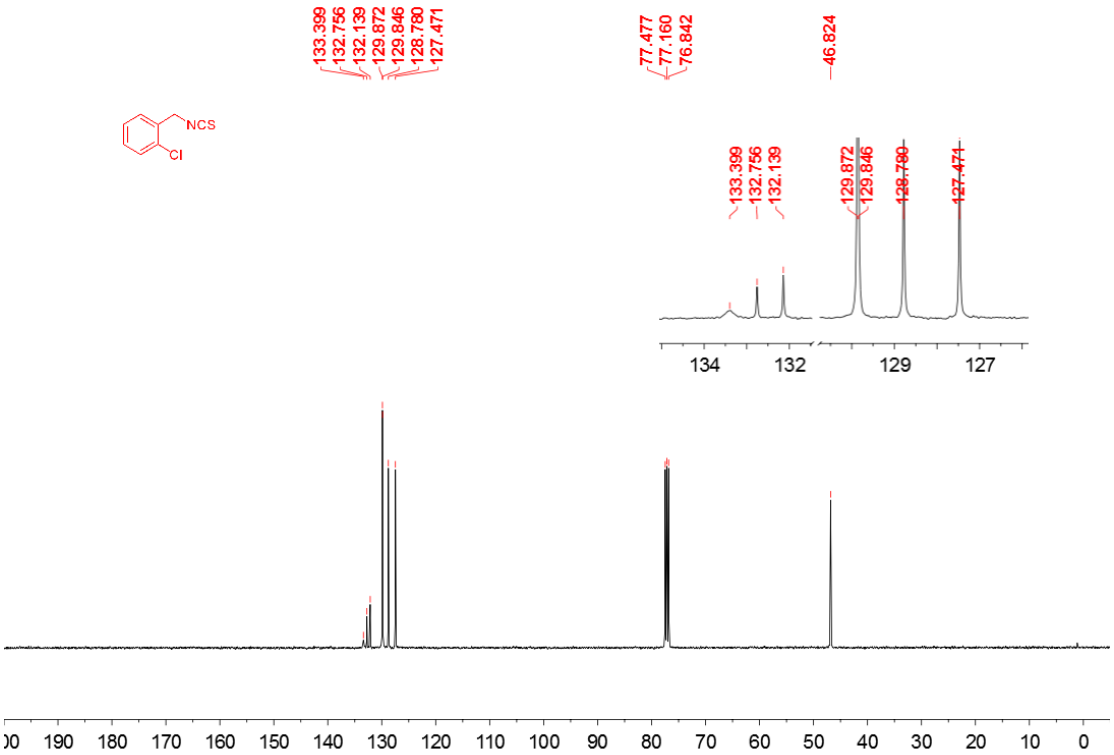
^{1}H NMR of Compound **2v**



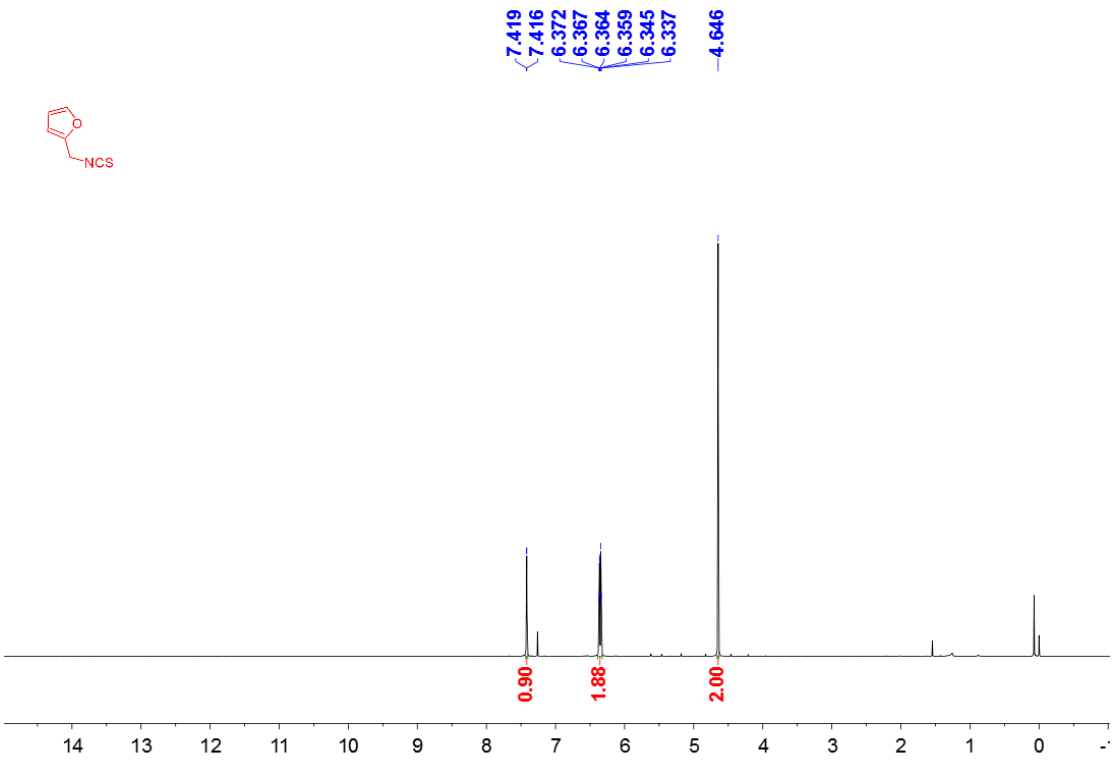
^{13}C NMR of Compound **2v**



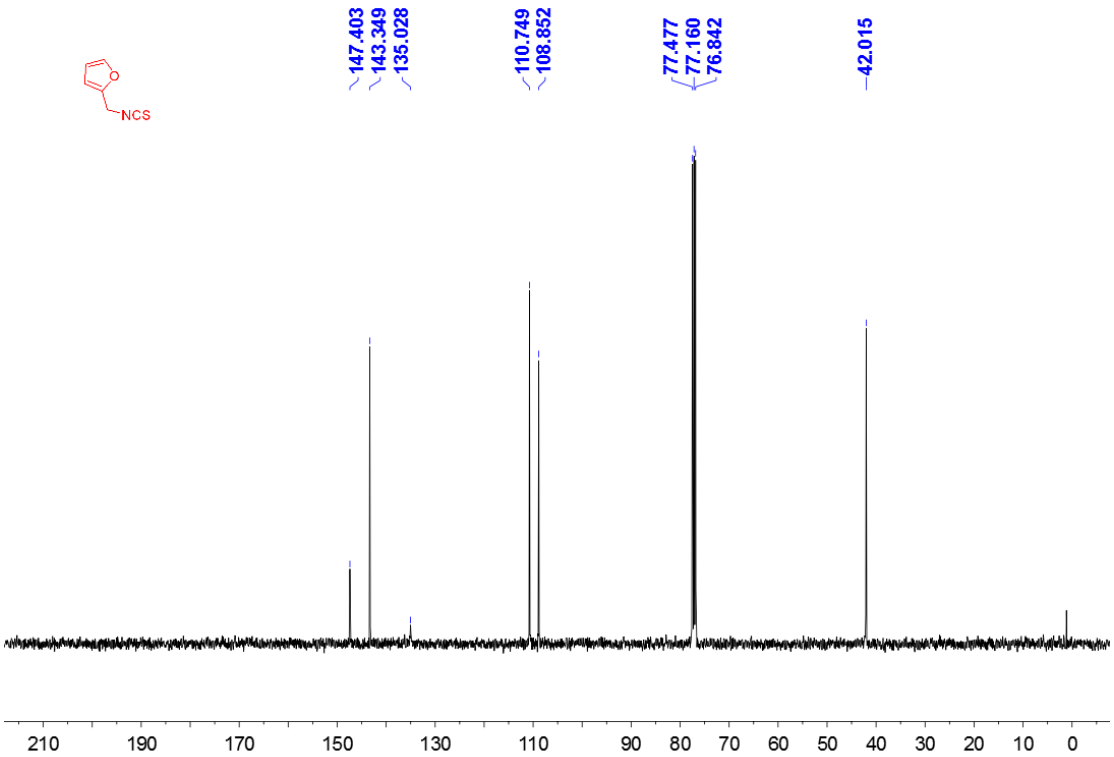
^{1}H NMR of Compound **2w**



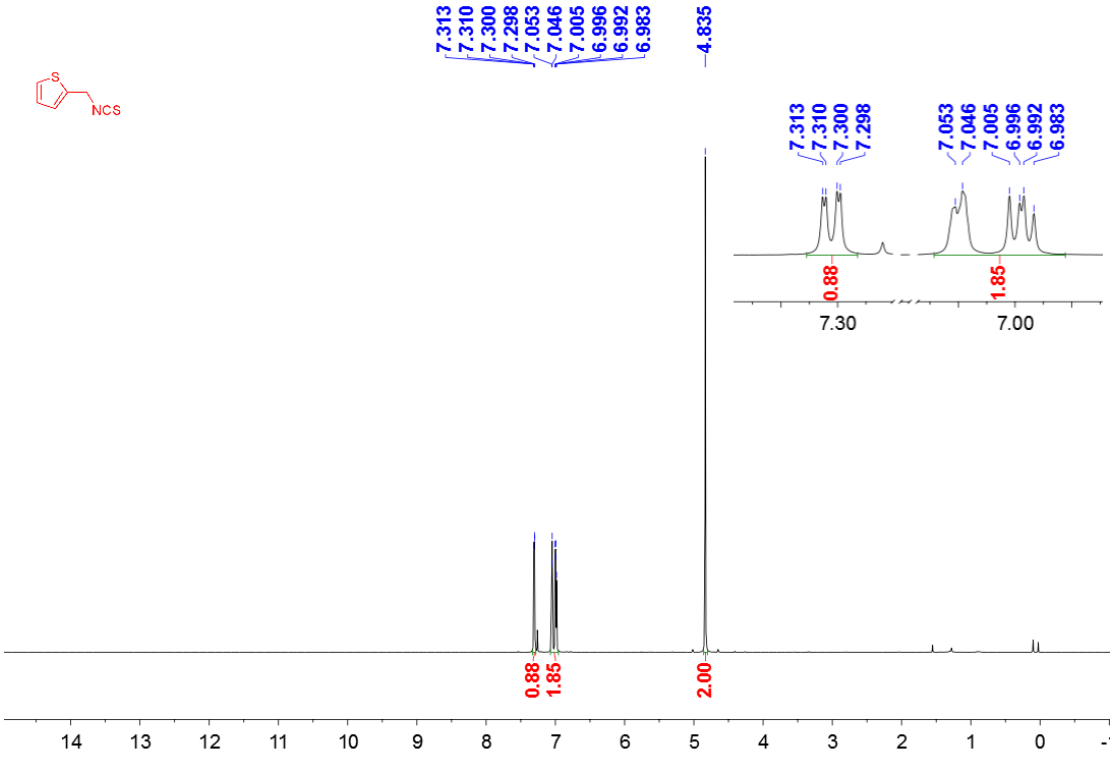
^{13}C NMR of Compound **2w**



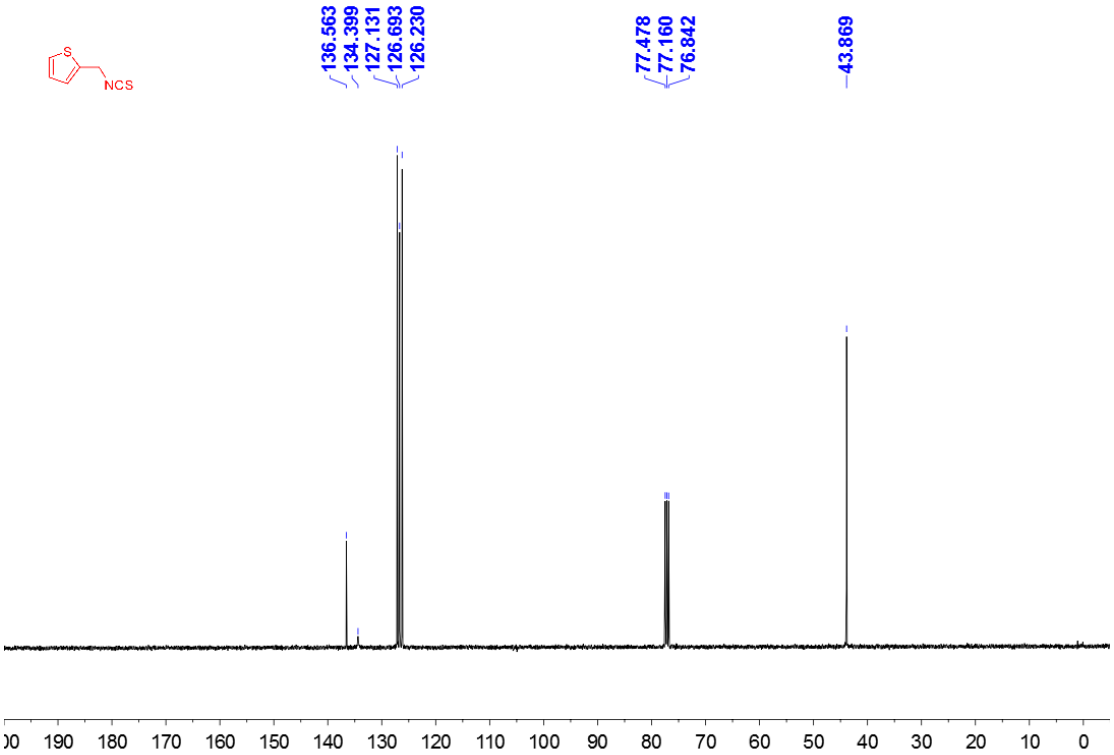
^{1}H NMR of Compound **2x**



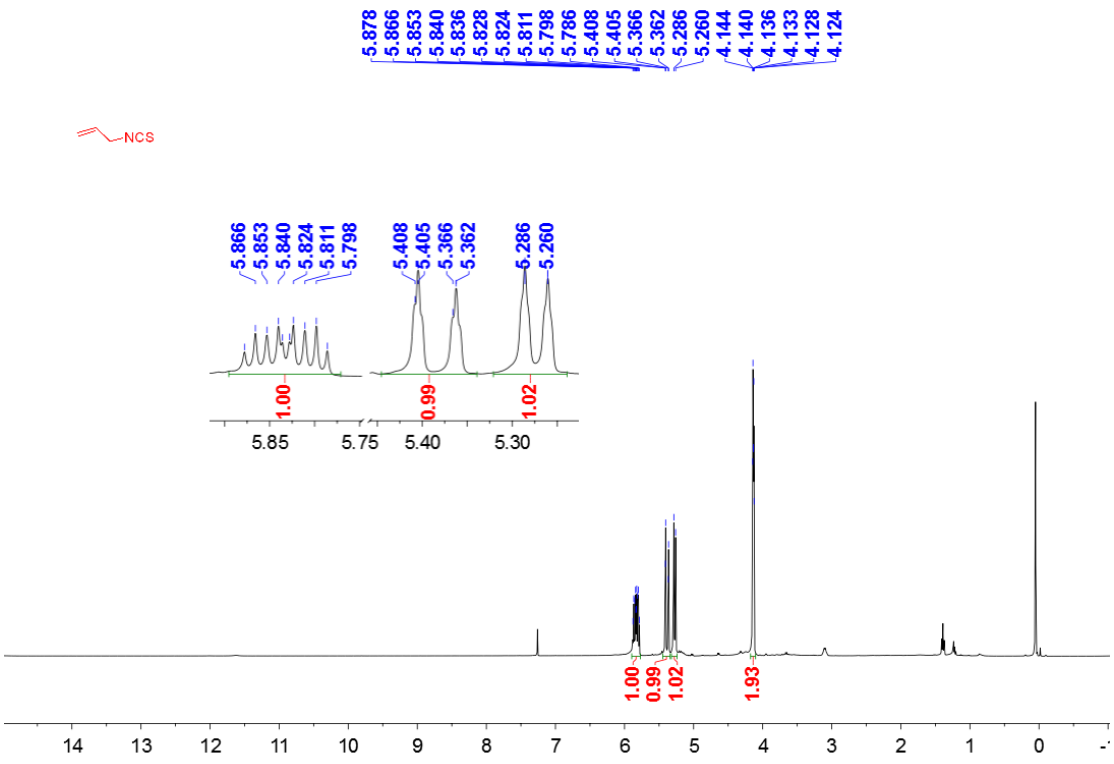
^{13}C NMR of Compound **2x**



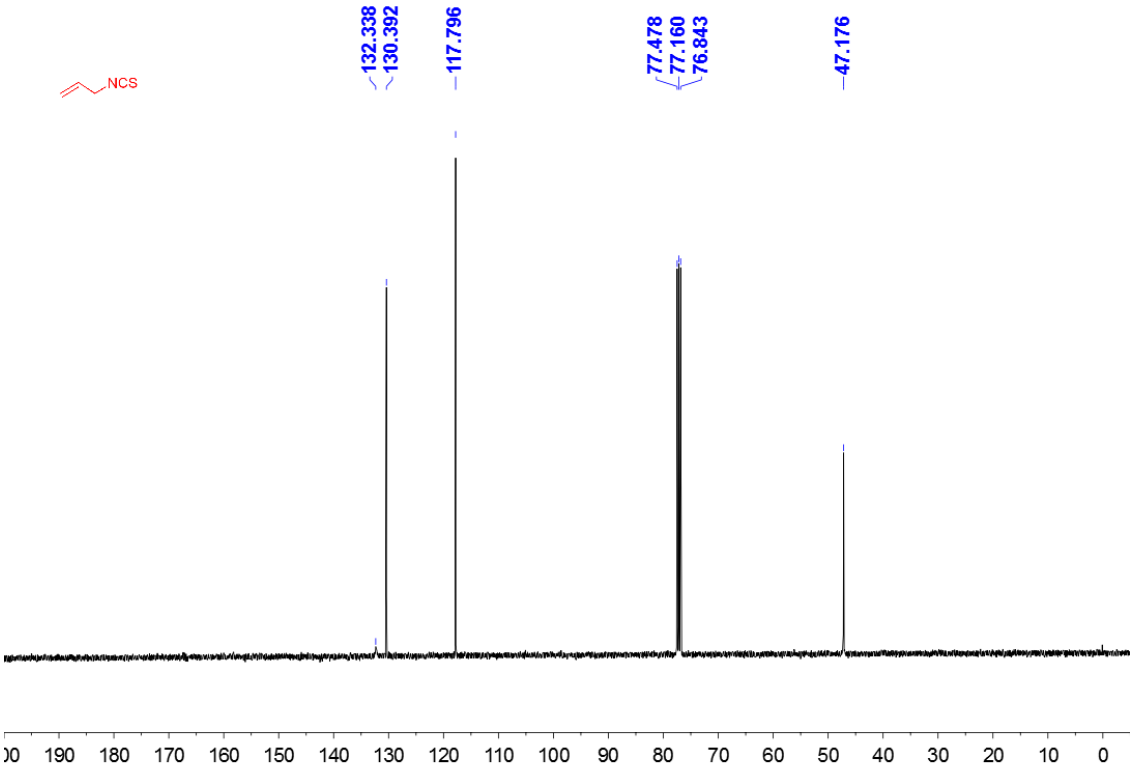
^{1}H NMR of Compound **2y**



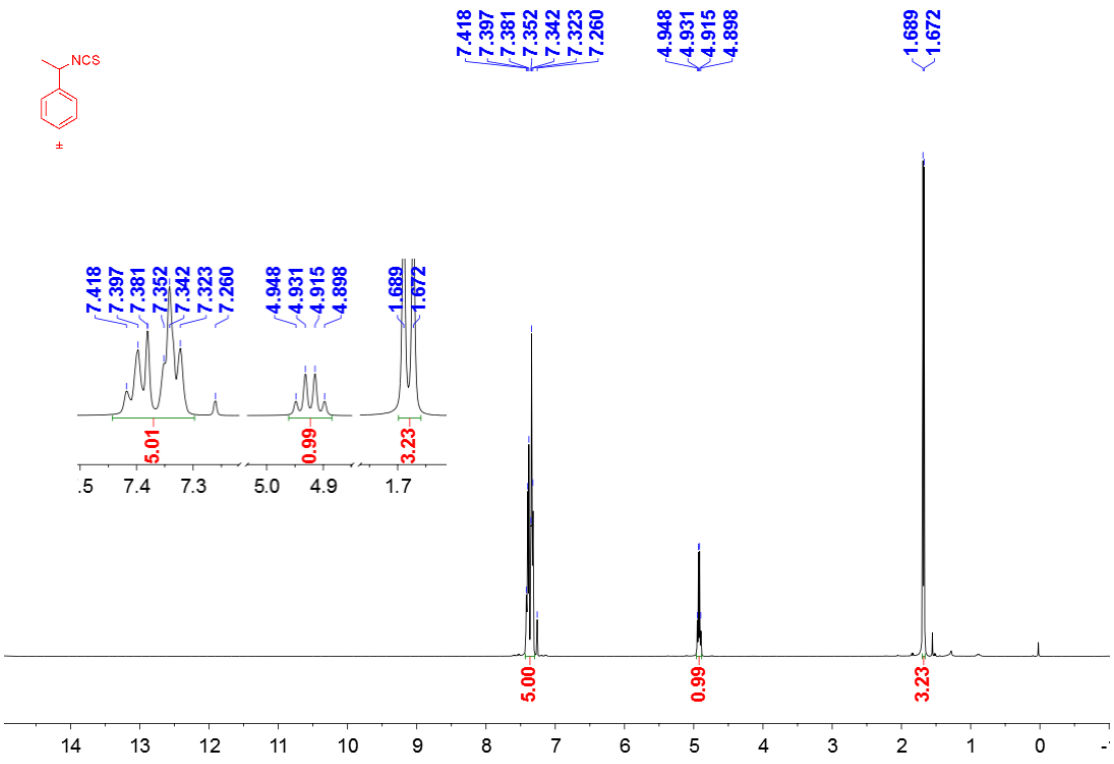
^{13}C NMR of Compound **2y**



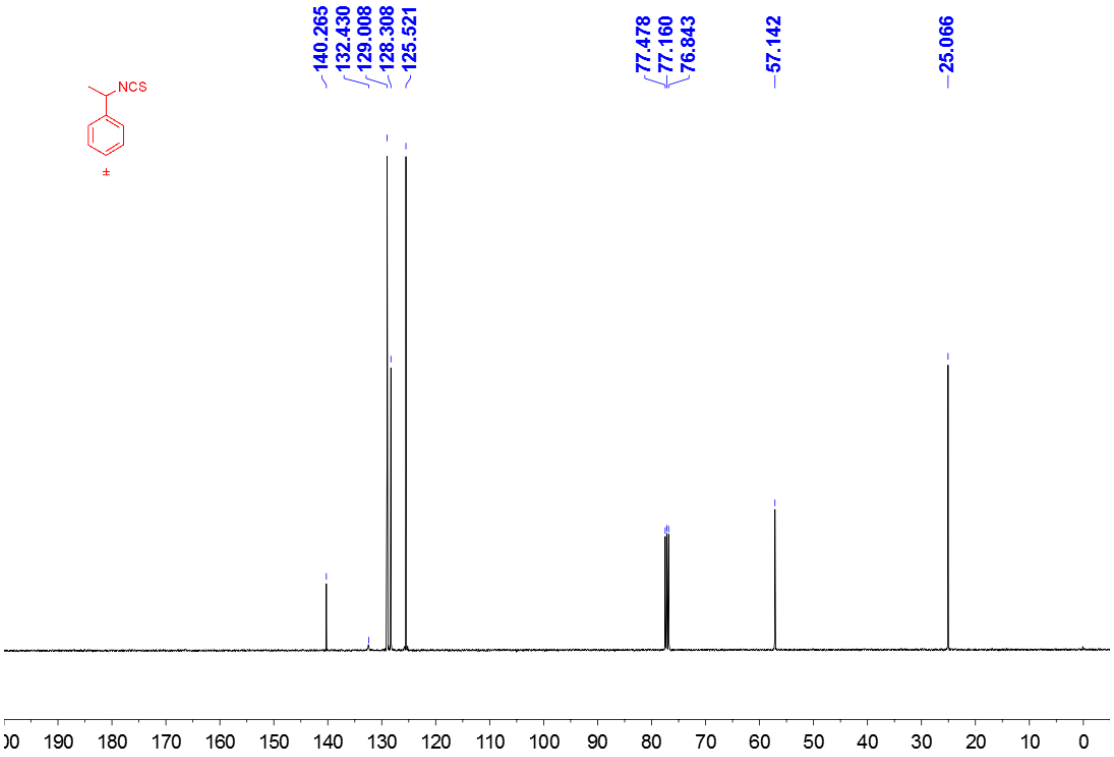
^{1}H NMR of Compound **2z**



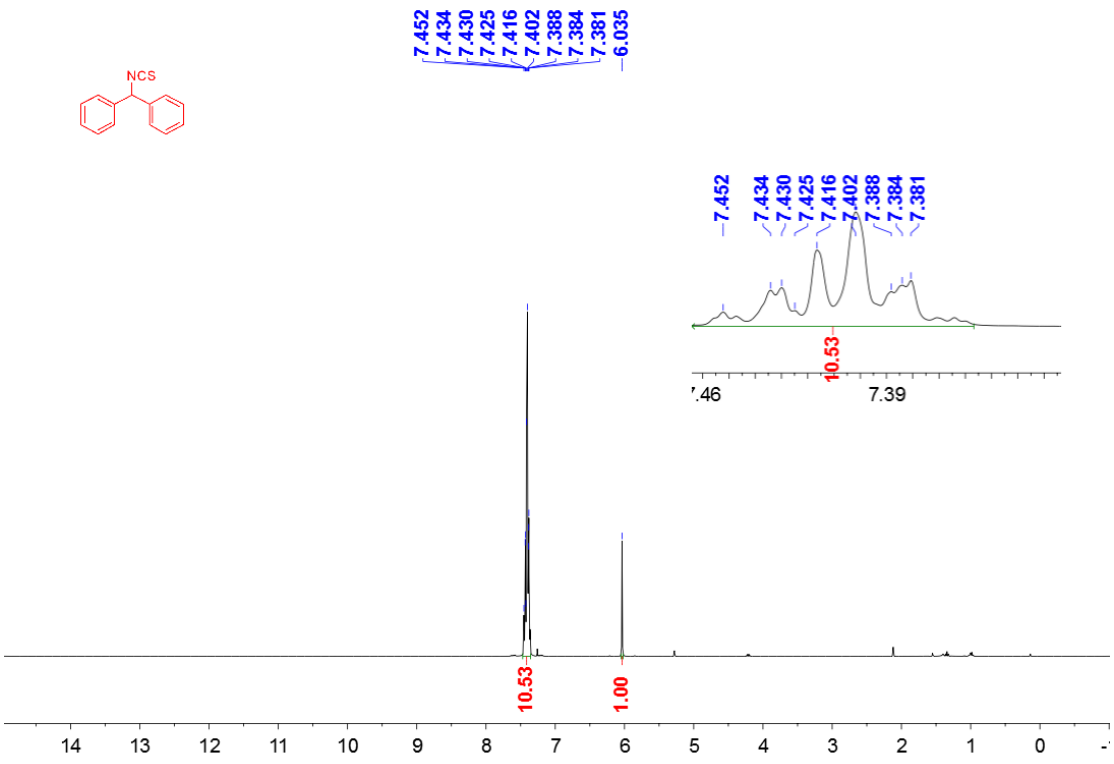
^{13}C NMR of Compound **2z**



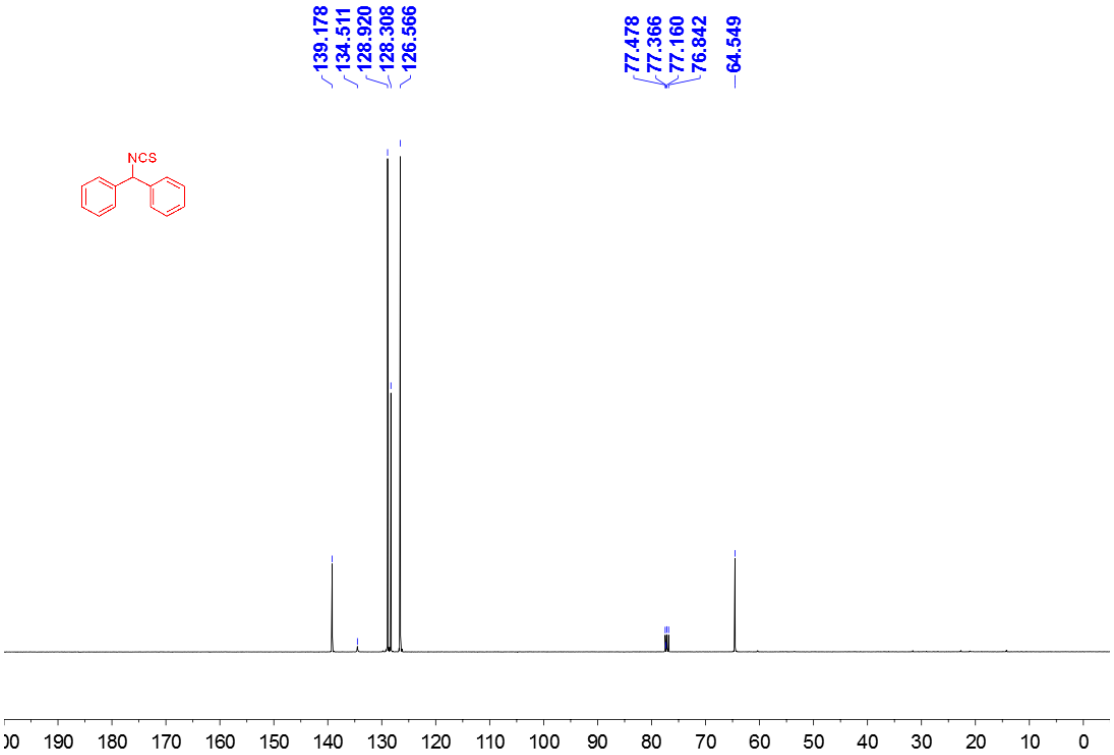
^{1}H NMR of Compound **2aa**



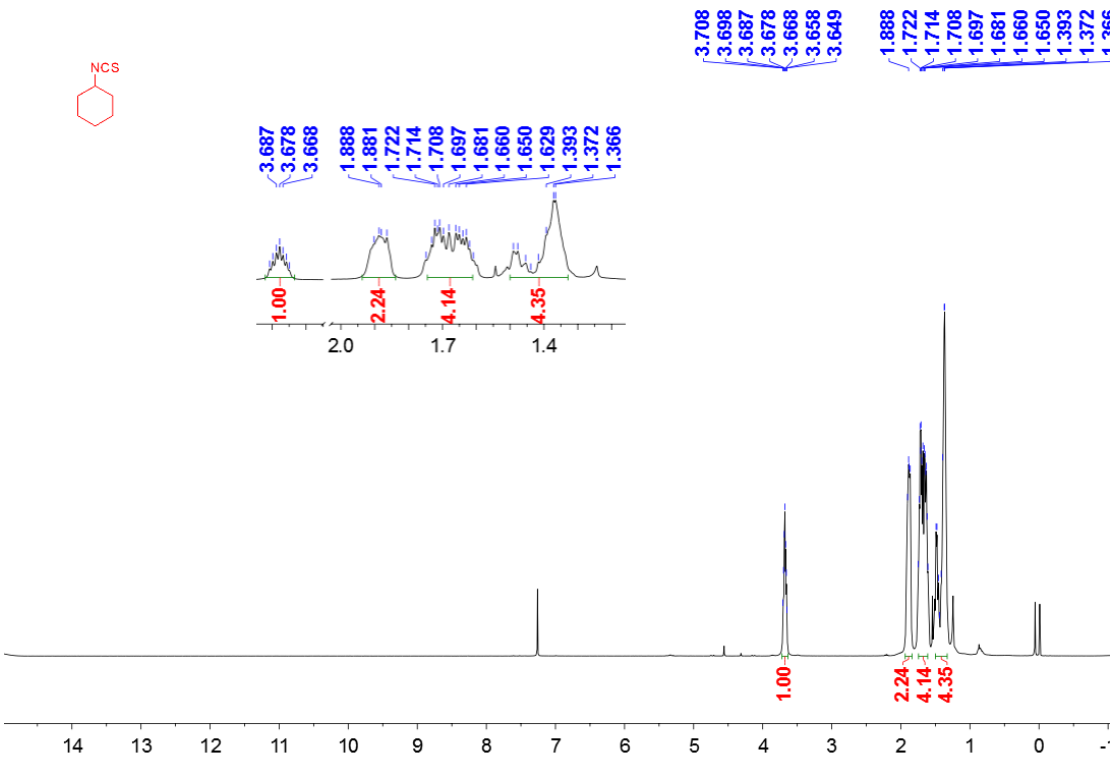
^{13}C NMR of Compound **2aa**



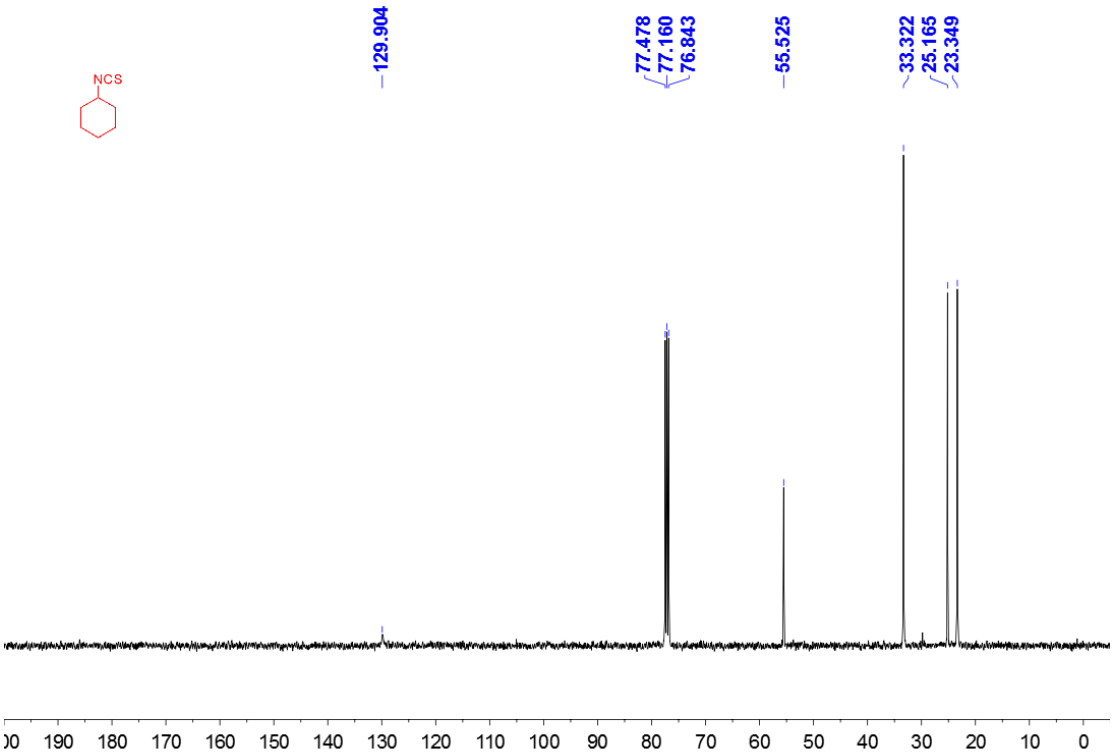
^{1}H NMR of Compound **2ab**



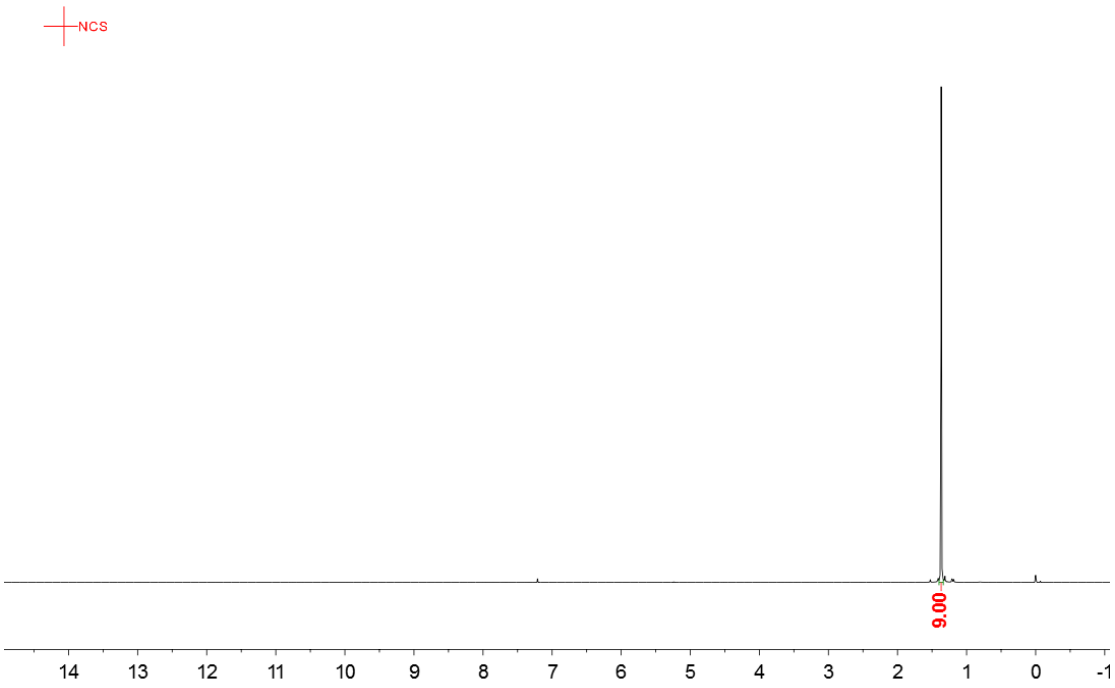
^{13}C NMR of Compound **2ab**



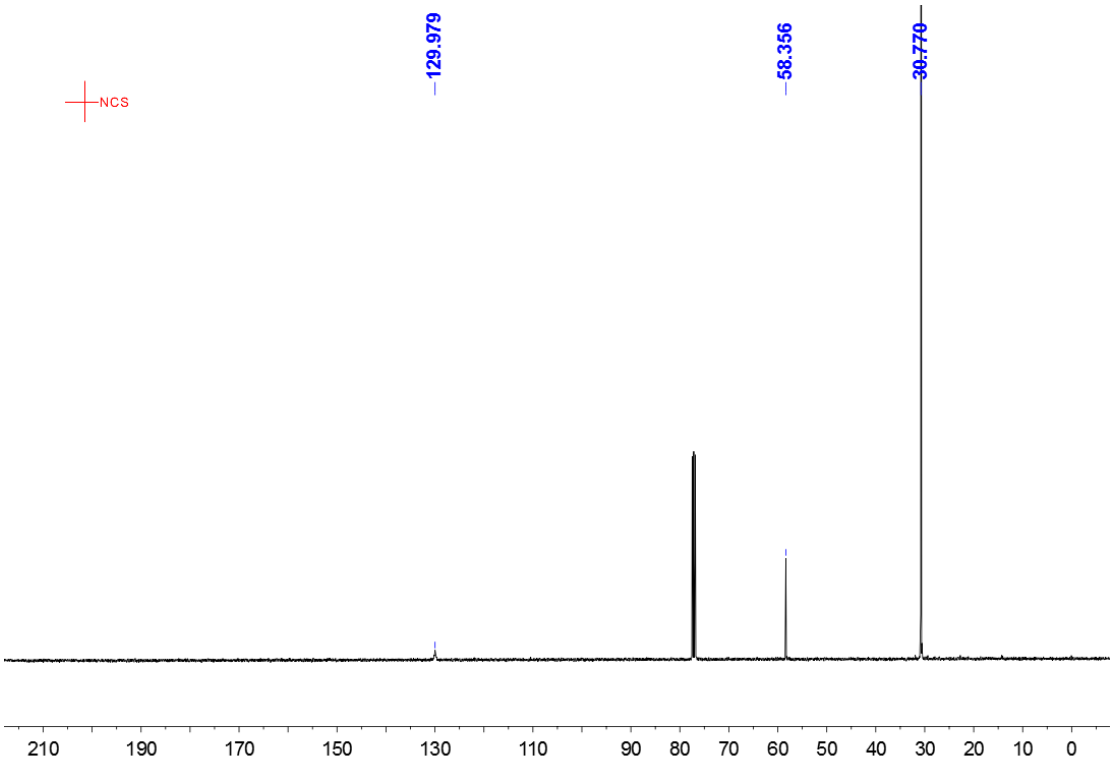
^{1}H NMR of Compound **2ac**



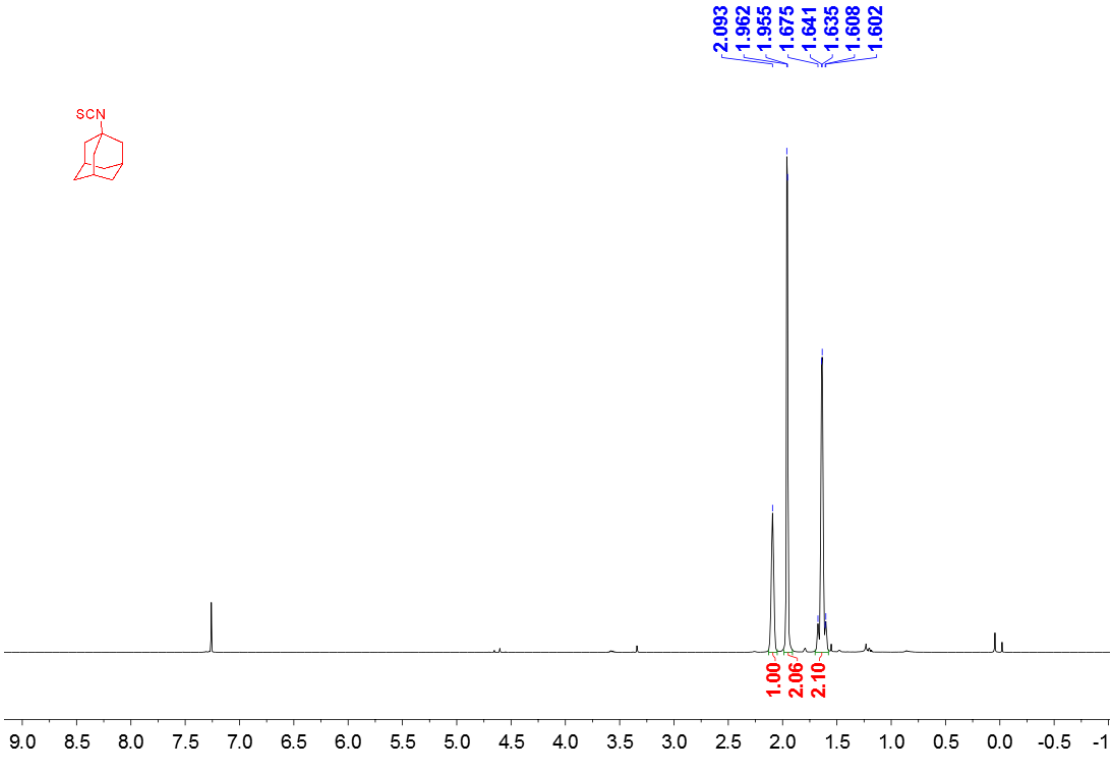
^{13}C NMR of Compound **2ac**



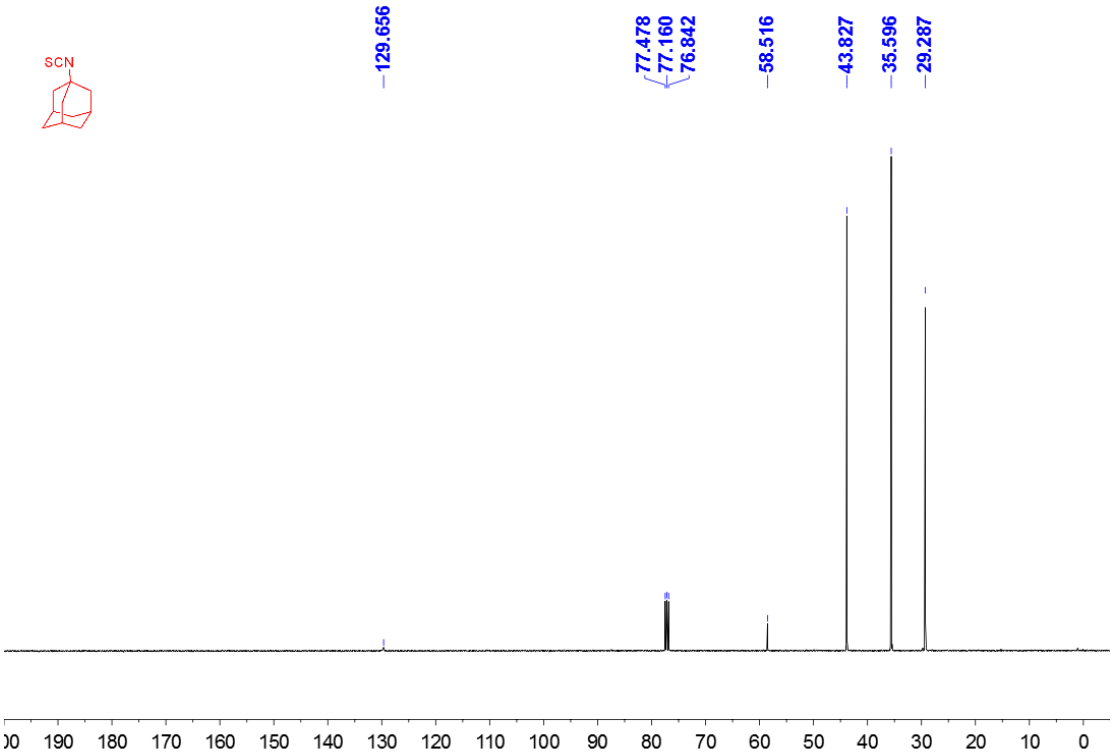
^{1}H NMR of Compound **2ad**



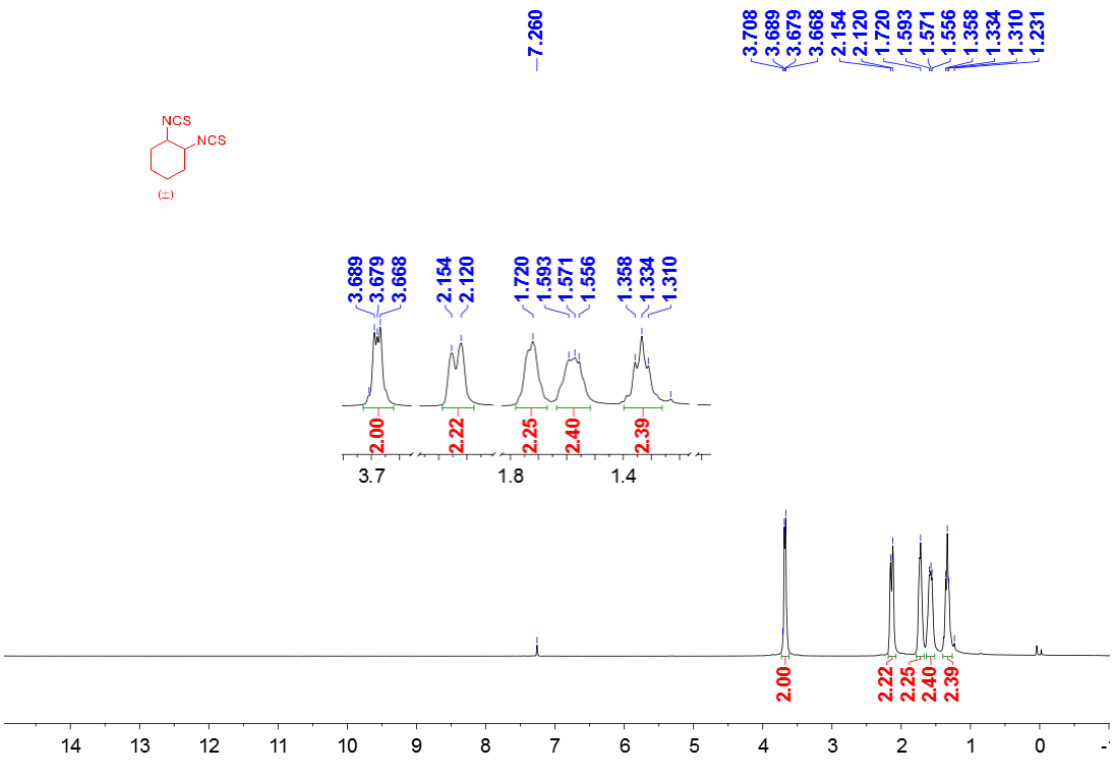
^{13}C NMR of Compound **2ad**



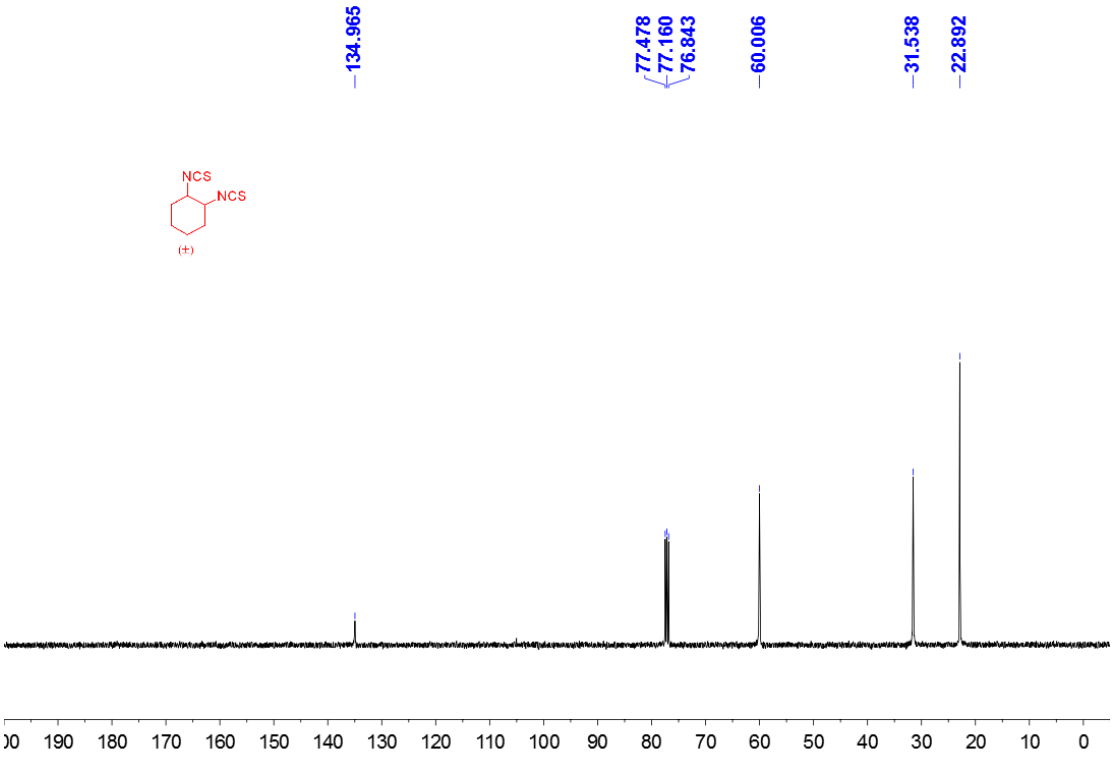
^{1}H NMR of Compound **2ae**



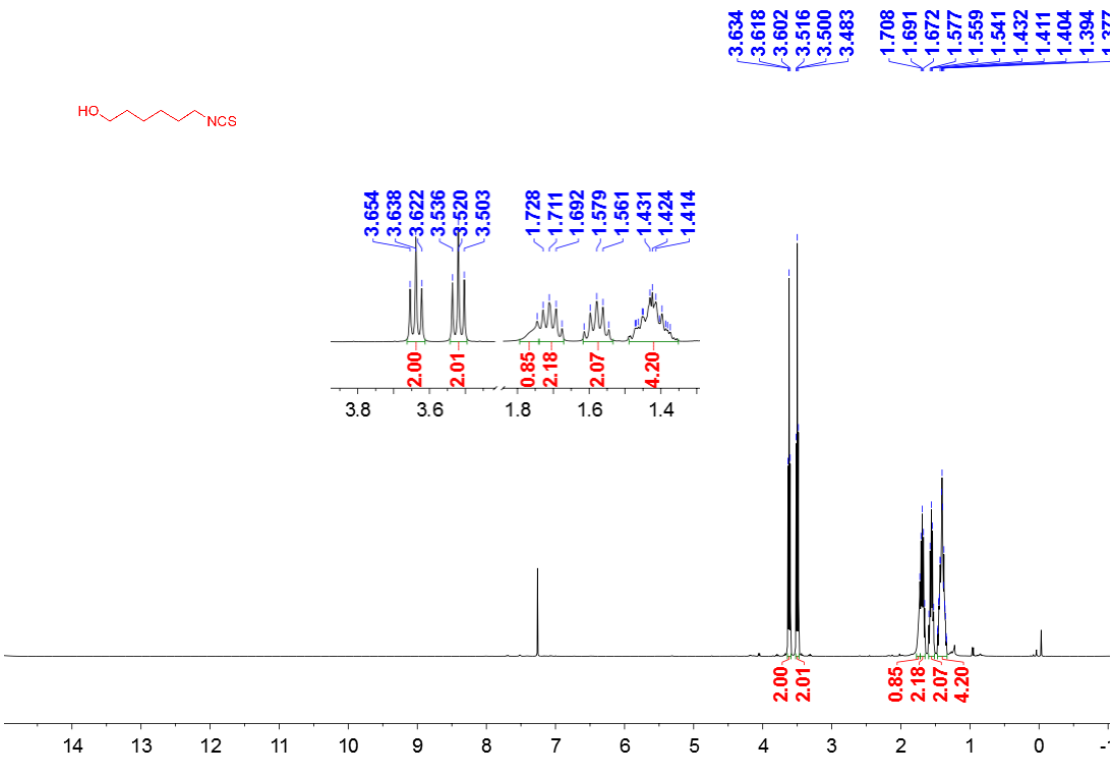
^{13}C NMR of Compound **2ae**



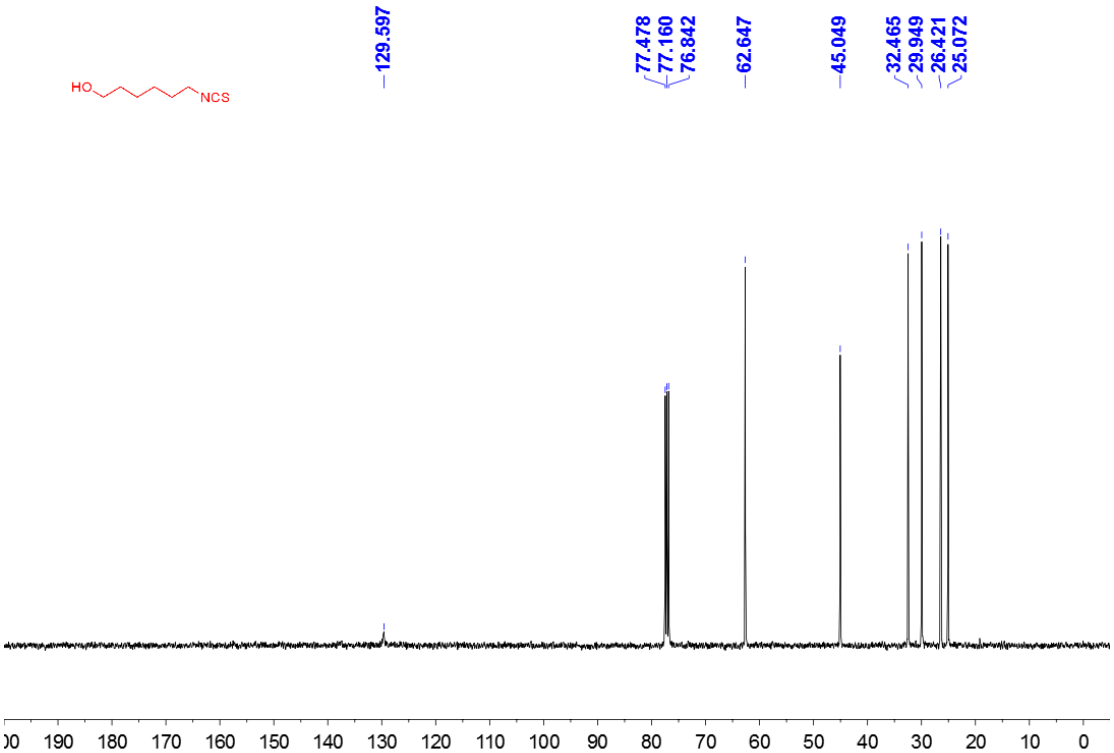
^{1}H NMR of Compound **2af**



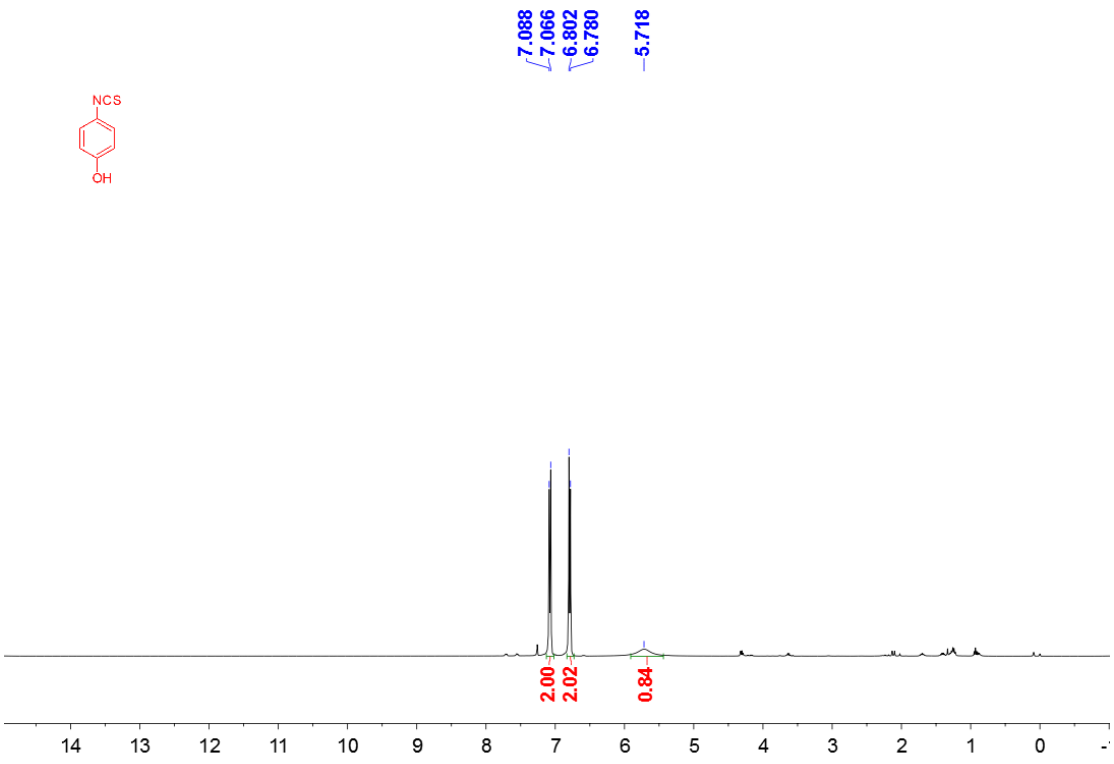
^{13}C NMR of Compound **2af**



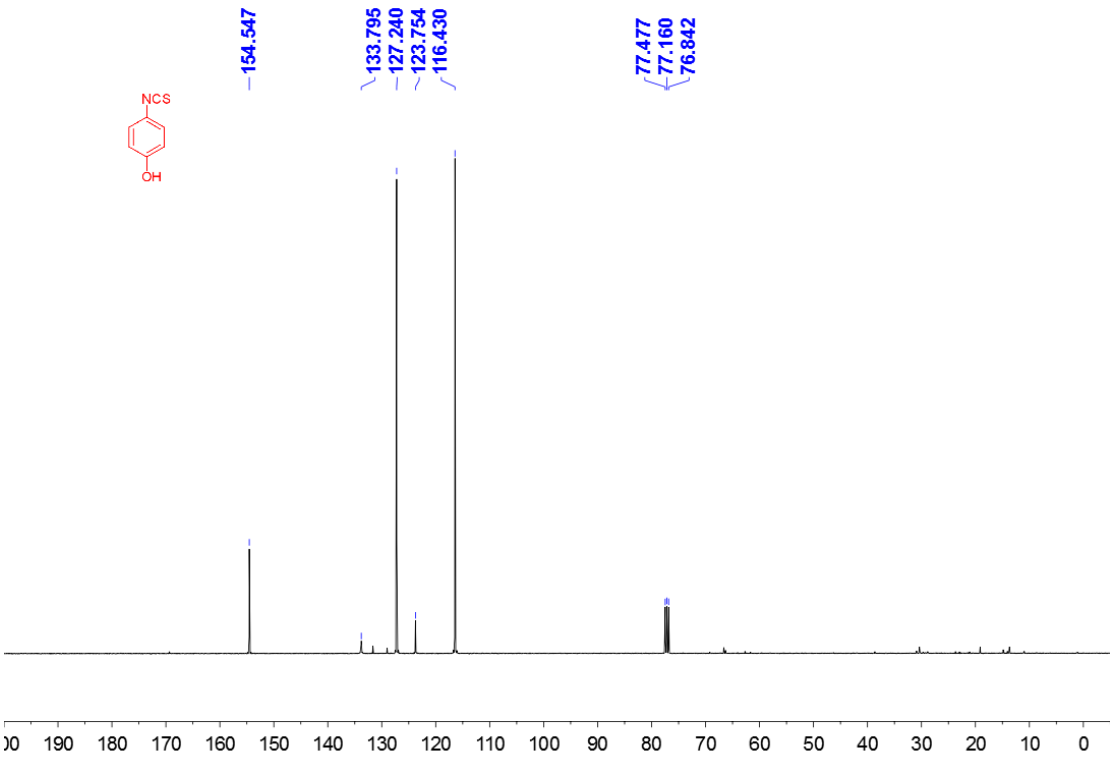
^{1}H NMR of Compound **2ag**



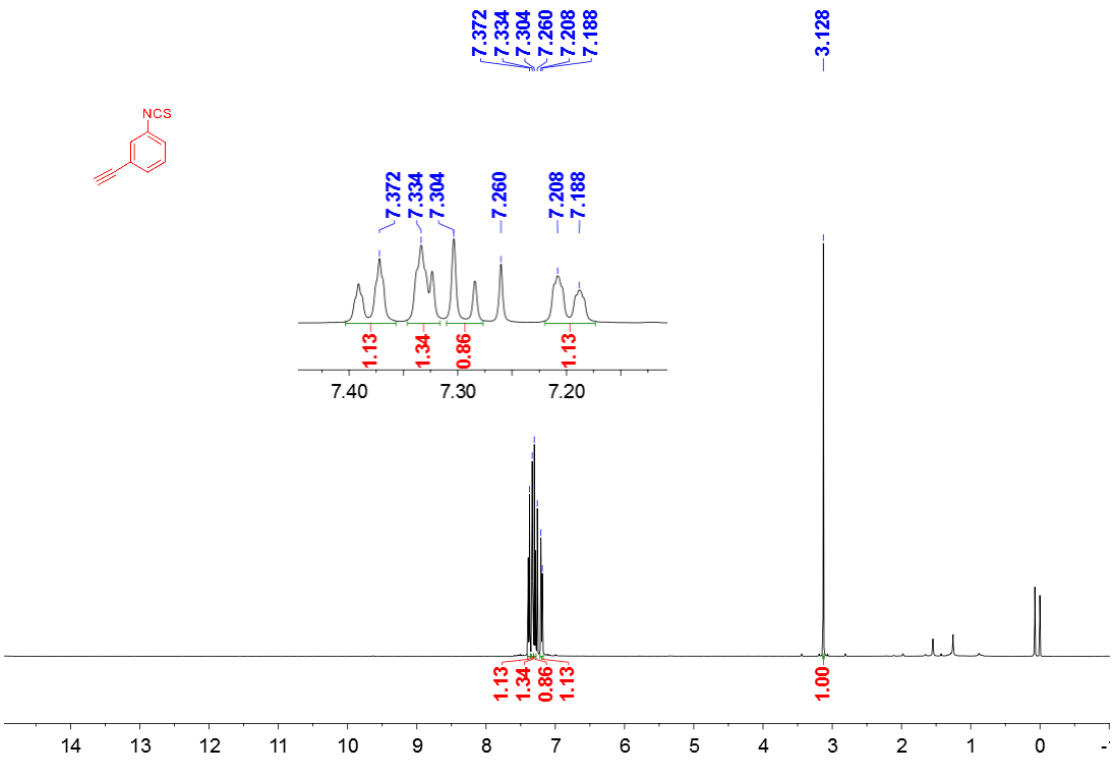
^{13}C NMR of Compound **2ag**



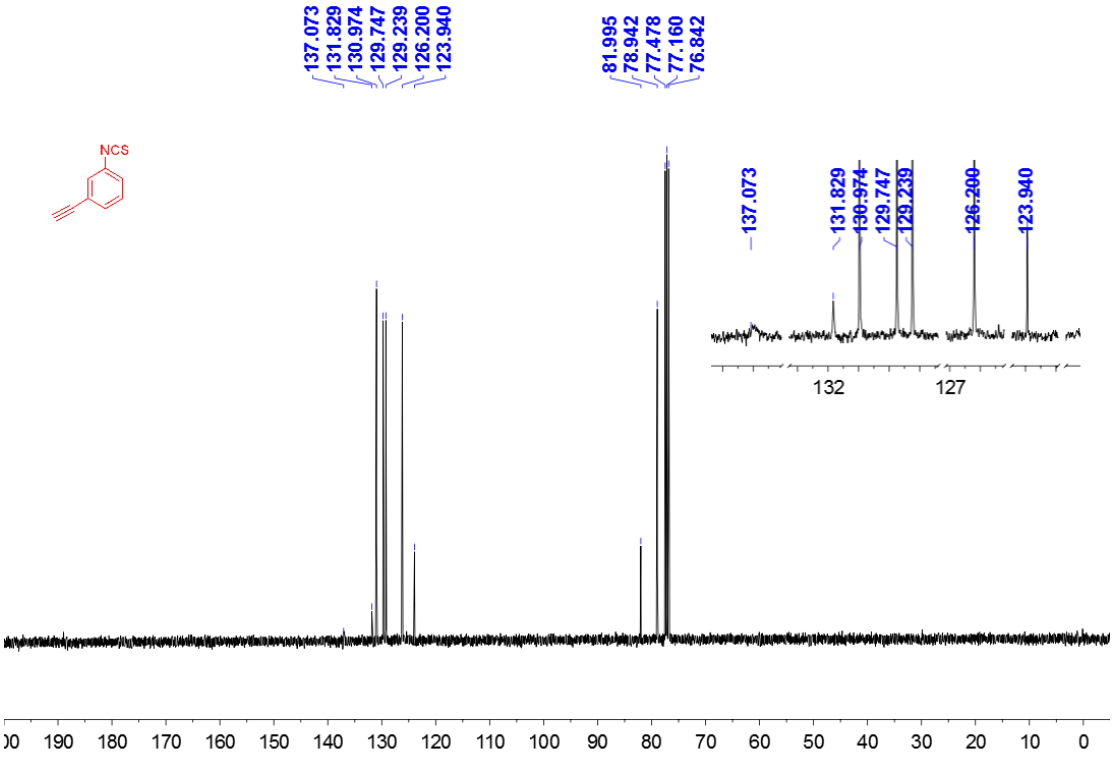
^{1}H NMR of Compound **2ah**



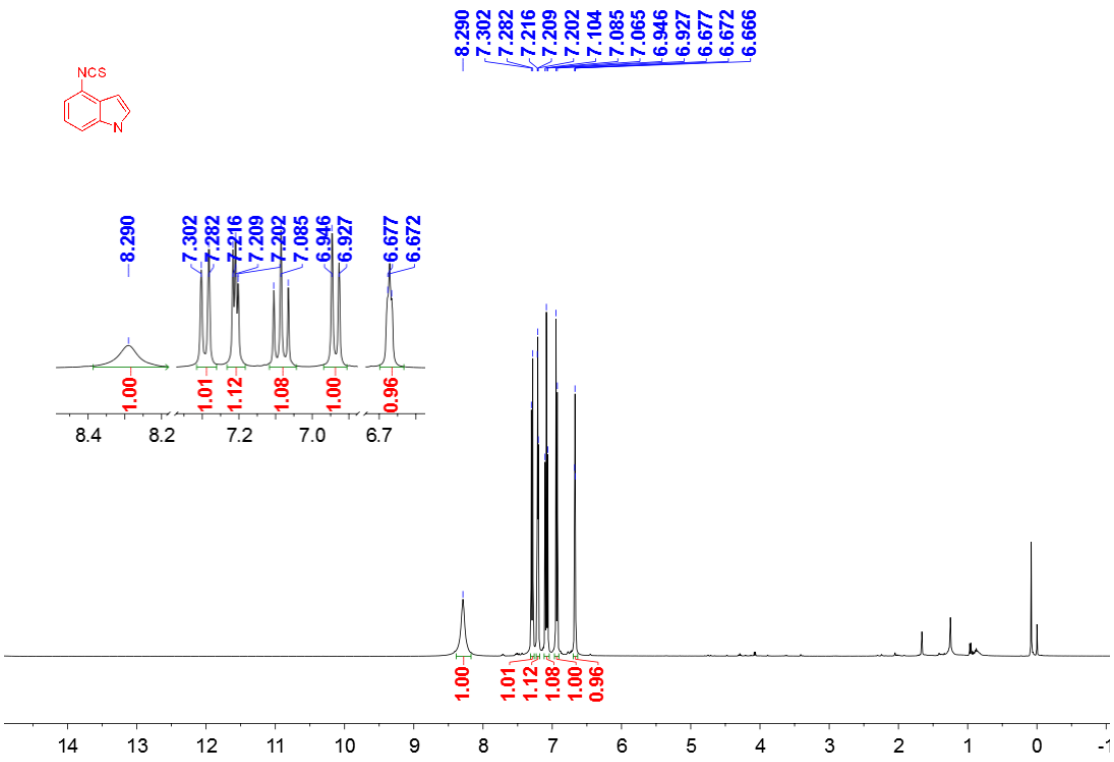
^{13}C NMR of Compound **2ah**



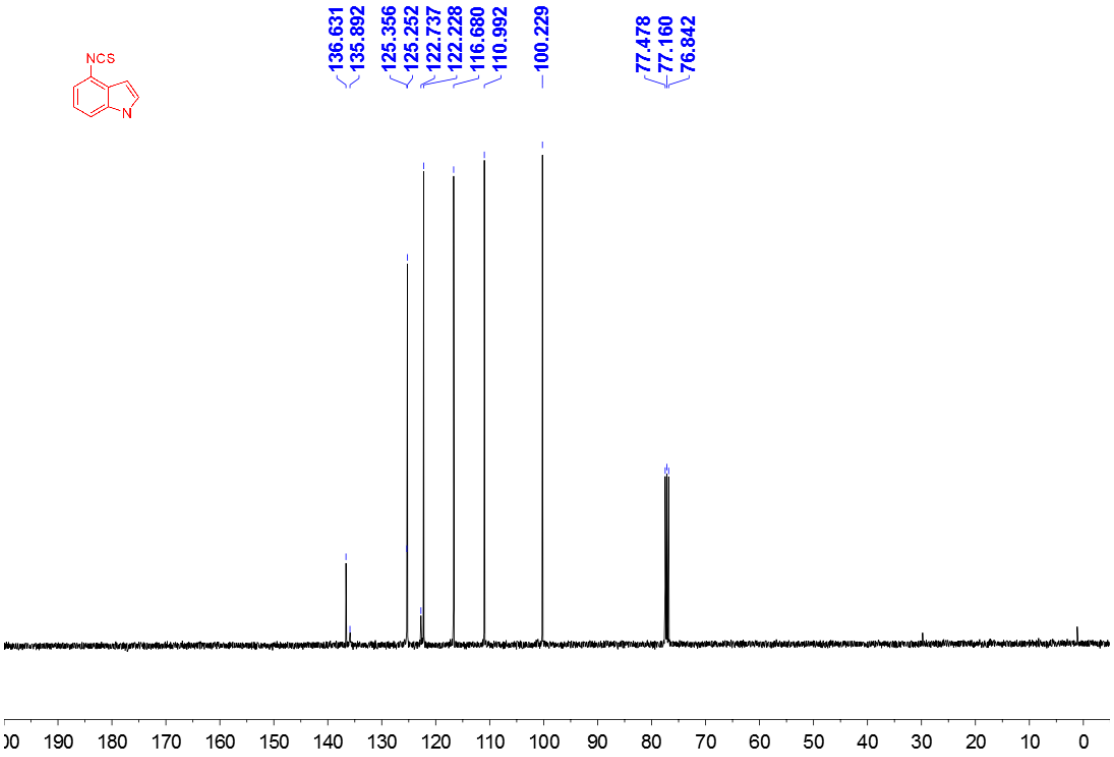
^{1}H NMR of Compound **2ai**



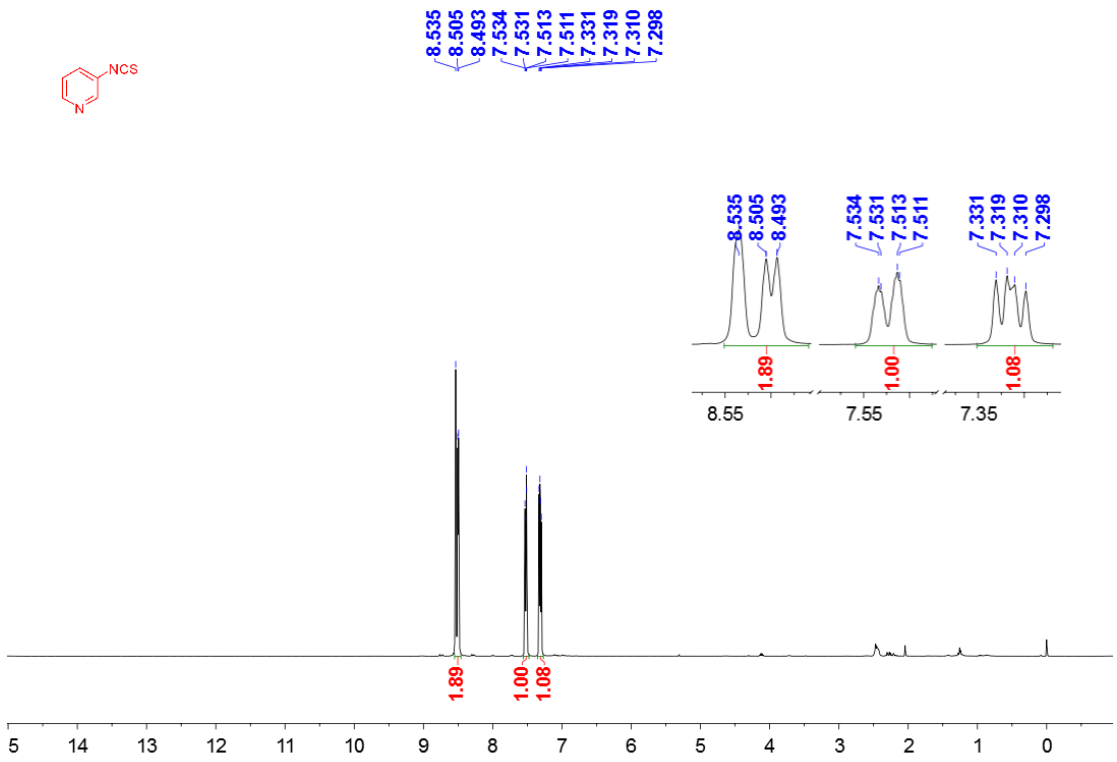
^{13}C NMR of Compound **2ai**



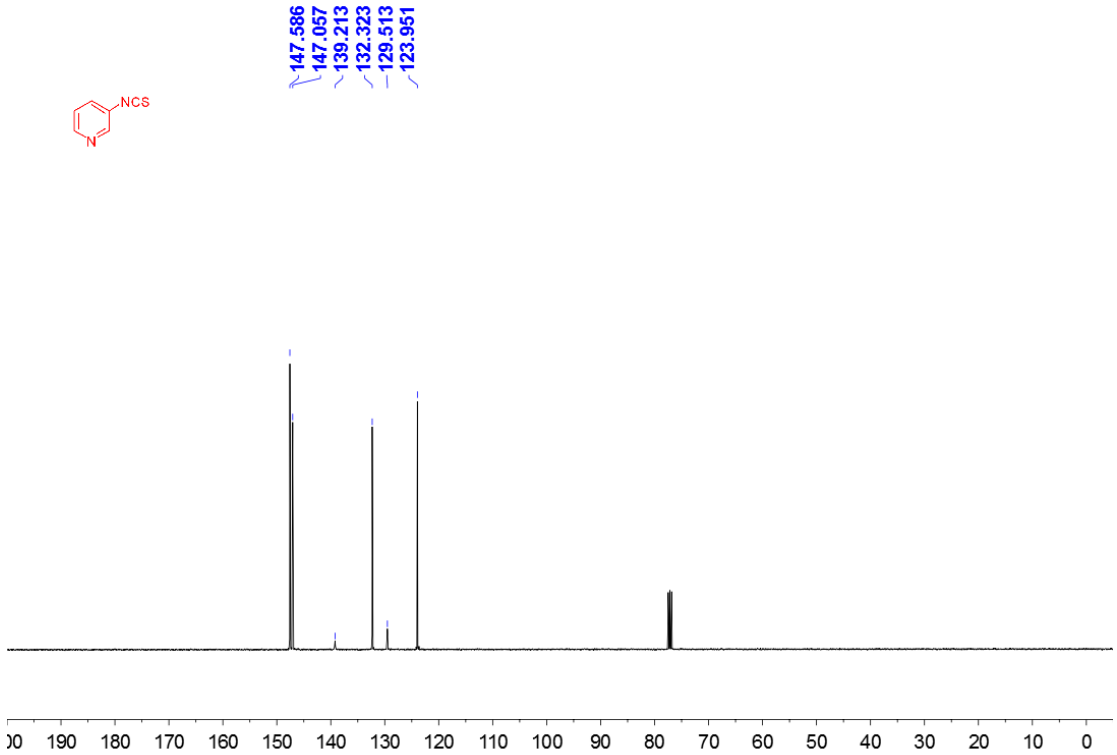
^{1}H NMR of Compound **2aj**



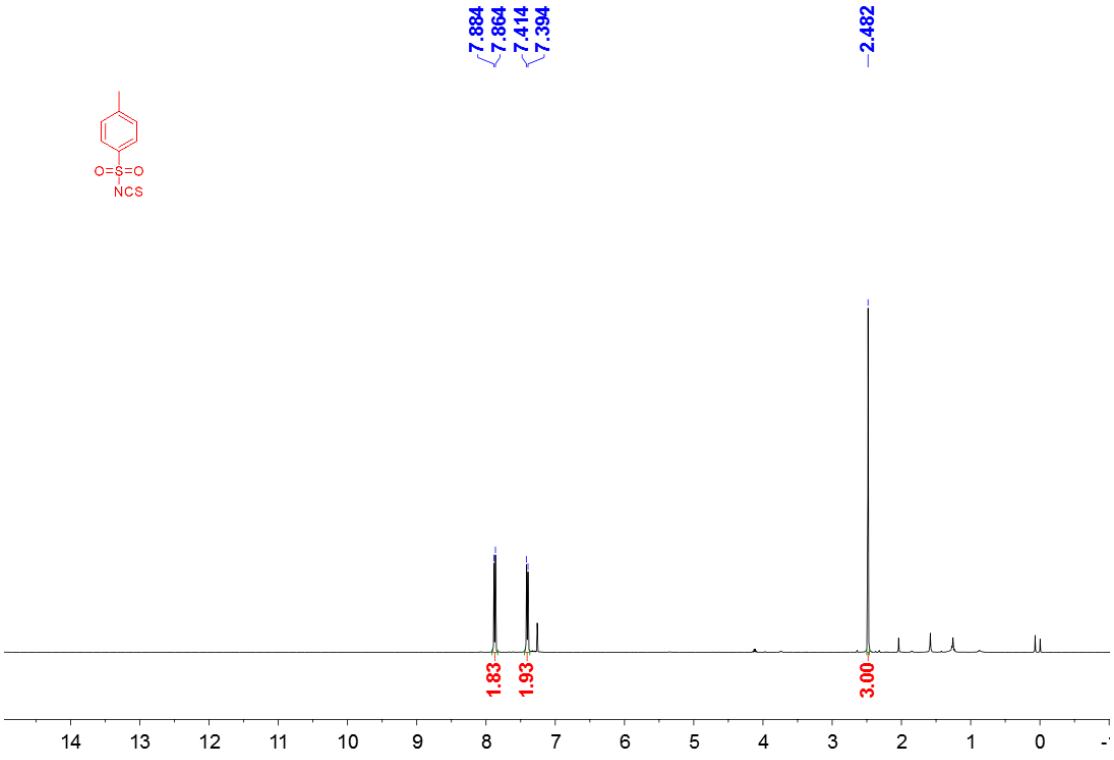
^{13}C NMR of Compound **2aj**



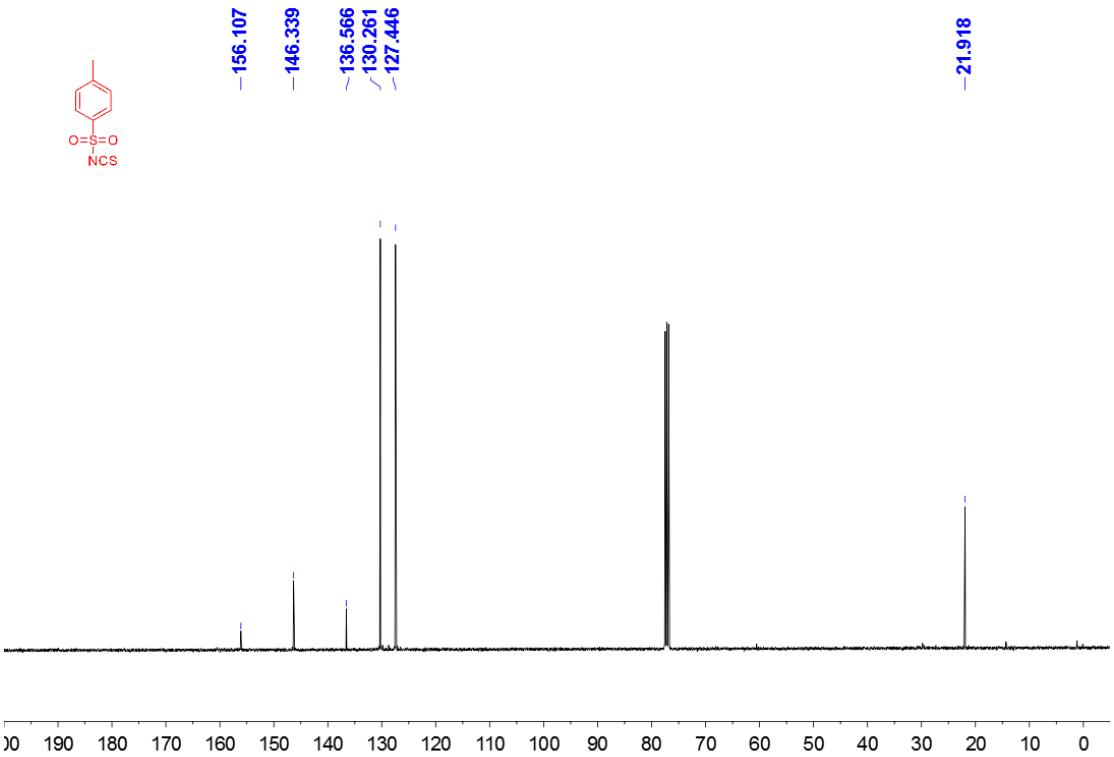
^{1}H NMR of Compound **2ak**



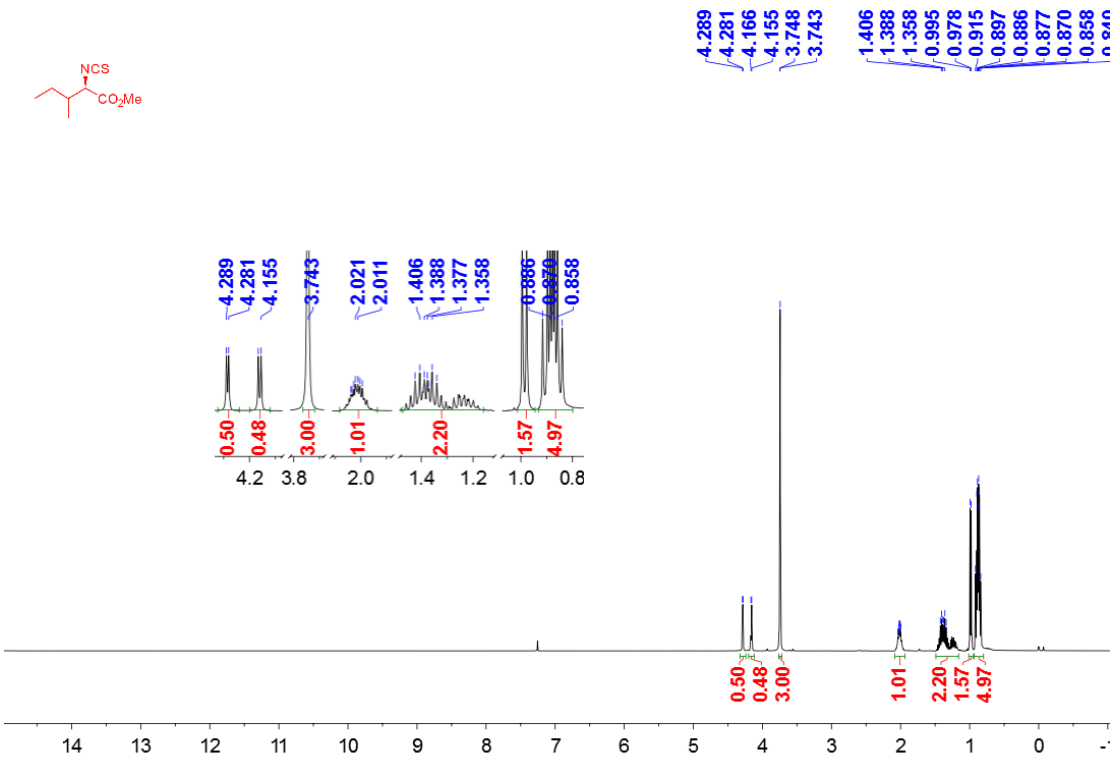
^{13}C NMR of Compound **2ak**



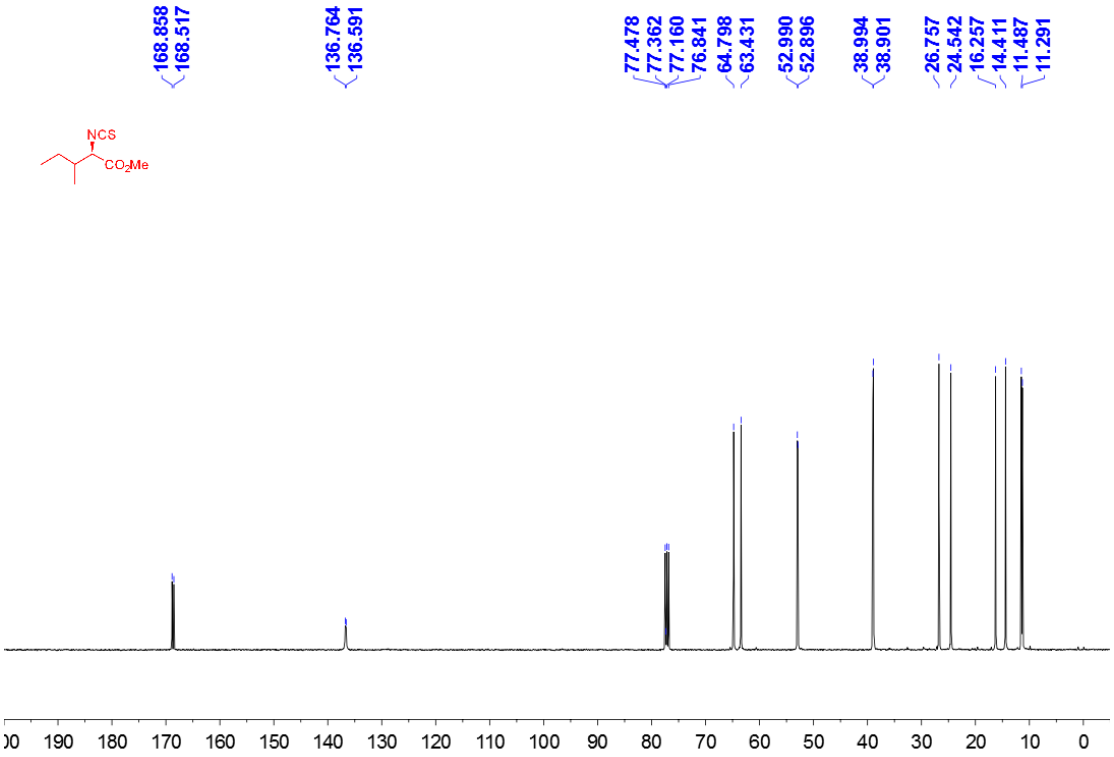
^{1}H NMR of Compound **2al**



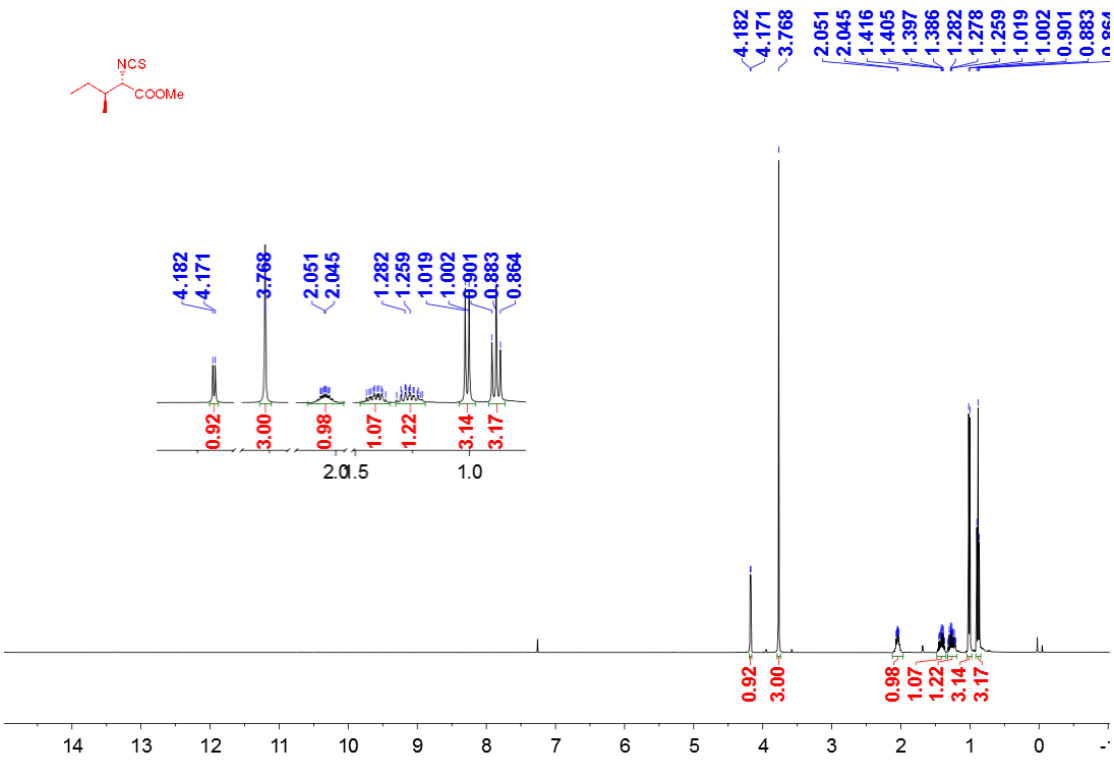
^{13}C NMR of Compound **2al**



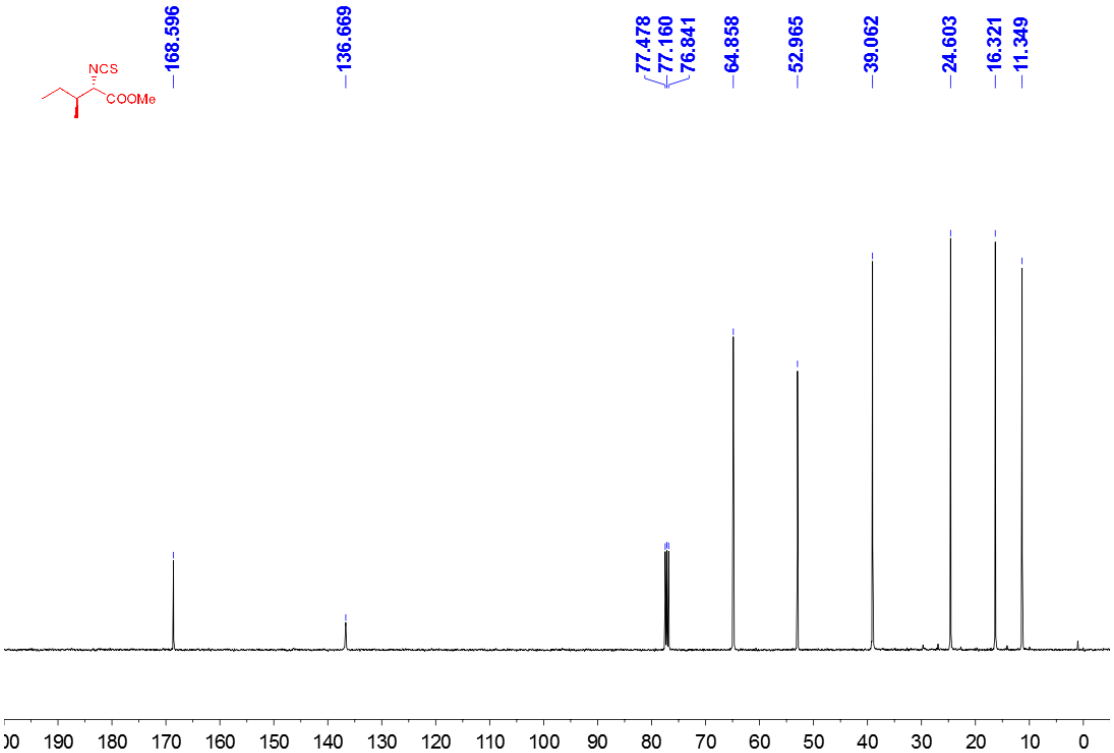
^{1}H NMR of Compound **11a and epi-11a**



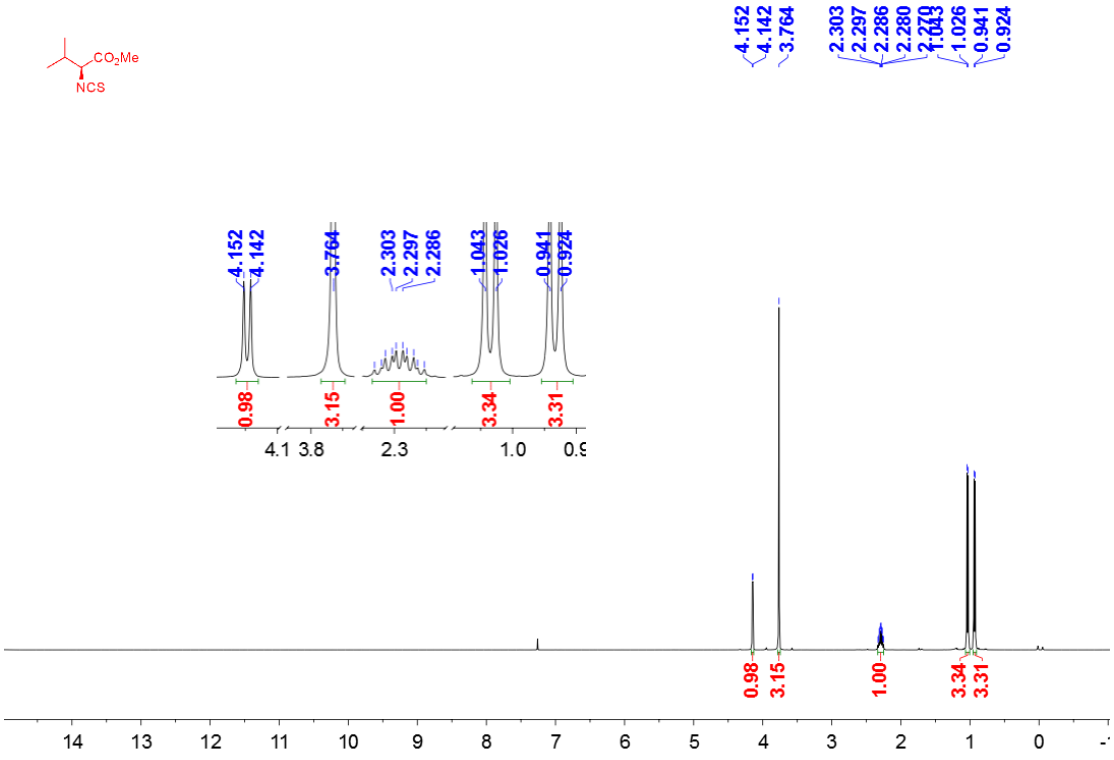
^{13}C NMR of Compound **11a and epi-11a**



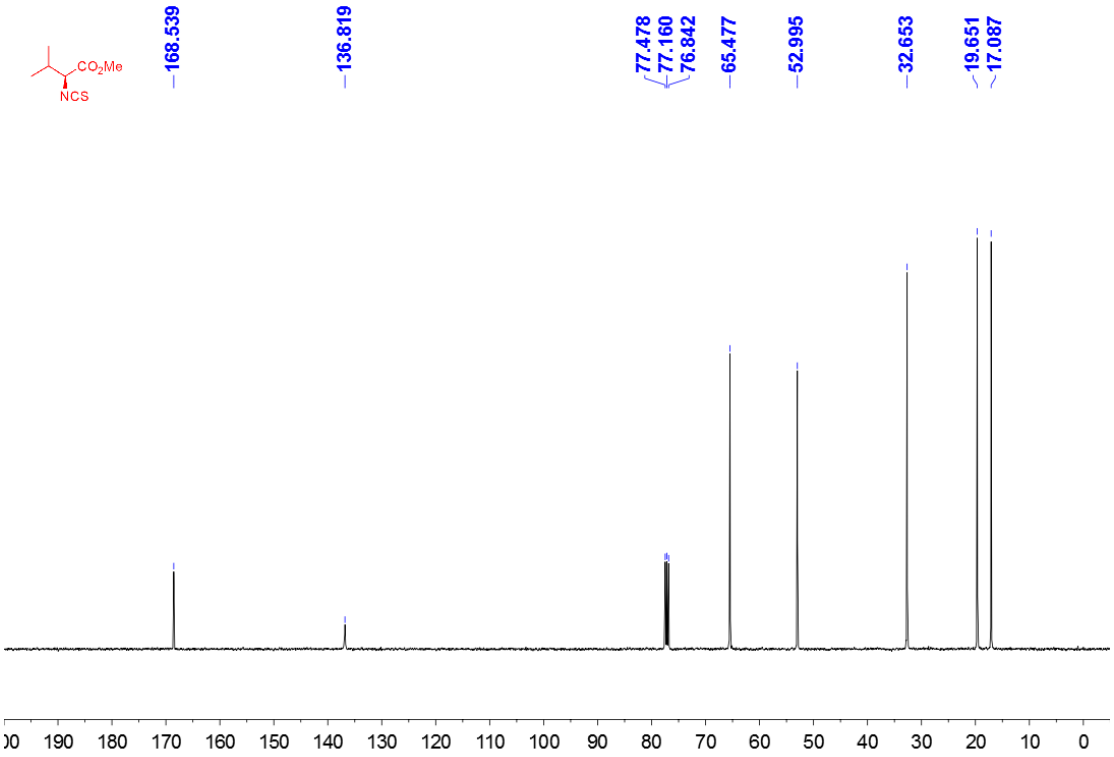
^{1}H NMR of Compound **11a**



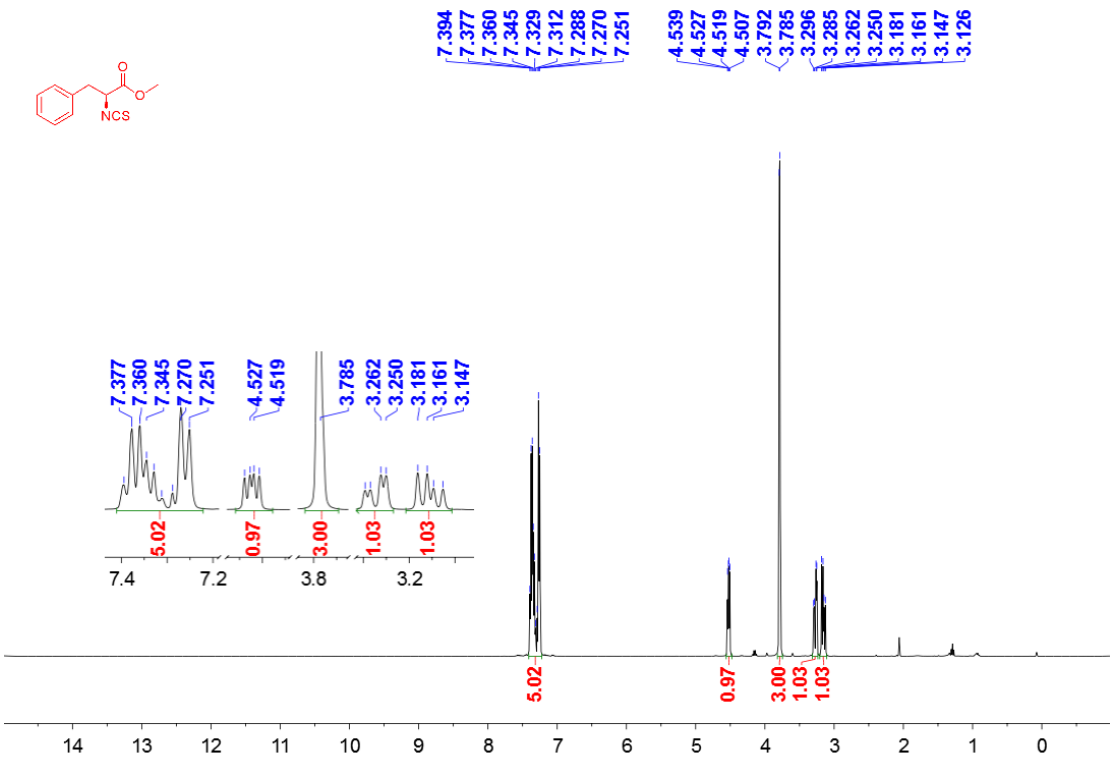
^{13}C NMR of Compound **11a**



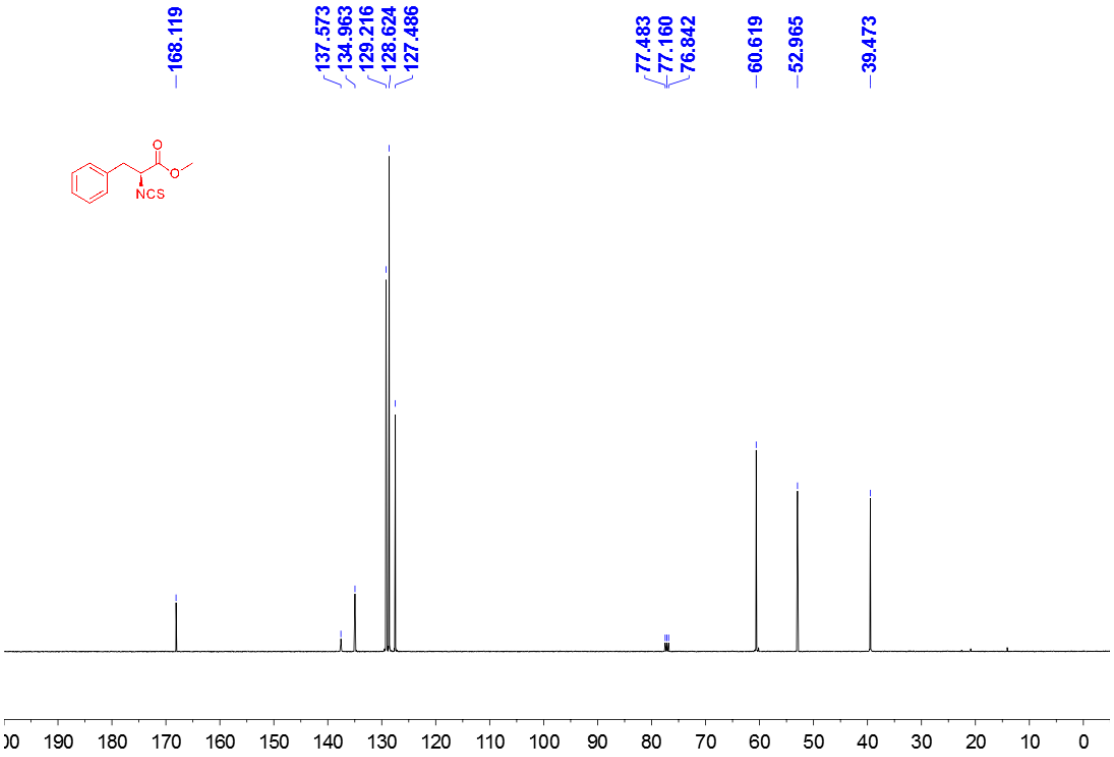
^{1}H NMR of Compound **11b**



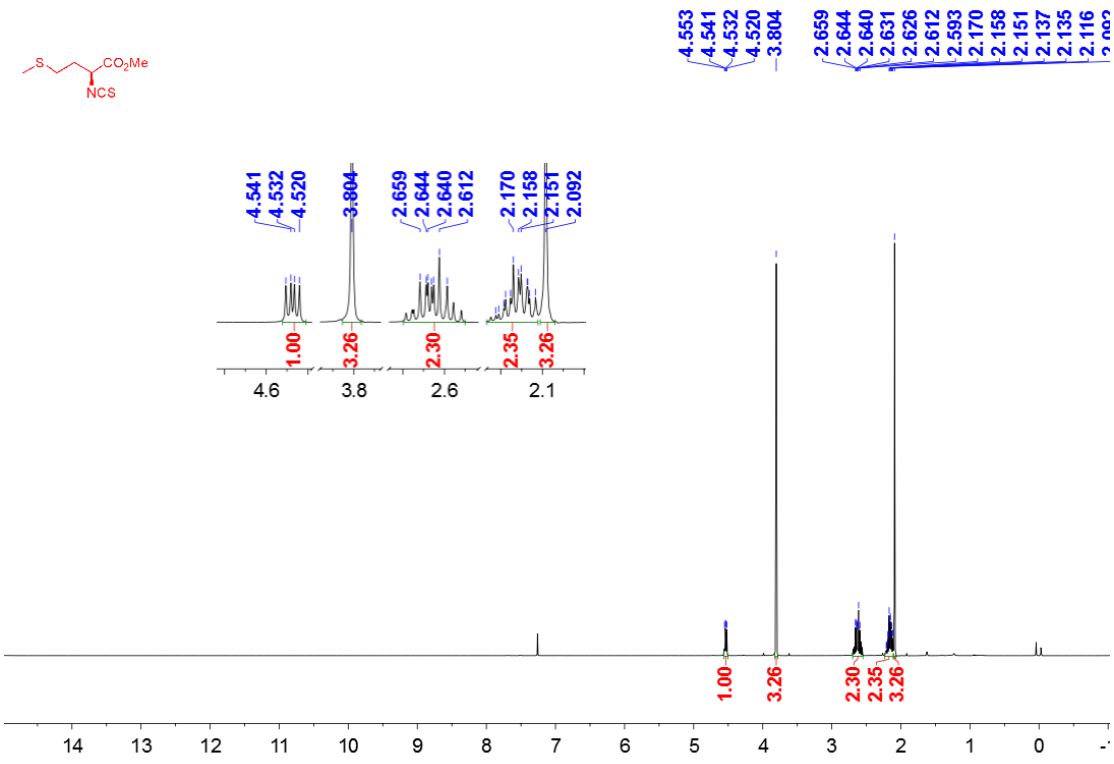
^{13}C NMR of Compound **11b**



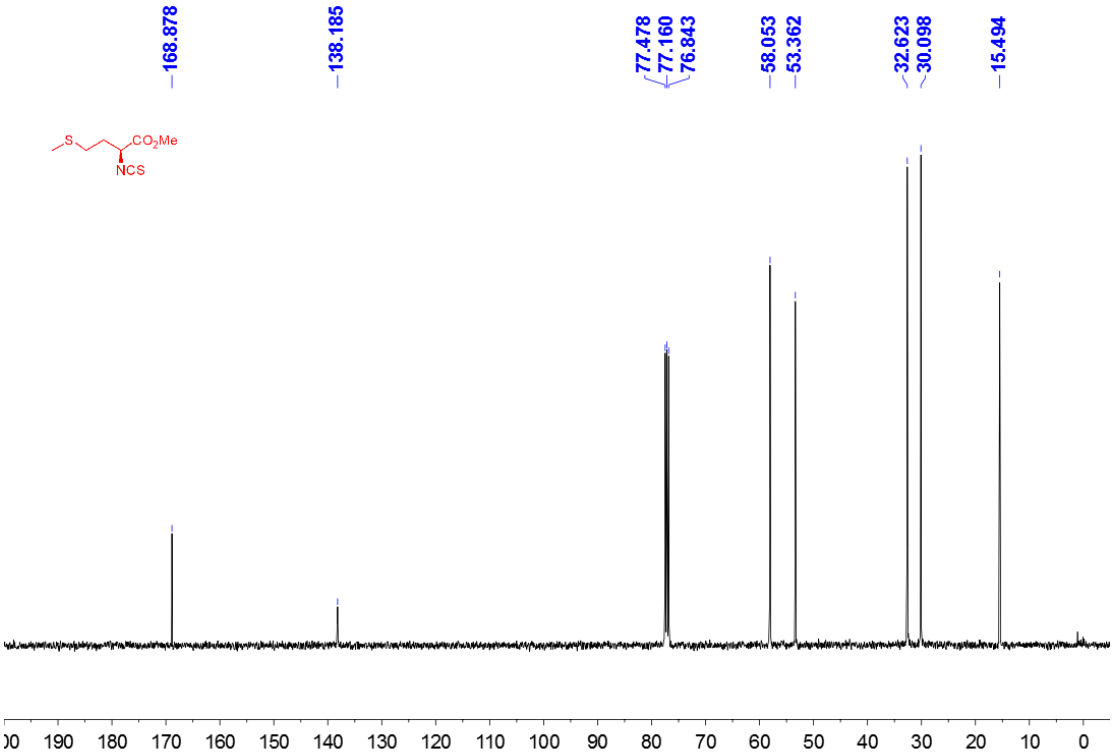
^{1}H NMR of Compound **11c**



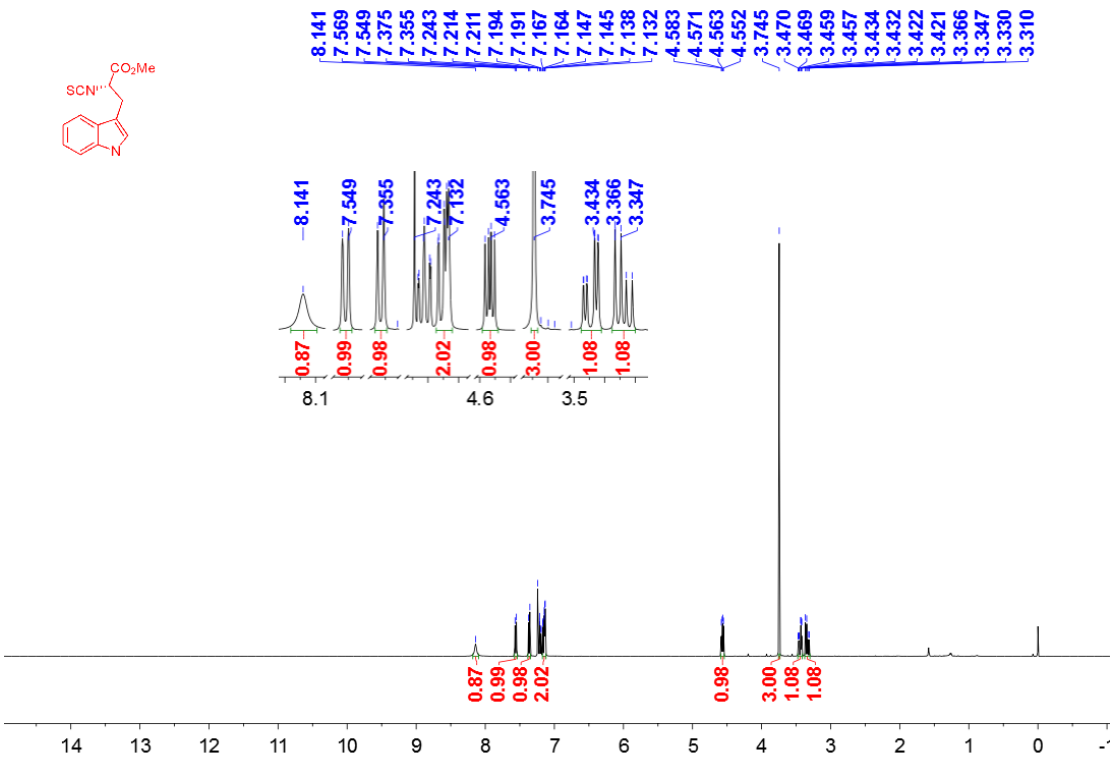
^{13}C NMR of Compound **11c**



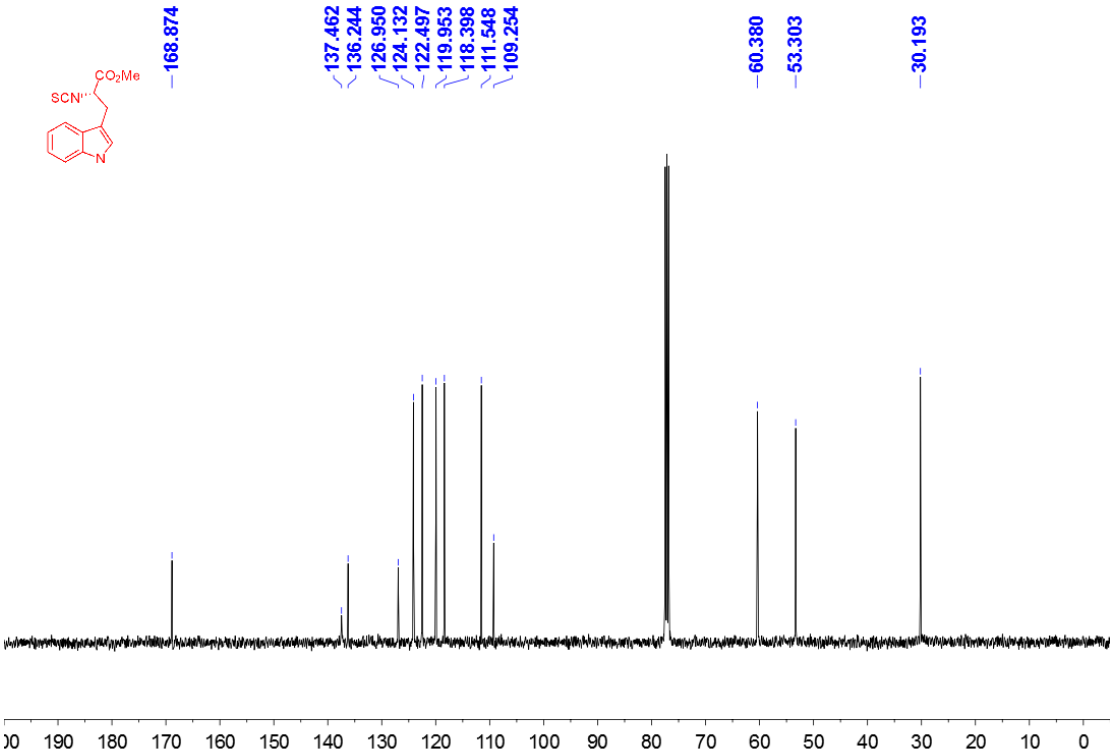
^{1}H NMR of Compound **11d**



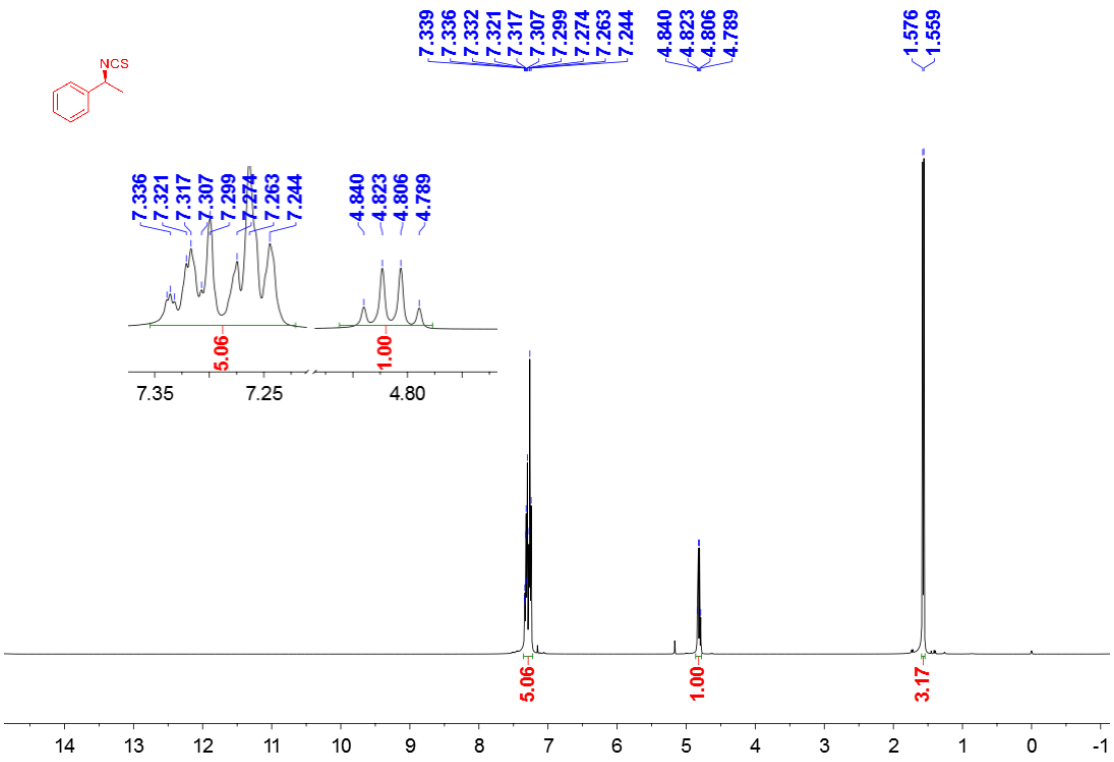
^{13}C NMR of Compound **11d**



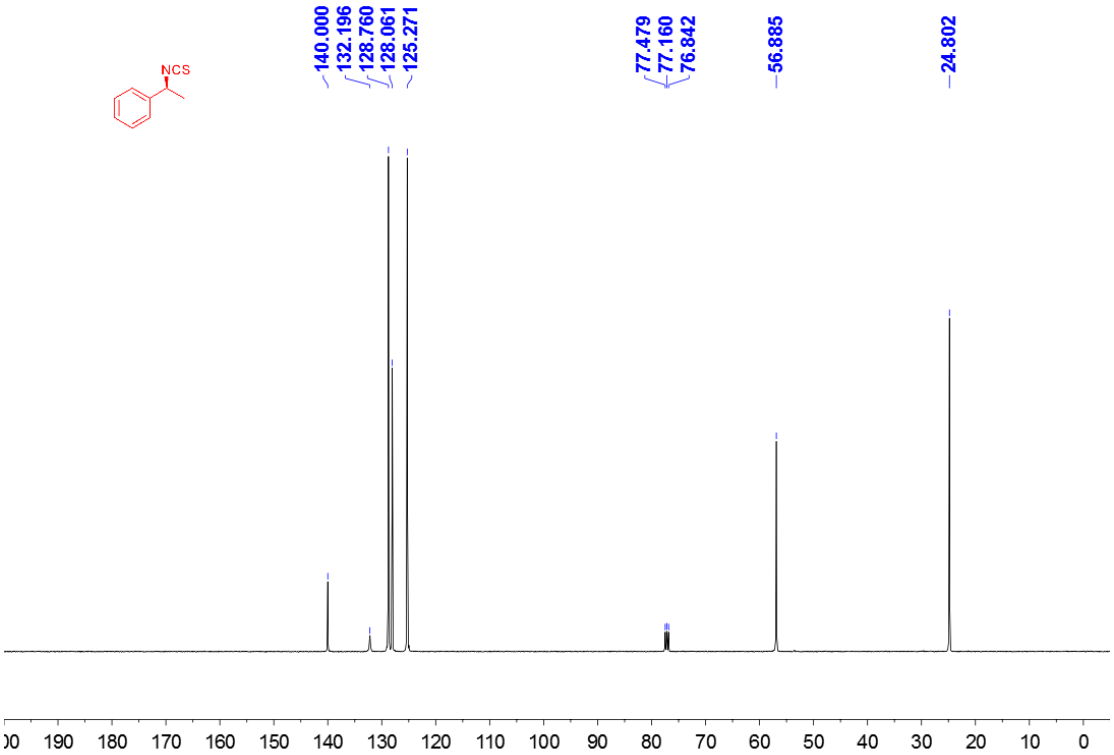
^{1}H NMR of Compound **11e**



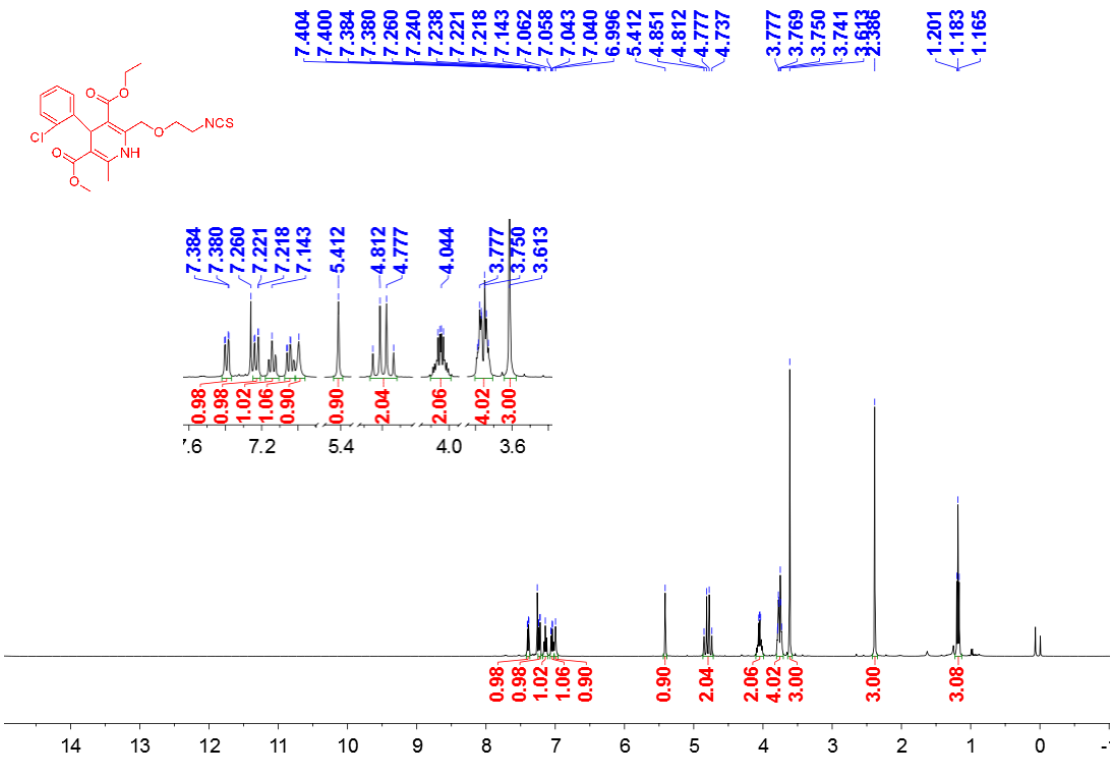
^{13}C NMR of Compound **11e**



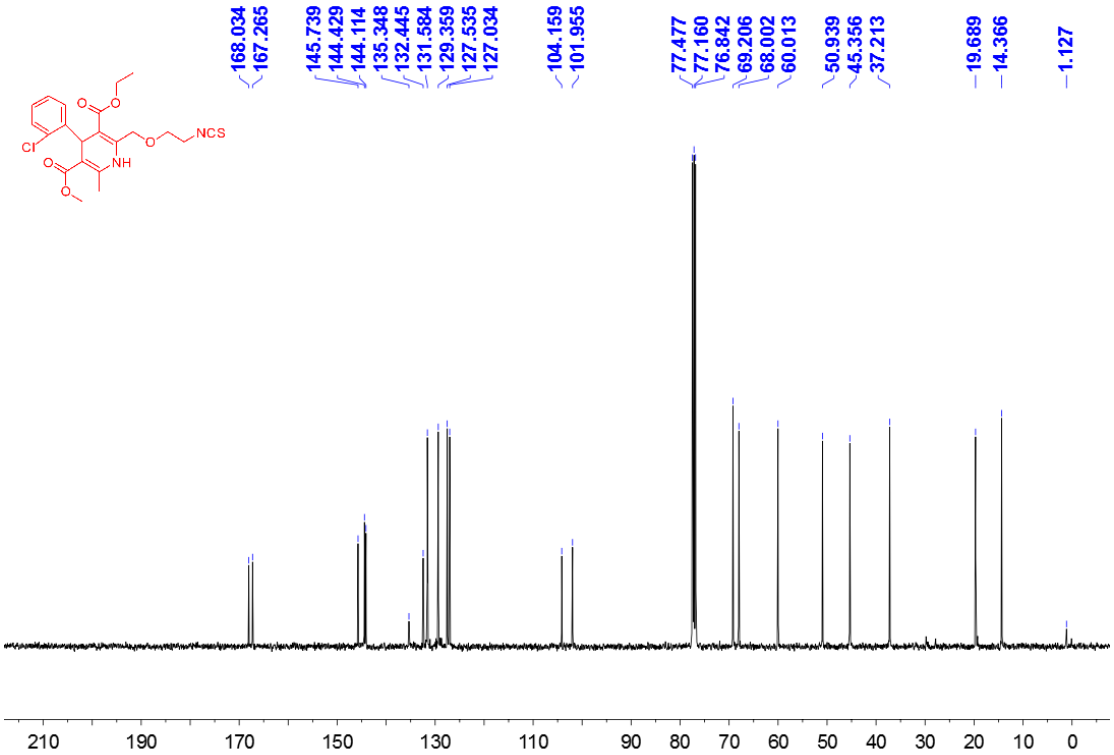
^{1}H NMR of Compound **11f**



^{13}C NMR of Compound **11f**

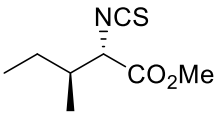


^{1}H NMR of Compound **13**

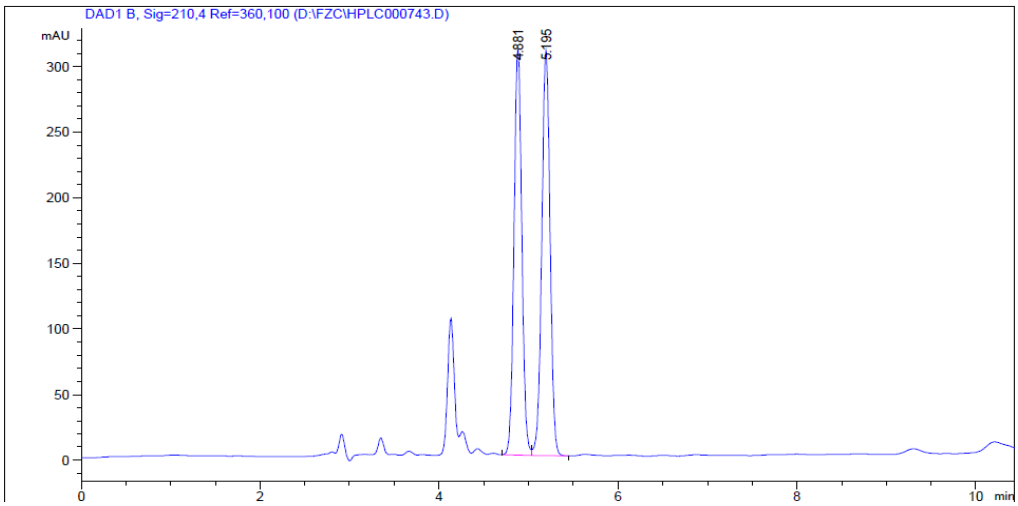


^{13}C NMR of Compound **13**

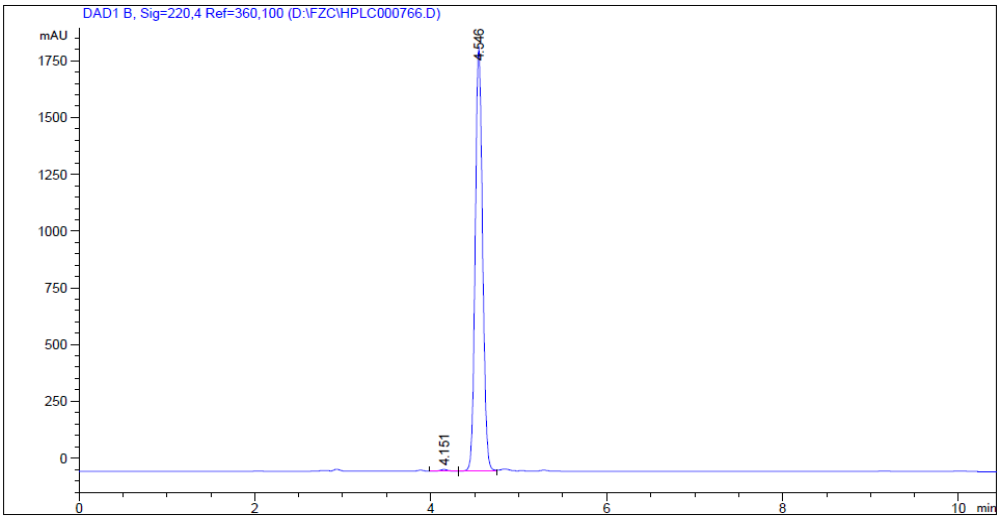
9.2. Copies of HPLC profiles of Chiral Product 11



11a, ee = 99 %

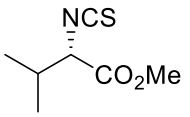


#	[min]		[min]	[mAU*s]	[mAU]	%
1	4.881	BV	0.0926	1872.99683	309.44669	48.4223
2	5.195	VB	0.0993	1995.05078	309.16745	51.5777

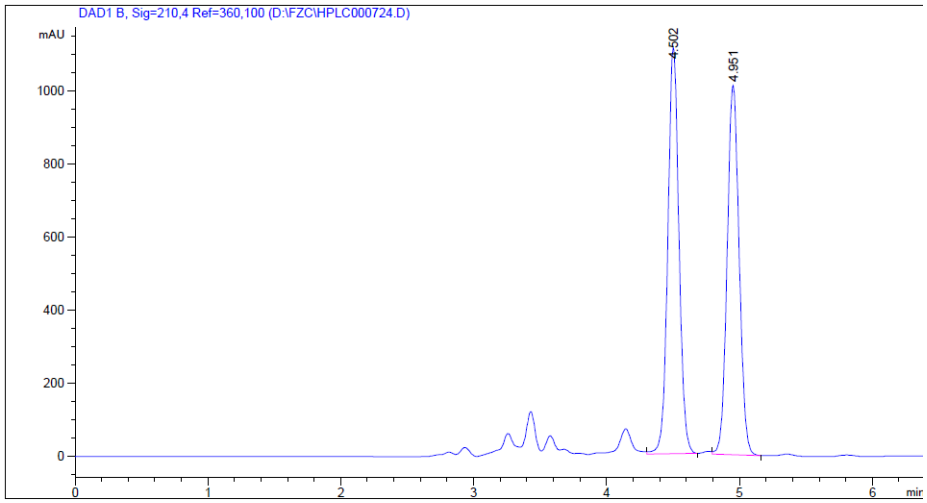


#	[min]		[min]	[mAU*s]	[mAU]	%
1	4.151	VB	0.0836	38.87138	7.13434	0.3565
2	4.546	BV	0.0902	1.08657e4	1859.88184	99.6435

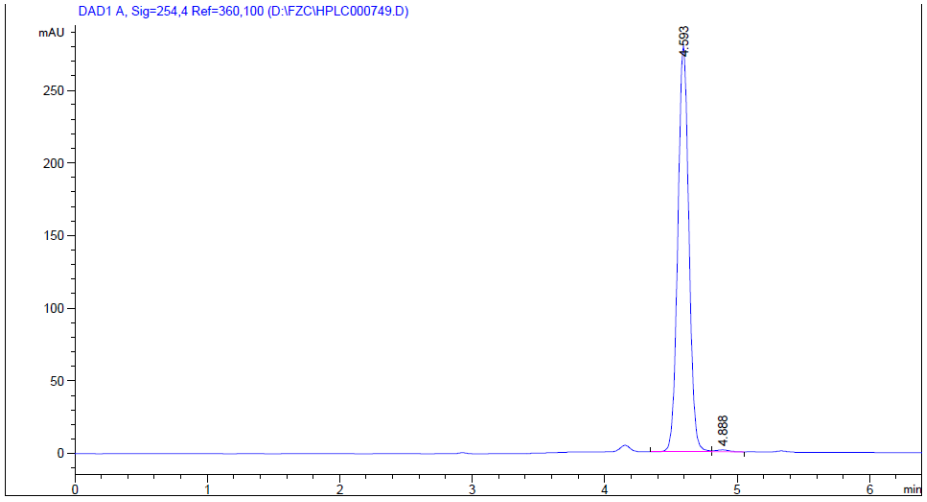
HPLC of Chiral Product **11a**



11b , ee = 99 %

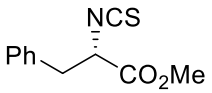


#	[min]		[min]	[mAU*s]	[mAU]	%
1	4.502	VB	0.0898	6460.12256	1112.27942	50.5667
2	4.951	VB	0.0969	6315.33252	1010.81927	49.4333

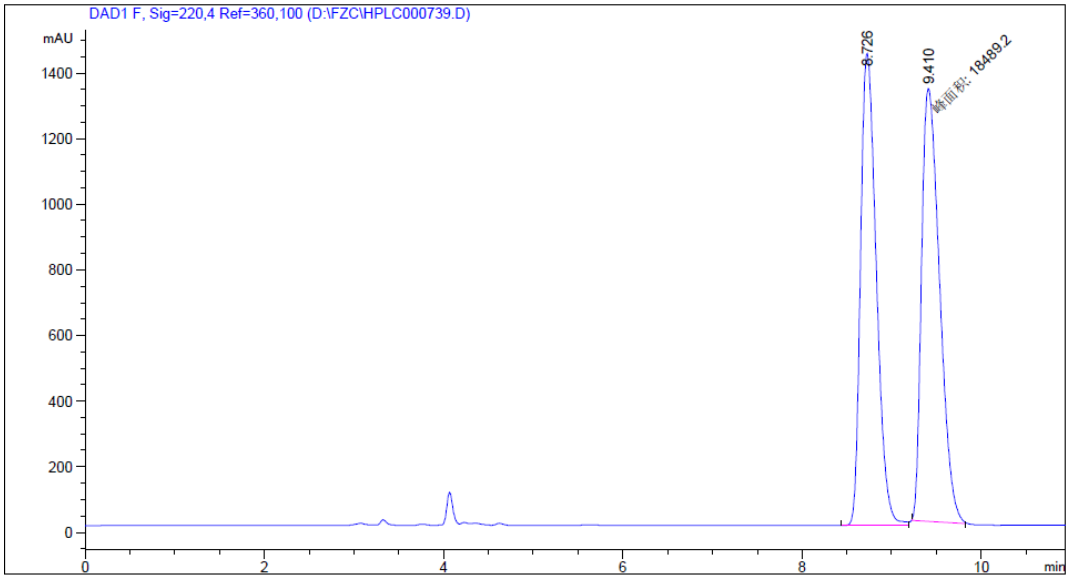


#	[min]		[min]	[mAU*s]	[mAU]	%
1	4.593	BV	0.0892	1609.82947	279.44308	99.4079
2	4.888	VB	0.1049	9.58809	1.34931	0.5921

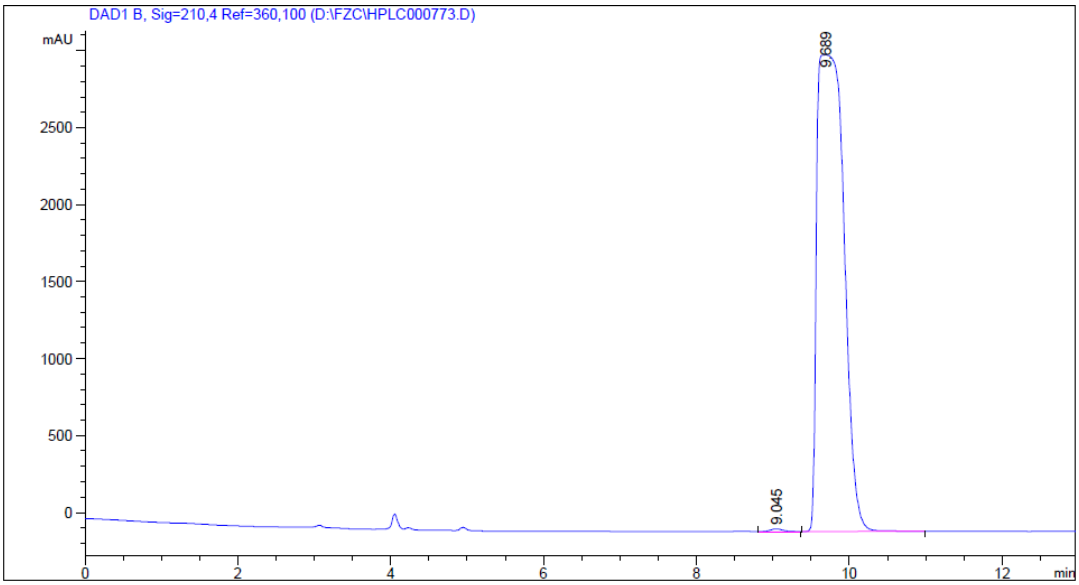
HPLC of Chiral Product **11b**



11c, ee = 99%

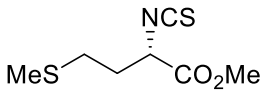


#	[min]		[min]	[mAU*s]	[mAU]	%
1	8.726	BV	0.1929	1.76185e4	1438.10608	48.7942
2	9.410	MM	0.2335	1.84892e4	1319.49512	51.2058

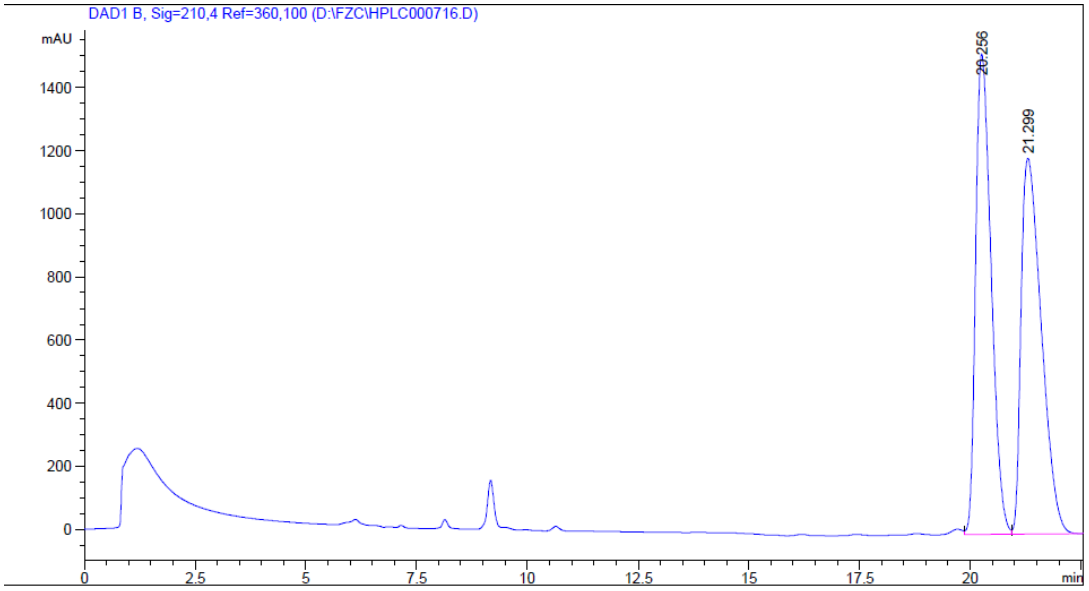


#	[min]		[min]	[mAU*s]	[mAU]	%
1	9.045	BB	0.1662	183.73738	16.98218	0.2420
2	9.689	BB	0.3654	7.57284e4	3096.01782	99.7580

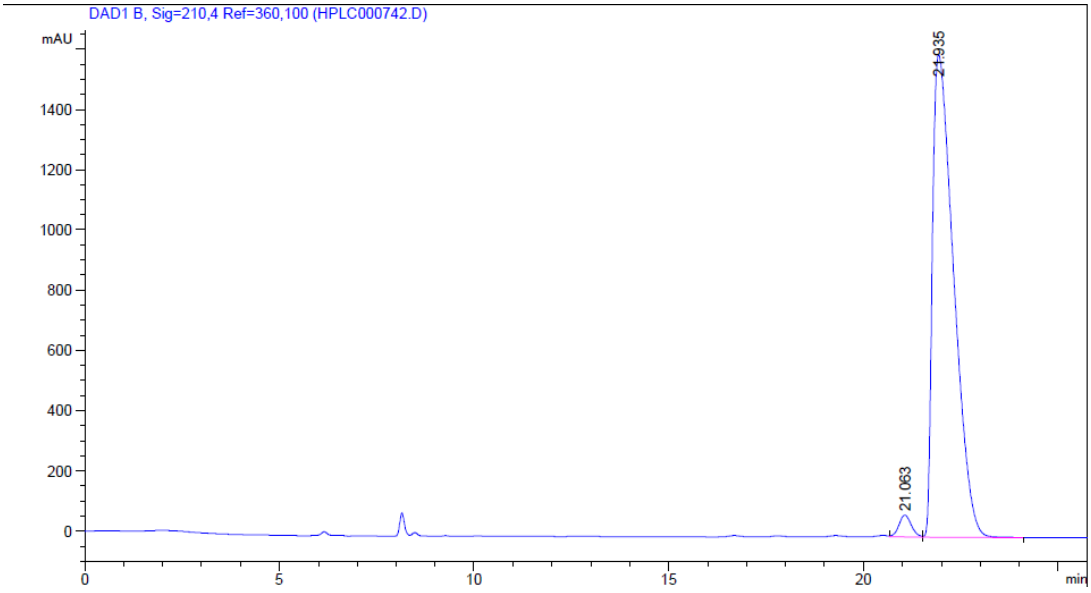
HPLC of Chiral Product **11c**



11d, ee = 94 %

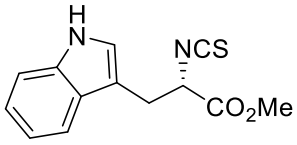


#	[min]		[min]	[mAU*s]	[mAU]	%
1	20.256	VV	0.3813	3.69627e4	1521.92480	49.4304
2	21.299	VBA	0.4985	3.78146e4	1190.76550	50.5696

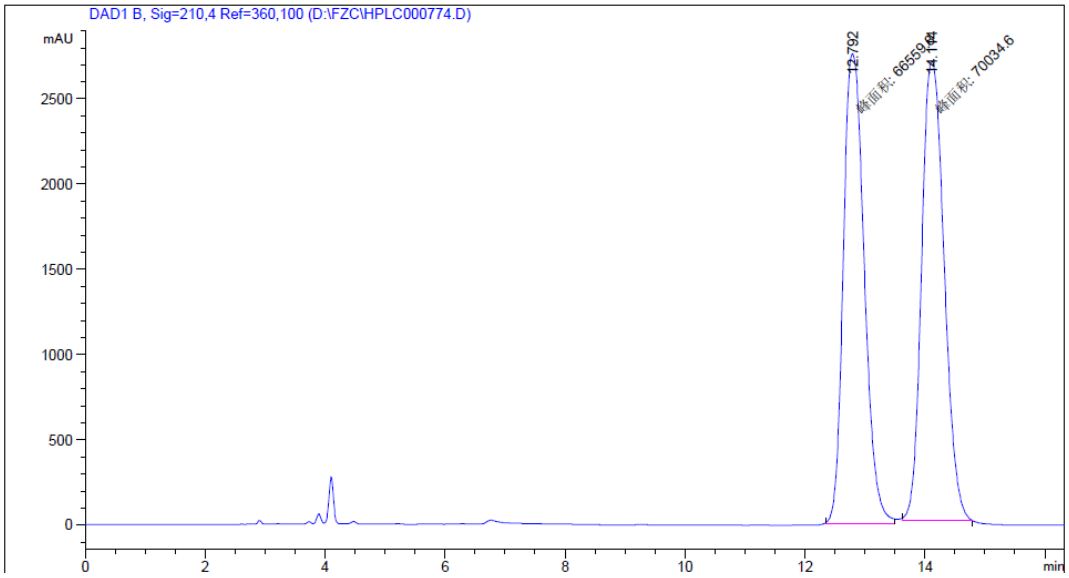


#	[min]		[min]	[mAU*s]	[mAU]	%
1	21.063	VV	0.3432	1619.51855	72.89110	2.6147
2	21.935	VB	0.5896	6.03204e4	1600.94751	97.3853

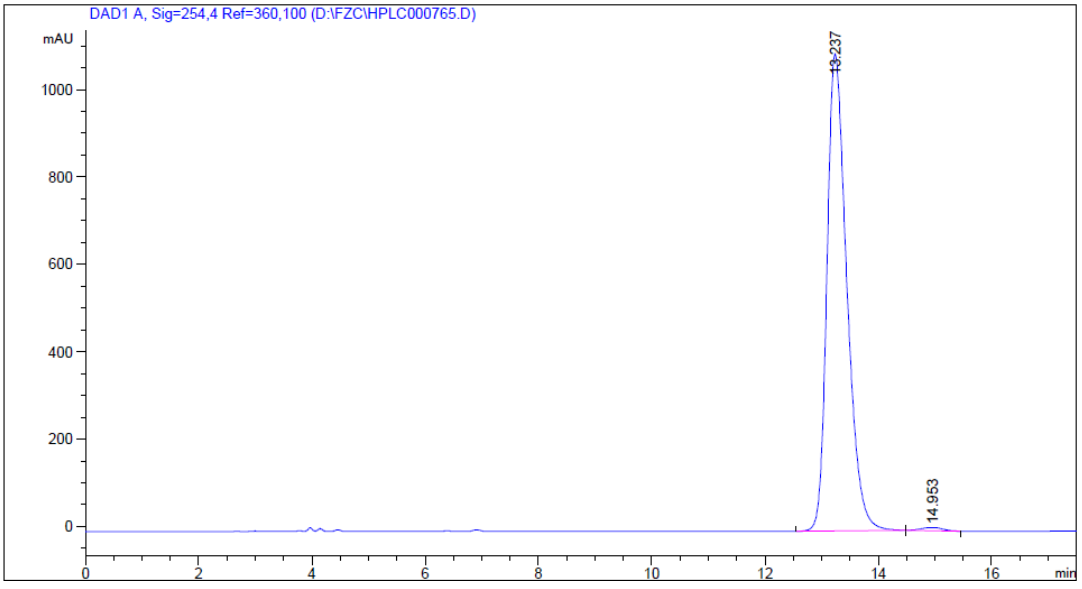
HPLC of Chiral Product **11d**



11e , ee = 98 % , OD-H, 1, 19, 80:20



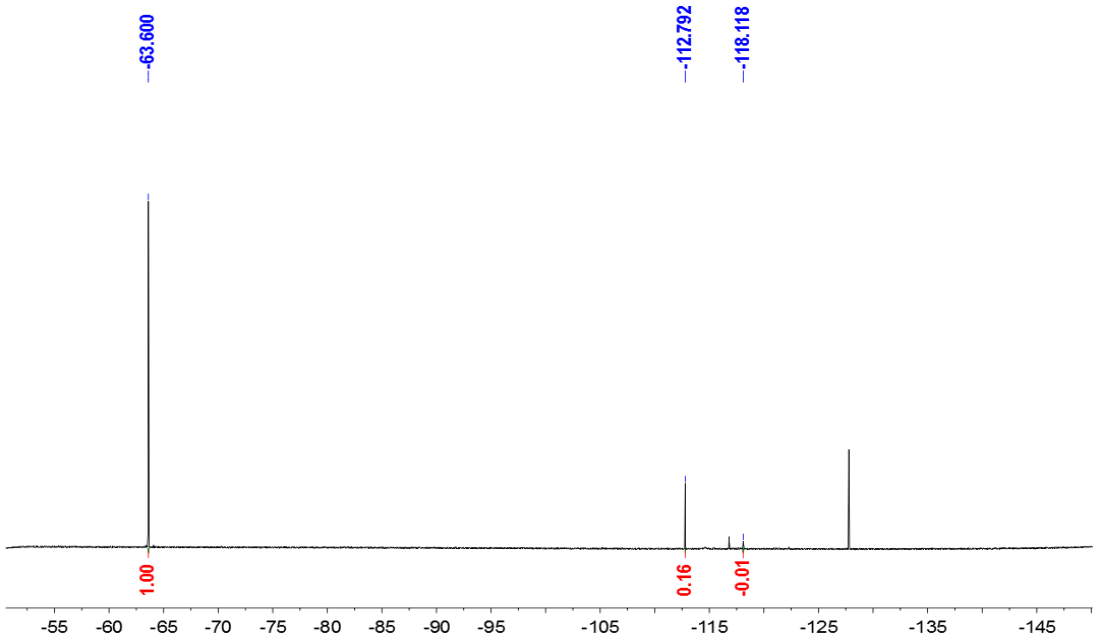
#	[min]		[min]	[mAU*s]	[mAU]	%
1	12.792	MM	0.4028	6.65598e4	2753.74976	48.7280
2	14.114	MM	0.4337	7.00346e4	2691.48975	51.2720



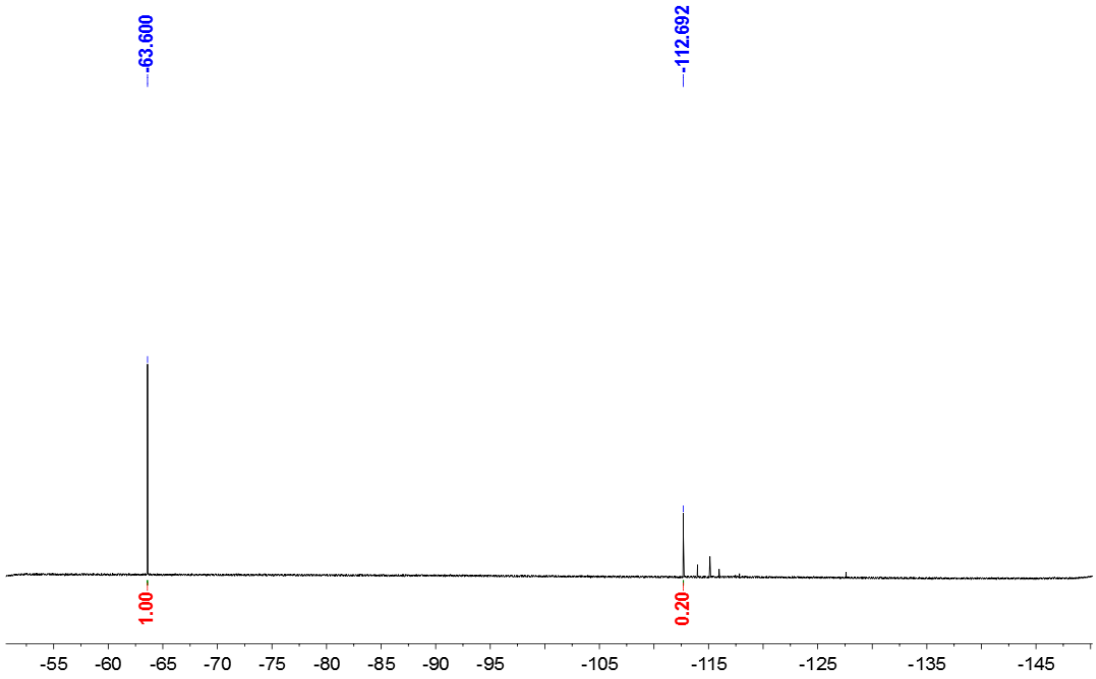
#	[min]		[min]	[mAU*s]	[mAU]	%
1	13.237	BB	0.3716	2.65277e4	1091.14551	99.2940
2	14.953	BB	0.4082	188.62254	7.47988	0.7060

HPLC of Chiral Product **11e**

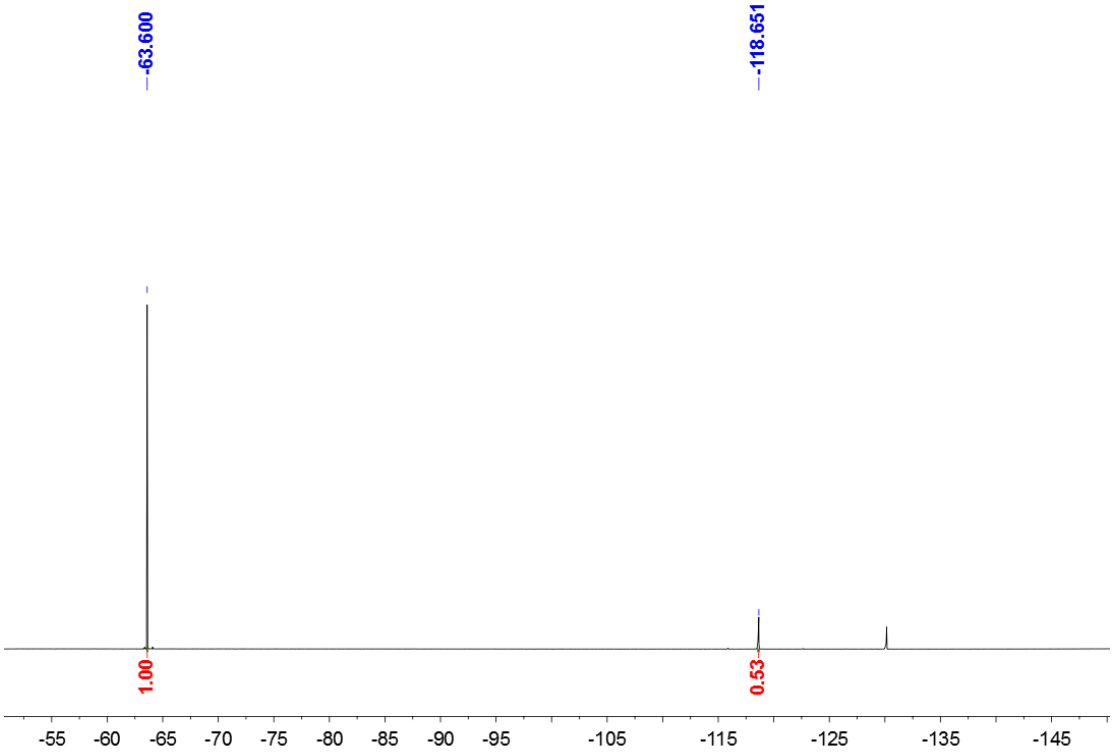
9.3. Copies of ^{19}F NMR Spectra in Optimization of the Conditions



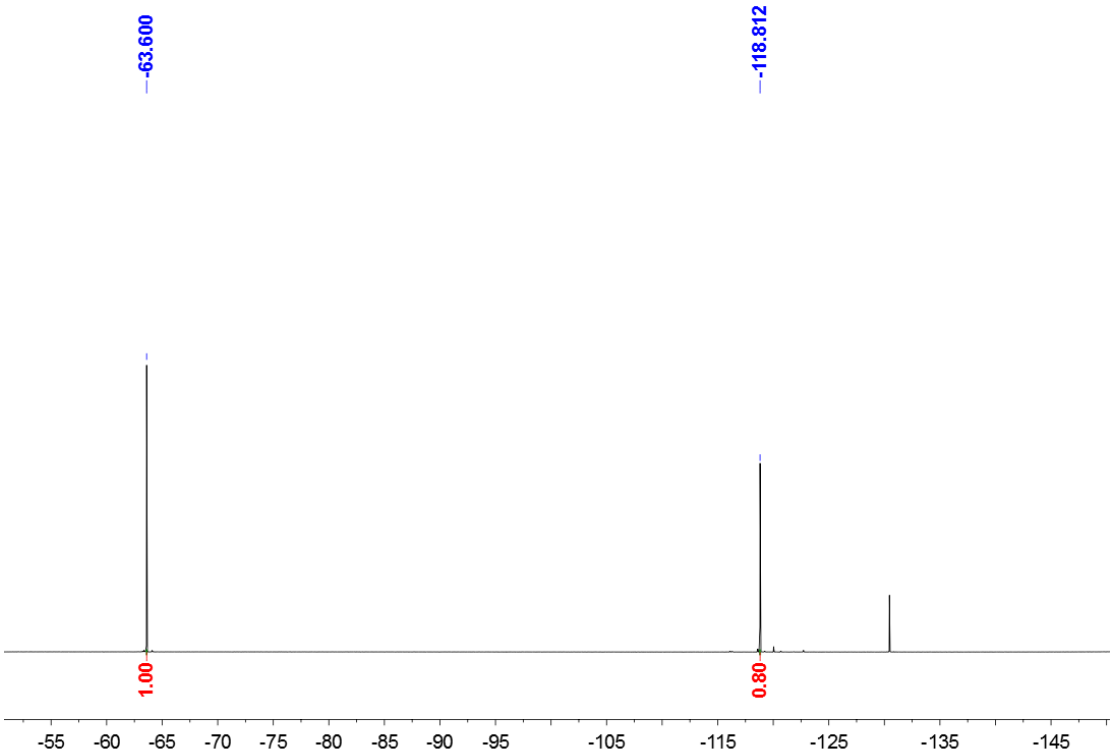
^{19}F NMR of Entry **1**



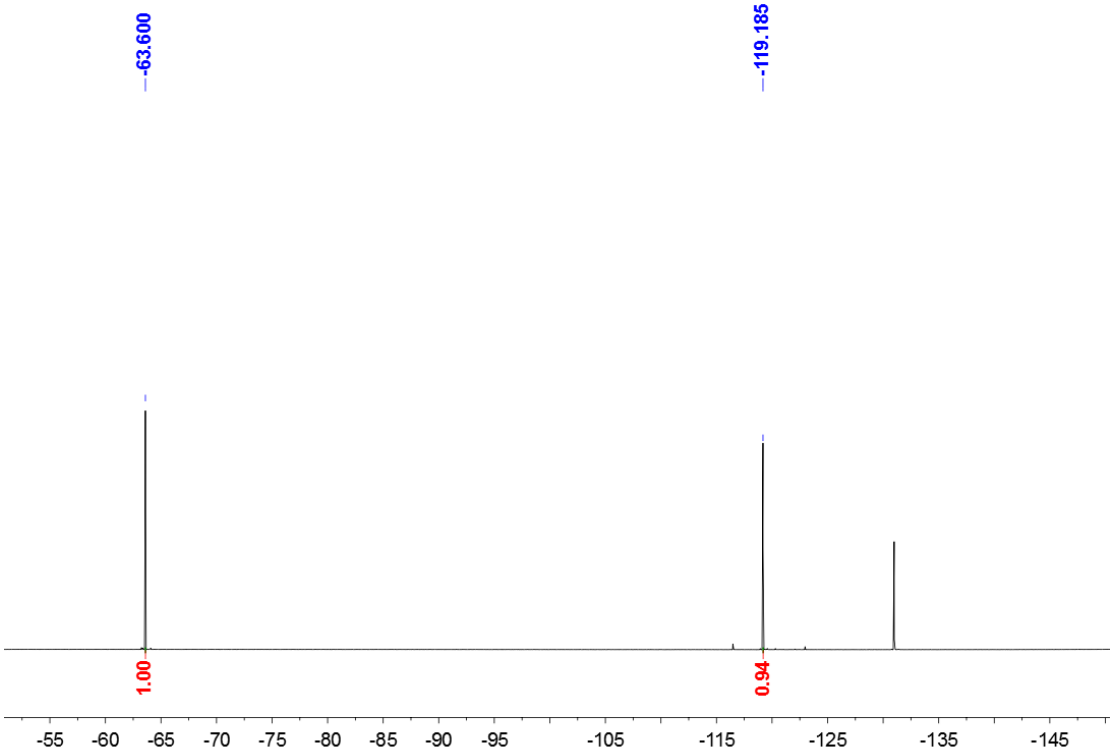
^{19}F NMR of Entry **2**



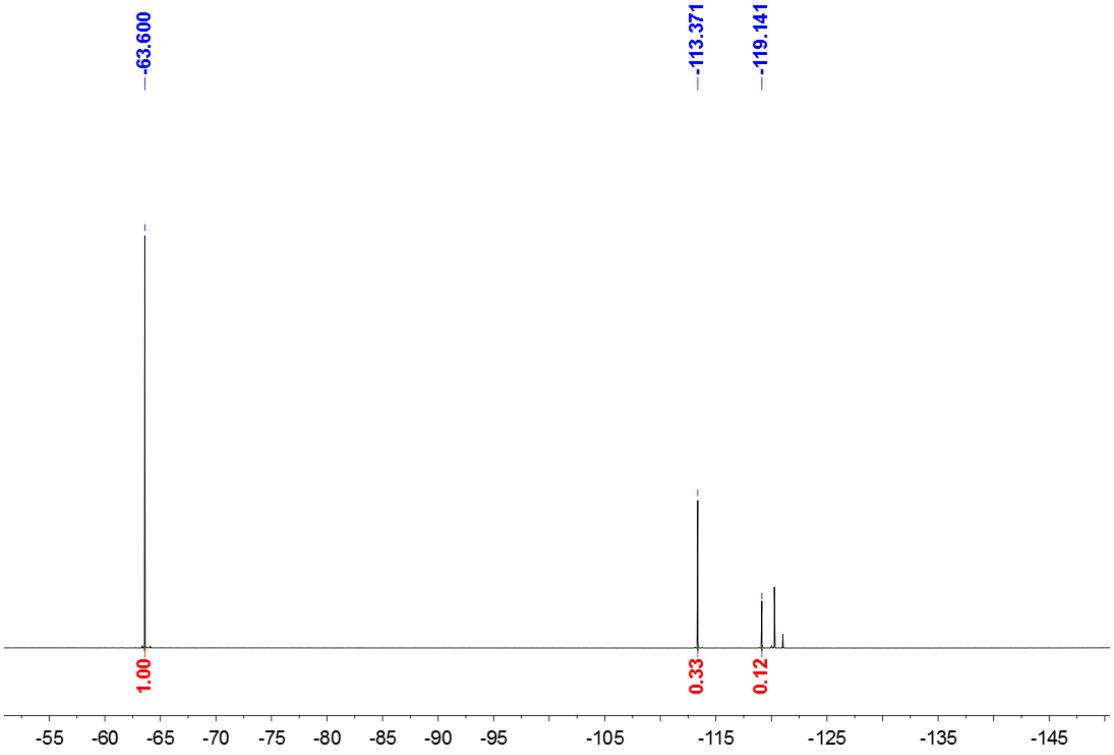
^{19}F NMR of Entry **3**



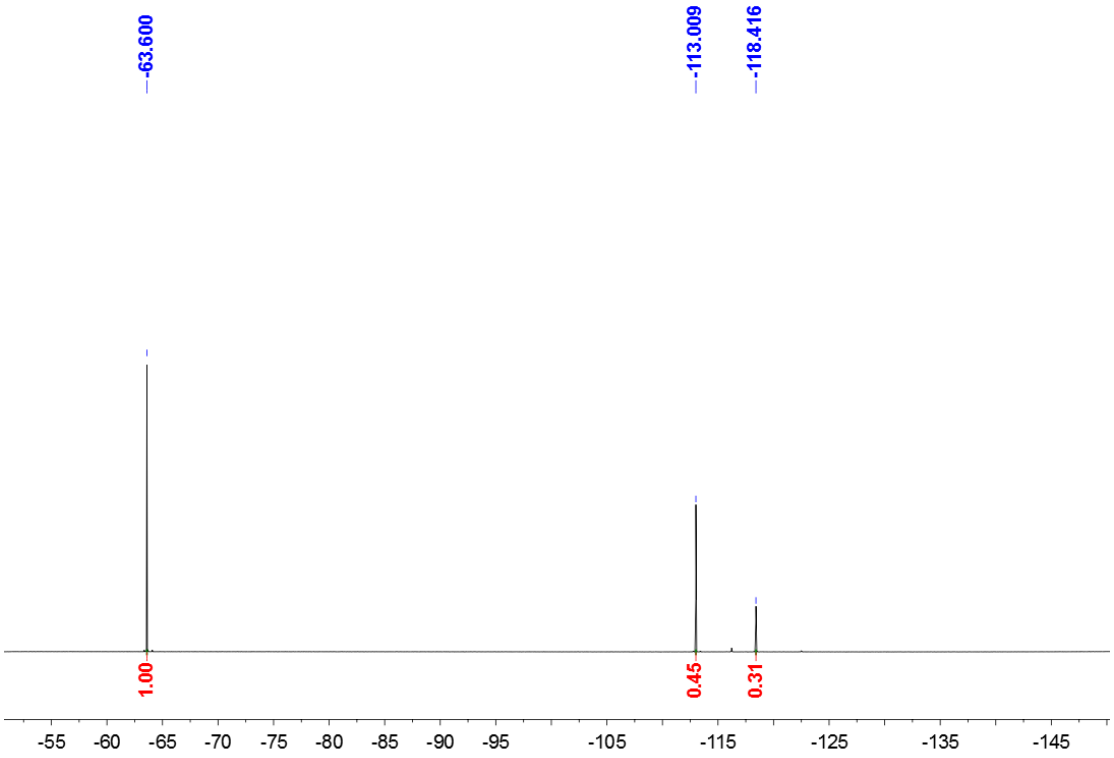
^{19}F NMR of Entry **4**



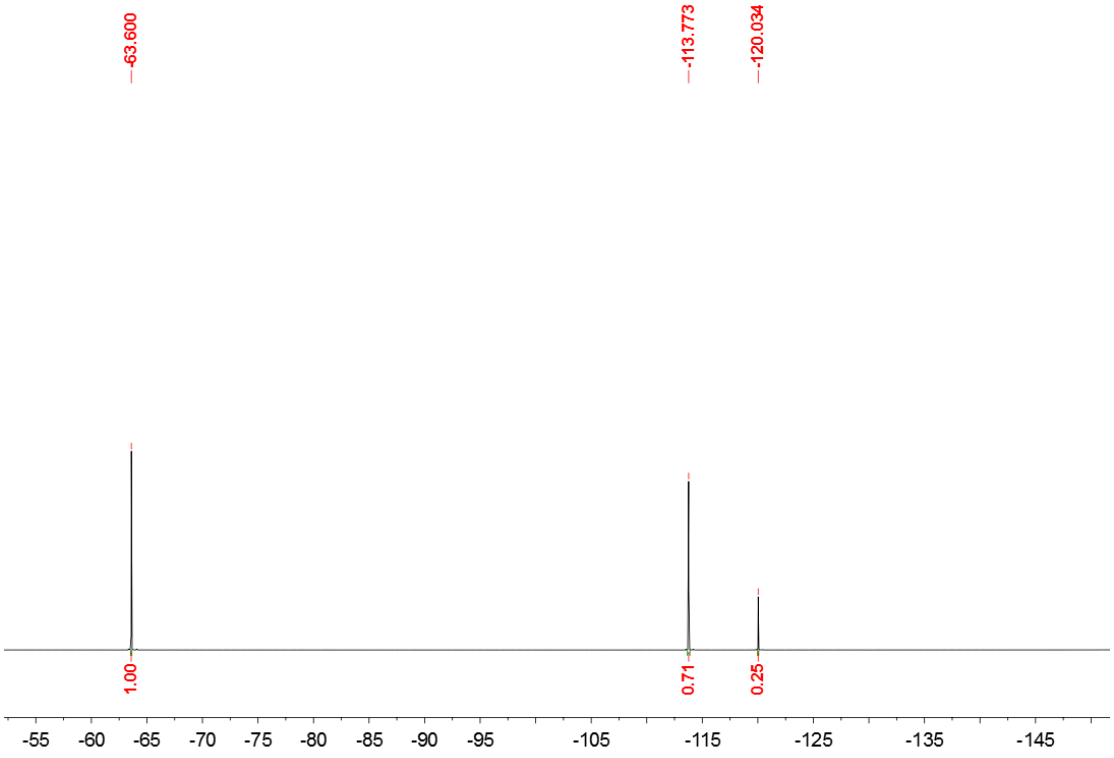
^{19}F NMR of Entry **5**



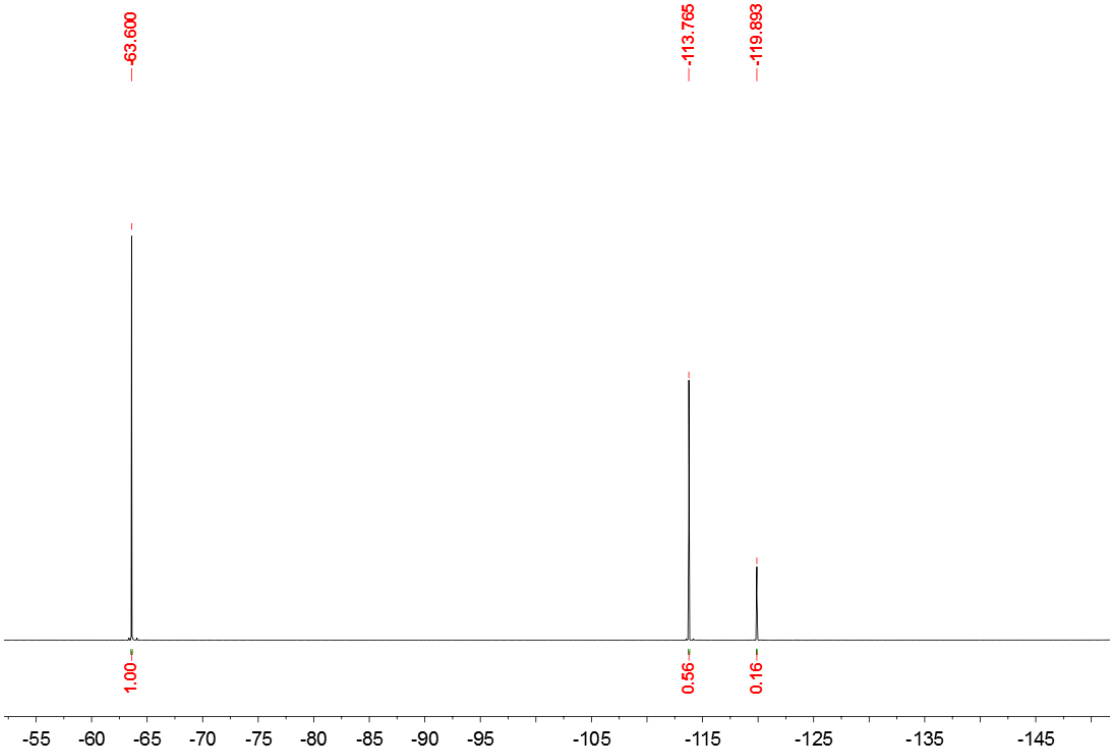
^{19}F NMR of Entry **6**



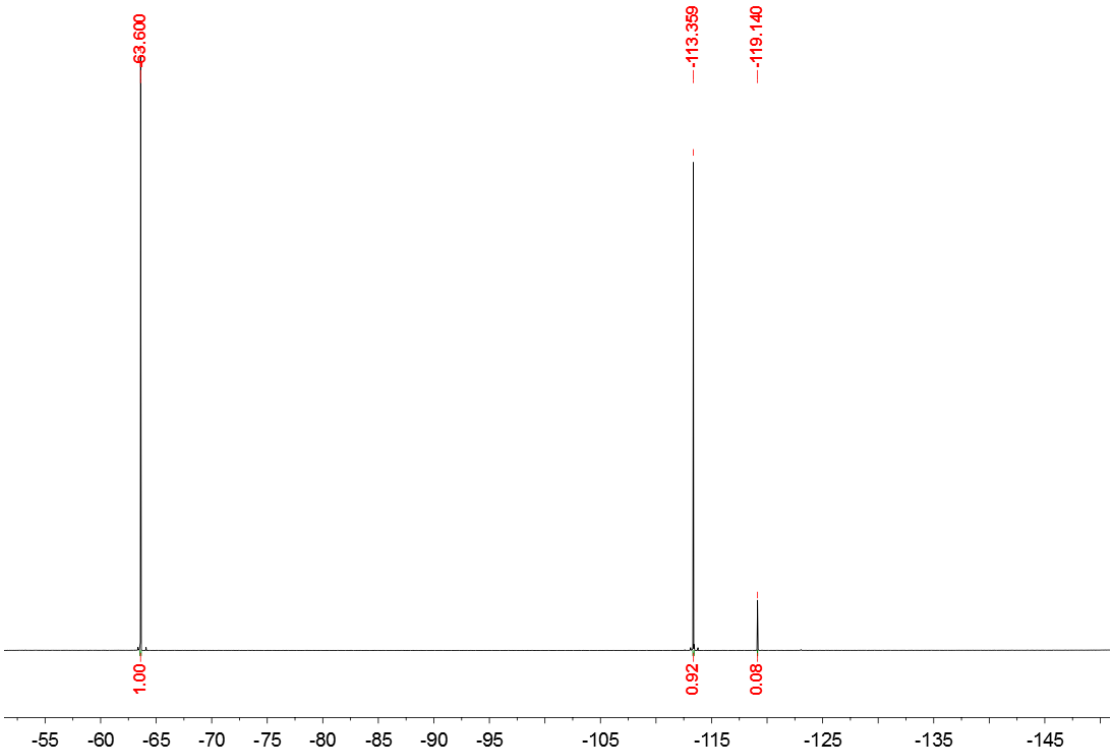
^{19}F NMR of Entry **7**



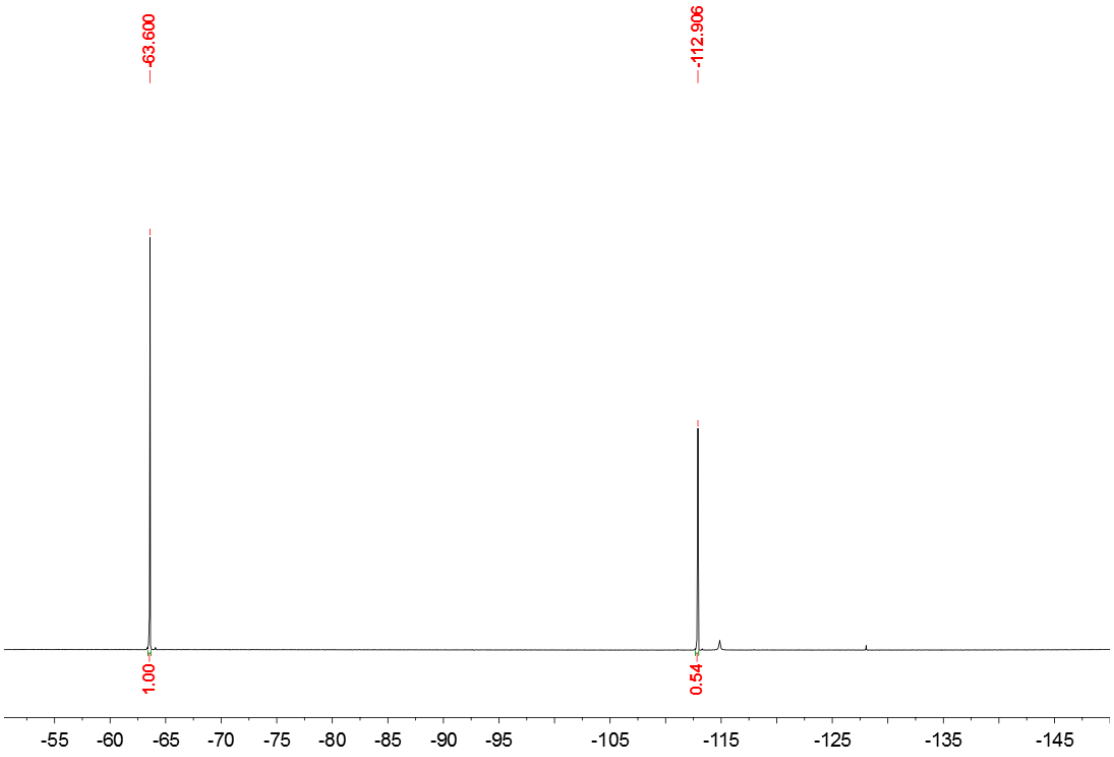
^{19}F NMR of Entry **8**



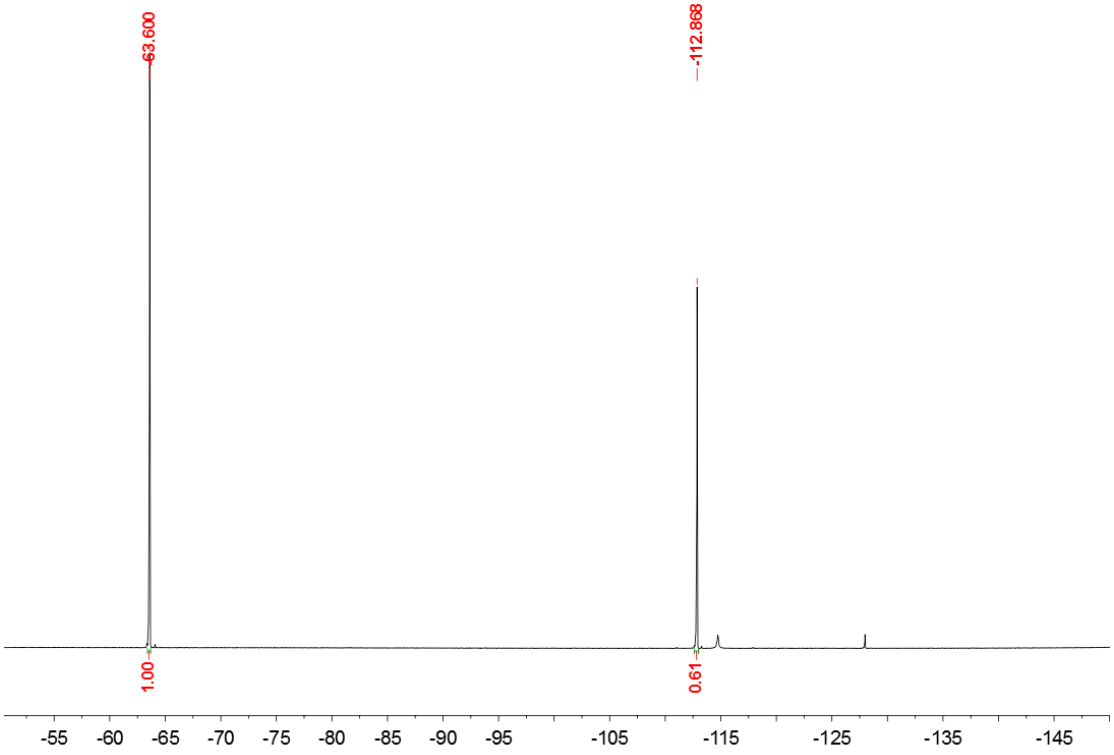
^{19}F NMR of Entry **9**



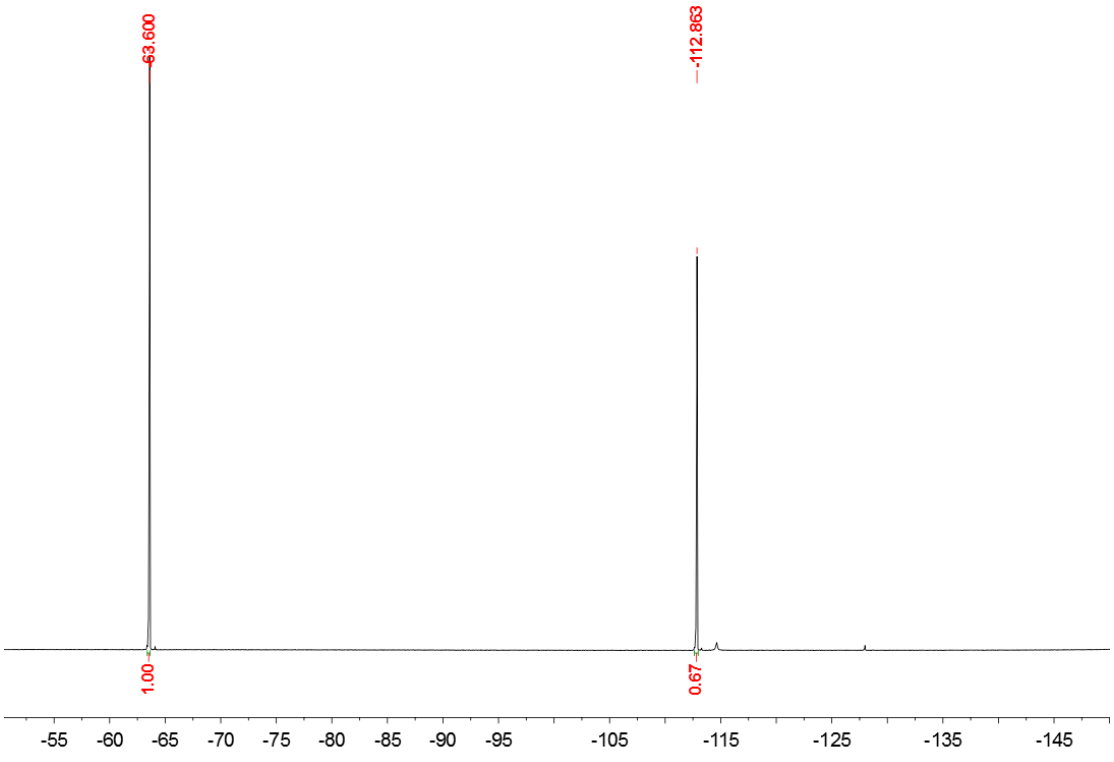
^{19}F NMR of Entry **10**



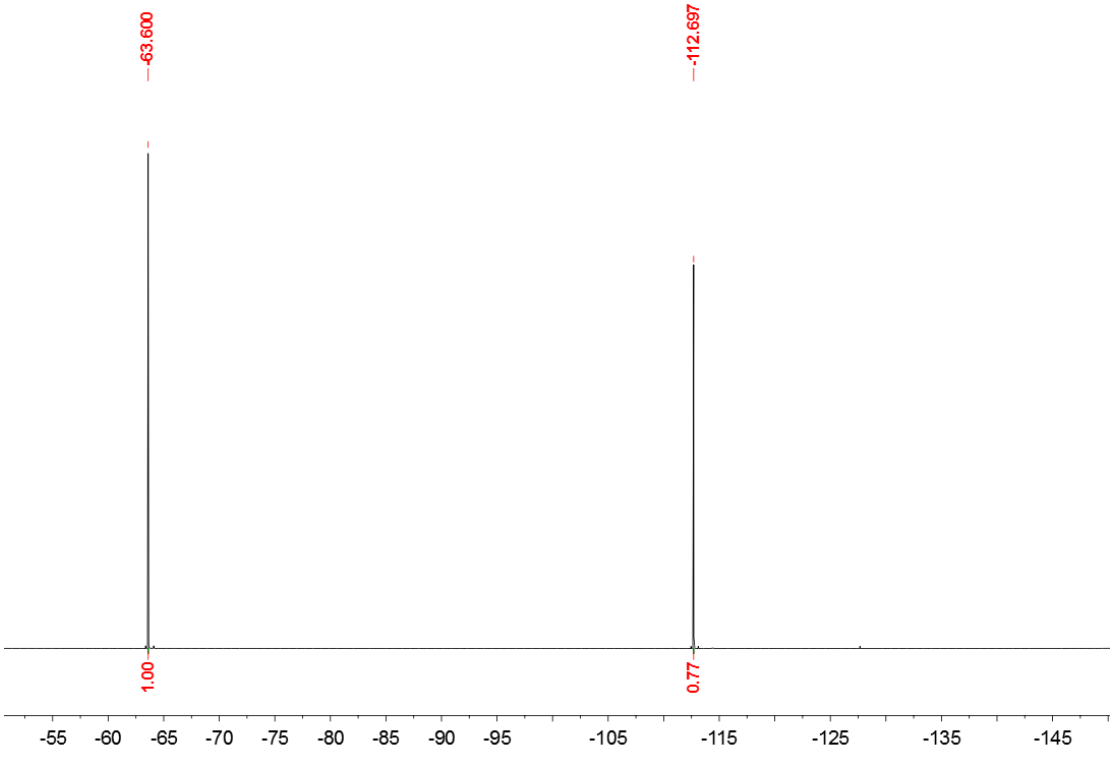
^{19}F NMR of Entry **11**



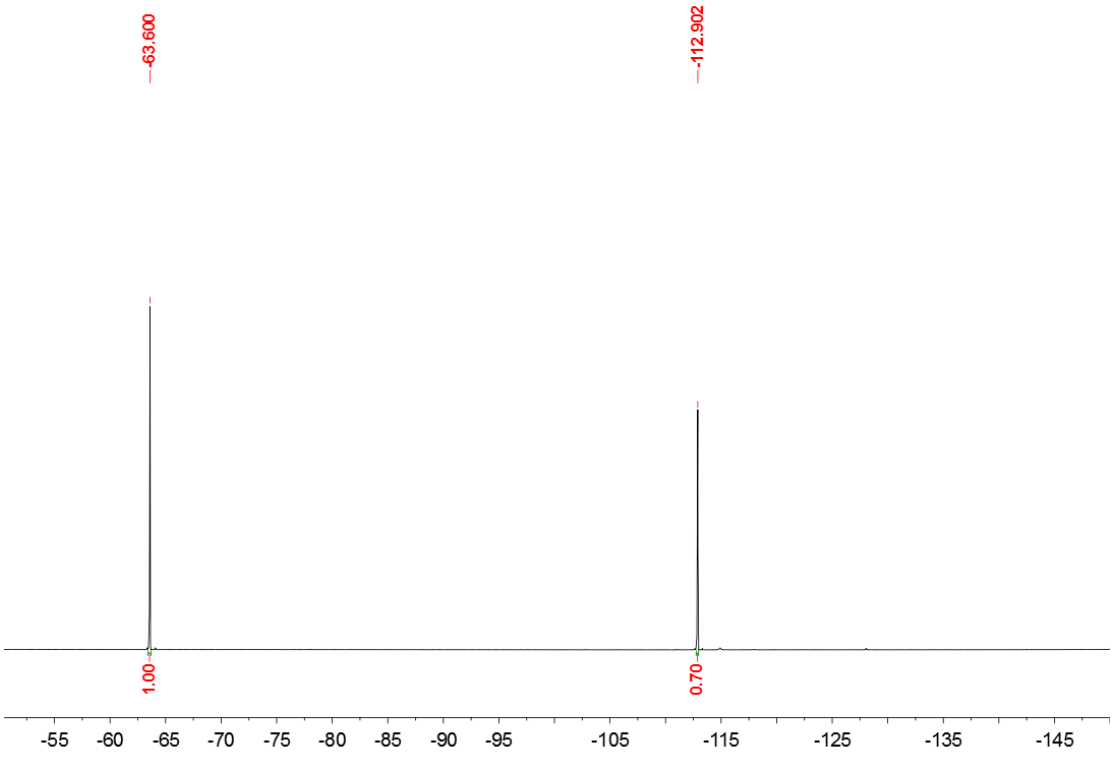
^{19}F NMR of Entry **12**



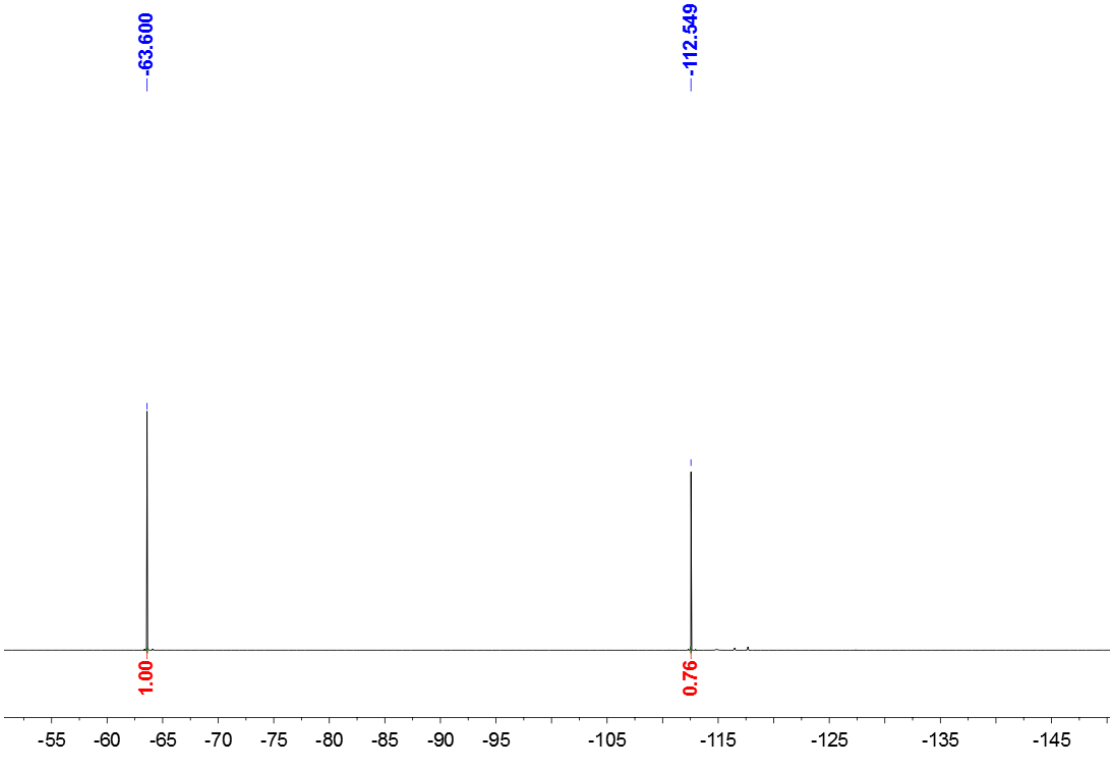
^{19}F NMR of Entry **13**



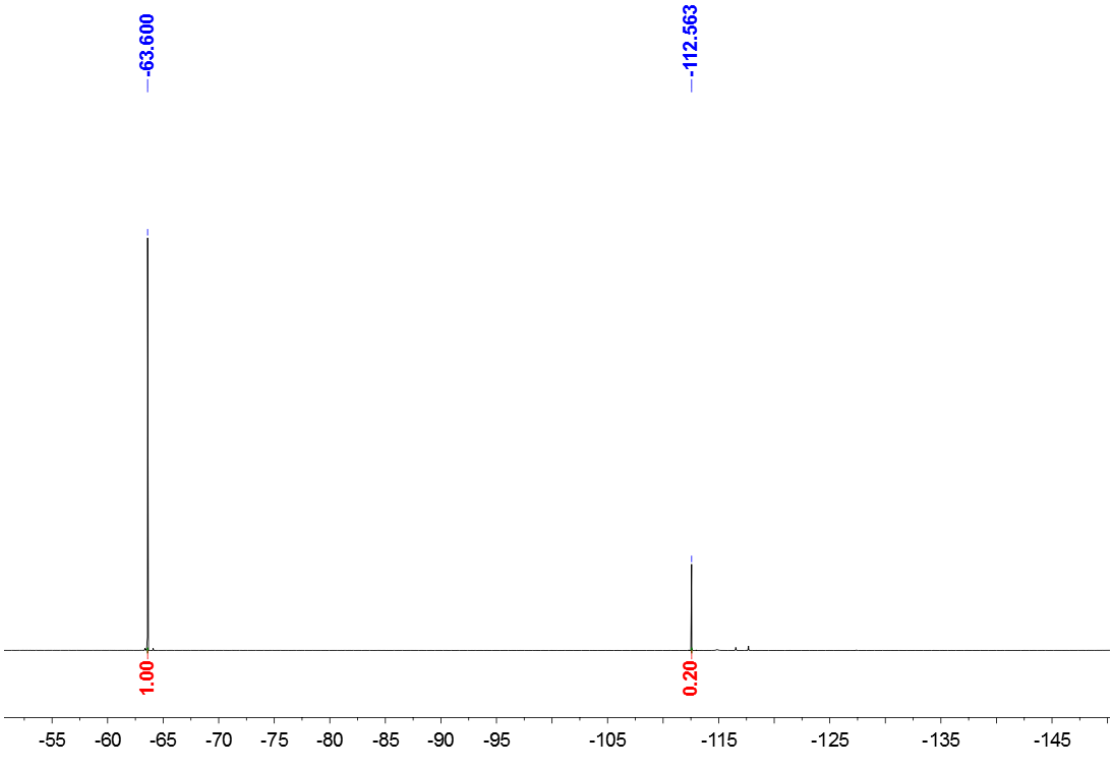
^{19}F NMR of Entry **14**



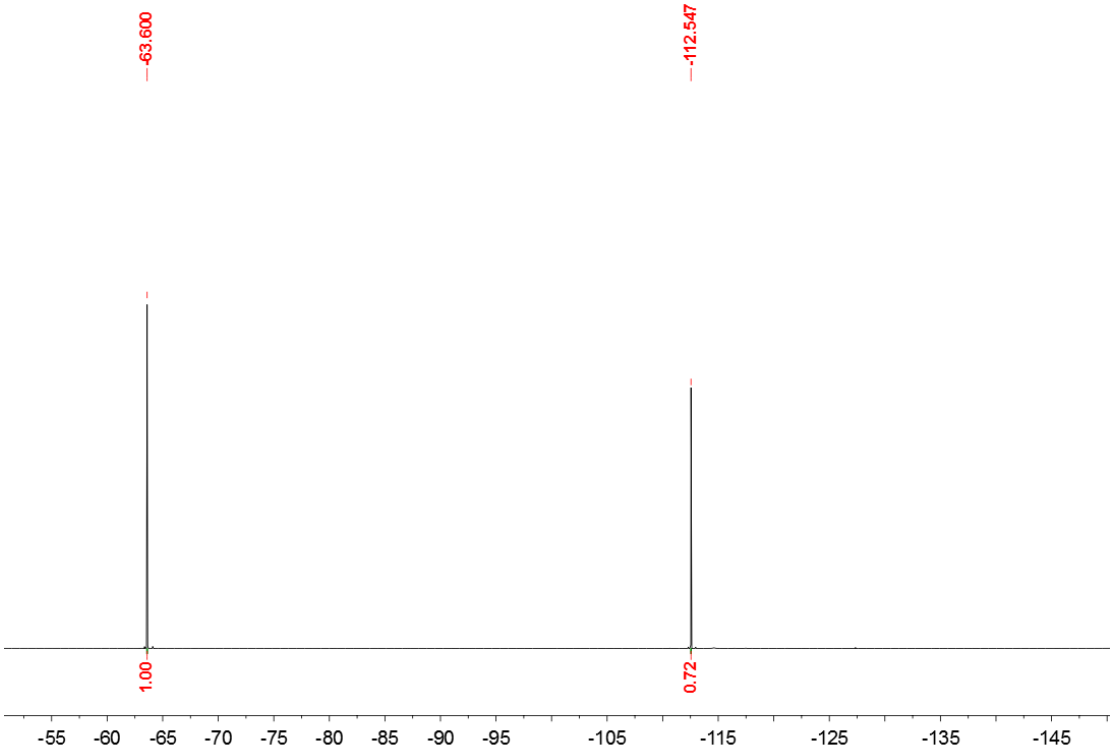
^{19}F NMR of Entry **15**



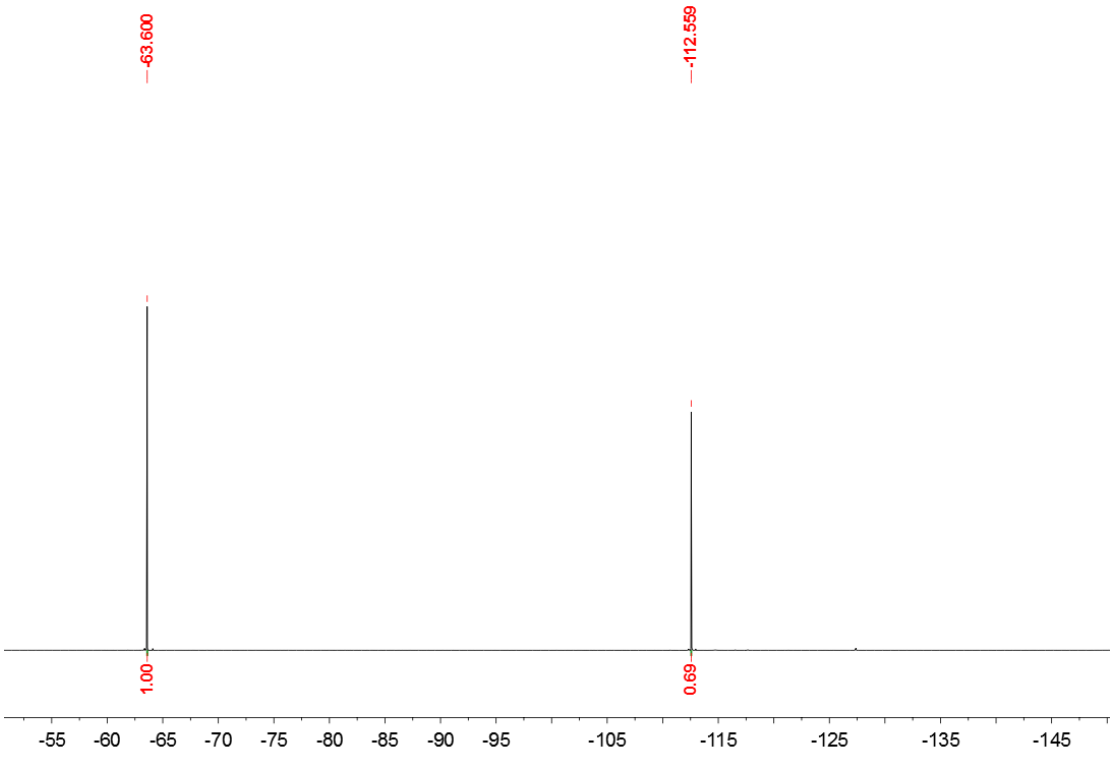
^{19}F NMR of Entry **16**



^{19}F NMR of Entry **17**

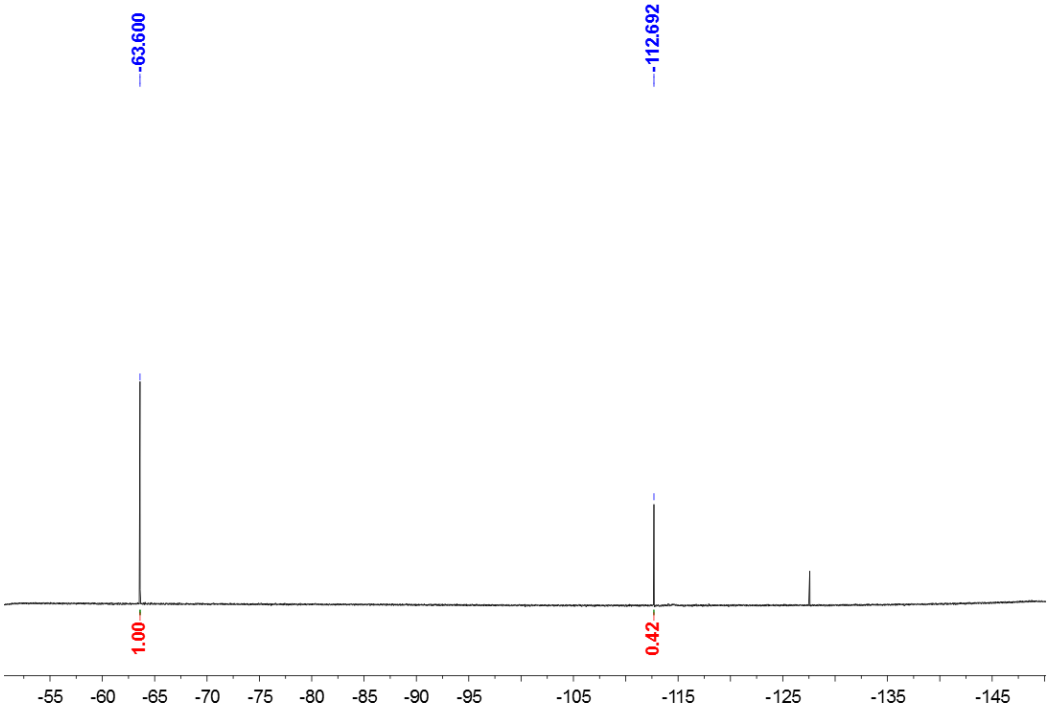


^{19}F NMR of Entry **18**

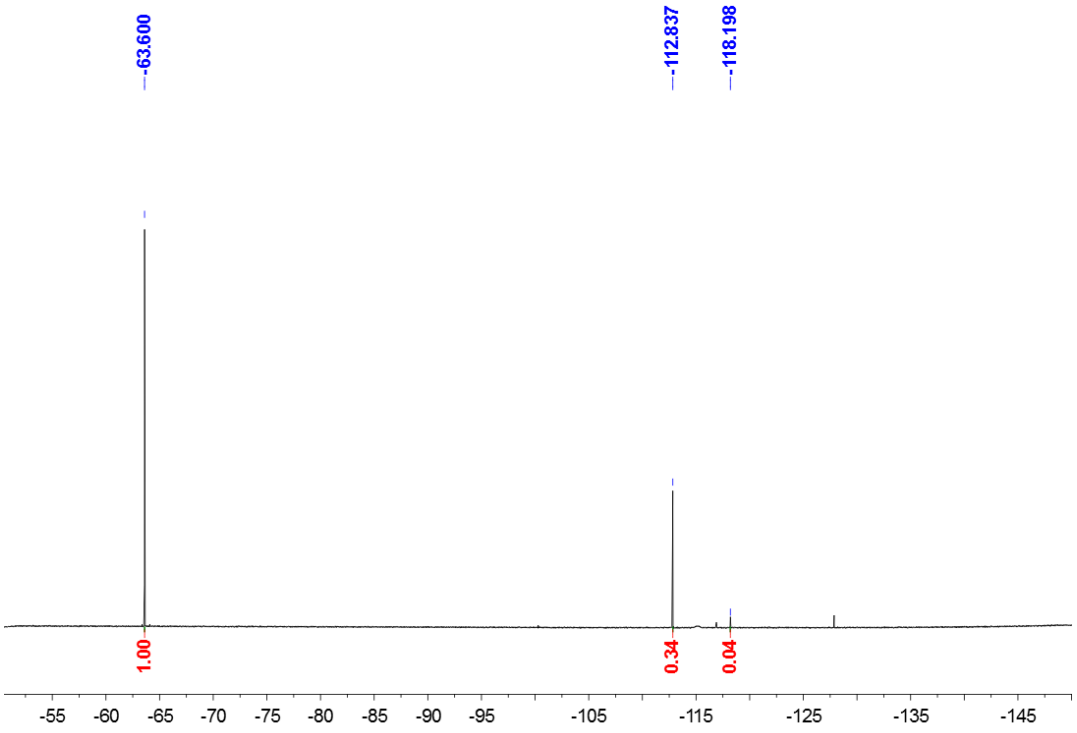


^{19}F NMR of Entry **19**

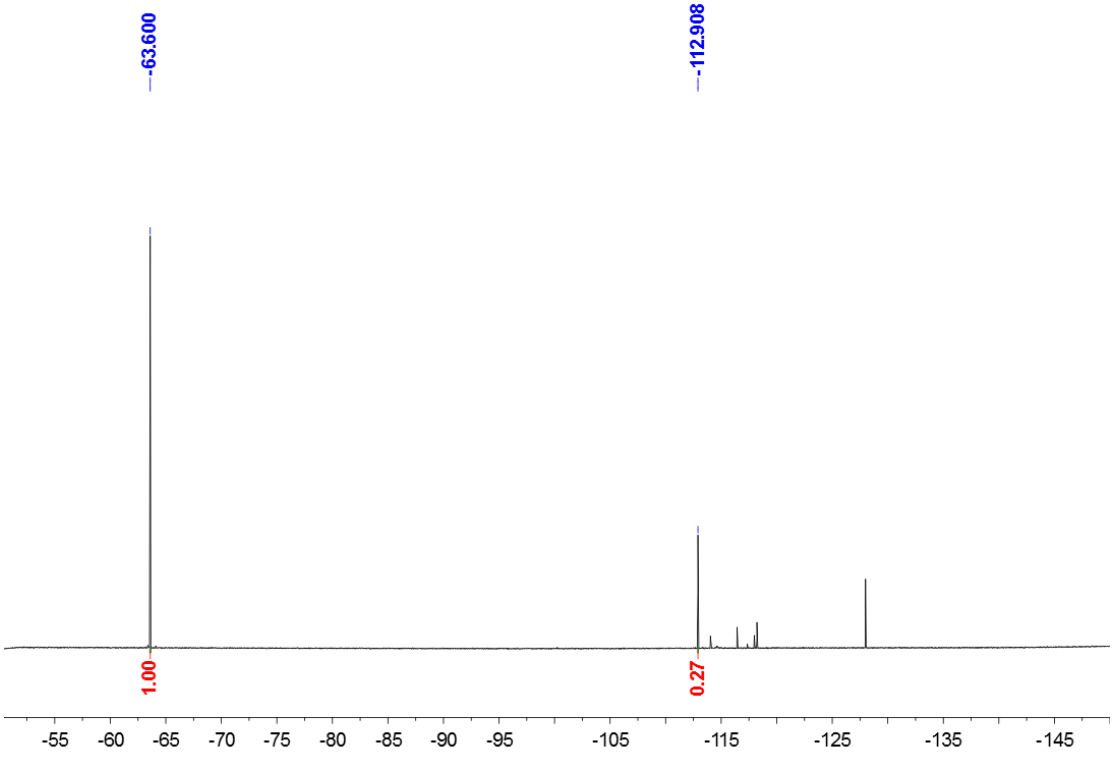
9.4 Copies of ^{19}F NMR Spectra in the effect of K_2CO_3 on the chemoselectivity with different oxidants (Table S18)



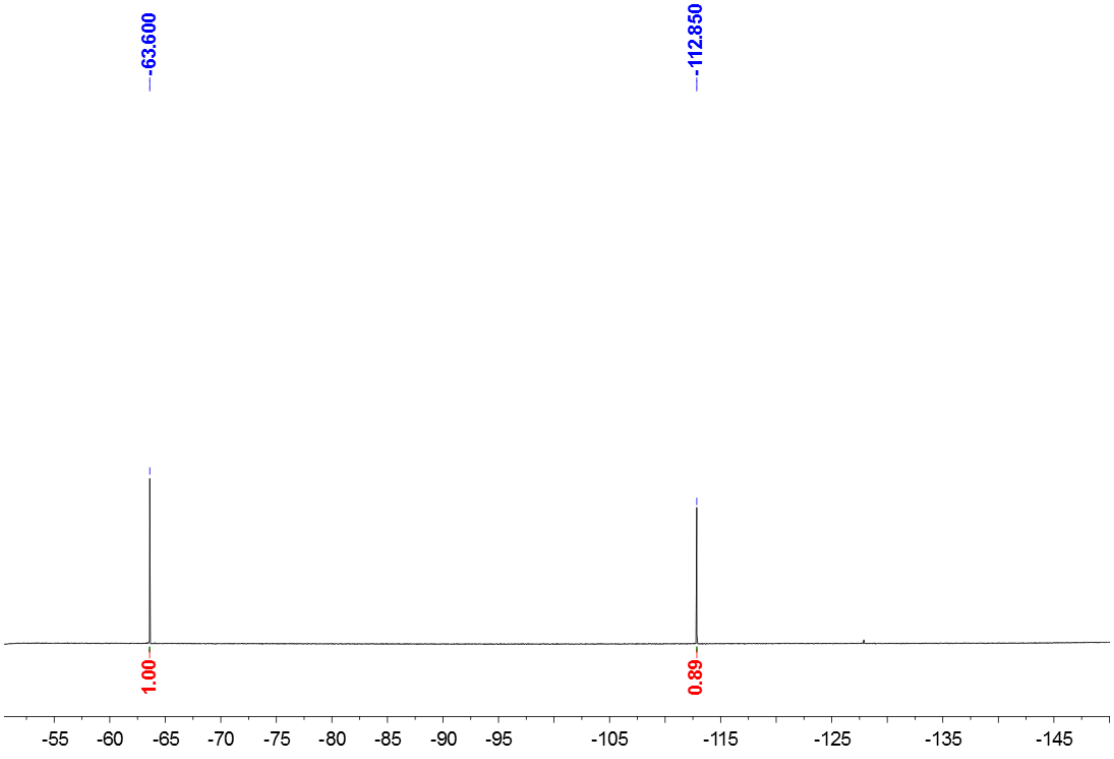
^{19}F NMR of Entry **1 in Table S18**



^{19}F NMR of Entry **2 in Table S18**

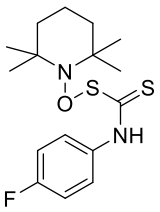


^{19}F NMR of Entry **3 in Table S18**



^{19}F NMR of Entry **4 in Table S18**

9.5. Copies of HRMS Spectra of the radical trapping product of radical speicies 6



$[M+H]^+$: Calculated: 343.1309;
Found: 343.1299