A nickel-catalyzed carbon-sulfur cross-coupling reaction with disulfides enabled by mechanochemistry

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Supporting Information

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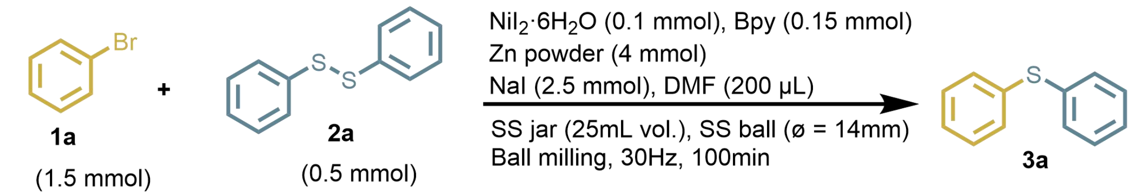
1. General Information

All chemicals were obtained from commercial sources and used without further purification. ^1H NMR and ^{13}C NMR spectra were obtained on Varian Mercury-VX300 and Bruker AVIII-400 spectrometers. Mass spectral data were obtained on a GCM-SQF2020V. All compounds were detected by ultraviolet light (254 nm and 365 nm) and iodine vapour. The synthesized products were purified by silica gel column chromatography. The ball mill used was a Retsch MM 400 mixing mill. Unless otherwise stated, the mechanochemical reactions were performed in 25 mL stainless steel jars with one stainless steel ball of 14 mm. Mechanochemical reactions were performed using mills and jars without any modifications or temperature control system.

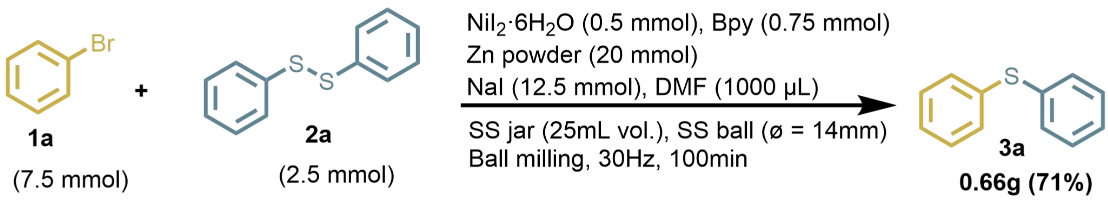
2. General procedures for the experiments

2.1 General Procedure



To a 25 mL stainless steel Jar was added a 14 mm stainless steel milling ball. A mixture of bromobenzene (1.5 mmol), phenyl disulfide (0.5 mmol, 109 mg), NiI_2 $6H_2O$ (0.1 mmol, 10 mol%), 2,2'-bipyridine (0.15 mmol, 15 mol%), DMF (200 μL), Zinc Powder (4 mmol, 8 equiv.) and NaI (2.5 mmol) were added to the jar, which was closed and placed on a ball mill. The reaction was milled for 100 min at 30 Hz. After the milling, the jar was opened and the mixture was rinsed into a conical flask using EtOAc (~40 mL). The mixture was filtered and concentrated under reduced pressure. The crude product was purified by column chromatography using petroleum as eluent to afford pure products. The procedure is applied for the preparation of all compounds. The identity and purity of the known products were determined by ^{1}H NMR and ^{13}C NMR spectroscopic analysis.

2.2 Procedure for the gram scale experiments

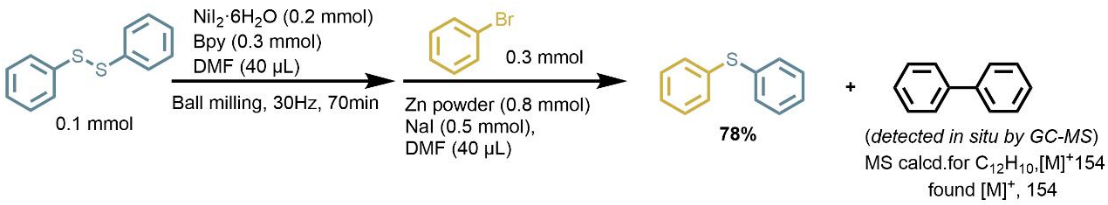


To a 25 mL stainless steel Jar was added a 14 mm stainless steel milling ball. A mixture of bromobenzene (7.5 mmol), phenyl disulfide (2.5 mmol, 546 mg), NiI_2 $6H_2O$ (0.21 g, 0.5 mmol, 10 mol%), 2,2'-bipyridine (0.117 g, 0.75 mmol, 15 mol%), DMF (1000 μL), Zinc Powder (1.308 g, 20 mmol, 8 equiv.) and NaI (1.874 g, 12.5mmol.) were all added to the jar, which was closed and placed on a ball mill. The reaction was milled for 100 min at 30 Hz. After the milling period, the jar was opened and the mixture was rinsed into a conical flask using EtOAc (100 mL). The mixture was filtered and concentrated under reduced pressure. The crude product was purified by column chromatography using petroleum as eluent to afford pure products. The yield of coupled product was determined to be 71% by column chromatography.

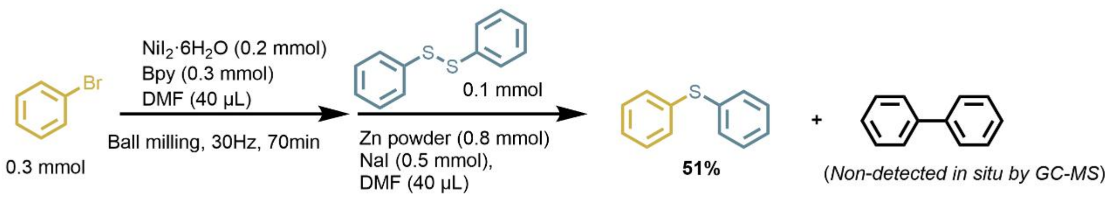
2.3 Procedure for radical trapping experiments

To a 25 mL stainless steel Jar was added a 14 mm stainless steel milling ball. A mixture of bromobenzene (1.5 mmol), phenyl disulfide (0.5 mmol, 109 mg), NiI_2 $6H_2O$ (0.1 mmol, 10 mol%), 2,2'-bipyridine (0.15 mmol, 15 mol%), DMF (200 µL), Zinc Powder (4 mmol, 8 equiv.) TEMPO (0.234 g, 3 equiv.) and NaI (2.5 mmol) were all added to the jar, which was closed and placed on a ball mill. The reaction was milled for 100 min at 30 Hz. After the milling period, the jar was opened and the mixture was rinsed into a conical flask using EtOAc (~40 mL). The mixture was filtered and concentrated under reduced pressure. The crude product was purified by column chromatography using petroleum as eluent to afford pure products. The yield of coupled product was determined to be 54% by column chromatography.

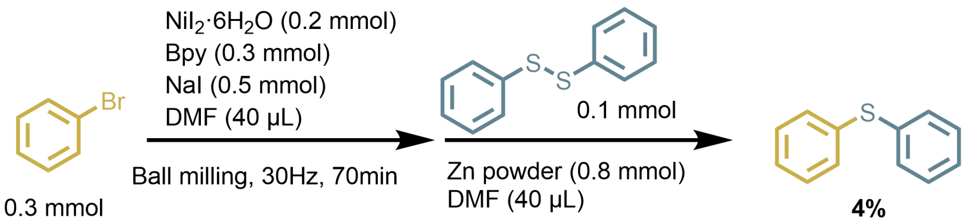
2.4 Control experiments



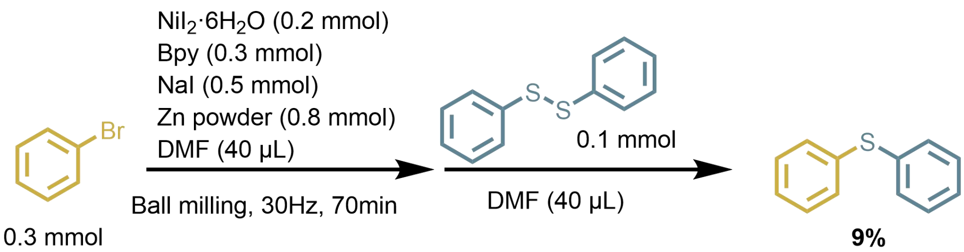
To a 25 mL stainless steel jar was added a 14 mm stainless steel milling ball. Phenyl disulfide (0.1 mmol, 218 mg), NiI_2 $6H_2O$ (0.2 mmol, 20 mol%), 2,2'-bipyridine (0.3 mmol; 30 mol%) and DMF (40µL) were added to the tank and allowed to react for 70 min. When the reaction is complete, quickly add bromobenzene (0.3 mmol), zinc powder (0.8 mmol, 8 equiv.), NaI (0.5 mmol) and DMF (40 µL), and place on a ball mill. Grinding was continued at 30 Hz for 100 minutes. After the milling period, the jar was opened and the mixture was rinsed into a conical flask using EtOAc (~40 mL). The mixture was filtered and concentrated under reduced pressure. The crude product was purified by column chromatography using petroleum as eluent to afford pure products. The yield of coupled product was determined to be 78% by column chromatography, and biphenyl was monitored by GC-MS.



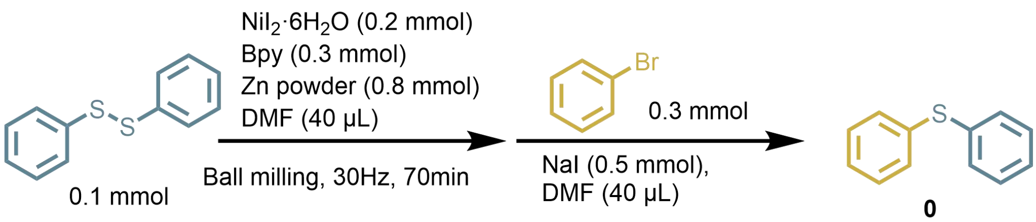
To a 25 mL stainless steel jar was added a 14 mm stainless steel milling ball. Bromobenzene (0.3 mmol), NiI_2 $6H_2O$ (0.2 mmol, 20 mol%), 2,2'-bipyridine (0.3 mmol; 30 mol%) and DMF (40 µL) were added to the tank and allowed to react for 70 min. When the reaction is complete, quickly add phenyl disulfide (0.1 mmol, 218 mg), zinc powder (0.8 mmol, 8 equiv.), NaI (0.5 mmol) and DMF (40 µL), and place on a ball mill. Grinding was continued at 30 Hz for 100 minutes. After the milling period, the jar was opened and the mixture was rinsed into a conical flask using EtOAc (~40 mL). The mixture was filtered and concentrated under reduced pressure. The crude product was purified by column chromatography using petroleum as eluent to afford pure products. The yield of coupled product was determined to be 51% by column chromatography, while biphenyl was not detected by GC-MS.



To a 25 mL stainless steel jar was added a 14 mm stainless steel milling ball. Bromobenzene (0.3 mmol), NiI_2 $6H_2O$ (0.2 mmol, 20 mol%), 2,2'-bipyridine (0.3 mmol; 30 mol%), NaI (0.5 mmol) and DMF (40 μL) were added to the tank and allowed to react for 70 min. When the reaction is complete, quickly add phenyl disulfide (0.1 mmol, 218 mg), zinc powder (0.8 mmol, 8 equiv.) and DMF (40 μL), and place on a ball mill. Grinding was continued at 30 Hz for 100 minutes. After the milling period, the jar was opened and the mixture was rinsed into a conical flask using EtOAc (~40 mL). The mixture was filtered and concentrated under reduced pressure. The crude product was purified by column chromatography using petroleum as eluent to afford pure products. The yield of coupled product was determined to be 4% by column chromatography.



To a 25 mL stainless steel jar was added a 14 mm stainless steel milling ball. Bromobenzene (0.3 mmol), NiI_2 $6H_2O$ (0.2 mmol, 20 mol%), 2,2'-bipyridine (0.3 mmol; 30 mol%), NaI (0.5 mmol), zinc powder (0.8 mmol, 8 equiv.) and DMF (40 μL) were added to the tank and allowed to react for 70 min. When the reaction is complete, quickly add phenyl disulfide (0.1 mmol, 218 mg), and DMF (40 μL), and place on a ball mill. Grinding was continued at 30 Hz for 100 minutes. After the milling period, the jar was opened and the mixture was rinsed into a conical flask using EtOAc (~40 mL). The mixture was filtered and concentrated under reduced pressure. The crude product was purified by column chromatography using petroleum as eluent to afford pure products. The yield of coupled product was determined to be 9% by column chromatography.



To a 25 mL stainless steel jar was added a 14 mm stainless steel milling ball. Phenyl disulfide (0.1 mmol, 218 mg), NiI_2 $6H_2O$ (0.2 mmol, 20 mol%), 2,2'-bipyridine (0.3 mmol; 30 mol%), zinc powder (0.8 mmol, 8 equiv.) and DMF (40 μL) were added to the tank and allowed to react for 70 min. When the reaction is complete, quickly add bromobenzene (0.3 mmol), NaI (0.5 mmol) and DMF (40 μL), and place on a ball mill. Grinding was continued at 30 Hz for 100 minutes. At the end of grinding, the jar was opened and rinsed with EtOAc. No product was detected by thin layer chromatography.

3. Optimisation studies

Table S1: Optimisation of Mechanochemical C-S Coupling

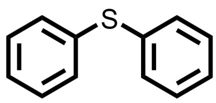
Entry	[Ni] & ligand ratio	Additive	Reductant	LAG	Time (min)	Milling Ball	Yield (%)	Remarks
1	CUI & Bpy (1:2)	NaI (3 mmol)	Zn Powder (3.5mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	-	Selected Catalyst & Ligand Ratio
2	$CoCl_2$ $6H_2O$ & Bpy (1:2)	NaI (3 mmol)	Zn Powder (3.5mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	37	
3	NiI_2 $6H_2O$ & 2,9-dm-1,10-phen (1:2)	NaI (3 mmol)	Zn Powder (3.5mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	-	
4	NiI_2 $6H_2O$ & 2,9-dm-4,7-dpphen (1:2)	NaI (3 mmol)	Zn Powder (3.5mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	-	
5	NiI_2 $6H_2O$ & Bpy (1:1)	NaI (3 mmol)	Zn Powder (3.5mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	66	
6	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (3 mmol)	Zn Powder (3.5 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	79	
7	NiI_2 $6H_2O$ & Bpy (1:2)	NaI (3 mmol)	Zn Powder (3.5 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	77	
8	NiI_2 $6H_2O$ & Bpy (1:1.5, 0.05 mmol Ni)	NaI (3 mmol)	Zn Powder (3.5 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	70	
9	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2 mmol)	Zn Powder (3.5 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	73	Selected Amount of NaI

10	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (3.5 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	81	
11	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (3 mmol)	Zn Powder (3.5 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	79	
12	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (3 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	77	Selected Zn
13	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (3.5 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	81	
14	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	85	
15	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4.5 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	52	
16	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Granular (4 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	17	
17	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn flake (4 mmol)	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	29	
18	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	-	DMF (0.24 µL/mg)	100	Ø 14 mm (1 ball)	-	
19	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMF (0.19 µL/mg)	100	Ø 14 mm (1 ball)	86	Selected LAGs
20	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMF (0.14µL/mg)	100	Ø 14 mm (1 ball)	62	
21	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMA (0.19 µL/mg)	100	Ø 14 mm (1 ball)	70	
22	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMSO (0.19 µL/mg)	100	Ø 14 mm (1 ball)	35	

23	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	CH_3OH (0.19µL/mg)	100	Ø 14 mm (1 ball)	59	
24	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	H_2O (0.19µL/mg)	100	Ø 14 mm (1 ball)	5	
25	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	CH_3CN (0.19µL/mg)	100	Ø 14 mm (1 ball)	42	
26	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	-	100	Ø 14 mm (1 ball)	-	
27	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMF (0.19 µL/mg)	70	Ø 14 mm (1 ball)	76	Reaction Time
28	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMF (0.19 µL/mg)	120	Ø 14 mm (1 ball)	69	
29	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMF (0.19 µL/mg)	100	Ø 14 mm (1 ball)	86	
30	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMF (0.19 µL/mg)	100	Ø 12 mm (1 ball)	75	Selected Milling Ball
31	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMF (0.19 µL/mg)	100	Ø 15 mm (1 ball)	47	
32	NiI_2 $6H_2O$ & Bpy (1:1.5)	NaI (2.5 mmol)	Zn Powder (4 mmol)	DMF (0.19 µL/mg)	100	Ø 14 mm (1 ball)	86	

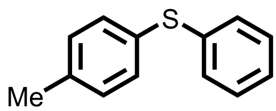
4. Characterisation Data

Diphenylsulfane **(3a)**[1]



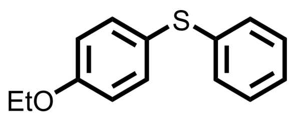
Prepared according to general procedure. Purified by column chromatography (PE) to give diphenylsulfane in the form of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (t, *J* = 6.5 Hz, 5H), 7.28 (d, *J* = 1.8 Hz, 3H), 7.21 (d, *J* = 3.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.69, 130.96, 129.13, 126.98. GCMS-EI (m/z): $[M]^+$ calcd for $C_{12}H_{10}S$, 186; found, 186.

phenyl(p-tolyl)sulfane **(3b)**[1]



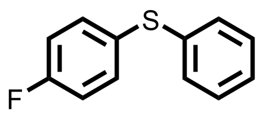
Prepared according to general procedure. Purified by column chromatography (PE) to give phenyl(p-tolyl)sulfane in the form of a yellow oil. ^{1}H NMR (300 MHz, DMSO) δ 7.43 – 7.32 (m, 2H), 7.28 (dd, *J* = 14.0, 5.8 Hz, 4H), 7.23 (s, 1H), 7.21 (d, *J* = 4.7 Hz, 2H), 2.31 (s, 3H).^{13}C NMR (75 MHz, DMSO) δ 137.66, 136.24, 132.08, 130.38, 130.33, 129.51, 129.45, 126.78, 20.71. GCMS-EI (m/z): $[M]^+$ calcd for $C_{13}H_{12}S$, 200; found, 200.

(4-ethoxyphenyl)(phenyl)sulfane **(3c)**[2]



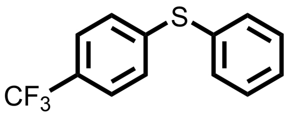
Prepared according to general procedure. Purified by column chromatography (PE) to give (4-ethoxyphenyl)(phenyl)sulfane in the form of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.36 (m, 2H), 7.26 – 7.19 (m, 2H), 7.13 (dd, *J* = 14.5, 7.2 Hz, 3H), 6.91 – 6.84 (m, 2H), 4.03 (q, *J* = 7.0 Hz, 2H), 1.42 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.13, 138.60, 135.30, 128.79, 128.02, 125.59, 123.90, 63.48, 14.69. GCMS-EI (m/z): $[M]^+$ calcd for $C_{14}H_{14}OS$, 230; found, 230.

(4-fluorophenyl)(phenyl)sulfane **(3d)**[1]



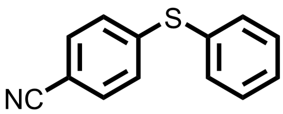
Prepared according to general procedure. Purified by column chromatography (PE) to give (4-fluorophenyl)(phenyl)sulfane in the form of a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.35 (m, 2H), 7.31 – 7.18 (m, 5H), 7.08 – 6.98 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6 (d, *J* = 246.8 Hz), 136.60, 134.04 (d, *J* = 8.2 Hz), 130.2 (d, *J* = 3 Hz), 129.90, 129.13, 126.71, 116.4 (d, *J* = 22.0 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -114.06. GCMS-EI (m/z): $[M]^+$ calcd for $C_{12}H_9FS$, 204; found, 204.

phenyl(4-(trifluoromethyl)phenyl)sulfane **(3e)**[1]



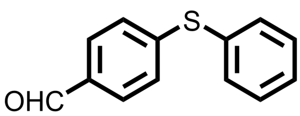
Prepared according to general procedure. Purified by column chromatography (PE) to give phenyl(4-(trifluoromethyl)phenyl)sulfane in the form of a colourless oil. ^{1}H NMR (400 MHz, DMSO) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.56 – 7.43 (m, 5H), 7.34 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (101 MHz, DMSO) δ 143.18, 133.91, 131.78, 130.50, 129.53, 128.58, 127.3 (q, *J* = 32.3 Hz), 126.5 (q, *J* = 4.0 Hz), 124.2 (q, *J* = 272.7 Hz). ^{19}F NMR (377 MHz, DMSO) δ -60.94. GCMS-EI (m/z): [M]$^+$ calcd for $C_{13}H_9F_3S$, 254; found, 254.

4-(phenylthio)benzonitrile **(3f)**[3]



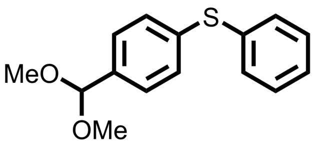
Prepared according to general procedure. Purified by column chromatography (PE) to give 4-(phenylthio)benzonitrile in the form of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 – 7.49 (m, 2H), 7.49 – 7.45 (m, 2H), 7.45 – 7.40 (m, 3H), 7.19 – 7.13 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.65, 134.42, 132.29, 130.76, 129.85, 129.32, 127.24, 118.72, 108.63. GCMS-EI (m/z): [M]$^+$ calcd for $C_{13}H_9NS$, 211; found, 211.

4-(phenylthio)benzaldehyde **(3g)**[4]



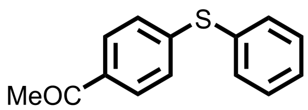
Prepared according to general procedure. Purified by column chromatography (PE) to give 4-(phenylthio)benzaldehyde in the form of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.91 (s, 1H), 7.75 – 7.68 (m, 2H), 7.56 – 7.49 (m, 2H), 7.46 – 7.40 (m, 3H), 7.24 (dd, *J* = 8.2, 1.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.11, 147.18, 134.31, 133.68, 131.27, 130.08, 129.76, 129.12, 127.19. GCMS-EI (m/z): [M]$^+$ calcd for $C_{13}H_{10}OS$, 214; found, 214.

(4-(dimethoxymethyl)phenyl)(phenyl)sulfane **(3h)**



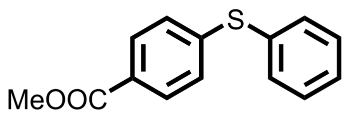
Prepared according to general procedure. Purified by column chromatography (PE/EA = 100/1) to give (4-(dimethoxymethyl)phenyl)(phenyl)sulfane in the form of a yellow oil. ^{1}H NMR (400 MHz, DMSO) δ 7.40 (d, *J* = 8.6 Hz, 2H), 7.38 – 7.35 (m, 3H), 7.35 – 7.29 (m, 4H), 5.37 (s, 1H), 3.24 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 137.85, 135.63, 134.89, 134.36, 131.47, 130.57, 130.08, 128.17, 128.07, 102.69, 53.08. GCMS-EI (m/z): [M]$^+$ calcd for $C_{15}H_{16}O_2S$, 260; found, 260.

1-(4-(phenylthio)phenyl)ethan-1-one **(3i)**[3]



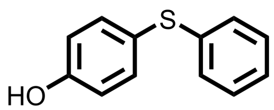
Prepared according to general procedure. Purified by column chromatography (PE) to give 1-(4-(phenylthio)phenyl)ethan-1-one in the form of a White solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 2H), 7.50 (dd, J = 6.6, 3.0 Hz, 2H), 7.44 – 7.37 (m, 3H), 7.21 (d, J = 8.3 Hz, 2H), 2.55 (d, J = 0.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.01, 144.83, 134.29, 133.78, 131.88, 129.59, 128.79, 128.71, 127.28, 26.41. GCMS-EI (m/z): $[M]^+$ calcd for $C_{14}H_{12}OS$, 228; found, 228.

methyl 4-(phenylthio)benzoate **(3j)**[4]



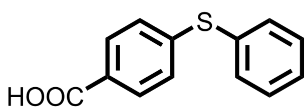
Prepared according to general procedure. Purified by column chromatography (PE/EA = 50/1) to give methyl 4-(phenylthio)benzoate in the form of a White solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 – 7.84 (m, 2H), 7.52 – 7.45 (m, 2H), 7.42 – 7.34 (m, 3H), 7.23 – 7.16 (m, 2H), 3.88 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.52, 144.27, 133.57, 132.28, 129.99, 129.53, 128.54, 127.46, 127.38, 51.96. GCMS-EI (m/z): $[M]^+$ calcd for $C_{14}H_{12}O_2S$, 244; found, 244.

4-(phenylthio)phenol **(3k)**[11]



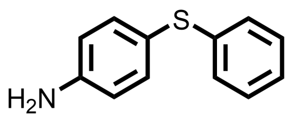
Prepared according to general procedure. Purified by column chromatography (PE/EA = 50/1) to give 4-(phenylthio)phenol in the form of a yellow oil. ^{1}H NMR (300 MHz, DMSO) δ 7.37 – 7.30 (m, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.18 – 7.04 (m, 3H), 6.88 – 6.80 (m, 2H). ^{13}C NMR (75 MHz, DMSO) δ 158.39, 138.72, 136.07, 129.19, 127.14, 125.67, 120.44, 116.85. GCMS-EI (m/z): $[M]^+$ calcd for $C_{12}H_{10}OS$, 202; found, 202.

4-(phenylthio)benzoic acid **(3l)**[7]



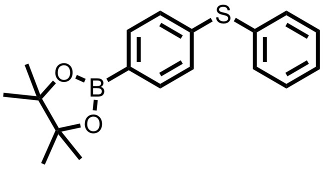
Prepared according to general procedure. Purified by column chromatography (PE/EA = 50/1) to give 4-(phenylthio)benzoic acid in the form of a White solid. ^{1}H NMR (300 MHz, DMSO) δ 7.90 – 7.81 (m, 3H), 7.75 – 7.67 (m, 2H), 7.48 (dt, J = 5.4, 3.4 Hz, 3H), 7.27 – 7.23 (m, 1H). ^{13}C NMR (75 MHz, DMSO) δ 166.68, 142.88, 133.35, 131.77, 131.36, 130.26, 130.07, 129.00, 128.51, 127.66, 126.97. HRMS(EI) m/z: $[M-H]^-$Calcd for $C_{13}H_{10}O_2S$, 230; found, 229.0327.

4-(phenylthio)aniline **(3m)**[3]



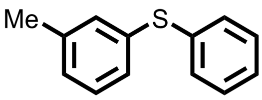
Prepared according to general procedure. Purified by column chromatography (PE/EA = 20/1) to give 4-(phenylthio)aniline in the form of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.25 – 7.16 (m, 2H), 7.15 – 7.05 (m, 3H), 6.70 – 6.63 (m, 2H), 3.74 (br. s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.86, 139.59, 136.02, 128.75, 127.25, 125.20, 120.50, 115.86. GCMS-EI (m/z): $[M]^+$ calcd for $C_{12}H_{11}NS$, 201; found, 201.

4,4,5,5-tetramethyl-2-(4-(phenylthio)phenyl)-1,3,2-dioxaborolane **(3n)**[3]



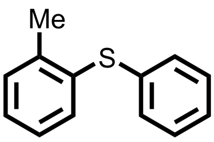
Prepared according to general procedure. Purified by column chromatography (PE/EA = 100/1) to give 4,4,5,5-tetramethyl-2-(4-(phenylthio)phenyl)-1,3,2-dioxaborolane in the form of a yellow oil. ^{1}H NMR (400 MHz, DMSO) δ 7.61 (dd, *J* = 11.6, 4.9 Hz, 3H), 7.46 – 7.35 (m, 4H), 7.24 (d, *J* = 8.2 Hz, 2H), 1.29 (d, *J* = 4.4 Hz, 12H). ^{13}C NMR (101 MHz, DMSO) δ 140.39, 136.82, 135.78, 133.57, 132.58, 131.44, 130.23, 128.87, 128.66, 126.01, 84.41, 84.21, 25.12. GCMS-EI (m/z): $[M]^+$ calcd for $C_{10}H_{12}O_2S$, 196; found, 196.

phenyl(m-tolyl)sulfane **(3o)**[1]



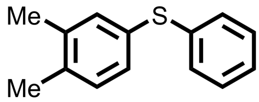
Prepared according to general procedure. Purified by column chromatography (PE) to give phenyl(m-tolyl)sulfane in the form of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 77.36 – 7.31 (m, 2H), 7.31 – 7.26 (m, 2H), 7.25 – 7.18 (m, 3H), 7.16 (d, *J* = 4.7 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.01, 136.06, 135.18, 131.80, 130.70, 129.08, 128.99, 128.29, 127.98, 126.80, 21.26. GCMS-EI (m/z): $[M]^+$ calcd for $C_{13}H_{12}S$, 200; found, 200.

phenyl(o-tolyl)sulfane **(3p)**[1]



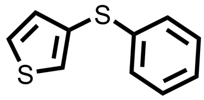
Prepared according to general procedure. Purified by column chromatography (PE) to give phenyl(o-tolyl)sulfane in the form of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 7.3, 1.6 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.25 (t, *J* = 3.3 Hz, 3H), 7.21 (d, *J* = 0.6 Hz, 2H), 7.18 – 7.10 (m, 1H), 2.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.95, 136.12, 132.97, 130.56, 129.60, 129.09, 129.03, 127.87, 127.48, 127.12, 126.68, 126.30, 20.52. GCMS-EI (m/z): $[M]^+$ calcd for $C_{13}H_{12}S$, 200; found, 200.

(3,4-dimethylphenyl)(phenyl)sulfane **(3q)**[7]



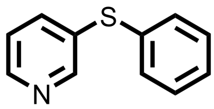
Prepared according to general procedure. Purified by column chromatography (PE) to give (3,4-dimethylphenyl)(phenyl)sulfane in the form of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, J = 7.0 Hz, 1H), 7.25 (d, J = 4.4 Hz, 3H), 7.23 – 7.13 (m, 3H), 7.09 (d, J = 7.9 Hz, 1H), 2.25 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.72, 137.32, 136.37, 133.52, 130.51, 129.93, 129.55, 129.03, 128.95, 127.49, 127.12, 126.21 (s), 19.66, 19.43. GCMS-EI (m/z): $[M]^+$ calcd for $C_{14}H_{14}S$, 200; found, 214.

3-(phenylthio)thiophene **(3r)**[9]



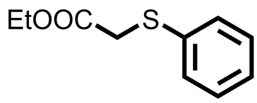
Prepared according to general procedure. Purified by column chromatography (PE) to give 3-(phenylthio)thiophene in the form of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H), 7.31 – 7.22 (m, 4H), 7.19 (dd, J = 10.7, 3.9 Hz, 1H), 7.06 (dd, J = 4.5, 1.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.28, 131.17, 129.28, 128.94, 128.36, 128.13, 126.68, 126.07. GCMS-EI (m/z): $[M]^+$ calcd for $C_{10}H_8S_2$, 192; found, 192.

3-(phenylthio)pyridine **(3s)**[1]



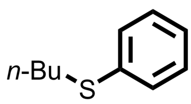
Prepared according to general procedure. Purified by column chromatography (PE) to give 3-(phenylthio)pyridine in the form of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, J = 5.8 Hz, 1H), 7.65 – 7.55 (m, 2H), 7.48 – 7.35 (m, 4H), 6.99 (ddd, J = 7.5, 4.9, 1.0 Hz, 1H), 6.88 (dd, J = 8.1, 0.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.46, 149.45, 136.68, 134.89, 130.95, 129.57, 129.04, 121.30, 119.82. HRMS(EI) m/z: $[M+H]^+$Calcd for $C_{11}H_9NS$, 187; found, 188.0522.

ethyl 2-(phenylthio)acetate **(3t)**[12]



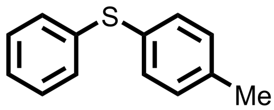
Prepared according to general procedure. Purified by column chromatography (PE/EA = 100/1) to give ethyl 2-(phenylthio)acetate in the form of a yellow oil. ^{1}H NMR (400 MHz, DMSO) δ 7.38 – 7.29 (m, 4H), 7.25 – 7.18 (m, 1H), 4.08 (q, J = 7.1 Hz, 2H), 3.86 (s, 2H), 1.13 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 169.71, 135.57, 129.51, 128.90, 126.77, 61.36, 35.37, 14.42. GCMS-EI (m/z): $[M]^+$ calcd for $C_{10}H_{12}O_2S$, 196; found, 196.

butyl(phenyl)sulfane **(3u)**[13]



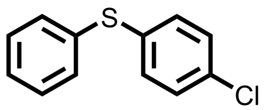
Prepared according to general procedure. Purified by column chromatography (PE) to give butyl(phenyl)sulfane in the form of a yellow oil. ^{1}H NMR (300 MHz, DMSO) δ 7.56 – 7.36 (m, 1H), 7.31 (d, J = 4.4 Hz, 4H), 7.22 – 7.12 (m, 1H), 2.99 – 2.90 (m, 2H), 1.60 – 1.33 (m, 4H), 0.88 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, DMSO) δ 136.58, 129.04, 127.95, 125.48, 31.70, 30.72, 21.34, 13.54. GCMS-EI (m/z): $[M]^+$ calcd for $C_{10}H_{14}S$, 166; found, 166.

phenyl(p-tolyl)sulfane **(4b)**[3]



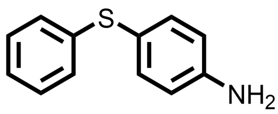
Prepared according to general procedure. Purified by column chromatography (PE) to give phenyl(p-tolyl)sulfane in the form of a colourless oil. ^{1}H NMR (400 MHz, DMSO) δ 77.36 – 7.31 (m, 2H), 7.30 – 7.26 (m, 2H), 7.23 (dd, J = 12.1, 5.0 Hz, 5H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 138.08, 136.66, 132.49, 130.83, 130.76, 129.90, 129.86, 127.22, 21.12. GCMS-EI (m/z): $[M]^+$ calcd for $C_{13}H_{12}S$, 200; found, 200.

(4-chlorophenyl)(phenyl)sulfane **(4c)**[5]



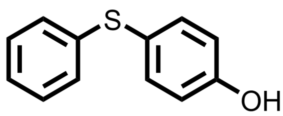
Prepared according to general procedure. Purified by column chromatography (PE) to give (4-chlorophenyl)(phenyl)sulfane in the form of a yellow oil. ^{1}H NMR (400 MHz, DMSO) δ 7.51 – 7.42 (m, 2H), 7.41 – 7.33 (m, 5H), 7.32 – 7.28 (m, 2H). ^{13}C NMR (101 MHz, DMSO) δ 134.83, 134.39, 132.46, 132.36, 131.78, 130.21, 129.96, 128.38. GCMS-EI (m/z): $[M]^+$ calcd for $C_{12}H_9ClS$, 220; found, 220.

4-(phenylthio)aniline **(4d)**[1]



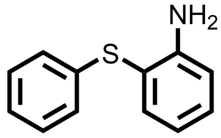
Prepared according to general procedure. Purified by column chromatography (PE/EA = 20/1) to give 4-(phenylthio)aniline in the form of a yellow solid. ^{1}H NMR (400 MHz, DMSO) δ 7.30 – 7.15 (m, 4H), 7.09 (t, J = 7.4 Hz, 1H), 7.03 (d, J = 7.3 Hz, 2H), 6.64 (d, J = 8.5 Hz, 2H), 5.51 (br. s, 2H). ^{13}C NMR (101 MHz, DMSO) δ 150.44, 140.63, 136.84, 129.40, 126.48, 125.42, 115.33, 115.21. GCMS-EI (m/z): $[M]^+$ calcd for $C_{12}H_{11}NS$, 201; found, 201.

4-(phenylthio)phenol **(4e)**[5]



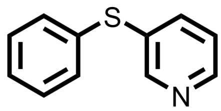
Prepared according to general procedure. Purified by column chromatography (PE/EA = 30/1) to give 4-(phenylthio)phenol in the form of a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 2H), 7.27 – 7.10 (m, 5H), 6.85 – 6.77 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.64, 138.17, 135.38, 128.91, 128.89, 128.30, 128.28, 125.86, 125.83, 124.56, 116.45, 116.43. GCMS-EI (m/z): $[M]^+$ calcd for $C_{12}H_{10}OS$, 202; found, 202.

2-(phenylthio)aniline **(4f)**[8]



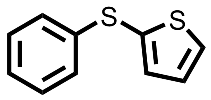
Prepared according to general procedure. Purified by column chromatography (PE/EA = 50/1) to give 2-(phenylthio)aniline in the form of a colourless oil. ^{1}H NMR (300 MHz, DMSO) δ 7.35 – 7.09 (m, 5H), 7.07 – 7.01 (m, 2H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.60 (t, *J* = 7.4 Hz, 1H), 5.37 (br. s, 2H). ^{13}C NMR (75 MHz, DMSO) δ 150.33, 130.01, 136.79, 131.10, 129.07, 126.39, 125.41, 116.80, 114.99, 112.02. GCMS-EI (m/z): $[M]^+$ calcd for $C_{12}H_{11}NS$, 201; found, 201.

3-(phenylthio)pyridine **(4g)**[6]



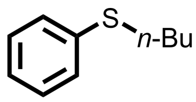
Prepared according to general procedure. Purified by column chromatography (PE) to give 3-(phenylthio)pyridine in the form of a yellow oil. ^{1}H NMR (400 MHz, DMSO) δ 8.41 (dd, *J* = 4.8, 1.0 Hz, 1H), 7.65 (td, *J* = 8.0, 1.9 Hz, 1H), 7.58 (dd, *J* = 6.4, 3.2 Hz, 2H), 7.52 – 7.44 (m, 3H), 7.15 (ddd, *J* = 7.4, 4.8, 0.9 Hz, 1H), 6.96 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 160.36, 150.05, 137.87, 135.09, 130.73, 130.31, 129.73, 121.58, 120.98. HRMS(EI) m/z: $[M+H]^+$Calcd for $C_{11}H_9NS$, 187, found, 188.0522.

2-(phenylthio)thiophene **(4h)**[10]



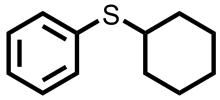
Prepared according to general procedure. Purified by column chromatography (PE) to give 2-(phenylthio)thiophene in the form of a yellow oil. ^{1}H NMR (400 MHz, DMSO) δ 7.83 (ddd, *J* = 16.5, 5.3, 1.2 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.35 – 7.26 (m, 2H), 7.24 – 7.09 (m, 4H). ^{13}C NMR (101 MHz, DMSO) δ 138.25, 137.13, 136.56, 134.36, 133.19, 129.80, 129.04, 128.86, 127.33, 126.89. GCMS-EI (m/z): $[M]^+$ calcd for $C_{10}H_8S_2$, 192; found, 192.

butyl(phenyl)sulfane **(4i)**[3]



Prepared according to general procedure. Purified by column chromatography (PE) to give butyl(phenyl)sulfane in the form of a yellow oil. ^{1}H NMR (400 MHz, DMSO) δ 7.31 (d, *J* = 4.2 Hz, 4H), 7.17 (dt, *J* = 8.6, 4.3 Hz, 1H), 3.00 – 2.90 (m, 2H), 1.61 – 1.34 (m, 4H), 0.88 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 137.01, 129.45, 128.41, 125.91, 32.16, 31.15, 21.75, 13.94. GCMS-EI (m/z): $[M]^+$ calcd for $C_{10}H_{14}S$, 166; found, 166.

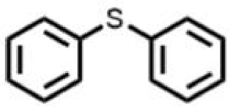
cyclohexyl(phenyl)sulfane **(4j)**[1]

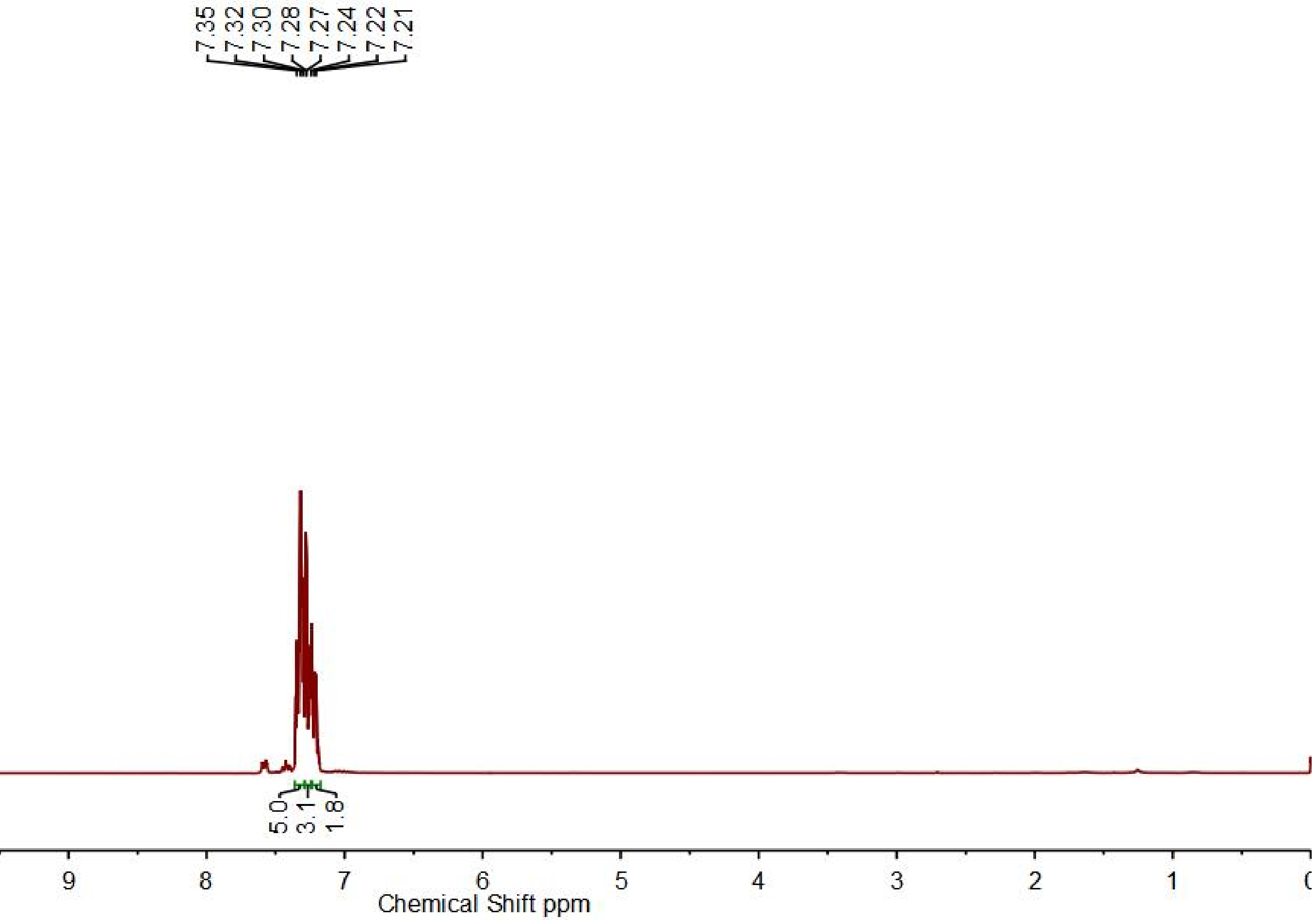


Prepared according to general procedure. Purified by column chromatography (PE) to give cyclohexyl(phenyl)sulfane in the form of a yellow oil. ^{1}H NMR (400 MHz, DMSO) δ 7.39 – 7.28 (m, 4H), 7.26 – 7.18 (m, 1H), 3.28 – 3.17 (m, 1H), 1.90 (dd, *J* = 9.3, 3.8 Hz, 2H), 1.70 (dd, *J* = 8.6, 4.0 Hz, 2H), 1.60 – 1.52 (m, 1H), 1.33 (ddd, *J* = 25.8, 11.9, 6.0 Hz, 5H). ^{13}C NMR (101 MHz, DMSO) δ 135.26, 131.13, 129.47, 126.86, 45.48, 33.24, 25.75, 25.74. GCMS-EI (m/z): $[M]^+$ calcd for $C_{12}H_{16}S$, 192; found, 192.

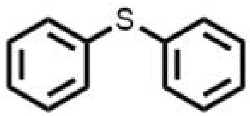
5. Spectroscopic Data

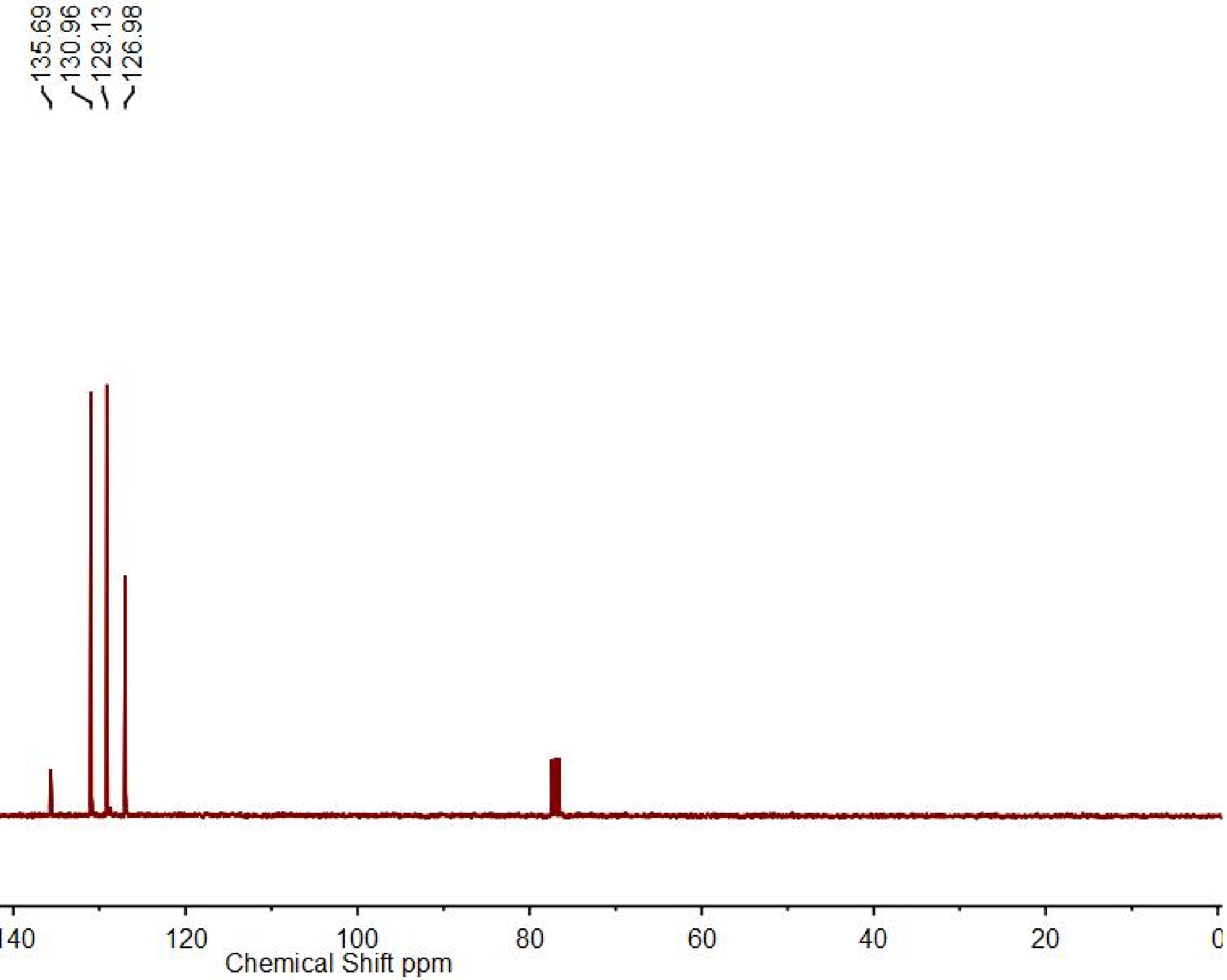
3a, $CDCl_3$, ^1H NMR 300 MHz



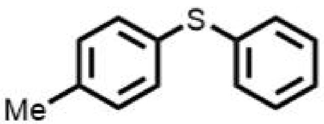


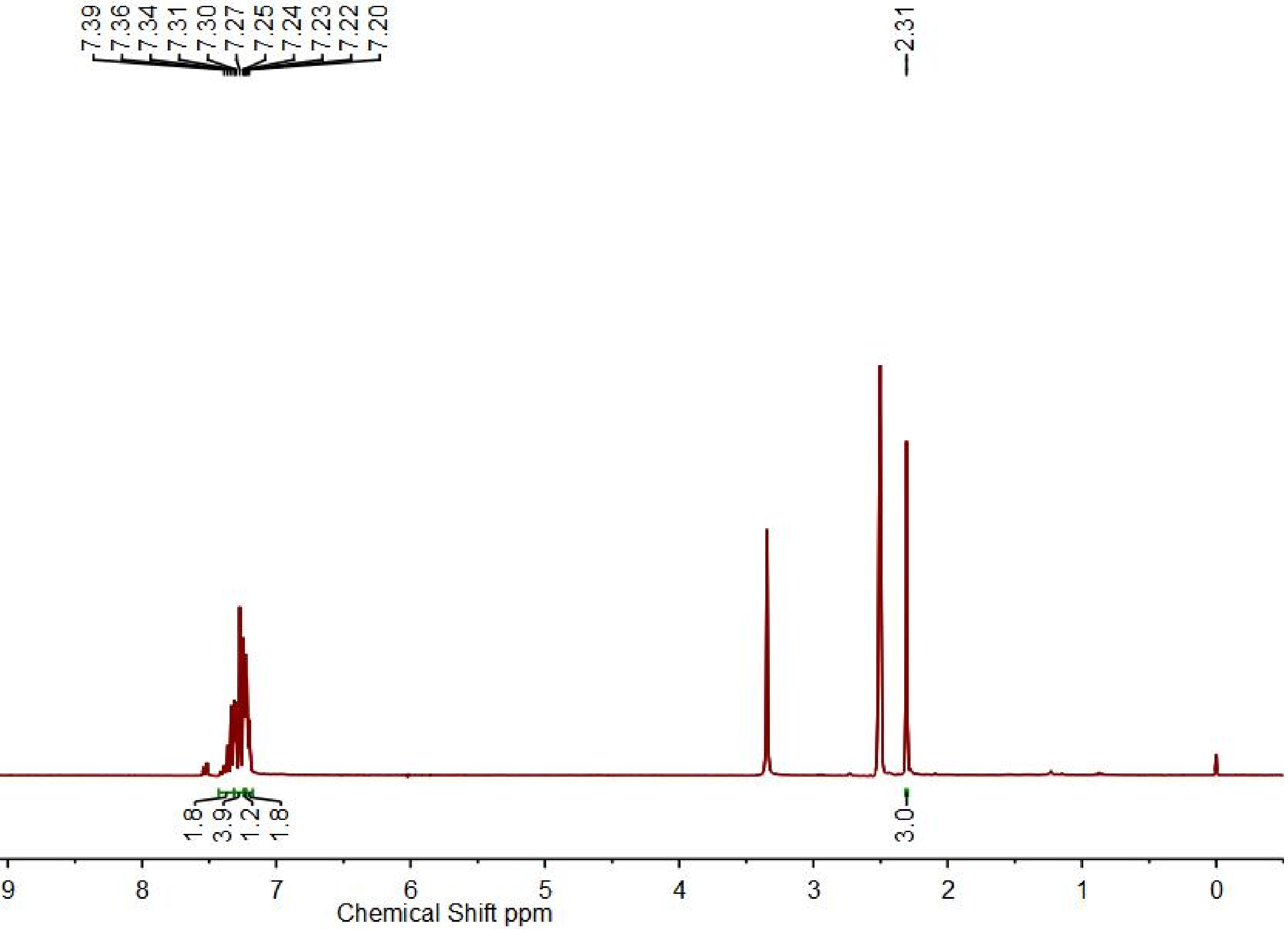
3a, $CDCl_3$, ^{13}C NMR 75 MHz



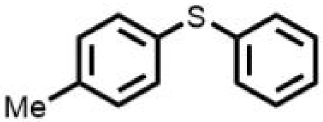


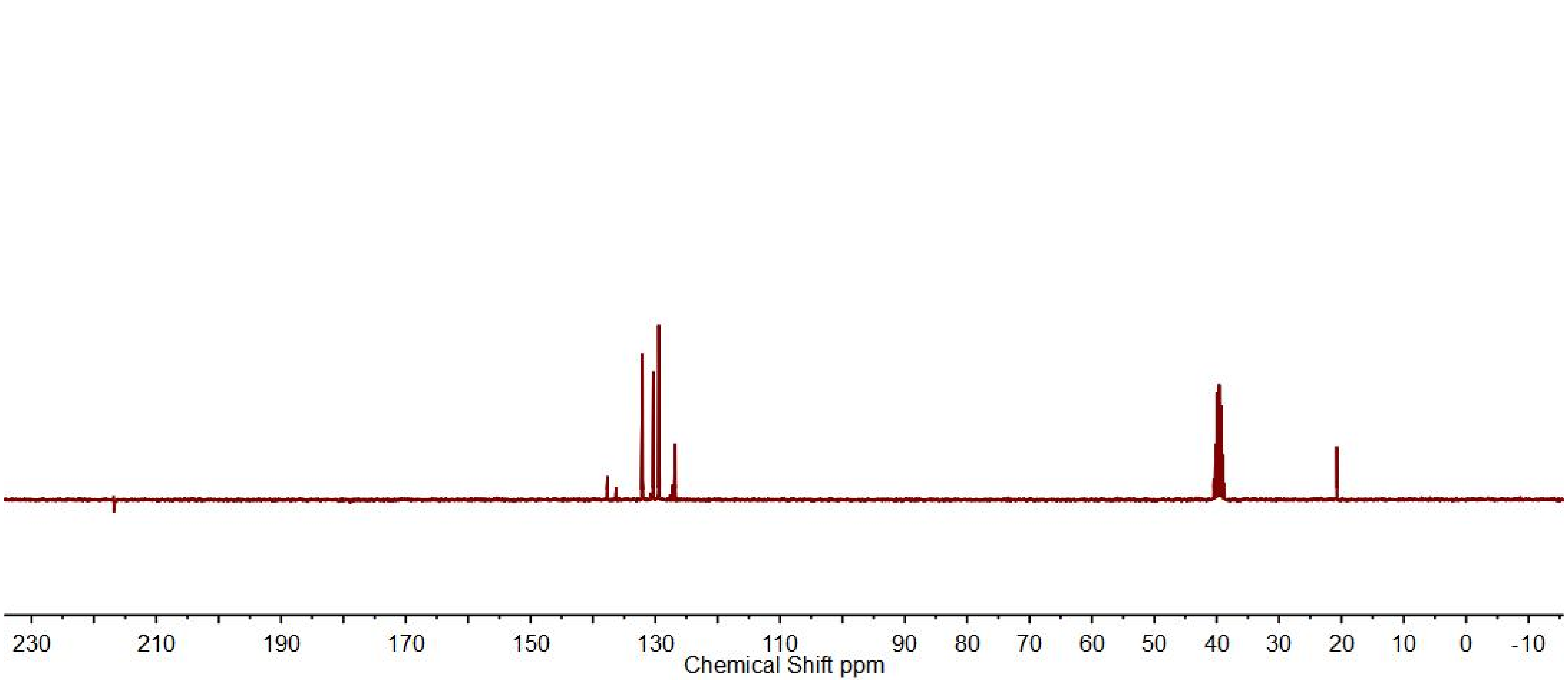
3b, DMSO-d_6, ^{1}H NMR 300 MHz



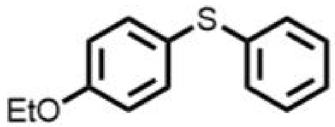


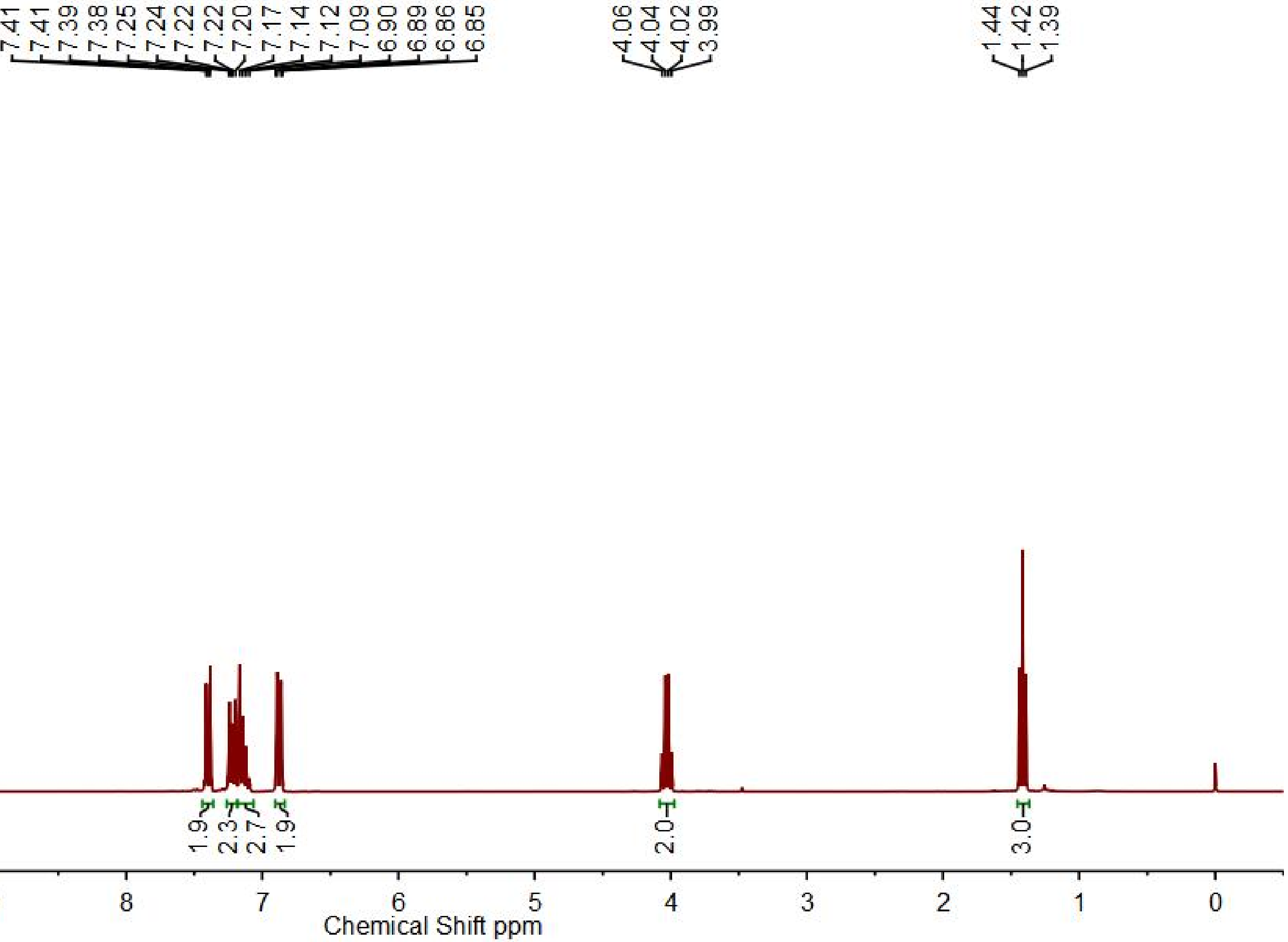
3b, DMSO-d_6, ^{13}C NMR 75 MHz



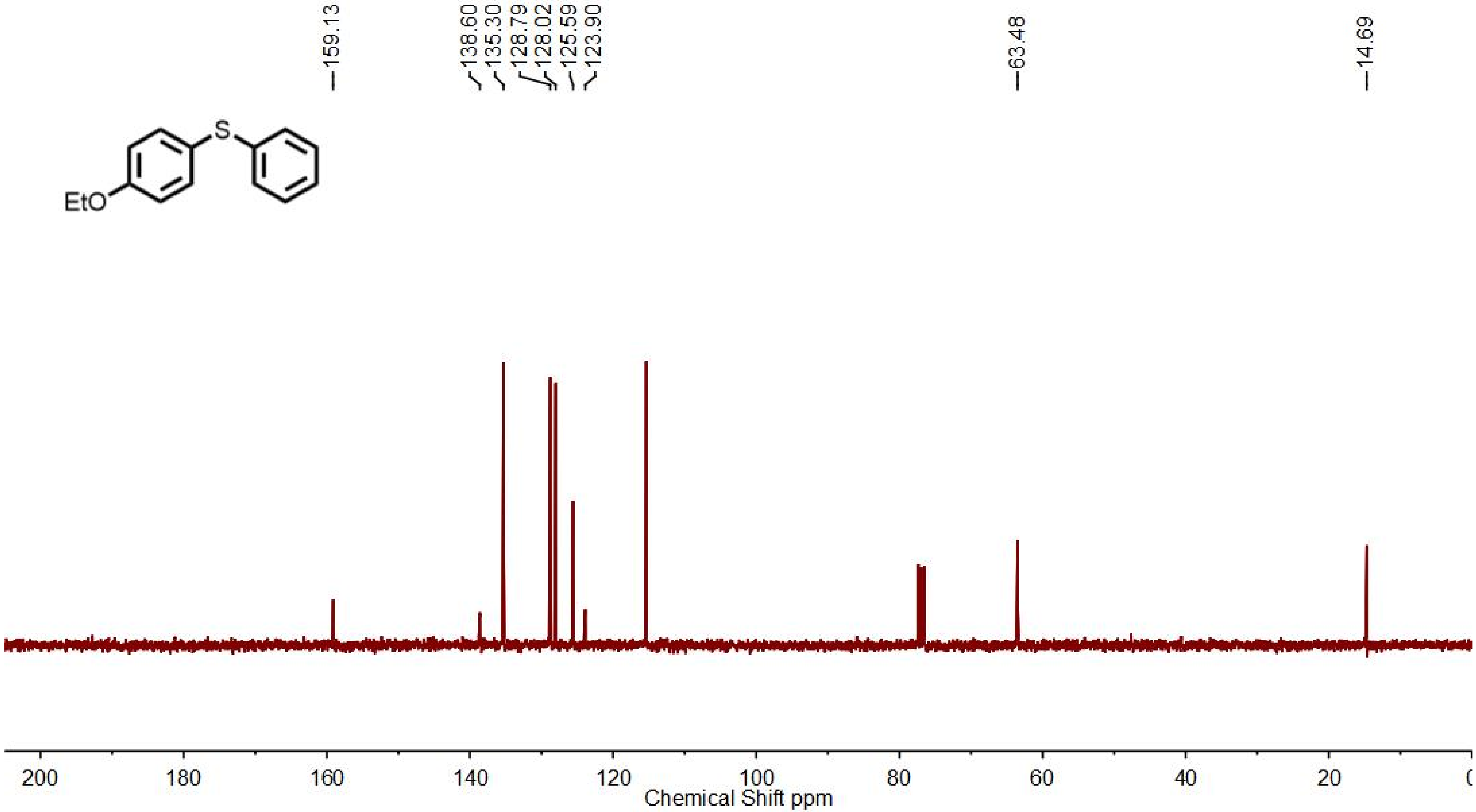


3c, $CDCl_3$, ^1H NMR 300 MHz

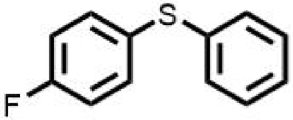


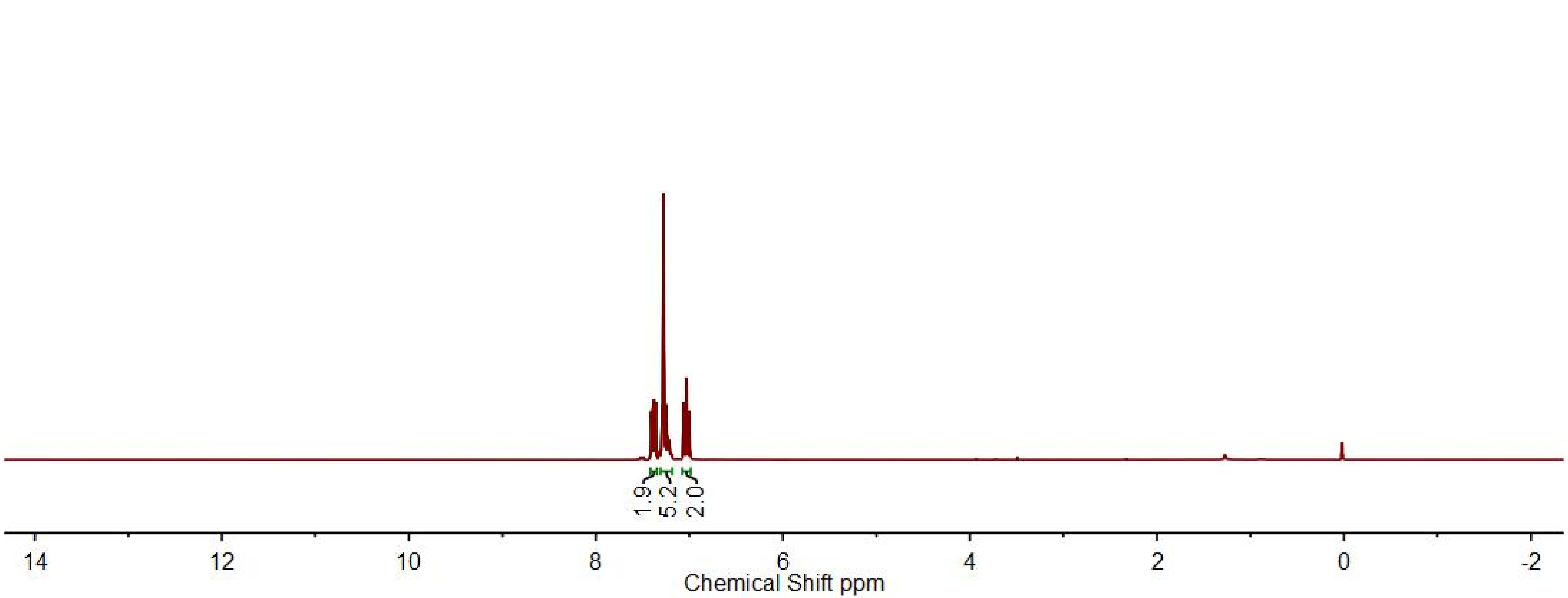


3c, $CDCl_3$, ^{13}C NMR 300 MHz

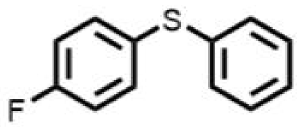


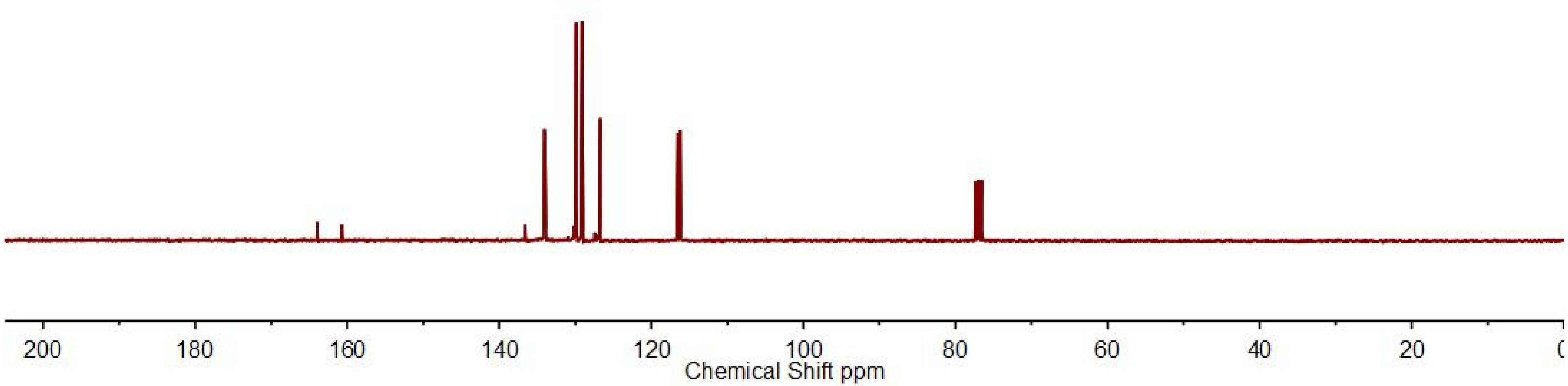
3d, $CDCl_3$, ^1H NMR 300 MHz



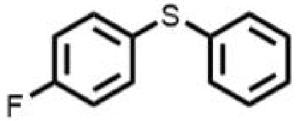


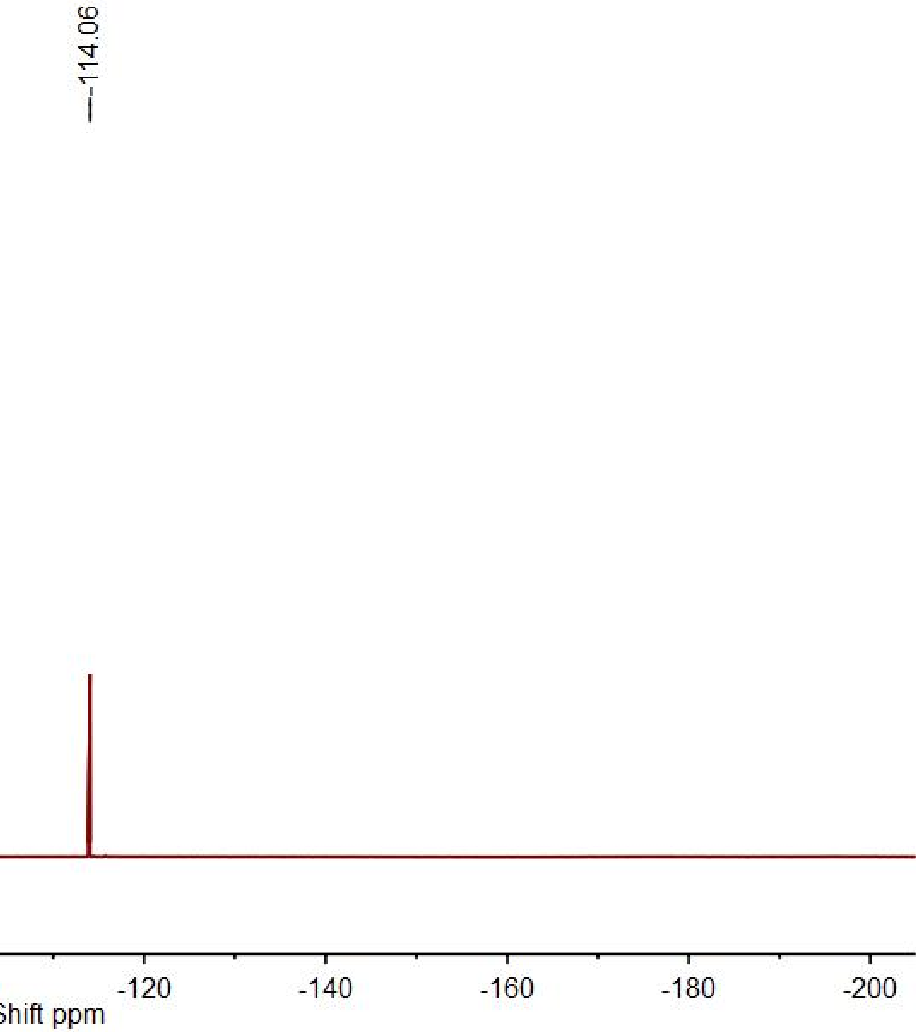
3d, $CDCl_3$, ^{13}C NMR 75 MHz



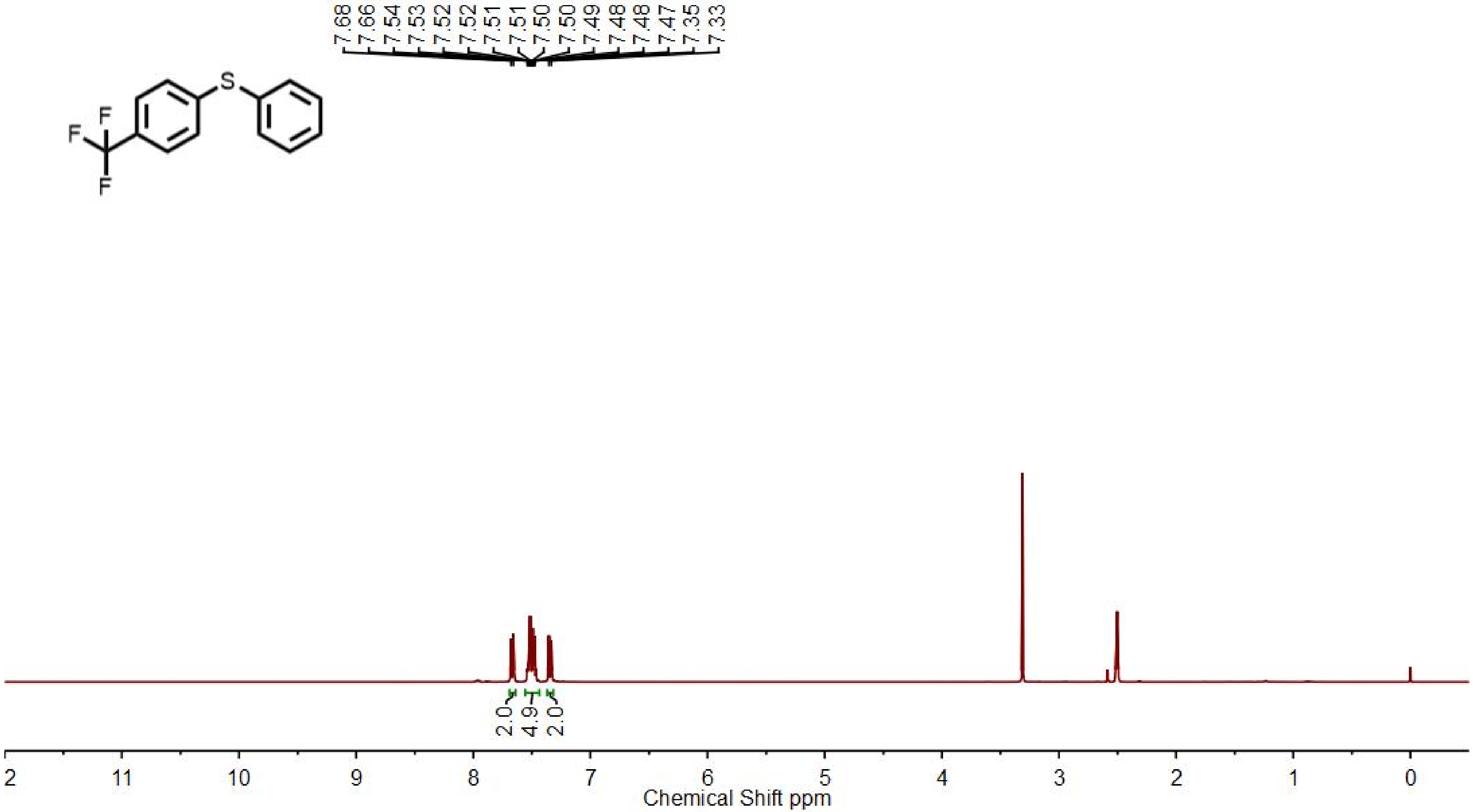


3d, $CDCl_3$, ^{19}F NMR 377 MHz

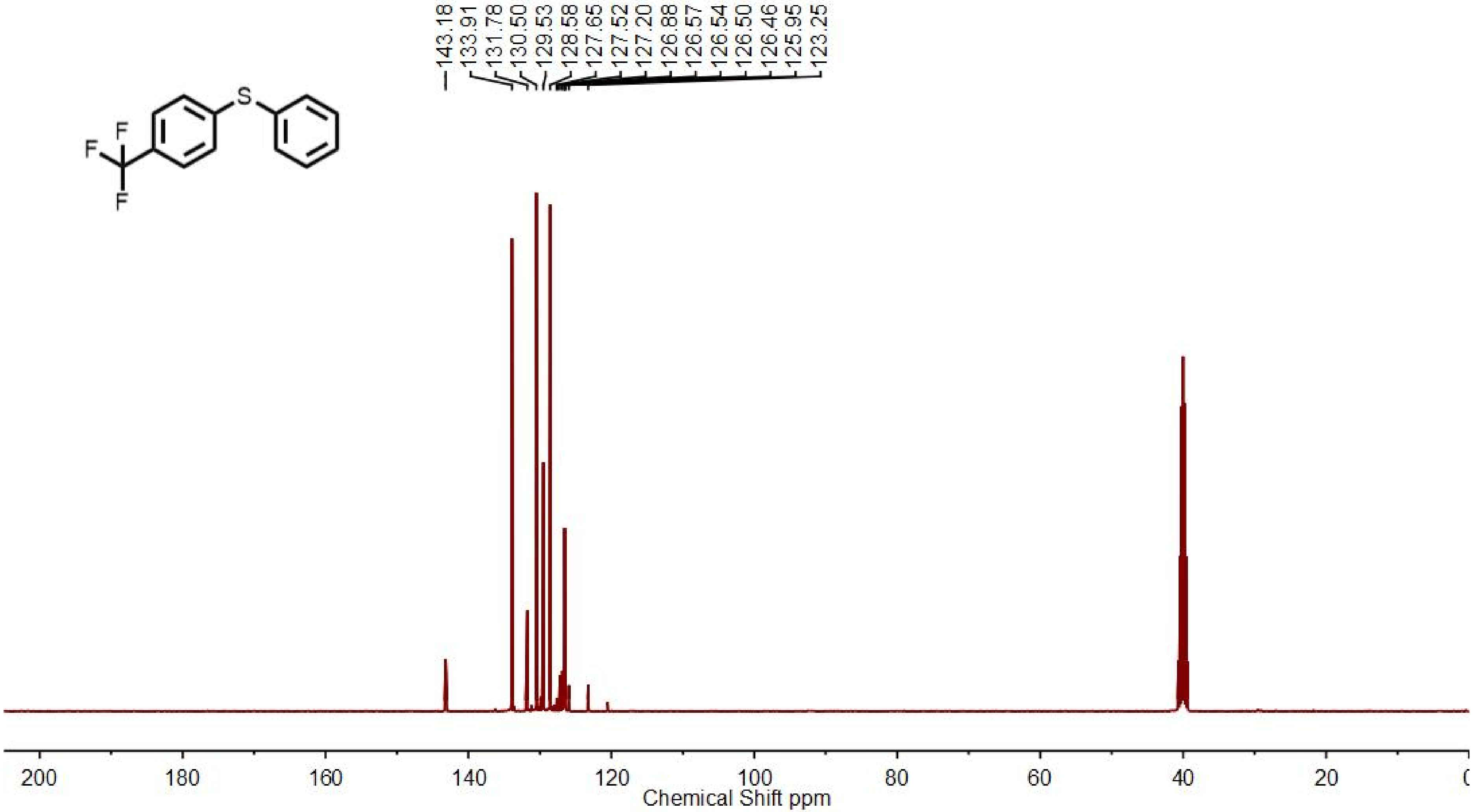




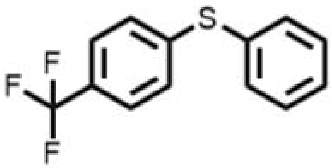
3e, DMSO-d_6, ^{1}H NMR 400 MHz

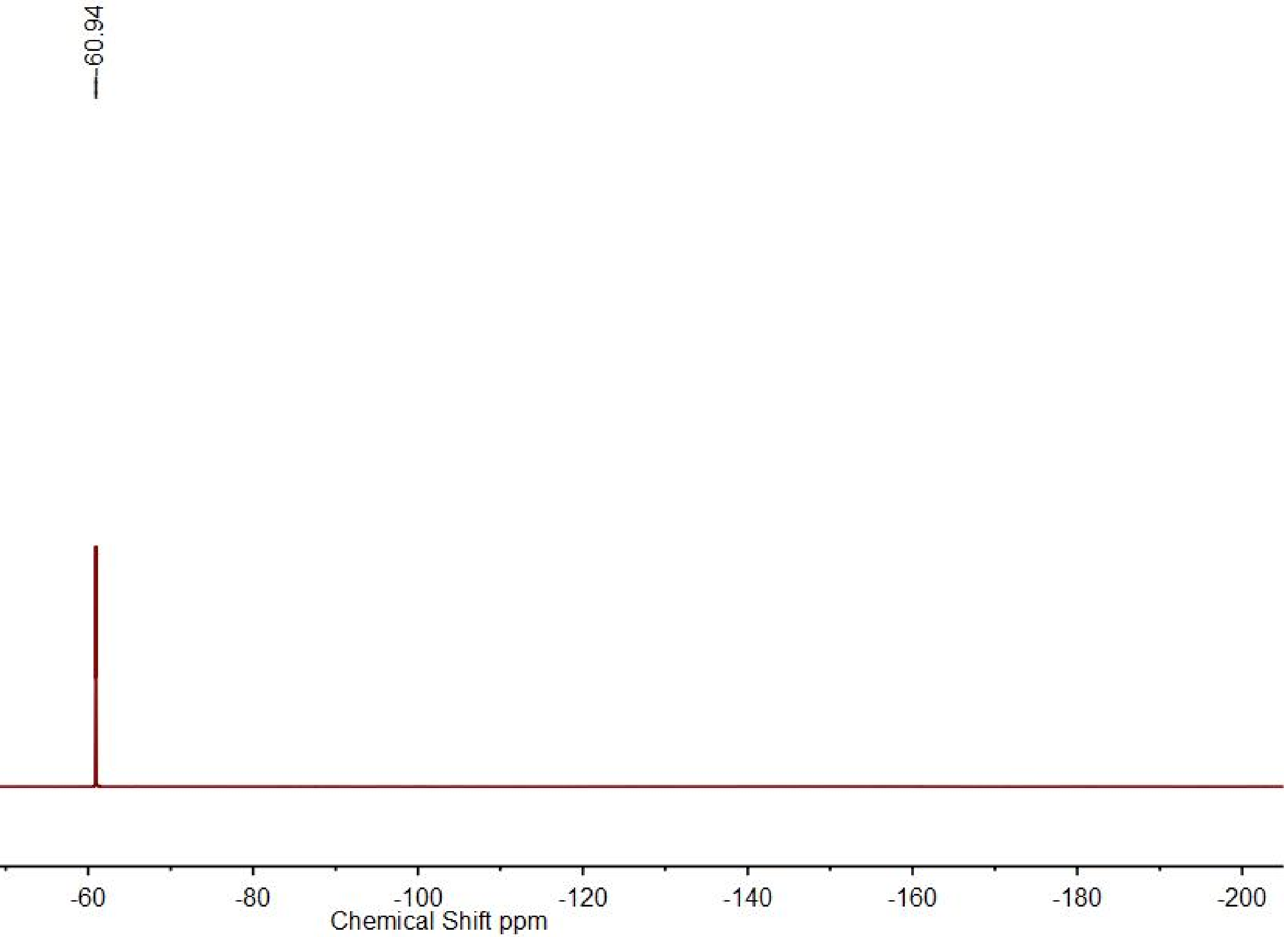


3e, DMSO-d_6, ^{13}C NMR 101 MHz

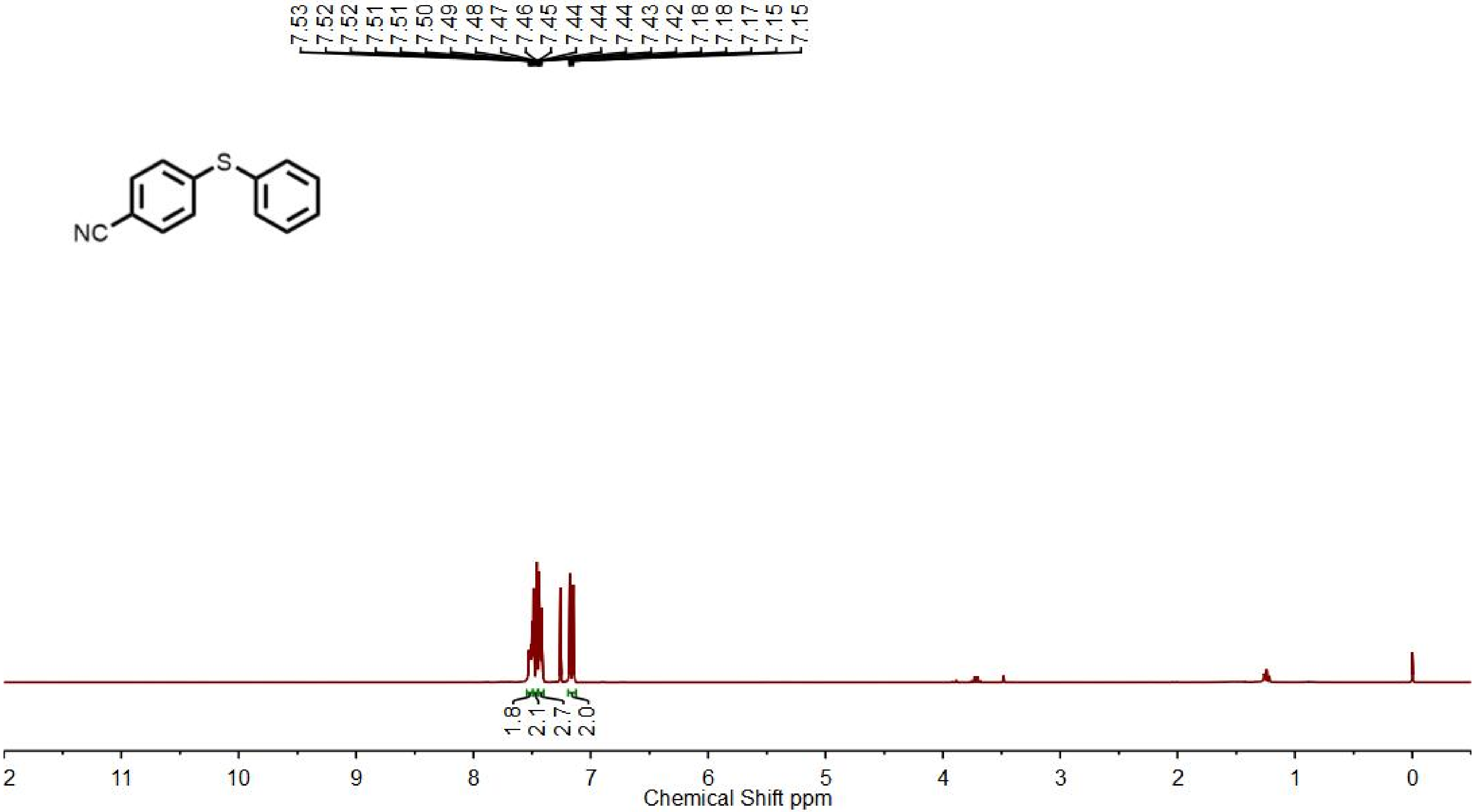


3e, DMSO-d_6, ^{19}F NMR 377 MHz

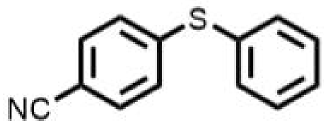


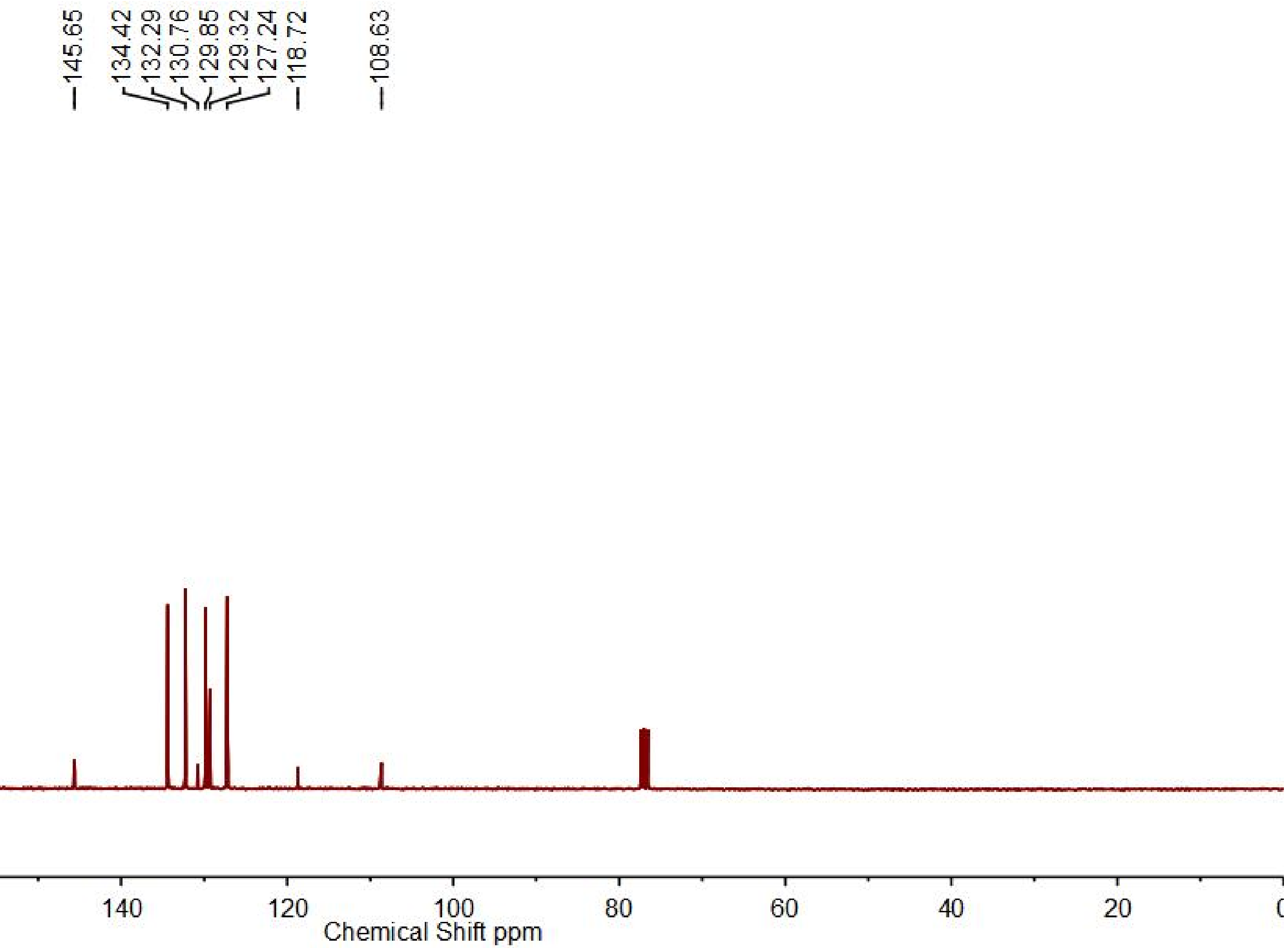


3f, $CDCl_3$, ^1H NMR 300 MHz

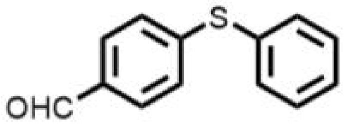


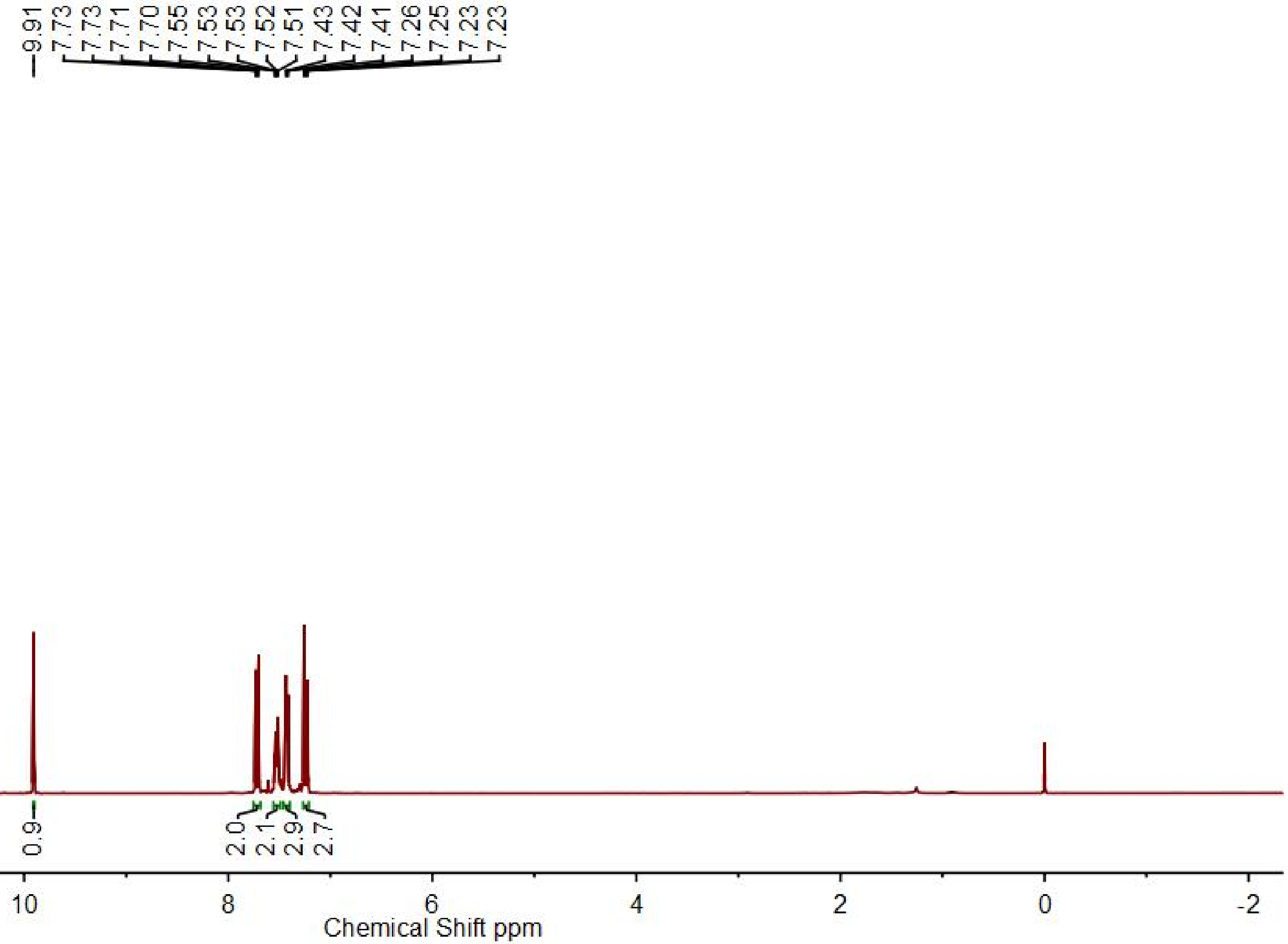
3f, $CDCl_3$, ^{13}C NMR 75 MHz



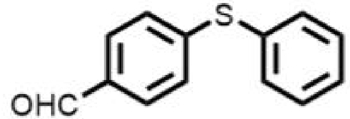


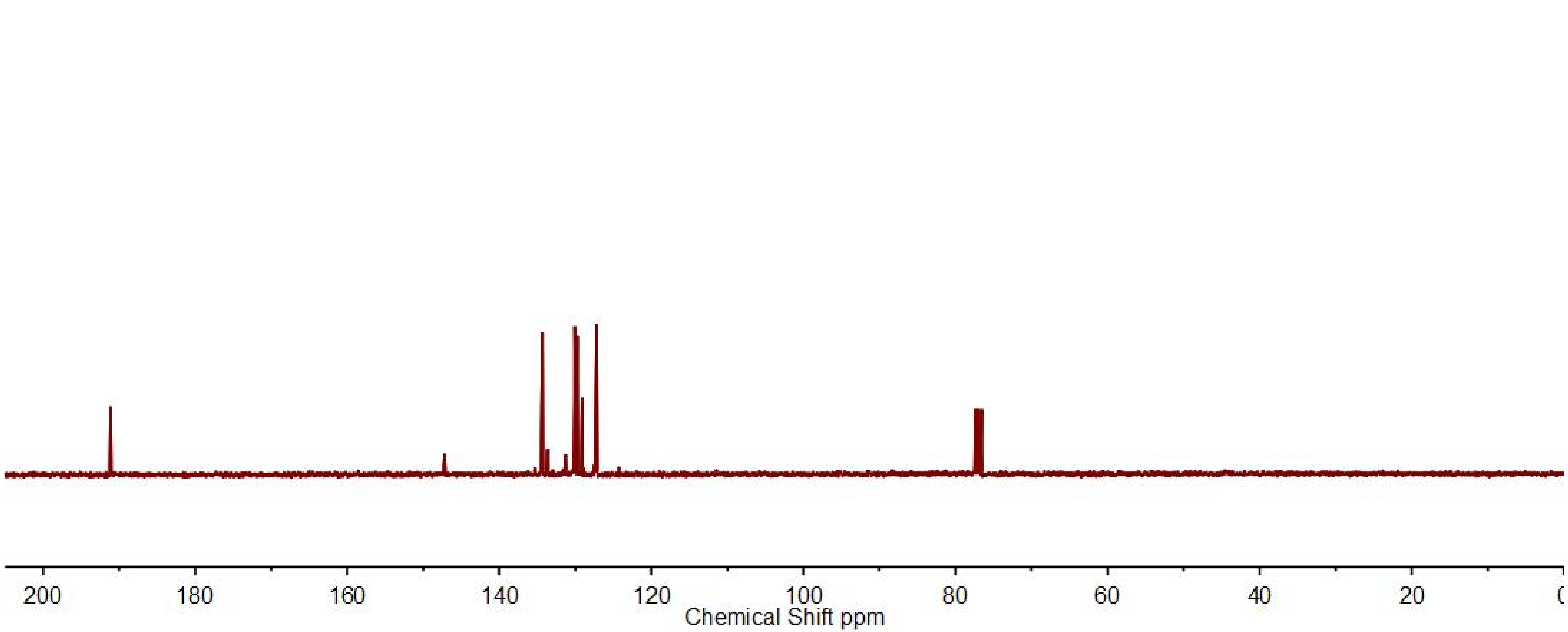
3g, $CDCl_3$, [1]H NMR 300 MHz



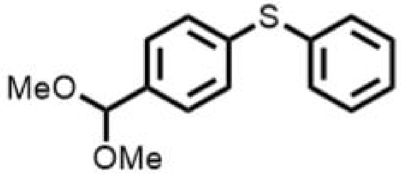


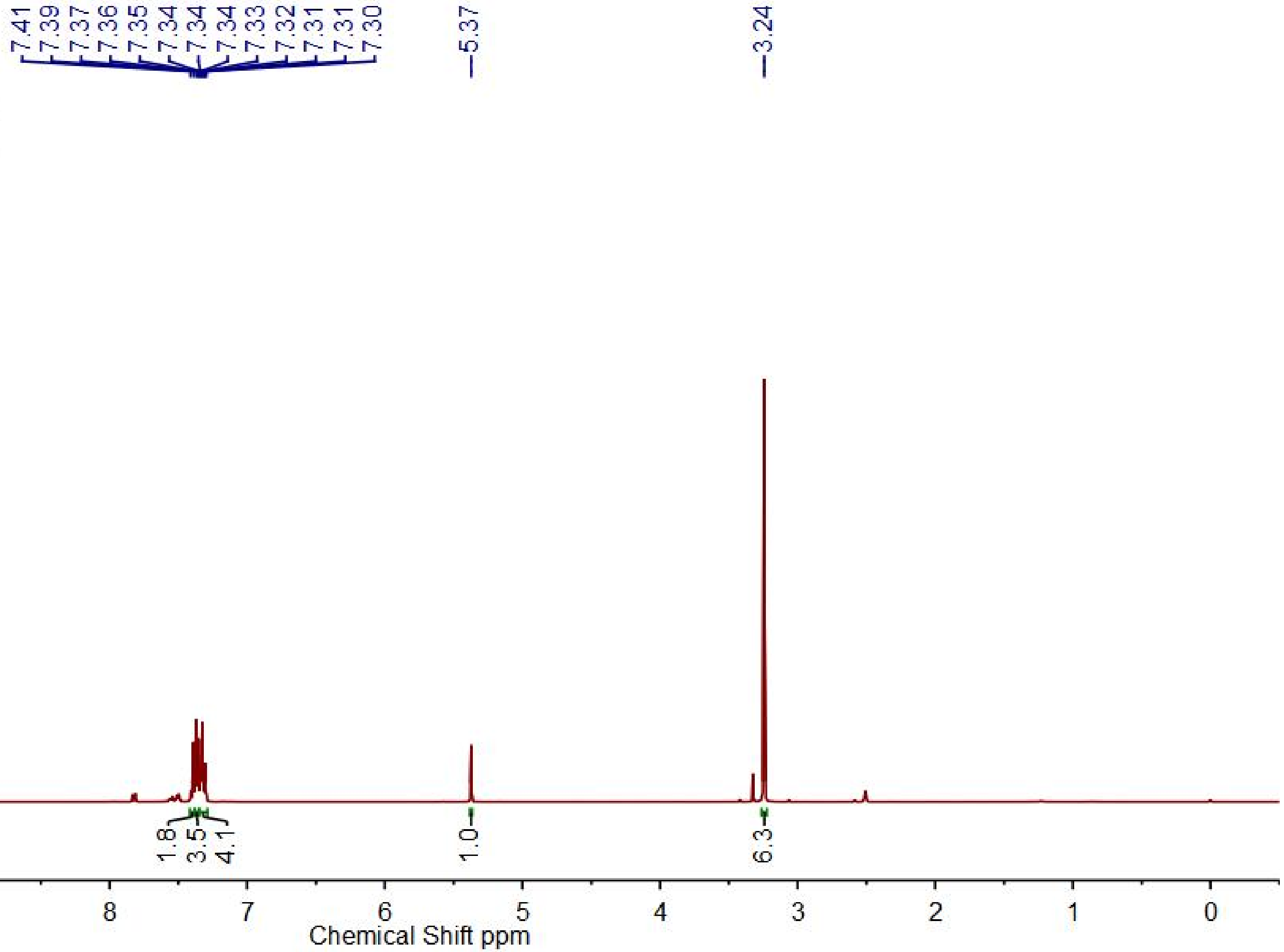
3g, $CDCl_3$, ^{13}C NMR 75 MHz



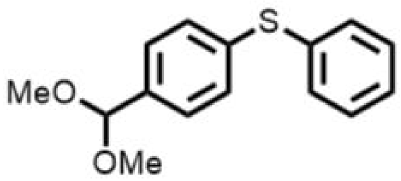


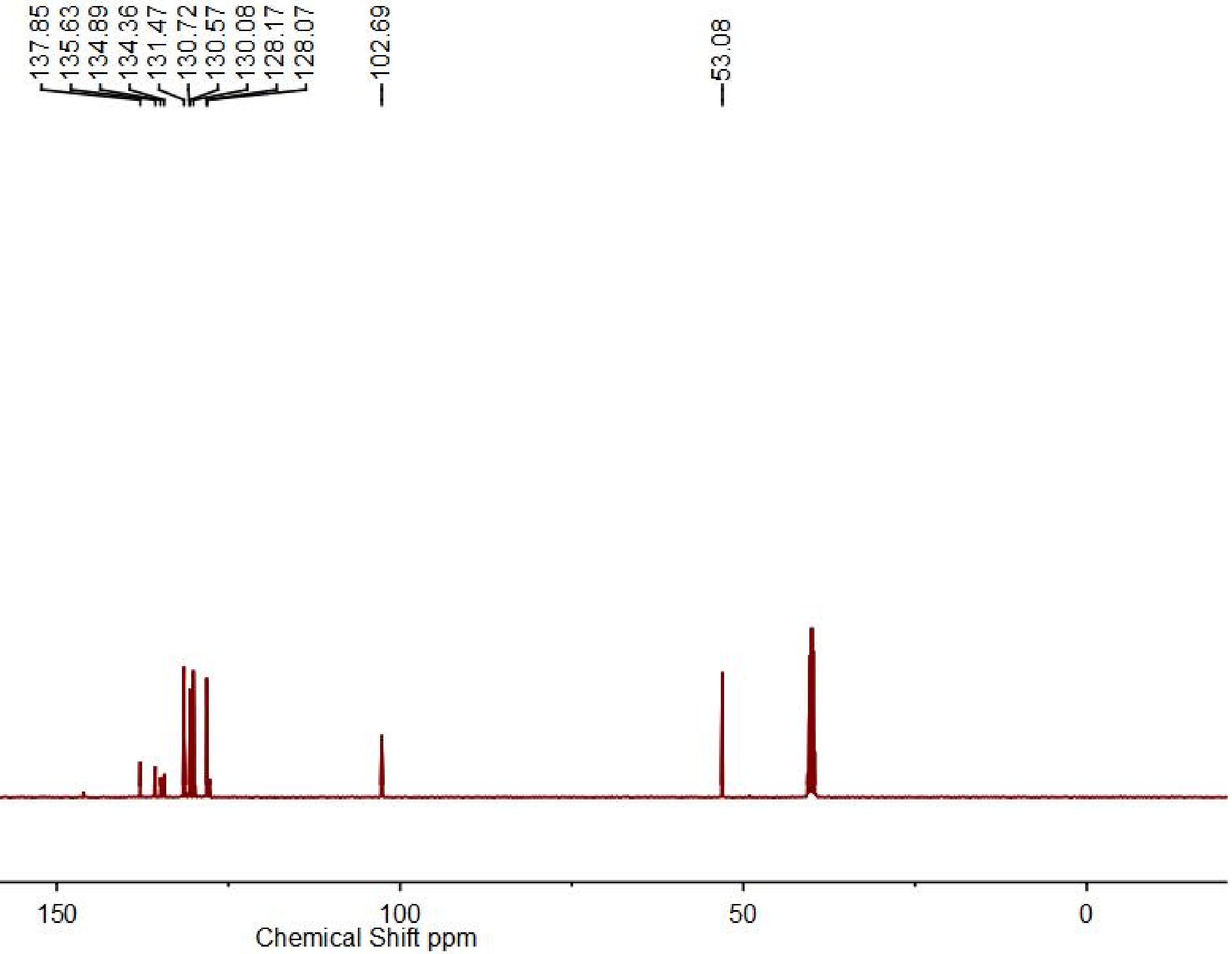
3h, DMSO-d_6, ^{1}H NMR 400 MHz



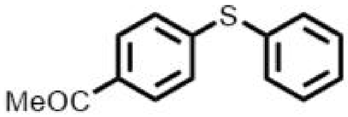


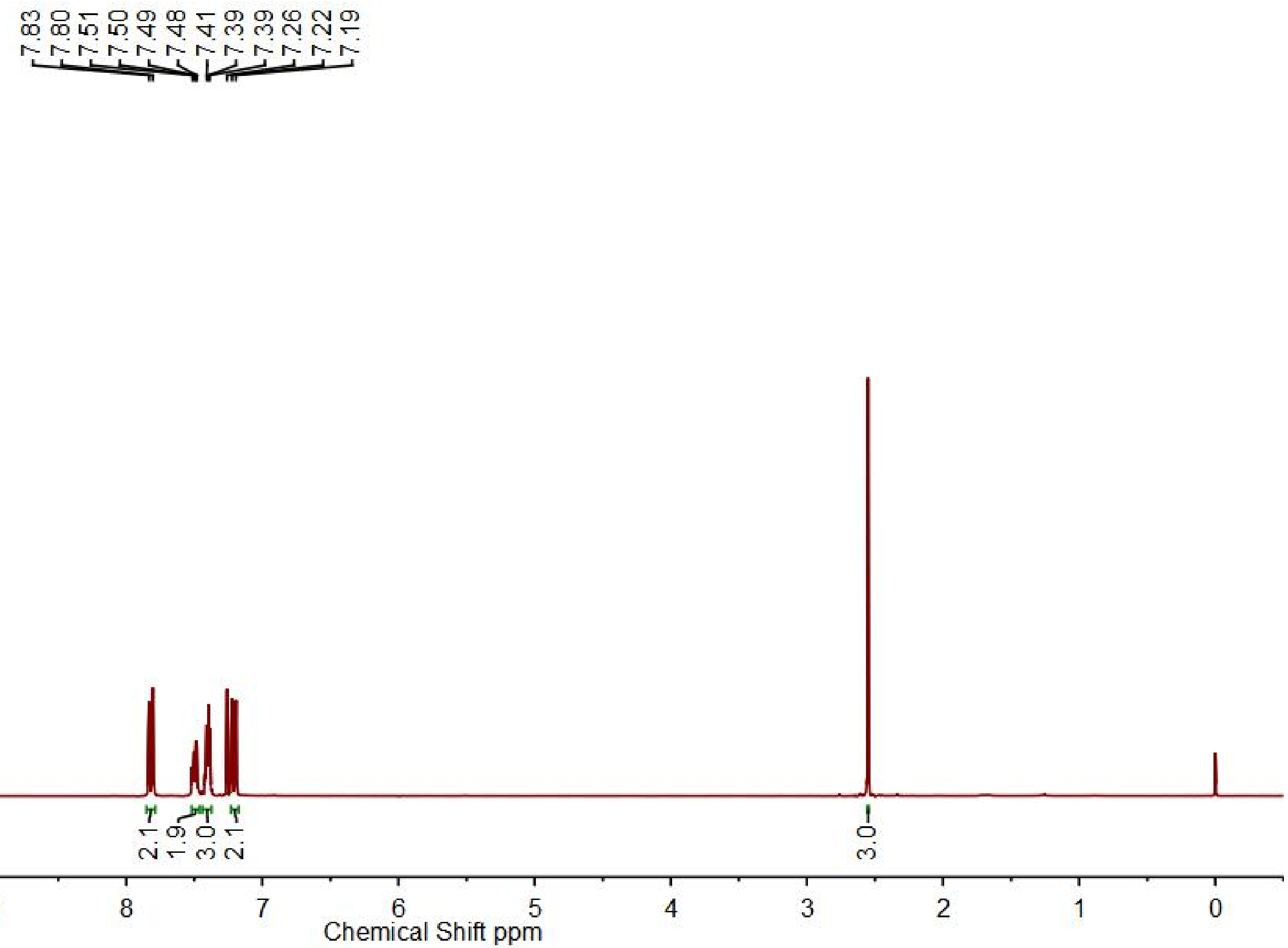
3h, DMSO-d_6, ^{13}C NMR 101 MHz



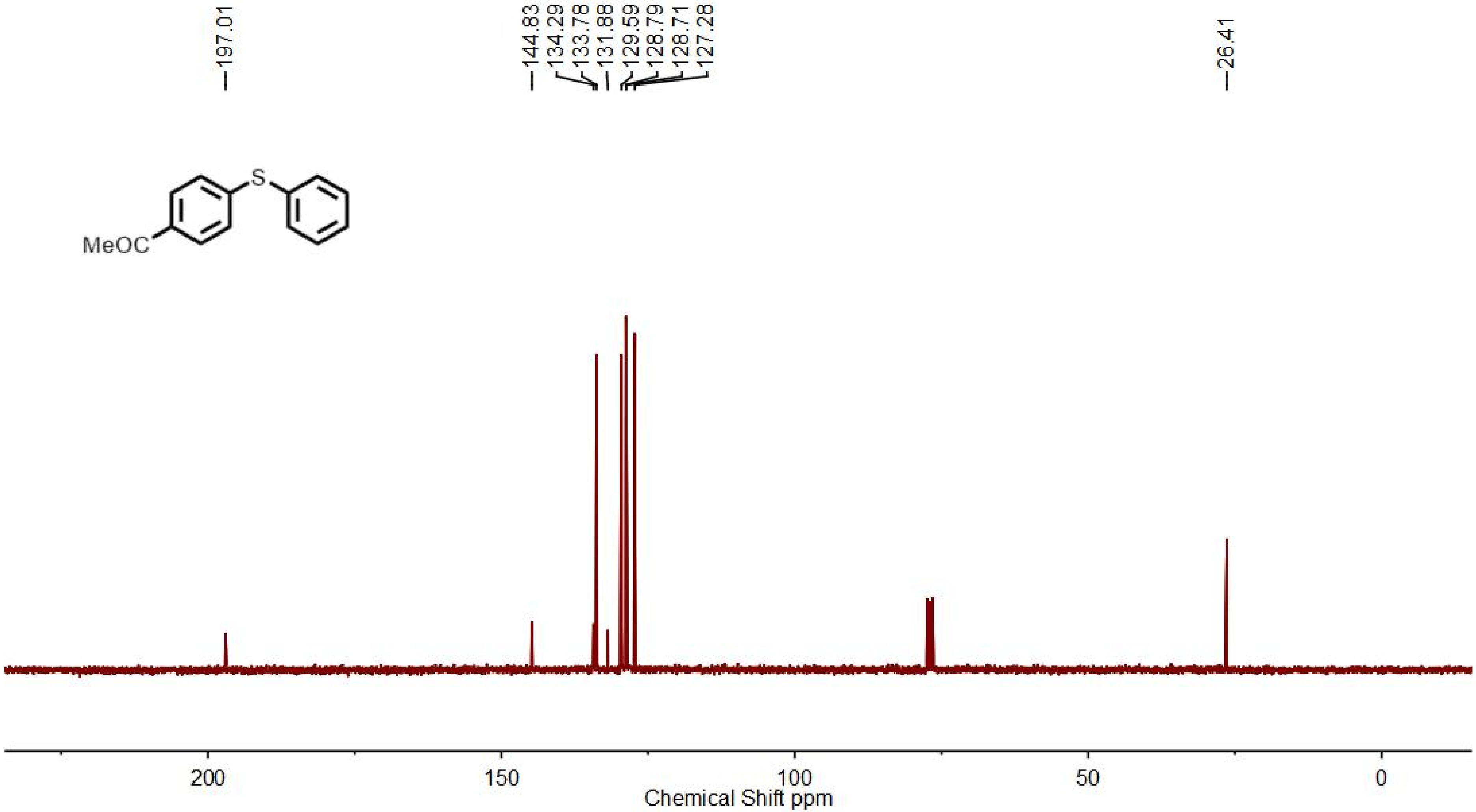


3i, $CDCl_3$, ^1H NMR 300 MHz

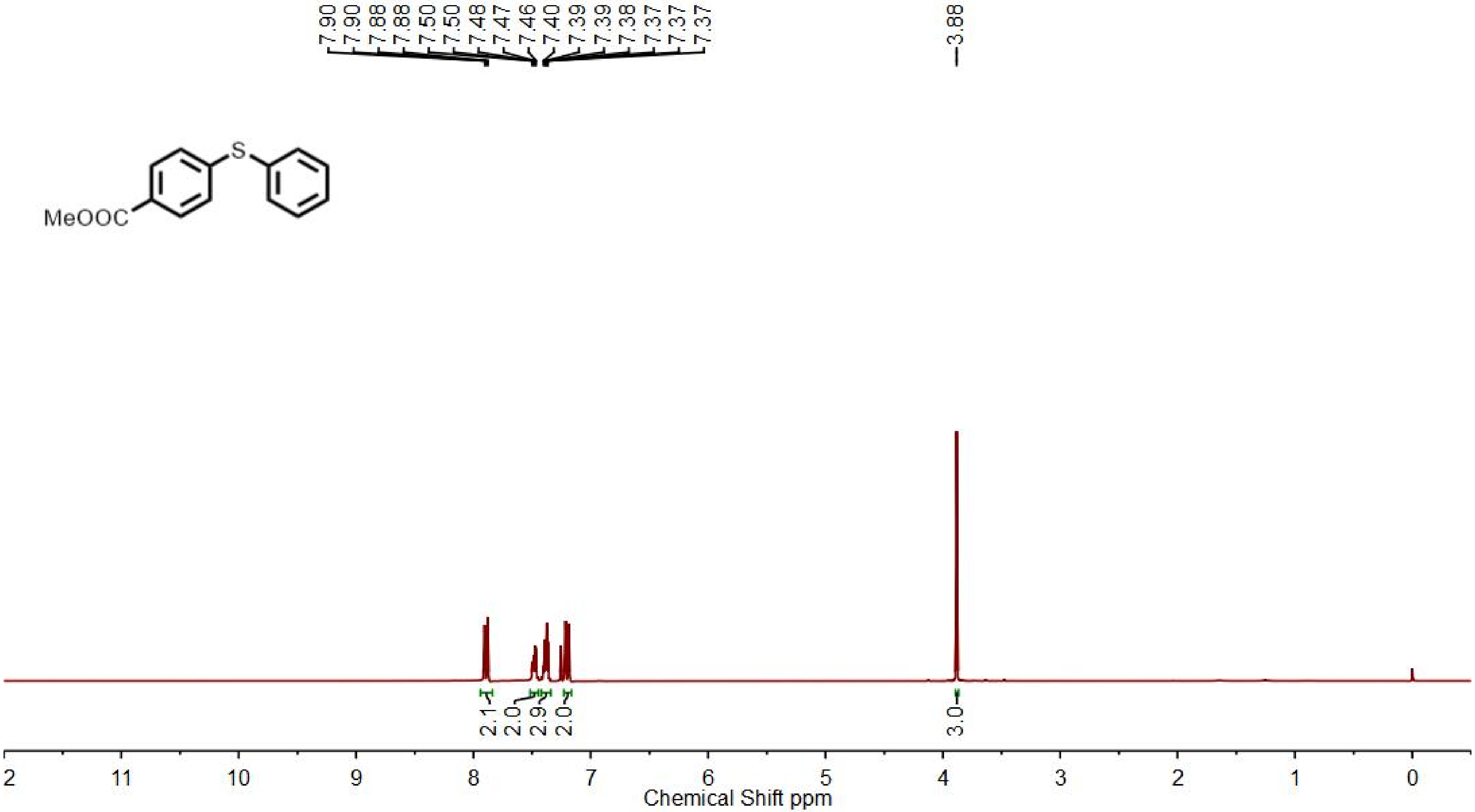




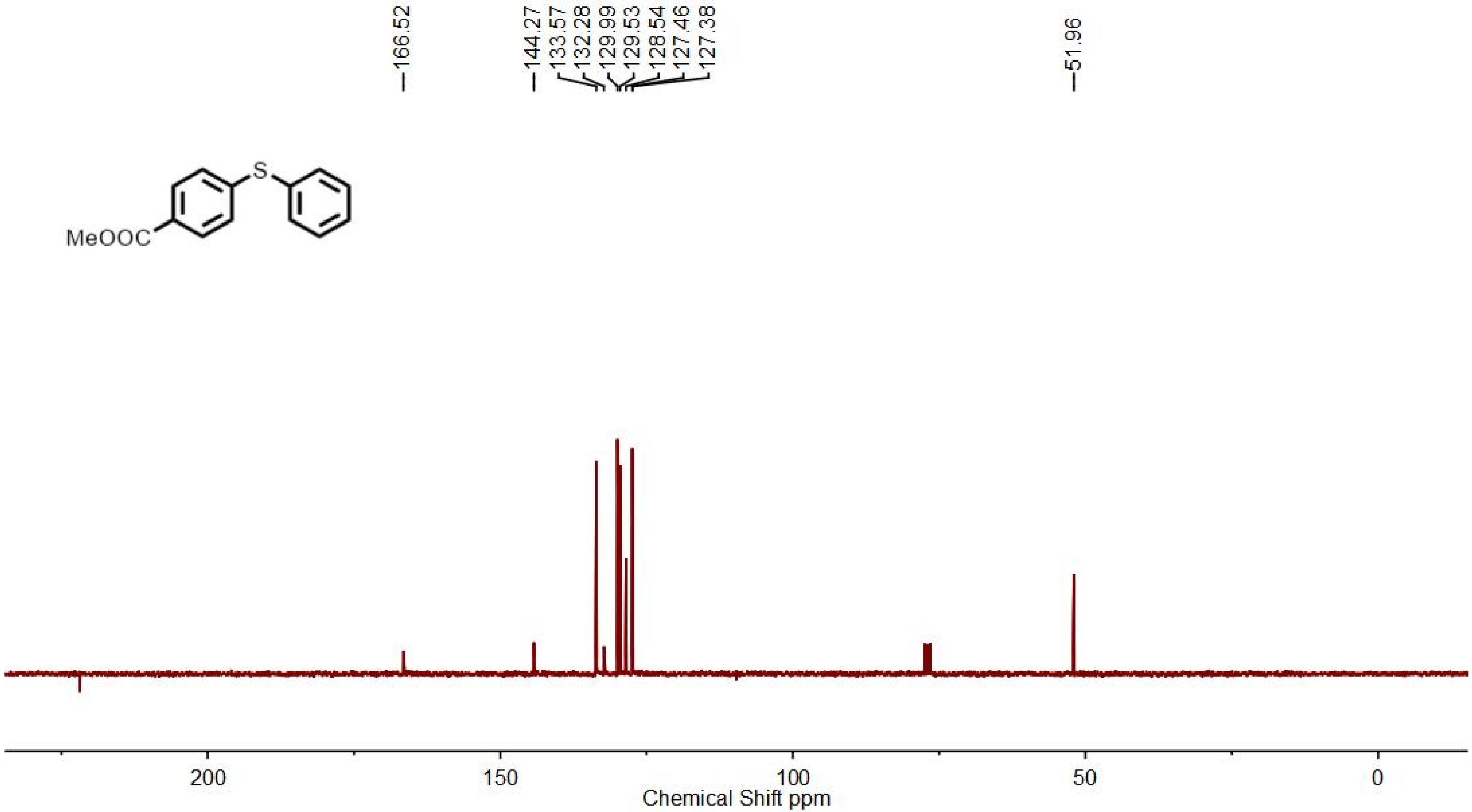
3i, $CDCl_3$, ^{13}C NMR 75 MHz



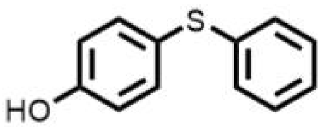
3j, $CDCl_3$, ^1H NMR 300 MHz

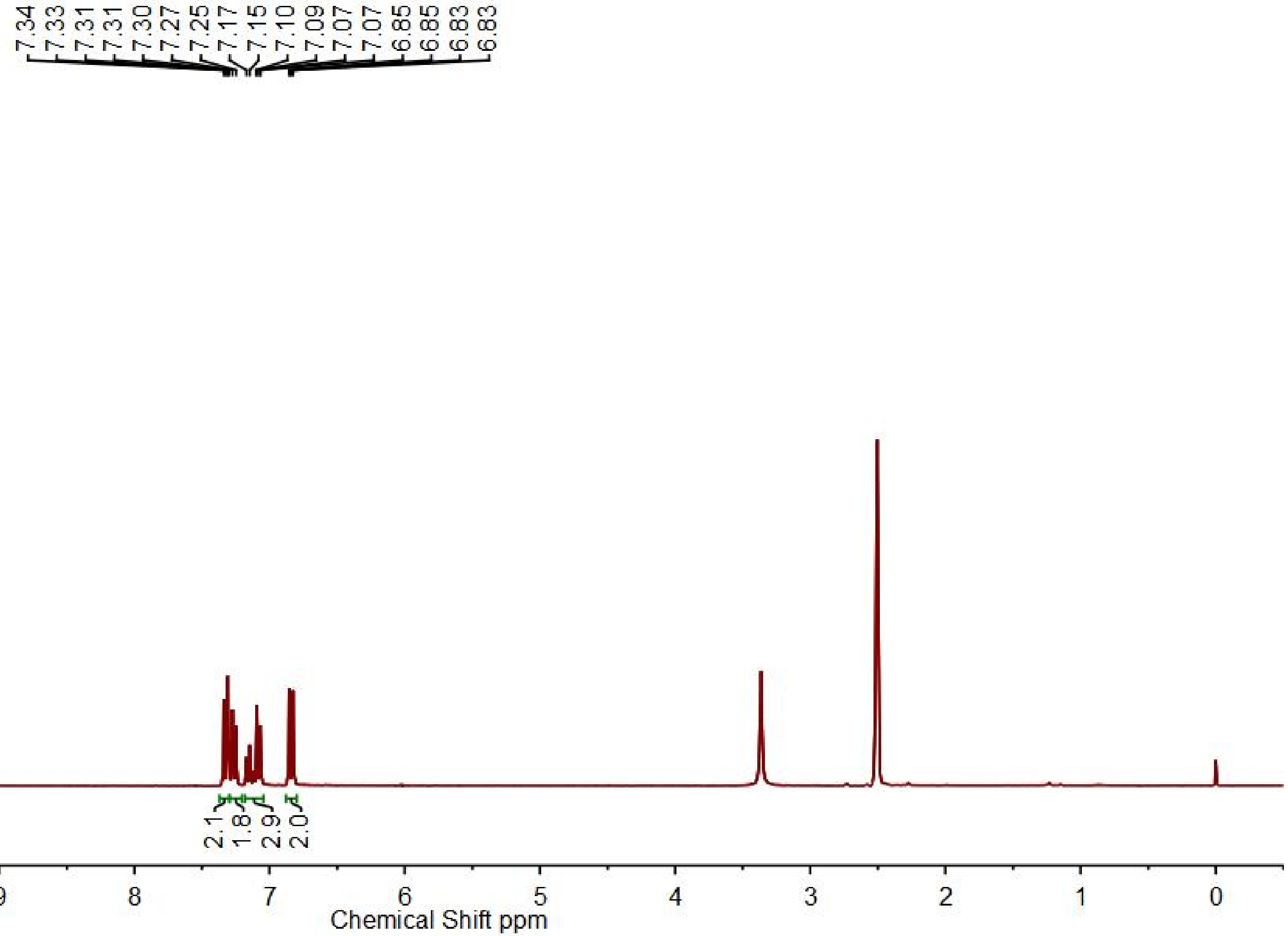


3j, $CDCl_3$, ^{13}C NMR 75 MHz

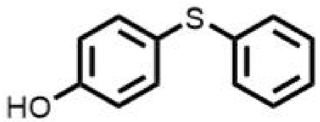


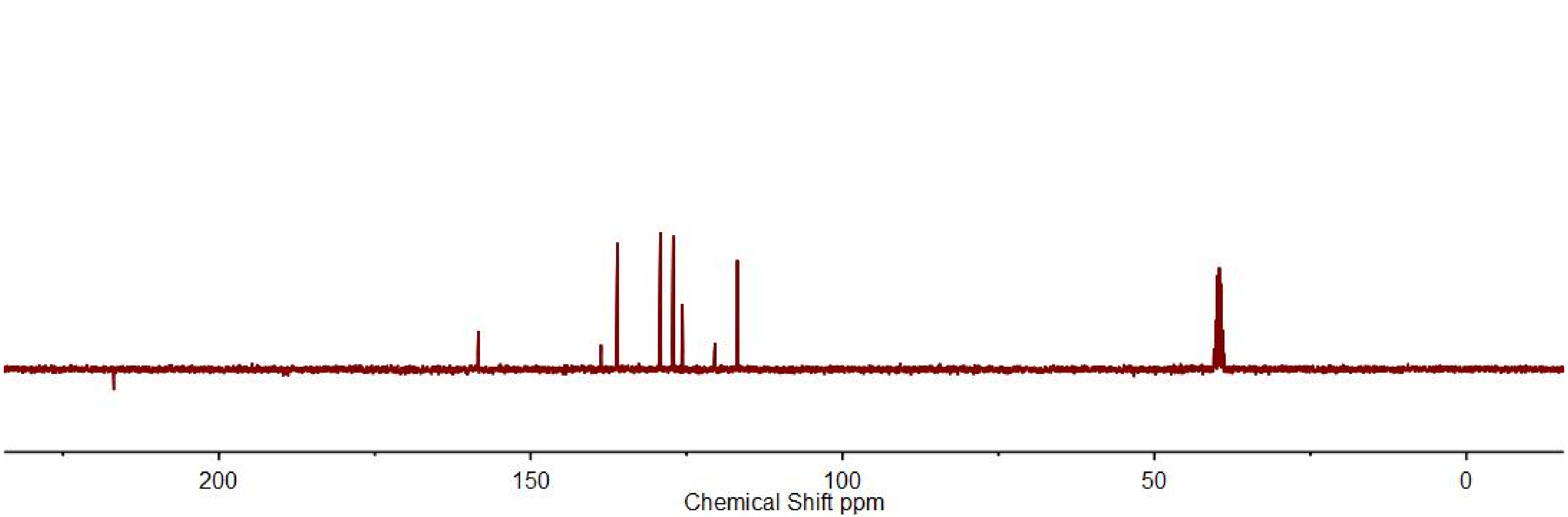
3k, $CDCl_3$, ^1H NMR 300 MHz



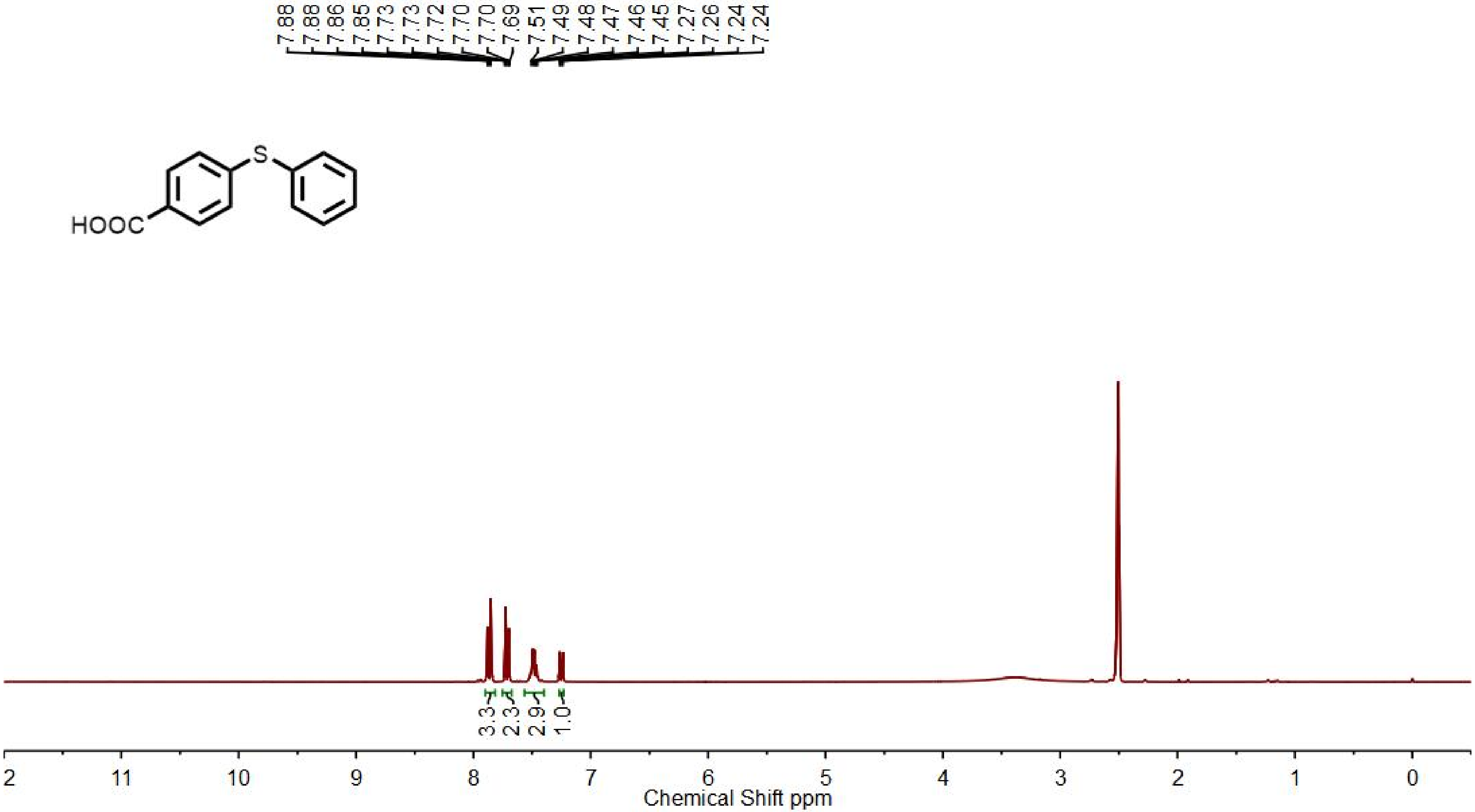


3k, $CDCl_3$, ^{13}C NMR 75 MHz

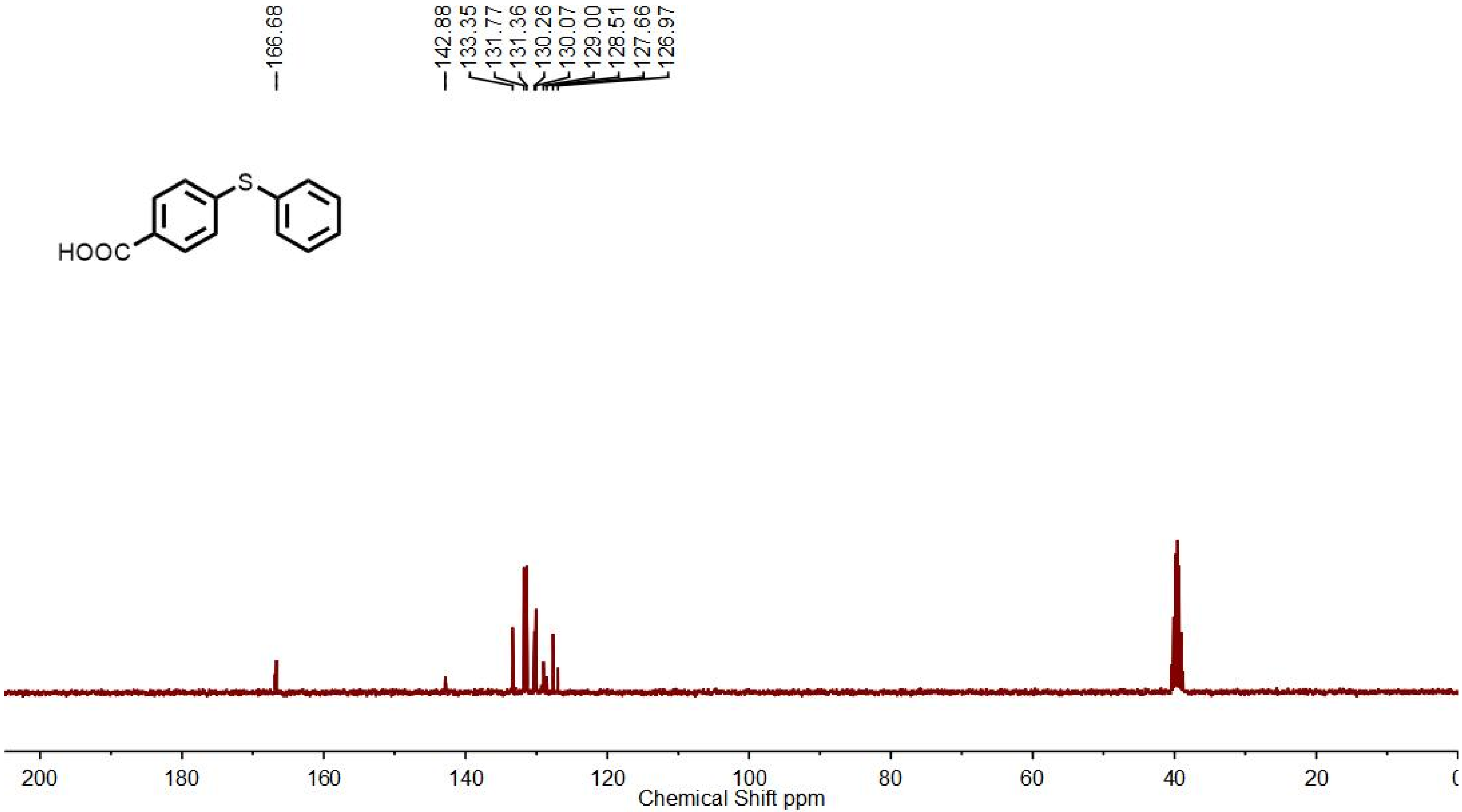




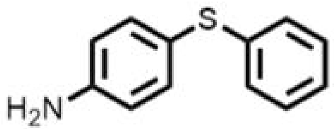
3l, DMSO-d_6, ^{1}H NMR 300 MHz

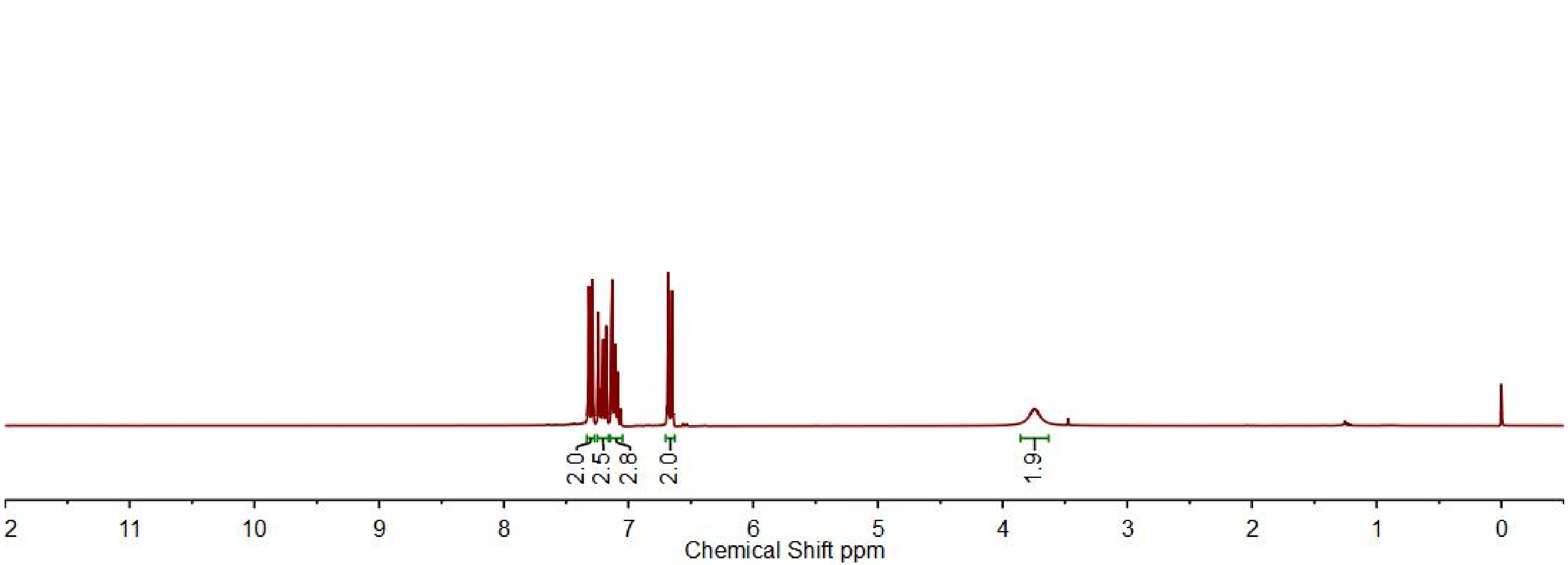


3l, DMSO-d_6, ^{1}H NMR 75 MHz

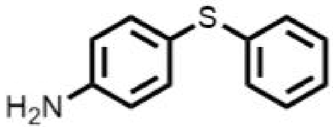


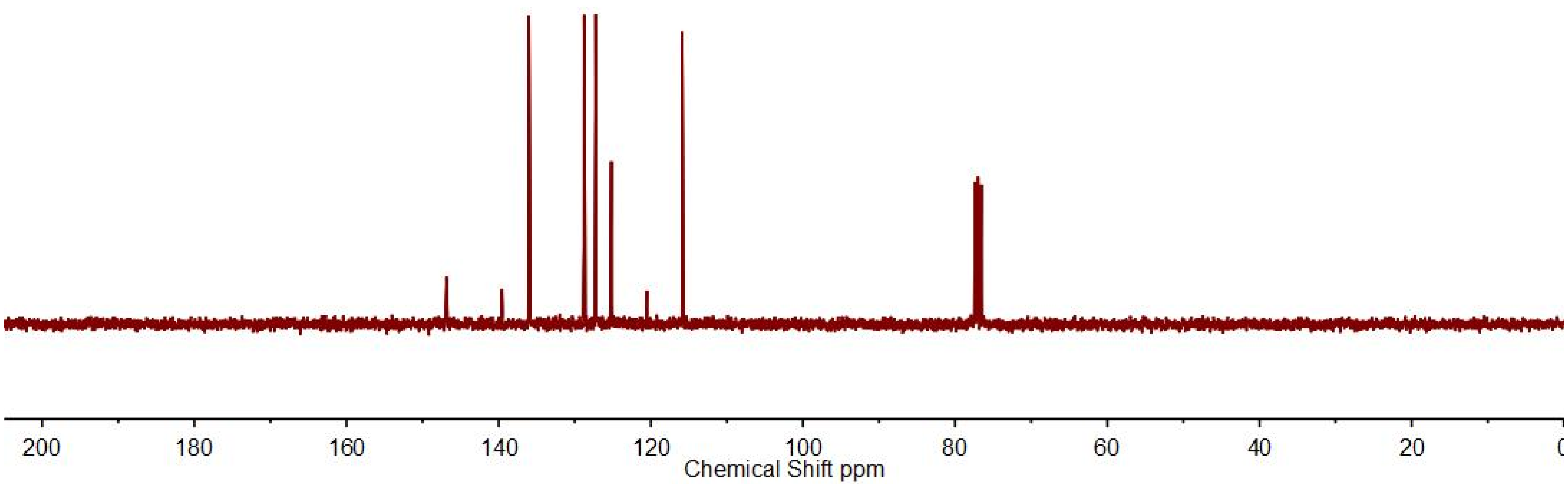
3m, $CDCl_3$, ^1H NMR 300 MHz



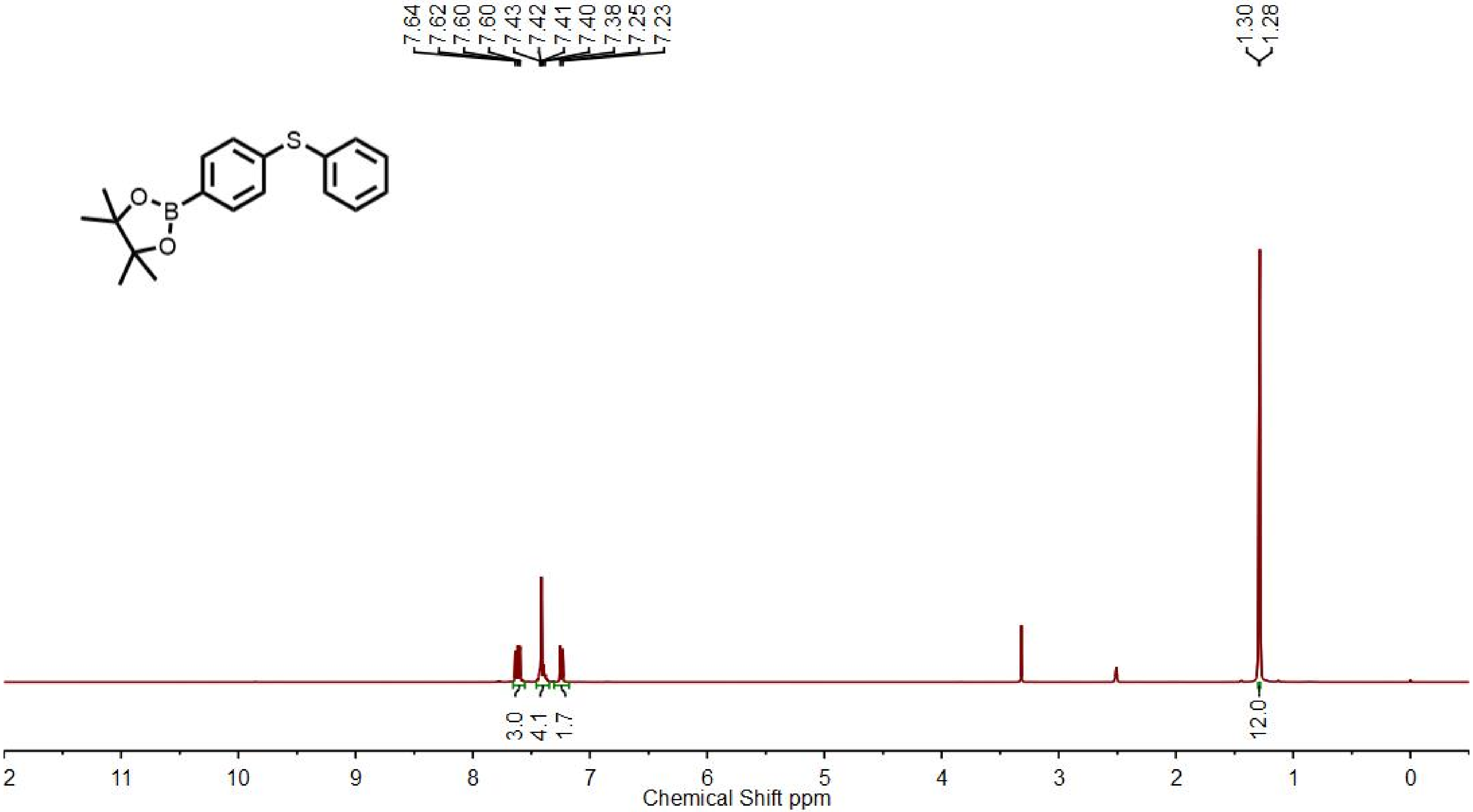


3m, $CDCl_3$, ^{13}C NMR 75 MHz

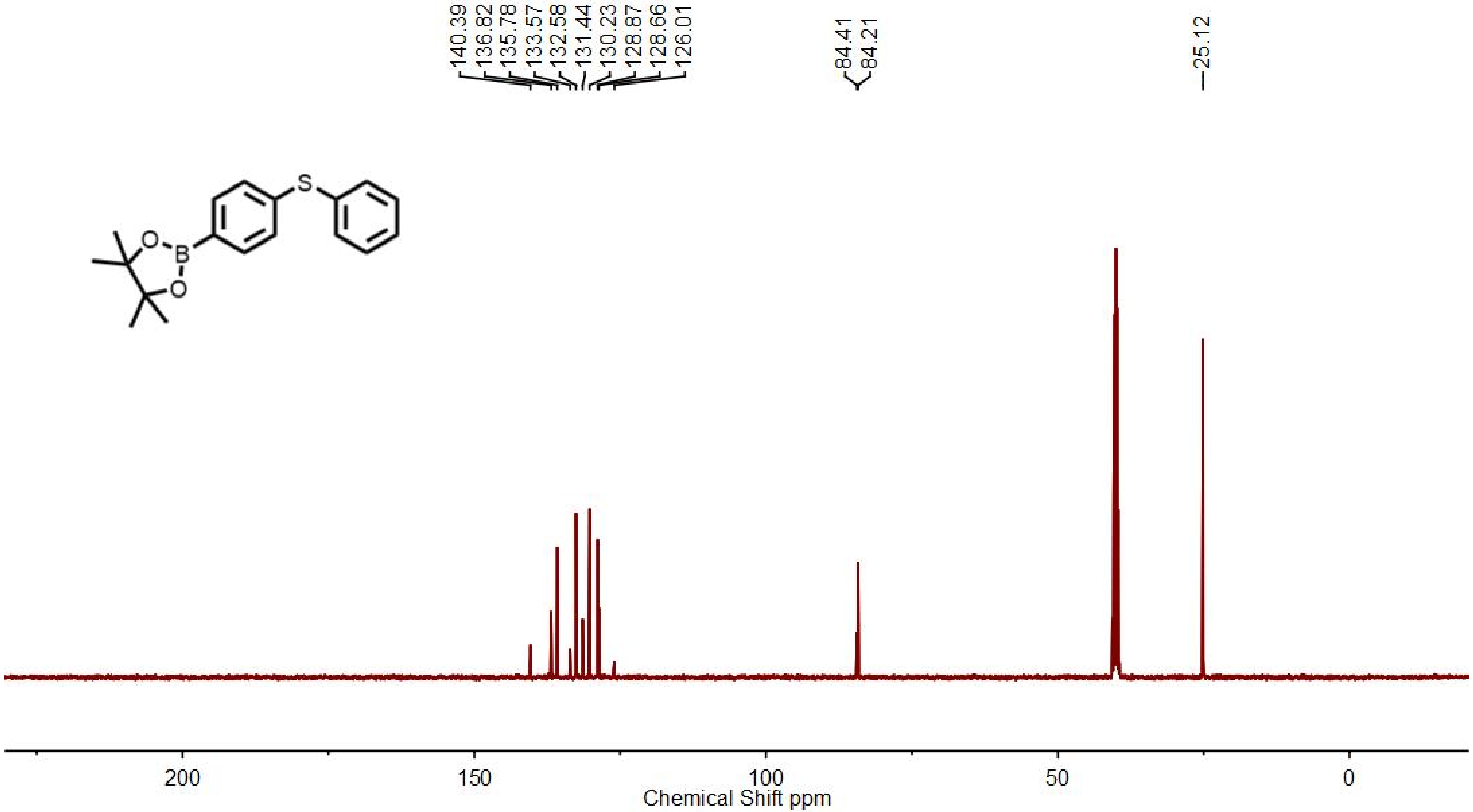




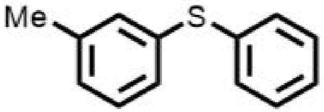
3n, DMSO-d_6, ^{1}H NMR 400 MHz

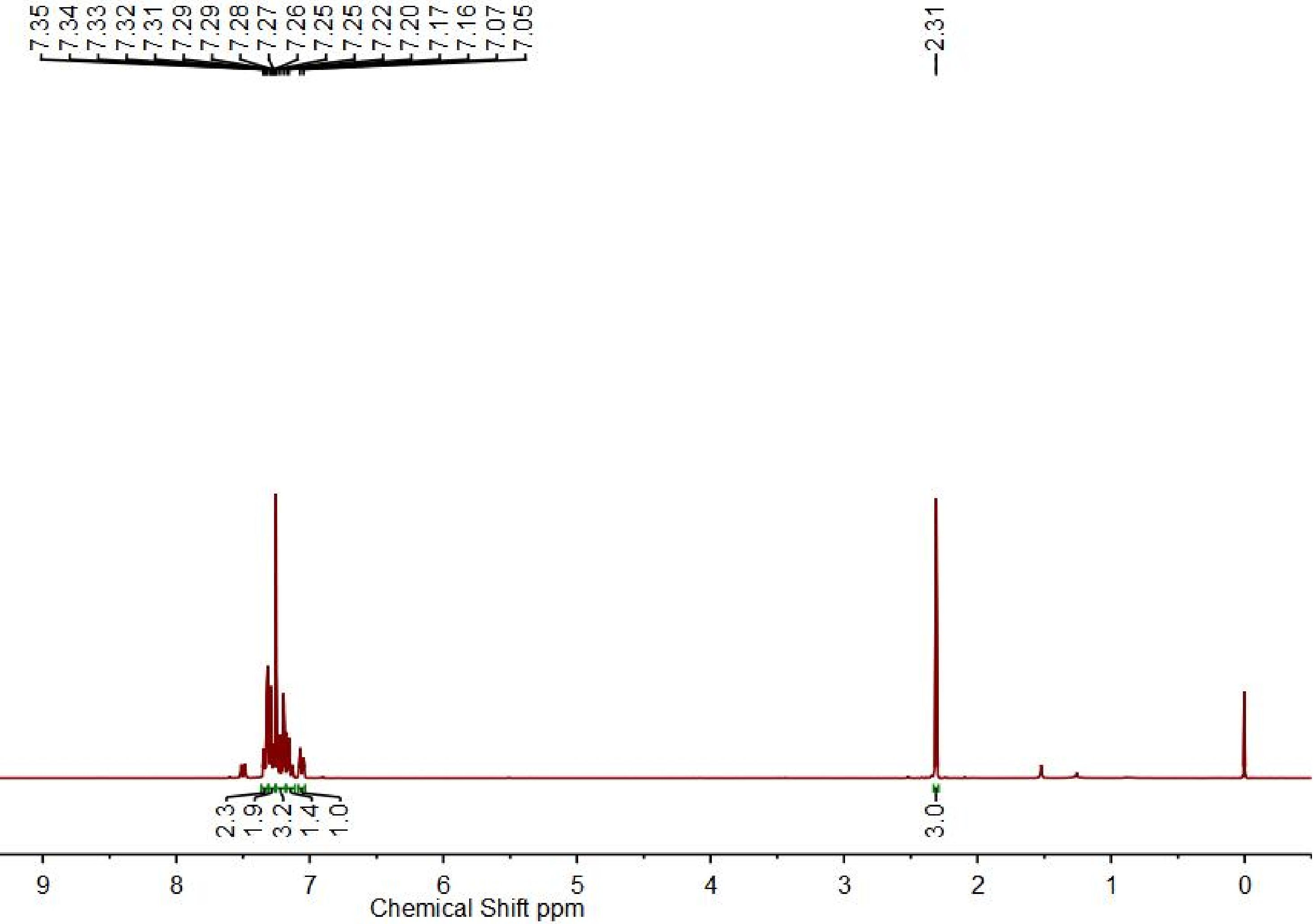


3n, DMSO-d_6, ^{13}C NMR 101 MHz

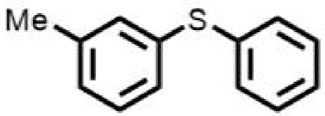


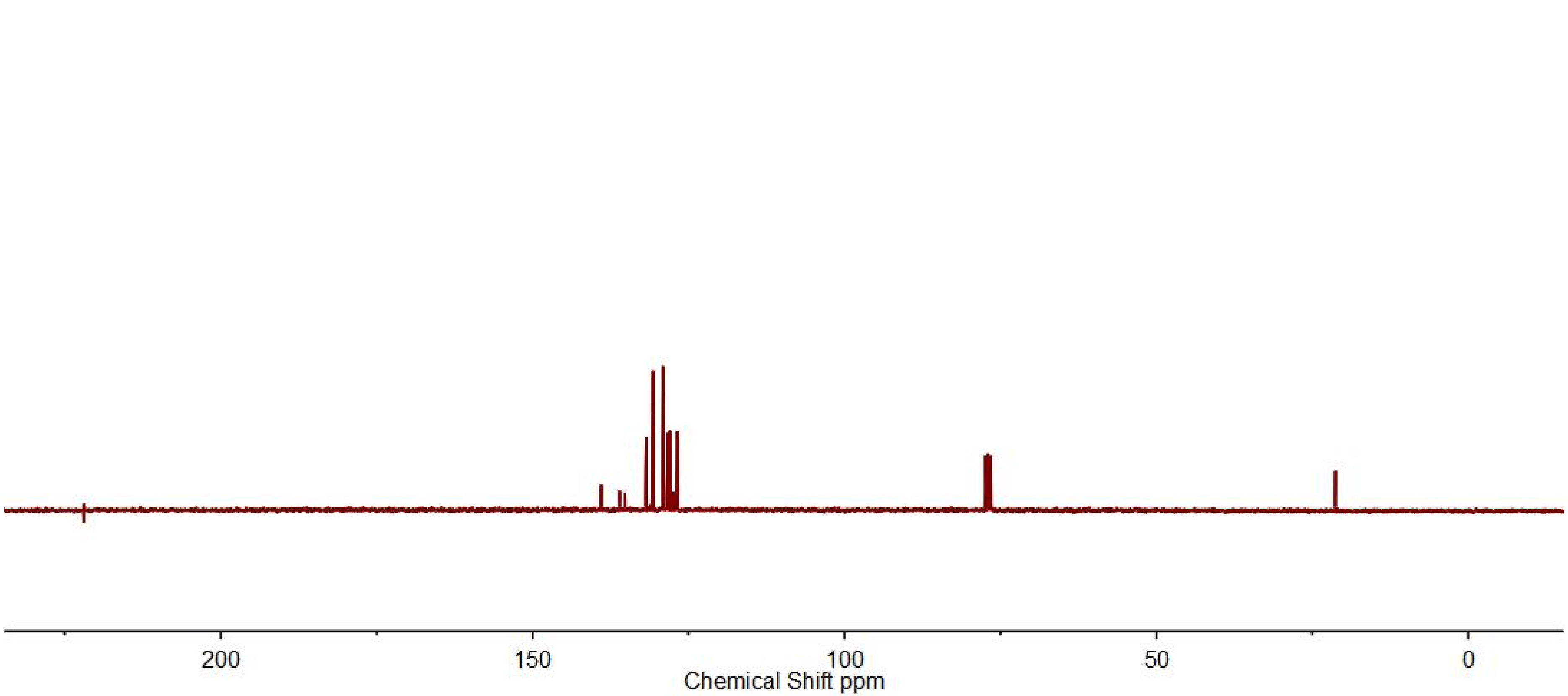
3o, $CDCl_3$, ^1H NMR 300 MHz



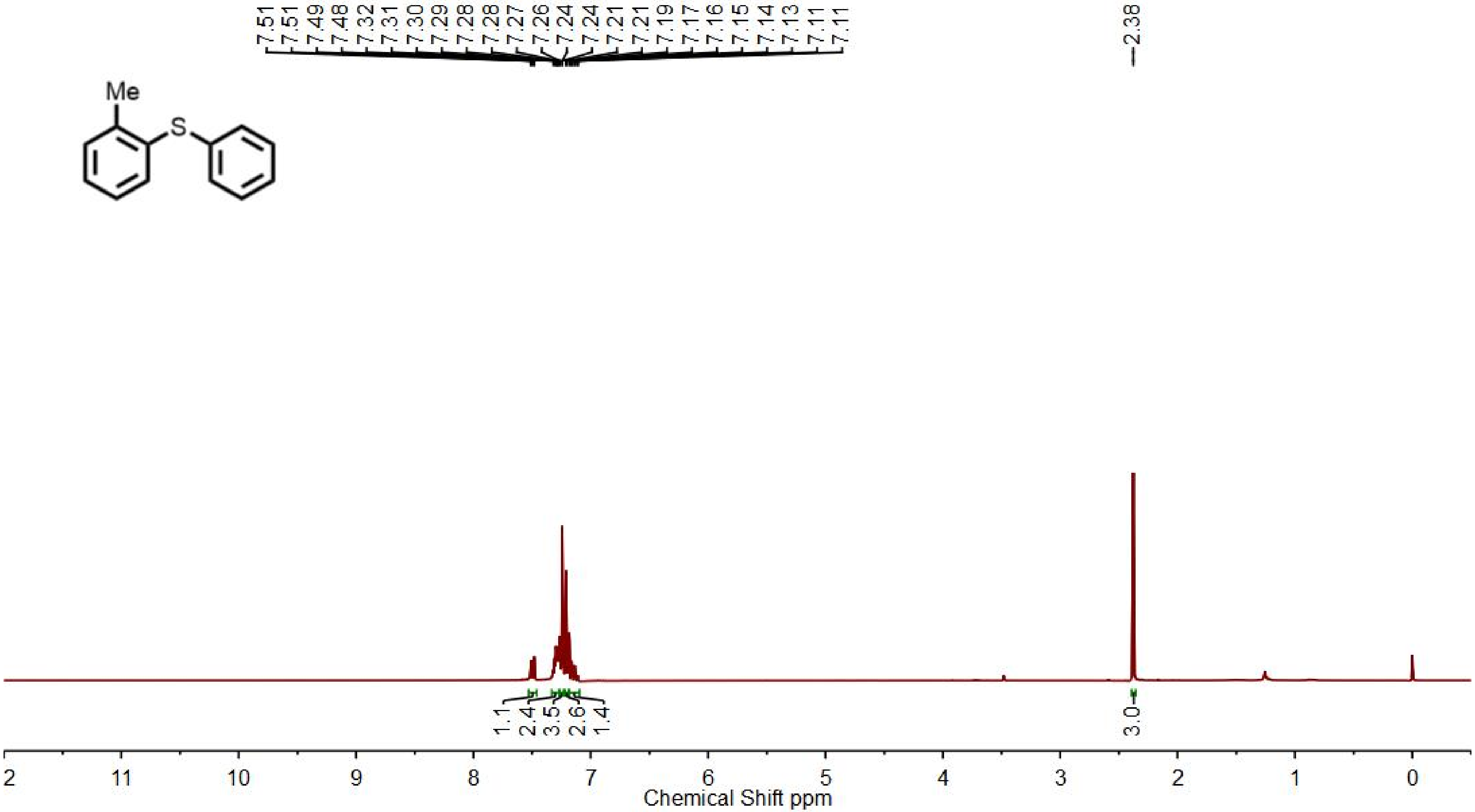


3o, $CDCl_3$, ^{13}C NMR 75 MHz

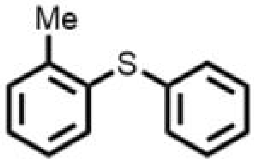


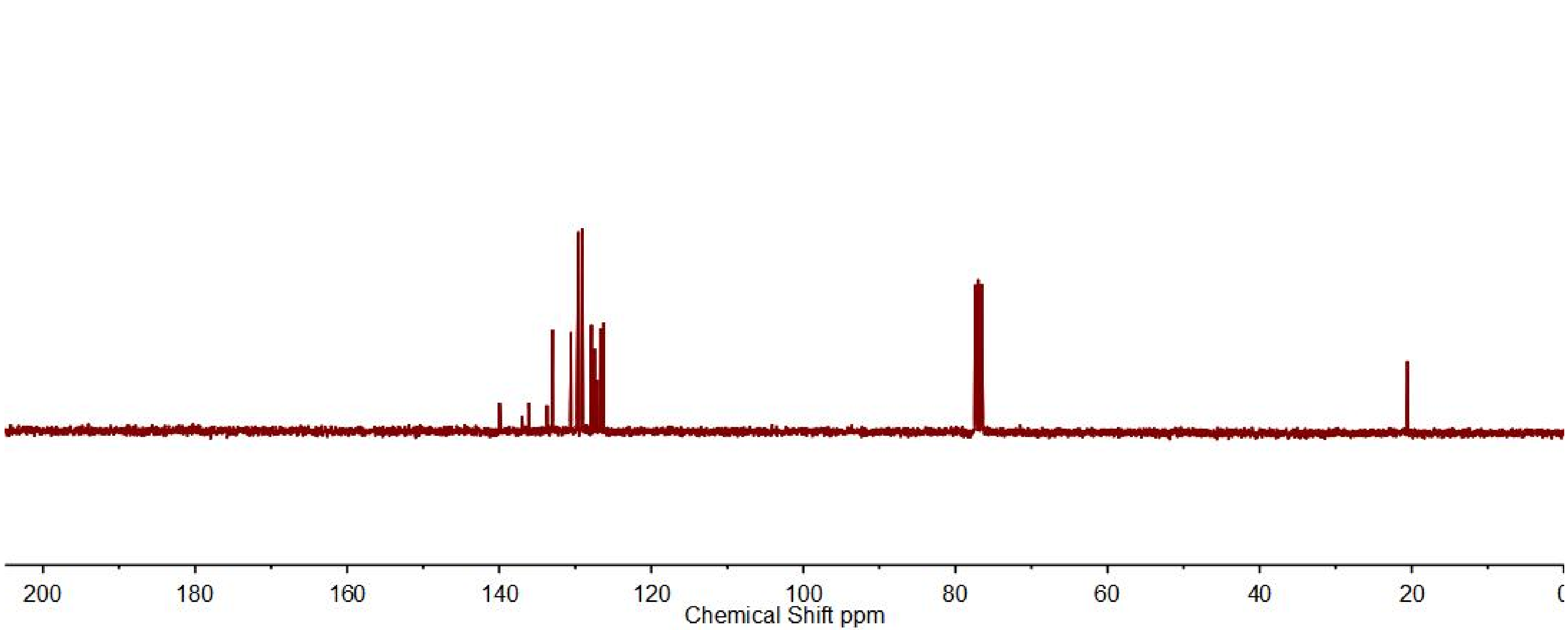


3p, $CDCl_3$, ^1H NMR 300 MHz

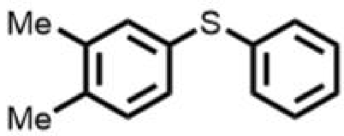


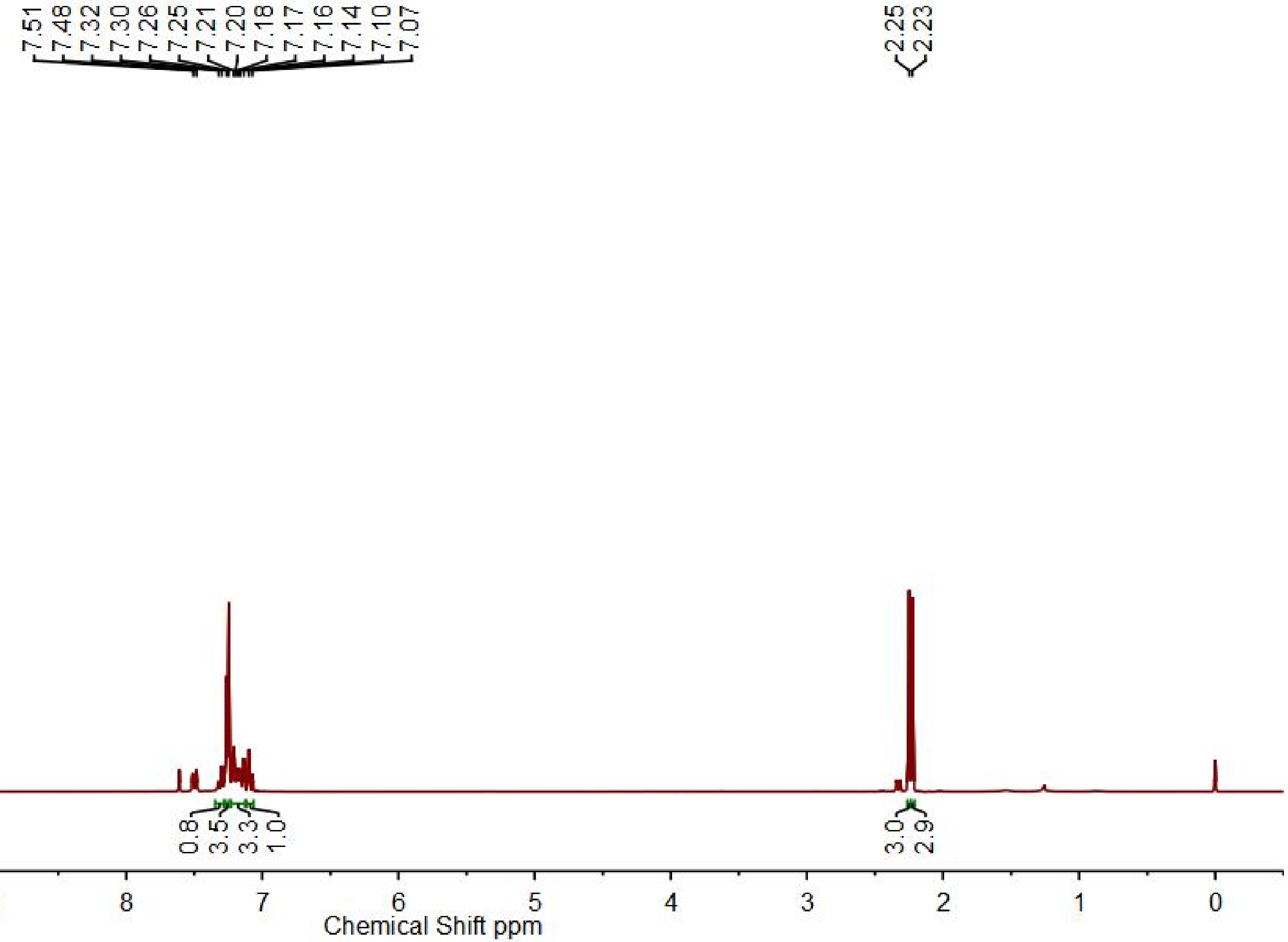
3p, $CDCl_3$, ^{13}C NMR 75 MHz



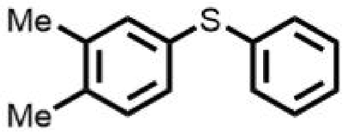


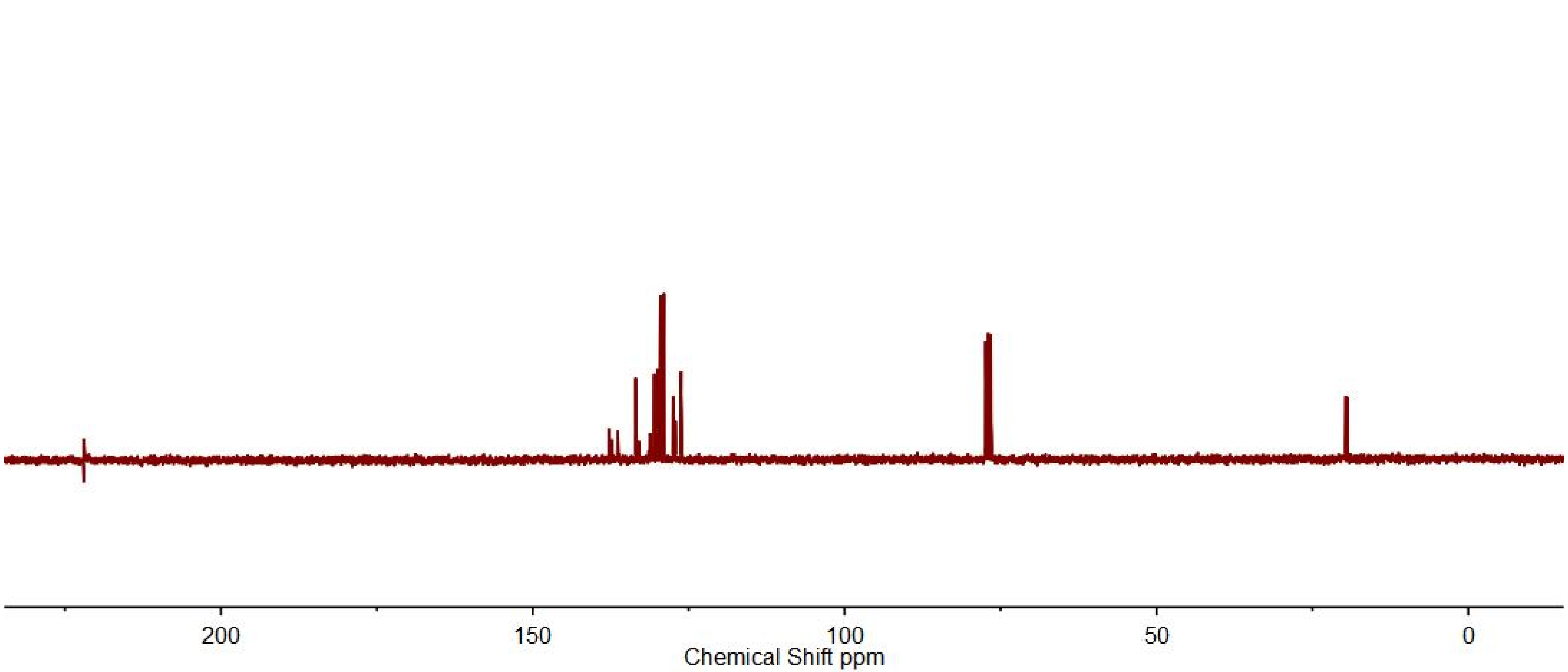
3q, $CDCl_3$, ^1H NMR 300 MHz



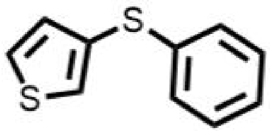


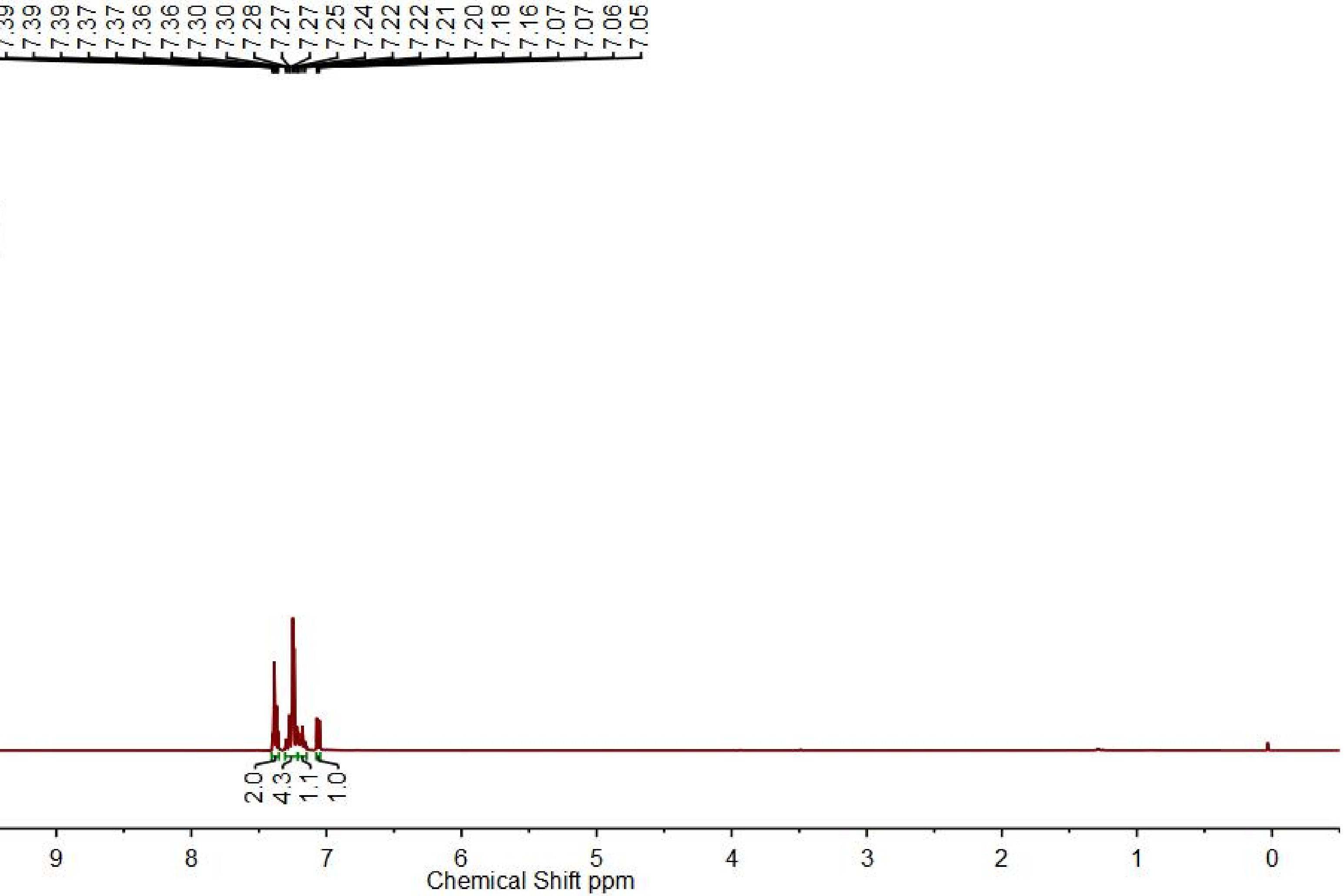
3q, $CDCl_3$, ^{13}C NMR 75 MHz



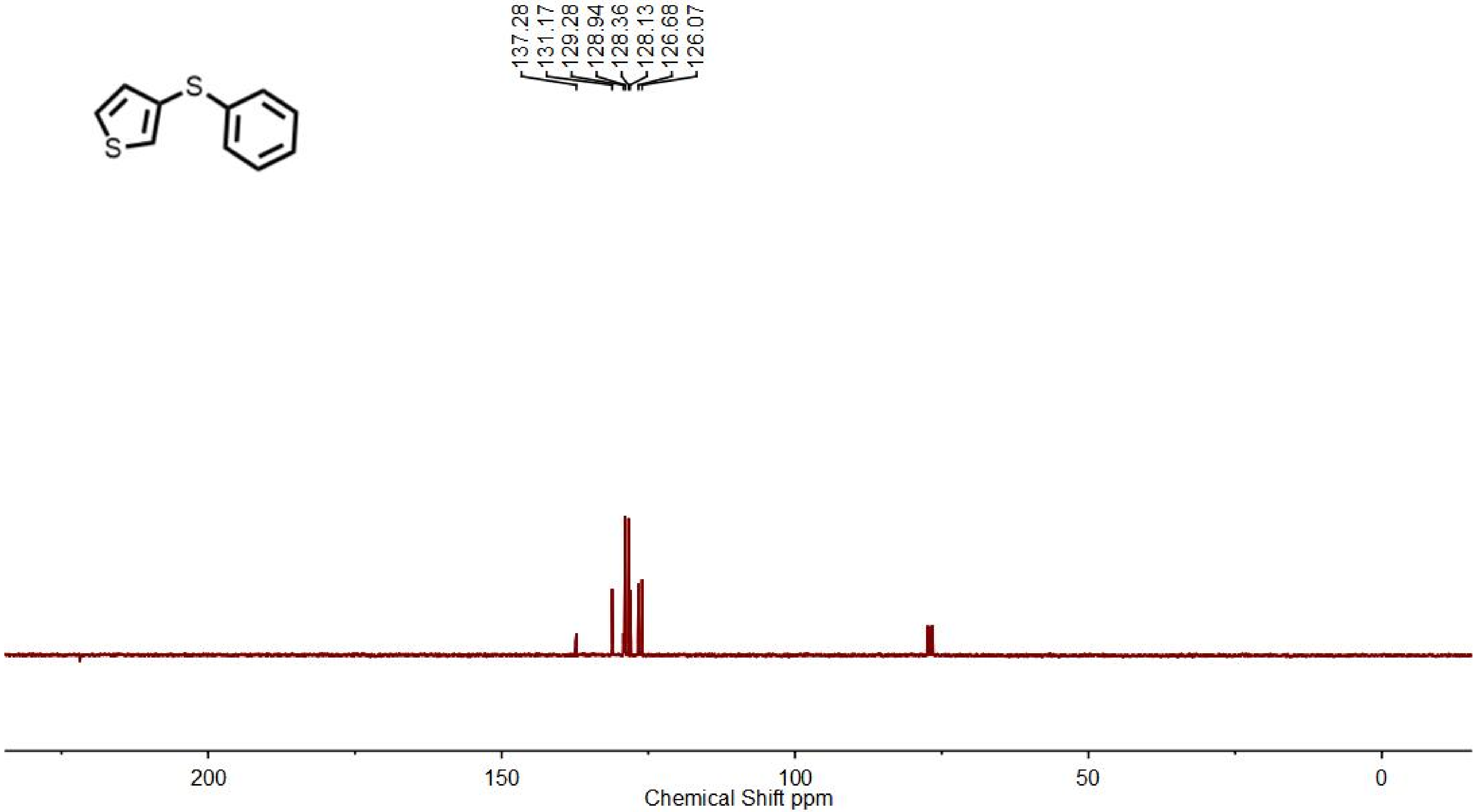


3r, $CDCl_3$, ^{13}C NMR 300 MHz

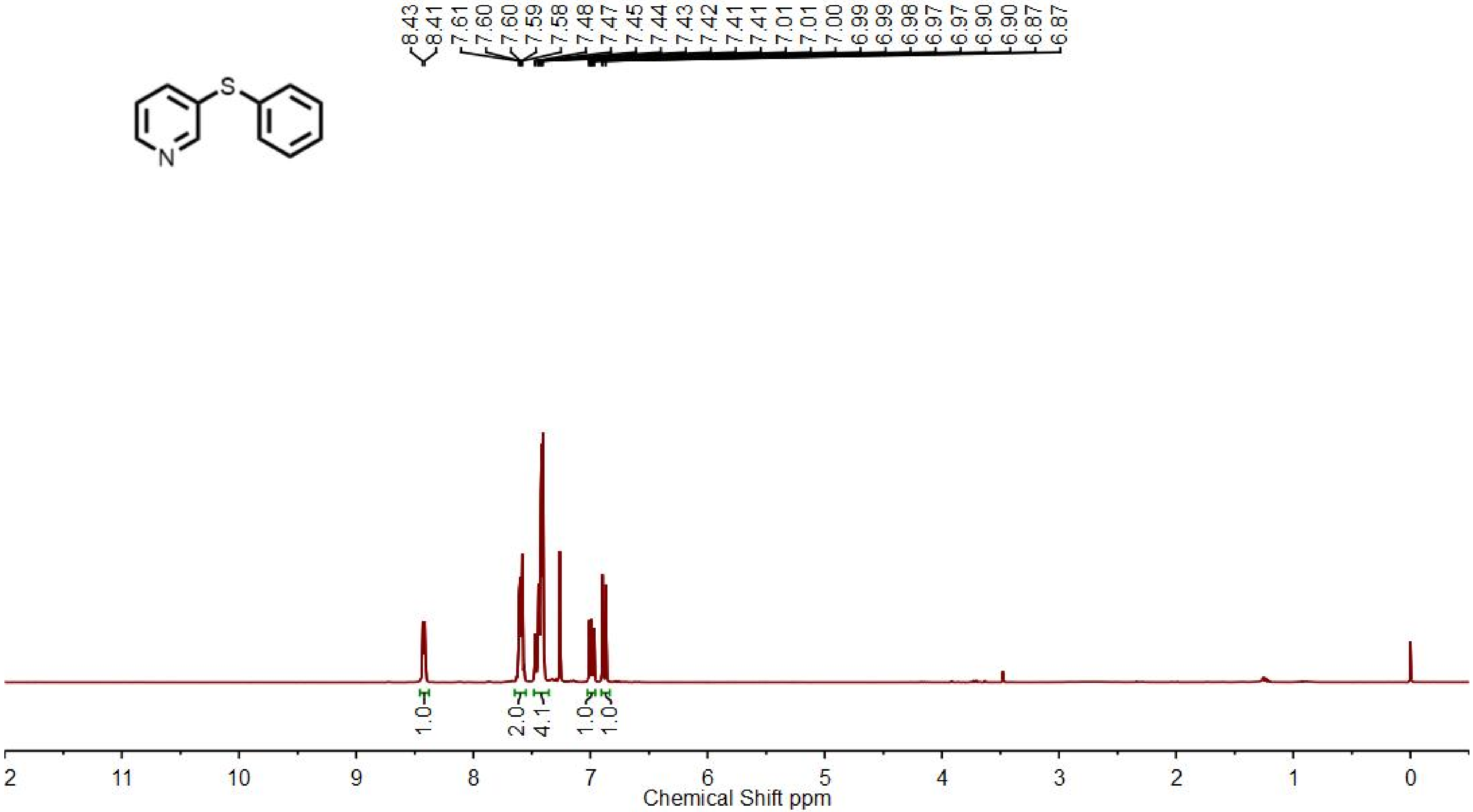




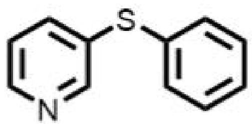
3r, $CDCl_3$, ^{13}C NMR 75 MHz

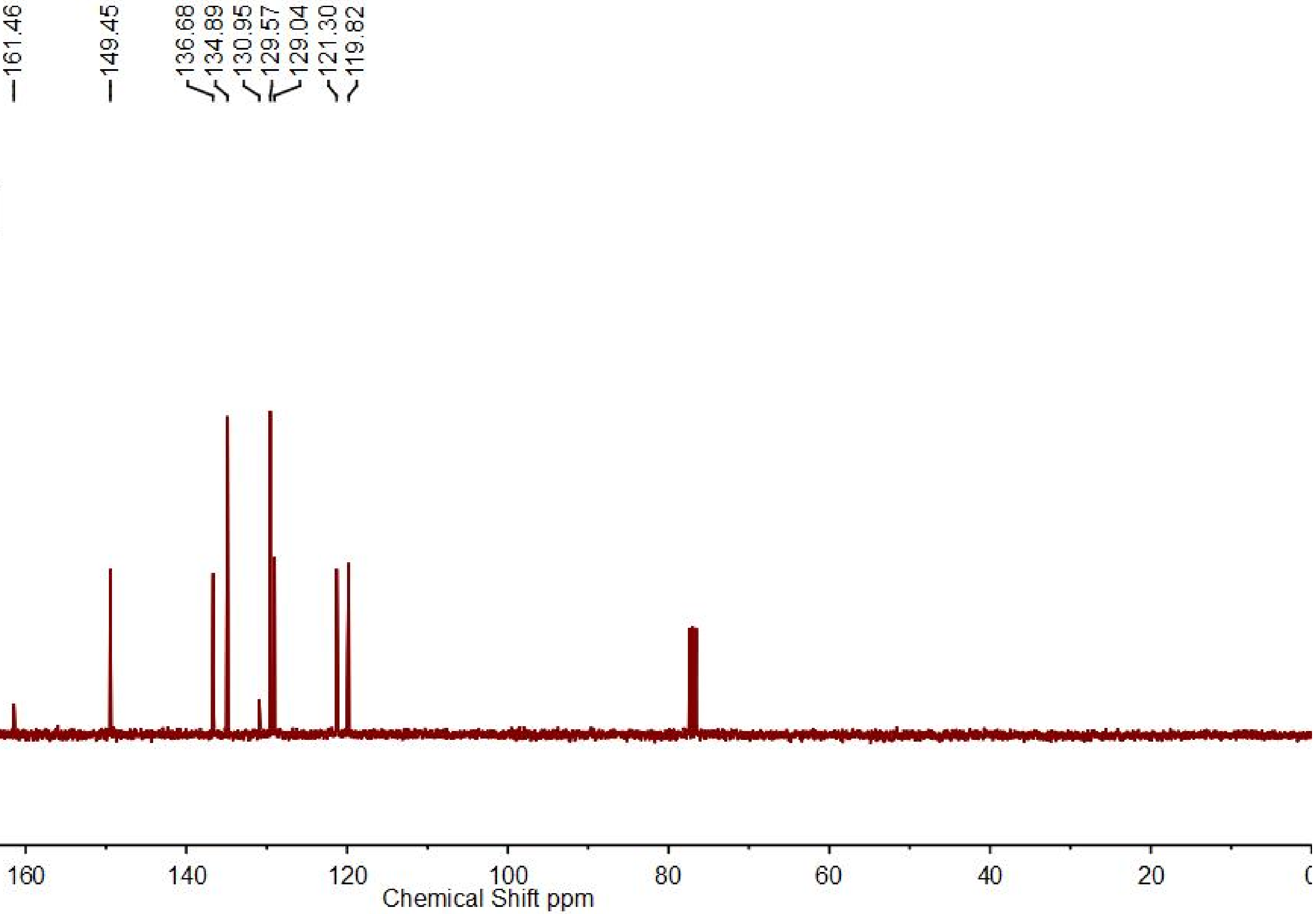


3s, $CDCl_3$, ^1H NMR 300 MHz

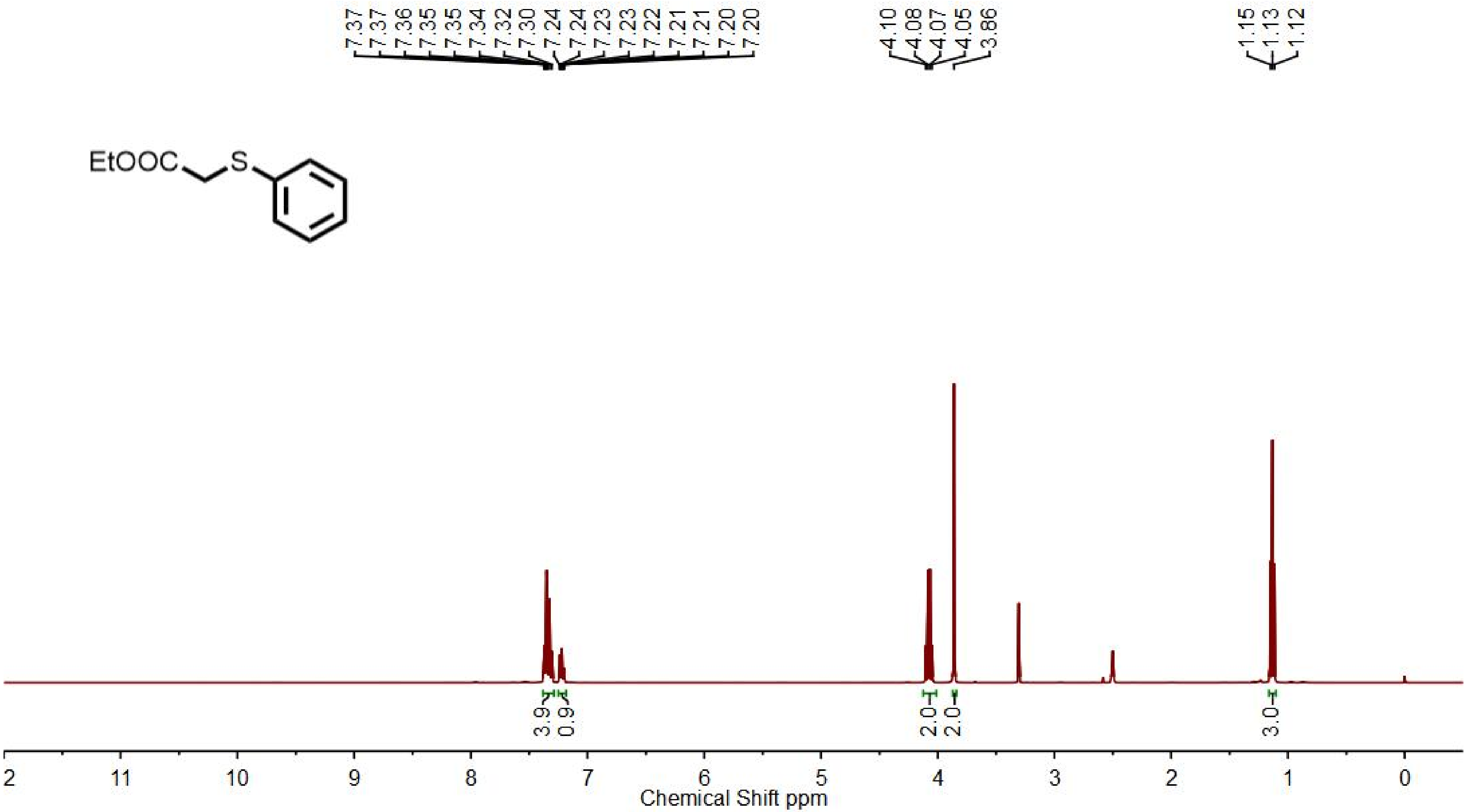


3s, $CDCl_3$, ^{13}C NMR 75 MHz

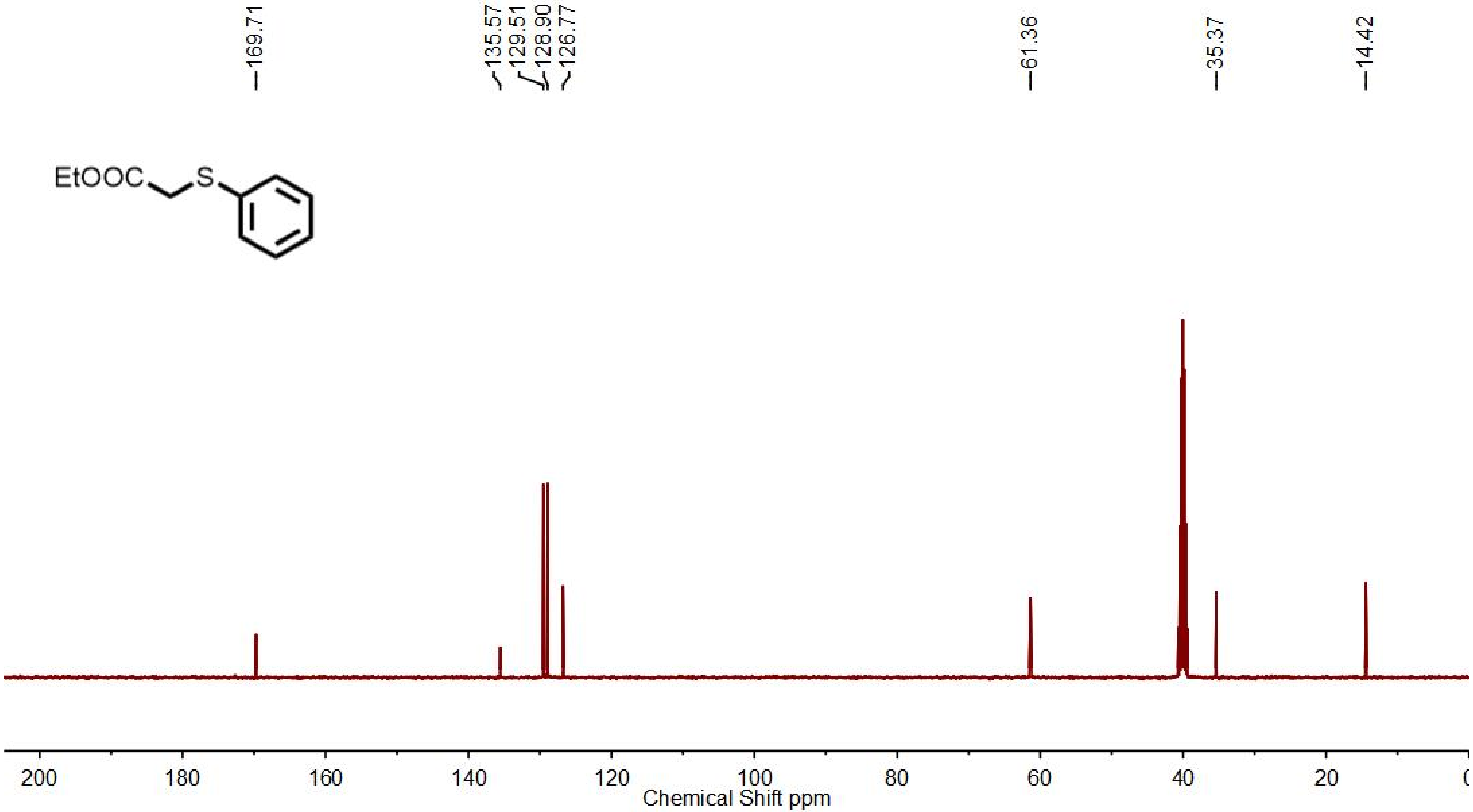




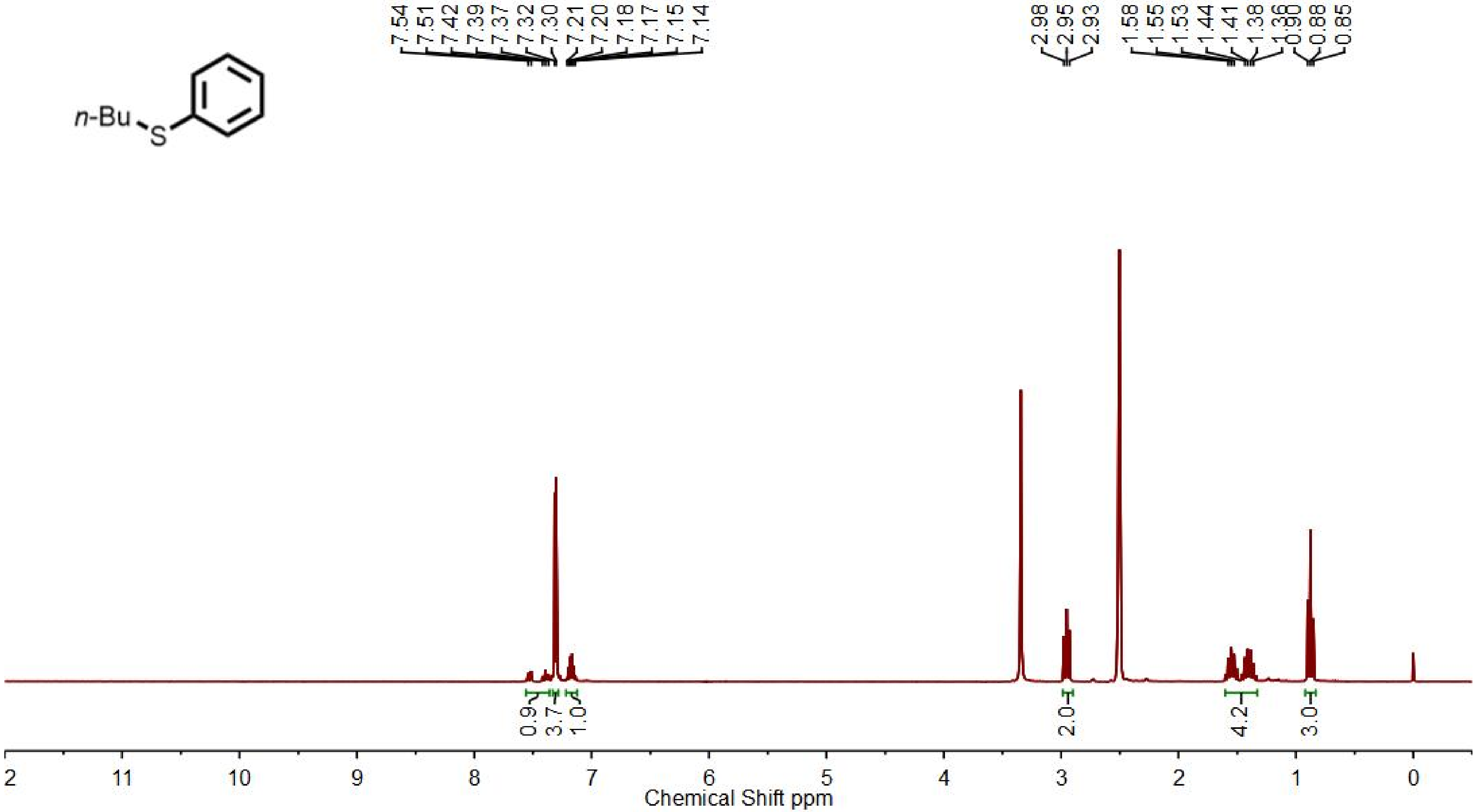
3t, DMSO-d_6, ^{1}H NMR 400 MHz



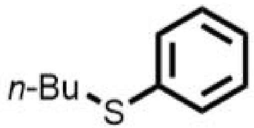
3t, DMSO-d_6, ^{13}C NMR 101 MHz

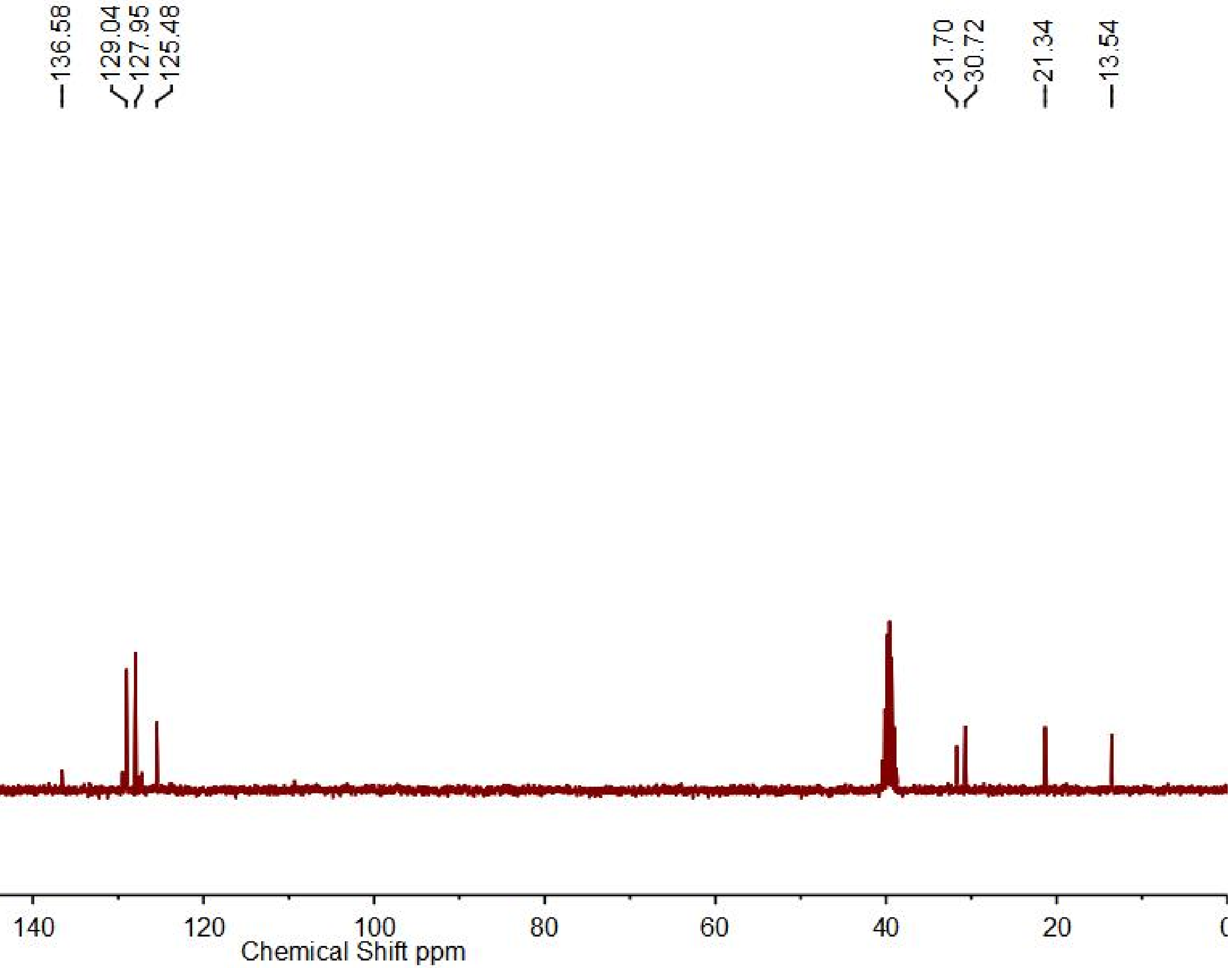


3u, DMSO-d_6, ^1H NMR 300 MHz

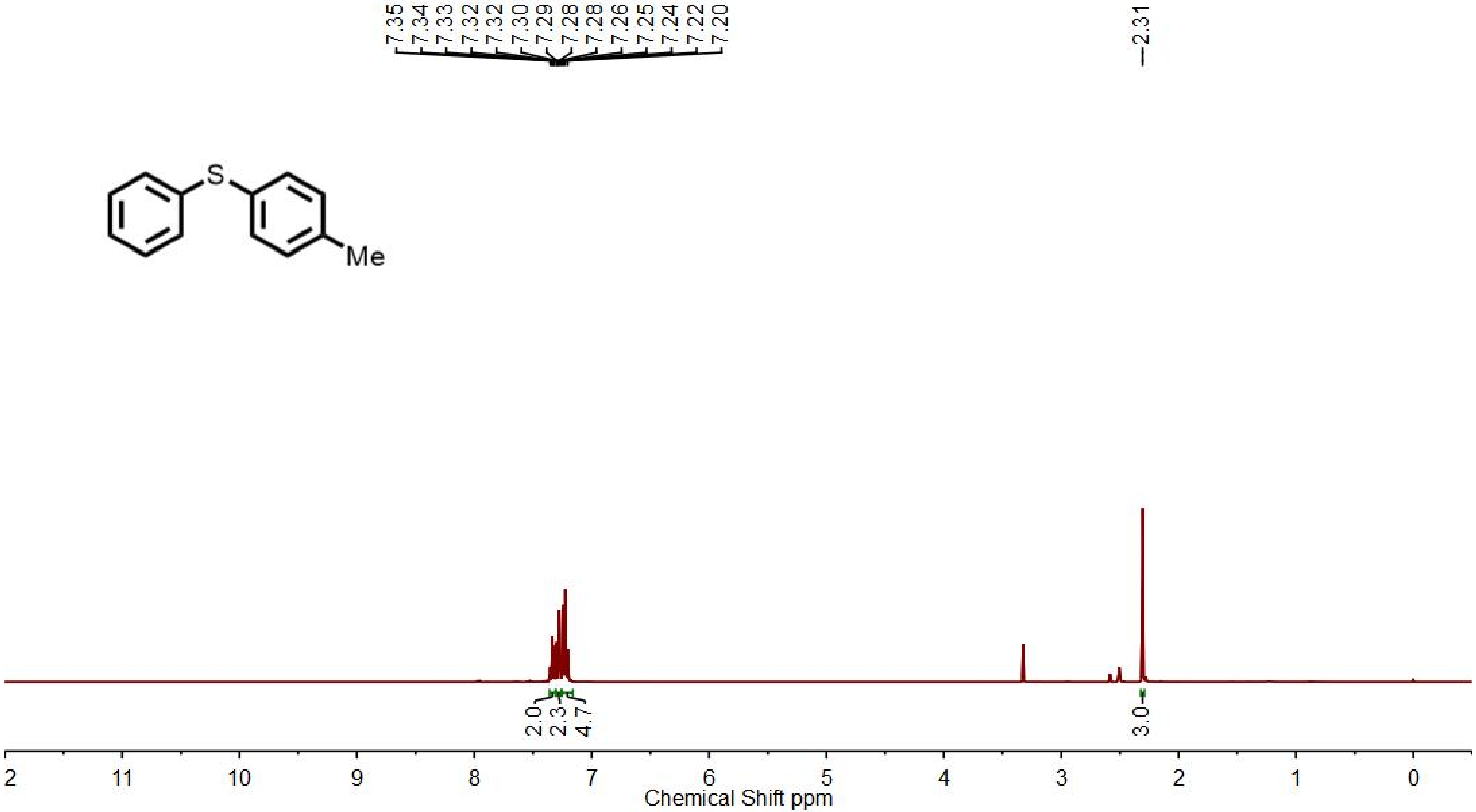


3u, DMSO-d_6, ^{13}C NMR 75 MHz

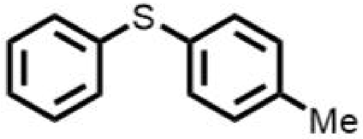


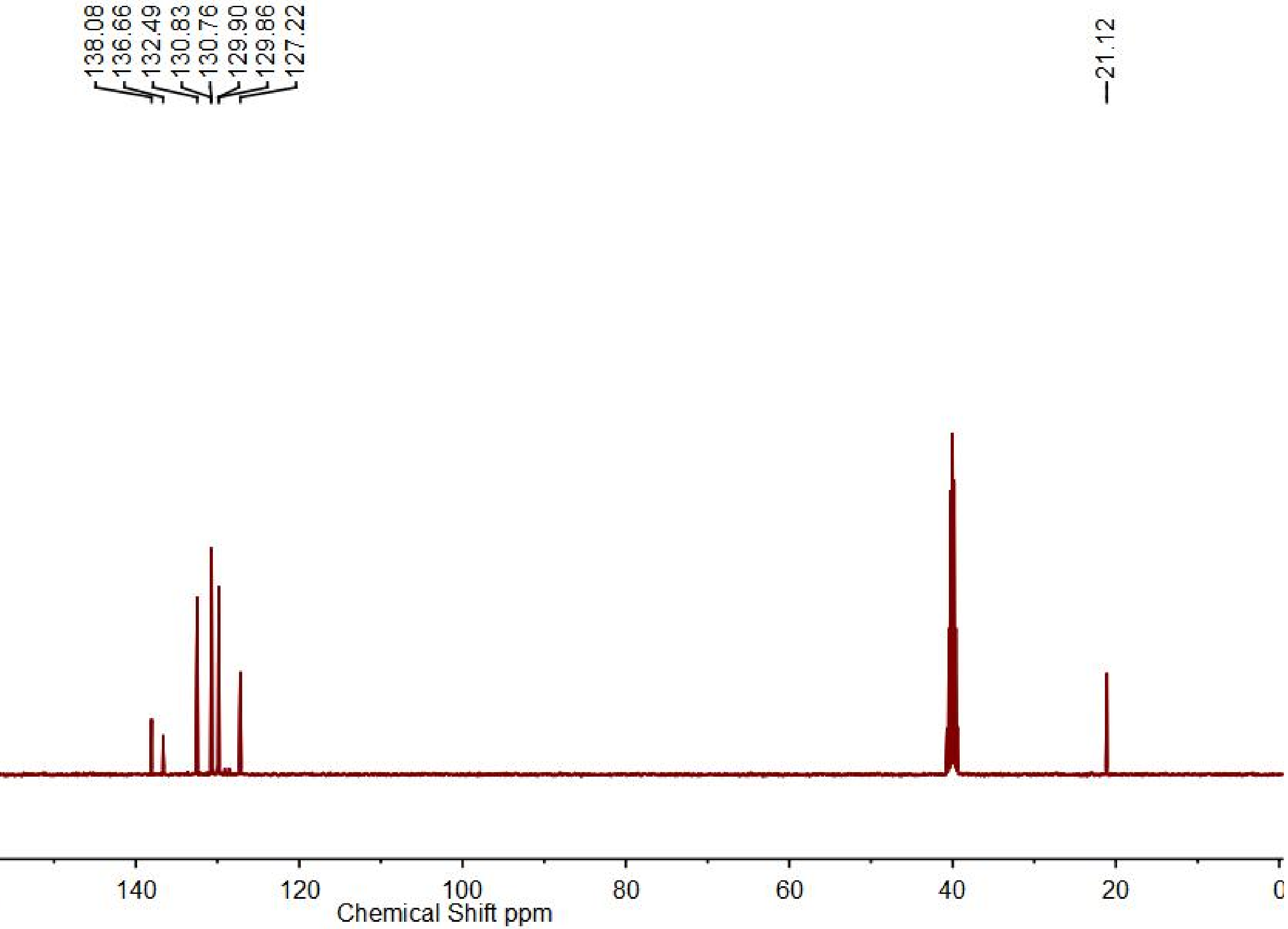


4b, DMSO-d_6, ^{1}H NMR 400 MHz

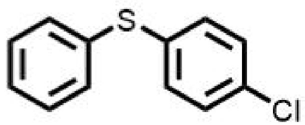


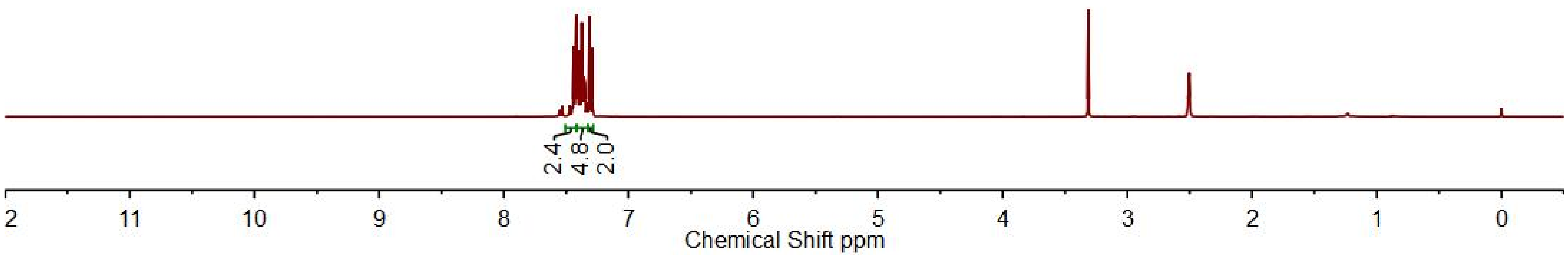
4b, DMSO-d_6, ^{13}C NMR 101 MHz



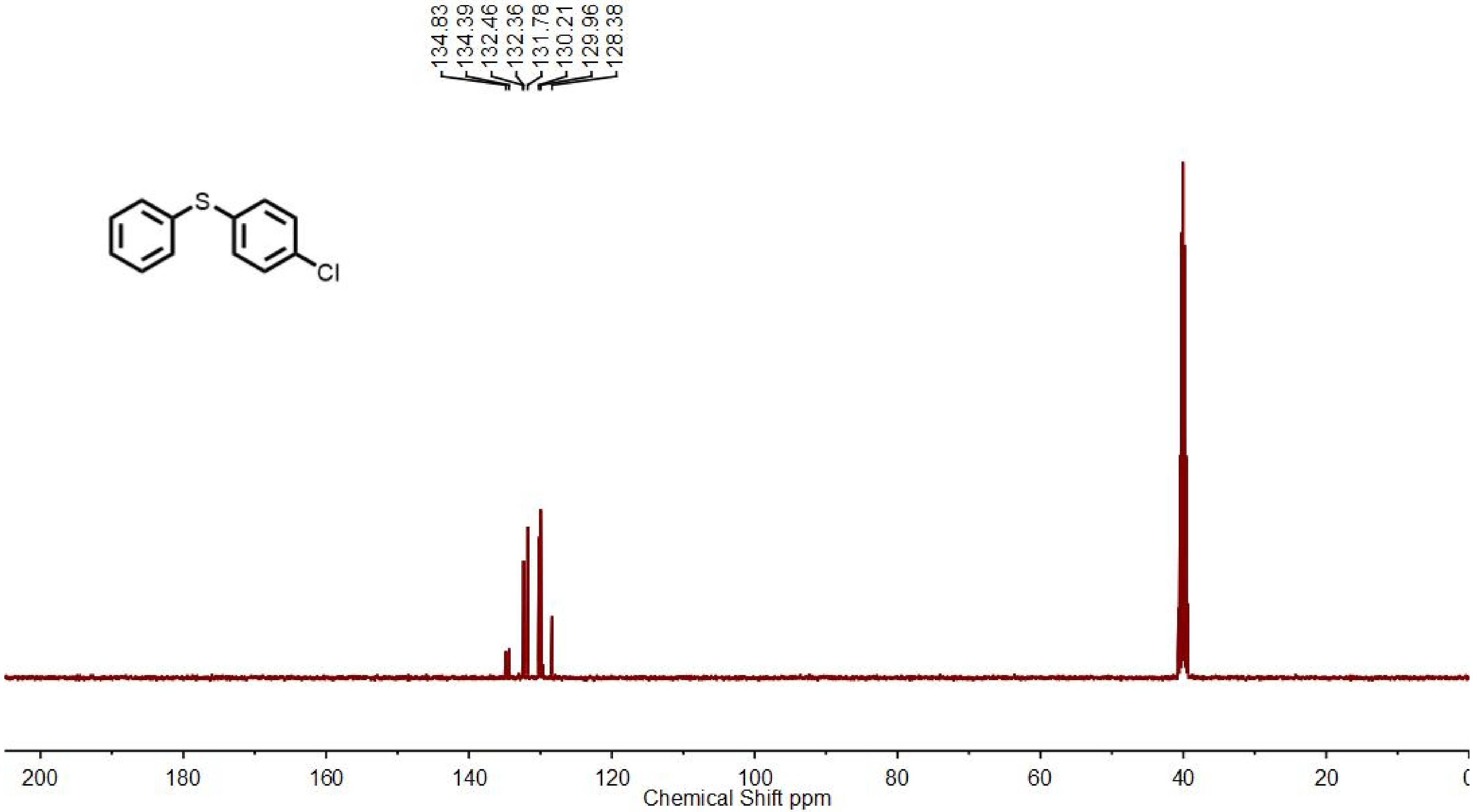


4c, DMSO-d_6, ^{1}H NMR 400 MHz

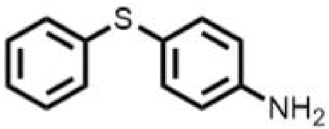


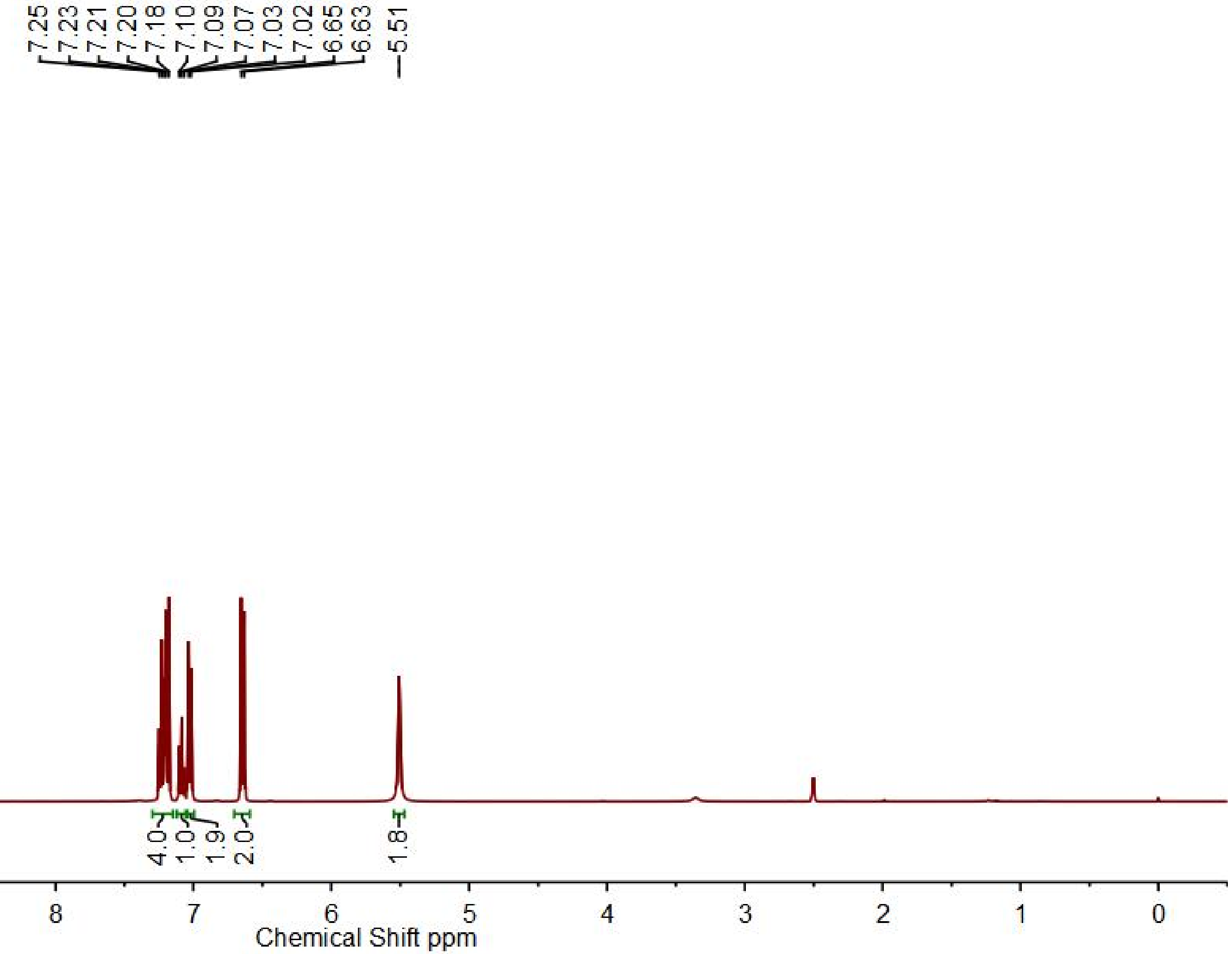


4c, DMSO-d_6, ^{13}C NMR 101 MHz

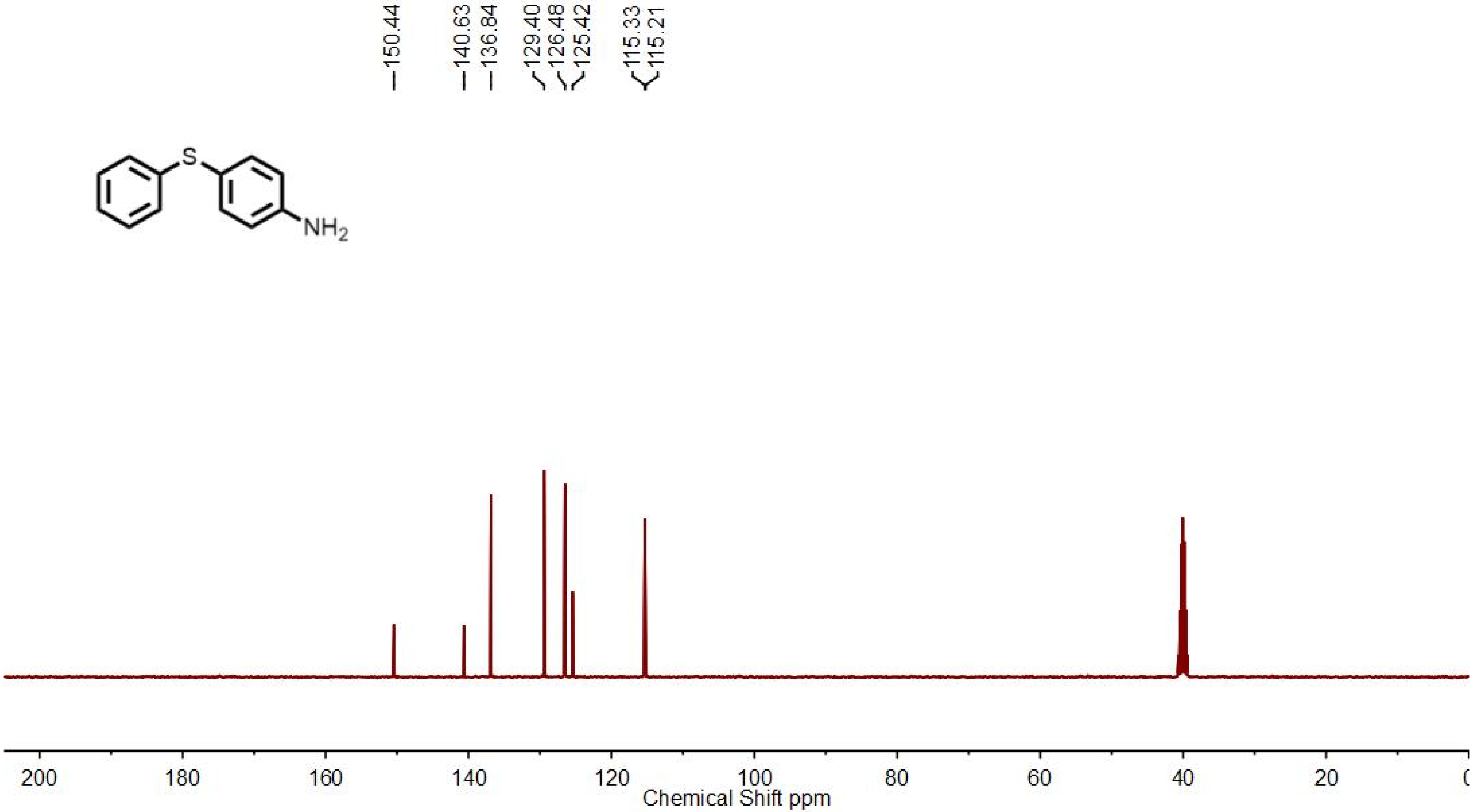


4d DMSO-d_6, ^{1}H NMR 400 MHz

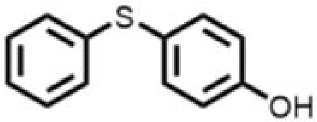


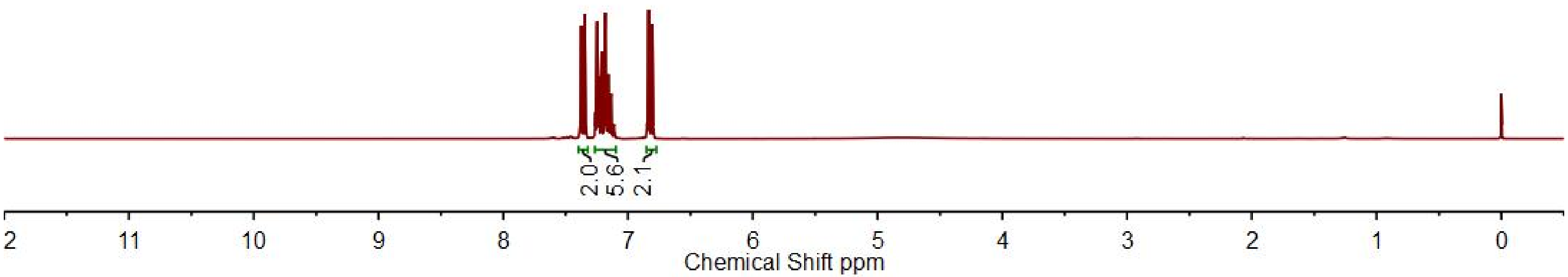


4d, DMSO-d_6, ^{13}C NMR 101 MHz

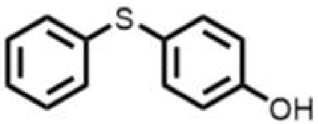


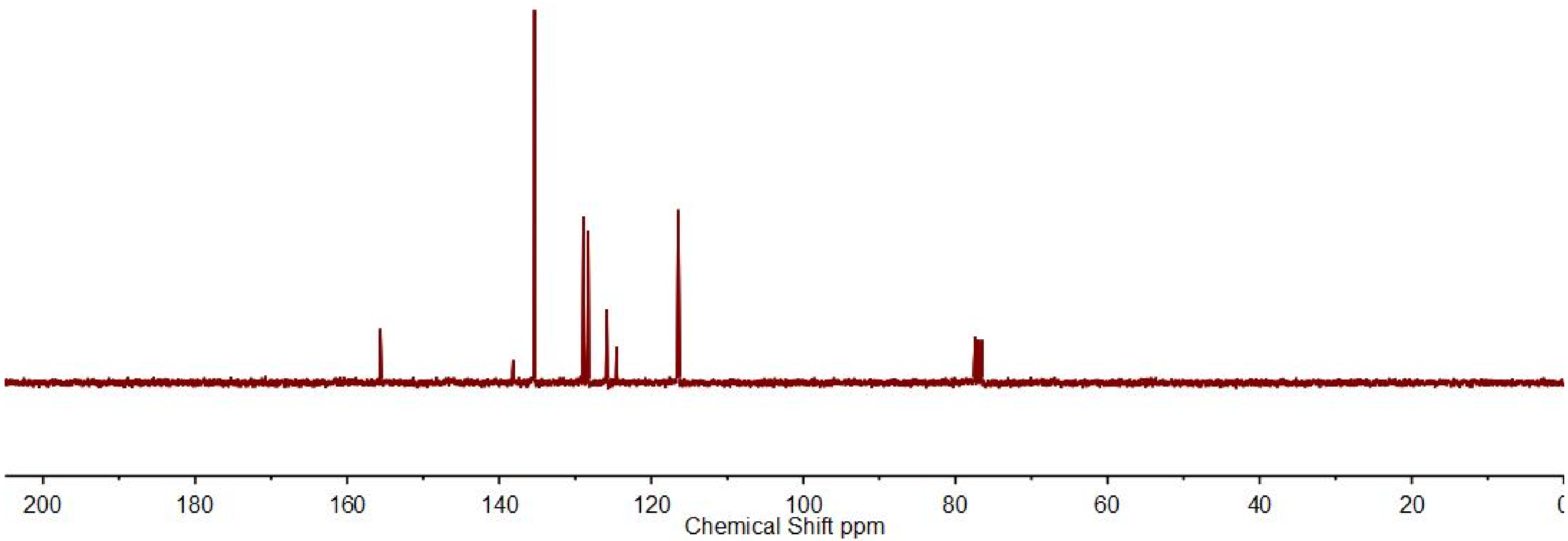
4e, $CDCl_3$, ^1H NMR 300 MHz



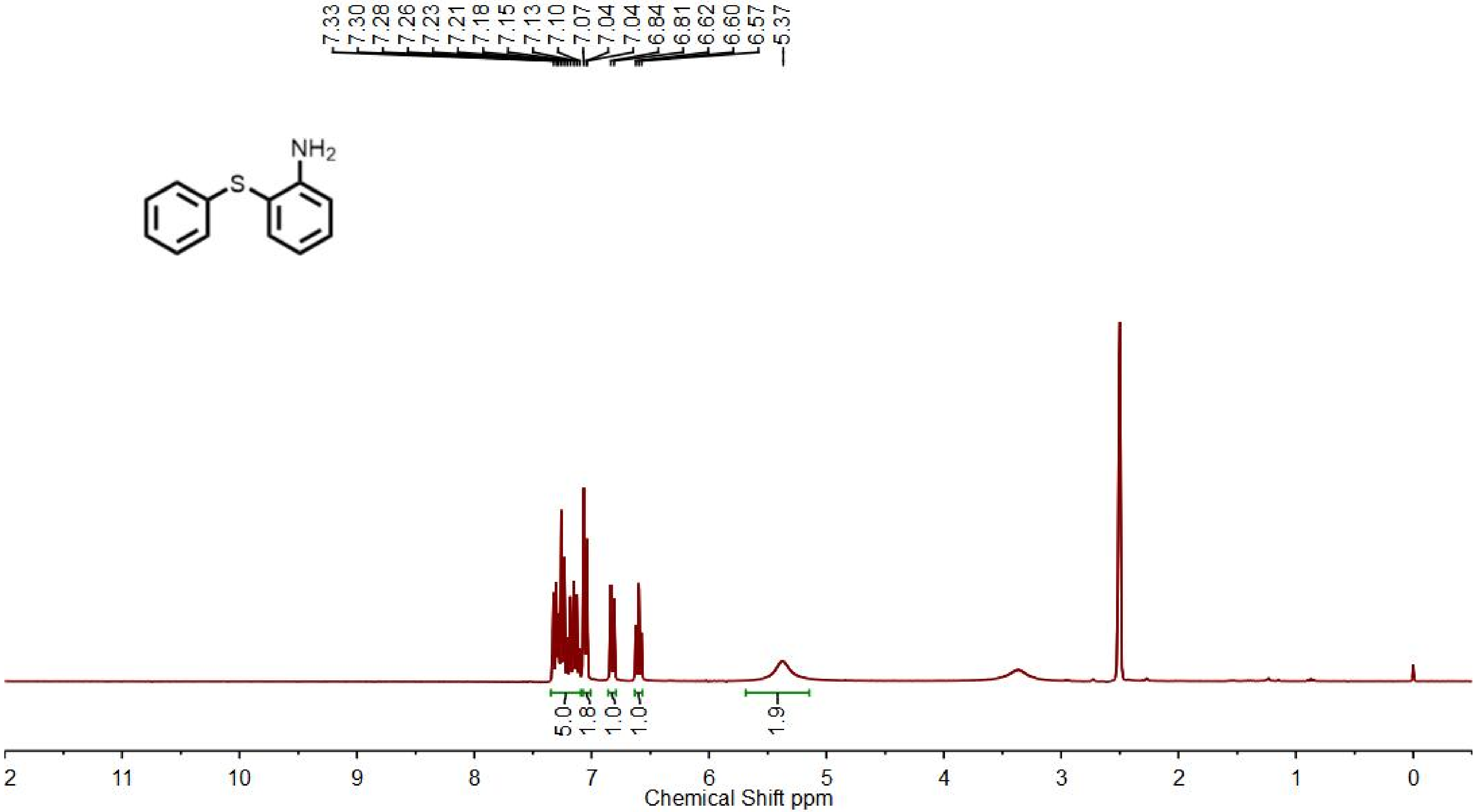


4e, $CDCl_3$, ^{13}C NMR 75 MHz

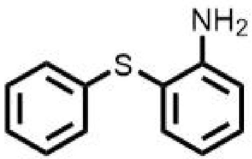


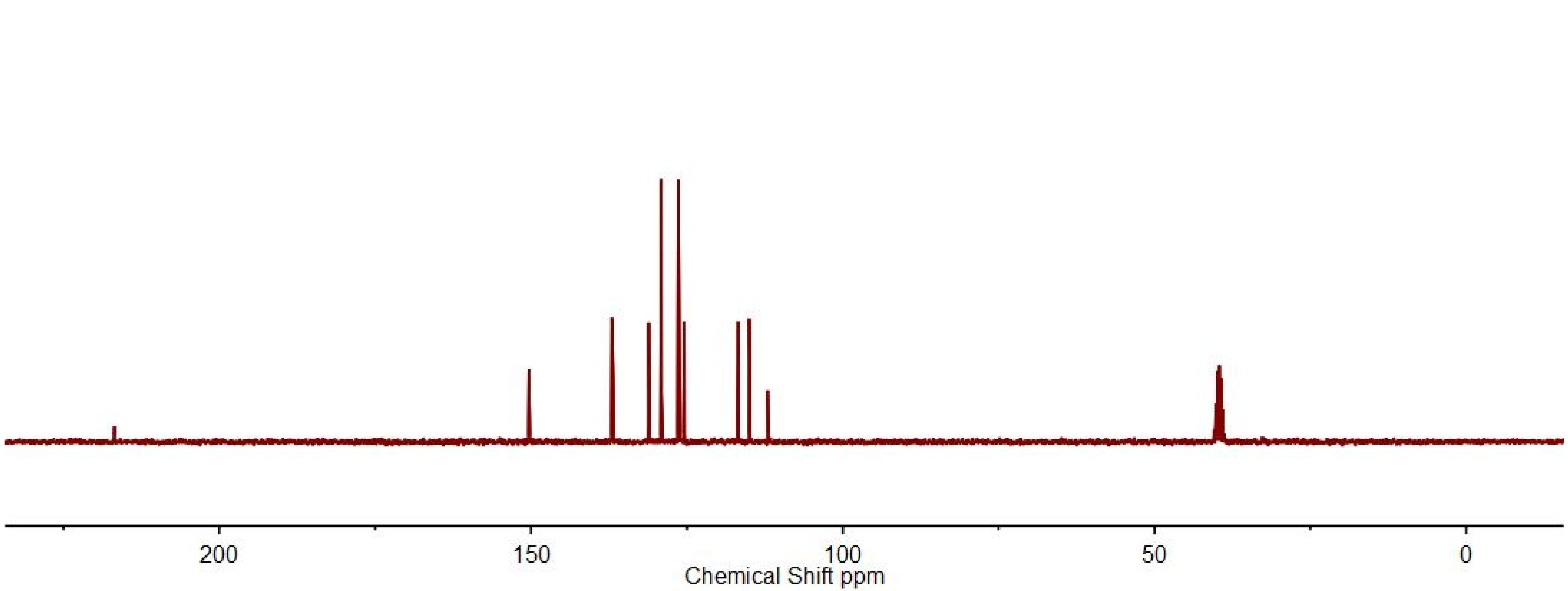


4f, DMSO-d_6, ^{1}H NMR 300 MHz

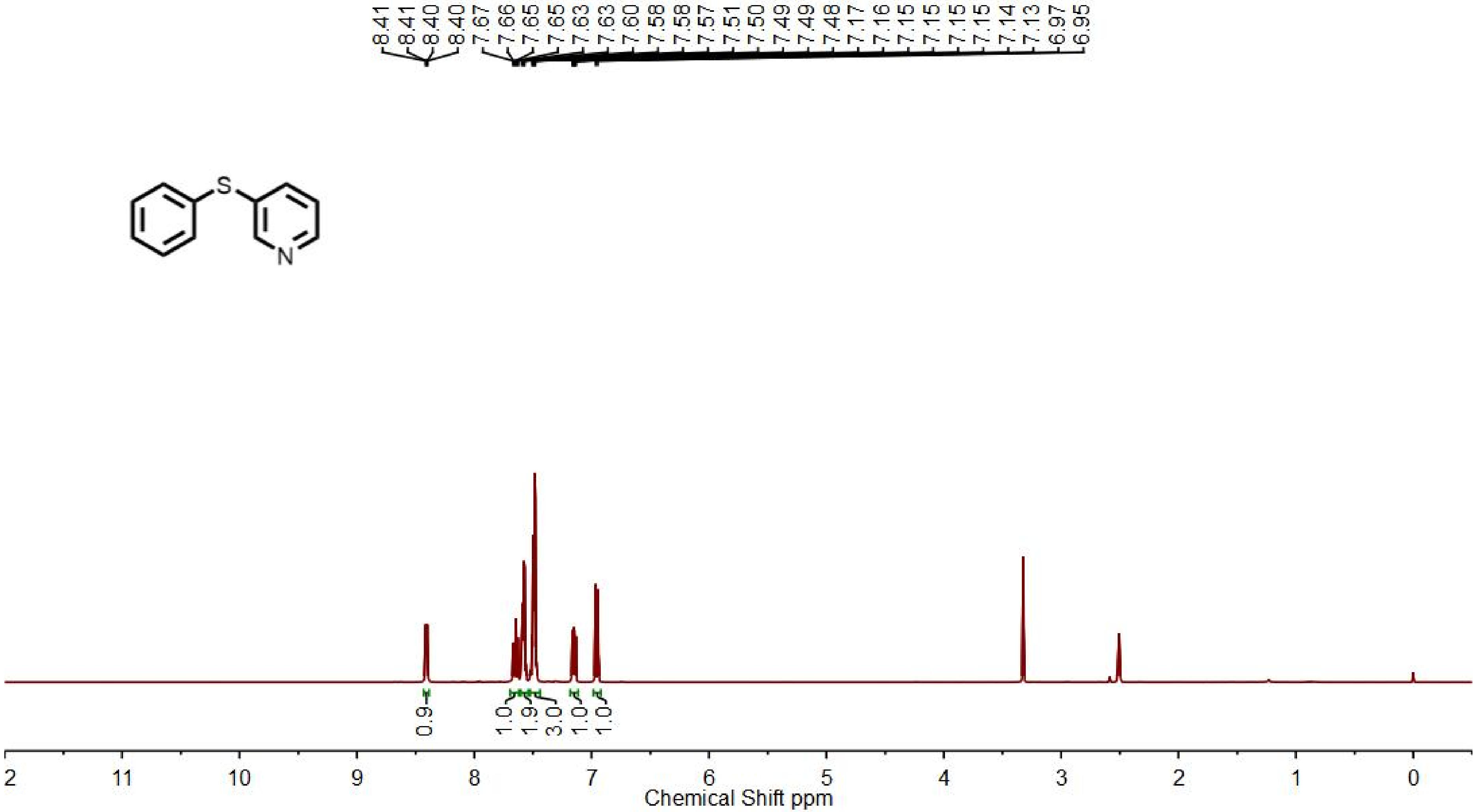


4f, DMSO-d_6, ^{13}C NMR 75 MHz

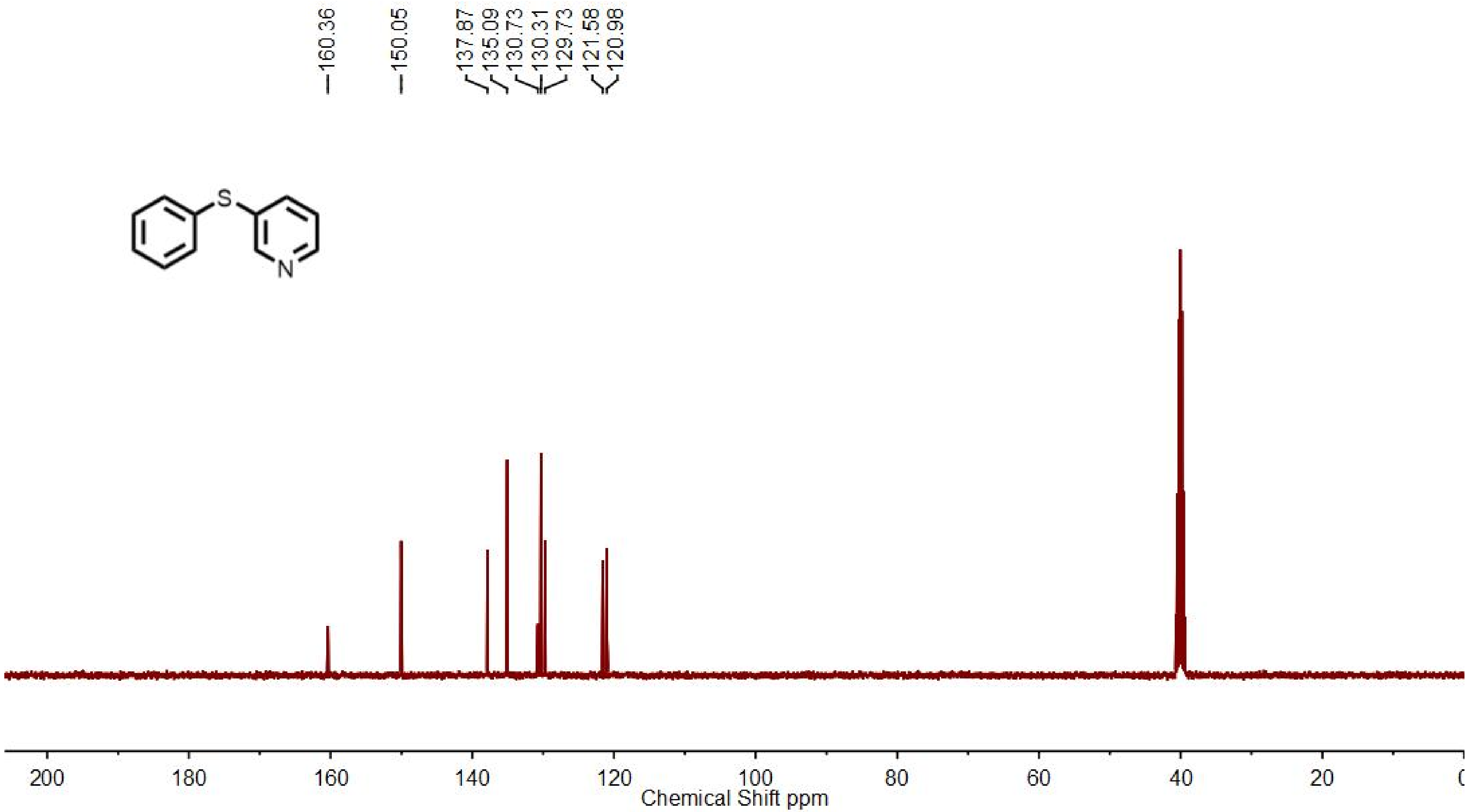




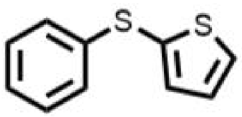
4g, DMSO-d_6, ^1H NMR 400 MHz

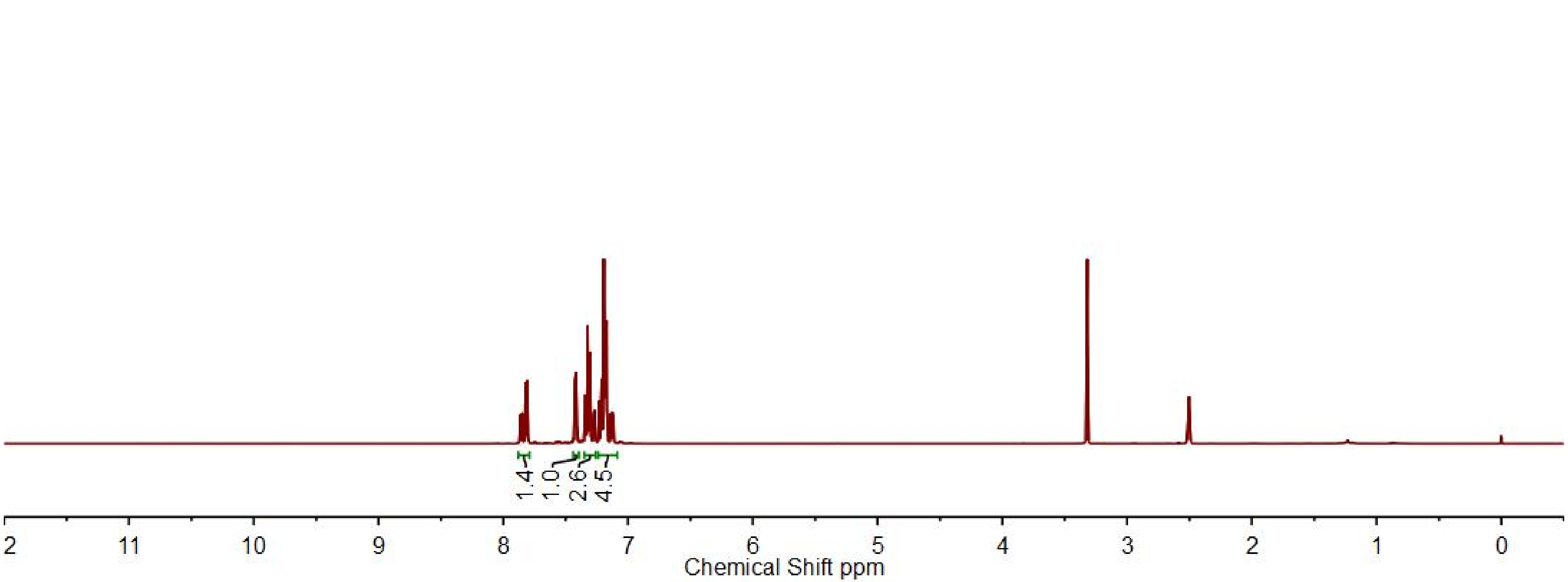


4g, DMSO-d_6, ^{13}C NMR 101 MHz

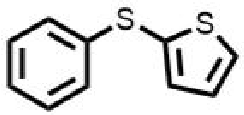


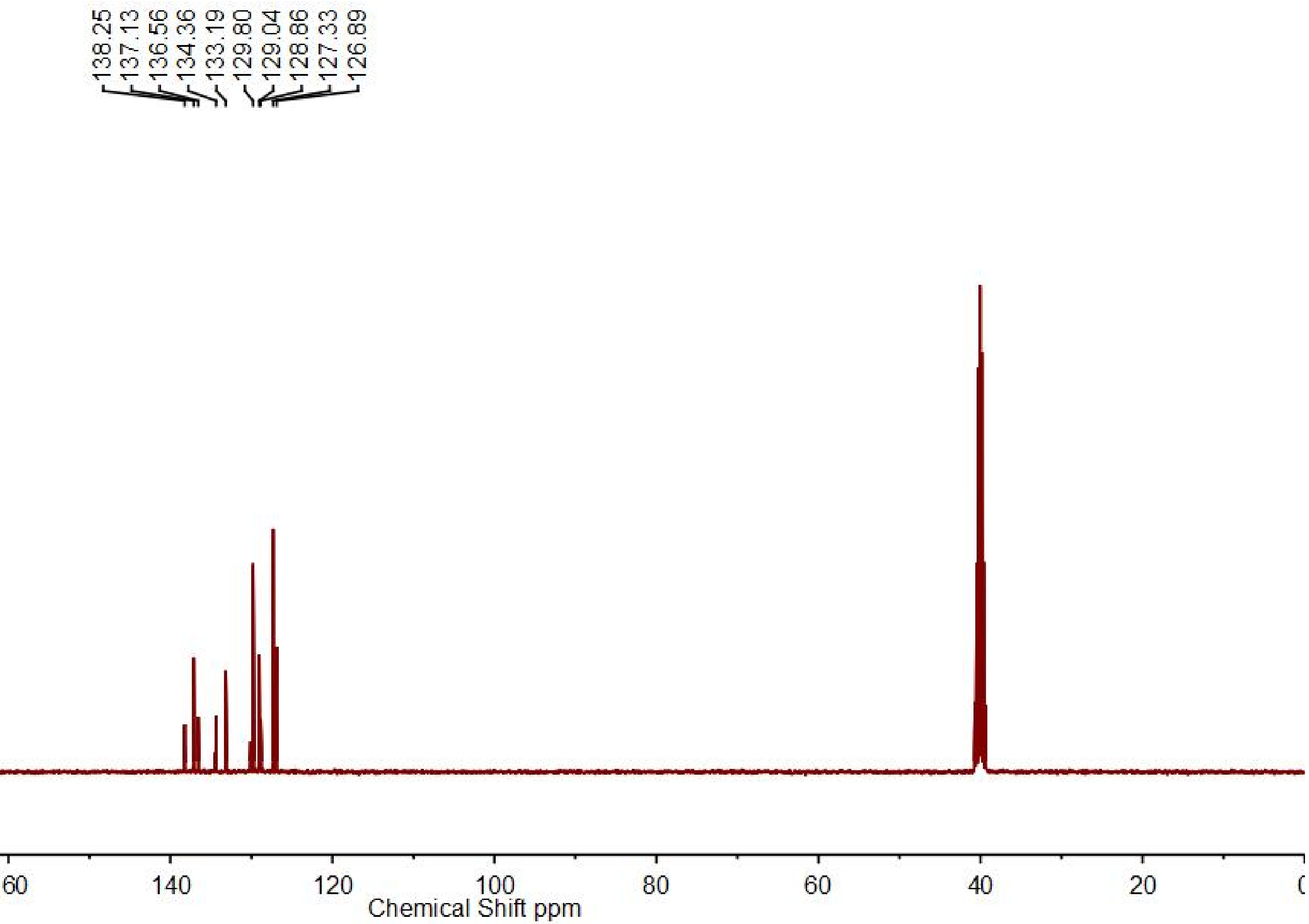
4h, DMSO-d_6, ^{1}H NMR 400 MHz



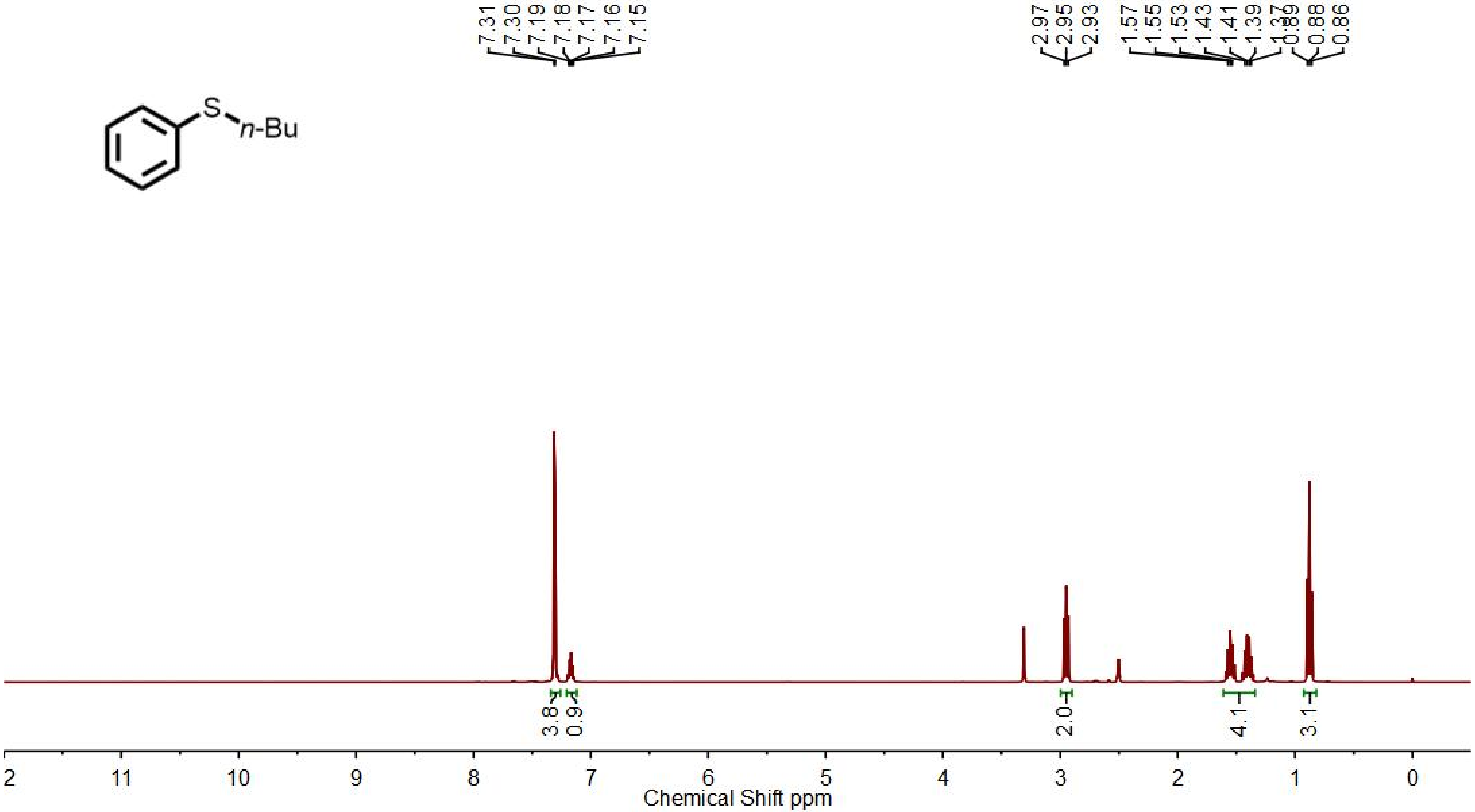


4h, DMSO-d_6, ^{13}C NMR 101 MHz

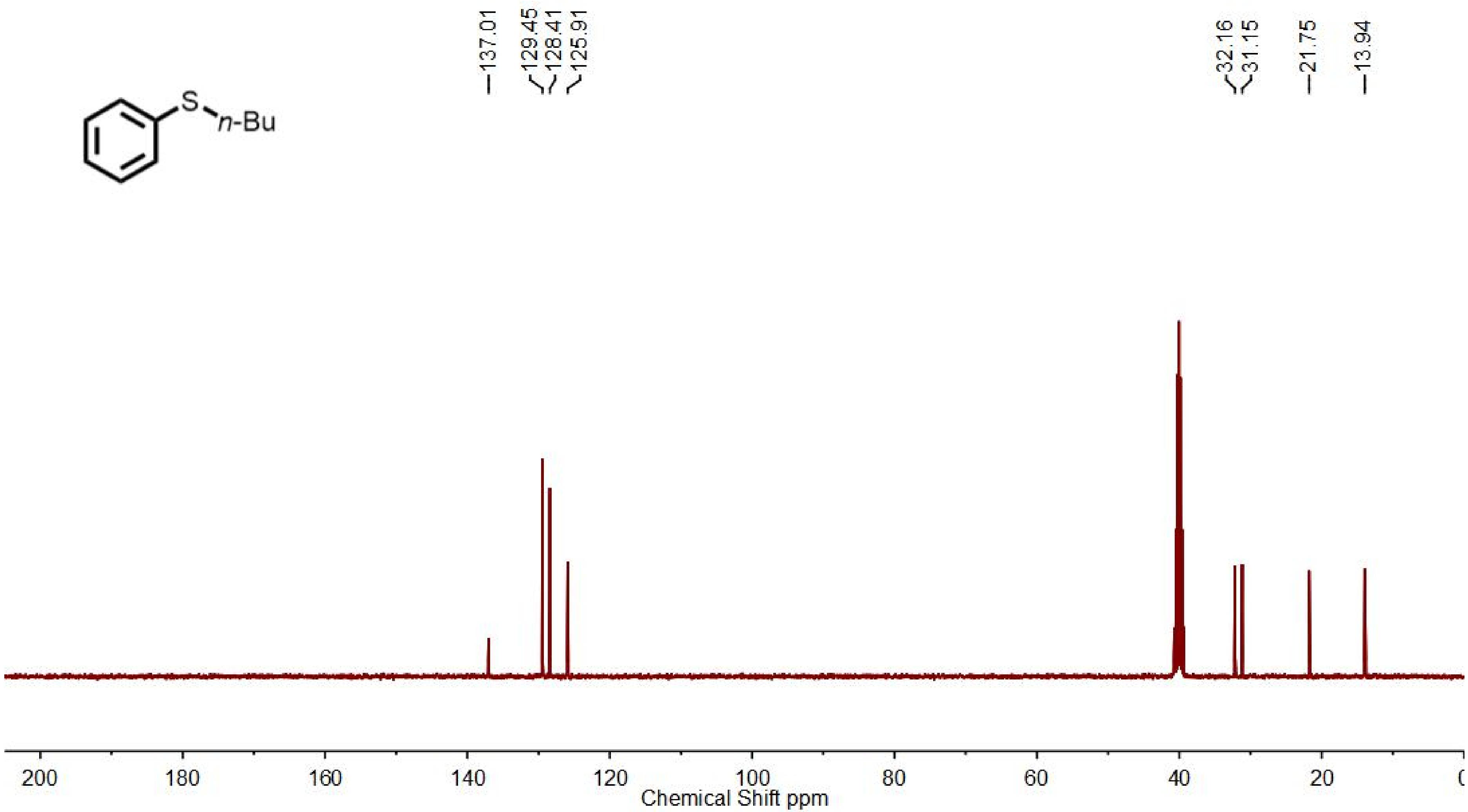




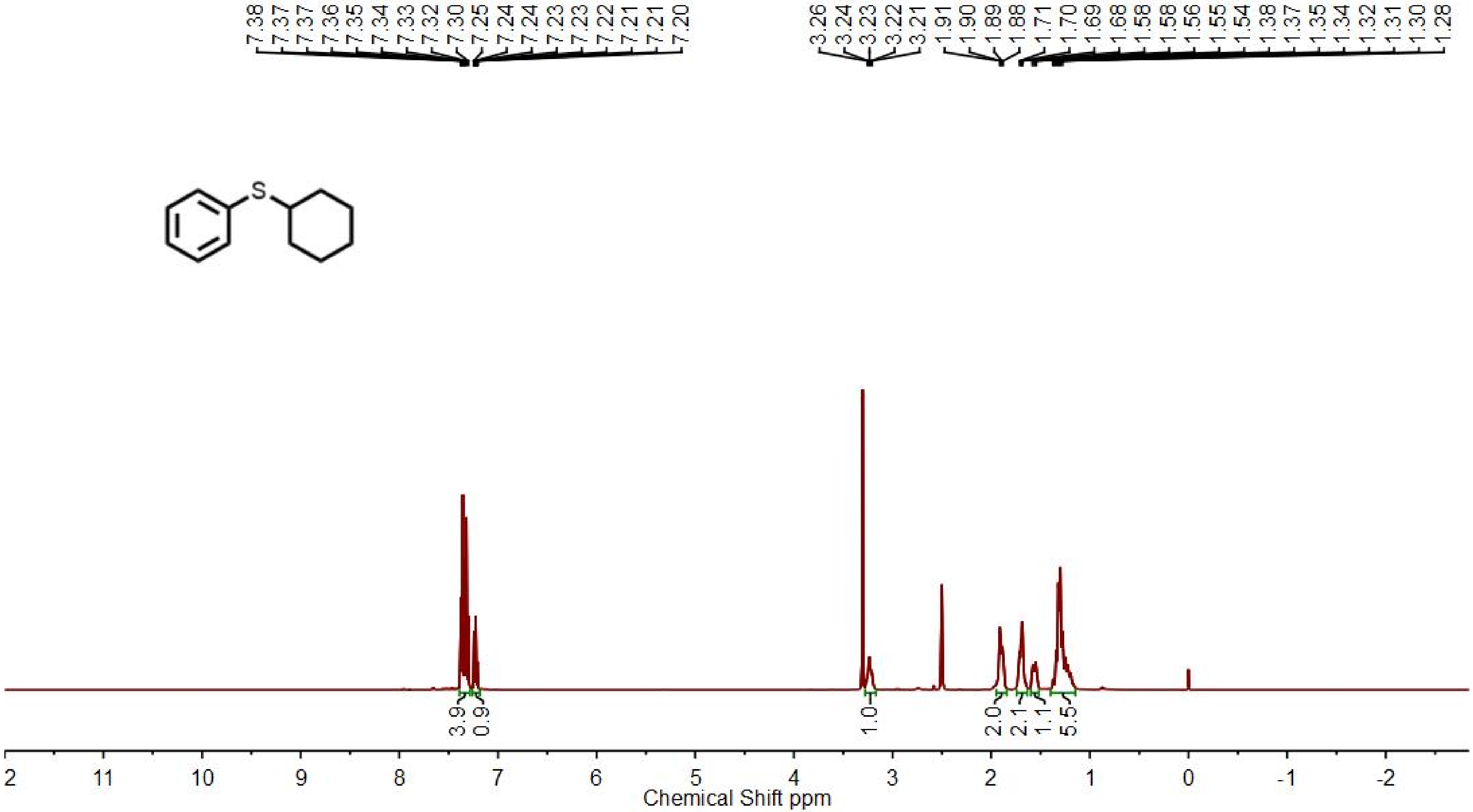
4i, DMSO-d_6, ^{1}H NMR 400 MHz



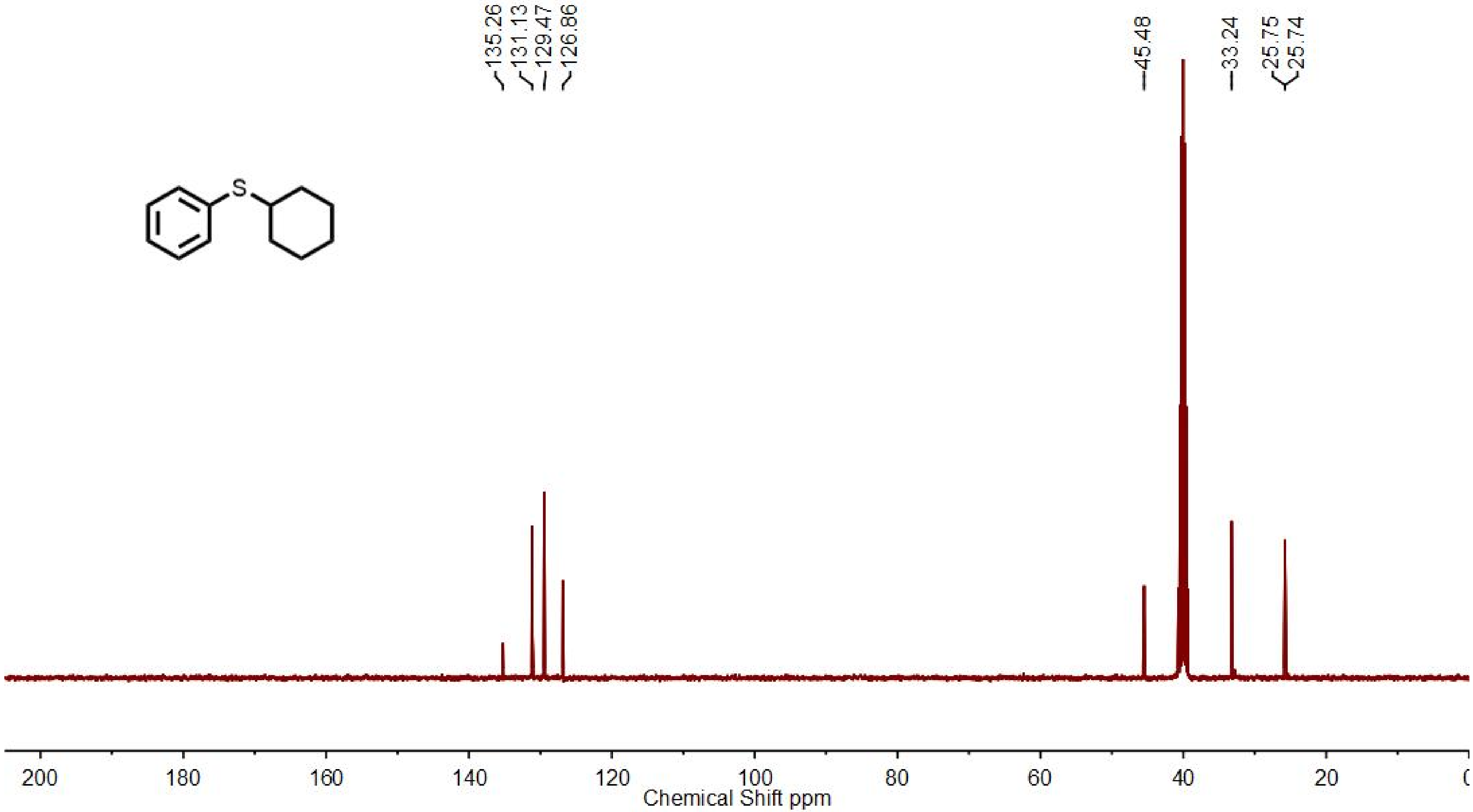
4i, DMSO-d_6, ^{13}C NMR 101 MHz



4j, DMSO-d_6, ^{1}H NMR 400 MHz

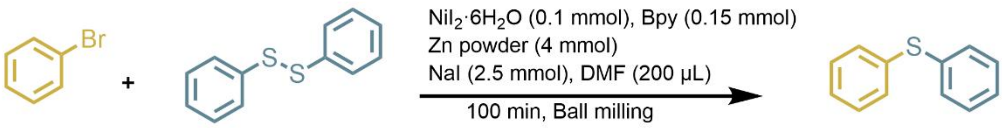


4j, DMSO-d_6, ^{13}C NMR 101 MHz



6. Green metrics for the C-S bond cross-coupling

Table S2 Calculation of green metrics for the mechanochemical to synthesize diphenyl sulfide **(3a)**



Yield of desired product (3a) = 86%

$$\text{Reaction mass efficiency (RME)} = \frac{\text{mass of product}}{\text{mass of stoichiometric reactants}} \times 100 = \frac{0.160}{0.1092 + 0.2355} \times 100 = 46\%$$

$$\text{Carbon efficiency (CE)} = \frac{\text{amount of carbon in product}}{\text{total carbon present in reactants}} \times 100 = \frac{12 \times 2}{12 + (3 \times 6)} \times 100 = 80\%$$

Reactant 1:	diphenyl disulfide	0.1092	1 mmol	FW 218.34
Reactant 2:	bromobenzene	0.2355	1.5 mmol	FW 157.01
Catalyst:	$NiI_2 \cdot 6H_2O$	0.0237	0.1 mmol	FW 237.69
Catalyst:	2,2'-Dipyridyl	0.0234	0.15 mmol	FW 156.19
Catalyst:	Zinc Powder	0.2615	4 mmol	FW 65.38
Additive:	NaI	0.3747	2.5 mmol	FW 149.89
Solvent:	N,N-Dimethylformamide	0.1896	2.5 mmol	FW 73.09
Product:	diphenylsulfane	0.160	0.86 mmol	FW 186.05

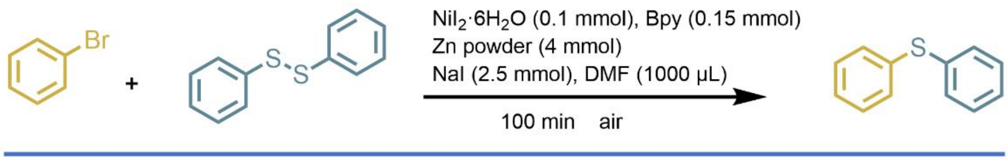
$$\text{E-factor} = \frac{\text{total waste}}{\text{total product}} = \frac{(0.1092 + 0.2355 + 0.0237 + 0.0234 + 0.2615 + 0.3747 + 0.1896) - 0.160}{0.160} = 6.61$$

Table S3 Calculation of EcoScale score for the mechanochemical to synthesize diphenyl sulfide **(3a)**

EcoScale points	Factor	Penalty
1 Yield	86%	7
2 Price (to obtain 10 mmol of end product)	diphenyl sulfide = 1.28 g = CNY 2.36 bromobenzene = 2.77 g = CNY 0.803 $NiI_2 \cdot 6H_2O$ = 0.29 g = CNY 0.11 2,2'-Dipyridyl = 0.276 g = CNY 0.243 Zinc Powder = 3.08 g = CNY 0.055 NaI = 4.407g = CNY 6.699 DMF = 2.94 ml = CNY 0.185 CNY 10.46 ＜10$	0
3 Safety	diphenyl disulfide (N) $NiI_2 \cdot 6H_2O$ (N) 2,2'-Dipyridyl (T) Zinc Powder (F) NaI (N) DMF (T)	5 5 5 5 5 5
4 Technical setup	common setup	0
5 Temperature/time	room temperature, 100 min	1
6 Workup and purification	classic chromatography	10
Penalty points total		48

EcoScale = 100 – 48 = 52

Table S4 Calculation of green metrics for the solution methods for the synthesis of diphenyl sulfide **(3a)** in air from phenyl disulfide and bromobenzene



Yield of desired product (3a) = 21%

$$\text{Reaction mass efficiency (RME)} = \frac{\text{mass of product}}{\text{mass of stoichiometric reactants}} \times 100 = \frac{0.0391}{0.1092 + 0.2355} \times 100 = 11\%$$

$$\text{Carbon efficiency (CE)} = \frac{\text{amount of carbon in product}}{\text{total carbon present in reactants}} \times 100 = \frac{12\times2}{12 + (3 \times 6)} \times 100 = 80\%$$

Reactant 1:	diphenyl disulfide	0.1092	0.5 mmol	FW 218.34
Reactant 2:	bromobenzene	0.2355	1.5 mmol	FW 157.01
Catalyst:	$NiI_2 \cdot 6H_2O$	0.0237	0.1 mmol	FW 237.69
Catalyst:	2,2'-Dipyridyl	0.0234	0.15 mmol	FW 156.19
Catalyst:	Zinc Powder	0.2615	4 mmol	FW 65.38
Additive:	NaI	0.3747	2.5 mmol	FW 149.89
Solvent:	N,N-Dimethylformamide	0.944	12.9 mmol	FW 73.09
Product:	diphenylsulfane	0.0391	0.21 mmol	FW 186.05

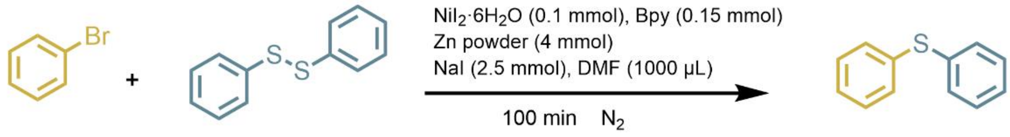
$$\text{E-factor} = \frac{\text{total waste}}{\text{total product}} = \frac{(0.1092 + 0.2355 + 0.0237 + 0.0234 + 0.2615 + 0.3747 + 0.944) - 0.0391}{0.0391} = 49.4$$

Table S5 Calculation of EcoScale score for the solution methods for the synthesis of diphenyl sulfide **(3a)** in air from phenyl disulfide and bromobenzene

EcoScale points	Factor	Penalty
1 Yield	21%	39.5
2 Price (to obtain 10 mmol of end product)	diphenyl sulfide = 1.28 g = CNY 2.36 bromobenzene = 2.77 g = CNY 0.803 $NiI_2 \cdot 6H_2O$ = 0.29 g = CNY 0.11 2,2'-Dipyridyl = 0.276 g = CNY 0.243 Zinc Powder = 3.08 g = CNY 0.055 NaI = 4.407g = CNY 6.699 DMF = 166.50 ml = CNY 10.47 CNY 20.74 ＜10$	0
3 Safety	diphenyl disulfide (N) $NiI_2 \cdot 6H_2O$ (N) 2,2'-Dipyridyl (T) Zinc Powder (F) NaI (N) DMF (T)	5 5 5 5 5 5
4 Technical setup	common setup	0
5 Temperature/time	room temperature, 100 min	1
6 Workup and purification	classic chromatography	10
Penalty points total		80.5

EcoScale = 100 – 80.5 = 19.5 (< 50; so, it is an inacceptable synthesis)

Table S6 Calculation of green metrics for the solution methods for the synthesis of diphenyl sulfide **(3a)** in N_2 from phenyl disulfide and bromobenzene



Yield of desired product (3a) = 13%

$$\text{Reaction mass efficiency (RME)} = \frac{\text{mass of product}}{\text{mass of stoichiometric reactants}} \times 100 = \frac{0.0242}{0.1092 + 0.2355} \times 100 = 7\%$$

$$\text{Carbon efficiency (CE)} = \frac{\text{amount of carbon in product}}{\text{total carbon present in reactants}} \times 100 = \frac{12\times 2}{12 + (3 \times 6)} \times 100 = 80\%$$

Reactant 1:	diphenyl disulfide	0.1092	0.5 mmol	FW 218.34
Reactant 2:	bromobenzene	0.2355	1.5 mmol	FW 157.01
Catalyst:	$NiI_2·6H_2O$	0.0237	0.1 mmol	FW 237.69
Catalyst:	2,2'-Dipyridyl	0.0234	0.15 mmol	FW 156.19
Catalyst:	Zinc Powder	0.2615	4 mmol	FW 65.38
Additive:	NaI	0.3747	2.5 mmol	FW 149.89
Solvent:	N,N-Dimethylformamide	0.944	12.9 mmol	FW 73.09
Product:	diphenylsulfane	0.0242	0.13 mmol	FW 186.05

$$\text{E-factor} = \frac{\text{total waste}}{\text{total product}} = \frac{(0.1092 + 0.2355 + 0.0237 + 0.0234 + 0.2615 + 0.3747 + 0.944) - 0.0242}{0.0242} = 80.5$$

Table S7 Calculation of EcoScale score for the solution methods for the synthesis of diphenyl sulfide **(3a)** in N_2 from phenyl disulfide and bromobenzene

EcoScale points	Factor	Penalty
1 Yield	13%	43.5
2 Price (to obtain 10 mmol of end product)	diphenyl sulfide = 1.28 g = CNY 2.36 bromobenzene = 2.77 g = CNY 0.803 $NiI_2 \cdot 6H_2O$ = 0.29 g = CNY 0.11 2,2'-Dipyridyl = 0.276 g = CNY 0.243 Zinc Powder = 3.08 g = CNY 0.055 NaI = 4.407g = CNY 6.699 DMF = 166.50 ml = CNY 10.47 CNY 20.74 ＜10$	0
3 Safety	diphenyl disulfide (N)	5
	$NiI_2 \cdot 6H_2O$ (N)	5
	2,2'-Dipyridyl (T)	5
	Zinc Powder (F)	5
	NaI (N)	5
	DMF (T)	5
4 Technical setup	common setup	0
5 Temperature/time	room temperature, 100 min	1
6 Workup and purification	classic chromatography	10
Penalty points total		84.5

EcoScale = 100 – 80.5 = 15.5 (< 50; so, it is an inacceptable synthesis)

References

[1] A. C. Jones, W. I. Nicholson, H. R. Smallman and D. L. Browne, A Robust Pd-Catalyzed C–S Cross-Coupling Process Enabled by Ball-Milling, *Org. Lett.,* 2020, **22**, 7433.

[2] E. Cui , D. Qiao, H. Li, L. Guo, C.-H. Tung and Y. Wang, Engaging Ag(0) single atoms in silver(I) salts-mediated C-B and C-S coupling under visible light irradiation, *J Catal.,* 2021, **402**, 255.

[3] K. D. Jones, D. J. Power, D. Bierer, K. M. Gericke and S. G. Stewart, Nickel Phosphite/Phosphine-Catalyzed C–S Cross-Coupling of Aryl Chlorides and Thiols, *Org. Lett.,* 2018, **20**, 208.

[4] M. Jiang, H. Li, H. Yang and H. Fu, Room-Temperature Arylation of Thiols: Breakthrough with Aryl Chlorides, *Angew. Chem. Int. Ed.,* 2016, **55**, 1.

[5] R. Sikari, S. Sinha, S. Das, A. Saha, G. Chakraborty, R. Mondal and N. D. Paul, Achieving Nickel Catalyzed C-S Cross Coupling under Mild Conditions using Metal-Ligand Cooperativity, *J. Org. Chem.,* 2019, **84**, 4072.

[6] R. Panigrahi, S. K. Sahu, P. K. Behera, S. Panda and L. Rout, $CuMoO_4$ Bimetallic Nanoparticles, An Efficient Catalyst for Room Temperature C-S Cross-coupling of Thiols and Haloarenes, *Chem. Eur. J.*, 2020, **26**, 620.

[7] G. Shen, Q. Lu, Z. Wang, W. Sun,Y. Zhang, X. Huang, M. Sun and Z. Wang, Environmentally Friendly and Recyclable $CuCl_2$-Mediated C–S Bond Coupling Strategy Using DMEDA as Ligand, Base, and Solvent, *Synthesis*, 2022, **54**, 184.

[8] A. Kumar, B. S. Bhakuni, C. D. Prasad, S. Kumar and S. Kumar, Potassium tert-butoxide-mediated synthesis of unsymmetrical diaryl ethers, sulfides and selenides from aryl bromides, *Tetrahedron*, 2013, **69**, 5383.

[9] C.-W. Chen, Y.-L. Chen, D. M. Reddy, K. Du, C.-E. Li, B.-H. Shih, Y.-J. Xue and C.-F. Lee, CuI/Oxalic Diamide-Catalyzed Cross-Coupling of Thiols with Aryl Bromides and Chlorides, *Chem. Eur. J.*, 2017, **23**, 10087.

[10] M. A. Fernández-Rodríguez and J. F. Hartwig, A General, Efficient, and Functional-Group-Tolerant Catalyst System for the Palladium-Catalyzed Thioetherification of Aryl Bromides and Iodides, *J. Org. Chem.*, 2009, **74**, 1663.

[11] Y.-C. Wong, T. T. Jayanth and C.-H. Cheng, Cobalt-Catalyzed Aryl−Sulfur Bond Formation, *Org. Lett.*, 2006, **8**, 5613.

[12] A. C. S. Reddy and P. Anbarasan, Rhodium-Catalyzed Rearrangement of S/Se-Ylides for the Synthesis of Substituted Vinylogous Carbonates, *Org. Lett.*, 2019, **21**, 9965.

[13] A. M. Wagner and M. S. Sanford, Transition-Metal-Free Acid-Mediated Synthesis of Aryl Sulfides from Thiols and Thioethers, *J. Org. Chem.*, 2014, **79**, 2263.