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

Supporting Information

One-Pot Tandem Reduction and Site-Selective Halogenation of Nitroarenes Using a Mixture of Tin Salts

Ganesh Kumar Dhandabani, [#[a]] Li-Te Chang,[#[a]] Hao-Yu Hsieh,[[b]] Chia-Ling Shih,[[b]] and Ling-Wei Hsin *[[a,b]]

[a] Center for Innovative Therapeutics Discovery, National Taiwan University, 17, Xuzhou Road, Room 936, Taipei 10055, Taiwan.

[b] School of Pharmacy, College of Medicine, National Taiwan University, 33, Linsen S. Road, Taipei 10050, Taiwan.

[#] Equal contribution to this manuscript

* Correspondence author: Email: lwhsin@ntu.edu.tw

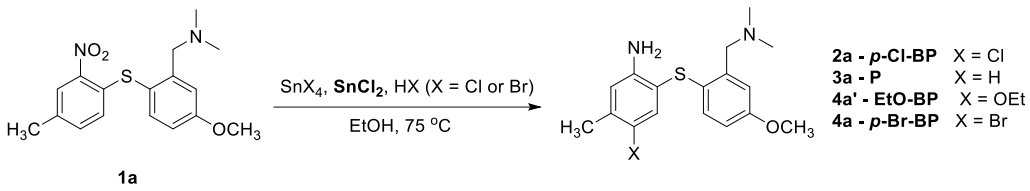
Table of Contents

1) General Information

NMR spectra were recorded on Bruker DPX-200, AV-400 and AV-600 FT-NMR spectrometers. The chemical shift (δ) values are reported in parts per million (ppm), and the coupling constants (*J*) are given in Hz. The spectra were recorded using $CDCl_3$ or DMSO-*d*6 as a solvent. ^{1}H NMR chemical shifts are referenced to tetramethylsilane (TMS) (0 ppm). ^{13}C NMR was referenced to $CDCl_3$ (77.16 ppm). The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; ddd, doublet of doublet of doublets; dt, doublet of triplets; td, triplet of doublets; m, multiplet. Thin-layer chromatography (TLC) was performed on Merck (art. 5715) silica gel plates and visualized under UV light (254 nm), upon treatment with iodine vapor, or upon heating after treatment with 5% phosphomolybdic acid in ethanol. Flash column chromatography was performed with Merck (art. 9385) 40 – 63 μm silica gel 60. Anhydrous tetrahydrofuran (THF) was distilled from sodium-benzophenone prior to use. Methane sulfonyl chloride (MsCl) was distilled from phosphorus pentoxide under reduced pressure prior to use. Mass spectra and high-resolution mass spectra (HRMS) was measured using the ESI (FT-MS solariX) at Academia Sinica, Taipei. Melting points were determined on an EZ-Melt (Automated melting point apparatus). All products reported showed ^{1}H NMR and ^{13}C NMR spectra in agreement with the assigned structures. Reaction progress and product mixtures were routinely monitored by TLC using Merck TLC aluminum sheets (silica gel 60 F254). Column chromatography was carried out with 230–400 mesh silica gel 60 (Merck)/neutral alumina and a mixture of *n*-hexane/ethyl acetate, or dichloromethane/methanol as an eluent. All the starting material was commercially available or prepared by following the reported literature methods.[1-13]

2) Studies on Parameters

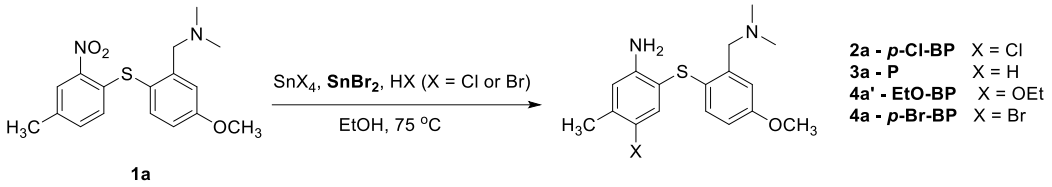
Table 1 Optimization of chlorination reaction conditions.



Entry	$SnCl_2$ eq.	SnX_4[a]	HX[a]	Results (LC area%)				
				p-Cl-BP **2a**	P **3a**	EtO-BP **4a'**	*p*-Br-BP **4a**	SM **1a**
1	5.0	-	Cl (1N)	30	61	4	-	-
2	3.0	-	Cl (1N)	51	31	12	-	-
3	-	Cl	Cl (2N)	6	2	1	-	88
4	0.5	Cl	Cl (2N)	17	2	2	-	76
5	1.0	Cl	Cl (2N)	36	6	9	-	45
6	1.5	Cl	Cl (2N)	54	8	12	-	20
7	2.0	Cl	Cl (2N)	63	13	15	-	3
8	2.5	Cl	Cl (2N)	65	15	15	-	-
9	3.0	Cl	Cl (2N)	64	10	15	-	-
10	4.0	Br	Cl (2N)	6	58	2	26	-
11	3.0	Br	Br (2.9N)	1	41	2	40	-

[a] Reaction condition: 5 eq SnX_4, 5 mL/mmol HX, 50 mL/mmol EtOH.

Table 2 Optimization of bromination reaction conditions.

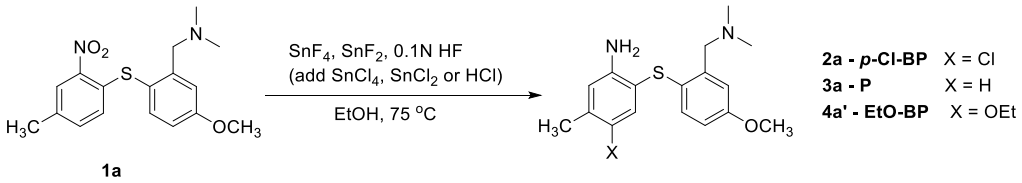


1a

Entry	$SnBr_2$ eq.	SnX_4[a]	HX[a]	Results (LC area%)				
				p-Cl-BP **2a**	P **3a**	EtO-BP **4a'**	*p*-Br-BP **4a**	SM **1a**
1	-	Br	Cl (2N)	-	1	2	-	95
2	0.5	Br	Cl (2N)	1	7	3	14	73
3	1.0	Br	Cl (2N)	1	18	2	11	64
4	1.5	Br	Cl (2N)	2	32	3	17	42
5	2.0	Br	Cl (2N)	2	41	2	24	24
6	2.5	Br	Cl (2N)	3	46	2	30	10
7	3.0	Br	Cl (2N)	3	52	2	33	-
8	3.5	Br	Cl (2N)	3	52	2	34	-
9	4.0	Br	Br (2.9N)	-	56	2	31	-
10	0.5	Cl	Br (2.9N)	2	7	2	4	85
11	1.0	Cl	Br (2.9N)	3	11	2	7	75
12	1.5	Cl	Br (2.9N)	4	19	2	13	60
13	2.0	Cl	Br (2.9N)	3	16	3	11	63
14	2.5	Cl	Br (2.9N)	6	33	3	19	35
15	3.0	Cl	Br (2.9N)	7	35	3	22	30
16	3.5	Cl	Br (2.9N)	7	32	4	23	29
17	4.0	Cl	Br (2.9N)	7	45	5	24	15

[a] Reaction condition: 5 eq SnX_4, 5 mL/mmol HX, 50 mL/mmol EtOH.

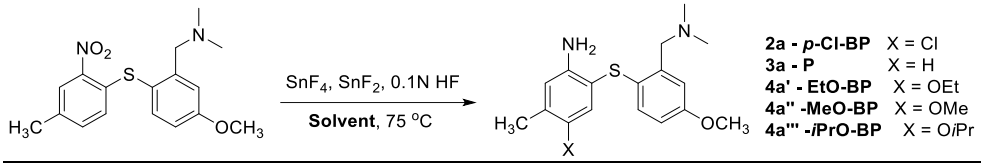
Table 3 Attempt for fluorination reaction.[a,b]



Entry	$SnCl_2$ equiv.	$SnCl_4$ equiv.	HCl	Results (LC area%)			
				p-Cl-BP **2a**	P **3a**	EtO-BP **4a'**	SM **1a**
1	-	-	-	-	4	4	92
2	-	-	+3N[c]	29	35	21	12
3	-	5.0	-	17	30	17	34
4	0.5		-	5	18	27	45
5	1.5		-	11	29	48	-
6	3.0		-	10	31	49	-

[a] Reaction condition: 5 eq SnF_4, 3 eq SnF_2, 5 mL/mmol of 0.1N HF, 50 mL/mmol EtOH; [b] no any fluorination product was detected in these studies; [c]use conc. HCl to form 3N HCl reaction mixture.

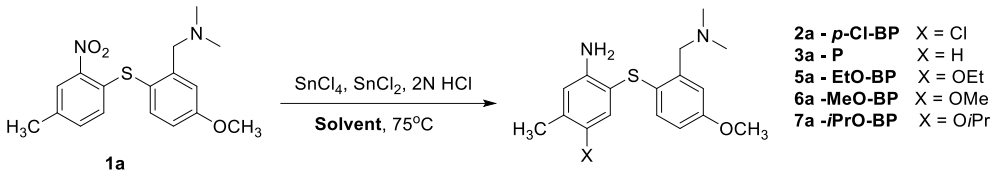
Table 4 Study of solvent effect for the *p*ara-substitution reactions.[a,b]



S.No	$SnCl_2$ eq.	Solvent	Results (LC area% of products)					
			p-Cl-BP **2a**	P **3a**	EtO-BP **4a'**	SM **1a**	MeO-BP **4a"**	*i*-PrO-BP **4a'"**
1	0.5	EtOH	5	18	27	45	-	-
	1.0		16	23	34	16	-	-
	1.5		11	29	48	-	-	-
	2.0		12	38	43	-	-	-
	2.5		9	29	49	-	-	-
	3.0		10	31	49	-	-	-
2	0.5	*i*-PrOH	-	3	-	90	-	3
	1.0		6	9	-	65	-	11
	1.5		13	18	-	46	-	18
	2.0		20	33	-	-	-	27
	3.0		20	33	-	-	-	27
3	1.0	DMF	1	5	-	60	-	-
	2.0		6	10	-	23	-	-
	3.0		6	18	-	-	-	-
4	1.0	*t*-BuOH	5	5	-	88	-	-
	2.0		21	27	-	23	-	-
	3.0		35	54	-	-	-	-
5	1.0	MeOH[c]	1	2	-	95	2	-
	2.0		21	12	-	42	23	-
	3.0		38	30	-	12	16	
6	1.0	Dioxane	-	2	-	96	-	-
	2.0		-	4	-	77	-	-
	3.0		-	13	-	43	-	-

[a] Reaction condition: 5 eq SnF_4, 5 mL/mmol of 0.1N HF, 50 mL/mmol solvent; [b] no any fluorination product was detected in these studies; [c] oil bath at 70°C.

Table 5 Study of solvent effect for *para*-chlorination reactions.[a]



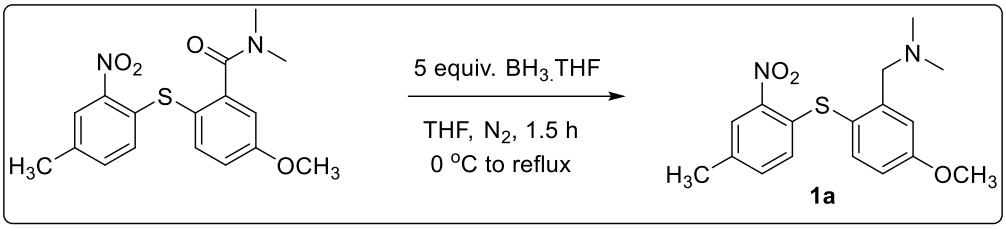
S.No	$SnCl_2$ eq.	Solvent	Results (LC area%)				
			p-Cl-BP **2a**	P **3a**	EtO-BP **4a'**	SM **1a**	MeO-BP **6a**
1	-	EtOH	6	2	1	88	-
	0.5		17	2	2	76	-
	1.0		36	6	9	45	-
	1.5		54	8	12	20	-
	2.0		63	13	15	3	-
	2.5		65	15	15		-
2	1.0	*t*-BuOH	37	9		48	-
	2.0		65	19		2	-
	3.0		63	22			-
3	1.0	MeOH[b]	35	3		58	2
	2.0		69	9		8	12
	3.0		75	14			9

[a] Reaction condition: 5 eq $SnCl_4$, 5 mL/mmol of 2N HCl, 50 mL/mmol solvent; [b] oil bath at 70°C.

3) General Experimental Procedures, Spectral Characterization.

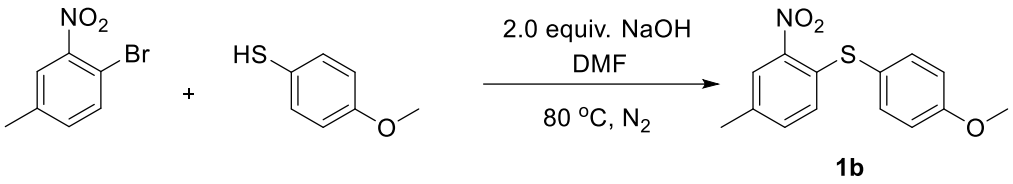
3.1) General Experimental Procedures and Spectral Characterization of Starting Materials.

General Procedure A: Synthesis of *N*,*N*-Dimethyl-2-(2-nitro-4-methylphenylthio)-5-methoxybenzylamine (1a).[1-12]



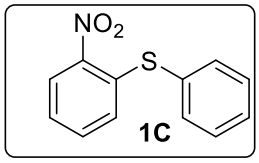
To a solution of 5-methoxy-2-(4-methyl-2-nitrophenylthio)-*N*,*N*-dimethylbenzamide[1] (368 mg, 1.06 mmol) in dry THF (32 mL) was added borane tetrahydrofuran complex solution (1 M in THF, 5.3 mL, 5.31 mmol) at 0°C. The mixture was stirred at reflux temperature under N_2 for 1.5 h and then cooled to rt. The conc. HCl (2.8 mL) was added to the mixture, stirred at rt under N_2 for 10 min and evaporated to afford a yellow oil. Water (31 mL) was added to the yellow oil and the solution was stirred at reflux temperature under N_2 for 30 min. The solution was adjusted to pH = 10-11 by sat. Na_2CO_3 and extracted with CH_2Cl_2 (30 mL × 3). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and evaporated. The crude product was chromatographed (silica gel, 1-2% MeOH in CH_2Cl_2) to afford a yellow oil **1a** (259 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.19 (s, 6H, -N(C*H*$_3$)$_2$), 2.35 (s, 3H, 4'-C*H*$_3$), 3.49 (s, 2H, 1-C*H*$_2$N(CH$_3$)$_2$), 3.88 (s, 3H, 5-OC*H*$_3$), 6.54 (d, *J* = 8.3 Hz, 1H, H-4), 6.88 (dd, *J* = 2.9, 8.5 Hz, 1H, H-5'), 7.11 (dd, *J* = 1.6, 8.3 Hz, 1H, H-3), 7.27 (s, 1H, H-6), 7.47 (d, *J* = 8.5 Hz, 1H, H-6'), 8.06 (s, 1H, H-3'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4 (4-*C*H$_3$), 45.5 (-N(*C*H$_3$)$_2$), 55.5 (5-OCH$_3$), 61.1 (1-*C*H$_2$N(CH$_3$)$_2$), 114.3 (C-4), 115.3 (C-6), 120.6 (C-1'), 126.0 (C-3'), 127.5 (C-3), 134.5 (C-6'), 134.9 (C-2), 136.7 (C-4'), 138.8 (C-5'), 144.5 (C-1), 145.8 (C-2'), 161.5 (C-5).

General Procedures B: Synthesis of (4-methoxyphenyl)(4-methyl-2-nitrophenyl)sulfane (1b)[1]



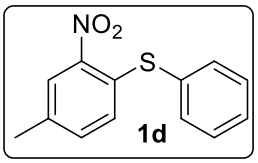
A mixture of 1-bromo-4-methyl-2-nitrobenzene (216 mg, 1.00 mmol), 4-methoxybenzenethiol (113 mL, 1.10 mmol), and NaOH (80 mg, 2.00 mmol) in dimethylformamide (5.0 mL) was flushed with N_2, and stirred at 80°C for 2 h. The reaction mixture was extracted with water (50 mL) and ethyl acetate (5 mL × 3). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and evaporated. The crude product was purified with flash column chromatography (silica gel, 20% CH_2Cl_2 in hexanes (500 mL)) to afford **1b** 269 mg (98%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 6.99 (d, *J* = 8.6 Hz, 2H), 6.71 (d, *J* = 8.3 Hz, 1H), 3.87 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.31, 144.81, 137.87, 137.39, 135.36, 134.79, 128.13, 126.03, 121.87, 115.84, 55.69, 20.63.

Synthesis of (2-Nitrophenyl)(phenyl)sulfane (4-methyl-2-nitrophenyl)(phenyl)sulfane (1c)[1]



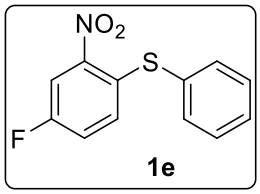
Compound **1c** was synthesized using 1-bromo-2-nitrobenzene (202 mg, 1.00 mmol), following general procedure B as a yellow color solid with71%) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (d, *J* = 8.2 Hz, 1H), 7.21 (td, *J* = 7.3, 0.8 Hz, 1H), 7.34 (td, *J* = 7.7, 1.1 Hz, 1H), 7.46-7.52 (m, 3H), 7.56-7.60 (m, 2H), 8.23 (dd, *J* = 8.2, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 125.0, 125.8, 128.4, 130.1, 130.2 (2C), 131.0, 133.5, 135.9 (2C), 139.5, 144.9.

Synthesis of (4-Methyl-2-nitrophenyl)(phenyl)sulfane (1d)[1]

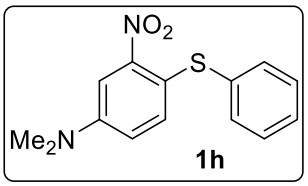


Compound **1d** was synthesized using 1-bromo-4-methyl-2-nitrobenzene (216 mg, 1.00 mmol) following general procedure B as a yellow solid with 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 6.76 (d, *J* = 8.3 Hz, 1H), 7.15 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.44-7.48 (m, 3H), 7.55-7.57 (m, 2H), 8.03 (d, *J* = 1.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 125.8, 128.5, 129.9, 130.1 (2C), 131.5, 134.7, 135.6, 135.7 (2C), 135.8, 145.1.

Synthesis of (4-Fluoro-2-nitrophenyl)(phenyl)sulfane (1e) and *N*,*N*-Dimethyl-3-nitro-4-(phenylthio)aniline (1h)[2]



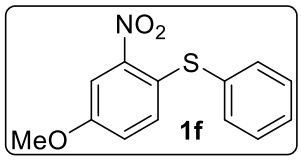
1e



1h

Compound **1e & 1h** were synthesized using 1-bromo-4-fluoro-2-nitrobenzene (220 mg, 1.00 mmol) following general procedure B as yellow solid and orange solid with 12% and 71% (the source of N(C*H*$_3$)$_2$) is DMF) yield, respectively. **1e:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.98 (s, 6H), 6.75 (dd, *J* = 9.0, 2.9, 1H), 6.91 (d, *J* = 9.0 Hz, 1H), 7.34-7.40 (m, 4H), 7.43-7.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.4 (2C), 107.4, 117.7, 120.6, 128.5, 129.6 (2C), 131.9, 133.6 (2C), 134.2, 148.6, 148.9; HRMS (ESI) calcd for $C_{14}H_{14}N_2NaO_2S$ $[M+Na]^+$, 297.0668; found, 297.0673. **1h:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (dd, *J* = 9.0, 5.2 Hz, 1H), 7.11 (td, *J* = 8.1, 2.8 Hz, 1H), 7.47-7.50 (m, 3H), 7.56-7.58 (m, 2H), 7.94 (dd, *J* = 8.3, 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.8 (d, *J* = 27 Hz), 121.5 (d, *J* = 21 Hz), 130.1 (d, *J* = 8 Hz), 130.3, 130.3 (2C), 130.9, 135.0 (d, *J* = 3 Hz), 135.9 (2C), 145.2 (d, *J* = 9 Hz) 159.5 (d, *J* = 248 Hz).

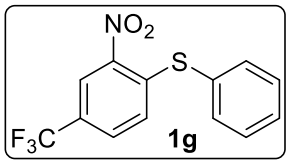
Synthesis of (4-Methoxy-2-nitrophenyl)(phenyl)sulfane (1f)[8]



1f

Compound **1f** was synthesized using 1-bromo-4-methoxy-2-nitrobenzene (232 mg, 1.00 mmol) following general procedure B as a yellow solid with 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 3H), 6.82 (d, *J* = 9.0 Hz, 1H), 6.96 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.44 (d, *J* = 2.3 Hz, 3H), 7.53 (t, *J* = 3.6 Hz, 2H), 7.68 (d, *J* = 2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 65.0, 109.1, 121.7, 129.6, 129.6, 130.0 (2C), 130.2, 132.1, 135.3 (2C), 146.1, 157.4

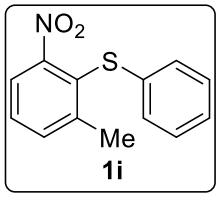
Synthesis of (2-Nitro-4-(trifluoromethyl)phenyl)(phenyl)sulfane (1g)[9]



1g

Compound **1g** was synthesized using 1-bromo-2-nitro-4-(trifluoromethyl)benzene (270 mg, 1.00 mmol) following general procedure B as a yellow solid with 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$) 6.96 (d, *J* = 8.6 Hz, 1H), 7.53-7.61 (m, 6H), 8.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 123.0 (q, *J* = 271 Hz),123.3 (q, *J* = 4 Hz), 127.2 (q, *J* = 34 Hz), 129.0, 129.6 (q, *J* = 3 Hz), 129.8, 130.6 (2C), 130.8, 136.1 (2C), 144.3, 144.8.

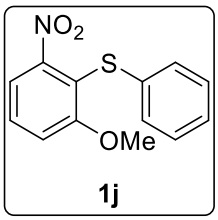
Synthesis of (2-Methyl-6-nitrophenyl)(phenyl)sulfane (1i)[10]



1i

Compound **1i** was synthesized using 2-bromo-1-methyl-3-nitrobenzene (216mg, 1.00 mmol) following general procedure B as a yellow solid with 84% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 7.07-7.09 (m, 2H), 7.14-7.17 (m, 1H), 7.20-7.25 (m, 2H), 7.38-7.46 (m, 2H), 7.54 (dd, *J* =7.4, 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 121.2, 125.5, 126.5, 128.2 (2C), 129.3 (2C), 129.7, 133.8, 135.5, 145.6, 155.7.

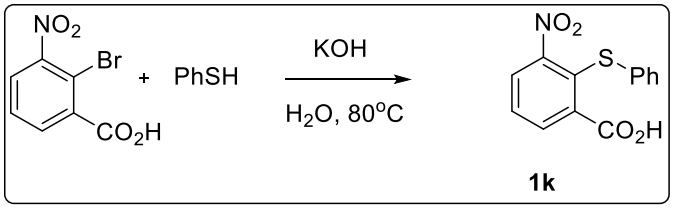
Synthesis of (2-Methoxy-6-nitrophenyl)(phenyl)sulfane (1j)



1j

Compound **1j** was synthesized using 2-bromo-1-methoxy-3-nitrobenzene (464 mg, 2.00 mmol) following general procedure B as a yellow solid with 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (s, 3H), 7.06 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.16-7.21 (m, 5H), 7.33 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.44 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.7, 114.7, 115.6, 116.6, 126.7, 128.9 (2C), 129.7 (2C), 130.4, 135.5, 155.1, 160.5; HRMS (ESI) calcd for $C_{13}H_{11}NaNO_3S$ $[M+Na]^+$, 284.0352; found, 284.0375.

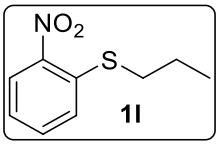
Synthesis of 3-Nitro-2-(phenylthio)benzoic acid (1k)[13]



1k

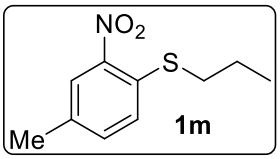
A mixture of 2-bromo-3-nitrobenzoic acid (403.2 mg, 2.00 mmol), benzenethiol (225.2 mL, 2.20 mmol), and KOH (316.8 mg, 4.40 mmol) in water (10.0 mL) was flushed with N_2, and stirred at 80°C for 1 h. The reaction mixture was extracted with water (40 mL) and CH_2Cl_2 (10 mL × 3). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and evaporated. The crude product was purified with flash column chromatography (silica gel, 4% MeOH in CH_2Cl_2) to afford **1k** (253.2 mg, 46%) as a brown solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.19-7.25 (m, 5H), 7.47 (t, J = 7.9 Hz, 1H), 7.88-7.91 (m, 2H), 8.47 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 127.4, 128.1, 128.2, 129.4 (2C), 131.6 (2C), 132.3, 133.8, 134.6, 136.5, 153.4, 170.9.

Synthesis of (2-Nitrophenyl)(propyl)sulfane (1l)[4]



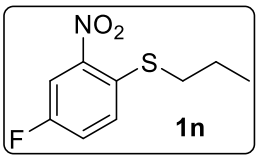
Compound **1l** was synthesized using 1-bromo-2-nitrobenzene (202 mg, 1.00 mmol) following the general procedure B as a yellow solid with 74% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, *J* = 7.4 Hz, 3H), 1.77 (q, *J* = 7.4 Hz, 2H), 2.95 (t, *J* = 7.4 Hz, 2H), 7.22-7.27 (m, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.53-7.57 (m, 1H), 8.19 (dd, *J* = 8.3, 1.3 Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 21.4, 34.3, 124.3, 126.1, 126.7, 133.5, 138.2, 146.1.

Synthesis of (4-Methyl-2-nitrophenyl)(propyl)sulfane (1m)[3]



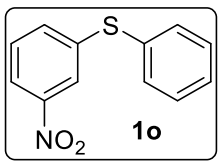
Compound **1m** was synthesized using 1-bromo-4-methyl-2-nitrobenzene (216 mg, 1.00 mmol) following general procedure B as a yellow solid with 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 (t, *J* = 7.3 Hz, 3H), 1.71-1.80 (m, 2H), 2.39 (s, 3H), 2.92 (t, *J* = 7.3 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 1H), 7.36 (dd, *J* = 8.4, 1.7 Hz, 1H), 8.00 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 20.5, 21.6, 34.5, 126.3, 126.8, 134.5, 134.6, 134.9, 146.3.

Synthesis of (4-Fluoro-2-nitrophenyl)(propyl)sulfane (1n)[5]



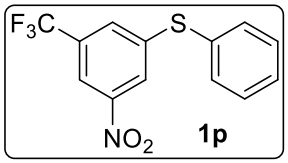
Compound **1n** was synthesized using 1-bromo-4-fluoro-2-nitrobenzene (220 mg, 1.00 mmol) following general procedure B as a yellow solid with 51% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, *J* = 7.3 Hz, 3H), 1.77 (q, *J* =7.4 Hz, 2H), 2.94 (t, *J* = 7.3 Hz, 2H), 7.41 (td, *J* = 7.2, 2.6 Hz, 1H), 7.38-7.42 (m, 1H), 7.92 (dd, *J* = 8.4, 2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 21.5, 34.8, 113.3 (d, *J* = 26 Hz), 121.4 (d, *J* = 22 Hz), 128.5 (d, *J* = 7 Hz), 133.5 (d, *J* = 3 Hz), 146.6 (d, *J* = 8 Hz), 159.2 (d, *J* = 247 Hz).

Synthesis of (3-Nitrophenyl)(phenyl)sulfane (1o)[12]



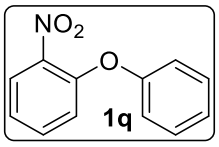
Compound **1o** was synthesized using 1-bromo-3-nitrobenzene (202 mg, 1.00 mmol) following general procedure B as a yellow solid with 52% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.42 (m, 4H), 7.46-7.50 (m, 3H), 7.98 (dt, *J* = 8.0, 1.0 Hz 1H), 8.02 (t, *J* = 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.0, 123.2, 129.0, 129.8, 129.9 (2C), 132.2, 133.5 (2C), 133.3, 140.6, 148.7.

Synthesis of (3-Nitro-5-(trifluoromethyl)phenyl)(phenyl)sulfane (1p)[11]



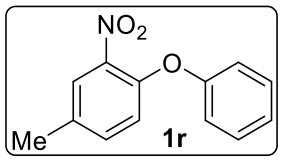
Compound **1p** was synthesized using 1-bromo-3-nitro-5-(trifluoromethyl)benzene (270 mg, 1.00 mmol) following general procedure B as a yellow solid with 67% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.48 (m, 3H), 7.51-7.55 (m, 2H), 7.67 (s, 1H), 8.07 (s, 1H), 8.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 117.6 (q, *J* = 4 Hz), 122.7 (q, *J* = 272 Hz), 124.9, 129.3 (q, *J* = 4 Hz), 130.2, 130.4 (2C), 132.4 (q, *J* = 4 Hz), 134.5 (2C), 144.8, 148.9.

Synthesis of 1-Nitro-2-phenoxybenzene (1q)



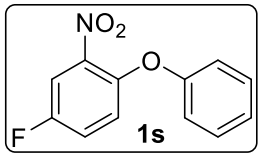
Compound **1q** was synthesized using 1-bromo-2-nitrobenzene (202 mg, 1.00 mmol) following general procedure B as a yellow solid with 74% of yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.03 (d, *J* = 3.3 Hz, 2H) 7.16-7.25 (m, 2H), 7.36-7.40 (m, 2H), 7.47-7.51 (m, 1H), 7.94 (dd, *J* = 8.1, 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 119.3 (2C), 120.5, 123.2, 124.6, 125.7, 130.1 (2C), 134.3, 141.3, 150.7, 155.8

Synthesis of 4-Methyl-2-nitro-1-phenoxybenzene (1r)[6]



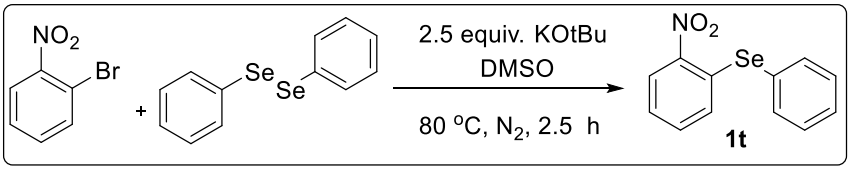
Compound **1r** was synthesized using 1-bromo-4-methyl-2-nitrobenzene (216 mg, 1.00 mmol) following general procedure B as a dark red solid with 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.99-7.02 (m, 2H), 7.12-7.16 (m, 1H), 7.30-7.36 (m, 3H), 7.75 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 118.7 (2C), 121.2, 124.2, 125.8, 130.0 (2C), 133.8, 135.0, 141.3, 148.2, 156.5

Synthesis of 4-Fluoro-2-nitro-1-phenoxybenzene (1s)[7]



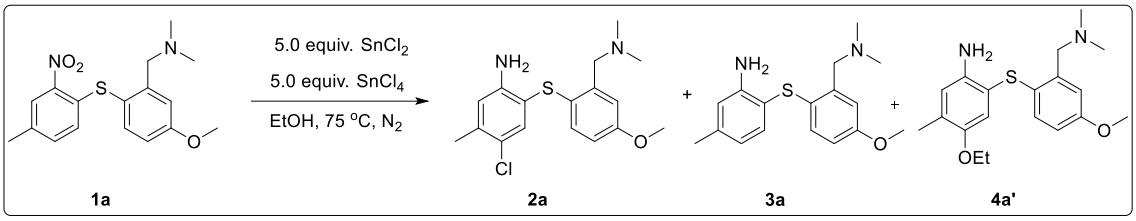
Compound **1s** was synthesized using 1-bromo-4-fluoro-2-nitrobenzene (220 mg, 1.00 mmol) following general procedure B as a yellow solid with 47% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00-7.06 (m, 3H), 7.17 (t, *J* = 7.4 Hz, 1H) 7.23-7.28 (m, 1H), 7.34-7.41 (m, 2H), 7.69 (dd, *J* = 7.7, 3.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.9, 118.7 (2C), 121.5 (d, *J* = 23 Hz), 122.7, 124.6, 130.2 (2C), 141.4 (d, *J* = 9 Hz) 146.9, 156.0, 158.3

Synthesis of (2-Nitrophenyl)(phenyl)selane (1t)[1]



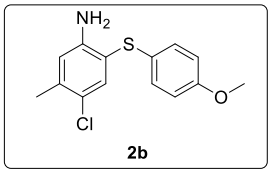
A mixture of 1-bromo-2-nitrobenzene (202 mg, 1.00 mmol), 1,2-diphenyldiselane (156 mg, 0.5 mmol), and *t*-BuOK (280 mg, 2.50 mmol) in DMSO (1.0 mL) was flushed with N_2, and stirred at 80°C for 2.5 h. The reaction mixture was extracted with water (50 mL) and ethyl acetate (5 mL × 3). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and evaporated. The crude product was purified with flash column chromatography (silica gel, 20% CH_2Cl_2 in hexanes (500 mL)) to afford **1t** (149 mg, 0.61 mmol, 61%) as a dark solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, *J* = 7.6 Hz, 1H), 7.26-7.33 (m, 2H), 7.45-7.52 (m, 3H), 7.70-7.72 (m, 2H), 8.32-8.34 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 125.9, 126.1, 128.2, 130.0, 130.2 (2C), 130.3, 133.8, 136.0, 137.5 (2C), 145.6.

General Procedure C: Synthesis of 1-(5-(2-Fluoroethoxy)-2-(4-methyl-2-nitrophenyl thio)-phenyl)-*N*,*N*-dimethylmethanamine (2a).

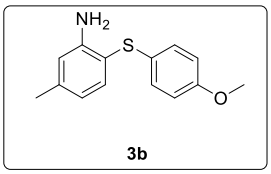


To a solution of compound **1a** (109 mg, 0.33 mmol) in ethanol (16.5 mL) and 2N HCl (1.7 mL) was added $SnCl_4$ (0.19 mL, 1.64 mmol) at rt. The reaction mixture was stirred at reflux temperature under N_2 for 0.5 h and $SnCl_2$ (31 mg, 0.16 mmol) was added every 0.5 h for six times at the same temperature. After 2 h, reaction completion was confirmed by TLC. Then, the mixture was evaporated and quenched with water (10 mL). The crude mixture was basified with 10% NaOH to pH > 12, extracted with CH_2Cl_2 (25 mL × 3), washed with brine, dried over $MgSO_4$ and evaporated. The crude product was chromatographed (silica gel, 2-3% MeOH (with 10% NH_4OH) in CH_2Cl_2) to afford a white oil **2a** (48.6 mg, 52%), **3a** (5.1 mg, 5%) and **4a'** (8 mg, 6%). **2a:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H), 2.29 (s, 6H), 3.53 (s, 2H), 3.77 (s, 3H), 6.56 (s, 1H), 6.69 (dd, *J* = 2.7, 8.6 Hz, 1H), 6.84 (d, *J* = 2.4 Hz, 1H), 6.97 (d, *J* = 8.6 Hz, 1H), 7.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 45.2, 55.3, 62.5, 113.6, 115.7, 116.1, 117.1, 122.4, 126.7, 130.9, 135.8, 137.9, 139.1, 147.0, 158.1; ESIHRMS calcd. for $C_{17}H_{21}ClN_2NaOS$ $[M+Na]^+$, 359.0961; found, 359.0957. **3a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 2.30 (s, 6H), 3.55 (s, 2H), 3.75 (s, 3H), 6.52 (d, *J* = 6.0 Hz, 1H), 6.53 (s, 1H), 6.65 (dd, *J* = 2.8, 8.6 Hz, 1H), 6.85 (d, *J* = 2.8 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 45.2, 55.3, 62.2, 113.4, 113.5, 115.79, 115.82, 119.3, 127.7, 129.9, 136.6, 138.5, 140.6, 148.3, 157.8; ESIHRMS calcd for $C_{17}H_{23}N_2OS$ $[M+H]^+$ and $[M+Na]^+$, 303.1531 and 325.1351; found, 303.1512 and 325.1355. **4a':** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, *J* = 7.0 Hz, 3H), 2.18 (s, 3H), 2.30 (s, 6H), 3.54 (s, 2H), 3.76 (s, 3H), 3.92 (q, *J* = 7.0 Hz, 2H), 6.58 (s, 1H), 6.66 (dd, *J* = 4.3, 13.0 Hz, 1H), 6.86 (d, *J* = 12.6 Hz, 1H), 6.86 (s, 1H), 6.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.0, 16.2, 45.3, 55.3, 62.3, 64.4, 113.47, 113.54, 115.8, 118.2, 119.6, 127.7, 129.4, 130.2, 138.4, 142.1, 149.9, 157.8; ESIHRMS calcd for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613; found, 347.1807 and 369.1623.

Synthesis of 4-Chloro-2-((4-methoxyphenyl)thio)-5-methylaniline (2b) and **2-((4-Methoxyphenyl)thio)-5-methylaniline (3b)**



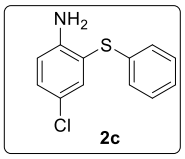
2b



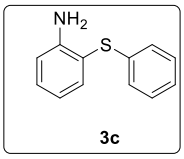
3b

Compound **2b & 3b** were synthesized using (4-methoxyphenyl)(4-methyl-2-nitrophenyl)sulfane (**1b**) following general procedure C for 2 h as white color solid **2w** and yellow color solid **3w** with 54% and 24% yield, respectively. **2b:** mp = 74-76ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.17 – 7.12 (m, 2H), 6.83 – 6.78 (m, 2H), 6.65 (s, 1H), 3.76 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.60, 146.12, 138.28, 135.59, 130.03, 126.28, 123.45, 117.59, 115.96, 114.90, 55.37, 20.03; ESIHRMS calcd for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613. **3b:** mp = 48-50ºC. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (d, *J* = 7.7 Hz, 1H), 7.09 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 2H), 6.56 (d, *J* = 12.0 Hz, 1H), 6.55 (d, *J* = 7.7 Hz, 1H), 3.74 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.23, 148.28, 141.09, 136.77, 129.15, 127.66, 119.97, 116.11, 114.85, 113.23, 55.44, 21.50; ESIHRMS calcd. for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613; found, 347.1807 and 369.1623.

Synthesis of 4-Chloro-2-(phenylthio)aniline (2c)[14] **and 2-(Phenylthio)aniline (3c).**



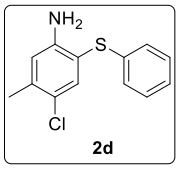
2c



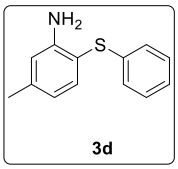
3c

Compounds **2c** & **3c** were synthesized using (2-nitrophenyl)(phenyl)sulfane (**1c**) following general procedure **C** for 2 h to afford **2c** & **3c** as brown oils. **2c:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (d, *J* = 2.4 Hz, 1H), 7.26-7.23 (m, 2H), 7.19-7.13 (m, 2H), 7.13-7.08 (m, 2H), 6.71 (d, *J* = 8.6 Hz, 1H), 4.28 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.38, 136.25, 135.88, 131.03, 129.30, 127.15, 126.10, 122.70, 116.41, 116.28. **3c:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.29-7.18 (m, 3H), 7.15-7.03 (m, 3H), 6.81-6.73 (m, 2H), 4.28 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.97, 137.61, 136.96, 131.27, 129.14, 126.62, 125.56, 118.89, 115.50, 114.53.

Synthesis of 4-Chloro-5-methyl-2-(phenylthio)aniline (2d) and 5-Methyl-2-(phenylthio) aniline (3d).



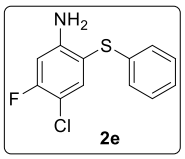
2d



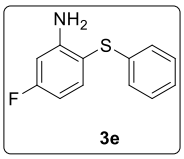
3d

Compounds **2d** & **3d** were synthesized using (4-methyl-2-nitrophenyl)(phenyl)sulfane (**1d**) following general procedure **C** for 2 h to afford **2d** as a green semi-solid and **3d** as a brown oil. **2d:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.24 -7.20 (m, 2H), 7.15 – 7.07 (m, 3H), 6.66 (s, 1H), 4.20 (s, 2H), 2.31 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.51, 139.25, 136.84, 136.47, 129.21, 126.70, 125.80, 123.23, 117.45, 113.20, 20.25; ESIHRMS calcd. for $C_{13}H_{13}ClNS$ $[M+H]^+$, 250.0457; found, 250.0457. **3d:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.8 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 2H), 7.10 (dd, *J* = 7.8, 3.0 Hz, 1H), 7.07 (dd, *J* = 5.7, 4.7 Hz, 2H), 6.62 (s, 1H), 6.59 (dd, *J* = 7.6, 1.7 Hz, 1H), 4.22 (s, 2H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.91, 141.76, 137.61, 129.08, 126.29, 125.34, 120.08, 116.66, 116.11, 111.15, 21.60.

Synthesis of 4-Chloro-5-fluoro-2-(phenylthio)aniline (2e) and 5-Fluoro-2-(phenylthio)aniline (3e)



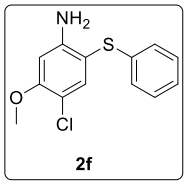
2e



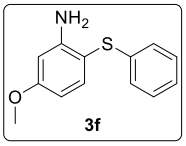
3e

Compound **2e & 3e** were synthesized using (4-fluoro-2-nitrophenyl)(phenyl)sulfane (**1e**) following general procedure C for 1 h as brown color solid **2e** and pale-yellow solid **3e** with 20% and 67% yield, respectively. **2e:** mp = 95-90ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 1H), 7.24 (t, *J* = 7.2 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 2H), 6.57 (d, *J* = 10.6 Hz, 1H), 4.42 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.35 (J_F = 249.15), 149.47 (J_F = 10.57), 138.52, 135.84, 129.19, 126.56, 125.96, 110.92, 109.39 (J_F = 18.12), 102.91 (J_F = 24.16); ESIHRMS calcd for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613; found, 347.1807 and 369.1623. **3e:** mp = 55-57ºC. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (t, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 2H), 6.55 – 6.40 (m, 2H), 4.40 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.01 (J_F = 247.64), 150.54 (J_F = 12.08), 139.35 (J_F = 6.04), 136.79, 129.05, 126.13, 125.49, 109.51, 105.81 (J_F = 21.14), 101.91 (J_F = 25.67). ESIHRMS calcd for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613; found, 347.1807 and 369.1623.

Synthesis of 4-Chloro-5-methoxy-2-(phenylthio)aniline (2f) and **5-Methoxy-2-(phenylthio)aniline (3f)**



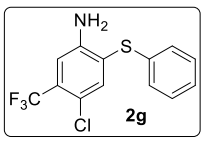
2f



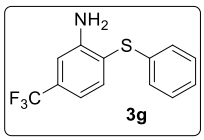
3f

Compound **2f & 3f** were synthesized using (4-Methoxy-2-nitrophenyl)(phenyl)sulfane (**1f**) following general procedure C for 2 h as yellow color solid **2f** and off-white color solid **3f** with 45% and 20% yield, respectively. **2f**: mp = 68-70ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H), 7.06 (d, *J* = 7.7 Hz, 2H), 6.36 (s, 1H), 4.35 (s, 2H), 3.88 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.32, 149.13, 138.19, 136.96, 129.05, 126.07, 125.49, 111.46, 105.92, 98.86, 56.11; ESIHRMS calcd for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613; found, 347.1807 and 369.1623. **3f:** mp = 90-92ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.4 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 2H), 7.06 (t, *J* = 12.8 Hz, 3H), 6.40 – 6.31 (m, 2H), 4.31 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.42, 150.33, 139.02, 137.86, 128.94, 125.78, 125.10, 105.67, 105.22, 100.32, 55.27; ESIHRMS calcd for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613; found, 347.1807 and 369.1623.

Synthesis of 4-Chloro-2-(phenylthio)-5-(trifluoromethyl)aniline (2g) and 2-(Phenylthio)-5-(trifluoromethyl)aniline (3g).



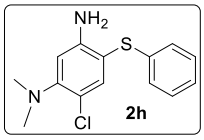
2g

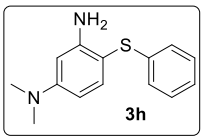


3g

Compounds **2g** & **3g** were synthesized using (2-nitro-4-(trifluoromethyl)phenyl)(phenyl)sulfane (**1g**) following general procedure **C** for 2 h to afford **2g** as a off-white solid and **3g** as a yellow oil. **2g:** mp = 48 - 49 ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.25-7.20 (m, 1H), 7.18 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.05 (s, 1H), 4.41 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 146.50, 137.83, 134.04, 129.59, 128.49, 127.05, 120.96, 119.72, 113.88; ESIHRMS calcd. for $C_{13}H_{10}ClFNS$ $[M+H]^+$, 304.0175; found, 304.0179. **3g**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 1H), 7.33 – 7.21 (m, 2H), 7.21 – 7.15 (m, 1H), 7.14 – 7.06 (m, 2H), 6.98 (s, 1H), 6.98 – 6.94 (m, 1H), 4.54 – 4.36 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.49, 137.19, 135.25, 132.81 (d, *J* = 32.4), 129.38, 127.67, 126.40, 124.02 (d, *J* = 272.6 Hz), 119.19, 114.96, 111.76.

Synthesis of 6-Chloro-*N1,N1*-dimethyl-4-(phenylthio)benzene-1,3-diamine (2h) and *N1,N1*-Dimethyl-4-(phenylthio)benzene-1,3-diamine (3h).

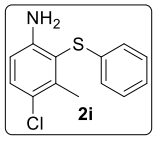


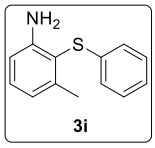


Compound **2h** & **3h** were synthesized using *N*,*N*-dimethyl-3-nitro-4-(phenylthio)aniline (**1h**) following general procedure **C** for 2 h to afford **2h** as a brown semi-solid and **3h** as a brown semi-solid. **2h:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.17 – 7.24 (m, 2H), 7.04 – 7.13 (m, 3H), 6.44 (s, 1H), 6.16 (dd, *J* = 8.6, 2.7 Hz, 1H), 2.83 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.04, 148.55, 137.07, 129.15, 126.33, 125.59, 125.55, 116.55, 107.81, 106.27, 43.62; ESIHRMS calcd. for $C_{14}H_{15}ClN_2S$ $[M+H]^+$, 279.0723; found, 279.0732.

3h: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.6 Hz, 1H), 7.21 – 7.17 (m, 2H), 7.09 – 7.02 (m, 3H), 6.20 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.11 (d, *J* = 2.7 Hz, 1H), 4.23 (s, 2H), 2.97 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.13, 150.16, 139.12, 138.82, 128.94, 125.59, 124.84, 104.34, 100.78, 98.20, 40.39.

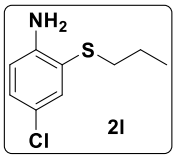
Synthesis of 4-Chloro-3-methyl-2-(phenylthio)aniline (2i) and 3-Methyl-2-(phenylthio)aniline (3i).

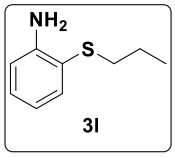




Compound **2i** & **3i** were synthesized using (2-methyl-6-nitro phenyl)(phenyl)sulfane (**1i**) following general procedure **C** for 2 h to afford **2i** as a brown semi-solid and **3i** as a white sold. **2i:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.8 Hz, 3H), 7.11 (t, *J* = 7.0 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 2H), 6.63 (d, *J* = 8.6 Hz, 1H), 4.42 (s, 2H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.51, 141.83, 136.03, 131.35, 129.14, 125.77, 125.39, 123.46, 113.56, 18.97; ESIHRMS calcd. for $C_{13}H_{12}ClNS$ $[M+H]^+$, 250.0457; found, 250.0462. **3i**: mp = 63 - 65 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 – 7.16 (m, 2H), 7.13 (d, *J* = 7.7 Hz, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.03 – 6.98 (m, 2H), 6.74 – 6.69 (m, 1H), 6.66 (dd, *J* = 8.1, 0.7 Hz, 1H), 4.36 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.87, 144.84, 136.82, 130.67, 129.13, 125.71, 125.12, 120.19, 113.84, 113.02, 21.71.

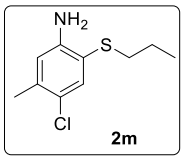
Synthesis of (5-Chloro-2-nitrophenyl)(propyl)sulfane (2l) and **(5-Chloro-2-nitrophenyl)(propyl)sulfane (3l)**

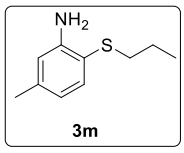




Compound **2l** & **3l** were synthesized using (2-nitrophenyl)(propyl)sulfane (**1l**) following general procedure C for 2 h as color loss oil **2l** and color loss oil **3l** with 63% and 21% yield, respectively. **2k:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (d, *J* = 2.4 Hz, 1H), 7.05 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.64 (d, *J* = 8.5 Hz, 1H), 4.31 (s, 2H), 2.84 – 2.64 (m, 2H), 1.64 – 1.53 (m, 2H), 0.99 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.54, 134.28, 129.12, 122.42, 119.94, 115.71, 36.83, 22.91, 13.30; ESIHRMS calcd for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613; found, 347.1807 and 369.1623. **3l:** ^{1}H NMR (600 MHz, δ 7.36 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.15 – 7.04 (m, 1H), 6.77 – 6.60 (m, 2H), 4.33 (s, 2H), 2.71 (t, *J* = 7.3 Hz, 2H), 1.58 (dd, *J* = 14.7, 7.3 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.17, 135.72, 129.44, 118.46, 118.30, 114.86, 36.89, 23.01, 13.35. ESIHRMS calcd for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613; found, 347.1807 and 369.1623.

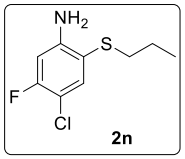
Synthesis of 4-Chloro-5-methyl-2-(propylthio)aniline (2m) and (4-Methyl-2-nitrophenyl) (propyl)sulfane (3m).

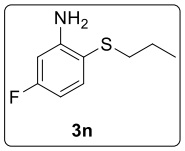




Compound **2m** & **3m** were synthesized using (4-methyl-2-nitrophenyl)(propyl)sulfane (**1m**) following general procedure **C** for 2 h to afford **2m** & **3m** as brown oils. **2m:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (s, 1H), 6.60 (s, 1H), 4.26 (s, 2H), 2.73 – 2.64 (m, 2H), 2.26 (s, 3H), 1.57 (d, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 146.91, 137.39, 135.39, 122.96, 117.03, 116.98, 37.29, 23.08, 20.07, 13.44; ESIHRMS calcd. for $C_{10}H_{14}ClN_S$ $[M+H]^+$, 216.0614; found, 216.0620. **3m:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 2.6 Hz, 1H), 6.56 (d, *J* = 0.9 Hz, 1H), 6.53 – 6.48 (m, 1H), 4.30 (s, 2H), 2.74 – 2.57 (m, 2H), 2.25 (s, 3H), 1.65 – 1.48 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.33, 139.98, 136.22, 119.66, 115.66, 115.08, 37.34, 23.14, 21.42, 13.45.

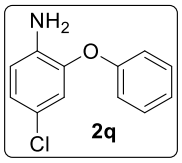
Synthesis of 4-Chloro-5-fluoro-2-(propylthio)aniline (2n) and 5-Fluoro-2-(propylthio)aniline (3n).

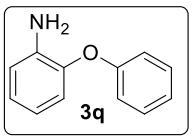




Compound **2n** & **3n** were synthesized using ((4-fluoro-2-nitrophenyl)(propyl)sulfane (**1n**) following general procedure **C** for 2 h to afford **2n** & **3n** as colorless oils. **2n:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.1 Hz, 1H), 6.50 (d, *J* = 10.6 Hz, 1H), 4.48 (s, 2H), 2.66 (dd, *J* = 7.6, 7.1 Hz, 2H), 1.56 (q, *J* = 7.7 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.99 (d, *J* = 247.8 Hz), 148.62 (d, *J* = 10.4 Hz, 137.33, 114.56, 108.87, 102.48 (d, *J* = 24.7 Hz), 37.46, 23.03, 13.39; ESIHRMS calcd. for $C_9H_{11}ClFNS$ $[M+H]^+$, 220.0363; found, 220.0362. **3n:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 -7.31 (dd, *J* = 6.7, 8.1 Hz, 1H), 6.42 (dd, *J* = 10.5, 2.7 Hz, 1H), 6.38 (td, *J* = 8.5, 2.7 Hz, 1H), 4.49 (s, 2H), 2.73 – 2.20 (m, 2H), 1.69 – 1.40 (m, 2H), 1.13 – 0.84 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) 164.05 (d, *J* = 245.6 Hz), 149.99 (d, *J* = 11.6 Hz), 137.96 (d, *J* = 10.0 Hz), 113.19, 105.31 (d, *J* = 22.0 Hz), 101.35 (d, *J* = 25.2 Hz), 37.29, 22.91, 13.28.

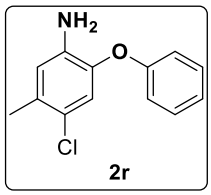
Synthesis of 4-Chloro-2-phenoxyaniline (2q)[14] and 2-Phenoxyaniline (3q).



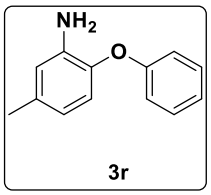


Compound **2q** & **3q** were synthesized using 1-nitro-2-phenoxybenzene (**1q**) following general procedure **C** for 90 minutes to afford **2q** as a brown oil and **3q** as an off-white solid. **2q:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.8 Hz, 2H), 7.10 (td, *J* = 7.4, 0.5 Hz, 1H), 7.01 – 6.96 (m, 2H), 6.92 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.82 (d, *J* = 2.3 Hz, 1H), 6.72 (d, *J* = 8.5 Hz, 1H), 3.80 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.79, 143.99, 137.30, 130.01, 124.54, 123.52, 122.78, 119.76, 117.85, 116.94. **3q**: mp = 42 - 44 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.98 – 6.95 (m, 3H), 6.87 (d, *J* = 1.1 Hz, 1H), 6.80 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.74 – 6.68 (m, 1H), 3.77 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.60, 143.16, 138.86, 129.81, 125.01, 122.73, 120.38, 118.86, 117.20, 117.58.

Synthesis of 4-Chloro-5-methyl-2-phenoxyaniline (2r) and 5-Methyl-2-phenoxyaniline (3r)



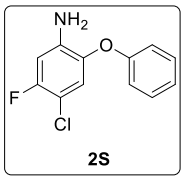
2r



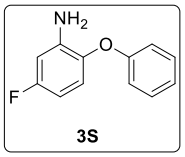
3r

Compound **2r & 3r** were synthesized using 4-methyl-2-nitro-1-phenoxybenzene (**1r**) following general procedure C for 3 h as brown color solid **2r** and off-white color solid **3r** with 72% and 20% yield, respectively. **2r:** mp = 52-54°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 2H), 7.08 (dd, *J* = 10.6, 4.2 Hz, 1H), 7.00 – 6.94 (m, 2H), 6.85 (s, 1H), 6.68 (s, 1H), 3.73 (s, 2H), 2.28 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.19, 141.54, 137.24, 132.20, 129.82, 123.01, 122.70, 120.55, 118.10, 117.16, 19.52; ESIHRMS calcd for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613; found, 347.1807 and 369.1623. **3r:** mp = 36-38°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (t, *J* = 8.0 Hz, 2H), 7.02 (t, *J* = 7.3 Hz, 1H), 6.98 – 6.91 (m, 2H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.64 (s, 1H), 6.53 (d, *J* = 8.1 Hz, 1H), 3.70 (s, 2H), 2.27 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.89, 140.64, 138.54, 134.82, 129.66, 122.33, 120.54, 119.45, 117.18, 116.67, 21.02; ESIHRMS calcd for $C_{19}H_{27}N_2O_2S$ $[M+H]^+$ and $C_{19}H_{26}N_2NaO_2S$ $[M+Na]^+$, 347.1793 and 369.1613; found, 347.1807 and 369.1623.

Synthesis of 4-Chloro-5-fluoro-2-phenoxyaniline (2s) and 5-Fluoro-2-phenoxyaniline (3s).



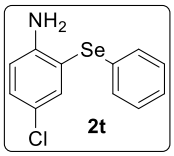
2S

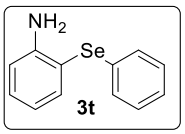


3S

Compounds **2s** & **3s** were synthesized using 4-fluoro-2-nitro-1-phenoxybenzene (**1s**) following general procedure **C** for 2h to afford **2s** & **3s** as colorless oils; **2s:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 2H), 7.10 (tt, *J* = 7.7, 1.0 Hz, 1H), 7.02 – 6.92 (m, 2H), 6.87 (d, *J* = 7.0 Hz, 1H), 6.60 (d, *J* = 10.2 Hz, 1H), 3.92 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.13, δ 155.27 (d, *J* = 243.0 Hz), 139.25, 138.85 (d, *J* = 9.7 Hz), 130.06, 123.44, 121.55, 117.23, 108.54 (d, *J* = 19.7 Hz), 103.76 (d, *J* = 25.8 Hz); ESIHRMS calcd. for $C_{12}H_9ClFNO$ $[M+H]^+$, 238.0435; found, 238.0440. **3s:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.95 – 6.91 (m, 2H), 6.82 (dd, *J* = 8.8, 5.4 Hz, 1H), 6.51 (dd, *J* = 9.9, 2.9 Hz, 1H), 6.42 – 6.37 (m, 1H), 3.87 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.21 (d, *J* = 240.5 Hz), 157.82, 140.34 (d, *J* = 11.4 Hz), 138.74, 129.83 (d, *J* = 13.2 Hz), 122.74, 121.66 (d, *J* = 10.2 Hz), 116.66, 104.76 (d, *J* = 23.5 Hz), 103.11 (d, *J* = 26.6 Hz).

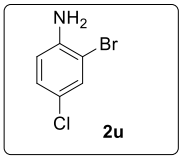
Synthesis of 4-Chloro-2-(phenylselanyl)aniline (2t)[15] and 2-(Phenylselanyl)aniline (3t).





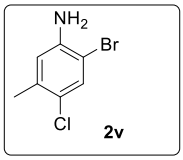
Compounds **2t** & **3t** were synthesized using (2-nitrophenyl)(phenyl)selane (**1t**) following general procedure **C** for 2h to afford **2t** as a brown oil and **3t** as a brown oil. **2t:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 2.4 Hz, 1H), 7.32 – 7.12 (m, 6H), 6.71 (d, *J* = 8.6 Hz, 1H), 4.27 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.19, 137.30, 130.93, 130.90, 129.95, 129.53, 126.80, 122.66, 115.98, 114.10. **3t:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.25 – 7.12 (m, 6H), 6.80 (dd, *J* = 8.0, 1.3 Hz, 1H), 6.70 (td, *J* = 7.5, 1.3 Hz, 1H), 4.29 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.73, 138.70, 131.81, 131.20, 129.48, 129.39, 126.34, 118.97, 115.16, 112.88.

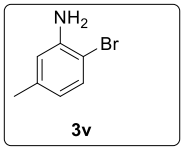
Synthesis of 2-Bromo-4-chloroaniline (2u).[16]



Compound **2u** was synthesized using 1-bromo-2-nitrobenzene (**1u**) following general procedure **C** for 2 h to afford **2u** as a white solid. **2u:** mp = 60 - 62 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (d, *J* = 2.3 Hz, 1H), 7.07 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.69 (d, *J* = 8.6 Hz, 1H), 4.08 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.98, 131.98, 128.49, 123.16, 116.34, 109.28.

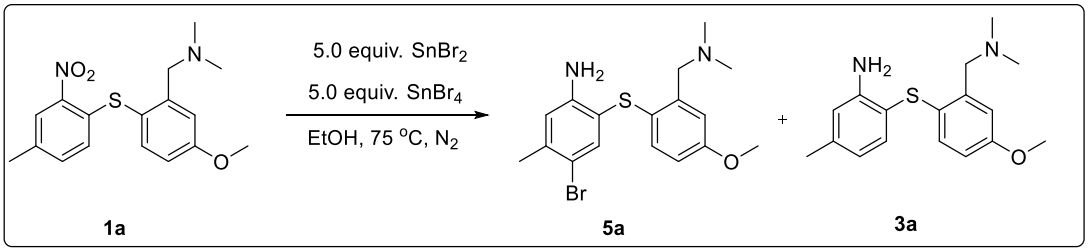
Synthesis of 2-Bromo-4-chloro-5-methylaniline (2v) and 2-Bromo-5-methylaniline (3v).





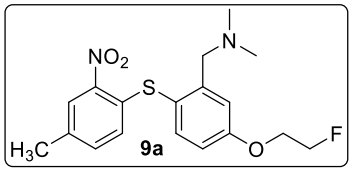
Compounds **2v** & **3v** were synthesized using 1-bromo-4-methyl-2-nitrobenzene (**1v**) following general procedure **C** for 2 h to afford **2v** as a white solid and **3v** as a colorless oil. **2v:** mp = 66 - 68°C;^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (s, 1H), 6.63 (d, *J* = 0.4 Hz, 1H), 3.99 (s, 2H), δ 2.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.71, 136.13, 131.91, 123.52, 117.36, 106.25, 19.76; ESIHRMS calcd. for C_7H_7BrClN $[M+H]^+$, 219.9529; found, 219.9527. **3v:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 0.9 Hz, 1H), 6.59 (d, *J* = 1.2 Hz, 1H), 6.48 – 6.47 (m, 1H), 3.99 (s, 2H), 2.22 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.88, 138.53, 132.35, 120.64, 116.59, 106.28, 21.15.

Synthesis of *N*,*N*-Dimethyl-2-(2-amino-4-methyl-5-bromophenylthio)-5-methoxybenzylamine (5a)



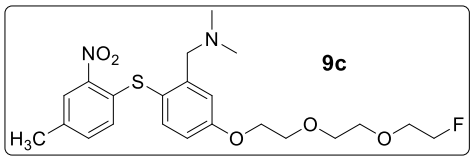
To a solution of compound **1a** (100 mg, 0.30 mmol) in EtOH (15 mL) and 2N HCl (1.5 mL) was added $SnBr_4$ (665 mg, 1.52 mmol) at rt. The reaction mixture was stirred at reflux temperature under N_2 for 0.5 h and $SnBr_2$ (42 mg, 0.15 mmol) was added every 0.5 h for seven times at the same temperature. Then the mixture was evaporated and quenched with water (10 mL). The crude mixture was basified with 10% NaOH to pH > 12, extracted with CH_2Cl_2 (25 mL × 3), IPA/CH_2Cl_2 (1/4, 10 mL × 2), washed with brine, dried over $MgSO_4$ and evaporated. The crude product was chromatographed (silica gel, 1-4% MeOH (with 10% NH_4OH) in CH_2Cl_2) to afford a white oil **3a** (43.5 mg, 48%), **5a** (24.6 mg, 22%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 9H), 3.53 (s, 2H), 3.76 (s, 3H), 6.57 (s, 1H), 6.69 (dd, *J* = 2.9, 8.7 Hz, 1H), 6.83 (d, *J* = 2.8 Hz, 1H), 6.97 (d, *J* = 8.6 Hz, 1H), 7.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8, 45.2, 55.3, 62.4, 111.5, 113.6, 116.1, 116.2, 117.1, 126.7, 131.0, 138.9, 139.1, 139.6, 147.6, 158.2; ESIHRMS calcd for $C_{17}H_{22}BrN_2OS$ $[M+H]^+$ and $C_{17}H_{21}BrN_2NaOS$ $[M+Na]^+$, 381.0636 and 403.0456; found, 381.0650 and 403.0474.

Synthesis of 1-(5-(2-Fluoroethoxy)-2-(4-methyl-2-nitrophenylthio)- phenyl)-*N*,*N*-dimethylmethanamine (9a).



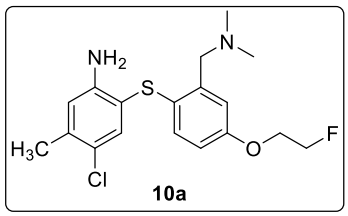
Compound **9a** was synthesized following general procedure A as a yellow oil with 73% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.19 (s, 6H), 2.35 (s, 3H), 3.49 (s, 2H), 4.31 (dt, *J* = 28.0, 4.1 Hz, 2H), 4.80 (dt, *J* = 47.3, 4.1 Hz, 2H), 6.53 (d, *J* = 8.3 Hz, 1H), 6.90 (dd, *J* = 8.5, 2.9 Hz, 1H), 7.12 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.27-7.31 (m, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 8.06 (m, 1H), ^{13}C NMR (50 MHz, $CDCl_3$) 20.5, 45.6 (2C), 61.1, 67.3 (d, *J* = 20.2 Hz), 81.9 (d, *J* = 170.1 Hz), 115.0, 115.9, 121.4, 126.1, 127.6, 134.7, 135.2, 136.6, 138.9, 144.7 146.1, 160.5; ESIHRMS calcd for $C_{18}H_{21}FN_2NaO_3S$ $[M+Na]^+$, 387.1155; found, 387.1141.

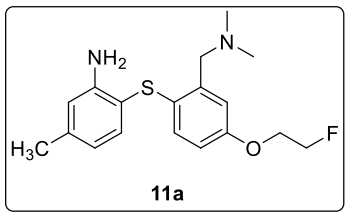
Synthesis of 1-(5-(2-(2-(2-Fluoroethoxy)ethoxy)ethoxy)-2-((4-methyl-2-nitrophenyl)thio) phenyl)-N,N-dimethylmethanamine (9b).



Compound **9b** was synthesized following general procedure A as a yellow oil with 72% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.27 (s, 3H), 2.28 (s, 6H), 3.52 (s, 2H), 3.69-3.73 (m, 5H), 3.77 (m, 1H), 3.83 (t, *J* = 4.8 Hz, 2H), 4.09 (t, *J* = 4.8 Hz, 2H), 4.56 (dt, *J* = 47.7, 4.2 Hz, 2H), 6.56 (s, 1H), 6.70 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.87 (d, *J* = 2.8Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 1H), 7.36 (s, 1H) ; ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.1, 45.4, 45.4, 62.6, 67.7, 69.9, 70.6 (d, *J* = 19.5 Hz), 71.0, 71.0, 83.3 (d, *J* = 168.0 Hz), 114.5, 115.9, 116.9, 117.3, 122.6, 127.1, 131.1, 135.9, 138.1, 139.3, 147.1, 157.6; ESIHRMS calcd for $C_{22}H_{30}ClFN_2NaO_3S$ $[M+Na]^+$, 479.1547; found 479.1547.

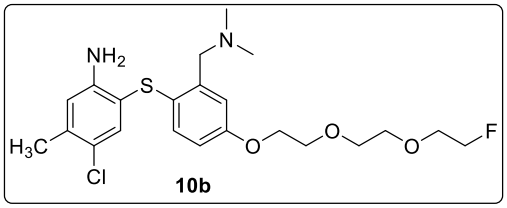
Synthesis of 4-Chloro-2-(2-((dimethylamino)methyl)-4-(2-fluoroethoxy)phenylthio)-5-methyl-benzenamine (10a) and 2-(2-((Dimethylamino)methyl)-4-(2-fluoroethoxy)phenyl-thio)-5-methyl- benzenamine (11a)



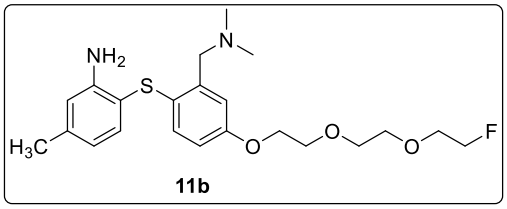


Compound **10a & 11a** were synthesized using 1-(5-(2-fluoroethoxy)-2-(4-methyl-2-nitrophenylthio)- phenyl)-*N*,*N*-dimethylmethanamine (**9a**) following general procedure C as color loss oil **10a** and color loss oil **11a** with 18% and 36% yield, respectively. **10a:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.28 (s, 3H), 2.29 (s, 6H), 3.52 (s, 2H), 4.17 (dt, *J* = 27.7, 4.2 Hz, 2H), 4.51 (bs, 2H), 4.72 (dt, *J* = 47.4, 4.2 Hz, 2H), 6.57 (s, 1H), 6.70 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.89 (d, *J* = 2.8 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 1H), 7.37 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.1, 45.4, 62.5, 67.4 (d, *J* = 21.0 Hz), 82.0 (d, *J* = 169.5 Hz), 114.4, 115.7, 116.9, 117.3, 122.7, 127.7, 131.0, 136.0, 138.2, 139.4, 147.2, 157.2; ESIHRMS calcd for $C_{18}H_{23}ClFN_2OS$ $[M+H]^+$,369.1204; found, 369.1218. **11a:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 3H), 2.30 (s, 6H), 3.54 (s, 2H), 4.16 (dt, *J* = 28.0, 4.1 Hz, 2H), 4.34 (bs, 2H), 4.71 (dt, *J* = 47.4, 4.1 Hz, 2H), 6.53-6.55 (m, 2H), 6.67 (dd, *J* = 8.6, 3.0 Hz, 1H), 6.87-6.90 (m, 2H), 7.30 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 45.5, 62.4, 67.3 (d, *J* = 20.0 Hz), 82.0 (d, *J* = 170.0 Hz), 113.3, 114.3, 116.0, 116.6, 119.6, 128.7, 129.9, 136.9, 138.8, 140.9, 148.6, 156.8; ESIHRMS calcd for $C_{18}H_{24}FN_2OS$ $[M+H]^+$, 335.1593; found, 335.1593.

Synthesis of 4-Chloro-2-(2-((dimethylamino)- methyl)-4-(2-(2-(2-fluoroethoxy)ethoxy)-ethoxy)phenylthio)-5-methyl- benzenamine (10b) and 2-(2-((Dimethylamino)methyl)-4-(2-(2-(2-fluoroethoxy)ethoxy)ethoxy)-phenylthio)-5-methylbenzenamine (11b).



10b



11b

Compound **10b & 11b** were synthesized using 1-(5-(2-(2-(2-fluoroethoxy)ethoxy)ethoxy)-2-((4-methyl-2-nitrophenyl)thio) phenyl)-N,N-dimethylmethanamine (**9c**) following general procedure C as color loss oil **10b** and color loss oil **11b** with 16% and 33% yield, respectively. **10b:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.27 (s, 3H), 2.28 (s, 6H), 3.52 (s, 2H), 3.69-3.73 (m, 5H), 3.77 (m, 1H), 3.83 (t, *J* = 4.8 Hz, 2H), 4.09 (t, *J* = 4.8 Hz, 2H), 4.56 (dt, *J* = 47.7, 4.2 Hz, 2H), 6.56 (s, 1H), 6.70 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.87 (d, *J* = 2.8Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 1H), 7.36 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) 20.1, 45.4, 45.4, 62.6, 67.7, 69.9, 70.6 (d, *J* = 19.5 Hz), 71.0, 71.0, 83.3 (d, *J* = 168.0 Hz), 114.5, 115.9, 116.9, 117.3, 122.6, 127.1, 131.1, 135.9, 138.1, 139.3, 147.1, 157.6; ESIHRMS calcd for $C_{22}H_{30}ClFN_2NaO_3S$ $[M+Na]^+$, 479.1547; found 479.1547. **11b:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 2.29 (s, 6H), 3.53 (s, 2H), 3.64-3.73 (m, 5H), 3.80-3.85 (m, 3H), 4.06-4.10 (m, 2H), 4.55 (dt, *J* = 47.7, 4.2 Hz, 2H), 6.52-6.54 (m, 2H), 6.67 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.87-6.89 (m, 2H), 7.30 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 45.4, 45.4, 62.4, 67.6, 69.9, 70.6 (d, *J* = 19.0 Hz), 71.0, 71.0, 83.3 (d, *J* = 168.0 Hz), 113.5, 114.4, 116.0, 116.7, 119.6, 128.1, 130.0, 136.8, 138.7 140.8, 148.4, 157.2; ESIHRMS calcd for $C_{22}H_{32}FN_2O_3S$ $[M+H]^+$, 423.2118; found, 423.2116.

4. References

1. a) Kumar, A.; Bhakuni, B. S.; Prasad, C. D.; Kumar, S.; Kumar, S. Potassium tert-butoxide-mediated synthesis of unsymmetrical diaryl ethers, sulfides, and selenides from aryl bromides. *Tetrahedron* **2013**, *69*, 5383-5392. b) Y.-Y. Huang, L.-T. Chang, H.-Y. Shen, Y.-H. Chen, K.-Y. Tzen, C.-Y. Shiue, L.-W. Hsin, *Bioorg. Chem.,* **2020**, *97*, 103654.

2. Yuan, H.; Beard, R. L.; Liu, X. X.; Donello, J. E.; Viswanath, V.; Garst, M. E. Benzofuran-2-sulfonamides derivatives as chemokine receptor modulators. *US20130231338 A1*, Sep 5, **2013**.

3. Crosignani, S.; Prêtre, A.; Jorand-Lebrun, C.; Fraboulet, G.; Seenisamy, J.; Augustine, J. K.; Missotten, M., Humbert, Y.; Cleva, C.; Abla, N.; Daff, H.; Schott, O.; Schneider, M.; Burgat-Charvillon, F.; Rivron, D.; Hamernig, I.; Arrighi,J. F.; Gaudet, M.; Zimmerli, S. C.; Juillard, P.; Johnson, Z. Discovery of potent, selective, and orally bioavailable alkynylphenoxyacetic acid CRTH2 (DP2) receptor antagonists for the treatment of allergic inflammatory diseases. *J. Med. Chem*. **2011**, *54*, 7299–7317.

4. Zienkiewicz, J.; Kaszynski, P. Fused-ring thiadiazines: preparation and crystallographic characterization of 3-phenyl derivative of benzo-, pyridio[2,3-*e*]-pyrazino[2,3-*e*]-, and tetrafluorobenzo-[1,2,4]thiadiazines. *J. Org. Chem*. **2004**, *69*, 2551-2561.

5. Otsubo, K.; Ochi, Y.; Nakai, M.; Mori, A. Quinolone compound and pharmaceutical composition. *WO2008150029 A1*, Dec 11, **2008**.

6. Wassmundt, F. W.; Pedemonte, R. P. An improved synthesis of dibenzofurans by a free-radical. *J. Org. Chem*. **1996**, *60*, 4991-4994.

7. Wang, M.; Gao, M.; Hutchins, G. D.; Zheng Q. H. Synthesis of [^{11}C]FEDAA1106 as a new PET imaging probe of peripheral benzodiazepine receptor expression. *E*ur. *J. Med. Chem*. **2009**, *44*, 2748–2753.

8. Bonnet, B.; Soullez, D.; Davioud-Charvet, E.; Landry, V.; Horvath, D.; Sergheraert, C.; New spermine and spermidine derivatives as potent inhibitors of *Trypanosoma cruzi* trypanothione reductase. *Bioorg. Med. Chem*. **1997**, *7*, 1249-1256.

9. Liu, C.; Zang, X.; Yu, B.; Yu, X.; Xu, Q. An eficient synthesis of unsymmetrical daiaryl thionethers. *Synlett*. **2011**, *8*, 1143–1148.

10. Moore, G. G. I.; Kenneth, H. J. Werkwijze ter bereiding van een herbicide verbinding. *DE2118190 A1*, Mar 9, **1972**.

11. Khalfina, I. A.; Rogozhnikova, O. Y.; Vlasov, V. M. Nucleophilic substitution of nitro group in 3,5-dinitrobenzotrifluoride. *Russ. J. Org. Chem.* **1996**, *32*, 1325-1331.

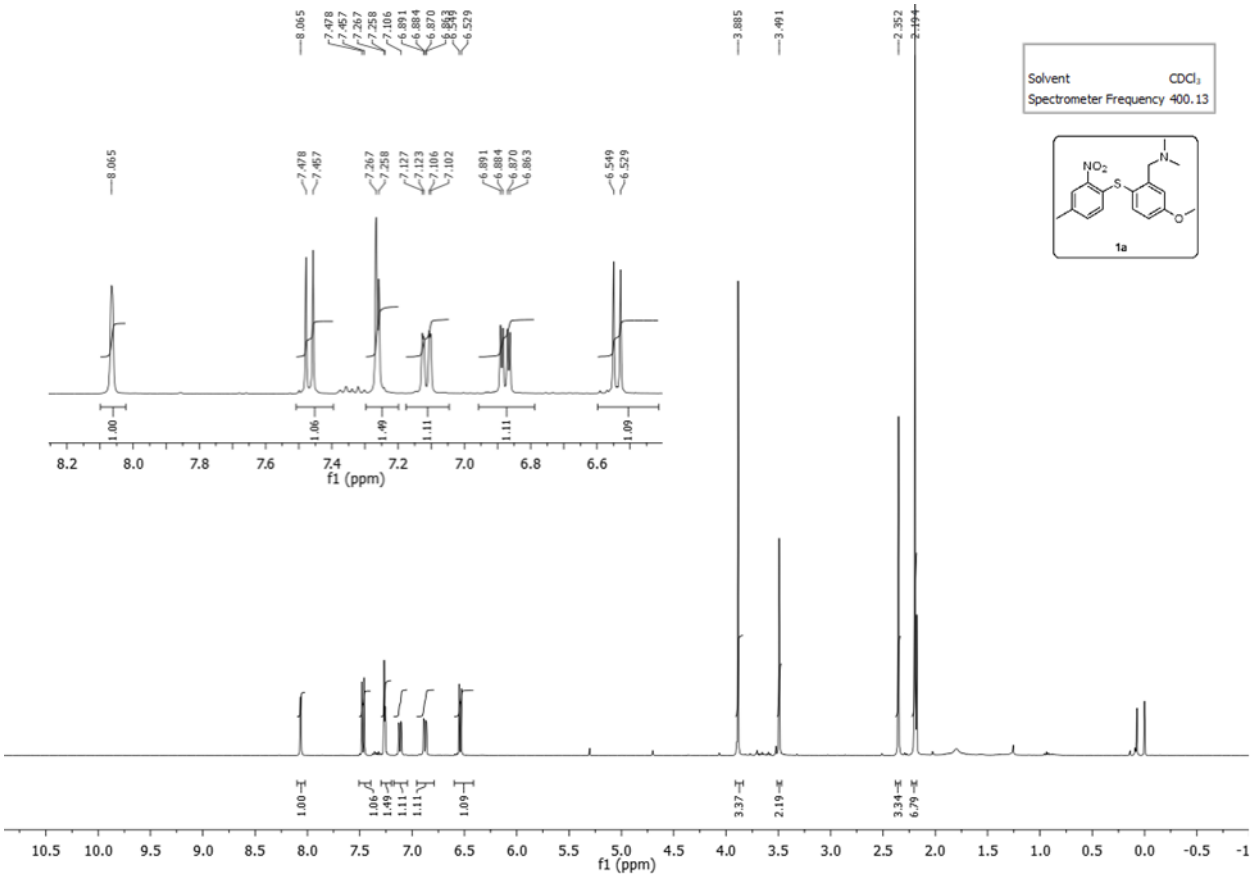
12. Itoh, T.; Mase, T. A general palladium-catalyzed coupling of aryl bromides/triflates and thiols. *Org. Lett.* **2004**, *6*, 4587-4590.

13. Pelz, K., Ernest, I.; Adlerová, E.; Metyšová J.; Protiva M. Neurotrope und psychotrope substanzen XXII. Weitere chlorderivate des 10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepins und einige verwandte stoffe. *Collect. Czech. Chem. Commun*. **1968**, *33*, 1852-1872.

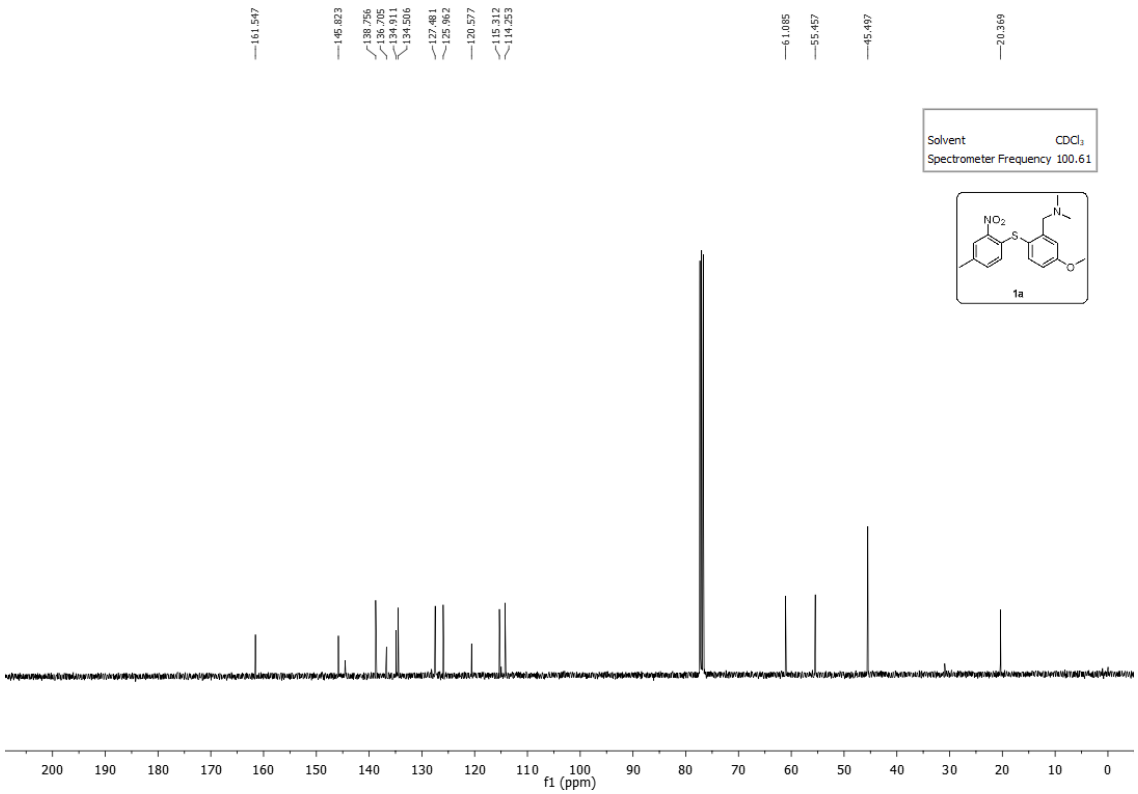
14. H. Tian, H. Yang, C. Zhu and H. Fu, Arylthiolation of Arylamine Derivatives with (Arylthio)-pyrrolidine-2,5-diones. *Adv. Synth. Catal.*, 2015, **357**, 481-488.

15. J. Rodrigues, S. Saba, A. C. Joussef, J. Rafique and A. L. Braga, KIO_3-Catalyzed C(sp^2)-H Bond Selenylation/Sulfenylation of (Hetero)arenes: Synthesis of Chalcogenated (Hetero)arenes and their Evaluation for Anti-Alzheimer Activity. *Asian J. Org. Chem.*, 2018, **7**, 1819-1824.

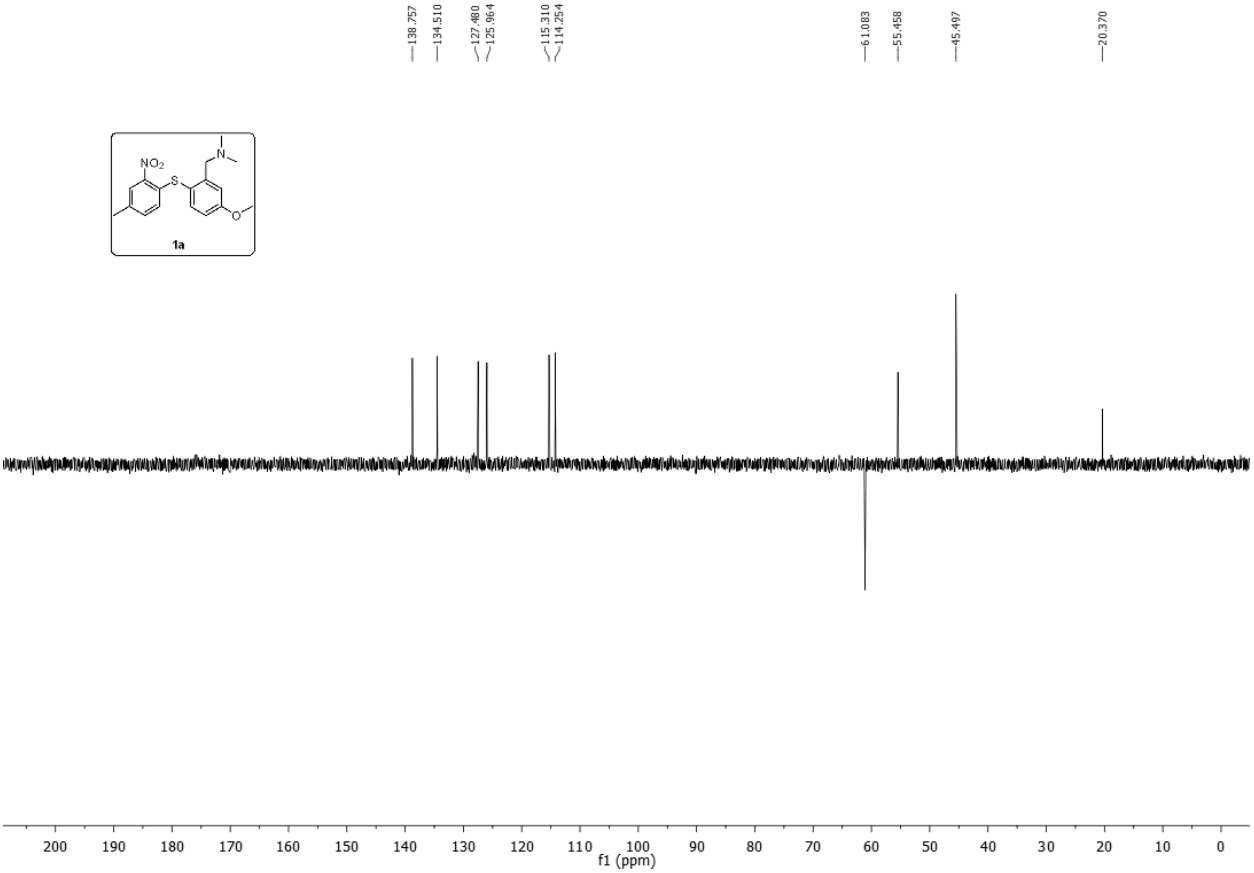
16. A. A. Ageshina, G. A. Chesnokov, M. A. Topchiy, I. V. Alabugin, M. S. Nechaev and A. F. Asachenko, Making endo-cyclizations favorable again: a conceptually new synthetic approach to benzotriazoles via azide group directed lithiation/cyclization of 2-azidoaryl bromides. *Org. Biomol. Chem.*, 2019, **17**, 4523-4534.



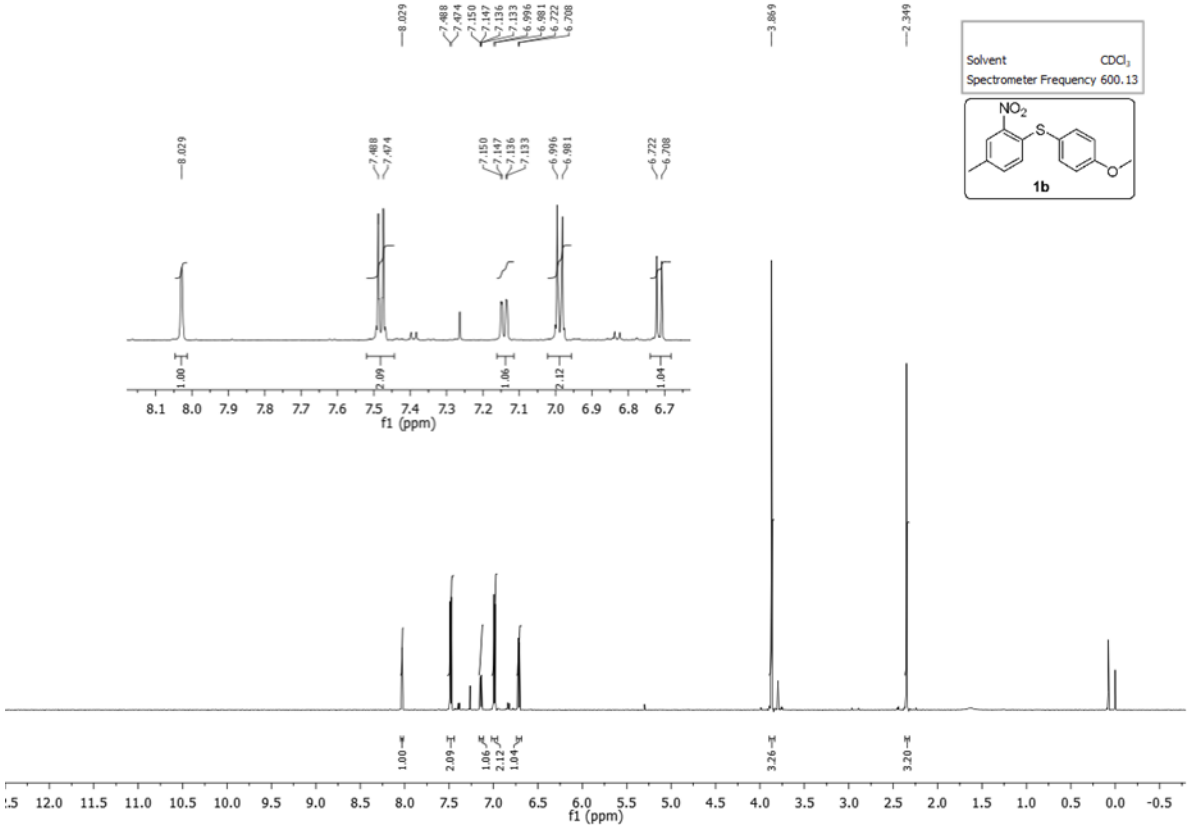
Compound **1a**, ^{1}H-NMR, 100MHz, $CDCl_3$



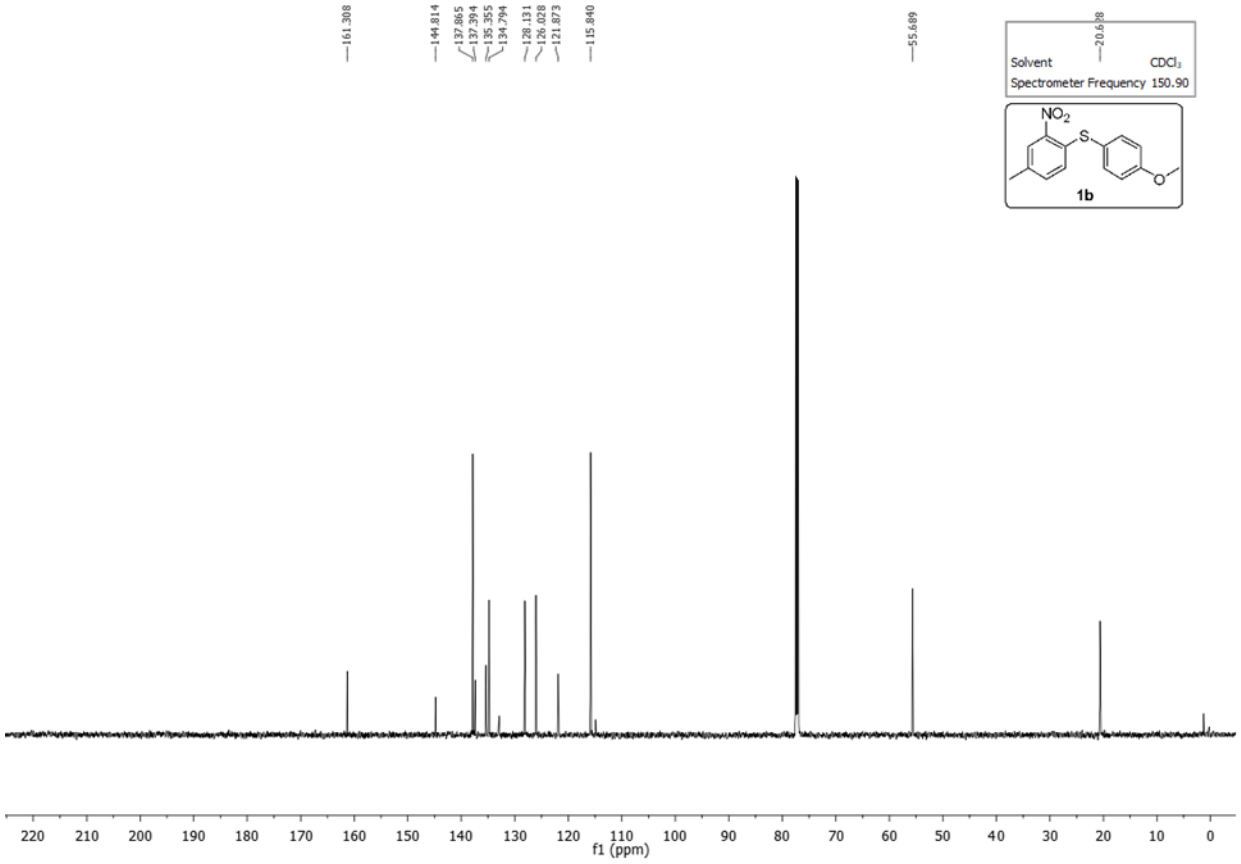
Compound **1a**, ^{13}C-NMR, 100MHz, $CDCl_3$



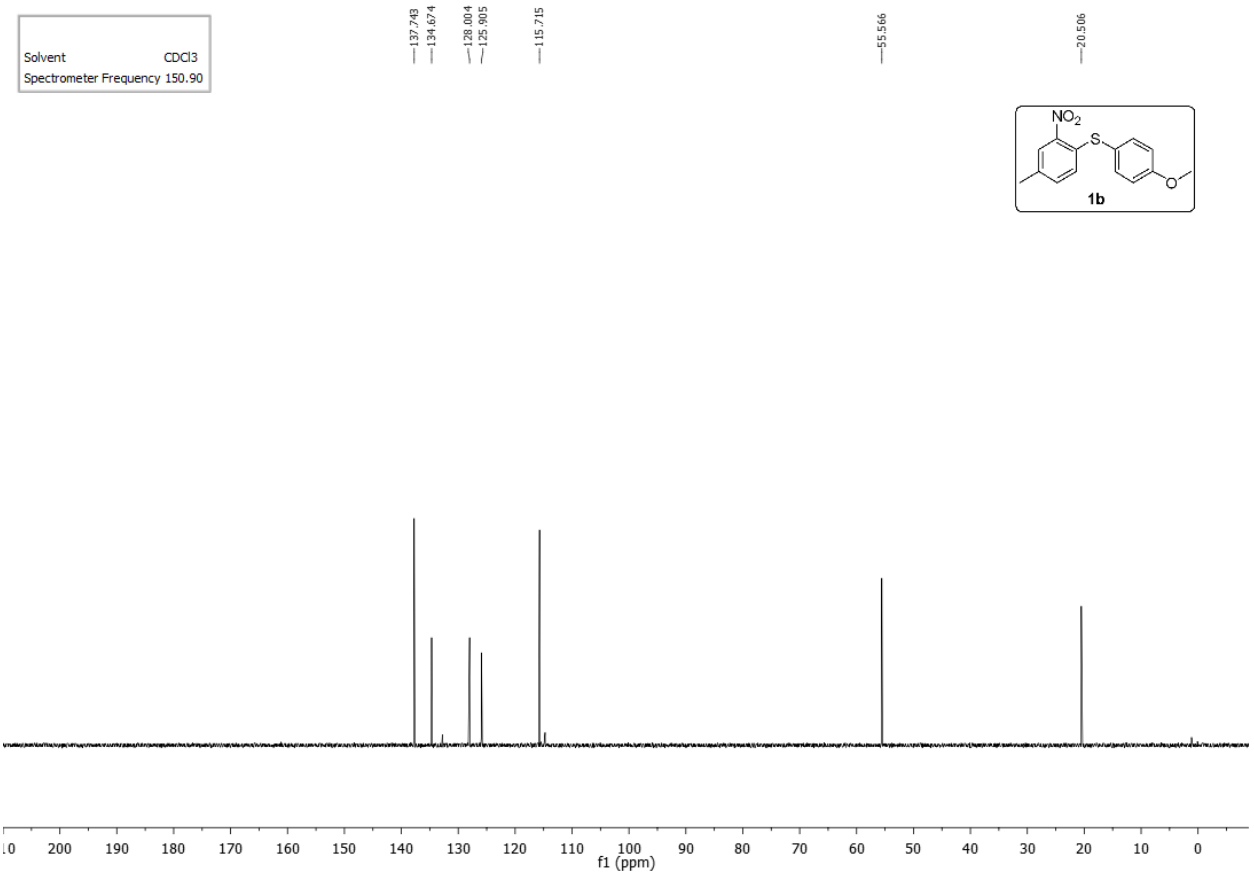
Compound **1a**, Dept135, 100MHz, $CDCl_3$



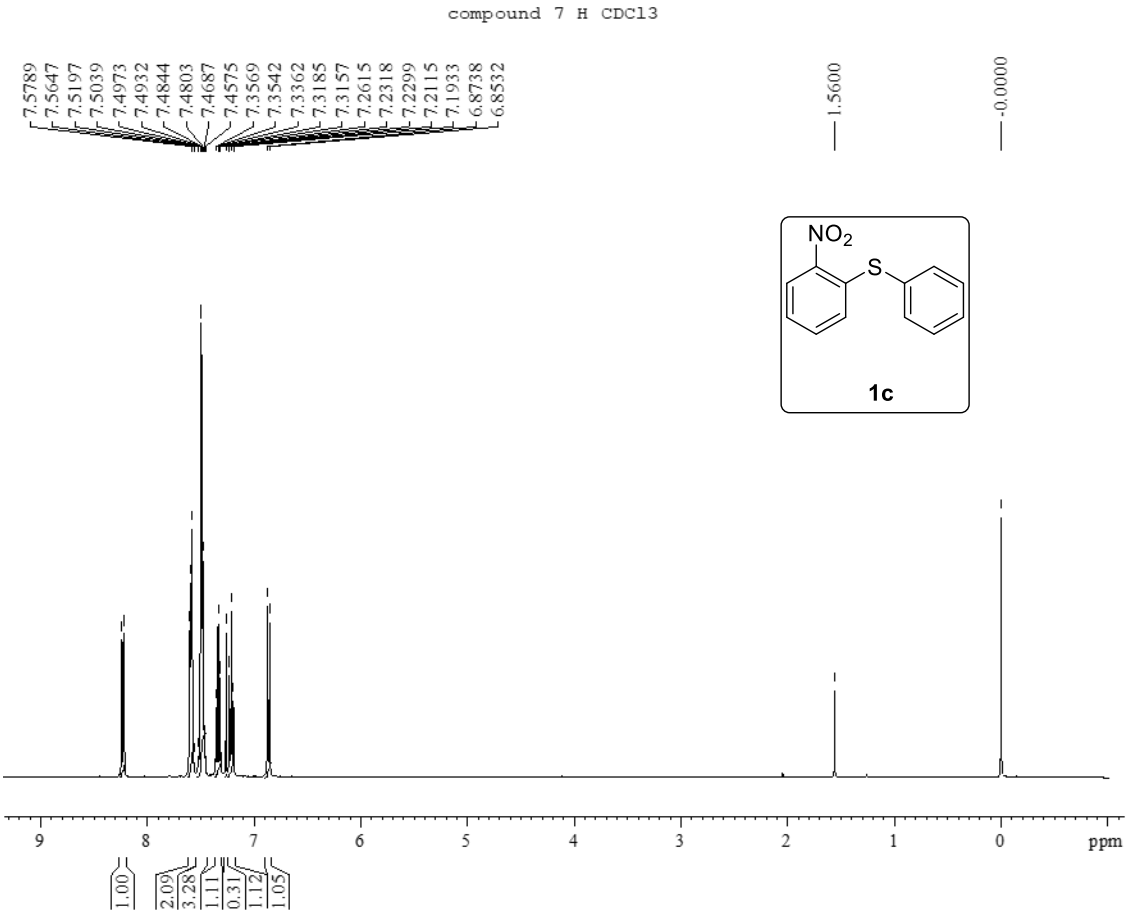
Compound **1b**, ^{1}H-NMR, 600MHz, $CDCl_3$



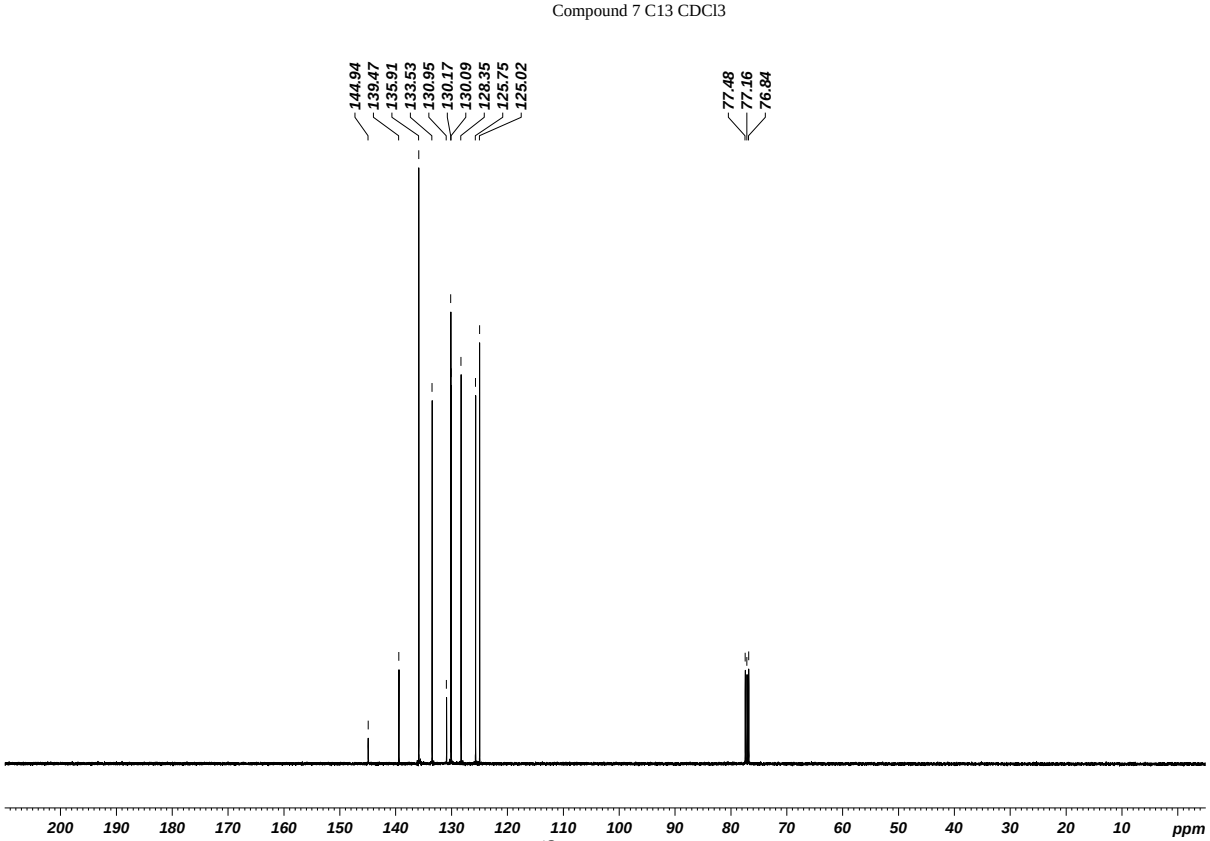
Compound **1b**, ^{13}C-NMR, 600MHz, $CDCl_3$



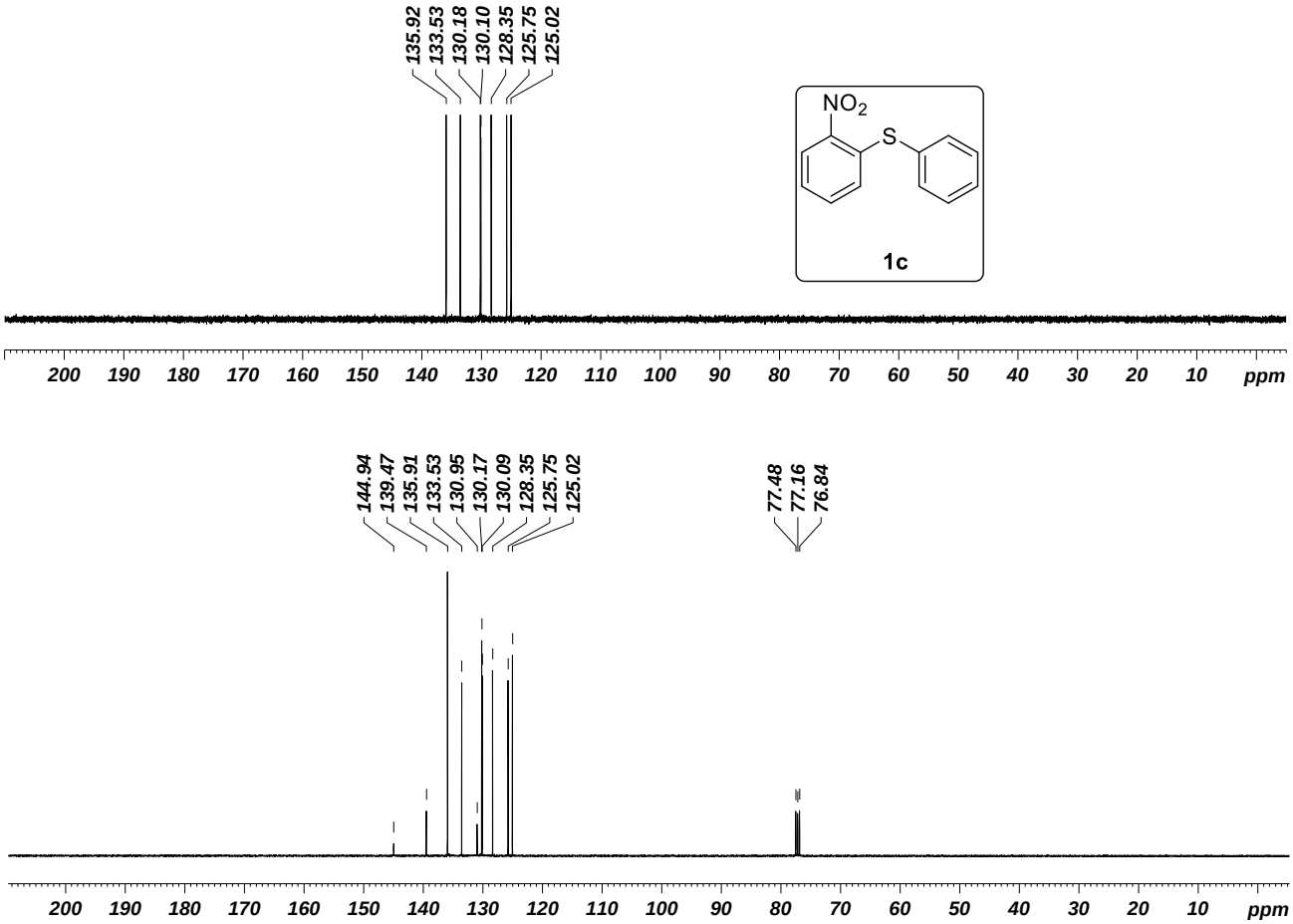
Compound **1b**, Dept135, ^{13}C-NMR, 155 MHz, $CDCl_3$



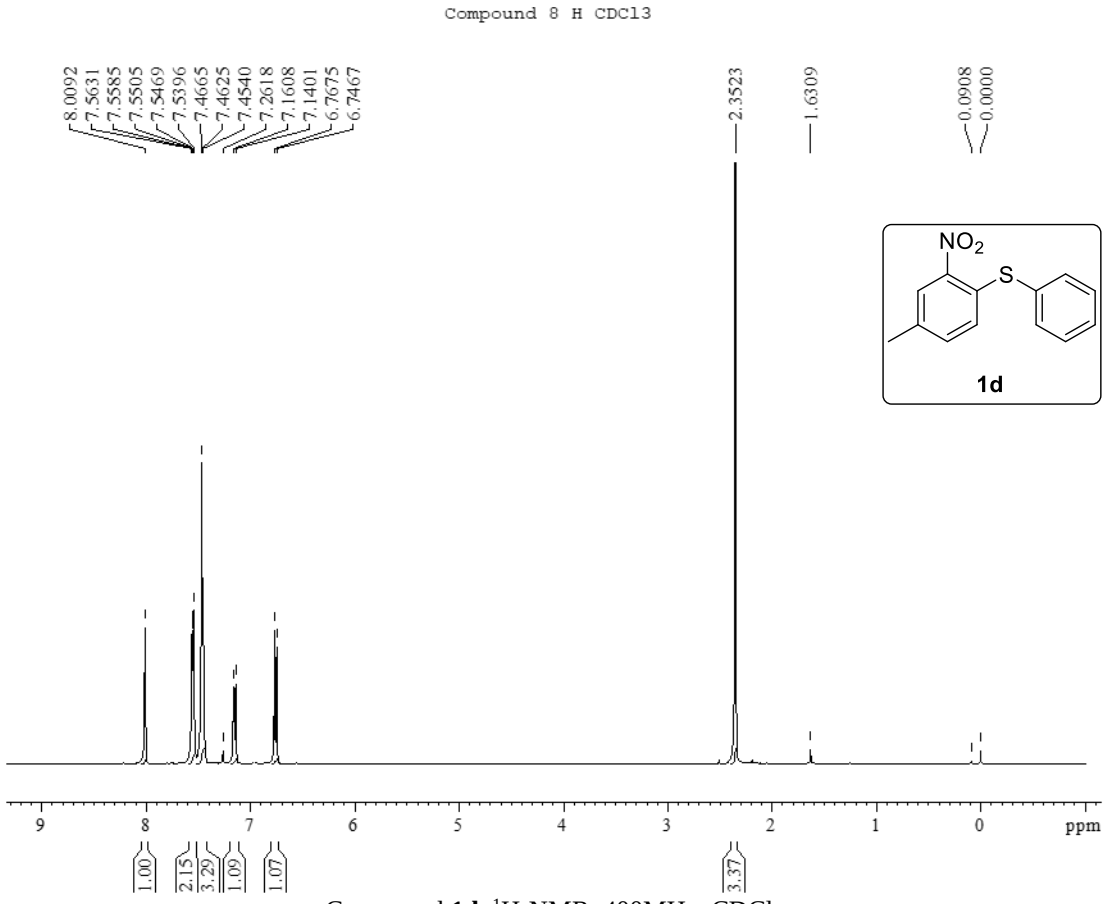
Compound **1c**, ^{1}H-NMR, 400MHz, $CDCl_3$



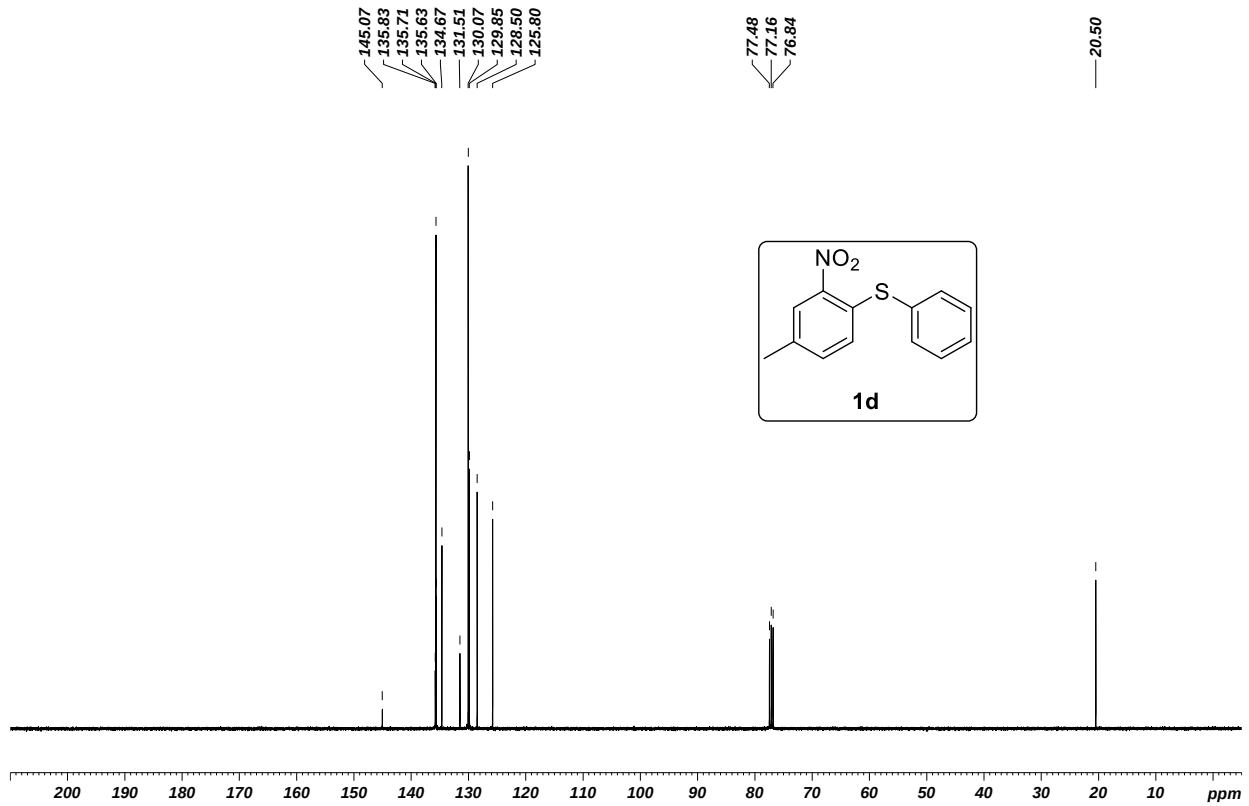
Compound **1c**, ^{13}C-NMR, 100MHz, $CDCl_3$



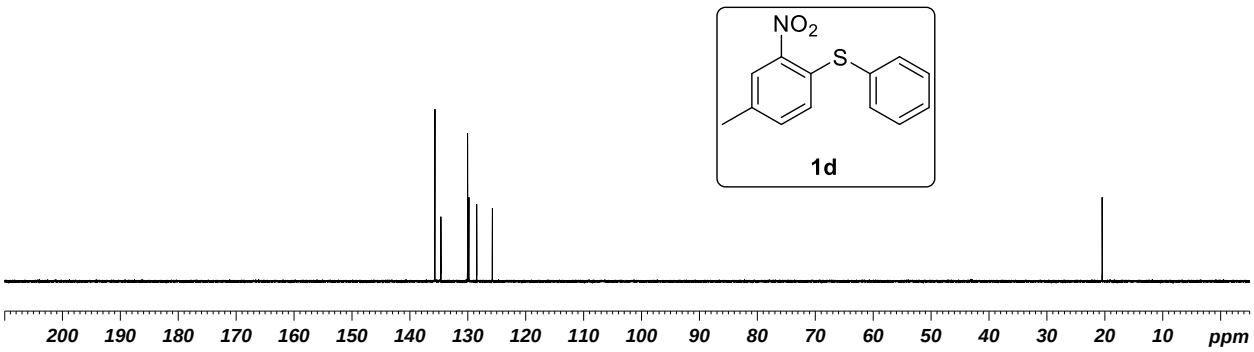
Compound **1c**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$

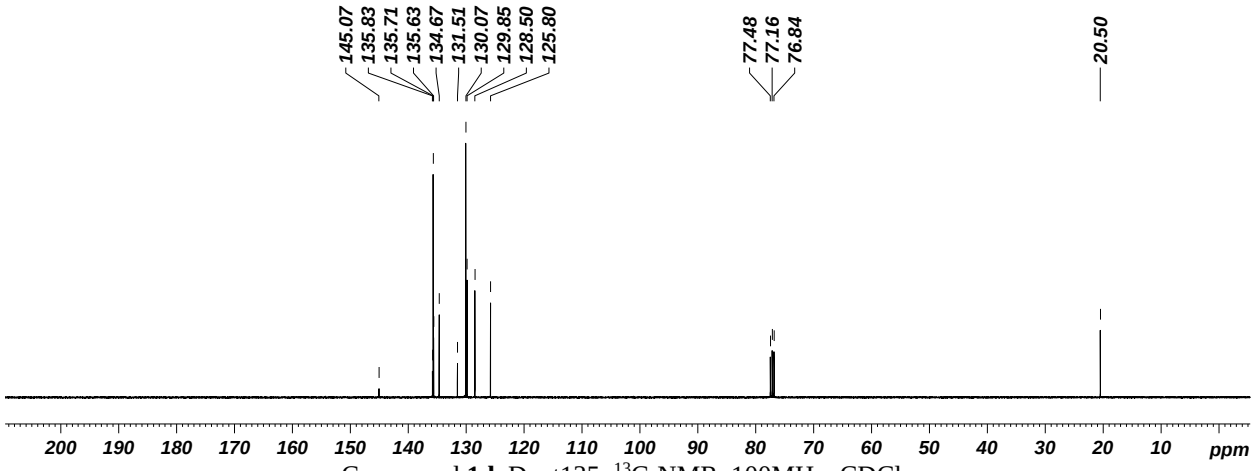


Compound **1d**, ^{1}H-NMR, 400MHz, $CDCl_3$

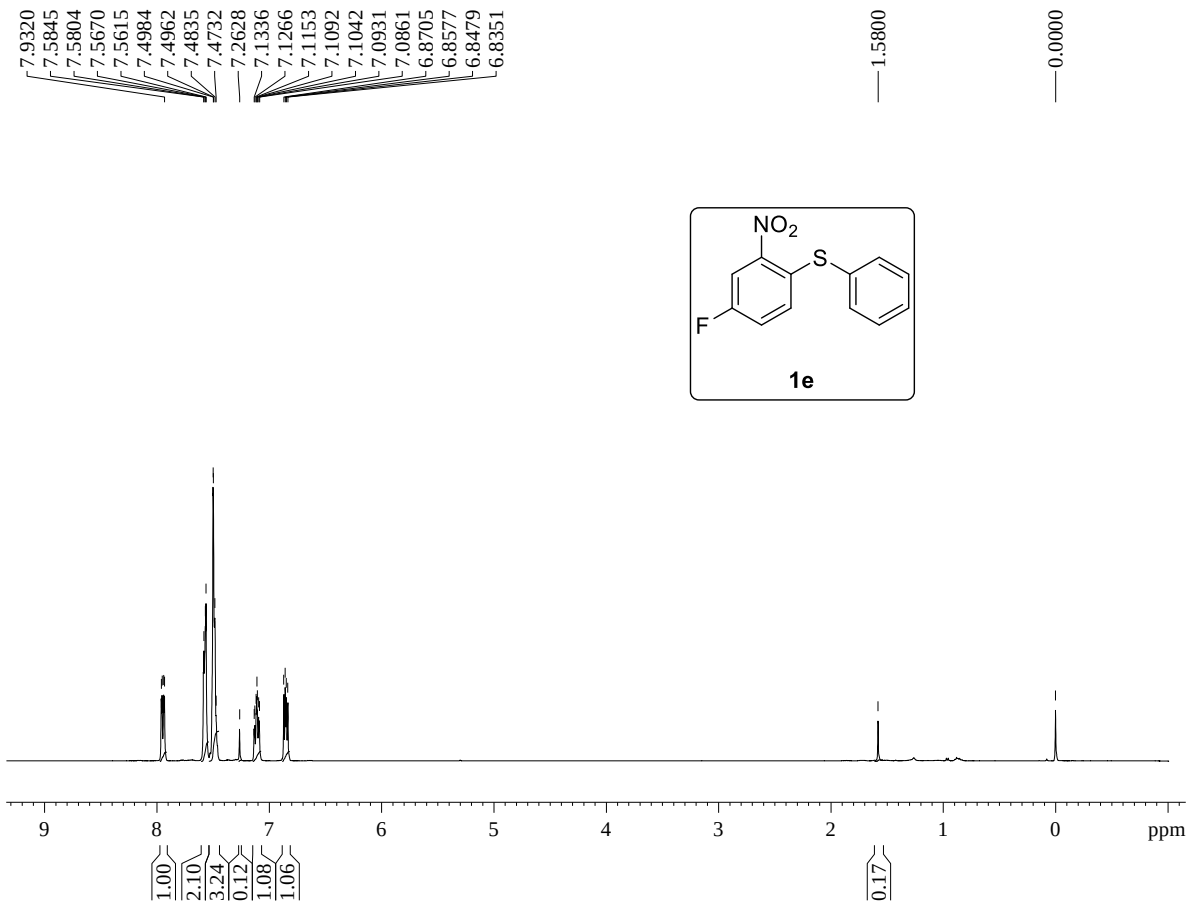


Compound **1d**, ^{13}C-NMR, 100MHz, $CDCl_3$

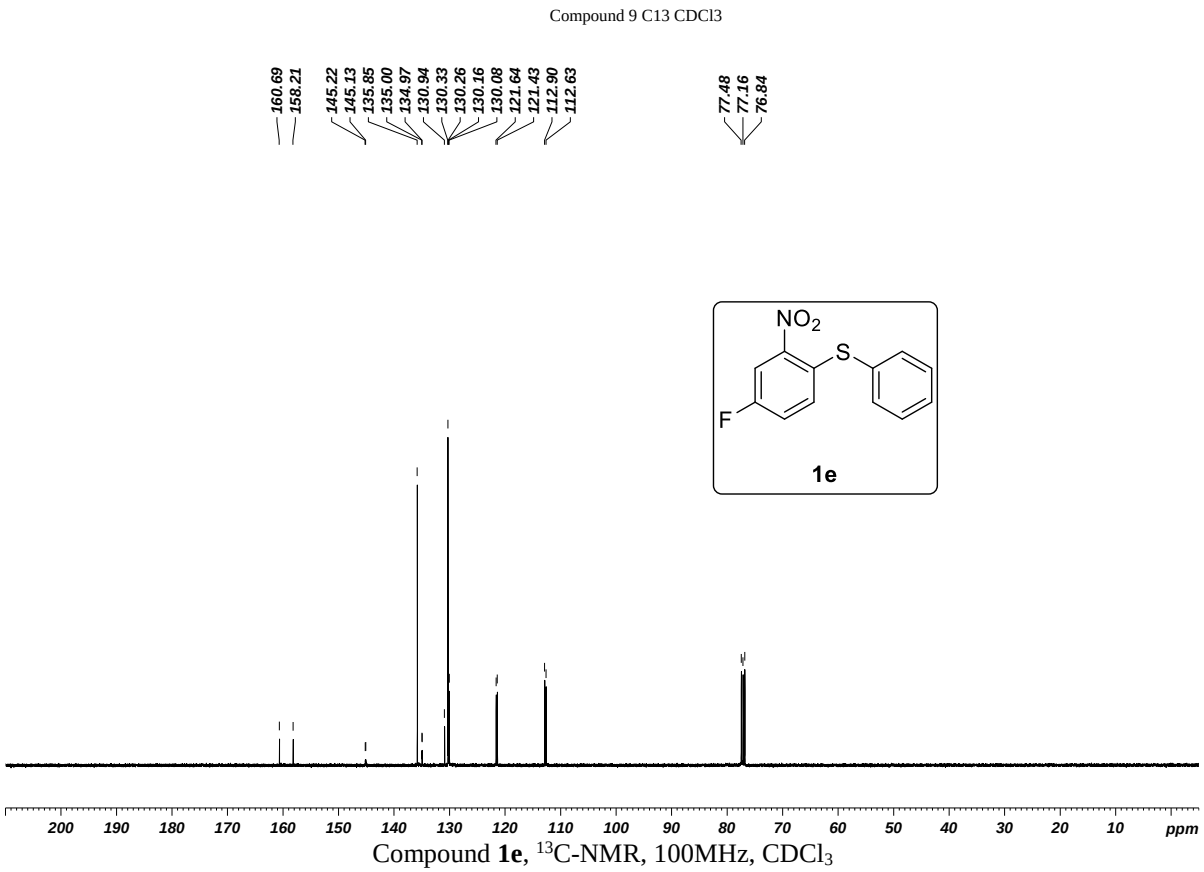




Compound **1d**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$

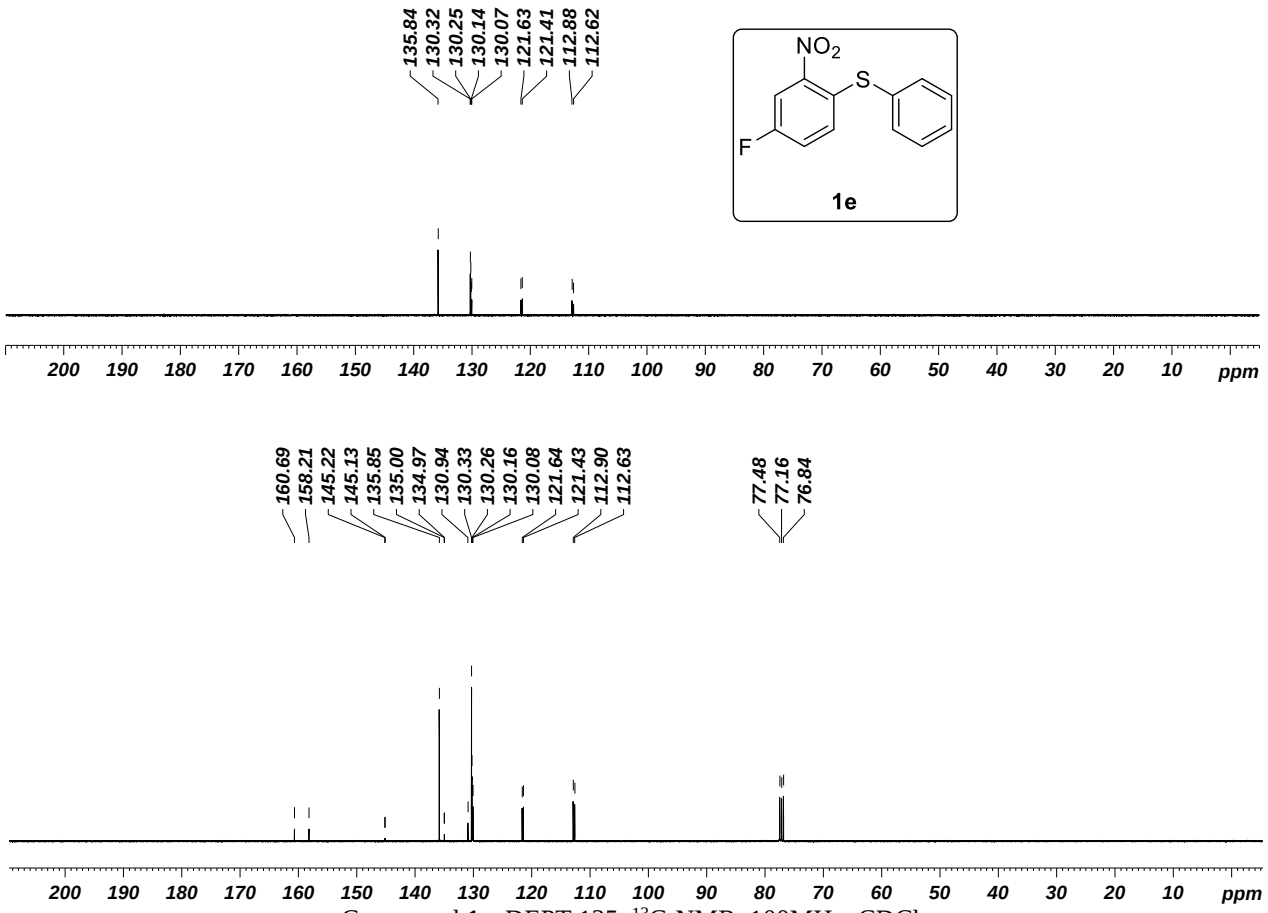


Compound **1e**, ^{1}H-NMR, 400MHz, $CDCl_3$

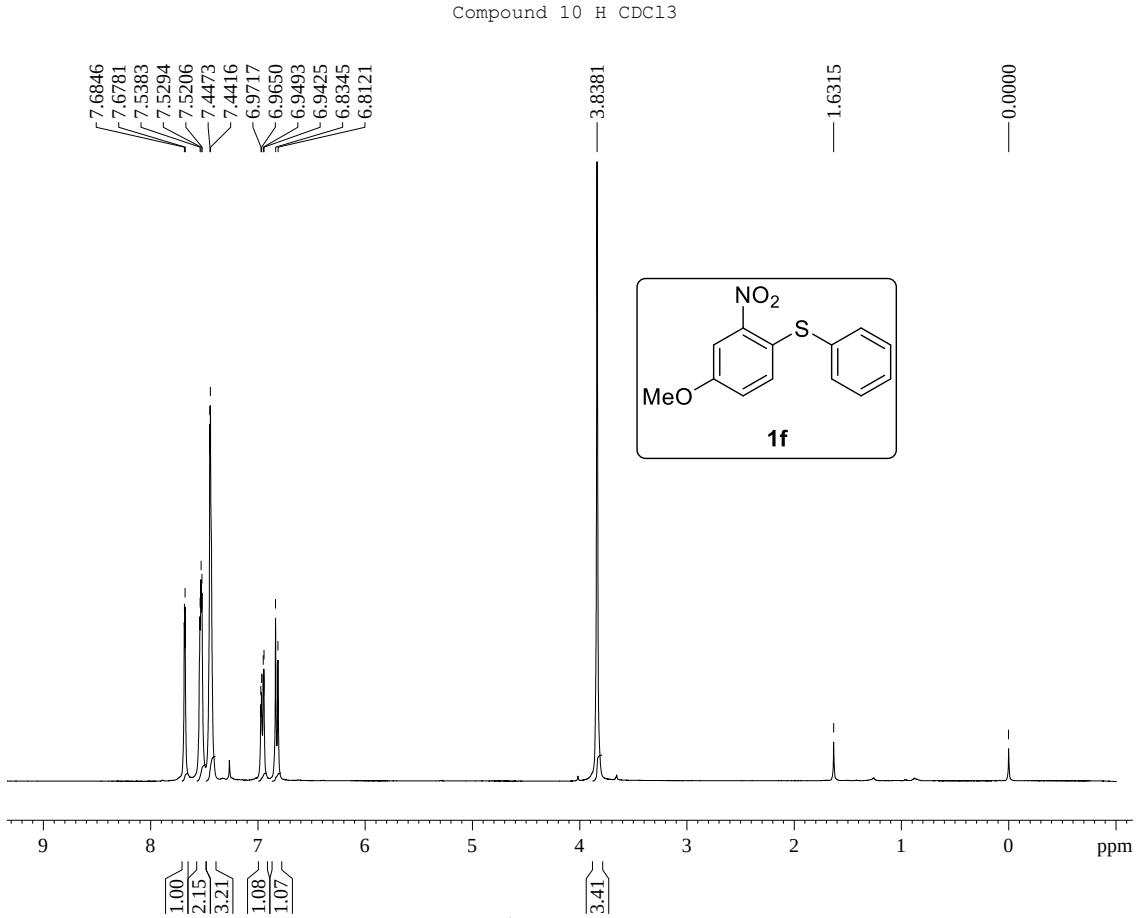


Compound **1e**, ^{13}C-NMR, 100MHz, $CDCl_3$

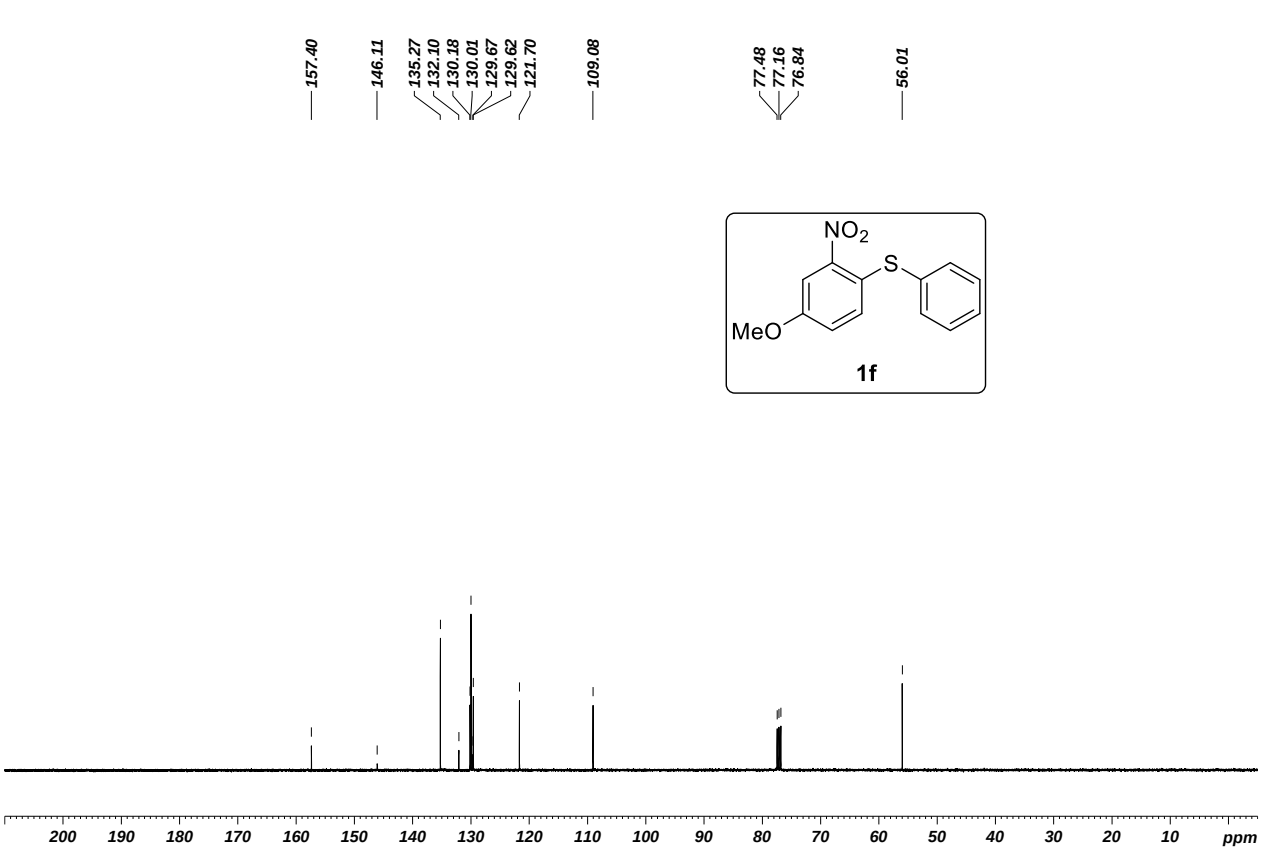
Compound 9 DEPT135 CDCl3



Compound **1e,** DEPT 135, ^{13}C-NMR, 100MHz, $CDCl_3$

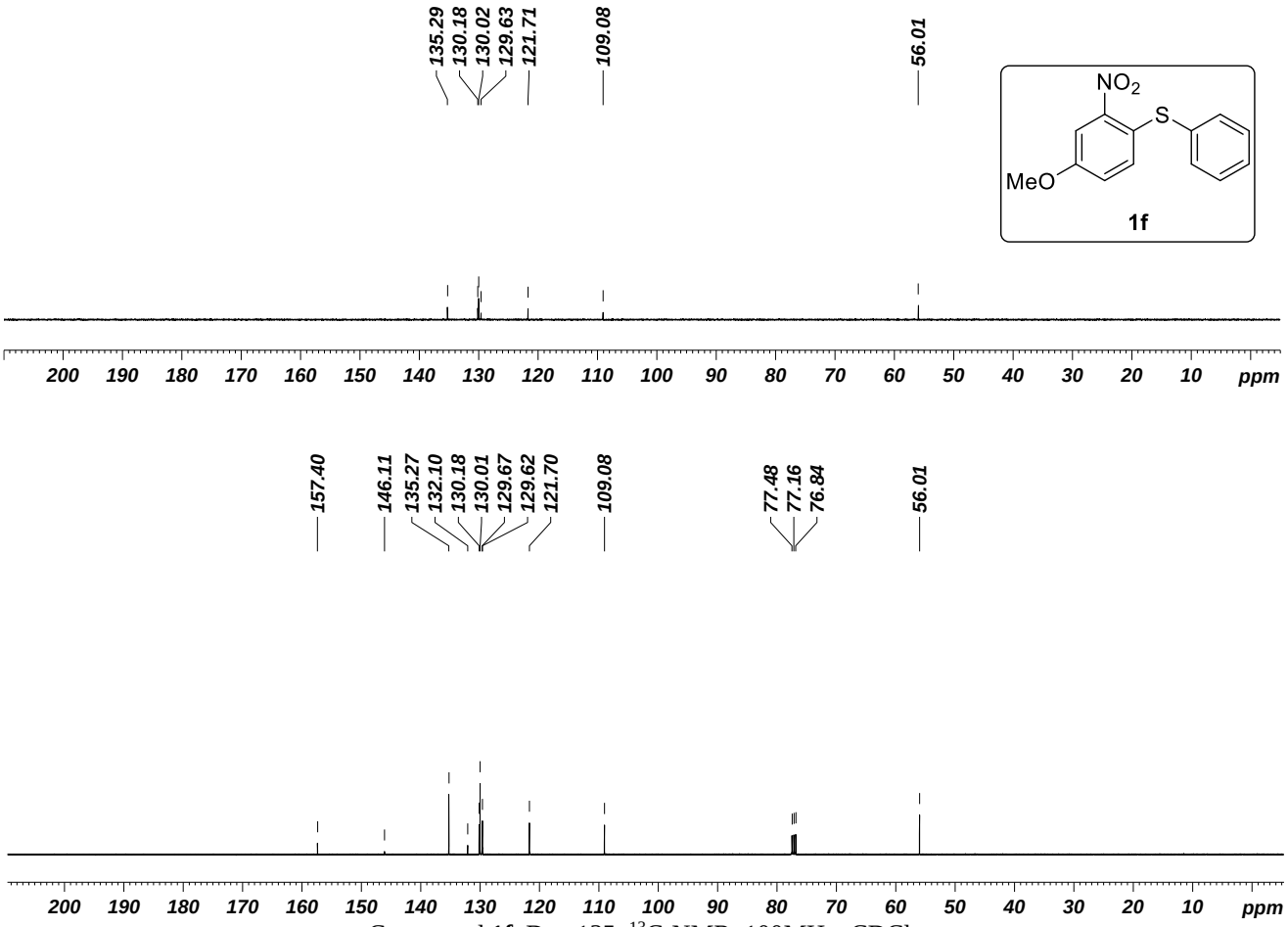


Compound **1f**, ^{1}H-NMR, 400MHz, $CDCl_3$

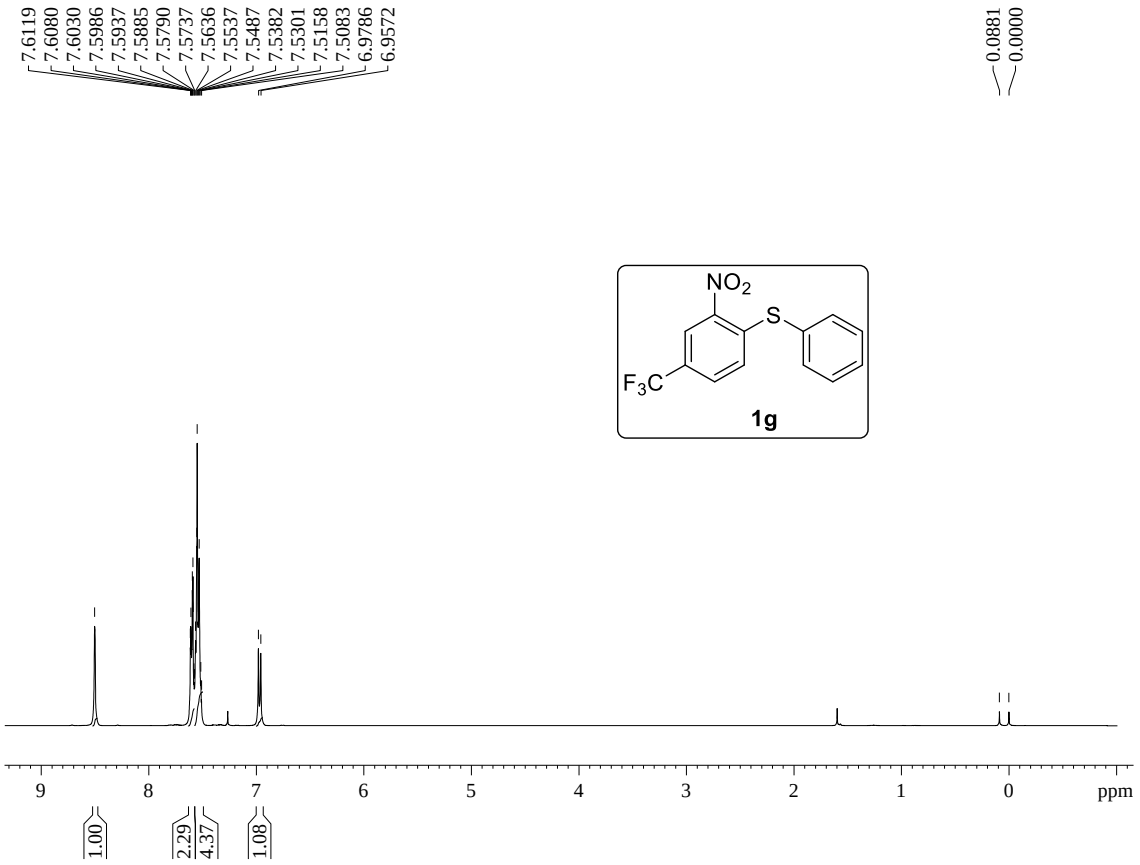


Compound **1f**, ^{13}C-NMR, 100MHz, $CDCl_3$

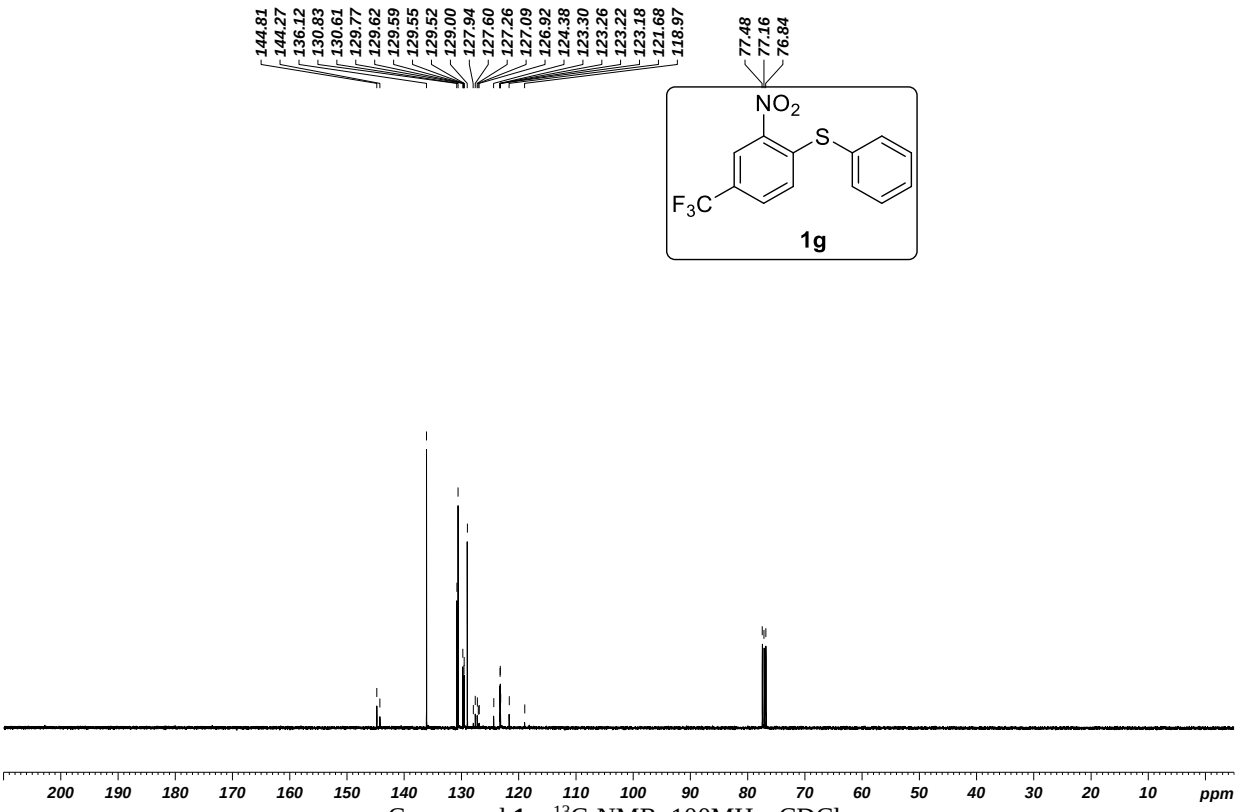
Compound 10 DEPT135 CDCl3



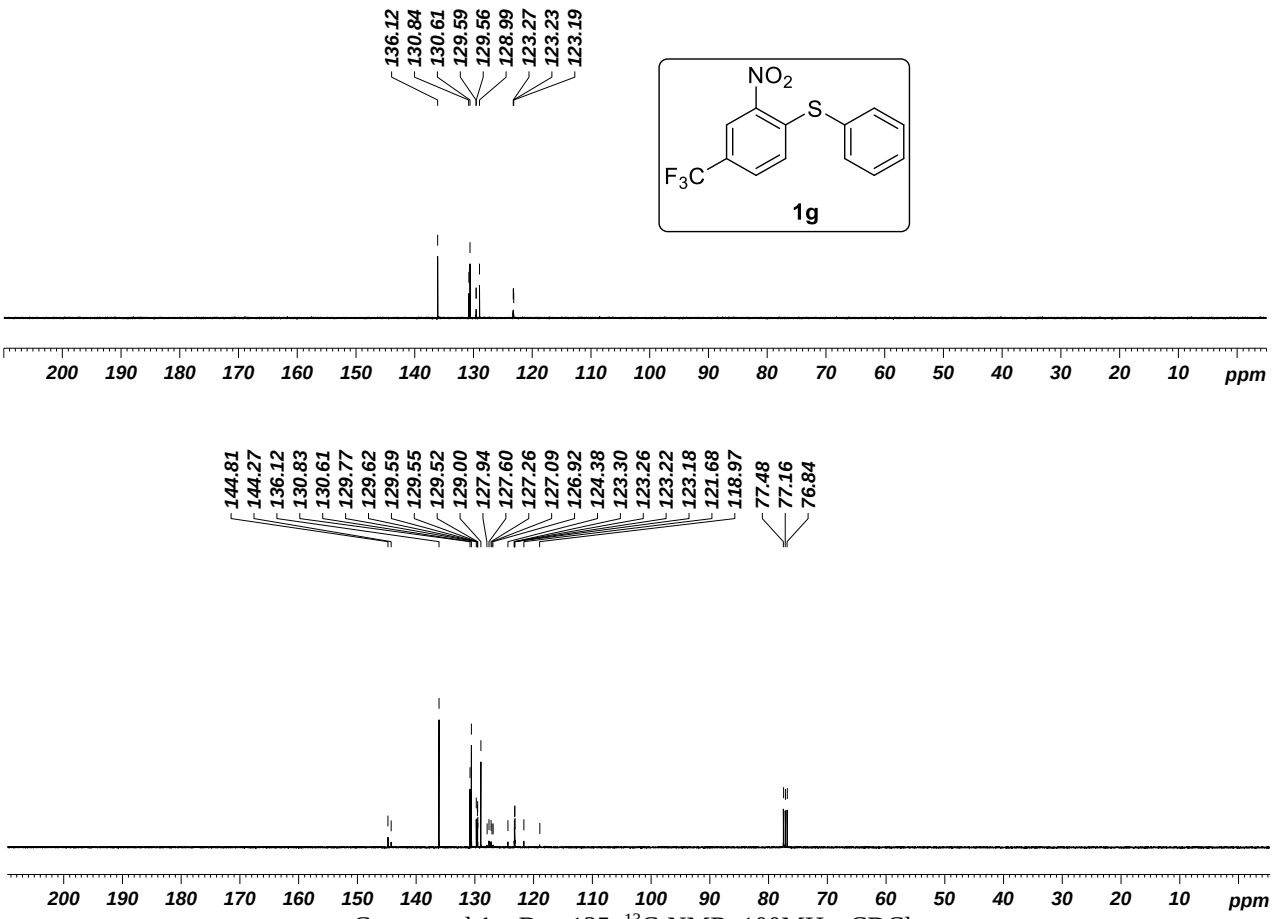
Compound **1f**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$



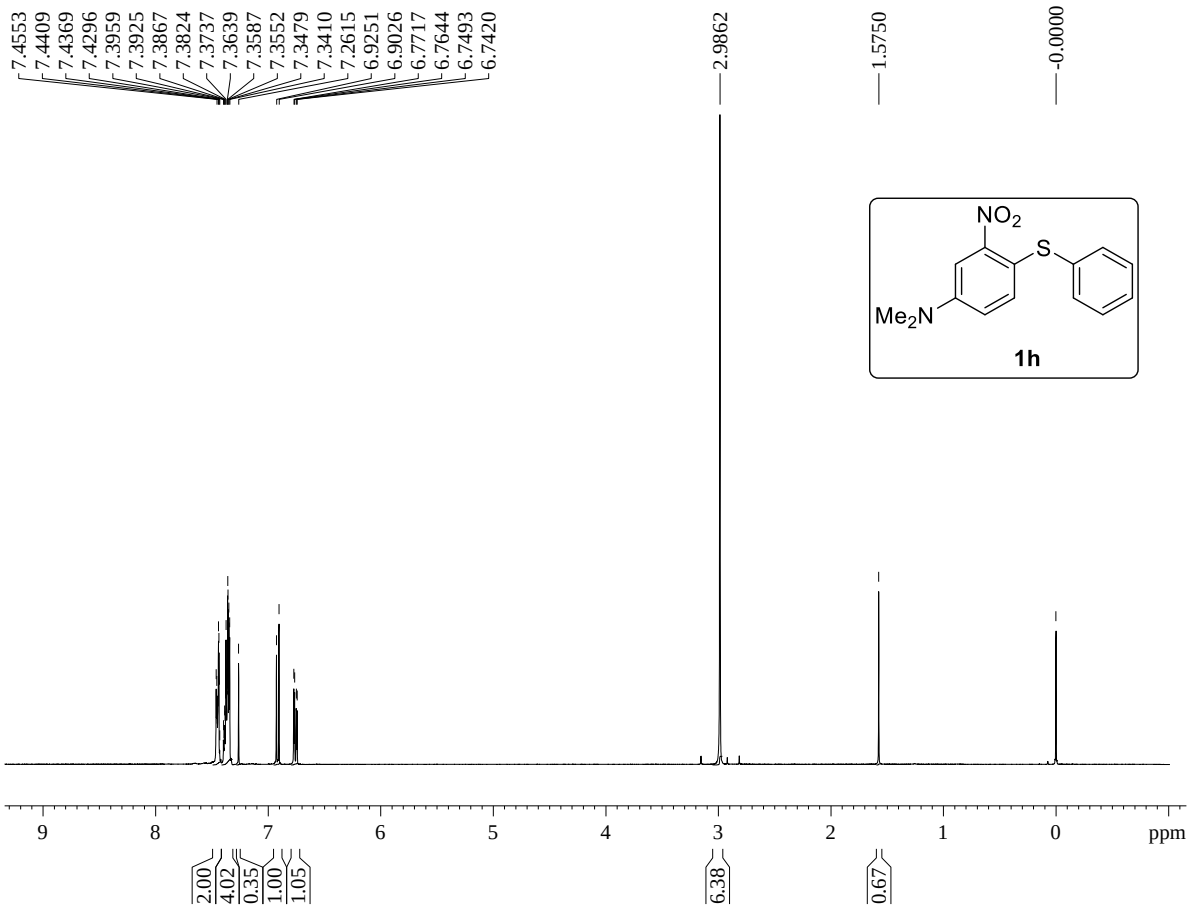
Compound **1g**, ^{1}H-NMR, 400MHz, $CDCl_3$



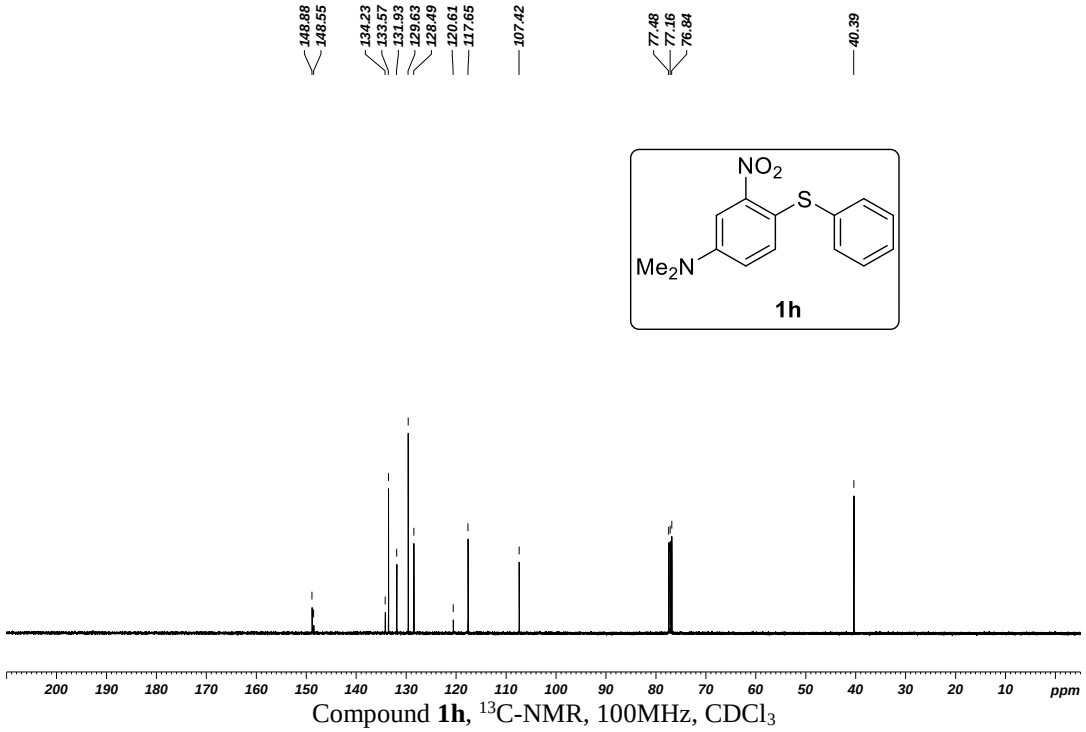
Compound **1g**, ^{13}C-NMR, 100MHz, $CDCl_3$



Compound **1g**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$

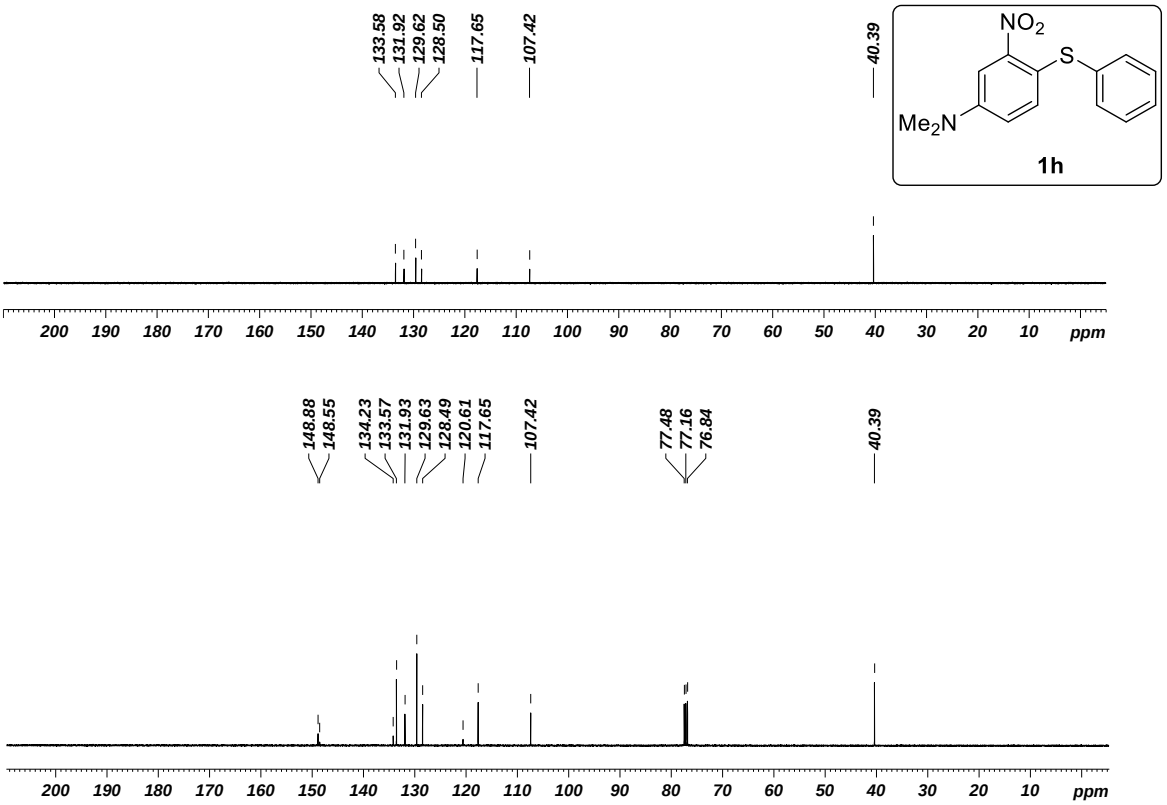


Compound **1h**, ^{1}H-NMR, 400MHz, $CDCl_3$

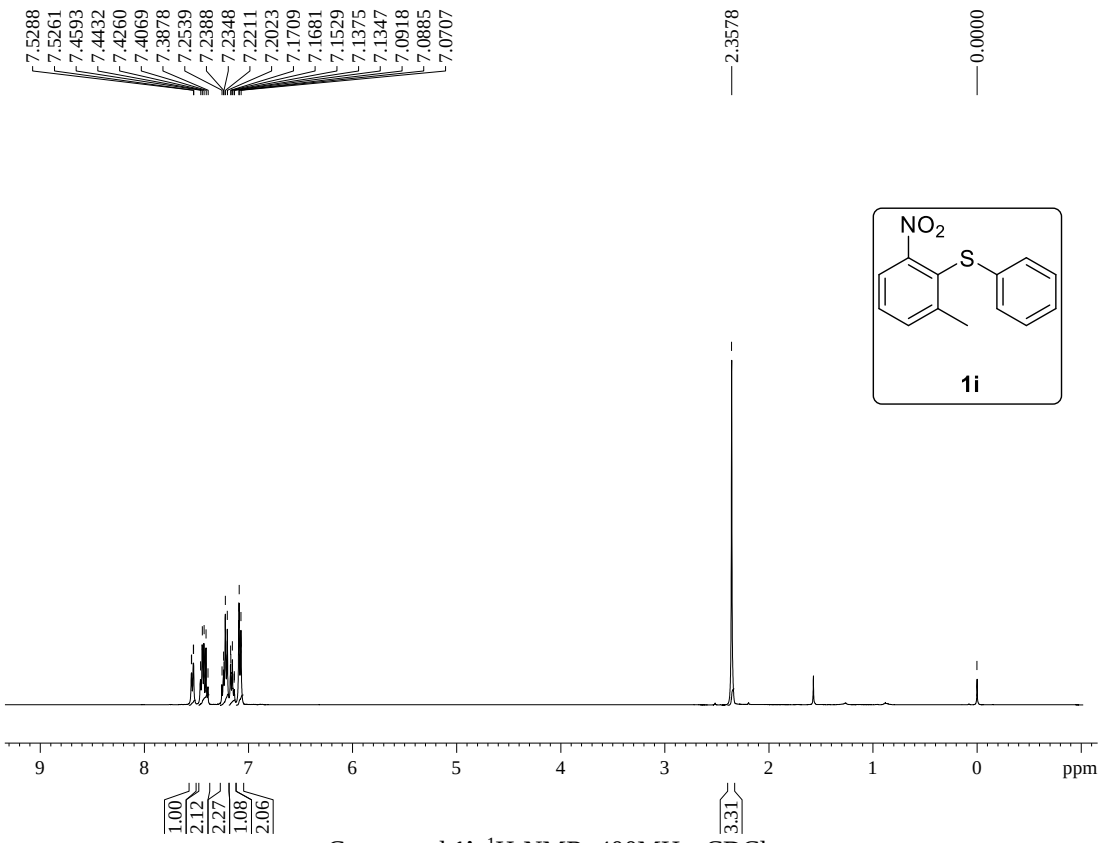


Compound **1h**, ^{13}C-NMR, 100MHz, $CDCl_3$

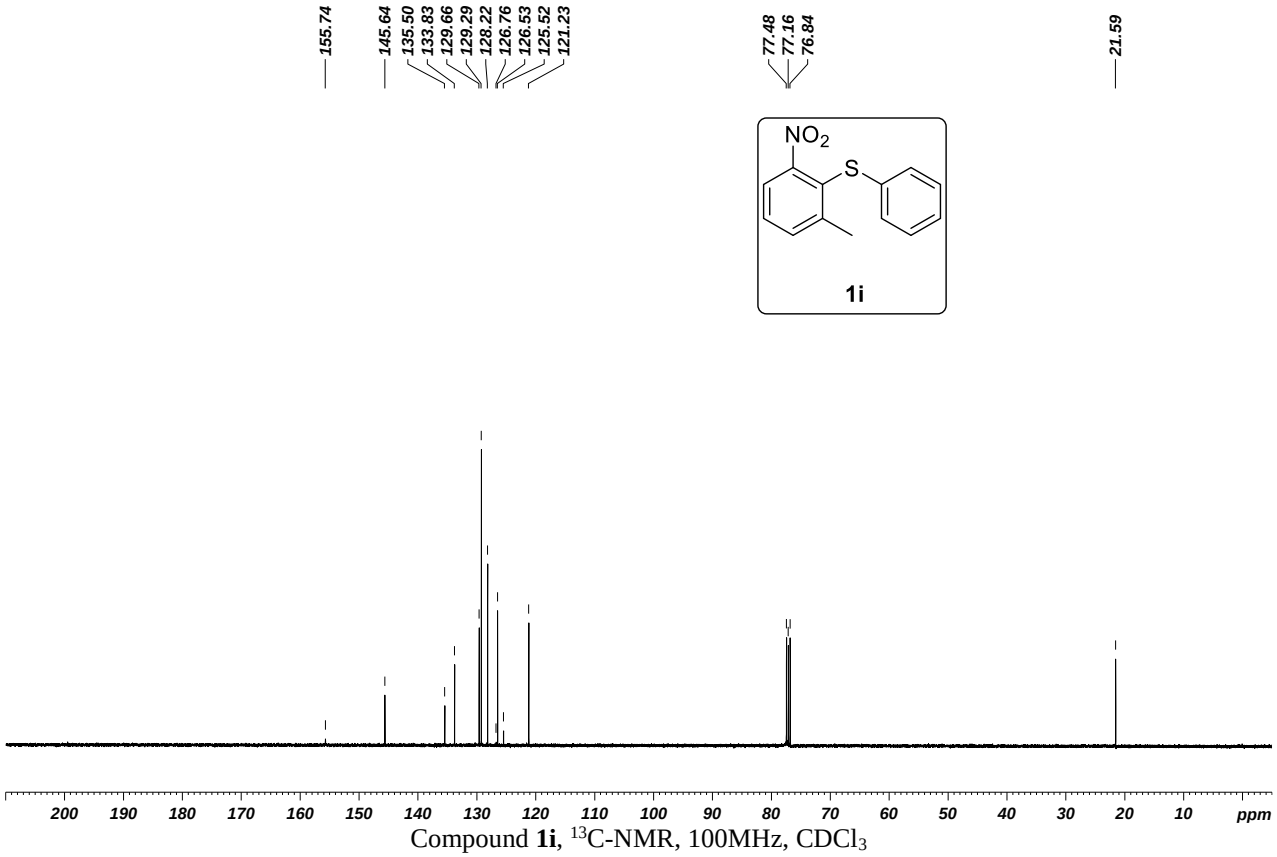
Compound 12 DEPT135 CDCl3



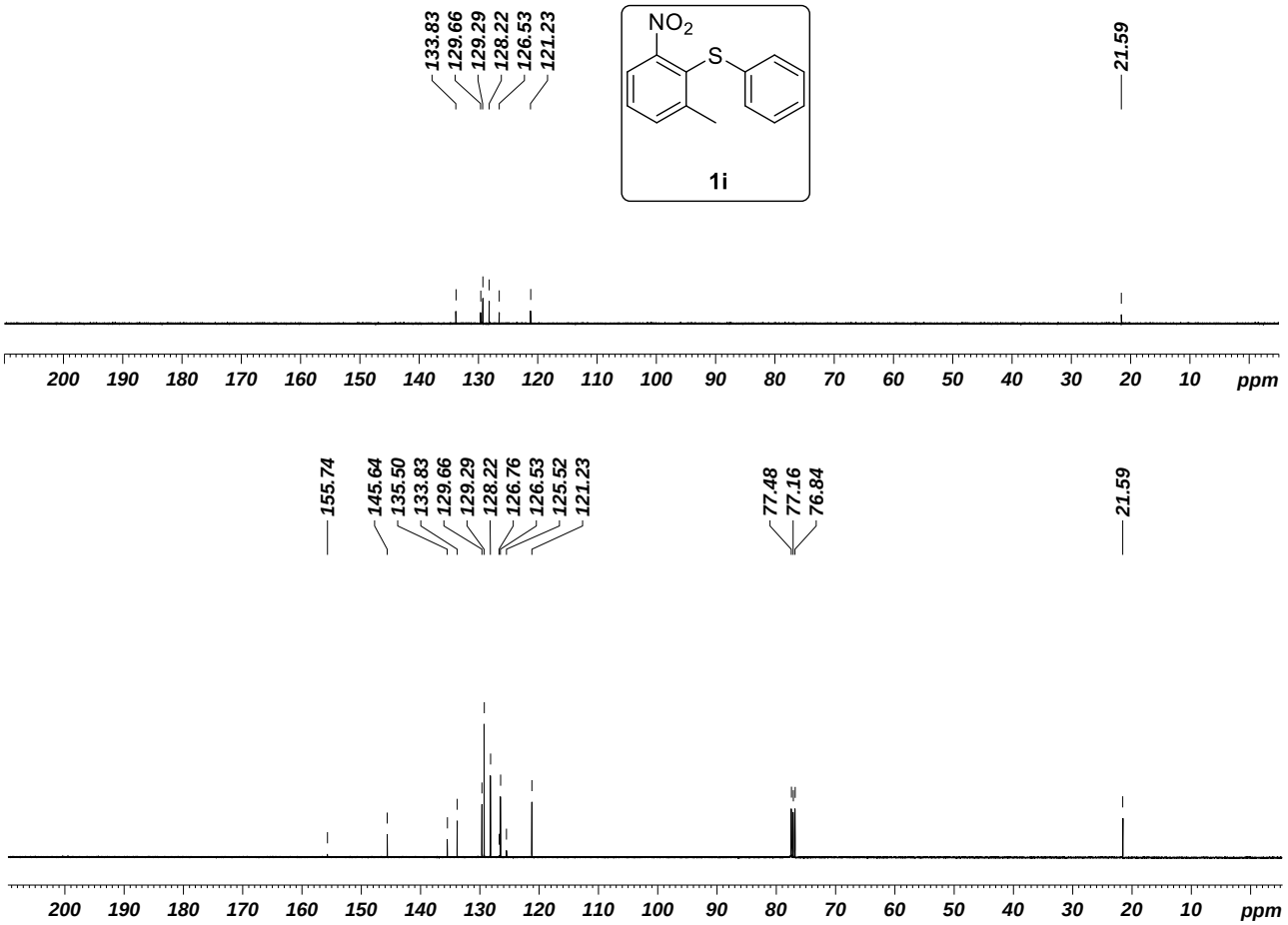
Compound **1h**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$



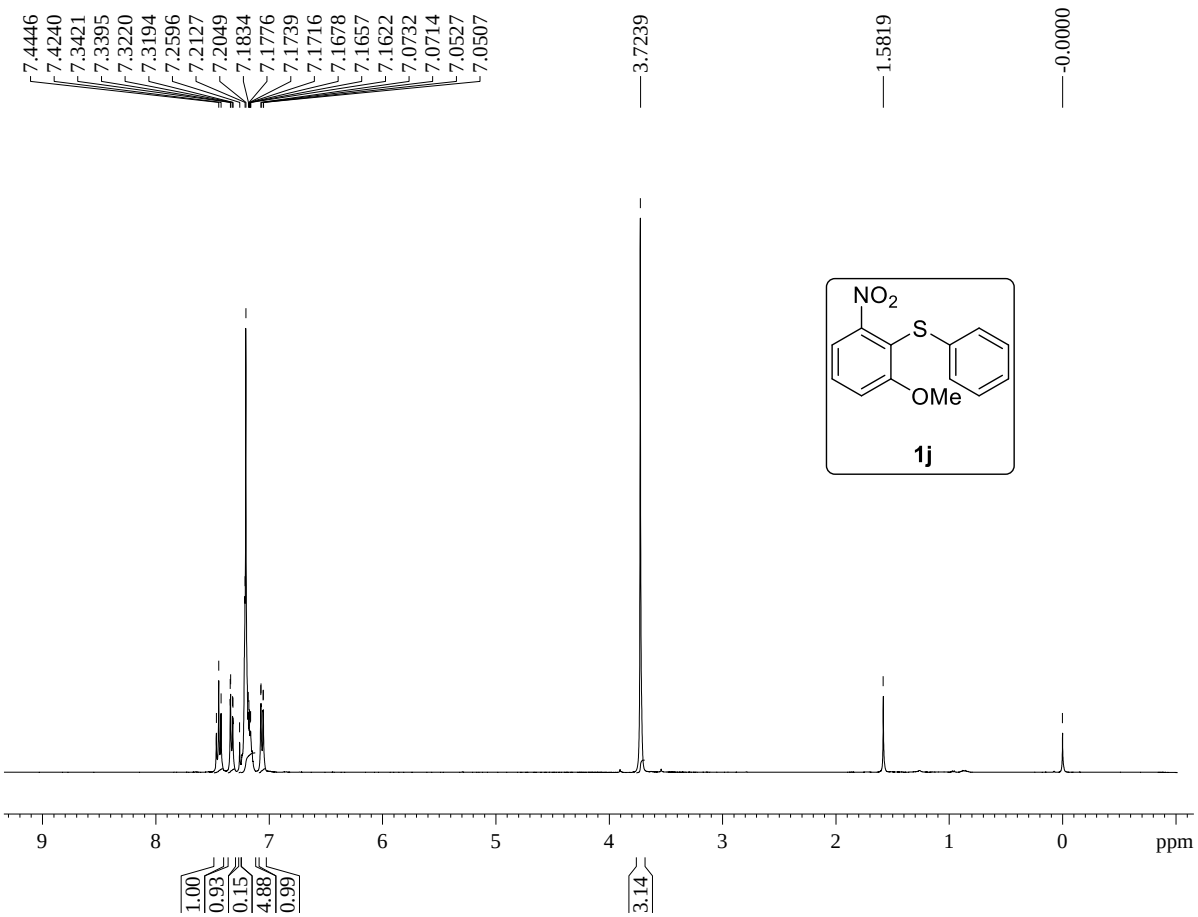
Compound **1i**, ^{1}H-NMR, 400MHz, $CDCl_3$



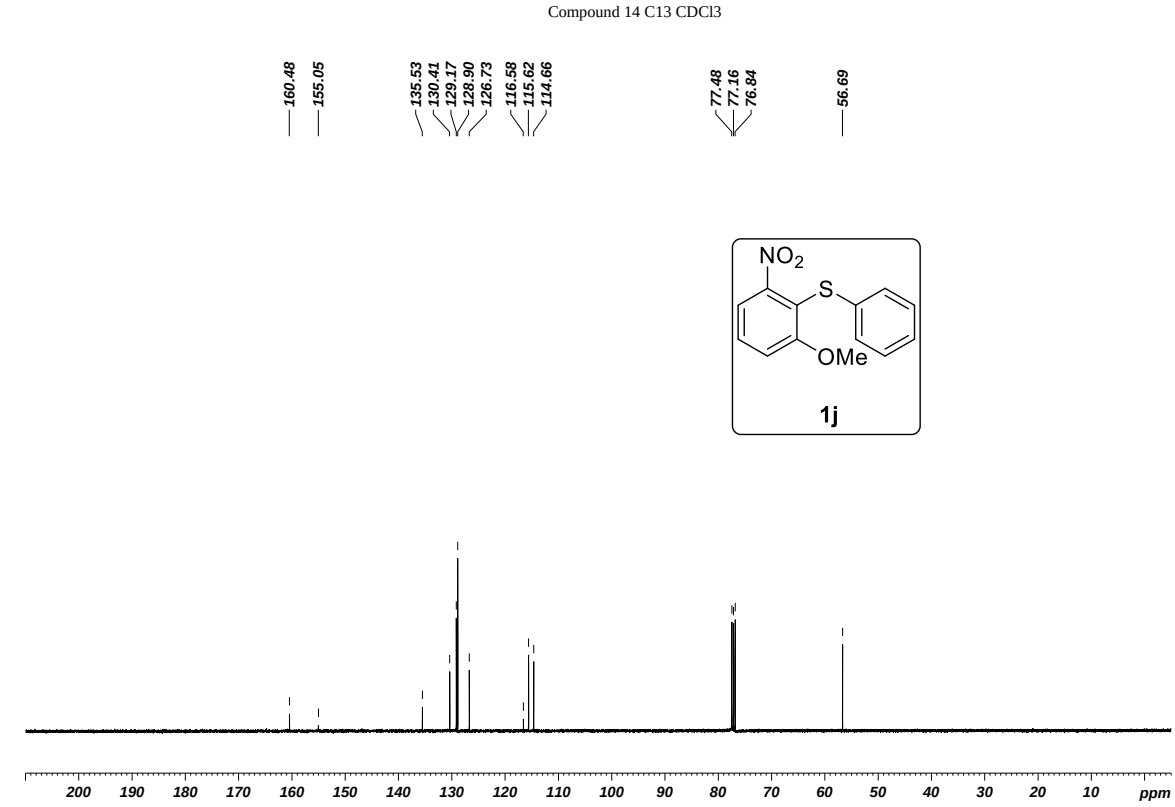
Compound **1i**, ^{13}C-NMR, 100MHz, $CDCl_3$



Compound **1i,** Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$

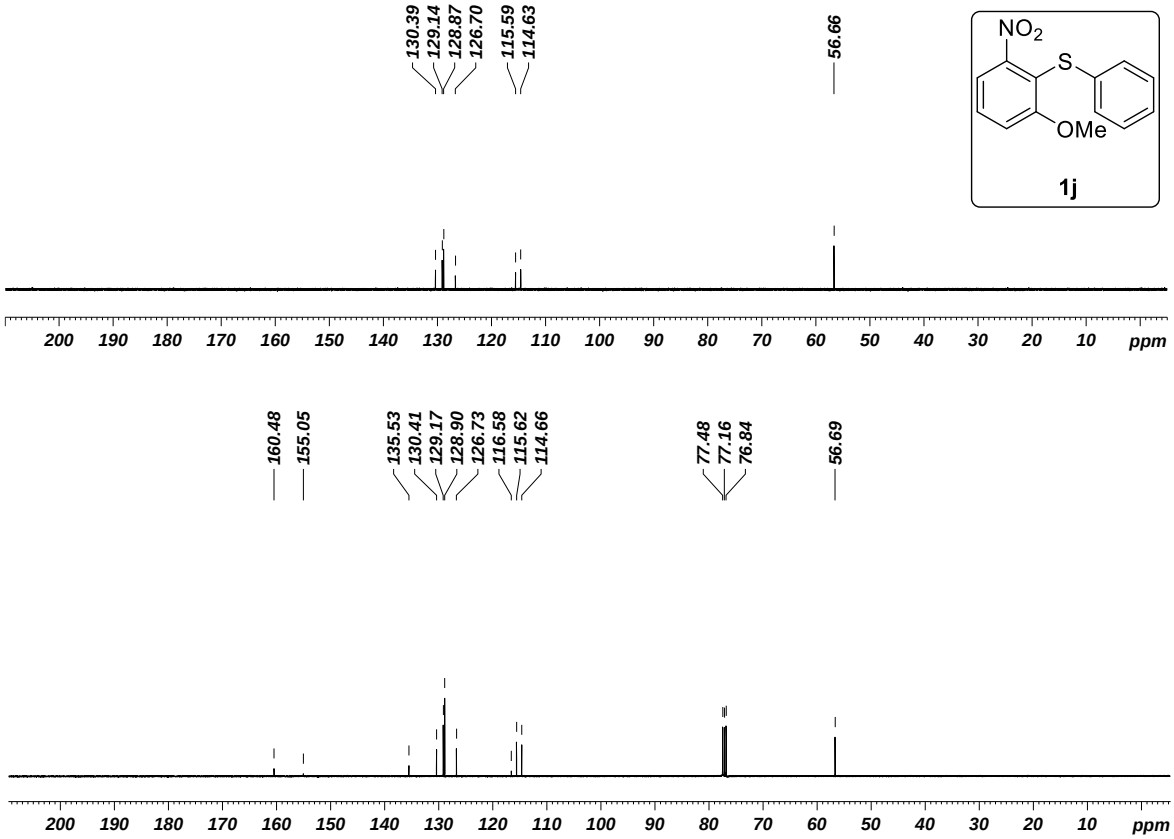


Compound **1j**, Dept135, ^{1}H-NMR, 400MHz, $CDCl_3$

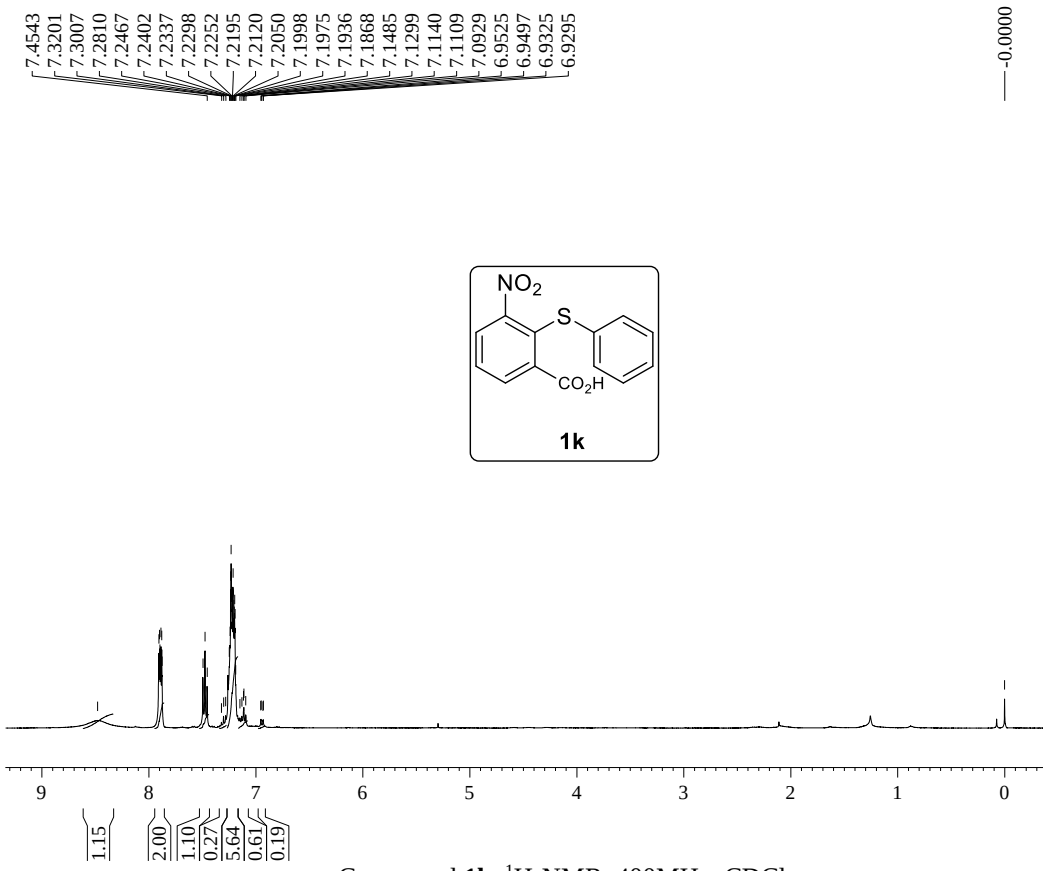


Compound **1j**, ^{13}C-NMR, 100MHz, $CDCl_3$

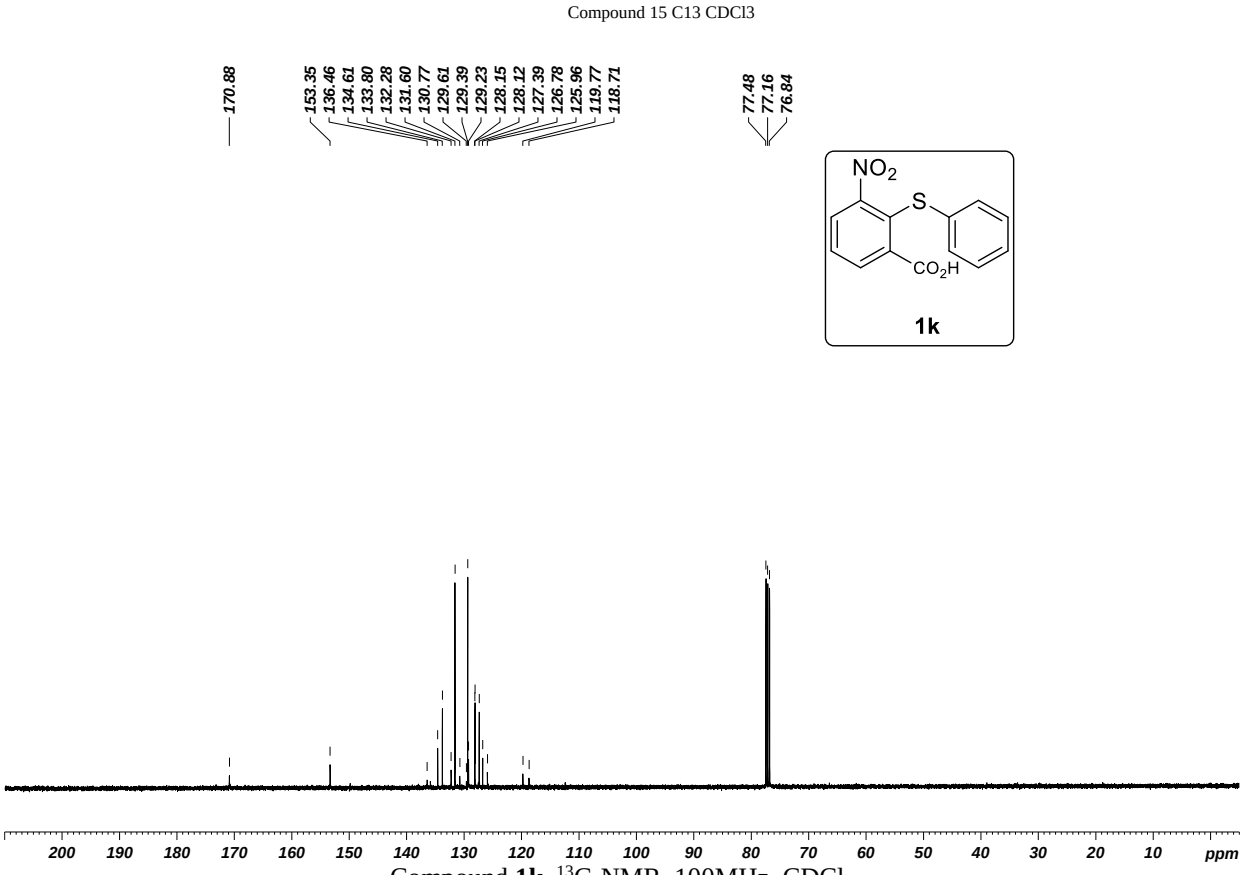
Compound 14 DEPT135 CDCl3



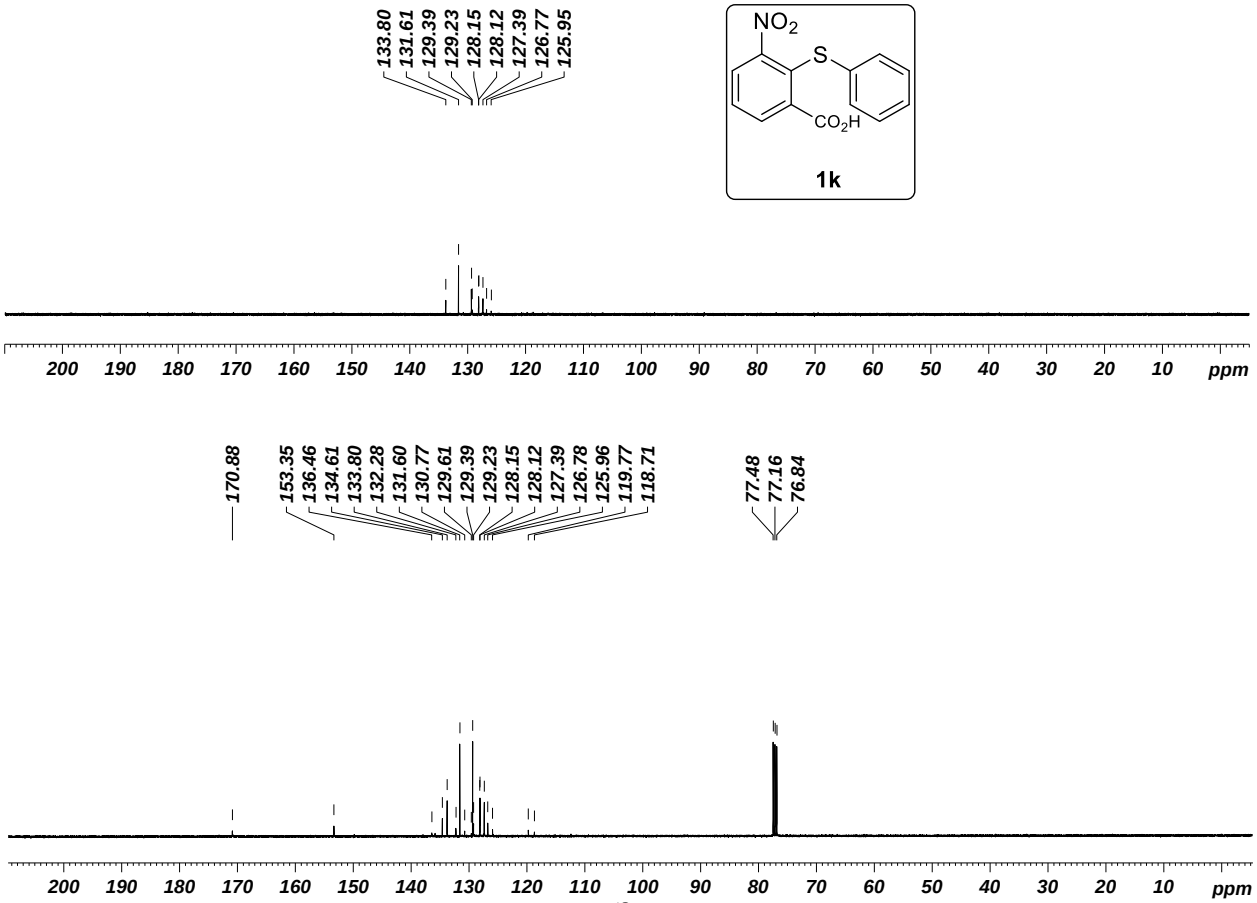
Compound **1j**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$



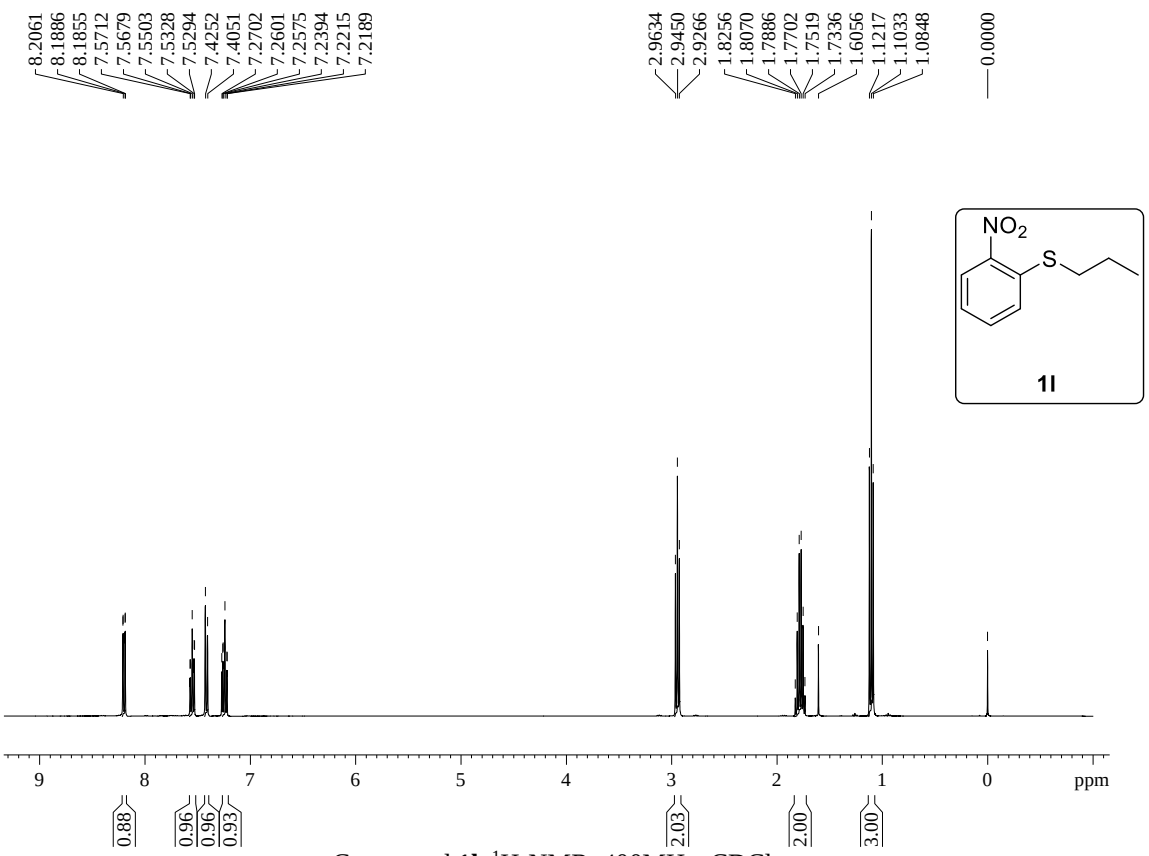
Compound **1k**, ^{1}H-NMR, 400MHz, $CDCl_3$



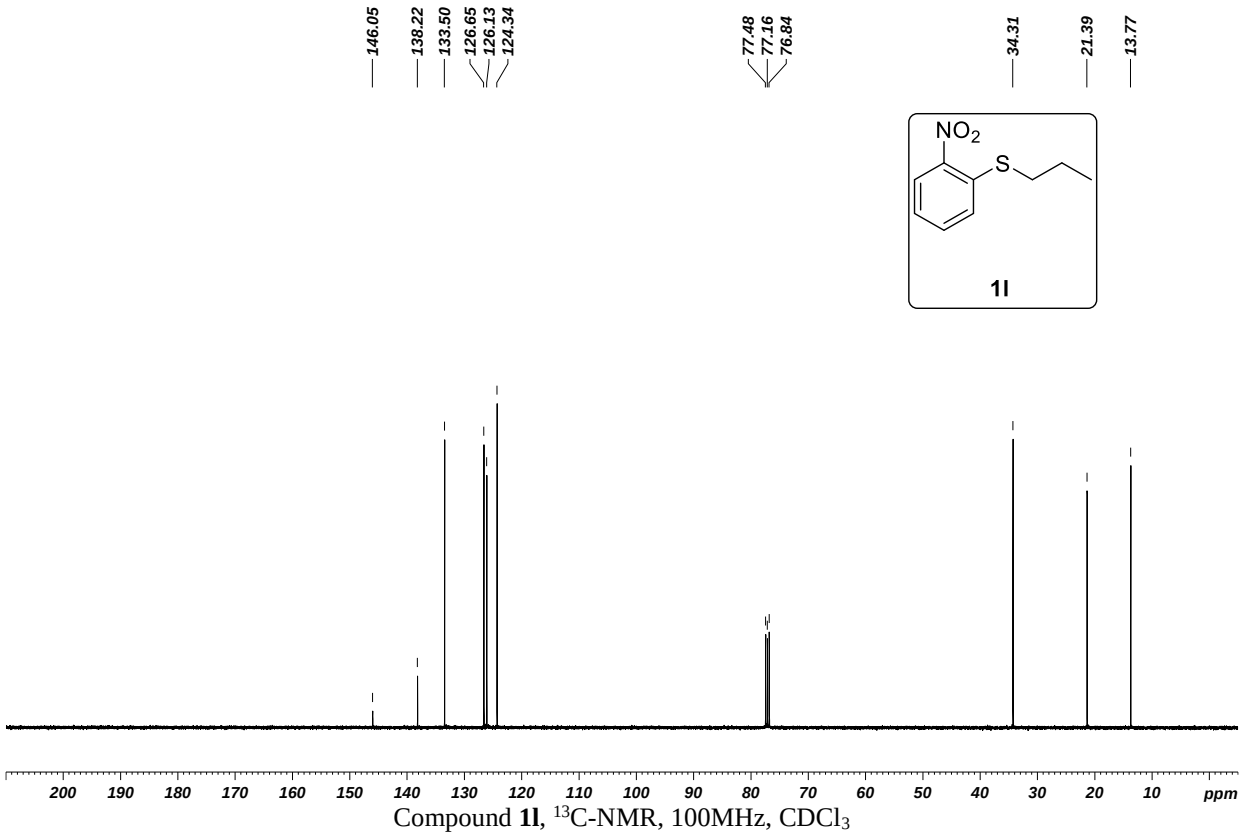
Compound **1k**, ^{13}C-NMR, 100MHz, $CDCl_3$



Compound **1k**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$

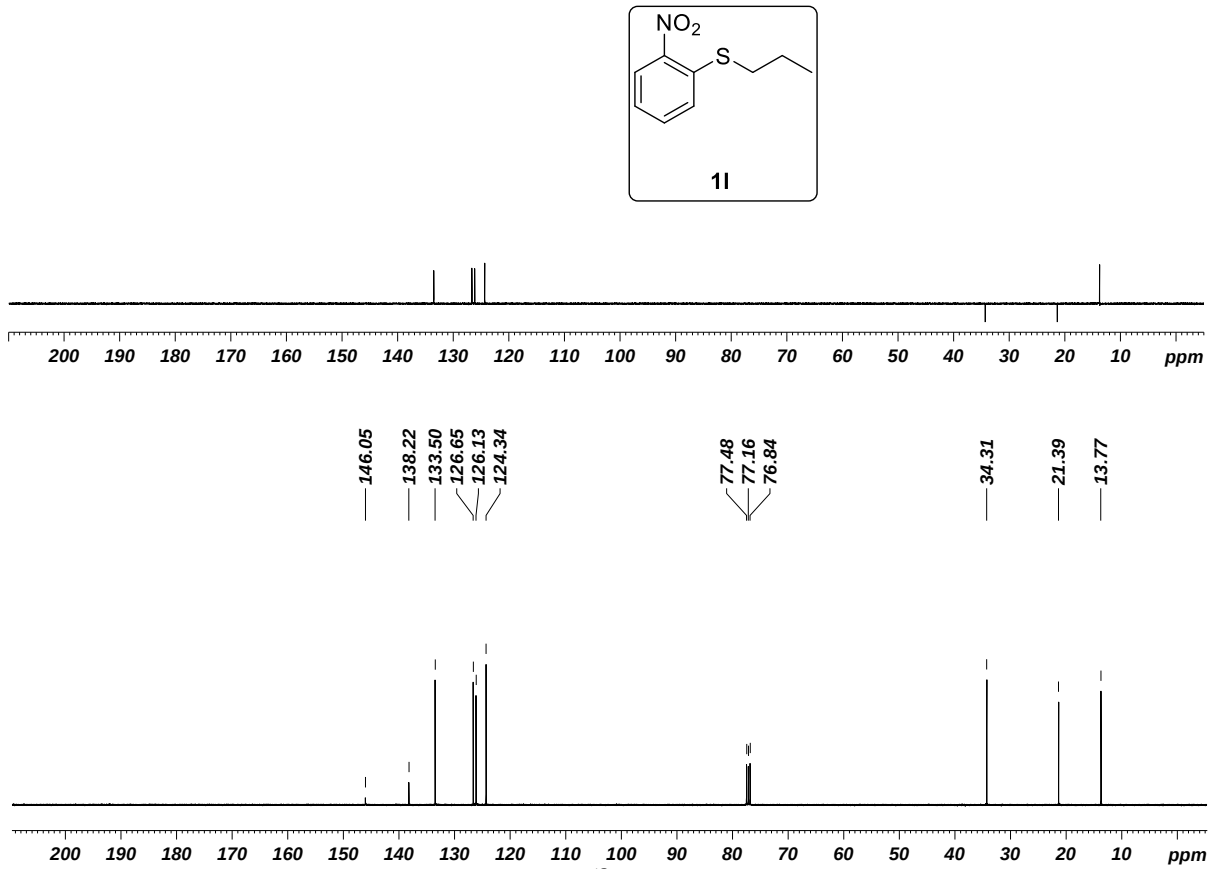


Compound **1l**, ^{1}H-NMR, 400MHz, $CDCl_3$

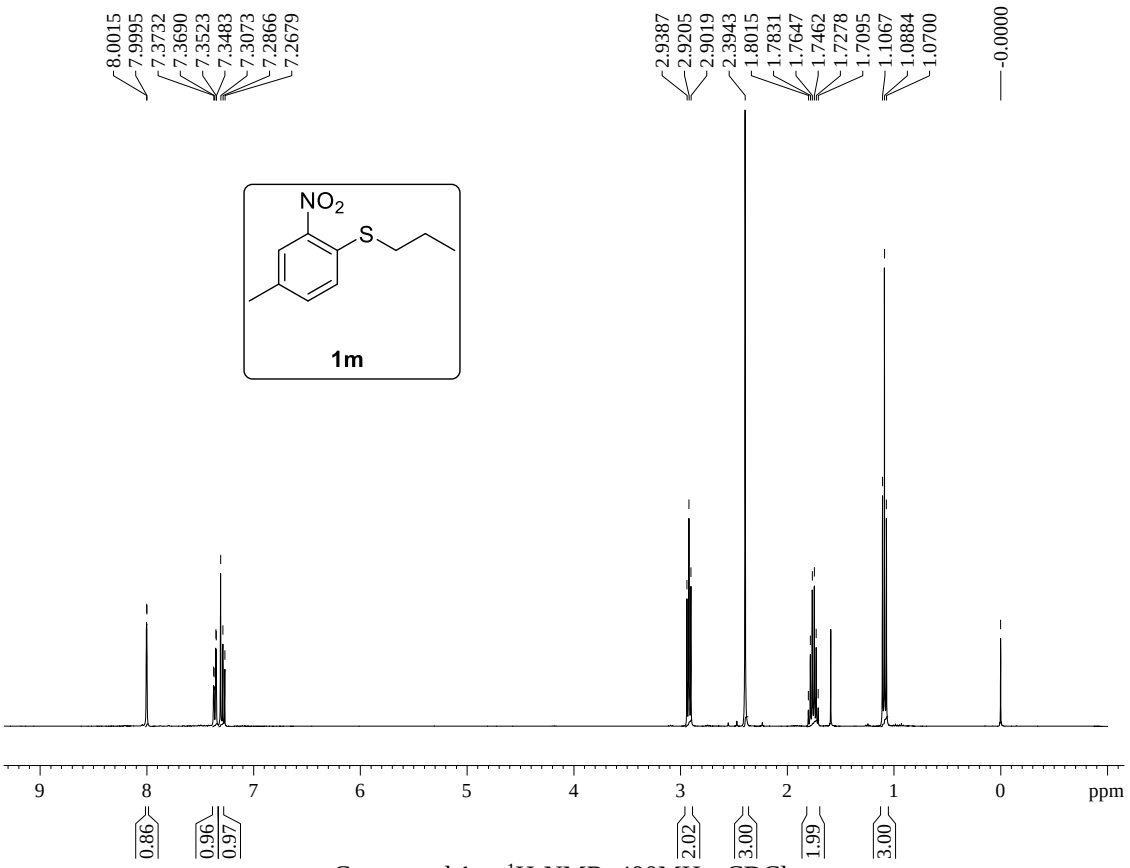


Compound **1l**, ^{13}C-NMR, 100MHz, $CDCl_3$

Compound 16 DEPT135 CDCl3

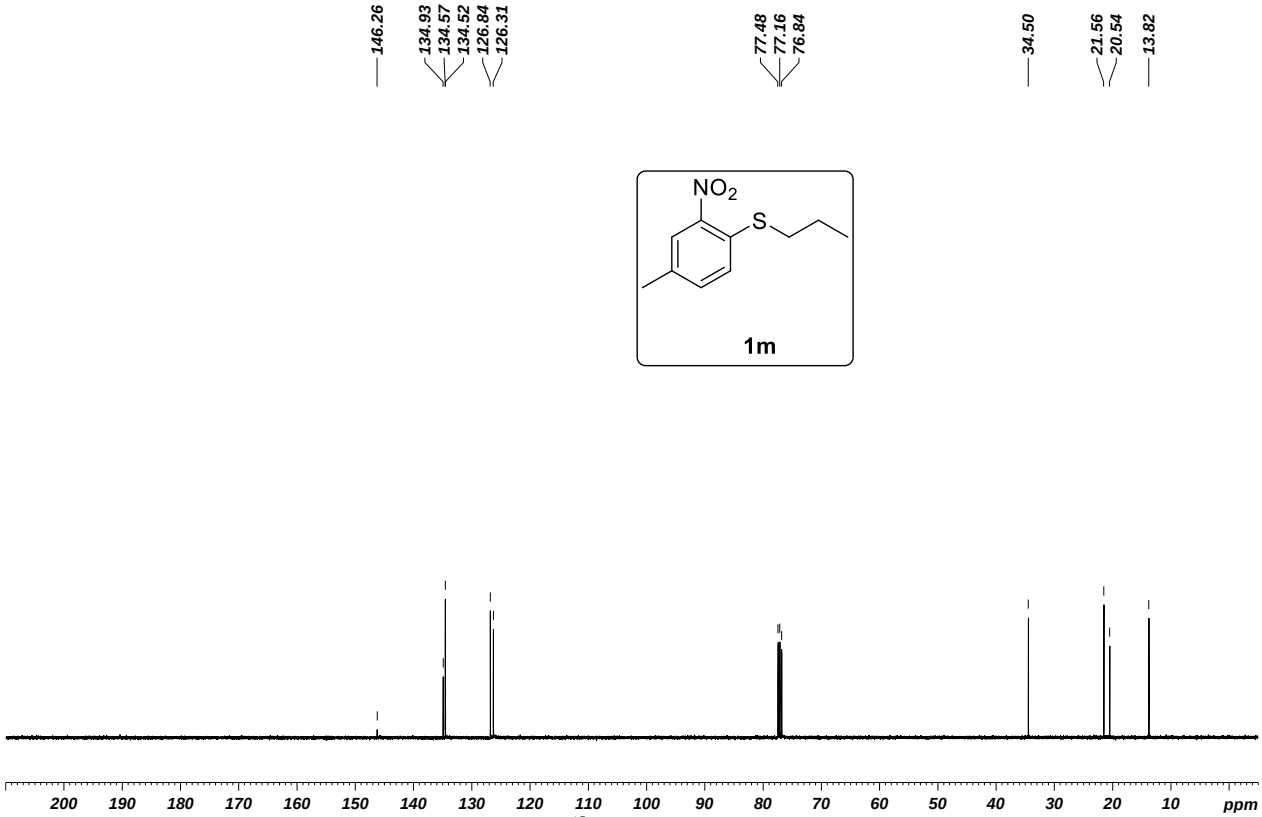


Compound **1l**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$



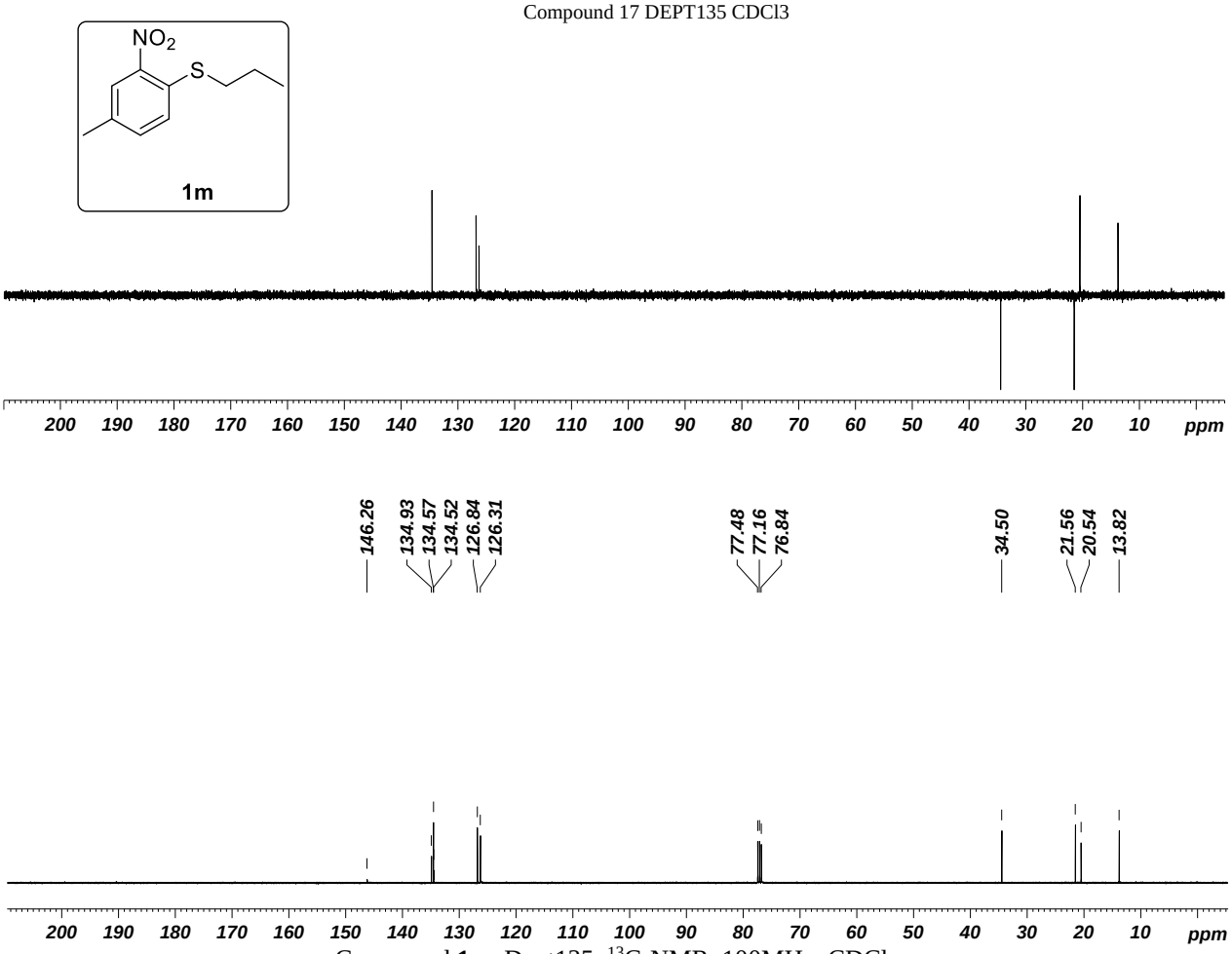
Compound **1m**, ^{1}H-NMR, 400MHz, $CDCl_3$

Compound 17 C13 CDCl3

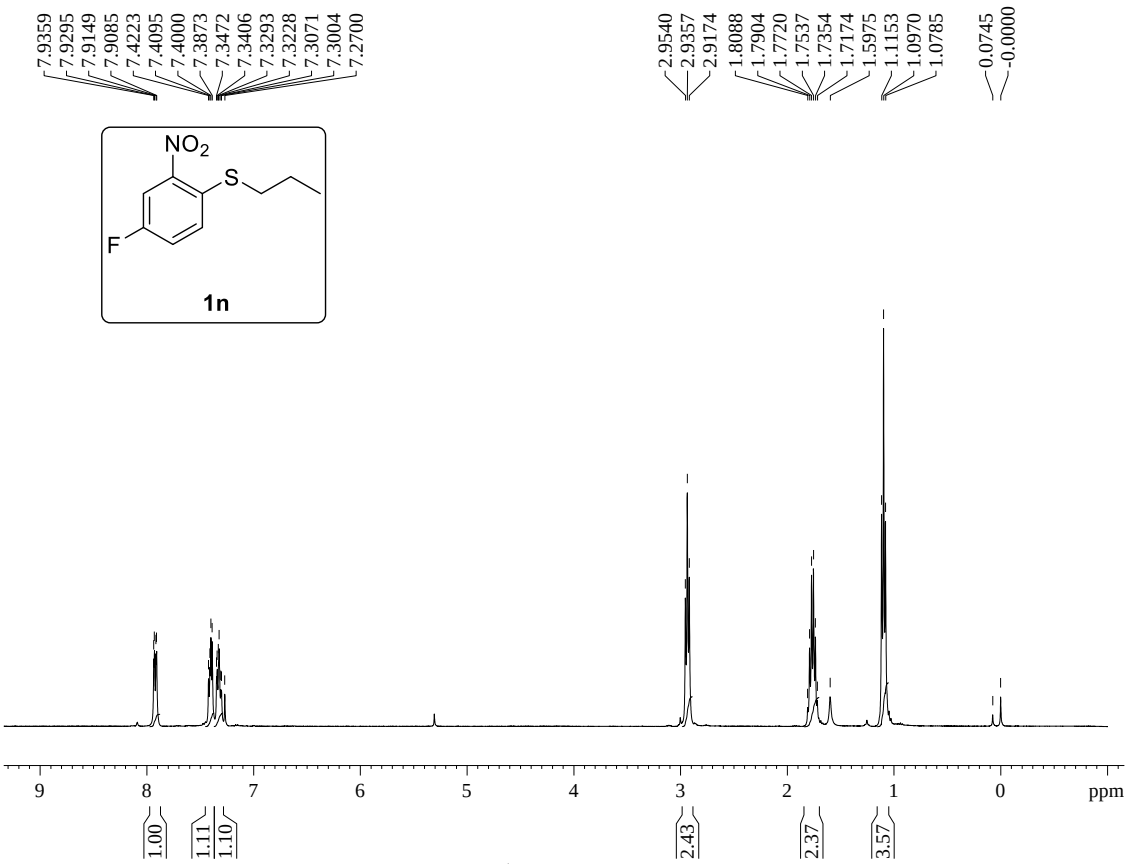


Compound **1m**, ^{13}C-NMR, 100MHz, $CDCl_3$

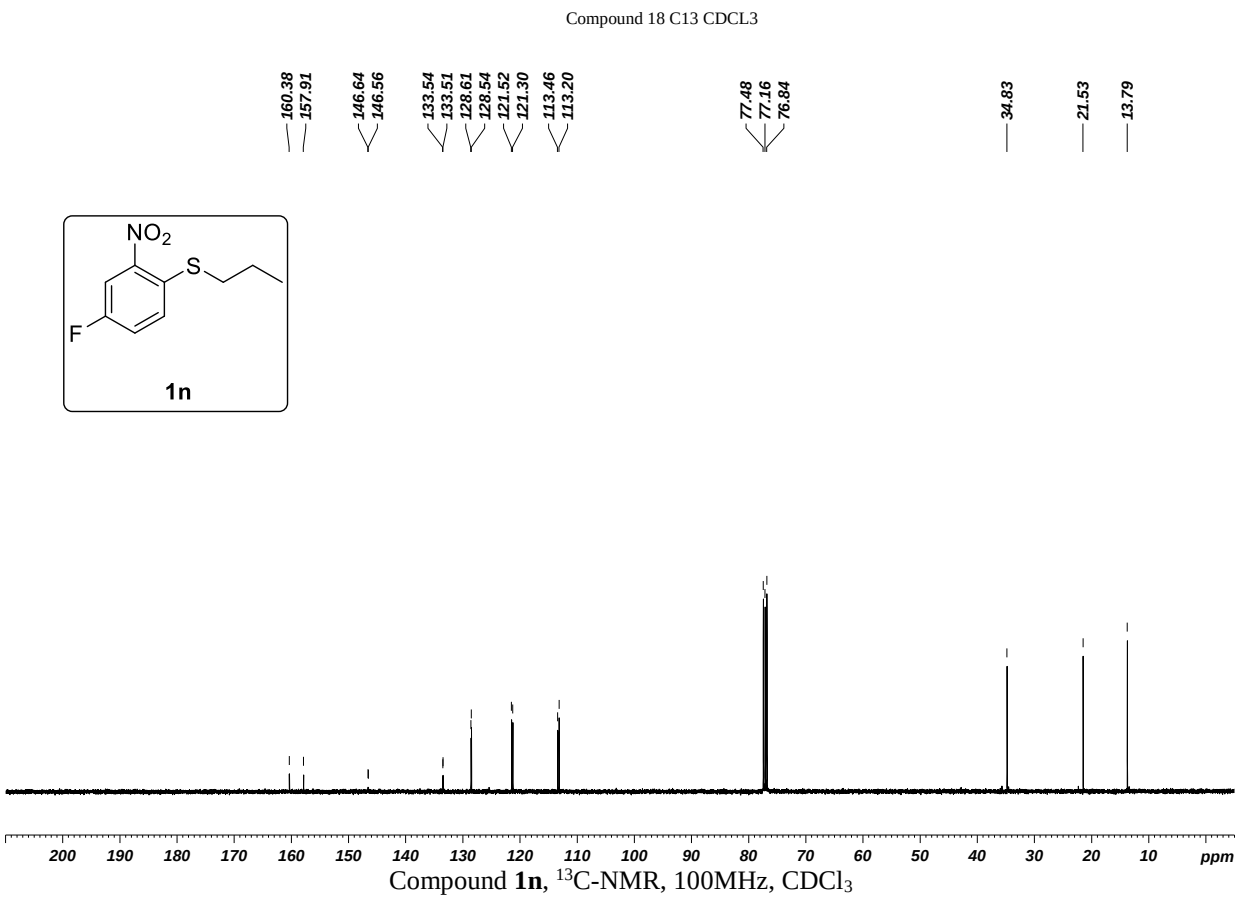
Compound 17 DEPT135 CDCl3



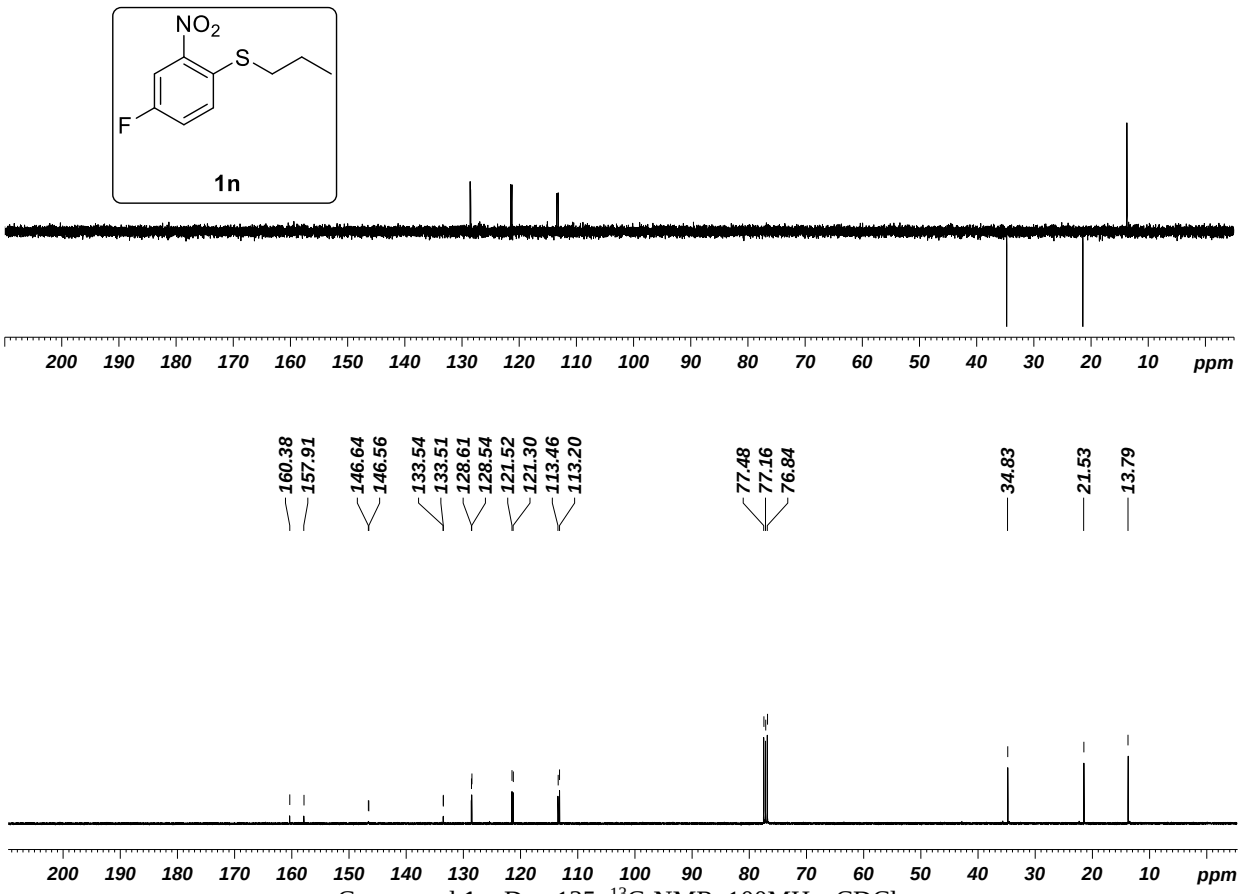
Compound **1m**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$



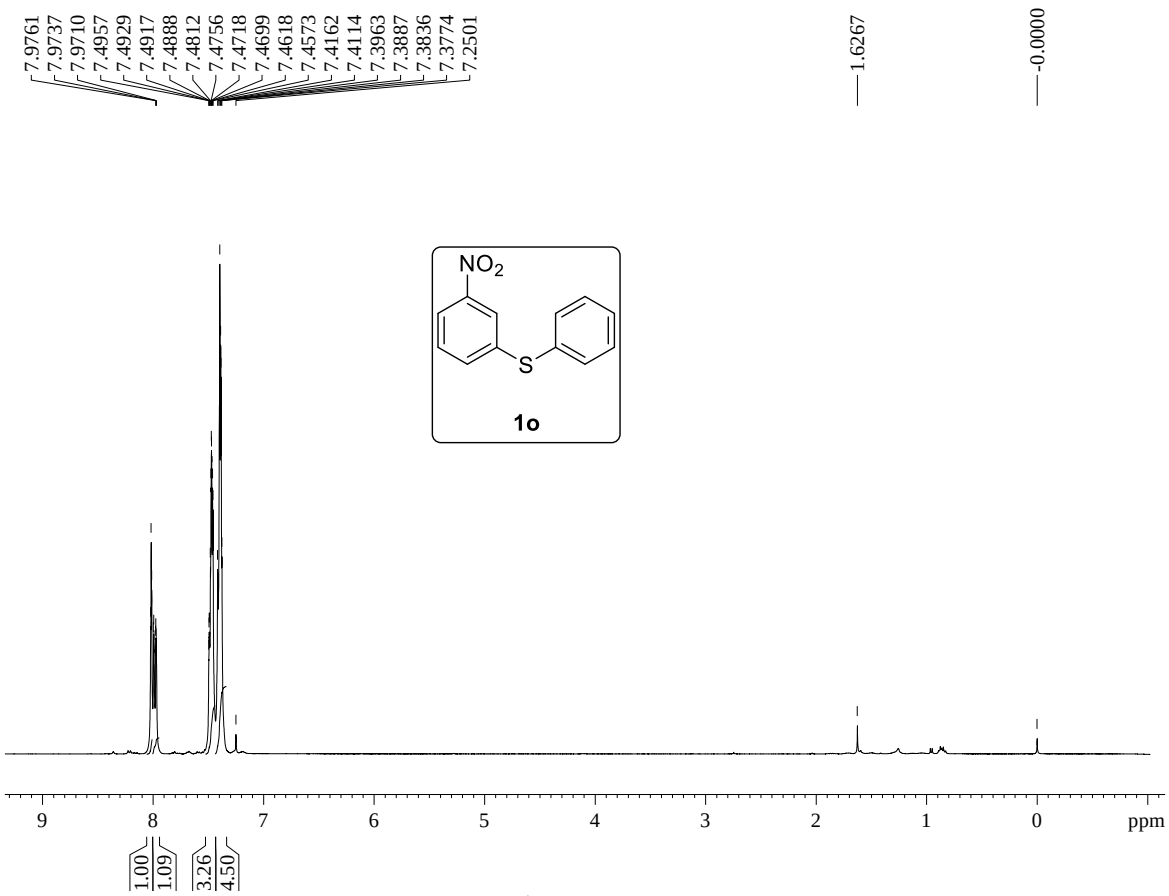
Compound **1n**, ^{1}H-NMR, 400MHz, $CDCl_3$



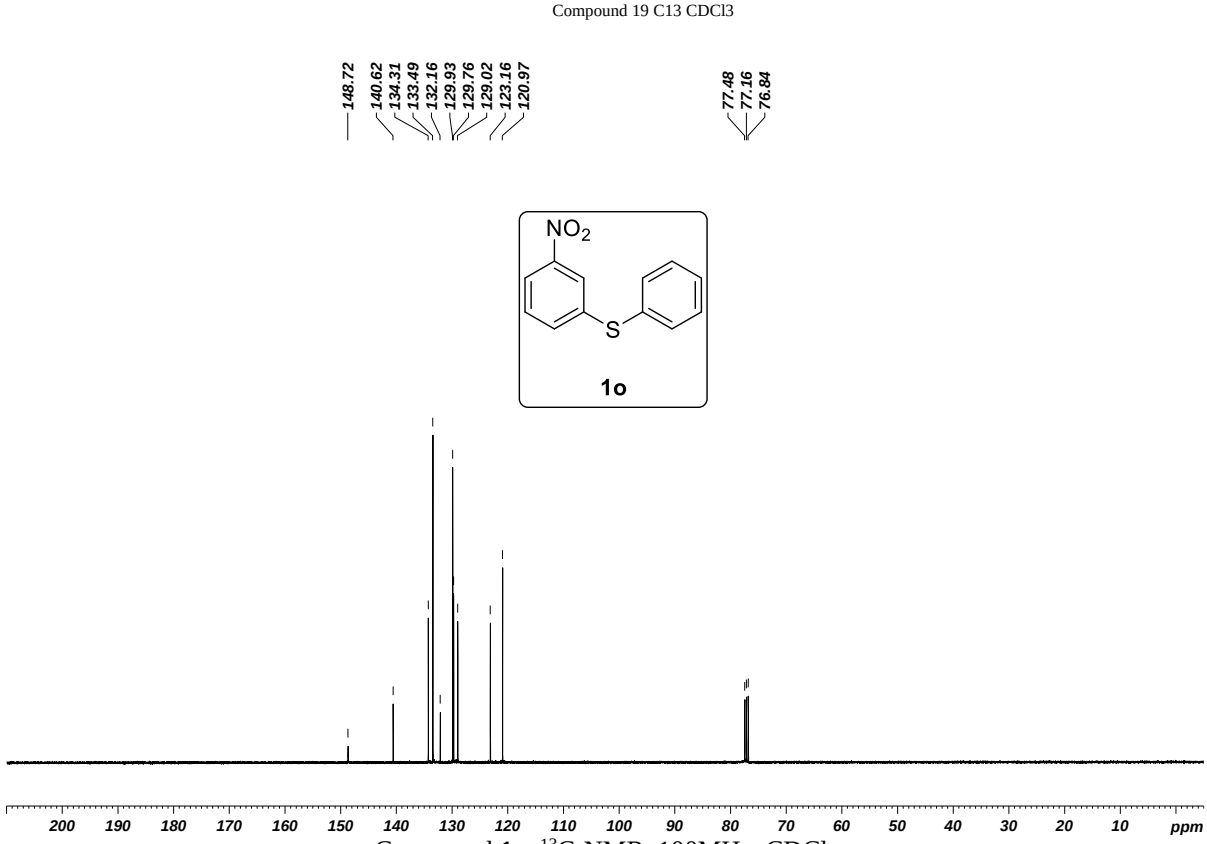
Compound **1n**, ^{13}C-NMR, 100MHz, $CDCl_3$



Compound **1n**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$

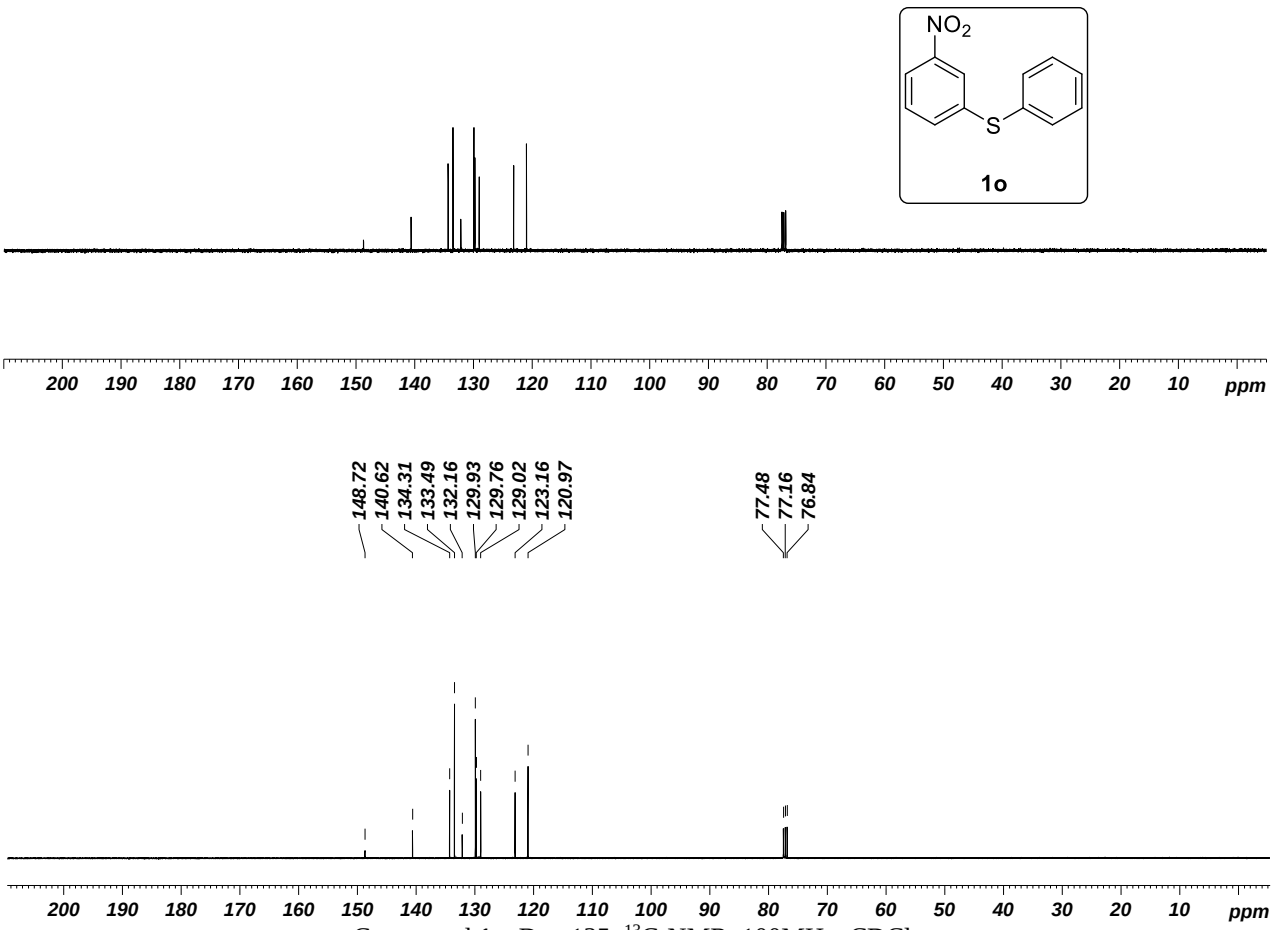


Compound **1o**, ^{1}H-NMR, 400MHz, $CDCl_3$

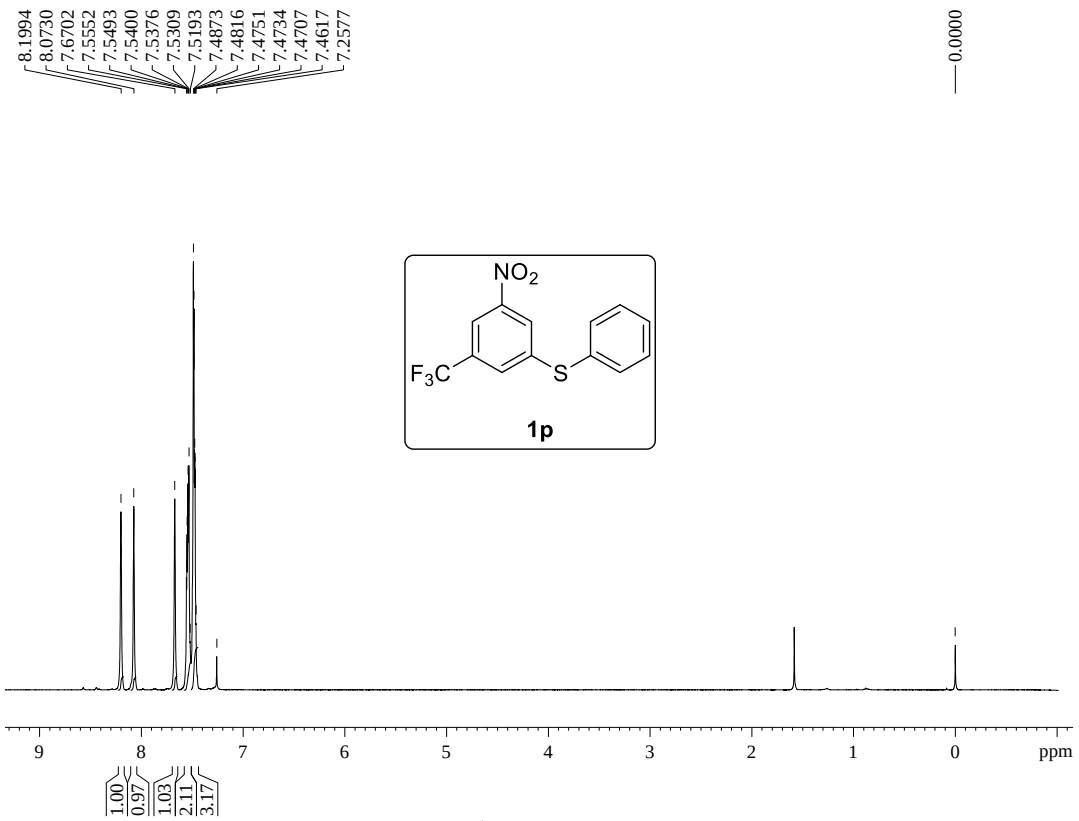


Compound **1o**, ^{13}C-NMR, 100MHz, $CDCl_3$

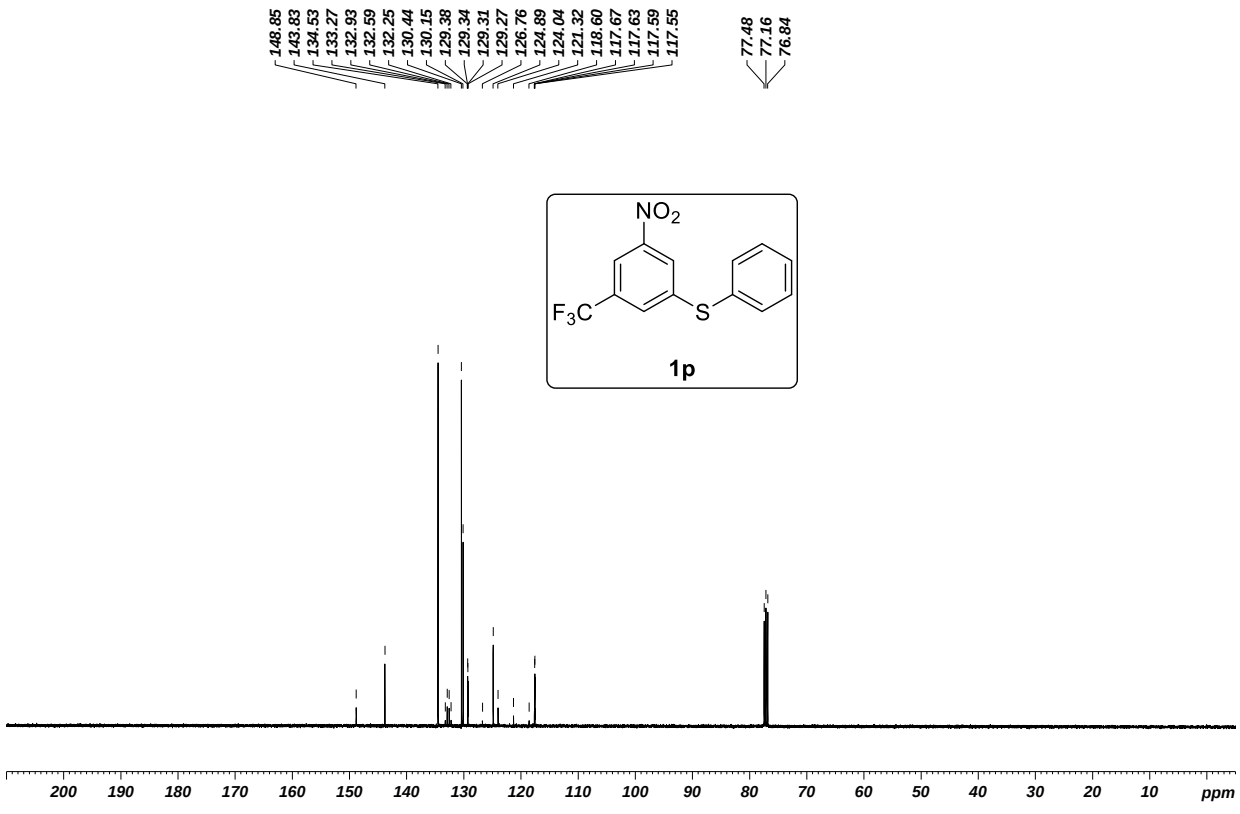
Compound 19 DEPT135 CDCl3



Compound **1o**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$

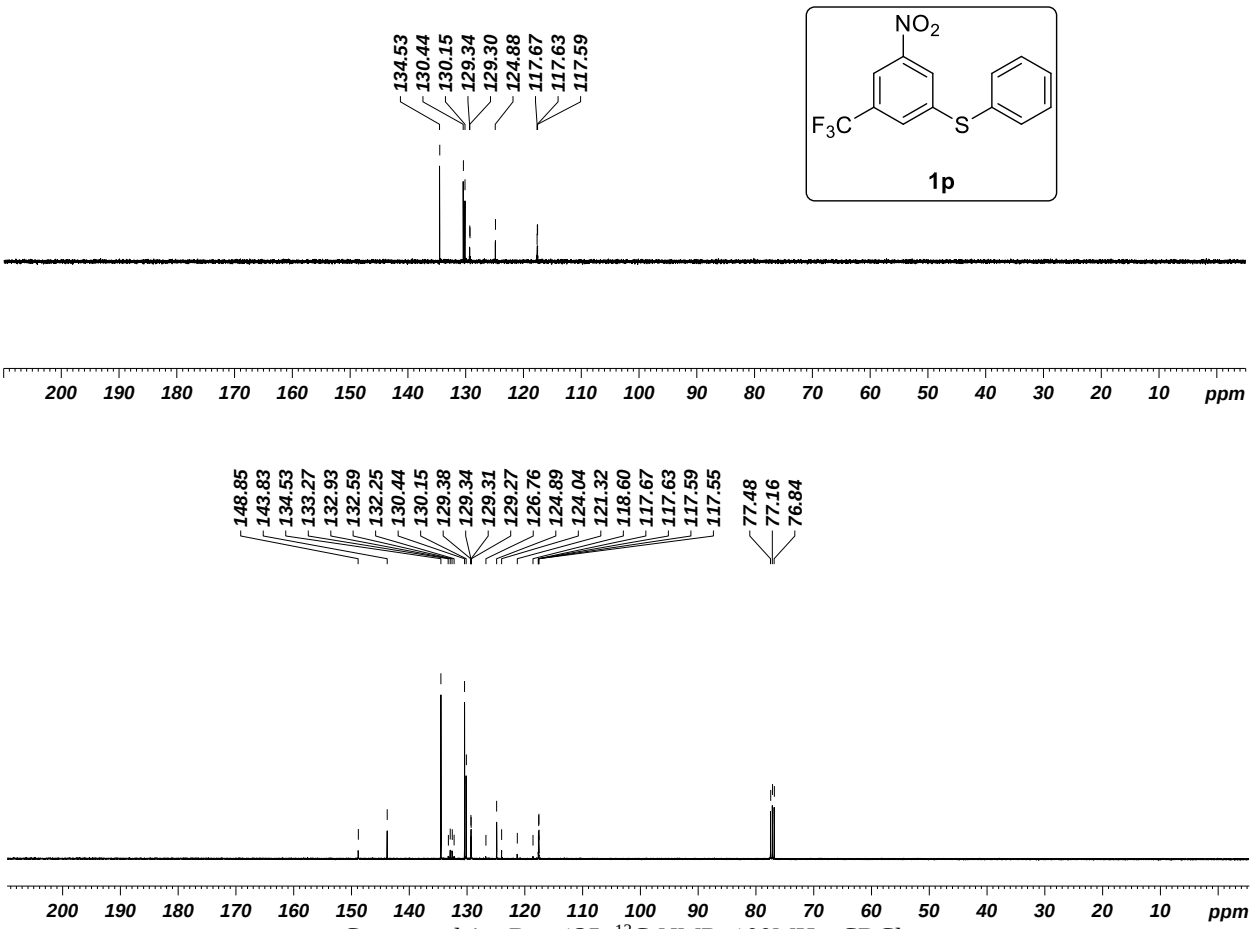


Compound **1p**, ^{1}H-NMR, 400MHz, $CDCl_3$

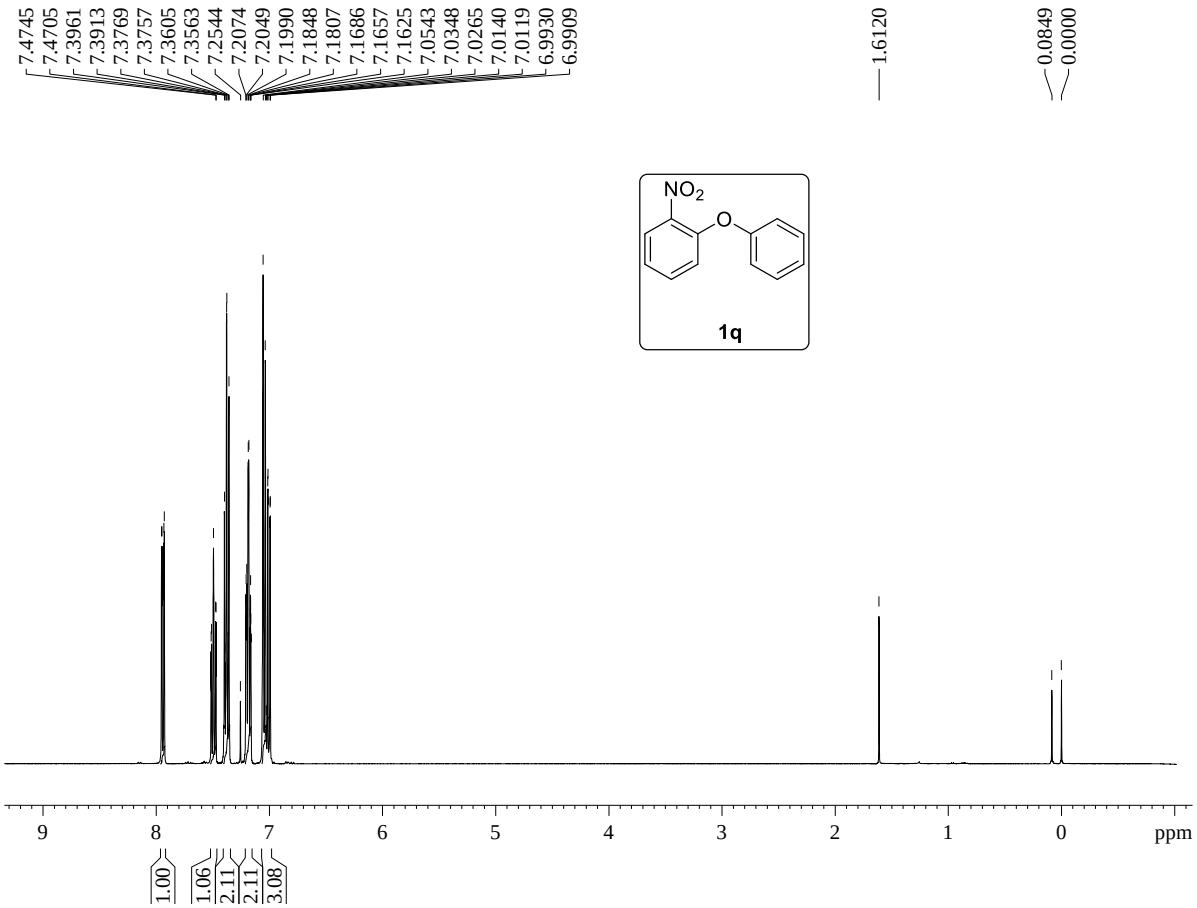


Compound **1p**, ^{13}C-NMR, 100MHz, $CDCl_3$

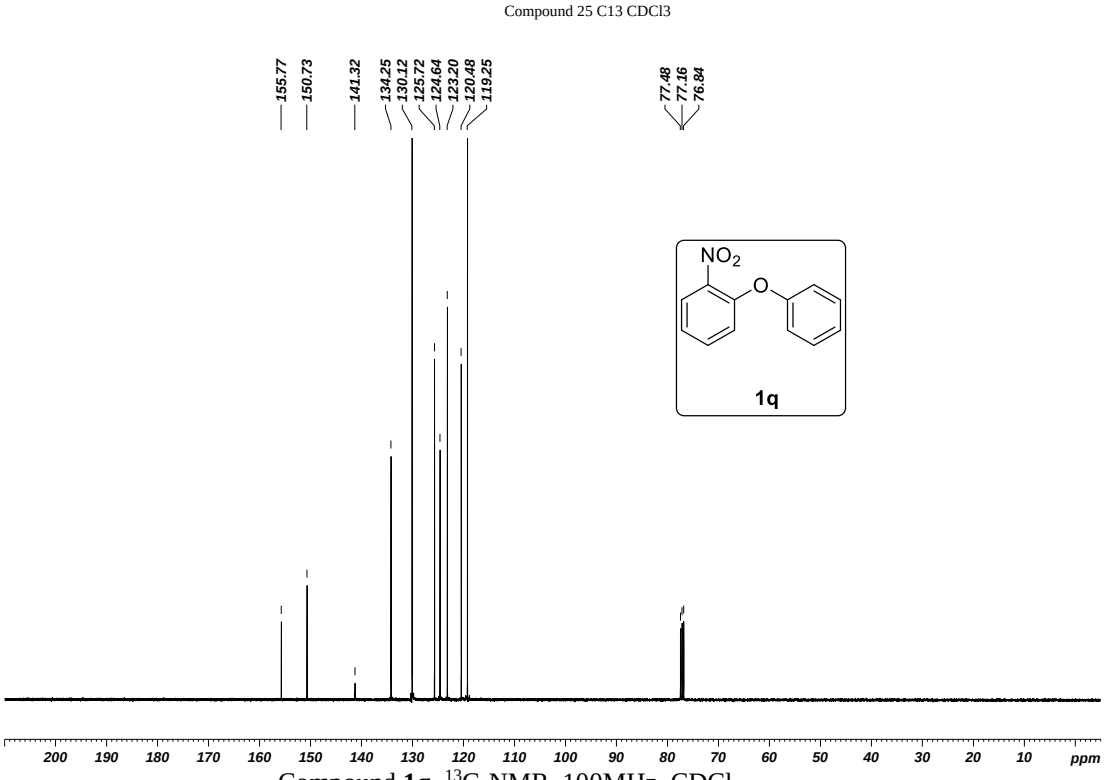
Compound 20 DEPT135 CDCl3



Compound **1p**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$

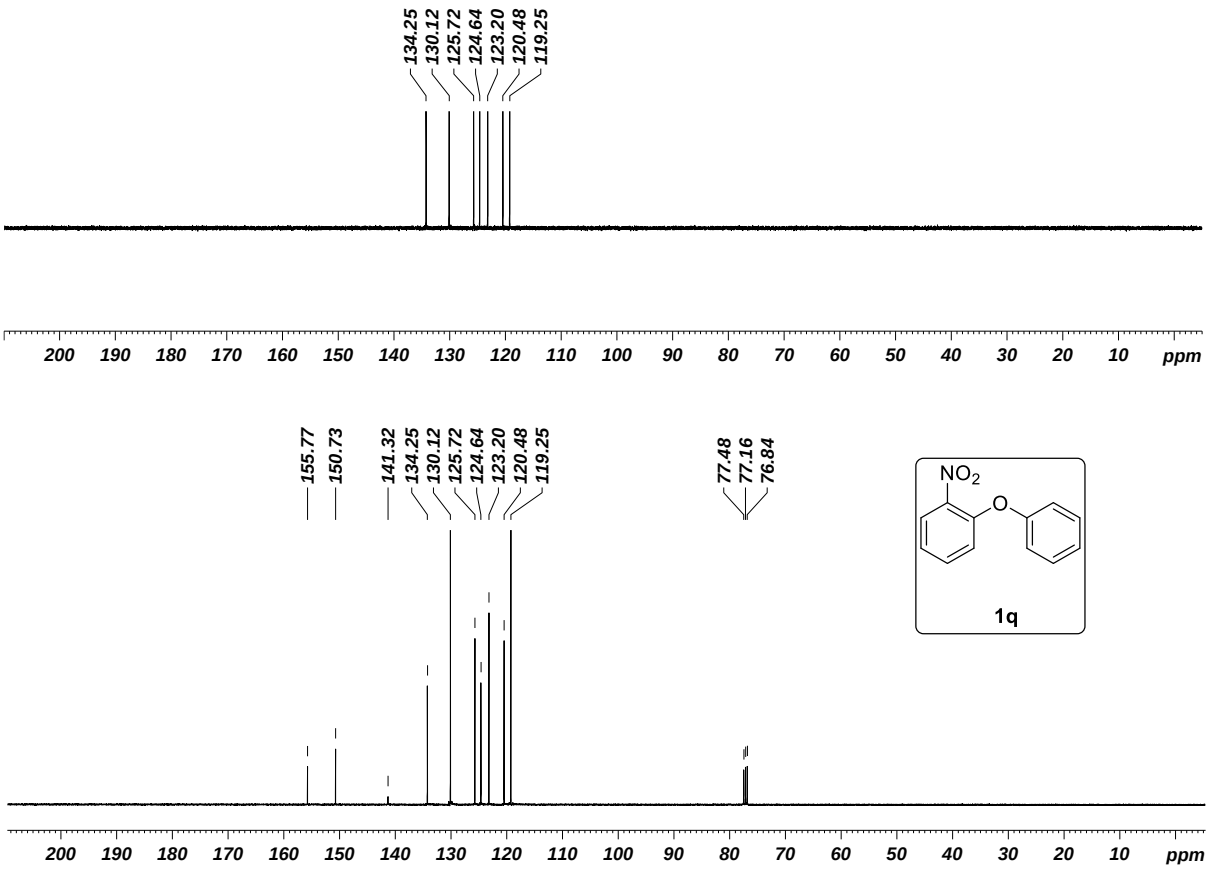


Compound **1q**, ^{1}H-NMR, 400MHz, $CDCl_3$

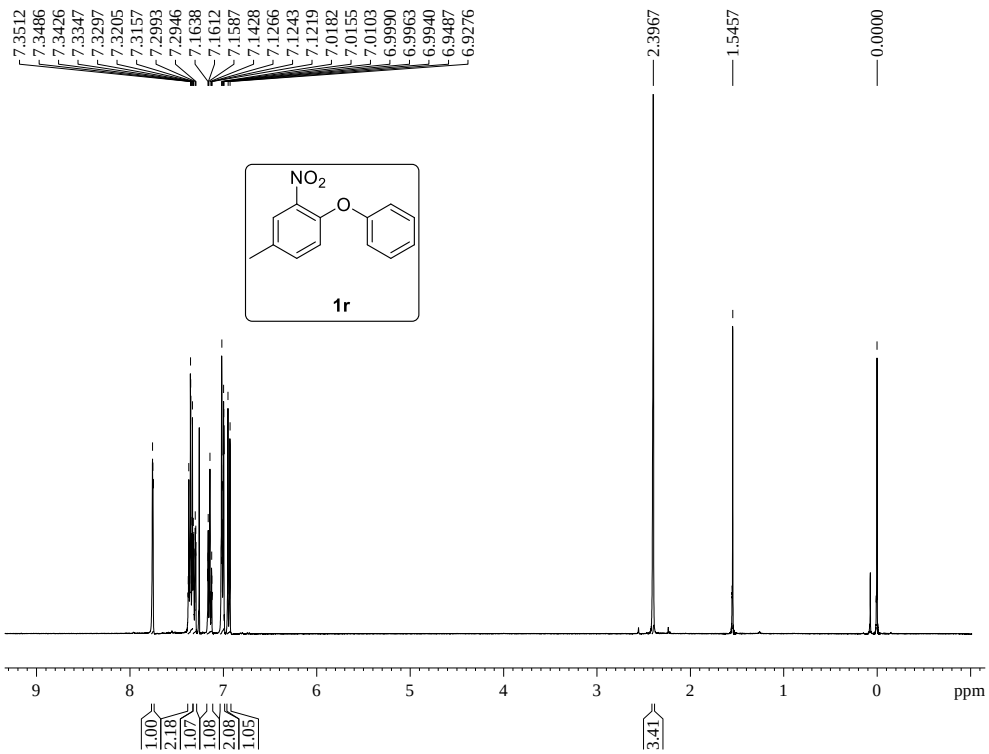


Compound **1q**, ^{13}C-NMR, 100MHz, $CDCl_3$

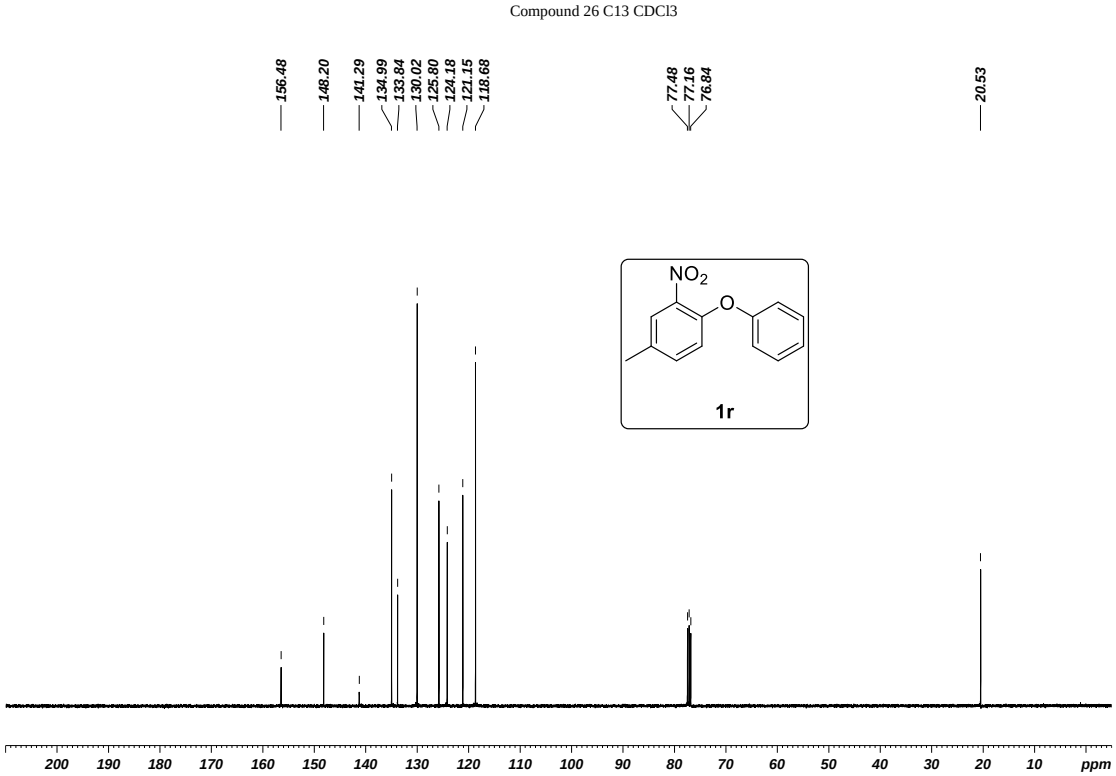
Compound 25 DEPT135 CDCl3



Compound **1q**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$

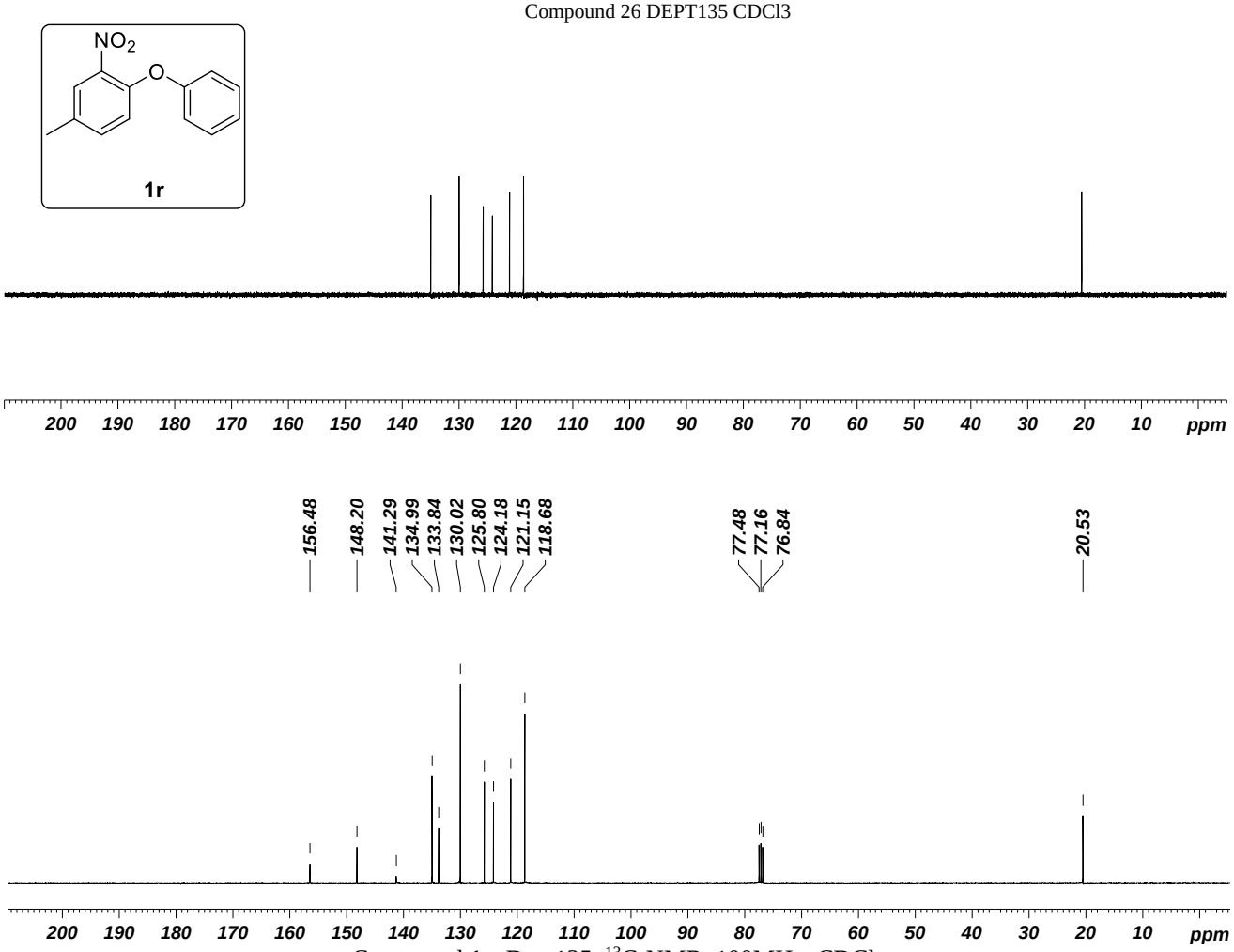


Compound **1r**, ^{1}H-NMR, 400MHz, $CDCl_3$

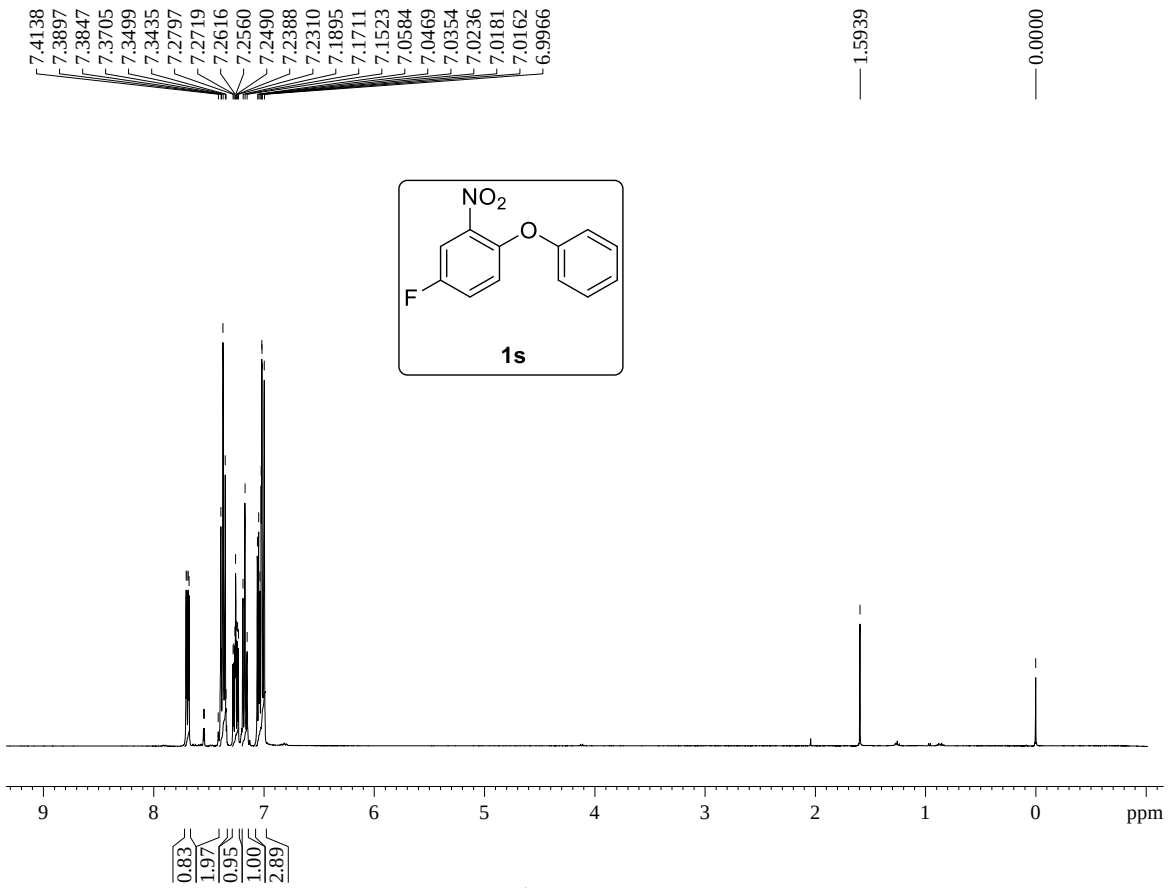


Compound **1r**, ^{13}C-NMR, 100MHz, $CDCl_3$

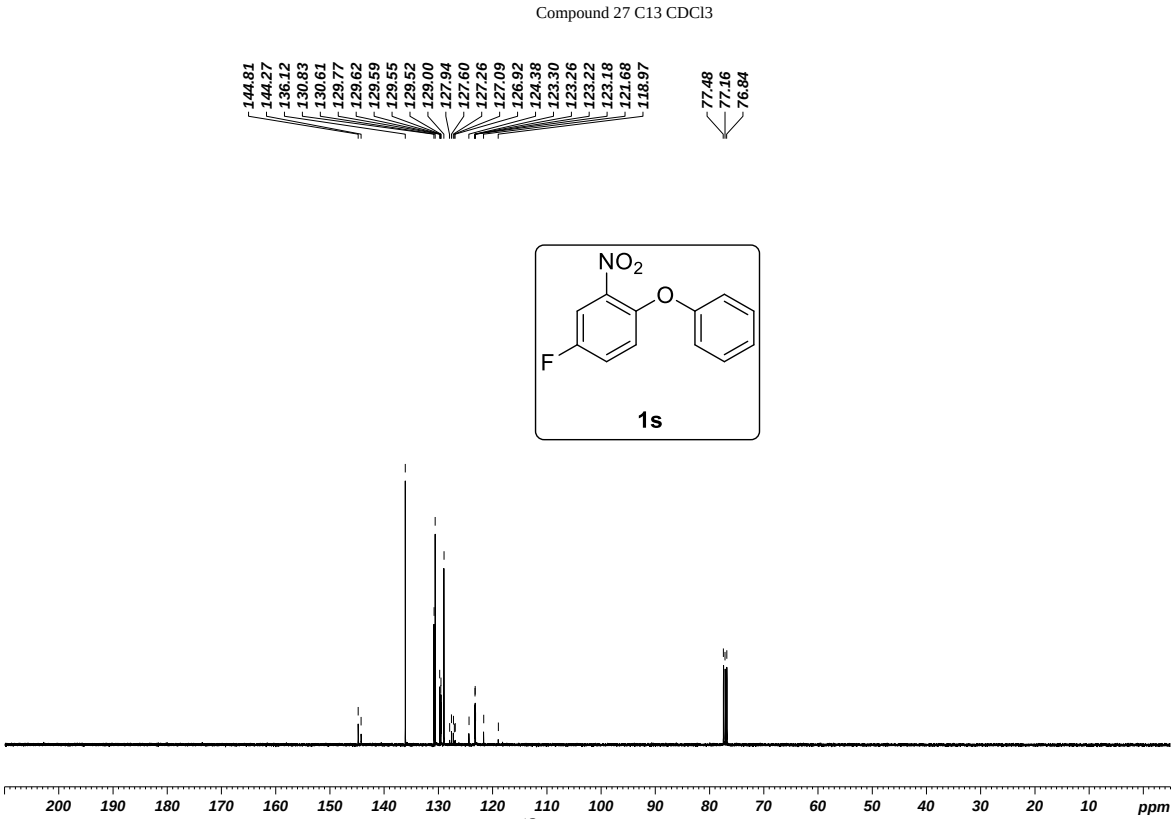
Compound 26 DEPT135 CDCl3



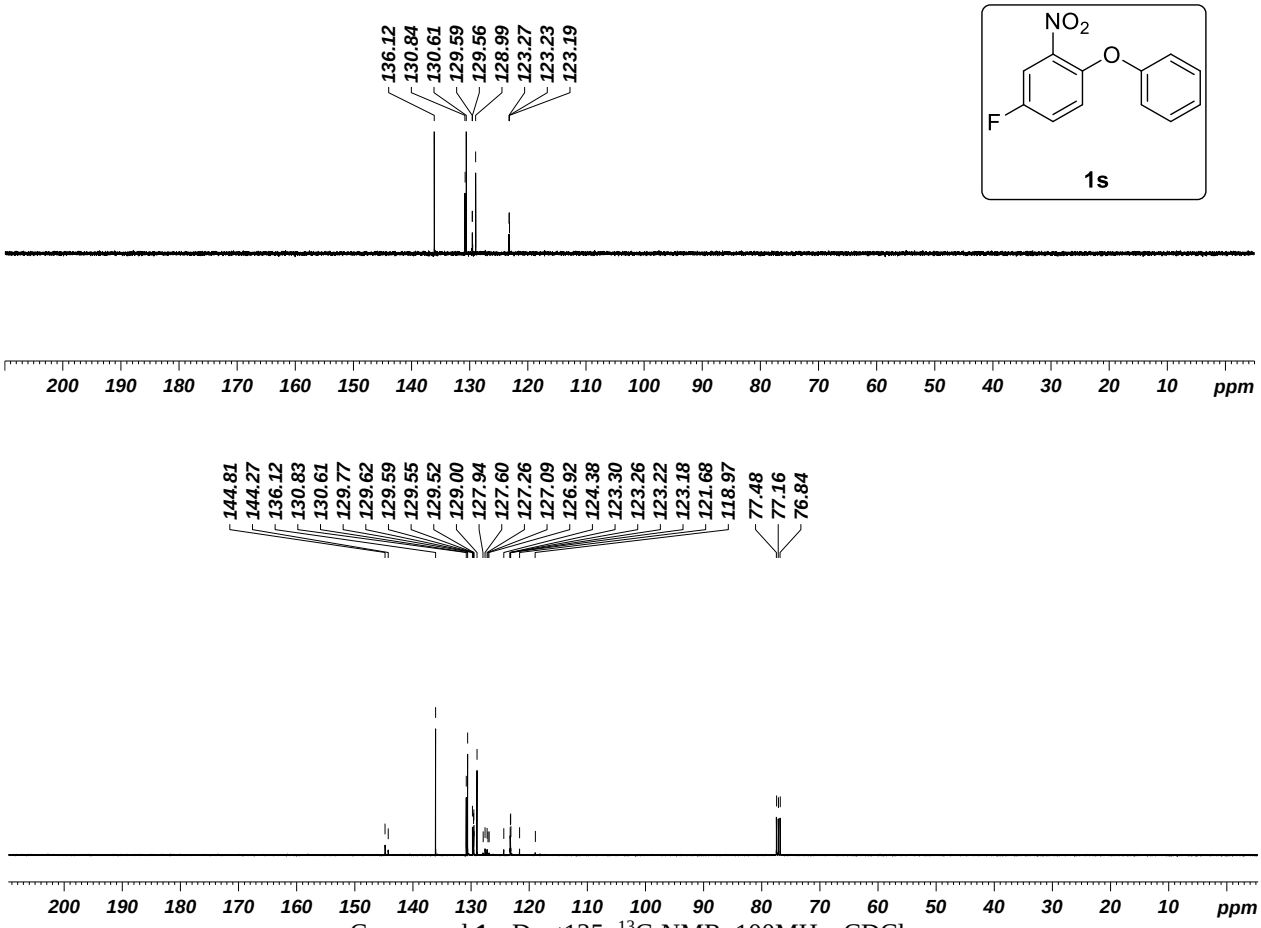
Compound **1r**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$



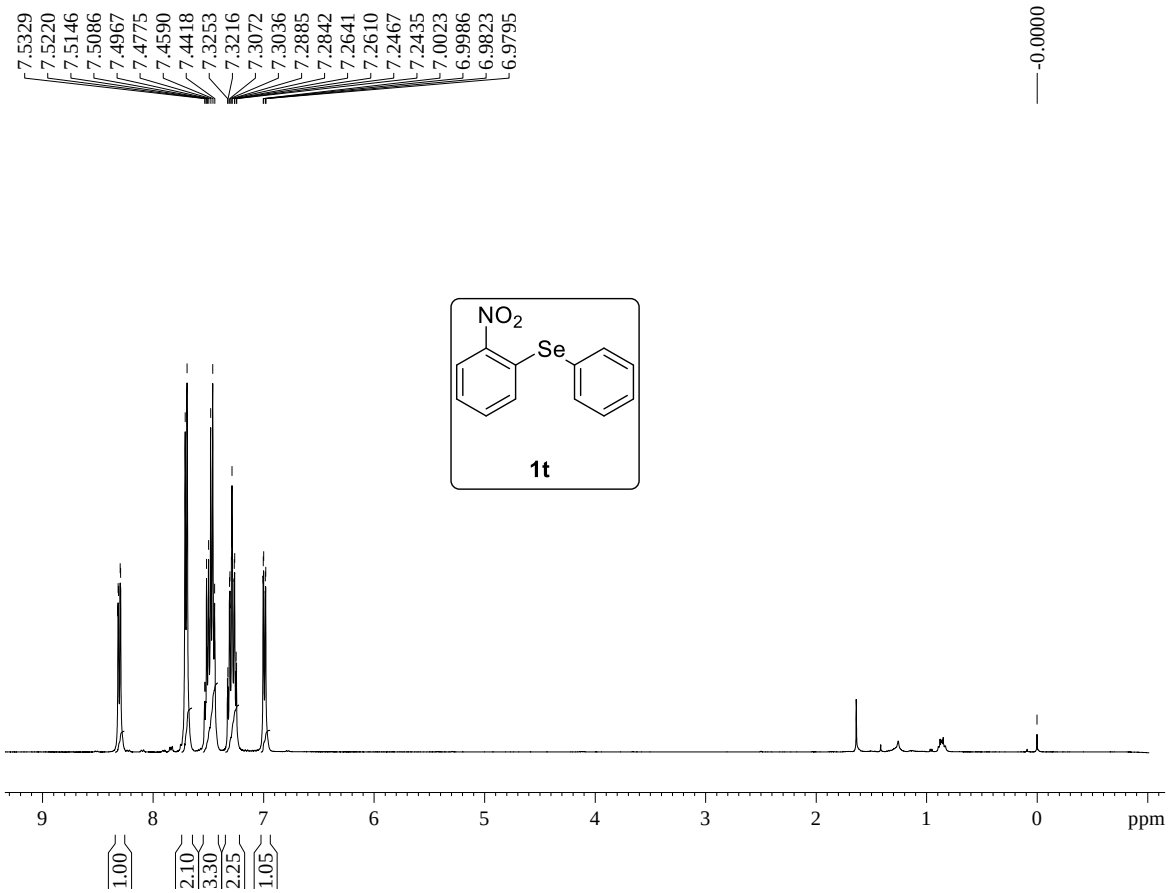
Compound **1s**, ^{1}H-NMR, 400MHz, $CDCl_3$



Compound **1s**, ^{13}C-NMR, 100MHz, $CDCl_3$

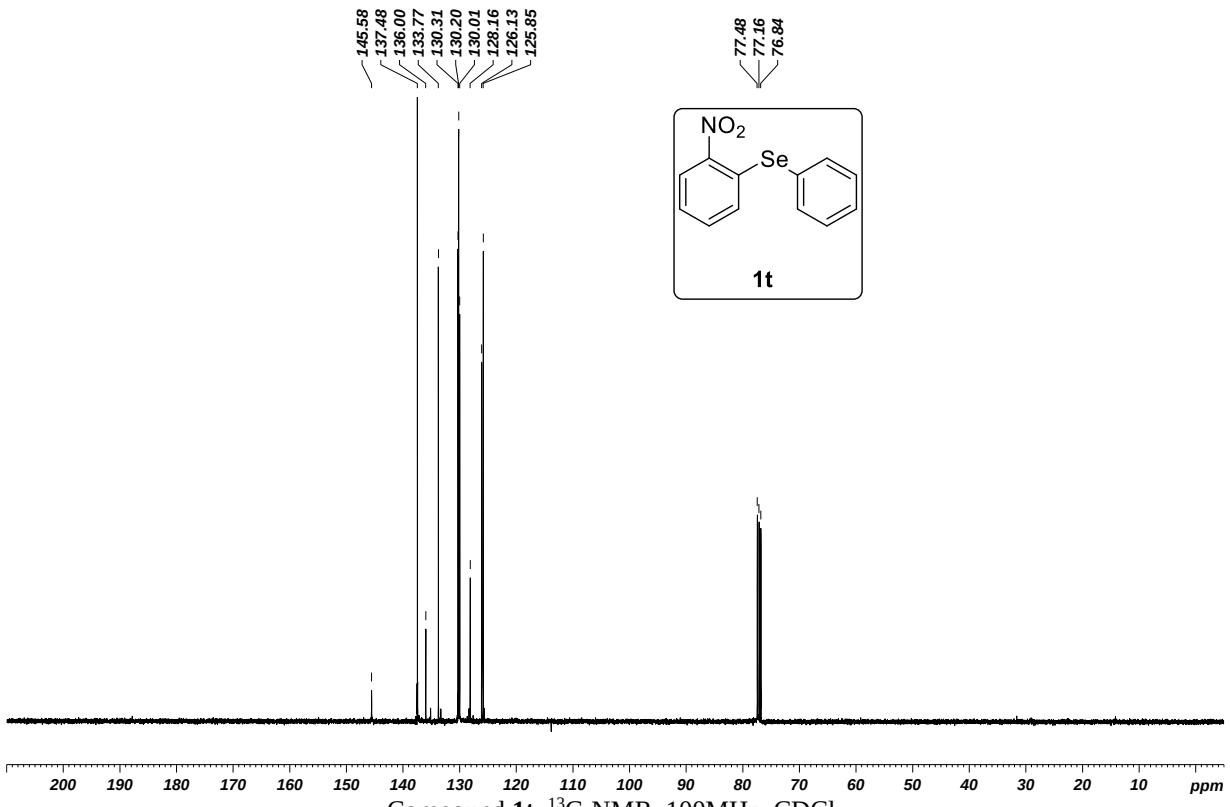


Compound **1s**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$



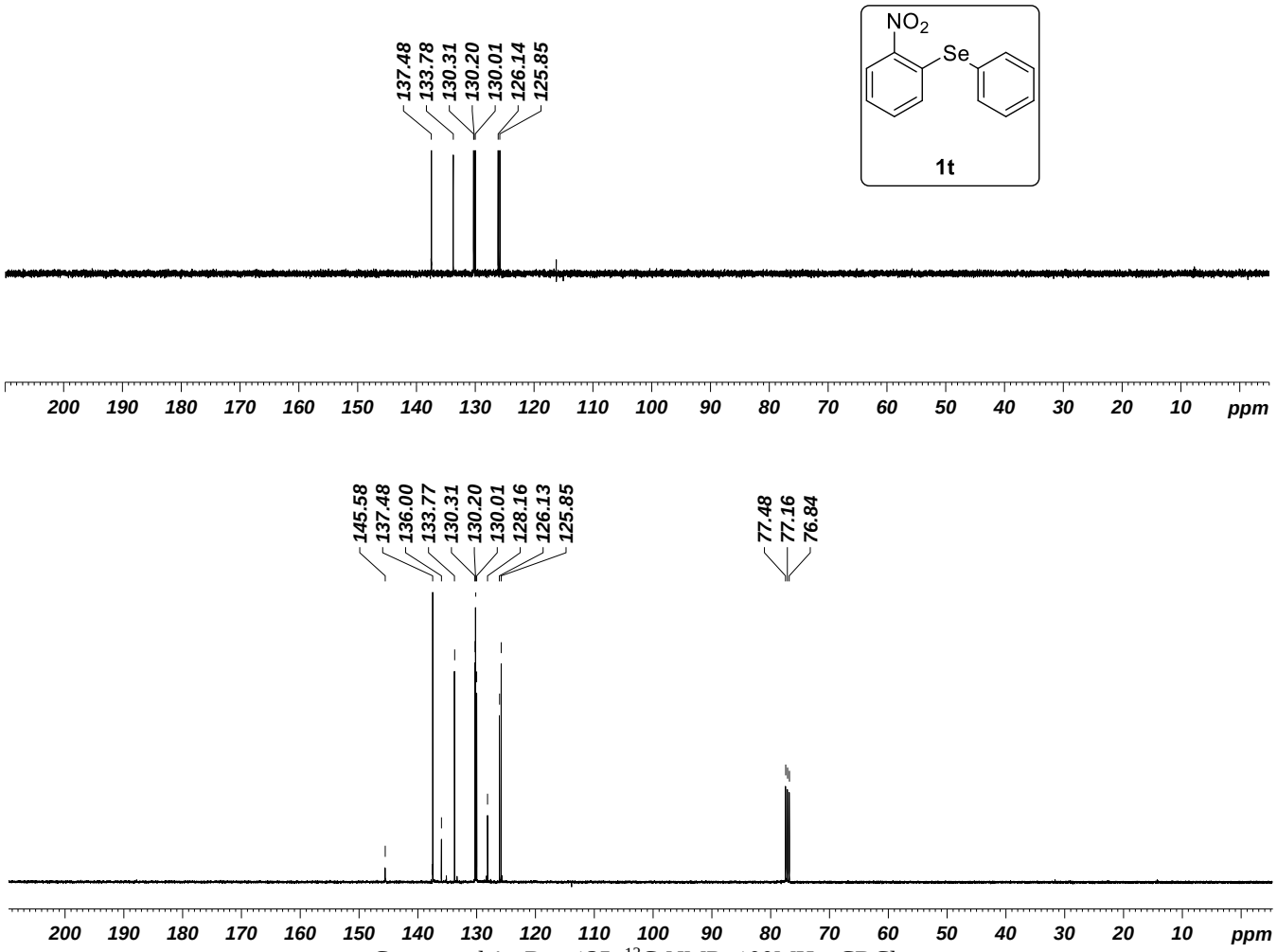
Compound **1t**, ^{1}H-NMR, 400MHz, $CDCl_3$

Compound 24 C13 CDCl3

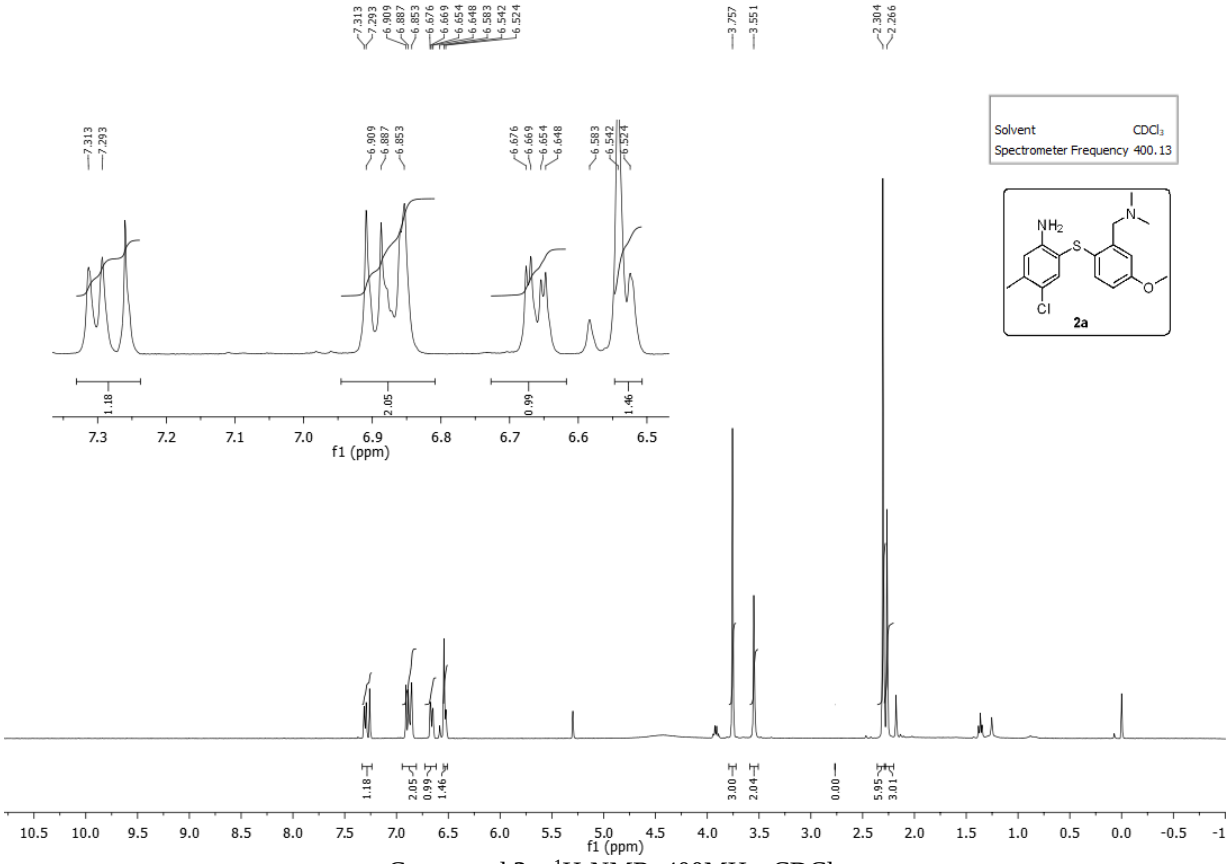


Compound **1t**, ^{13}C-NMR, 100MHz, $CDCl_3$

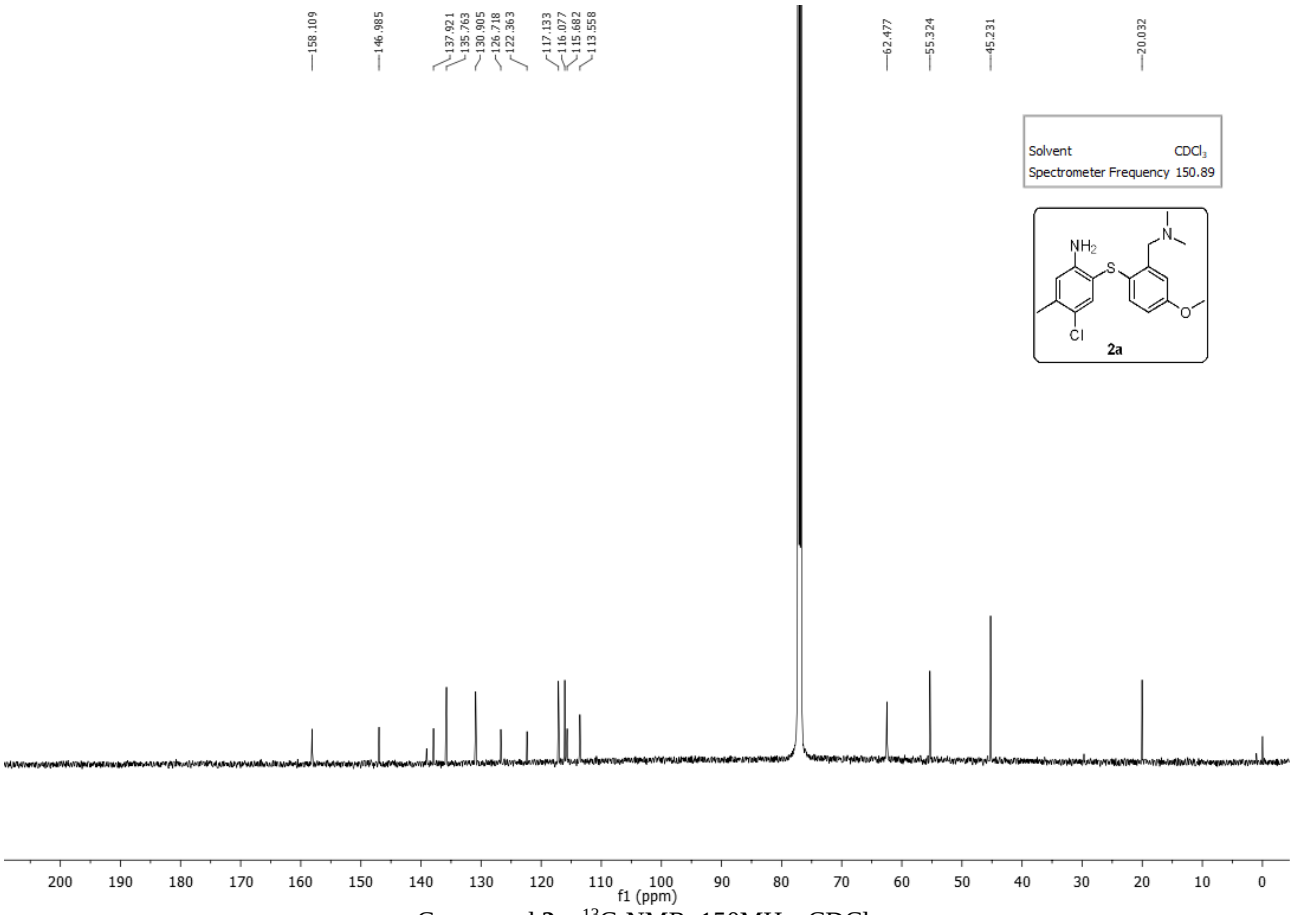
compound 24 DEPT135 CDCl3



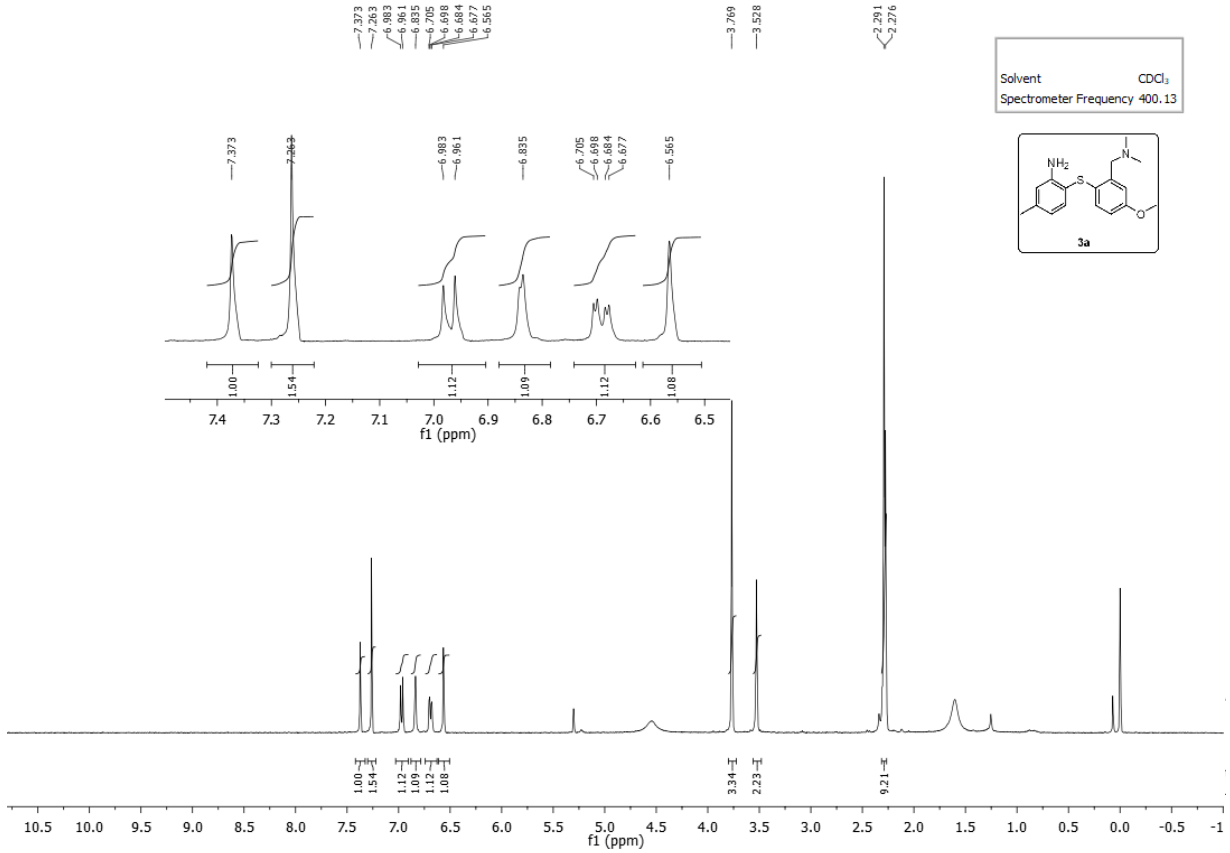
Compound **1t**, Dept135, ^{13}C-NMR, 100MHz, $CDCl_3$



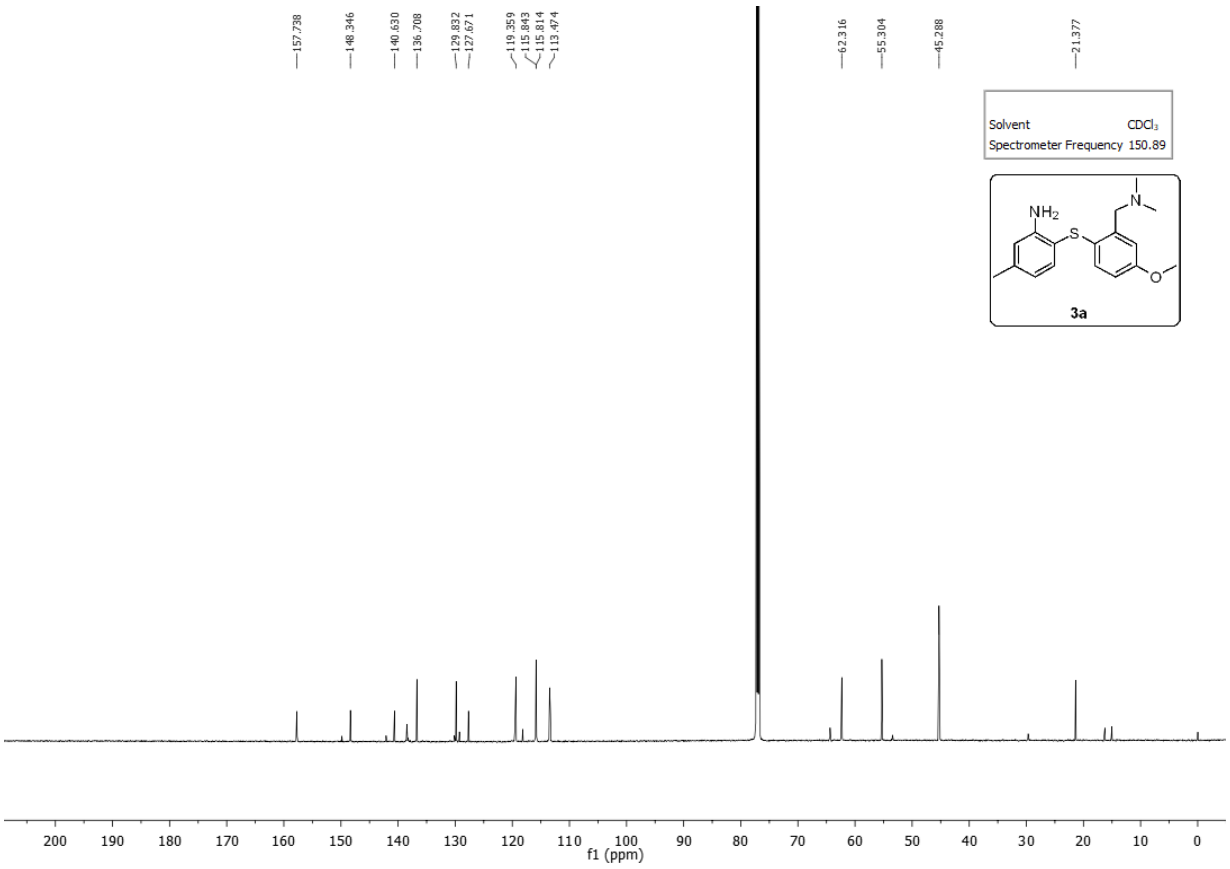
Compound **2a**, ^{1}H-NMR, 400MHz, $CDCl_3$



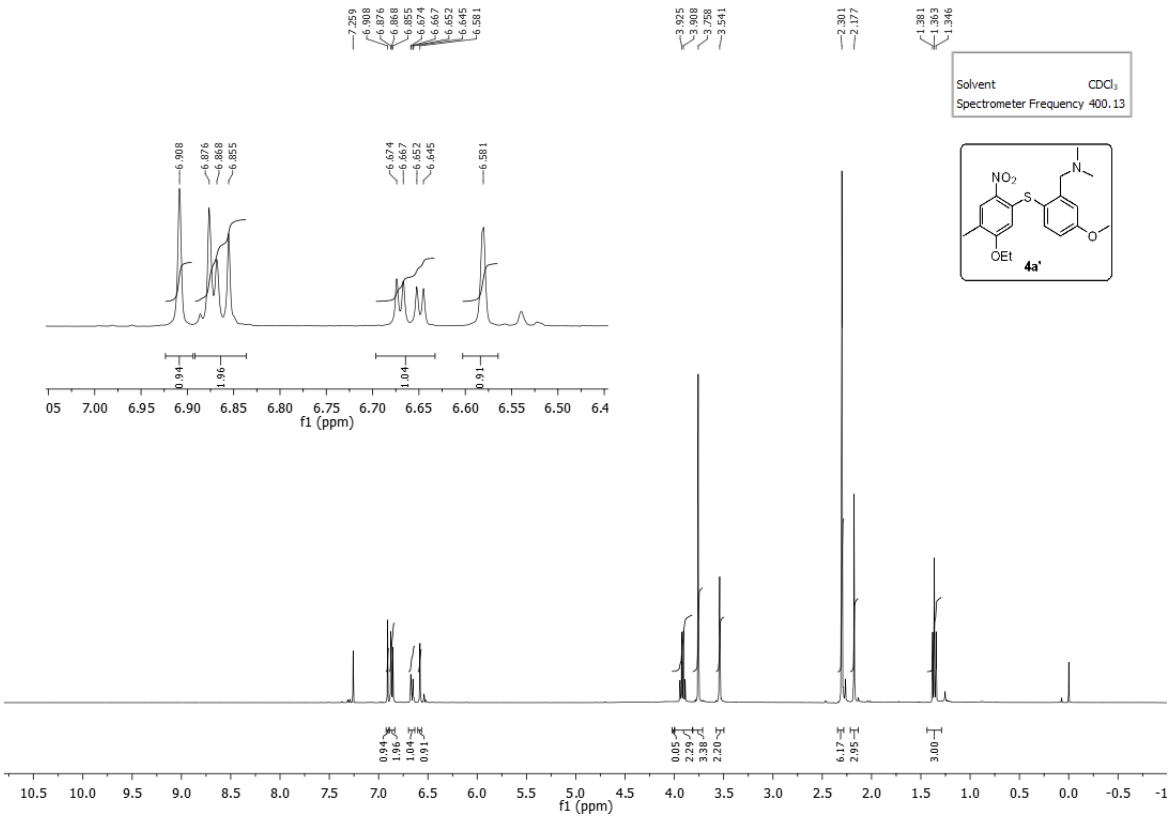
Compound **2a**, ^{13}C-NMR, 150MHz, $CDCl_3$



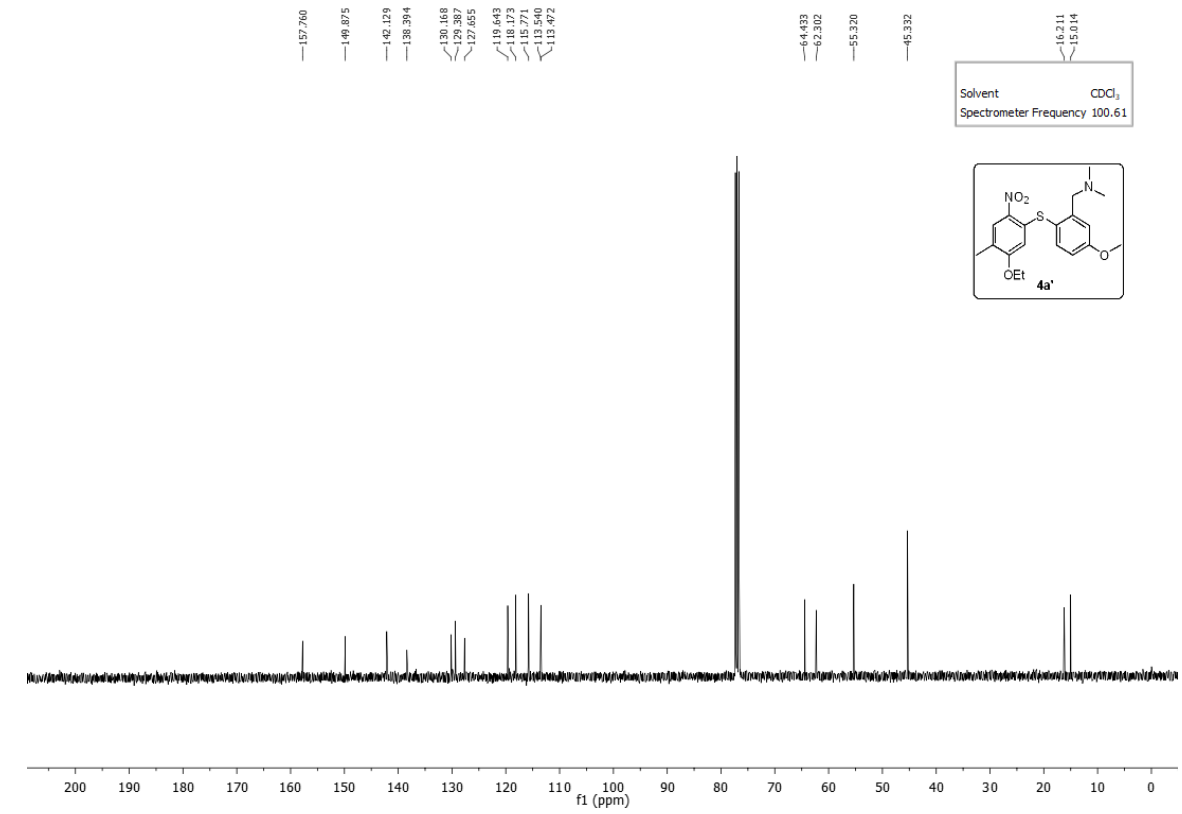
Compound **3a**, ^{1}H-NMR, 400MHz, $CDCl_3$



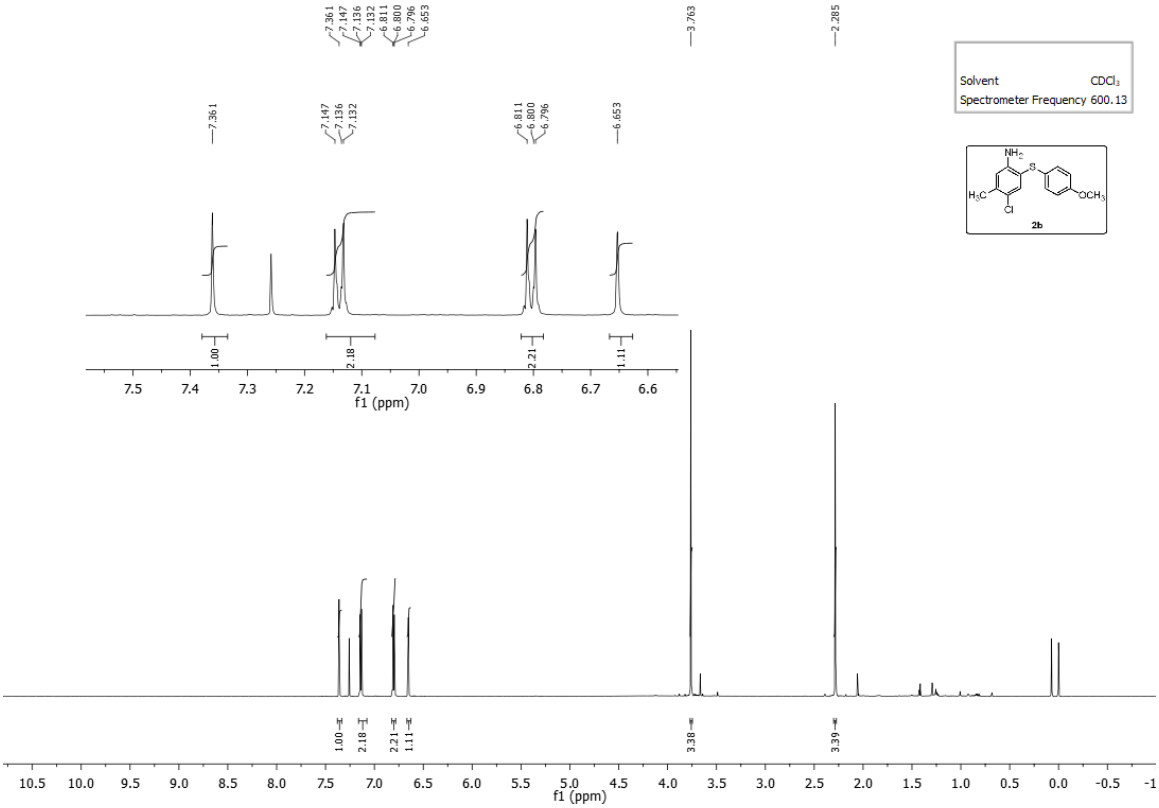
Compound **3a**, ^{13}C-NMR, 150MHz, $CDCl_3$



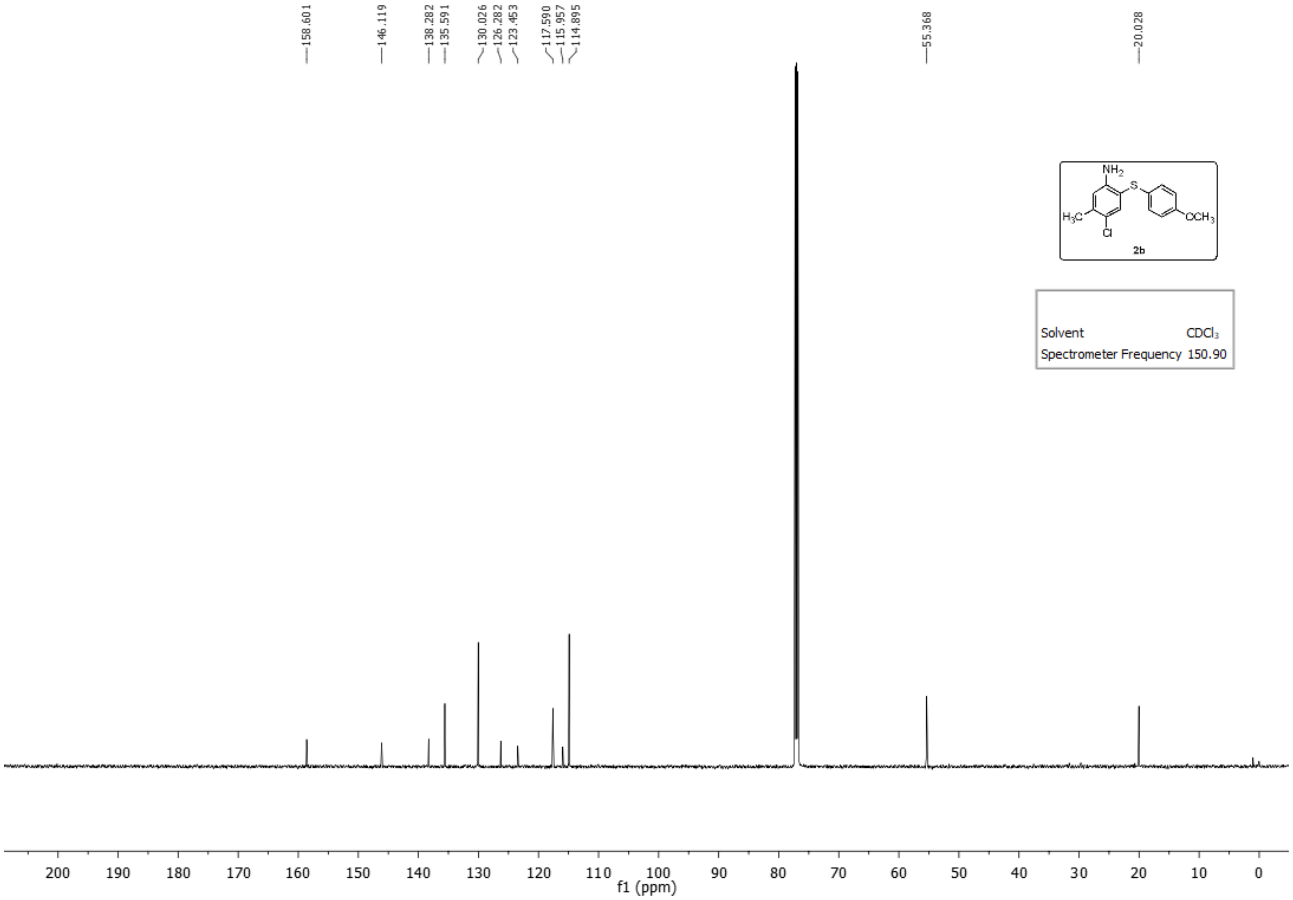
Compound **4a'**, ^{1}H-NMR, 400MHz, $CDCl_3$



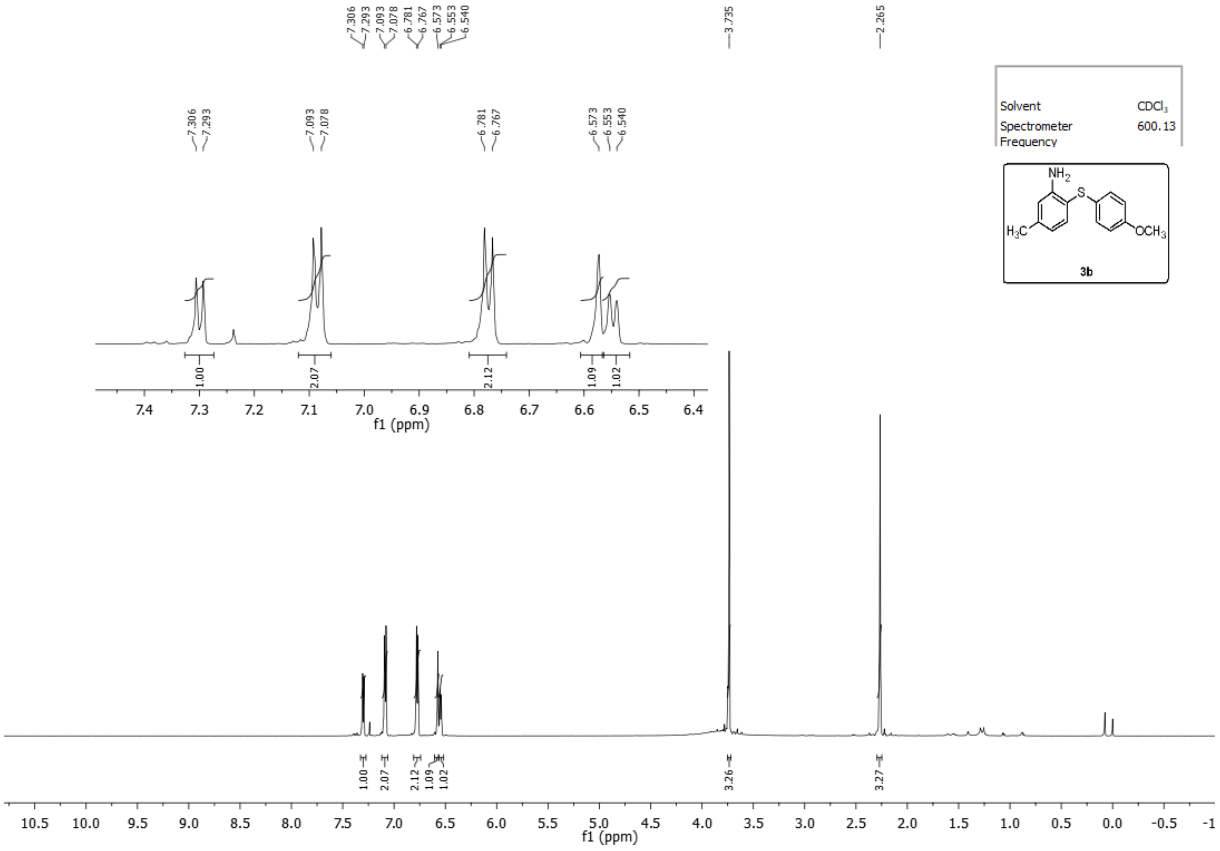
Compound **4a'**, ^{13}C-NMR, 100MHz, $CDCl_3$



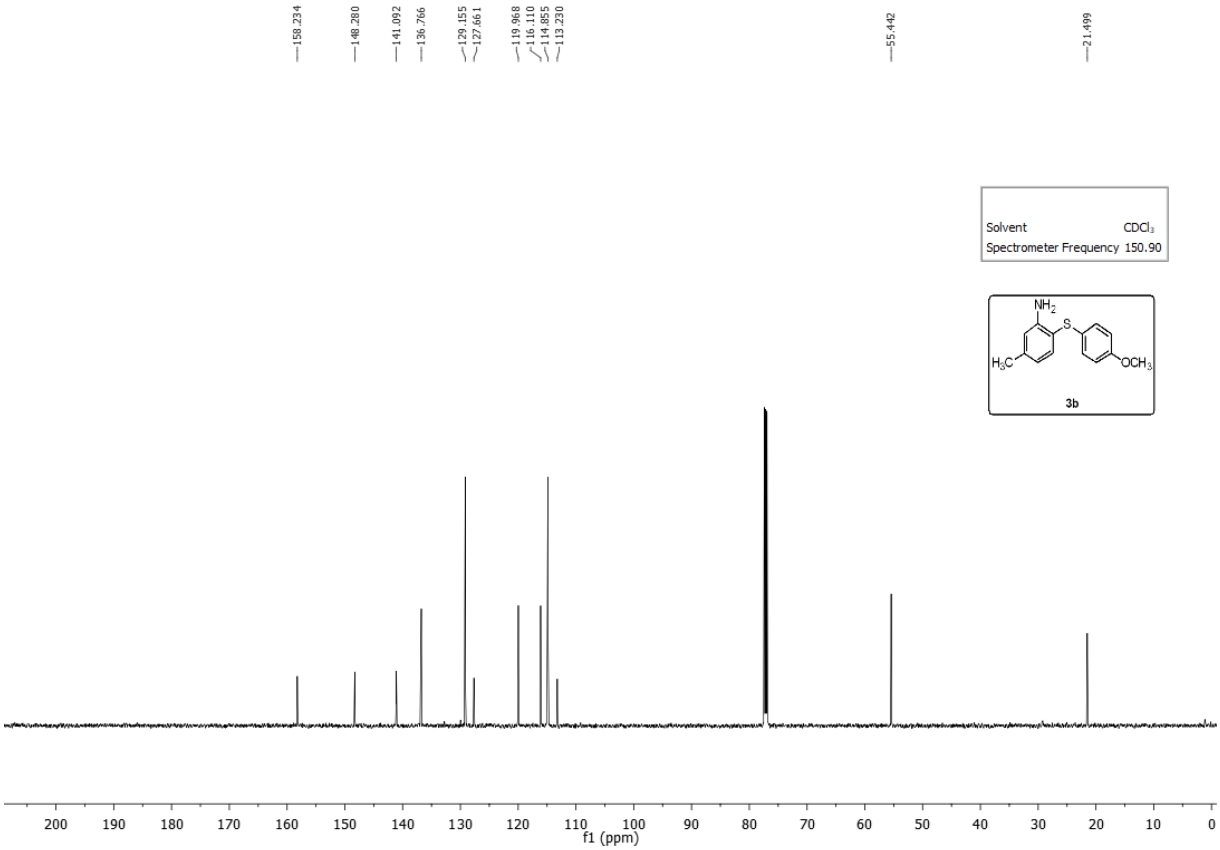
Compound **2b**, ^{1}H-NMR, 600MHz, $CDCl_3$



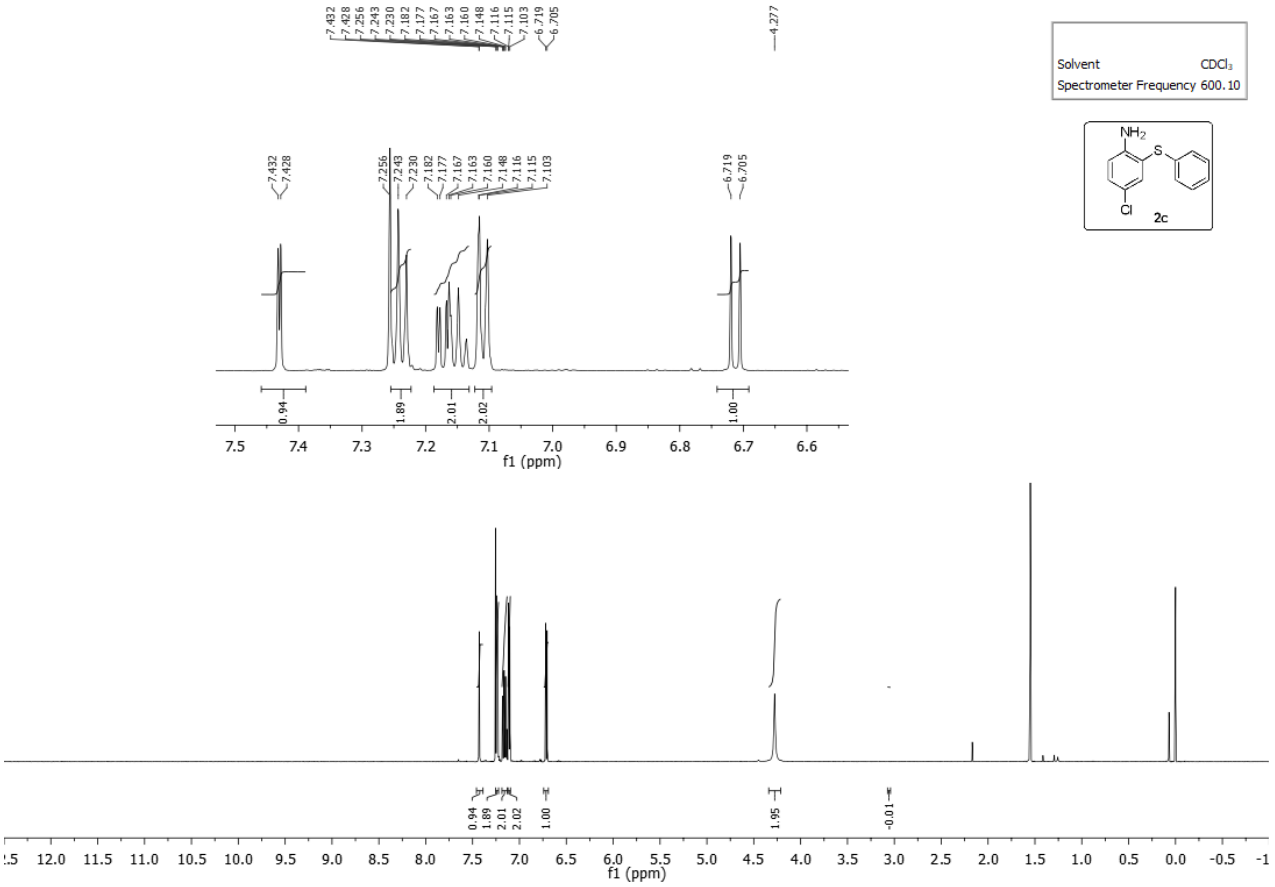
Compound **2b**, ^{13}C-NMR, 150MHz, $CDCl_3$



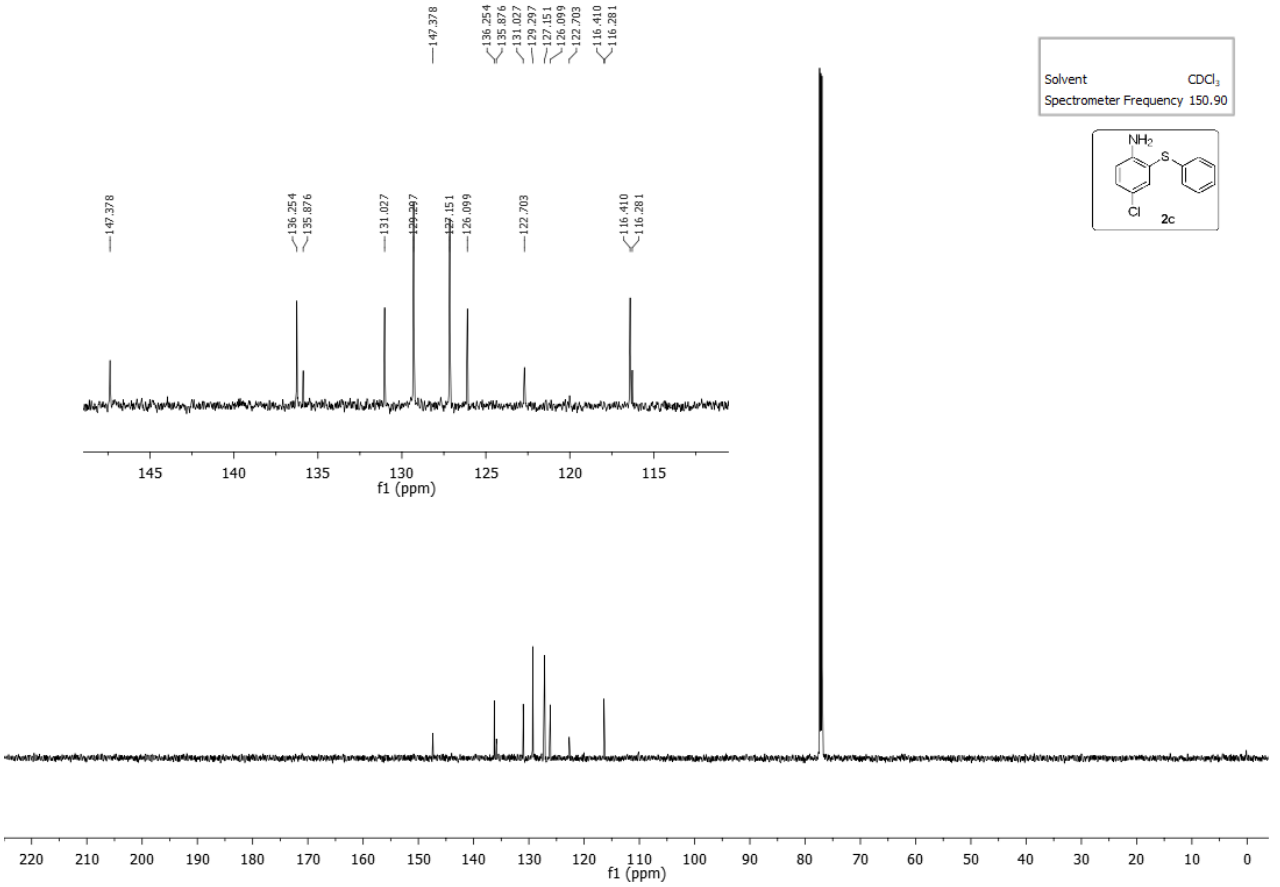
Compound **3b**, ^{1}H-NMR, 600MHz, $CDCl_3$



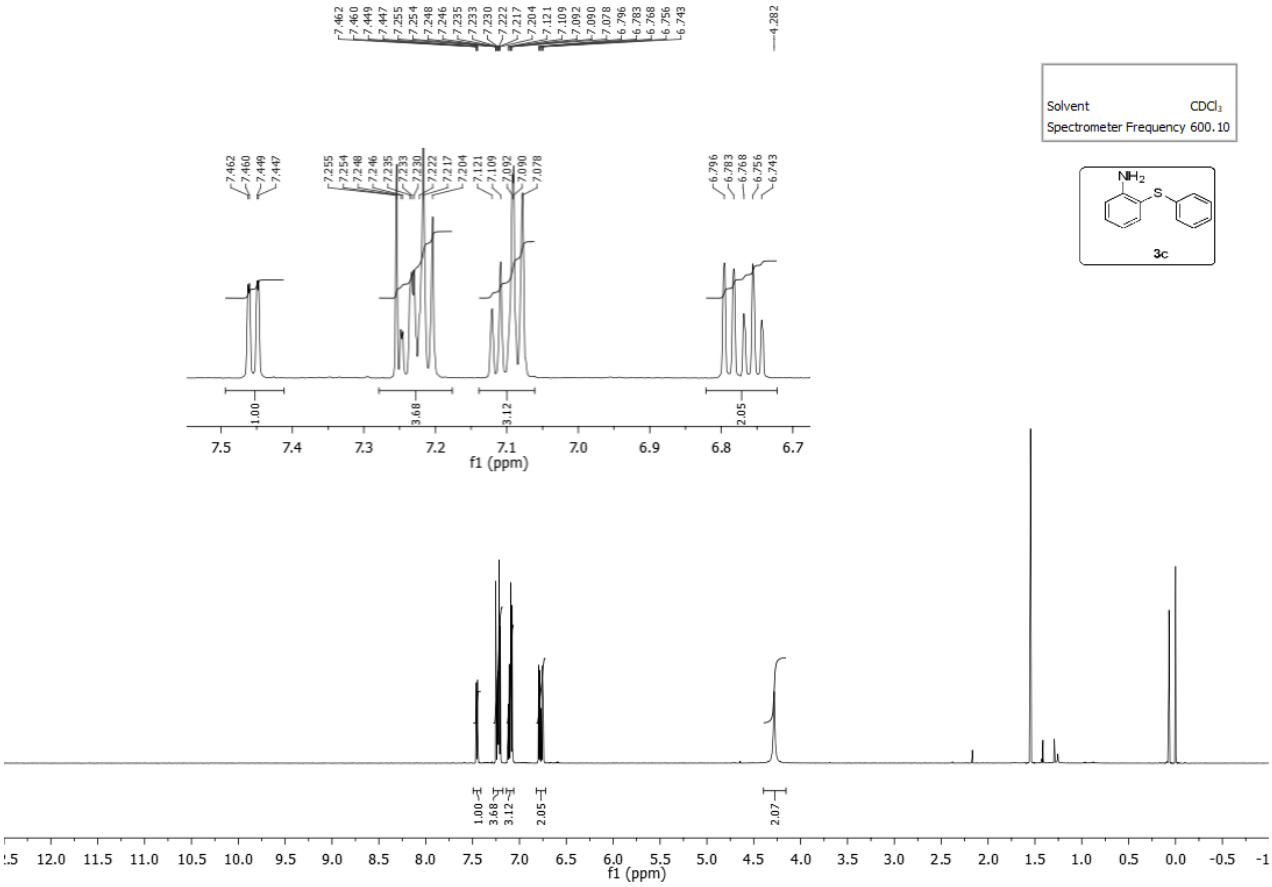
Compound **3b**, ^{13}C-NMR, 150MHz, $CDCl_3$



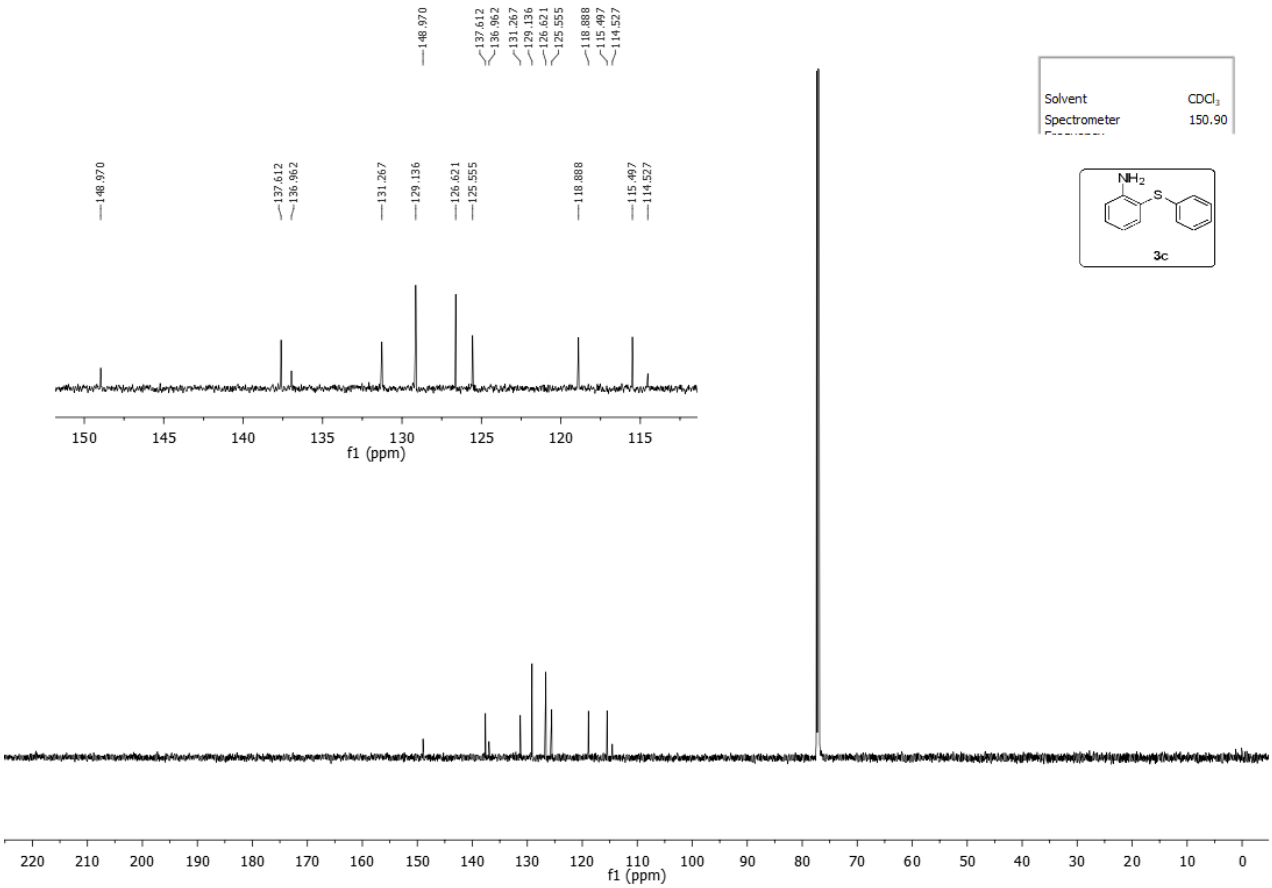
Compound **2c**, ^{1}H-NMR, 600MHz, $CDCl_3$



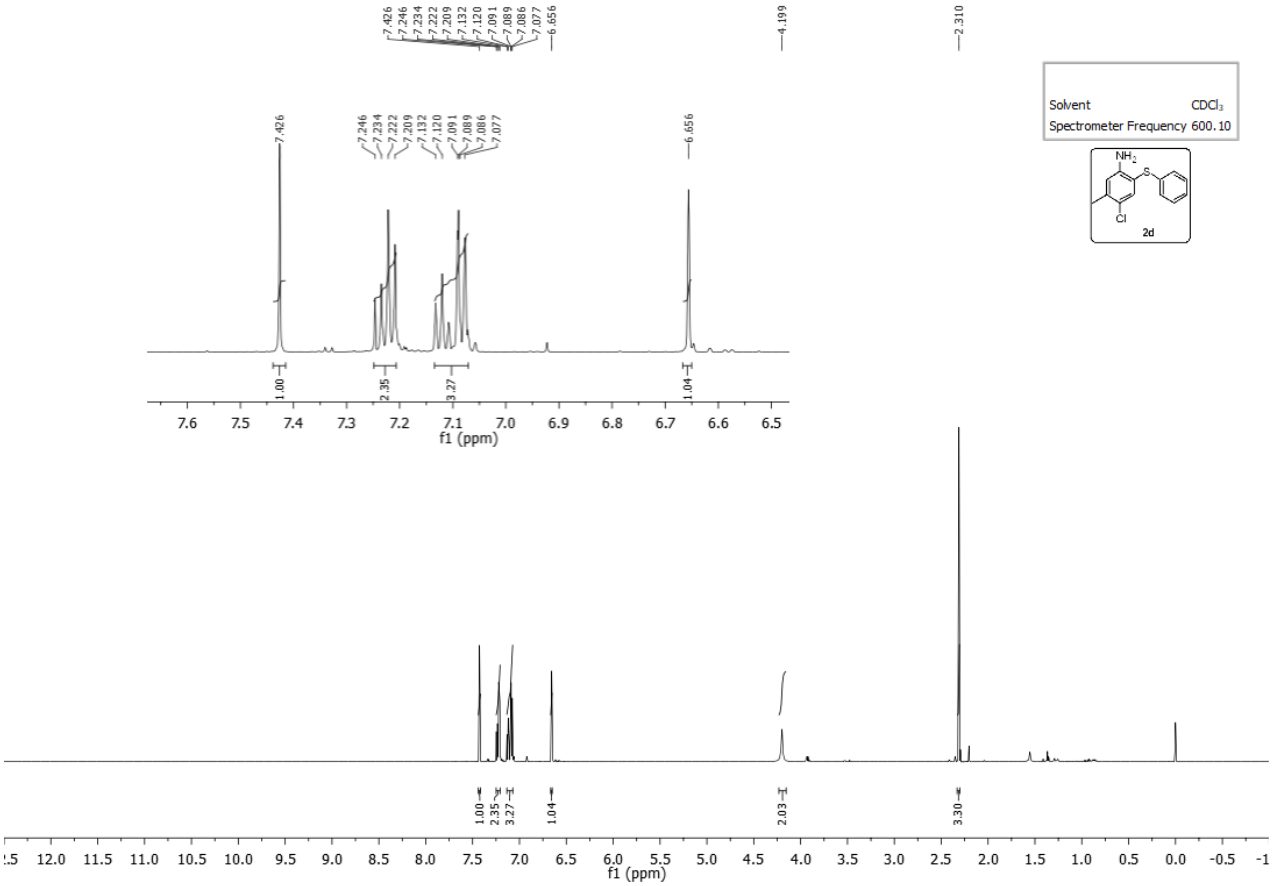
Compound **2c**, ^{13}C-NMR, 150MHz, $CDCl_3$



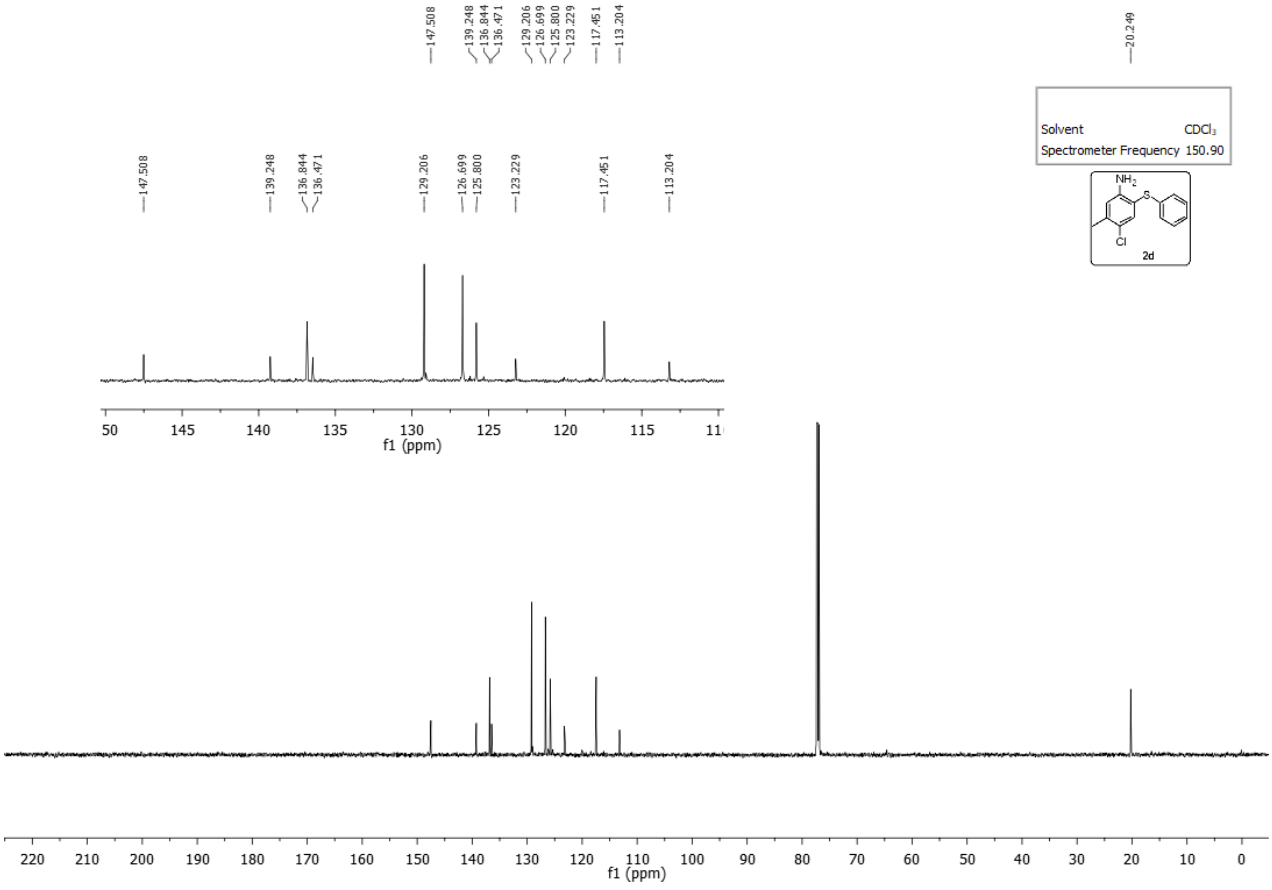
Compound **3c**, ^{1}H-NMR, 600MHz, $CDCl_3$



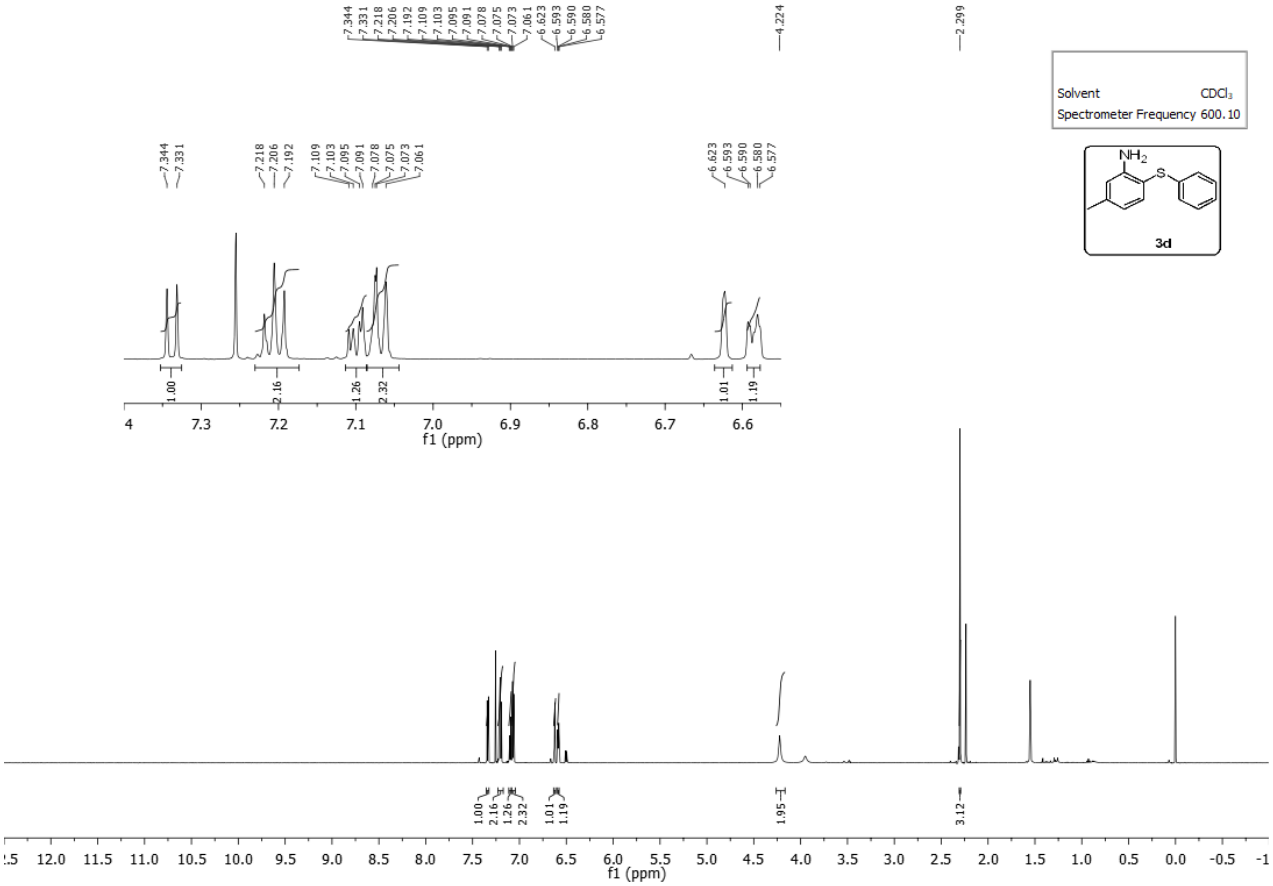
Compound **3c**, ^{13}C-NMR, 150MHz, $CDCl_3$



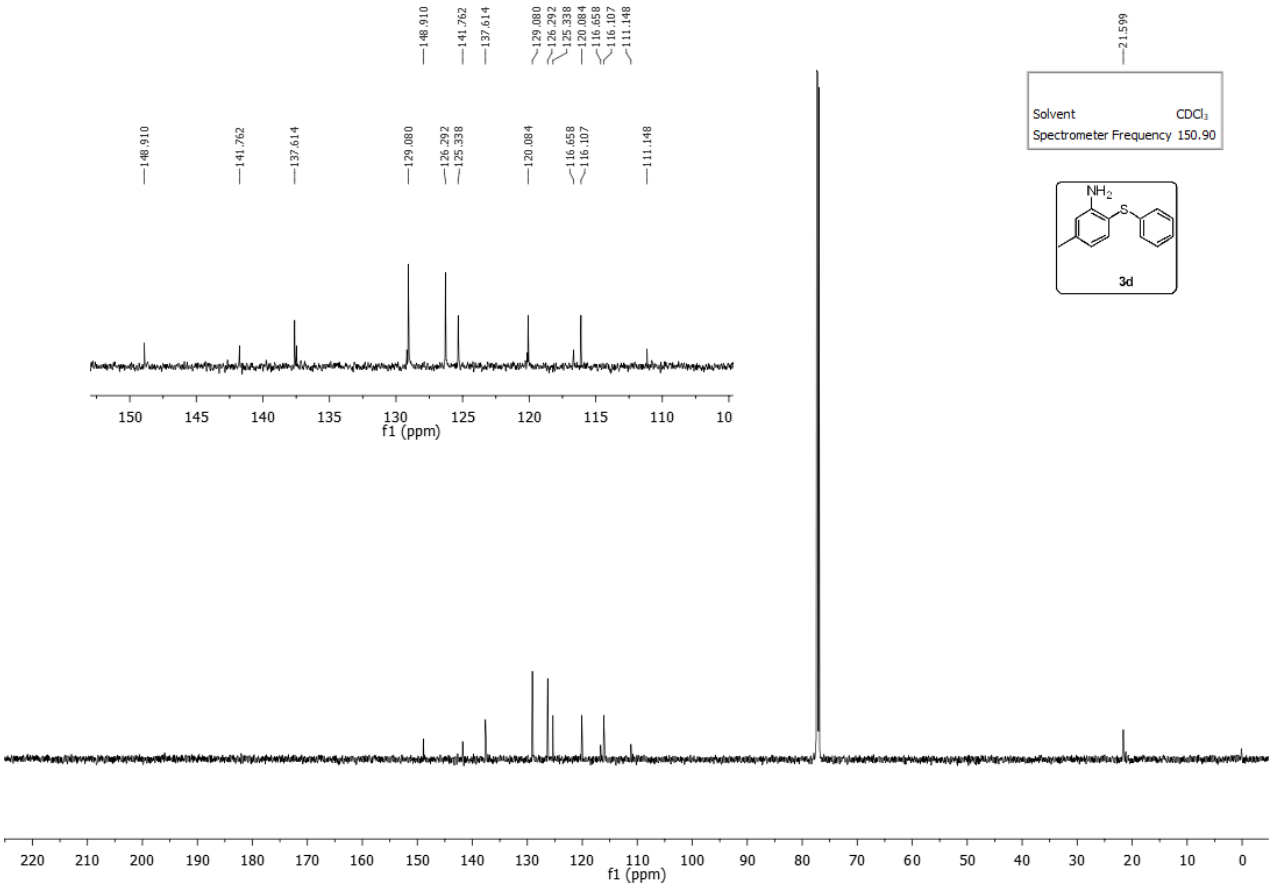
Compound **2d**, ^{1}H-NMR, 600MHz, $CDCl_3$



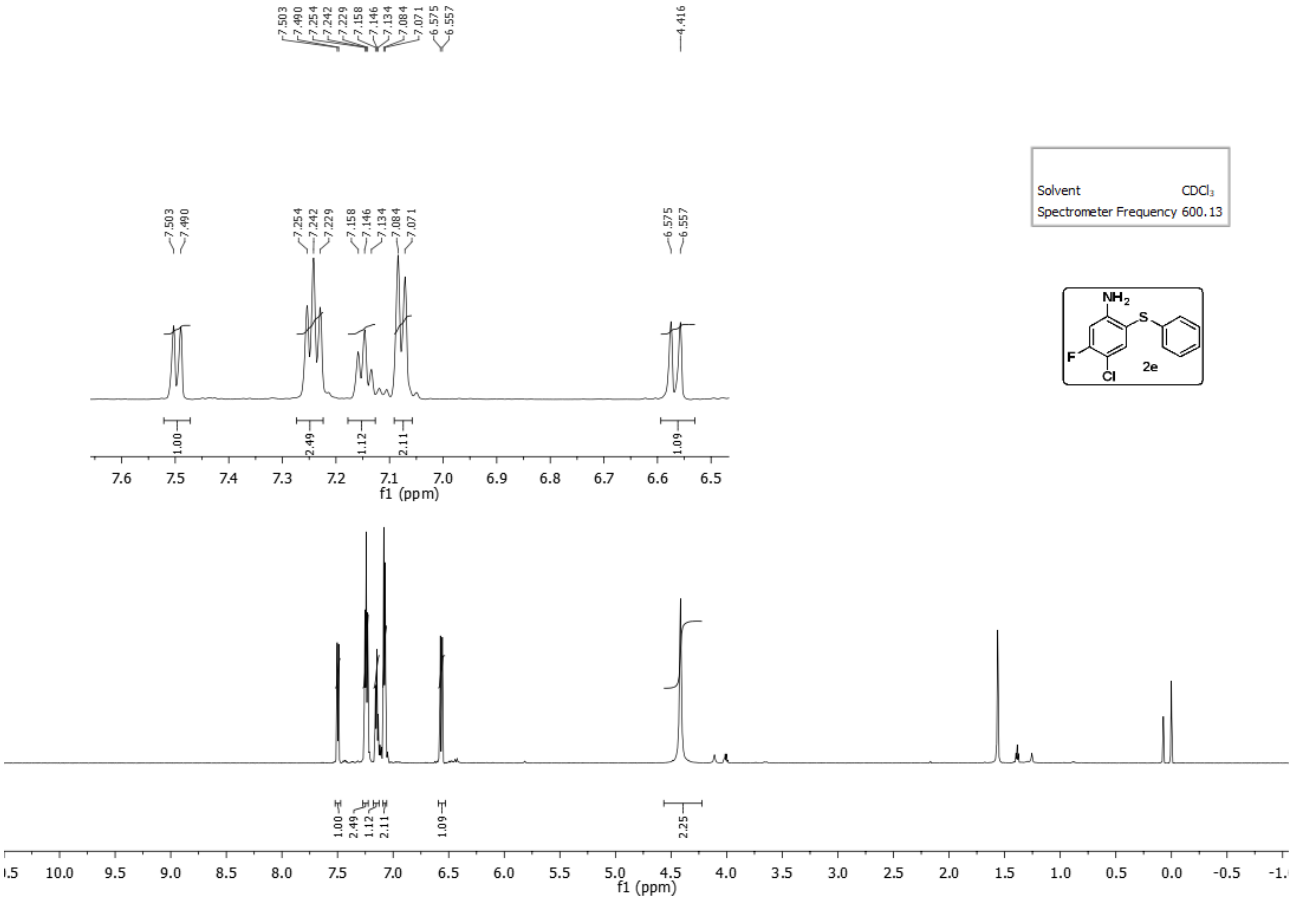
Compound **2d**, ^{13}C-NMR, 150MHz, $CDCl_3$



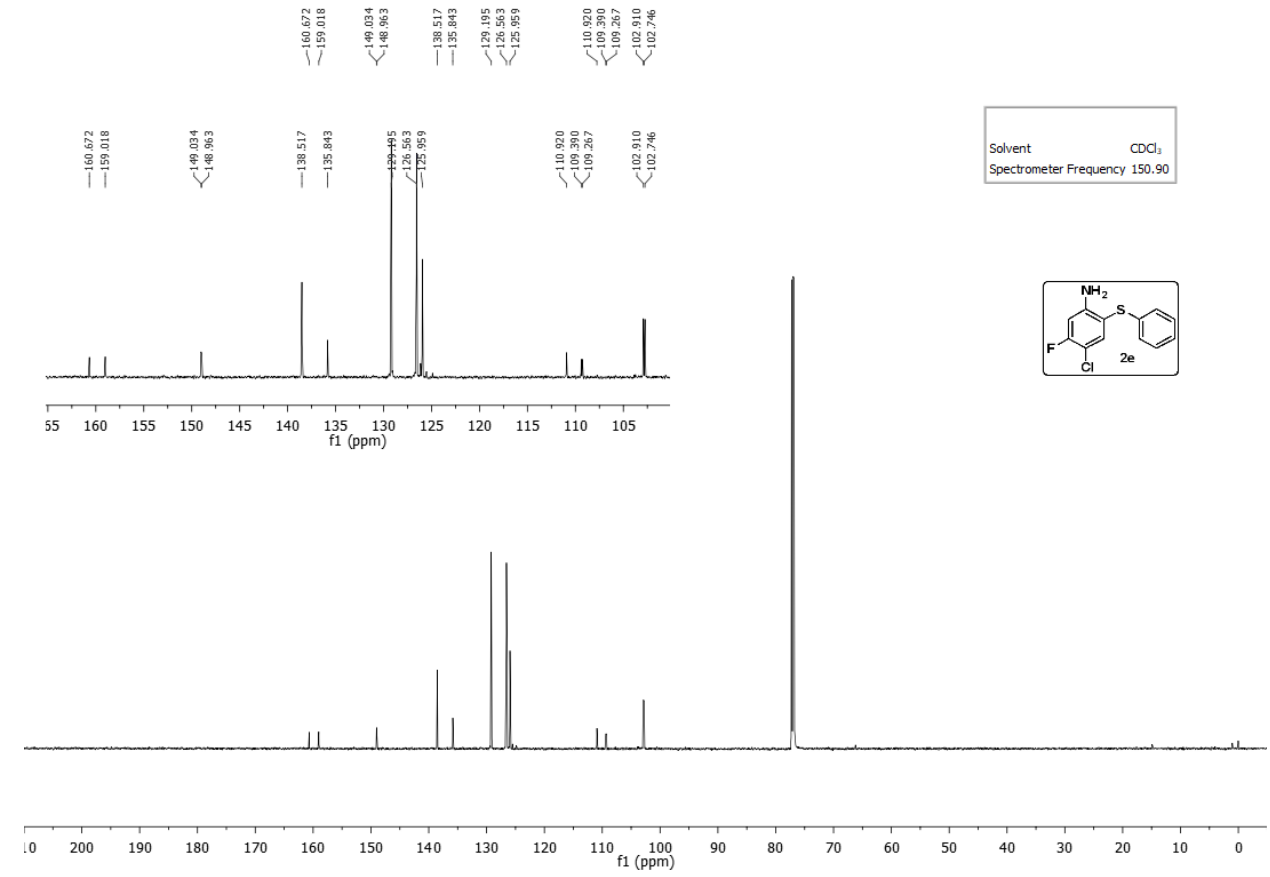
Compound **3d**, ^{1}H-NMR, 600MHz, $CDCl_3$



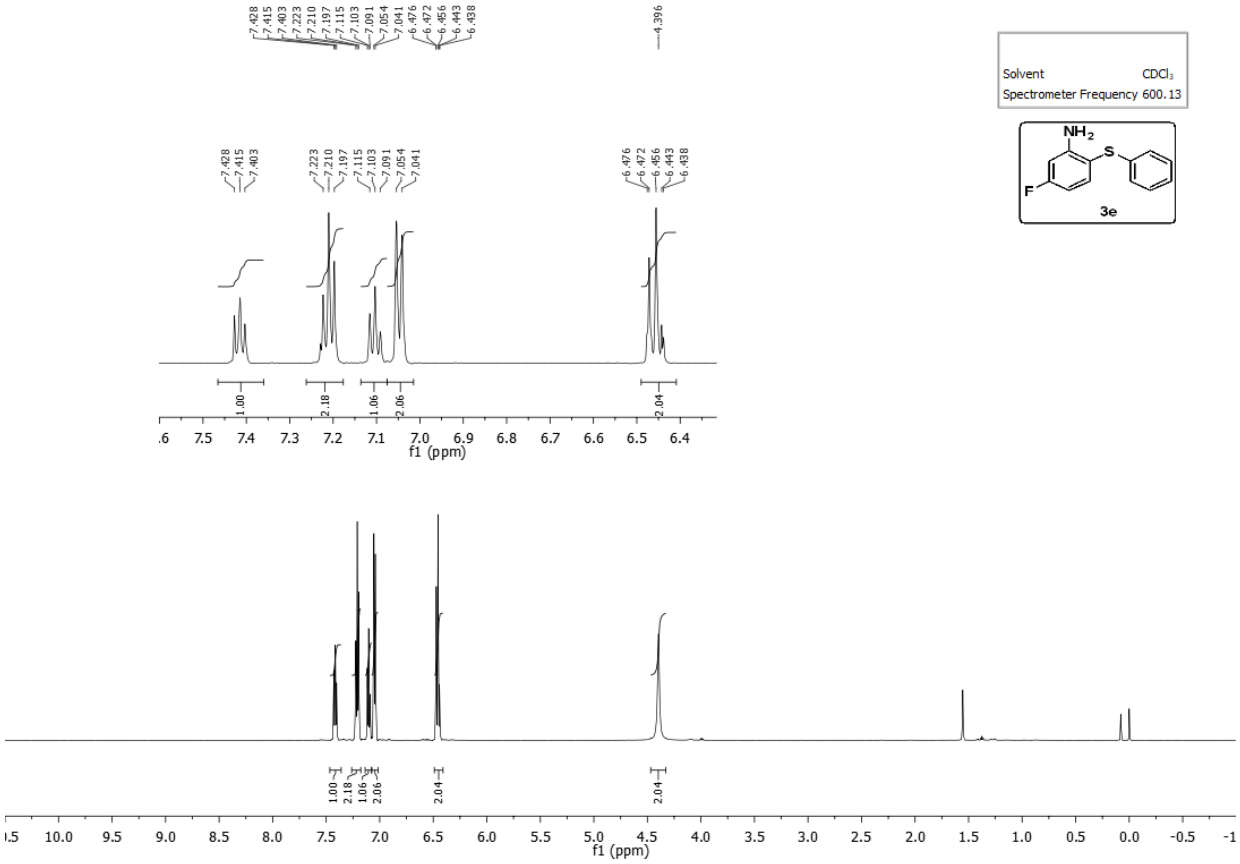
Compound **3d**, ^{13}C-NMR, 150MHz, $CDCl_3$



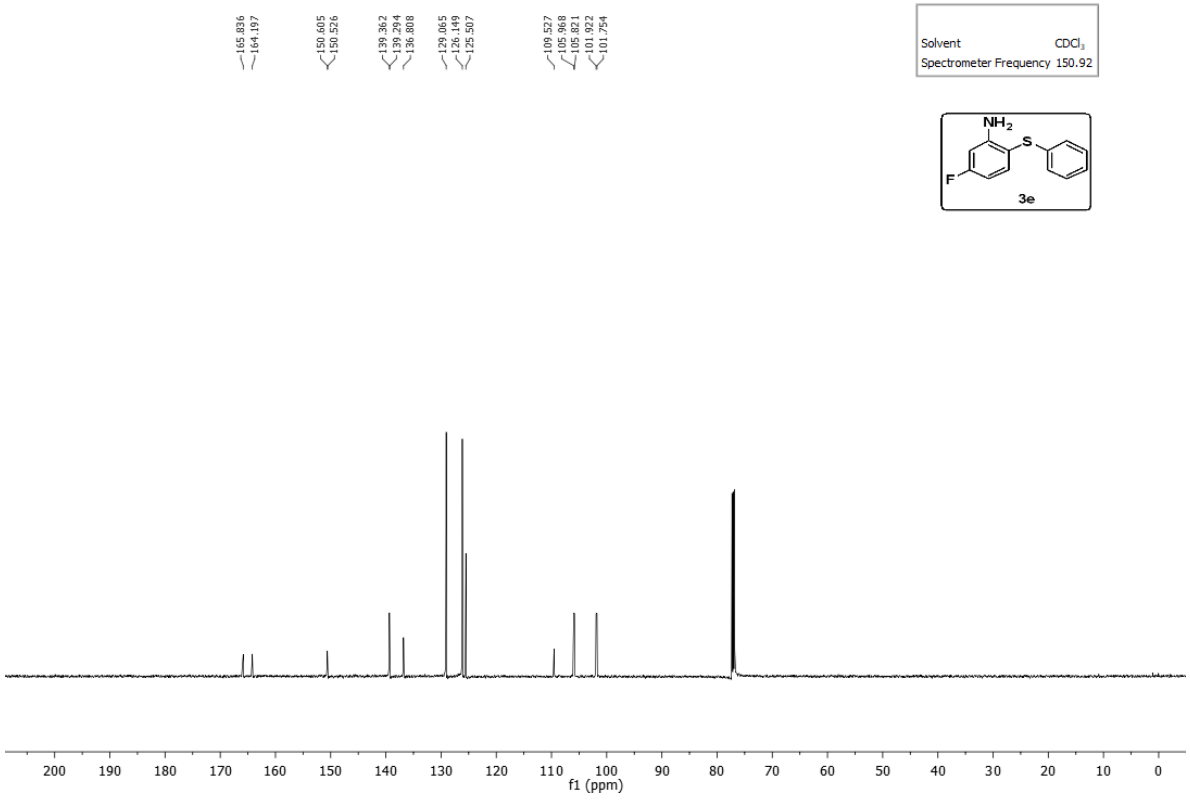
Compound **2e**, ^{1}H-NMR, 600MHz, $CDCl_3$



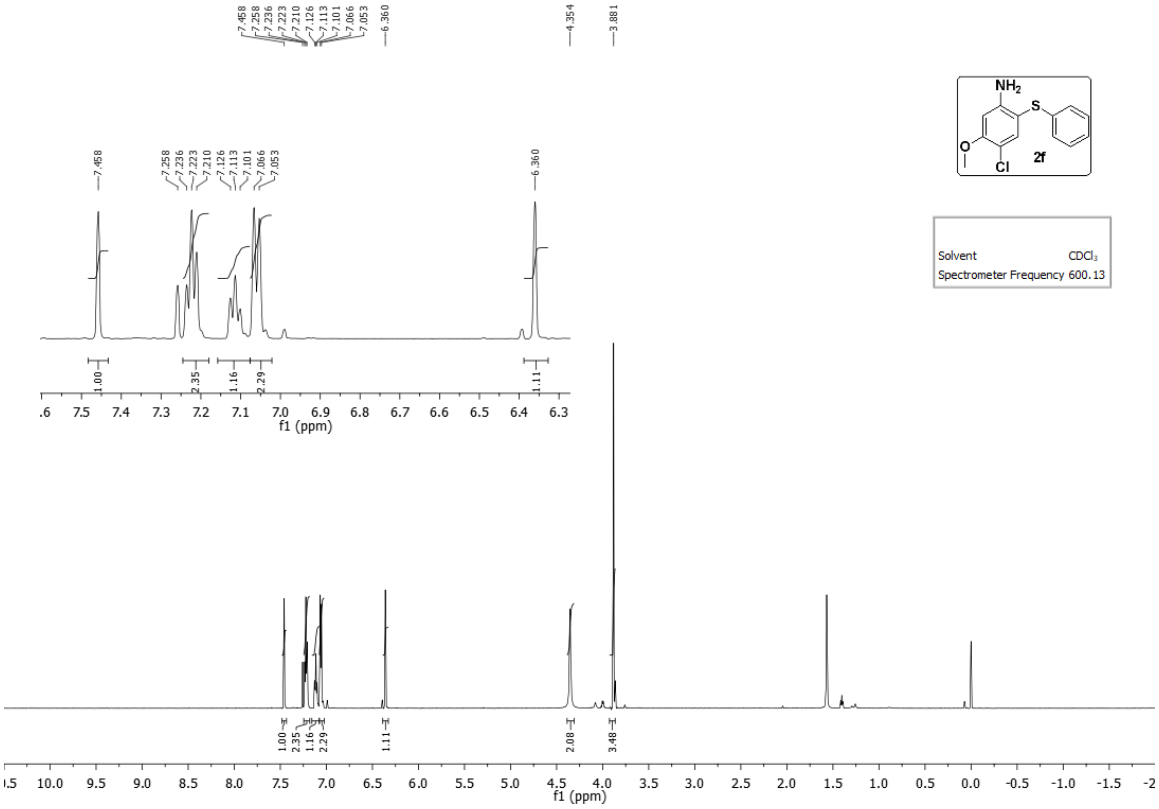
Compound **2e**, ^{13}C-NMR, 150MHz, $CDCl_3$



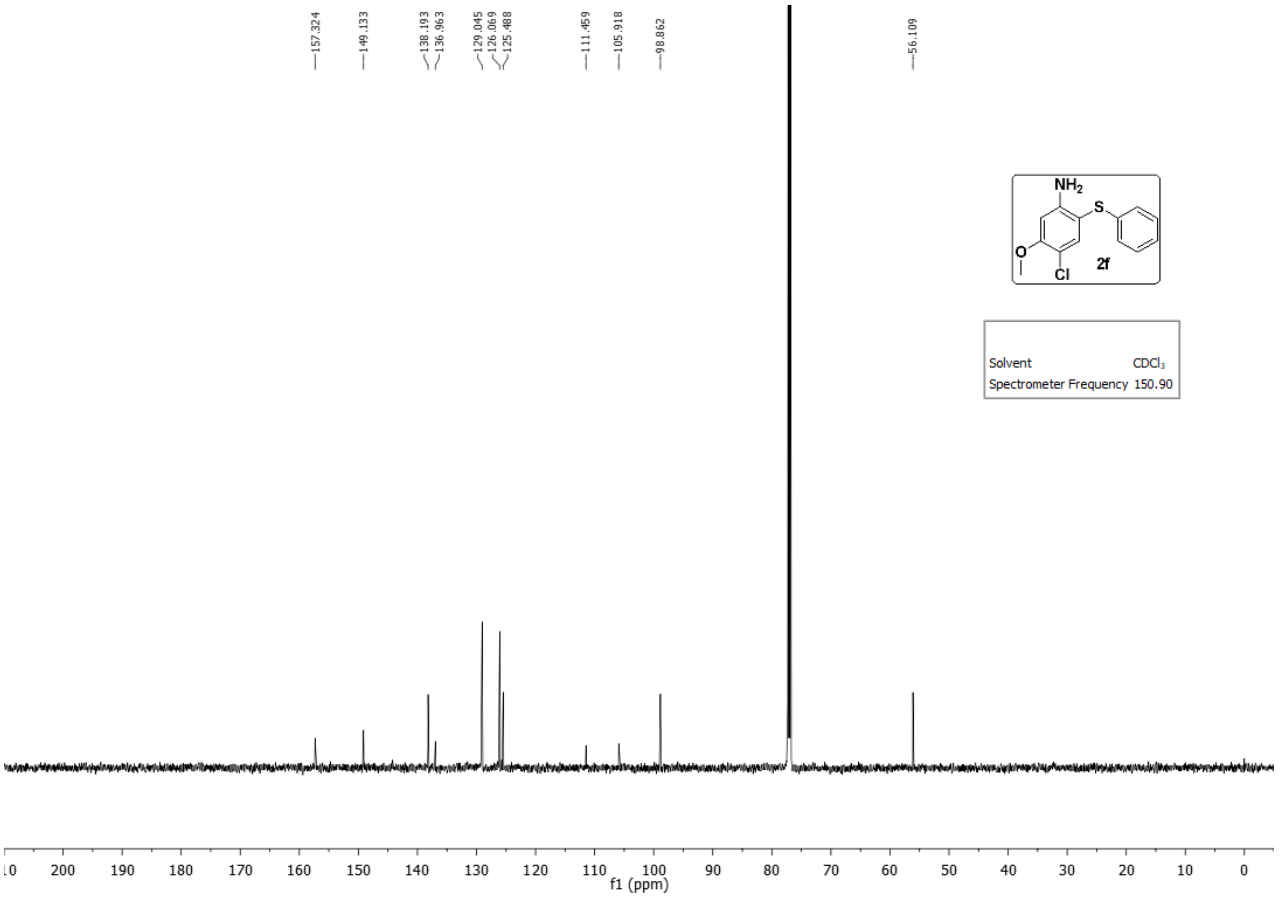
Compound **3e**, ^{1}H-NMR, 600MHz, $CDCl_3$



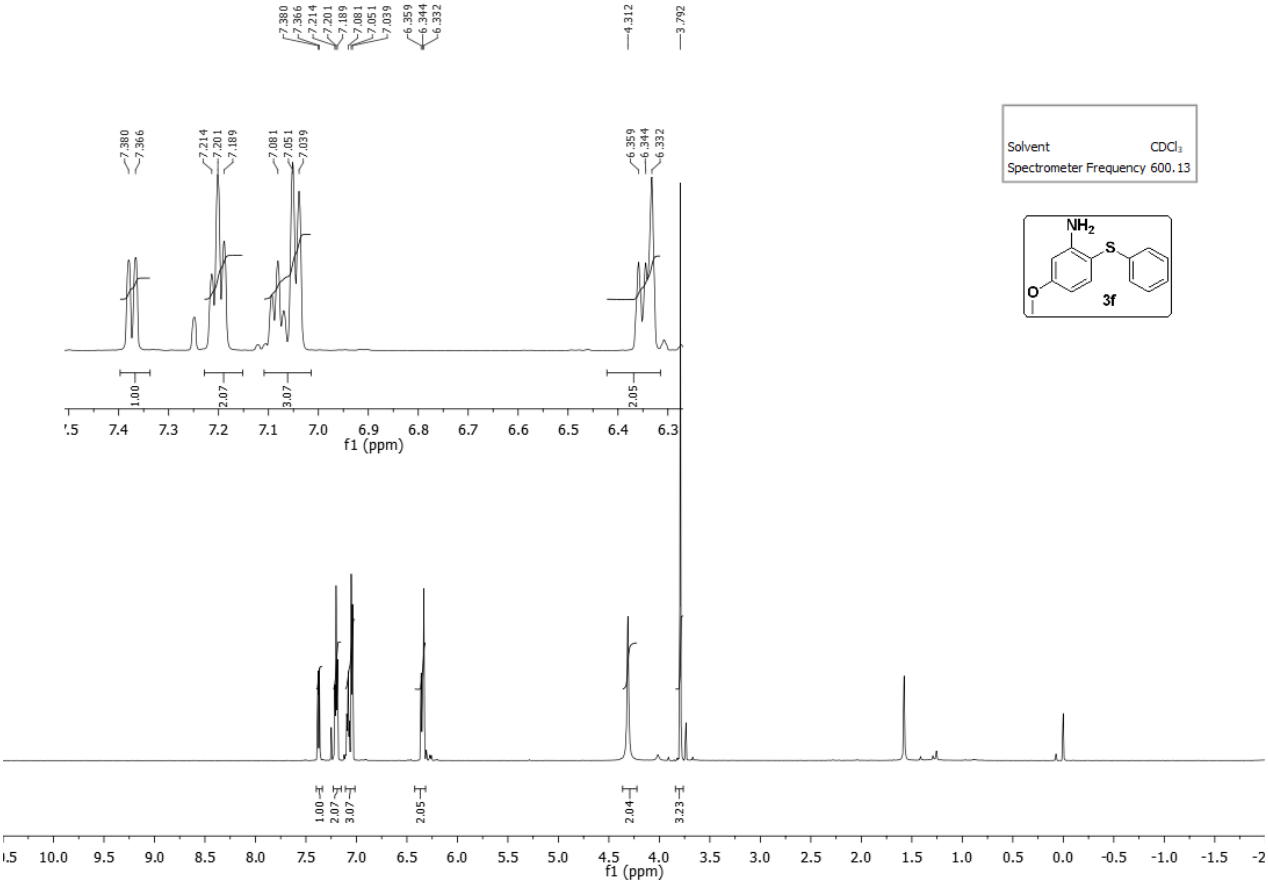
Compound **3e**, ^{13}C-NMR, 150MHz, $CDCl_3$



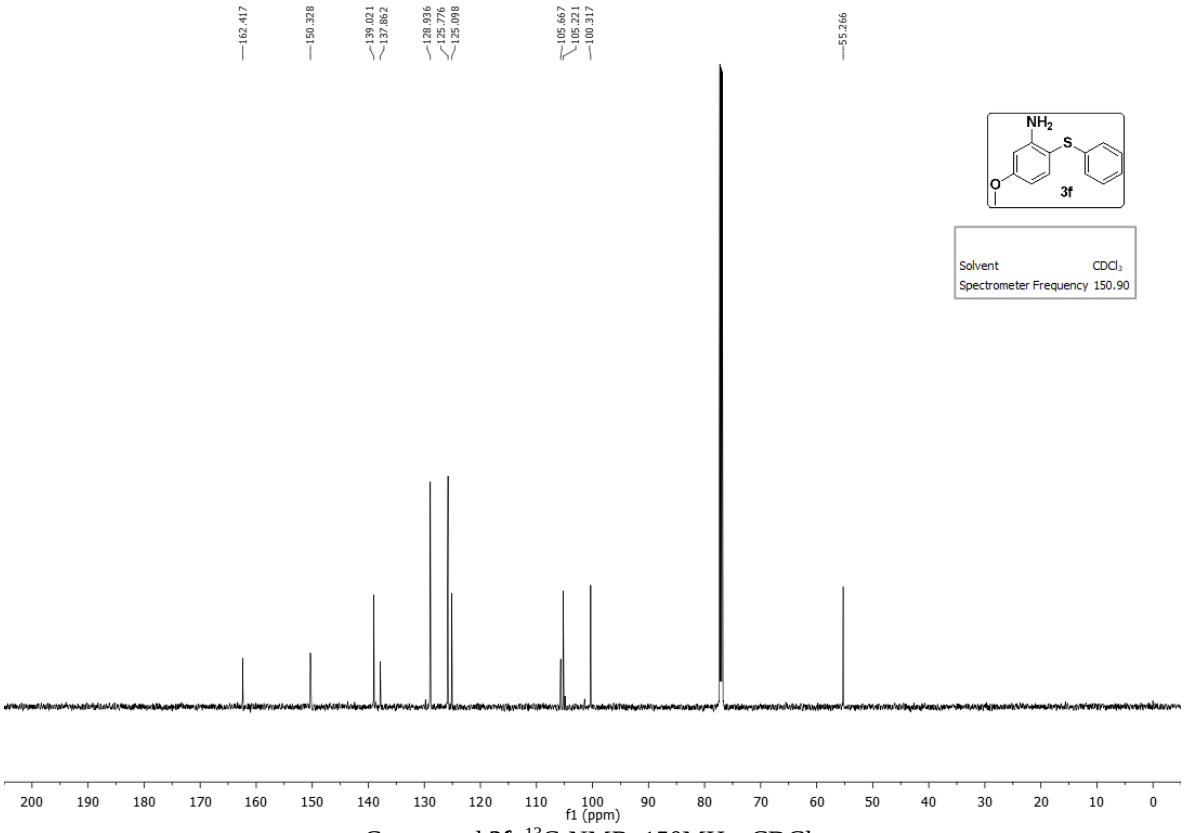
Compound **2f**, ^{1}H-NMR, 600MHz, $CDCl_3$



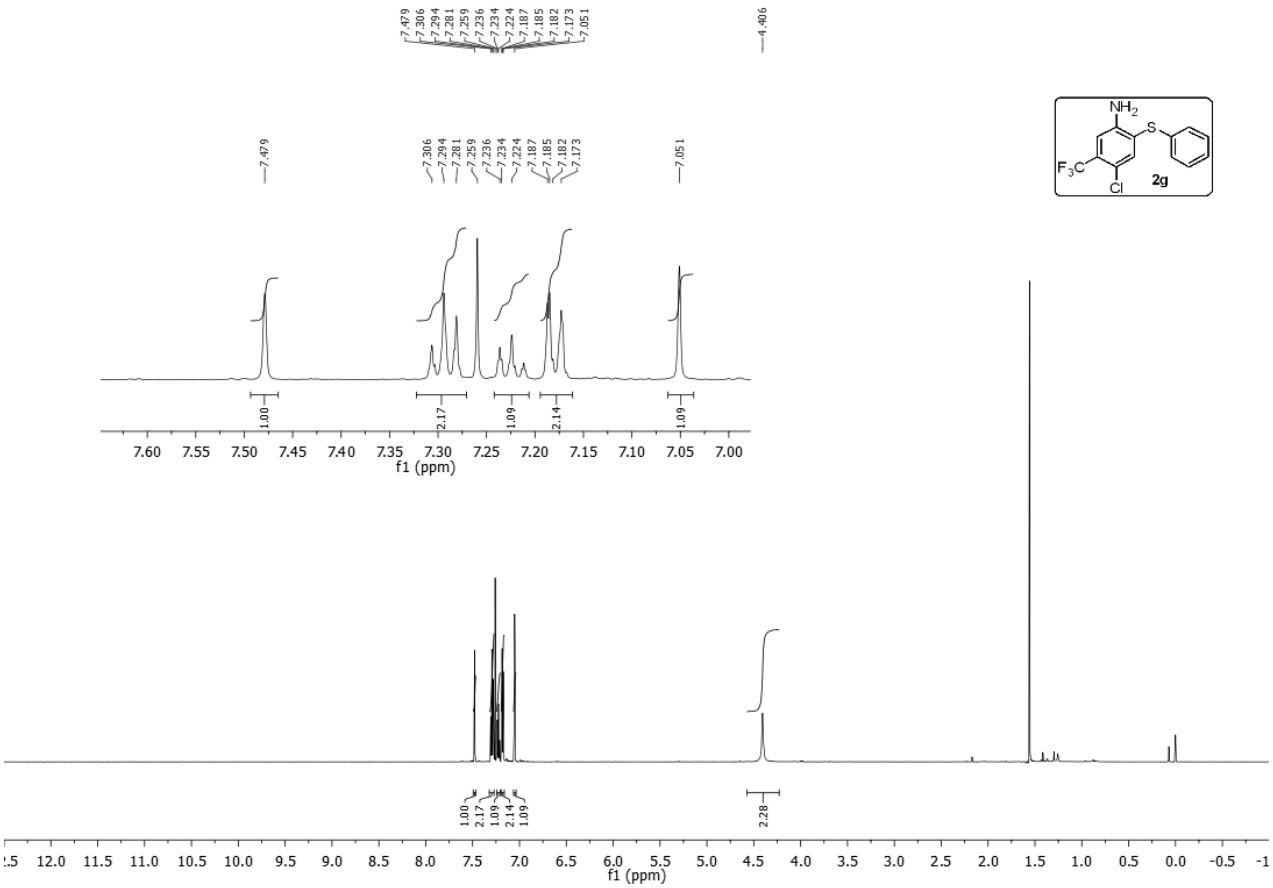
Compound **2f**, ^{13}C-NMR, 150MHz, $CDCl_3$



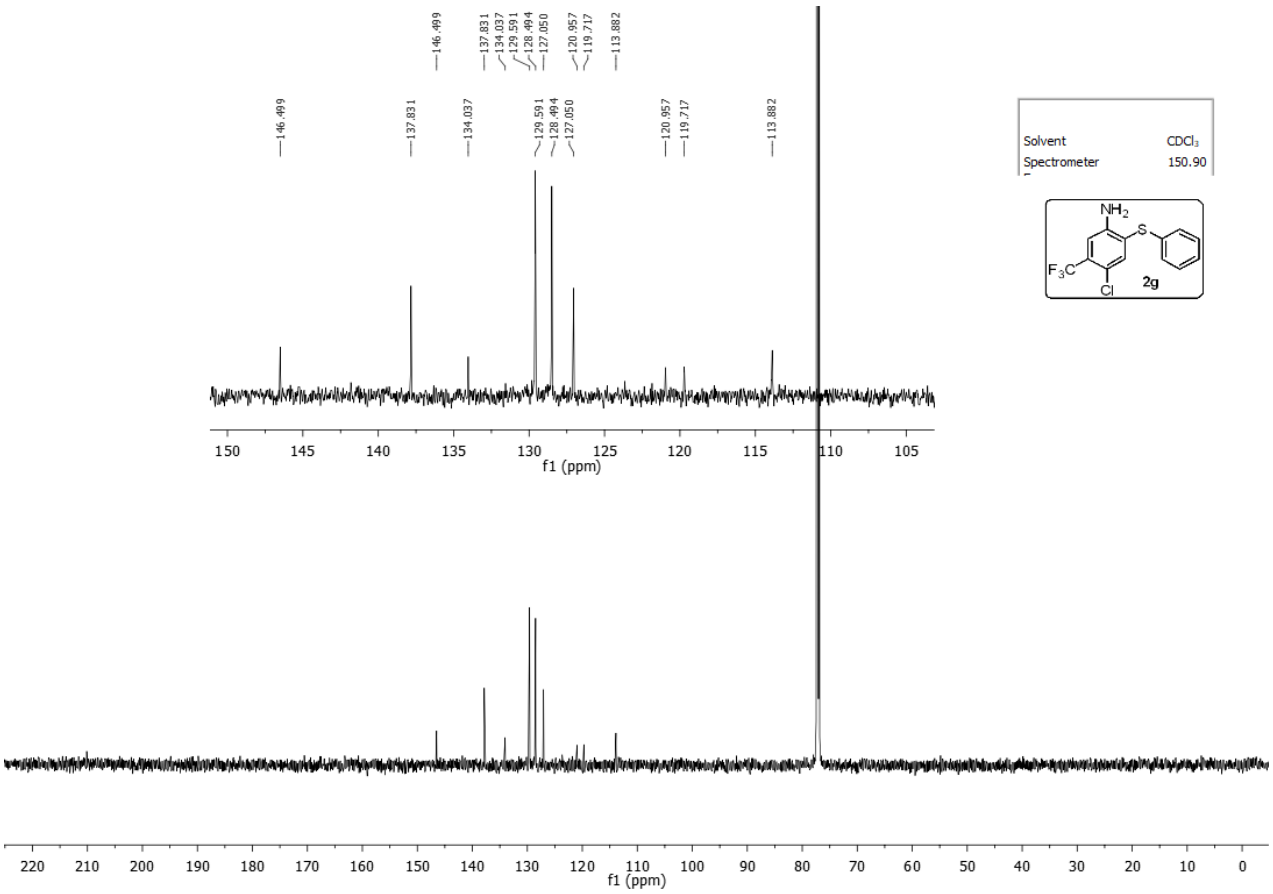
Compound **3f**, ^{1}H-NMR, 600MHz, $CDCl_3$



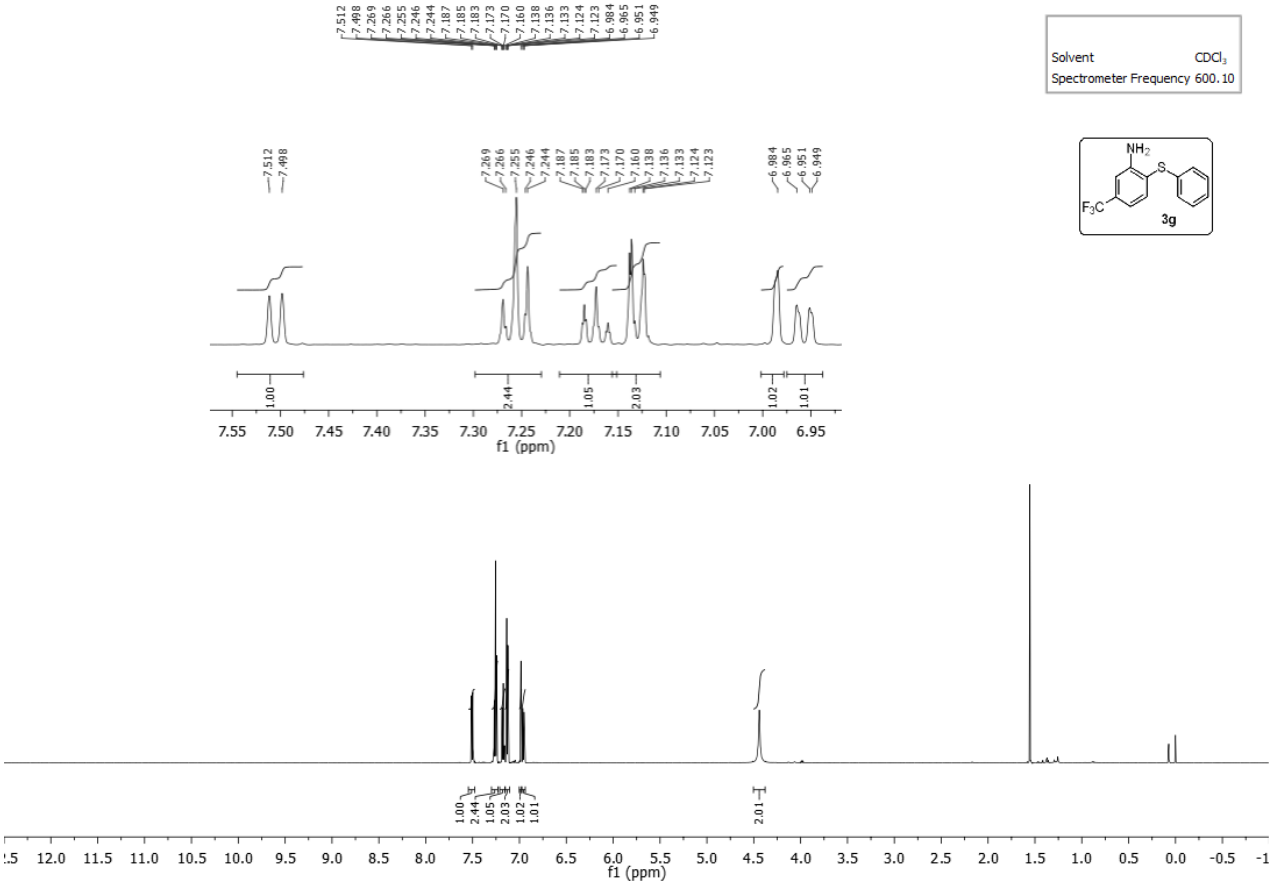
Compound **3f**, ^{13}C-NMR, 150MHz, $CDCl_3$



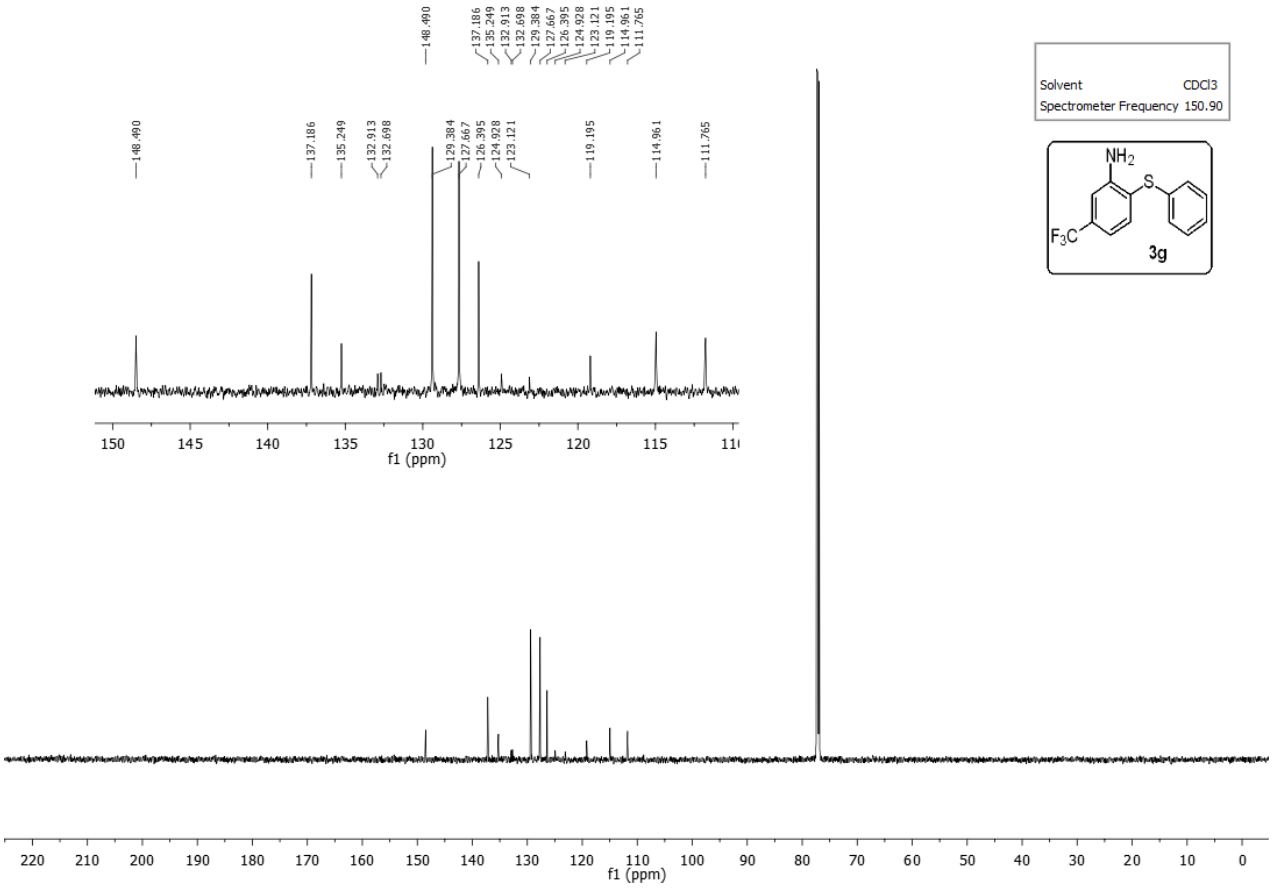
Compound **2g**, ^{1}H-NMR, 600MHz, $CDCl_3$



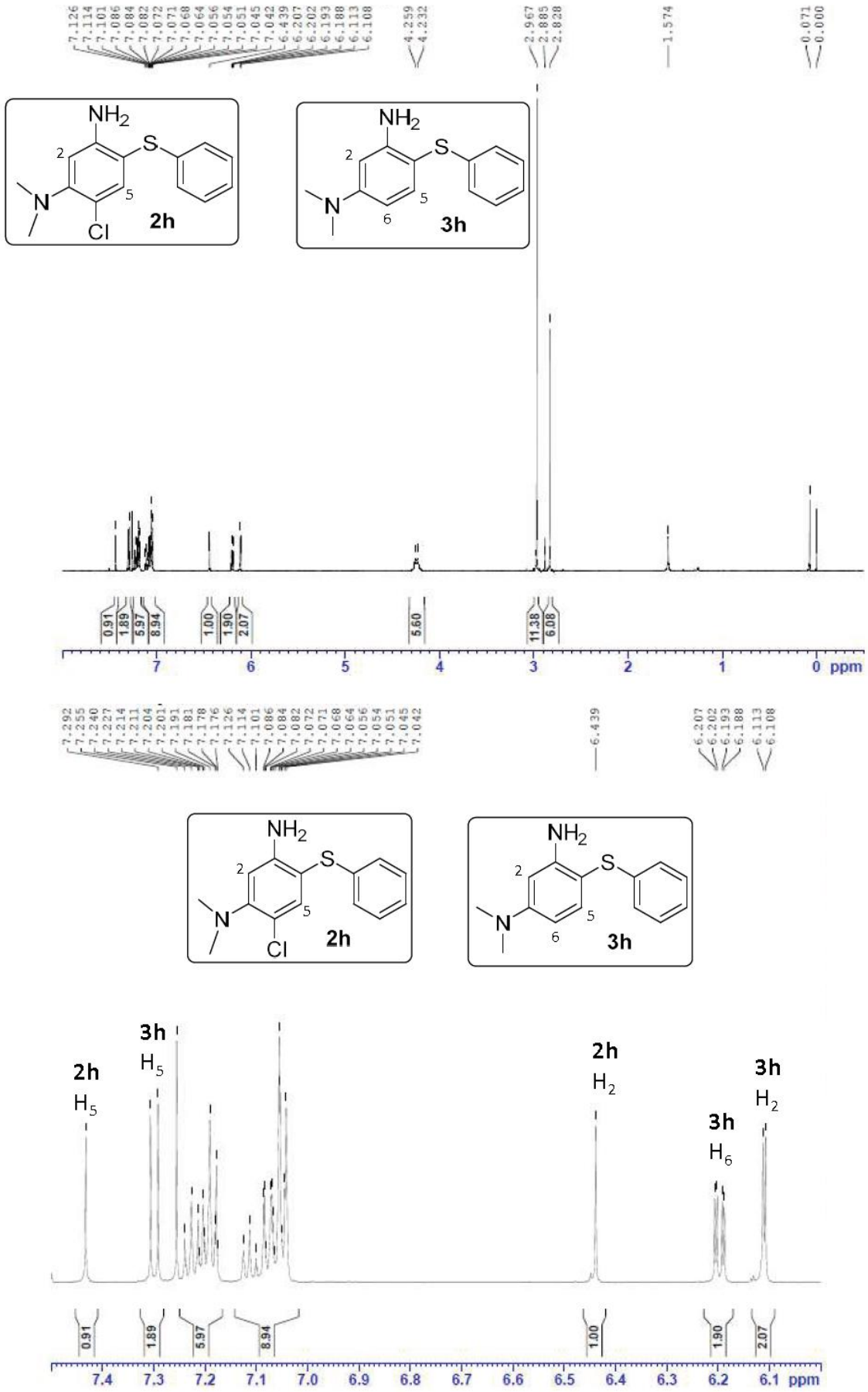
Compound **2g**, ^{13}C-NMR, 150MHz, $CDCl_3$



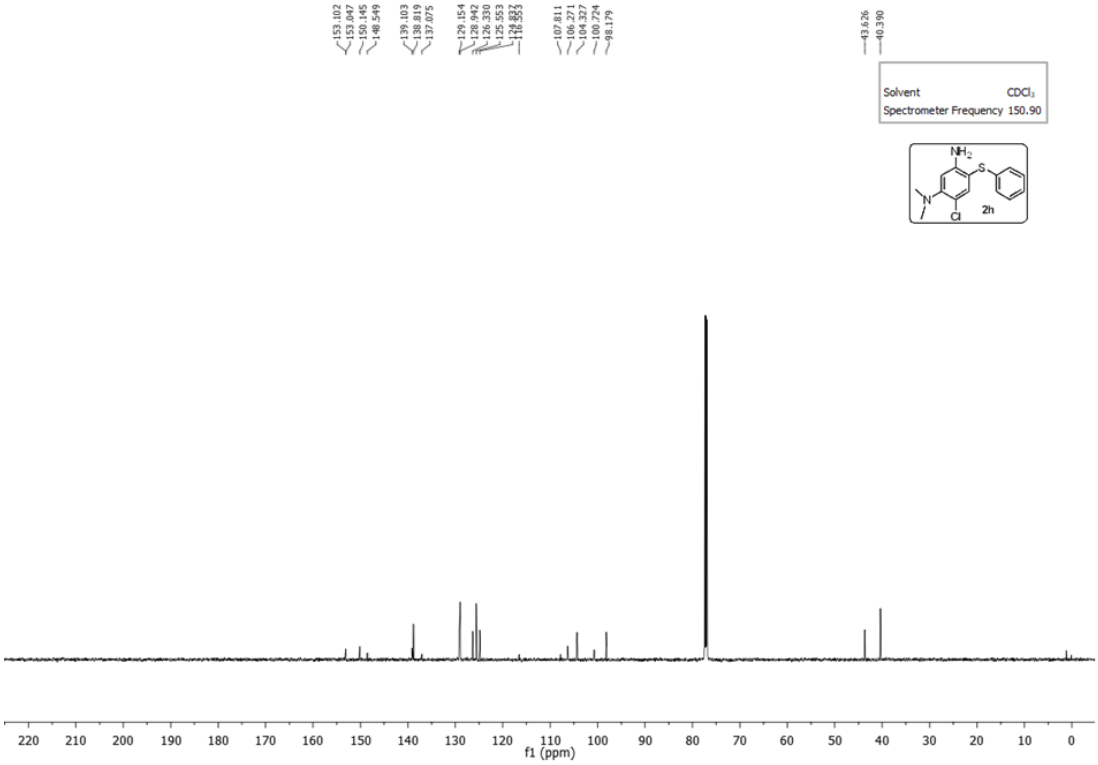
Compound **3g**, ^{1}H-NMR, 600MHz, $CDCl_3$



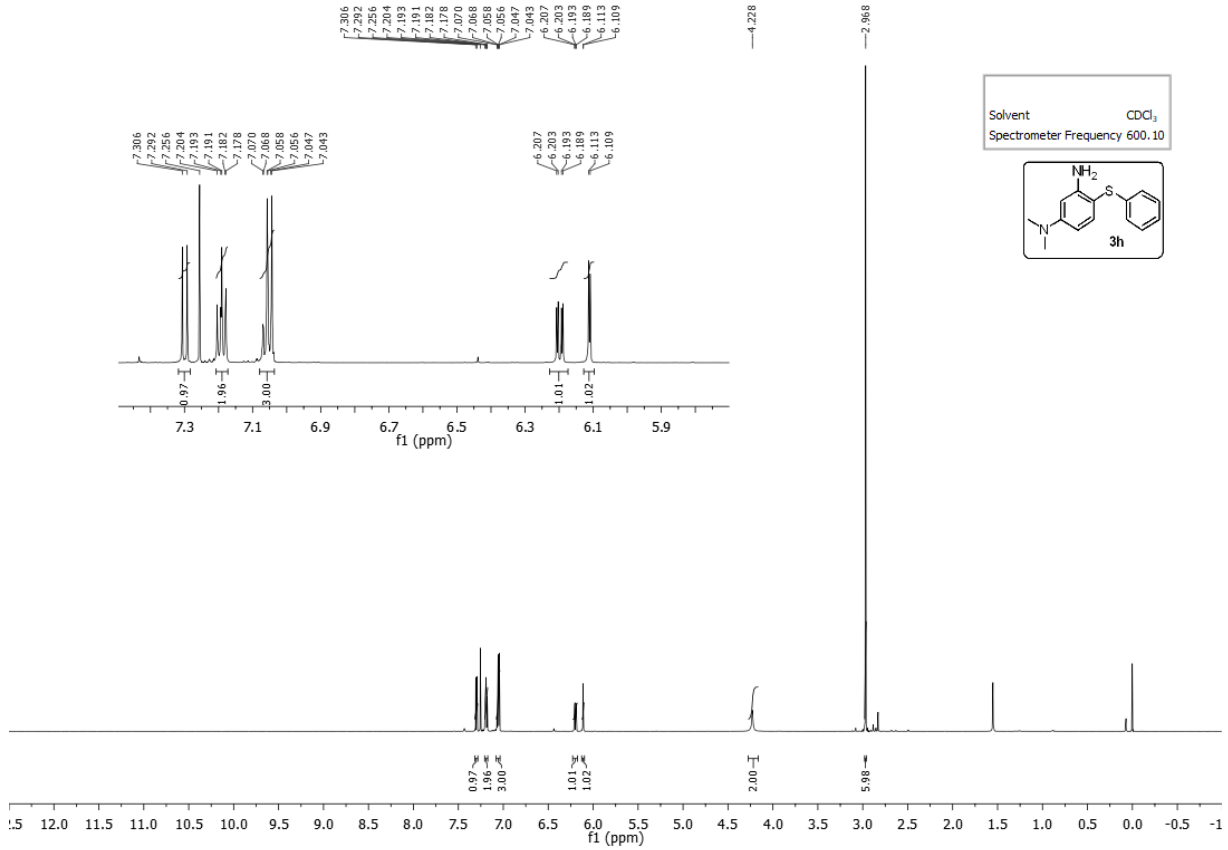
Compound **3g**, ^{13}C-NMR, 150MHz, $CDCl_3$



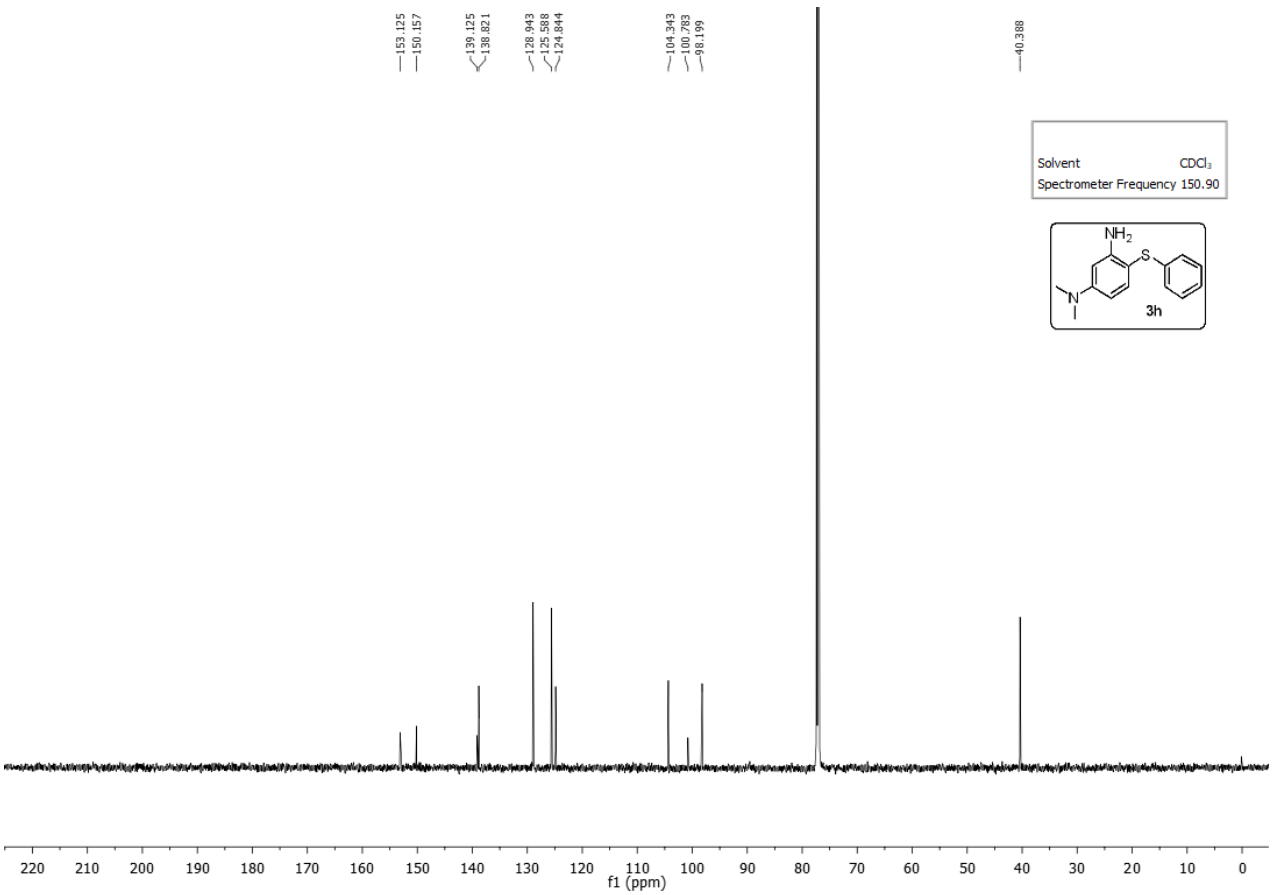
A mixture of compounds **2h** and **3h** (ratio=1:2), ^{1}H-NMR, 600MHz, $CDCl_3$



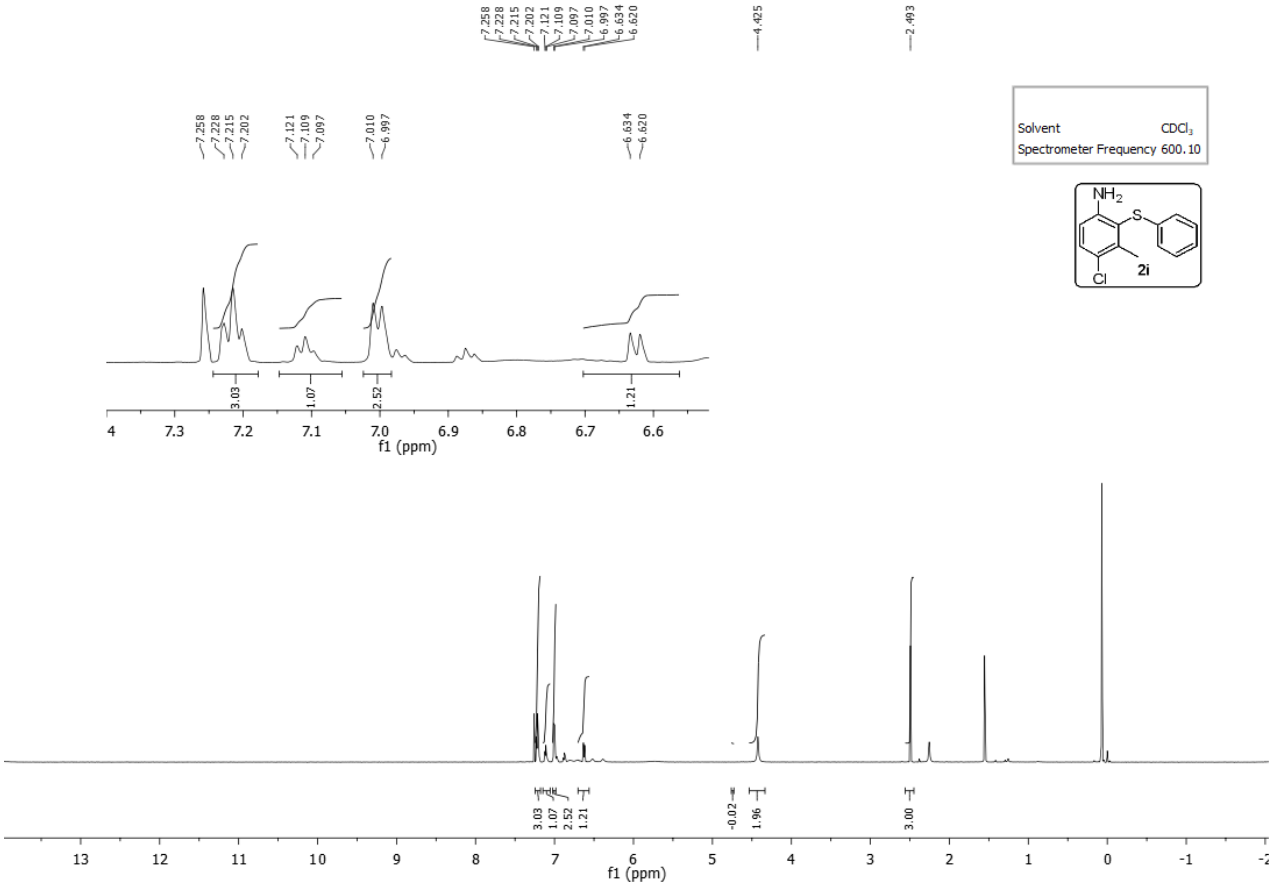
A mixture of compounds **2h** and **3h** (ratio=1:2), ^{13}C-NMR, 150MHz, $CDCl_3$



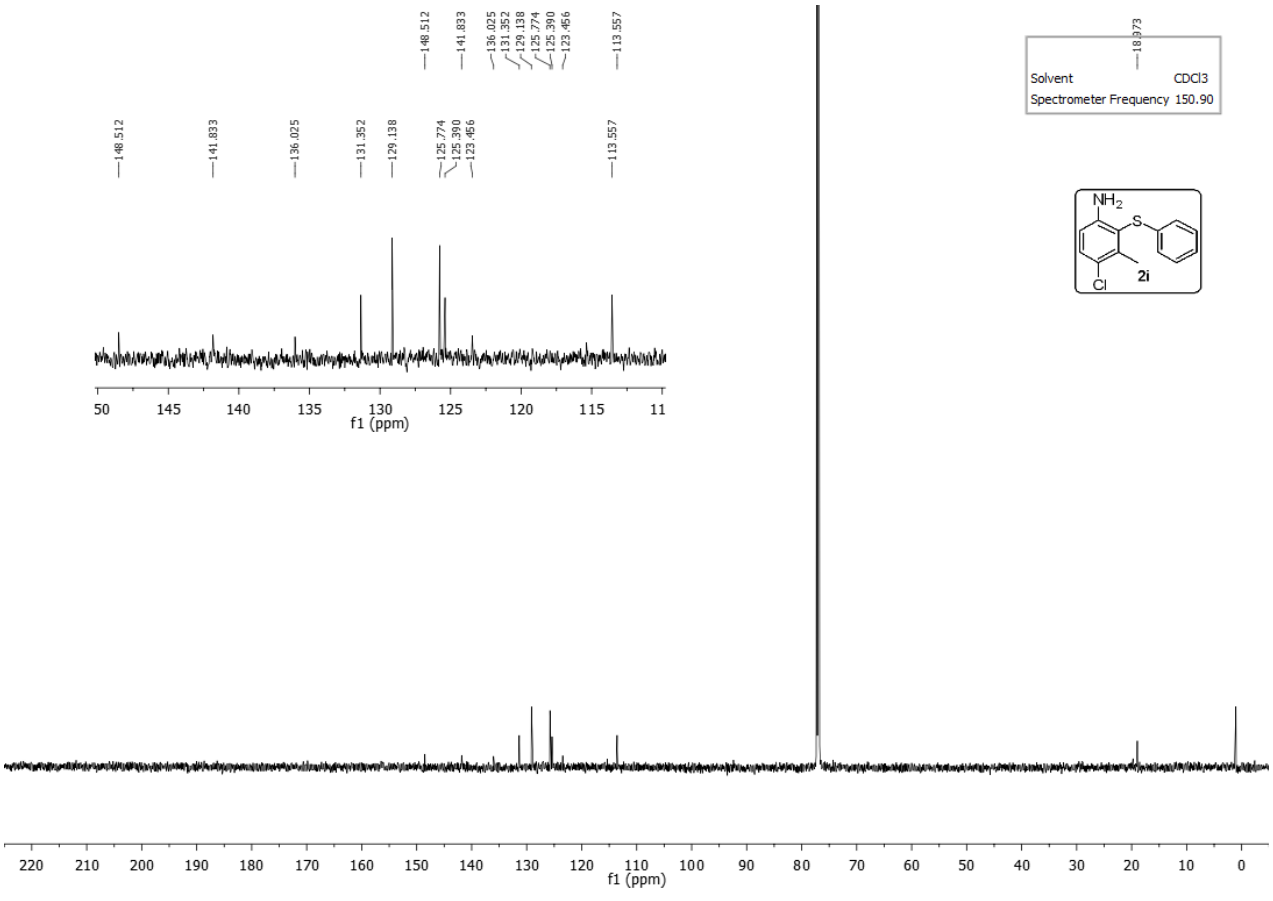
Compound **3h**, ^{1}H-NMR, 600MHz, $CDCl_3$



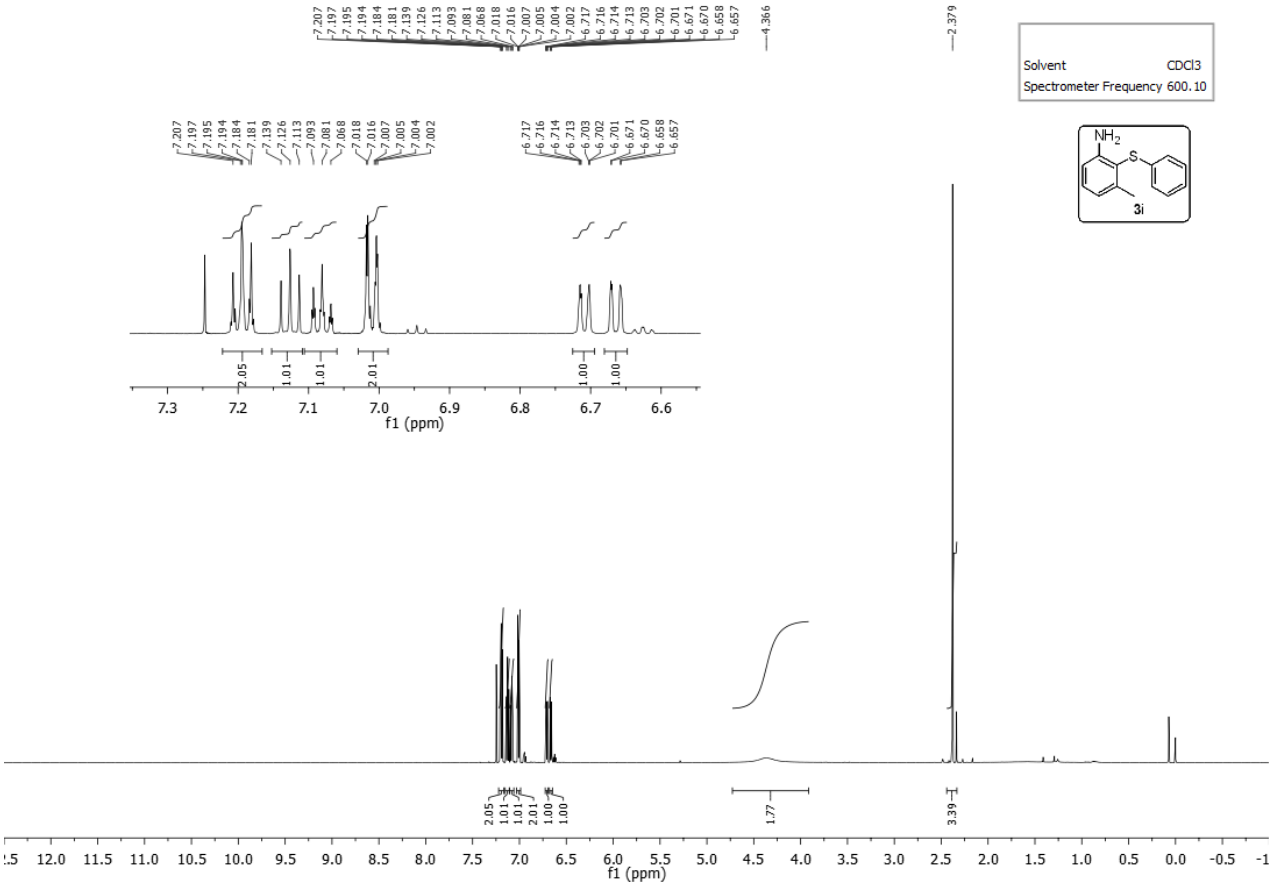
Compound **3h**, ^{13}C-NMR, 150MHz, $CDCl_3$



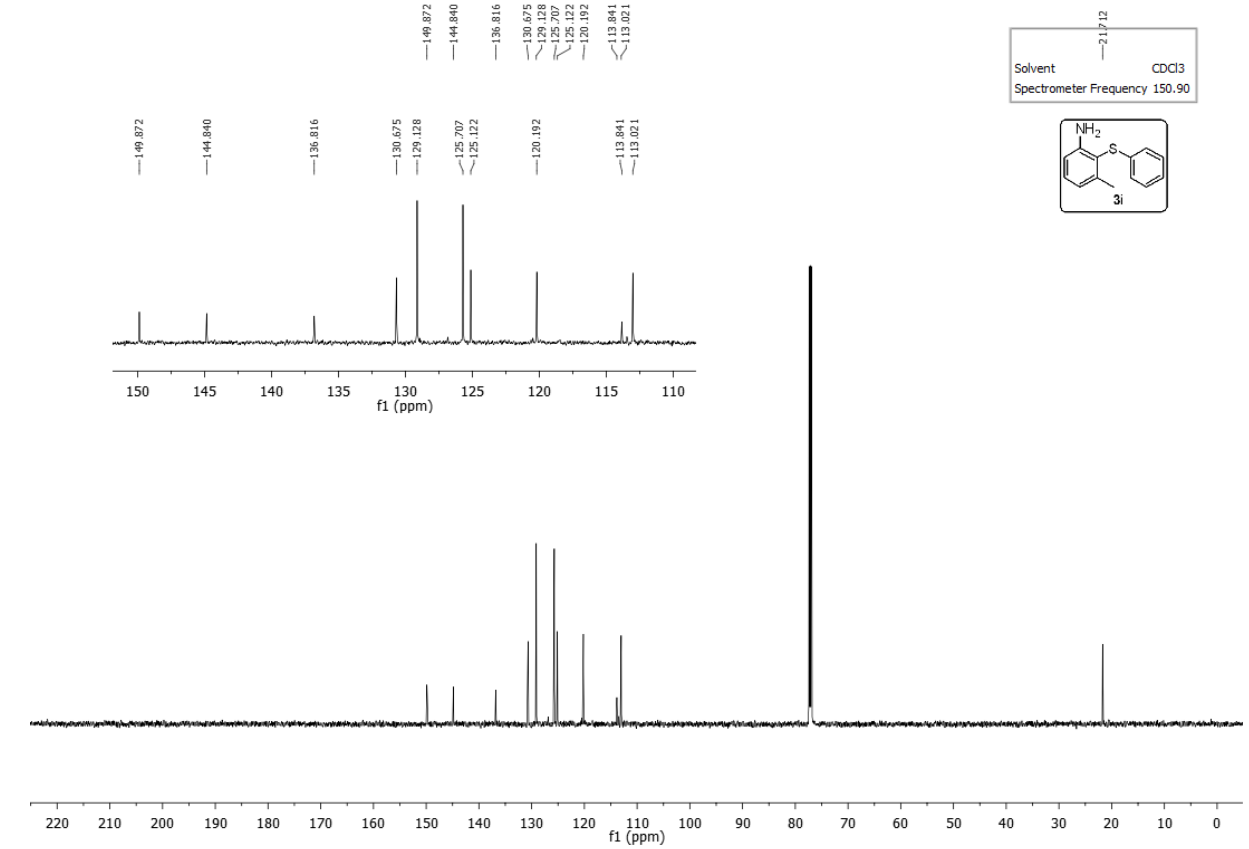
Compound **2i**, ^{1}H-NMR, 600MHz, $CDCl_3$



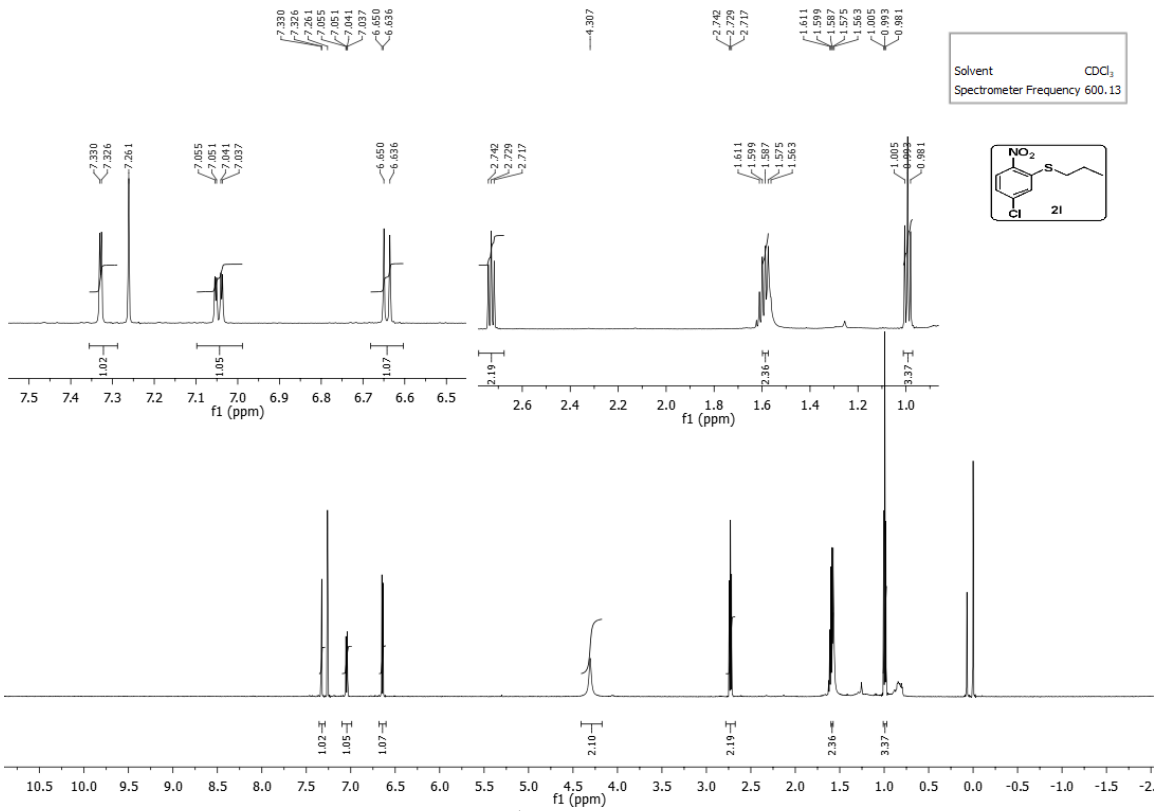
Compound **2i**, ^{13}C-NMR, 150MHz, $CDCl_3$



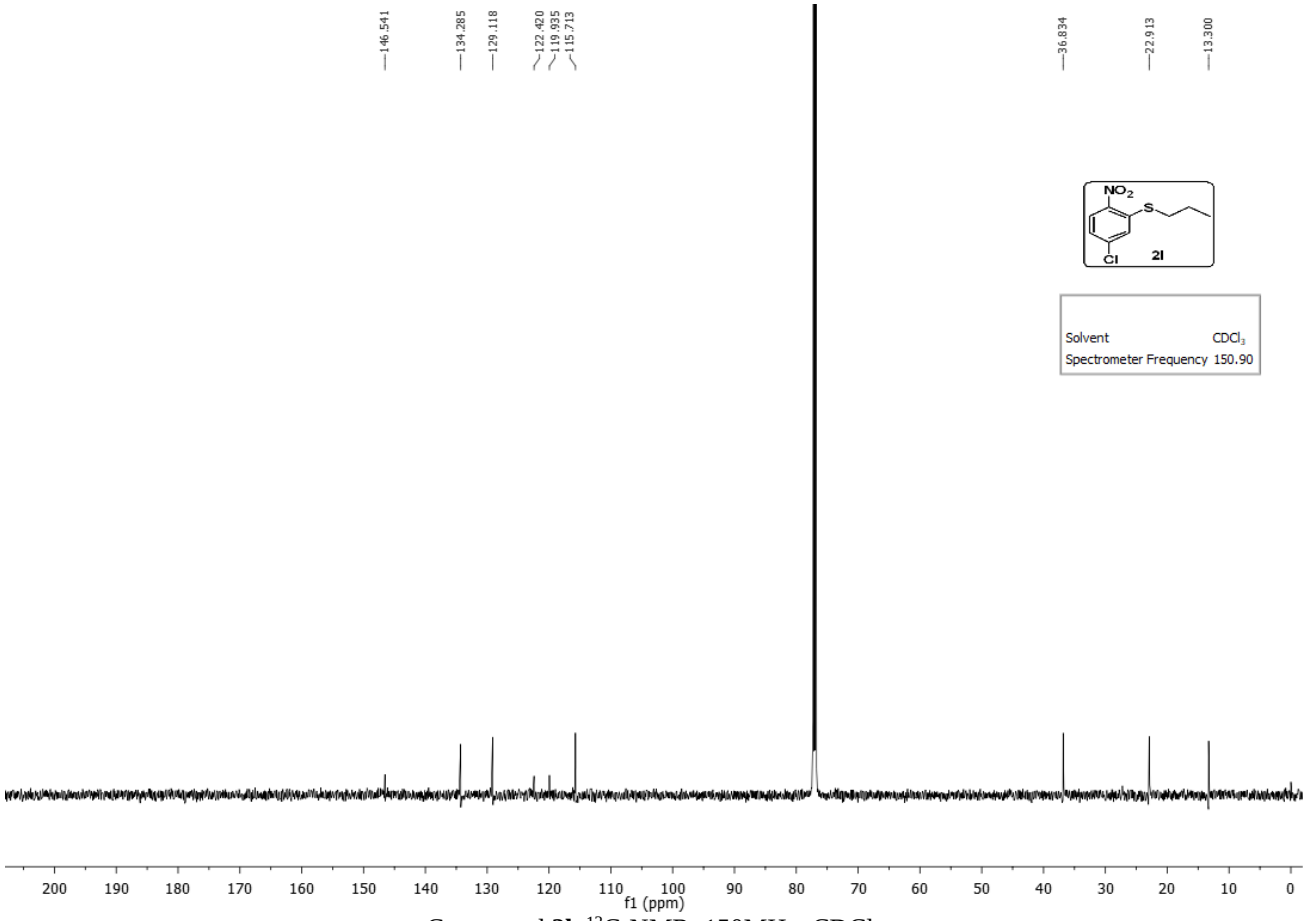
Compound **3i**, ^{1}H-NMR, 600MHz, $CDCl_3$



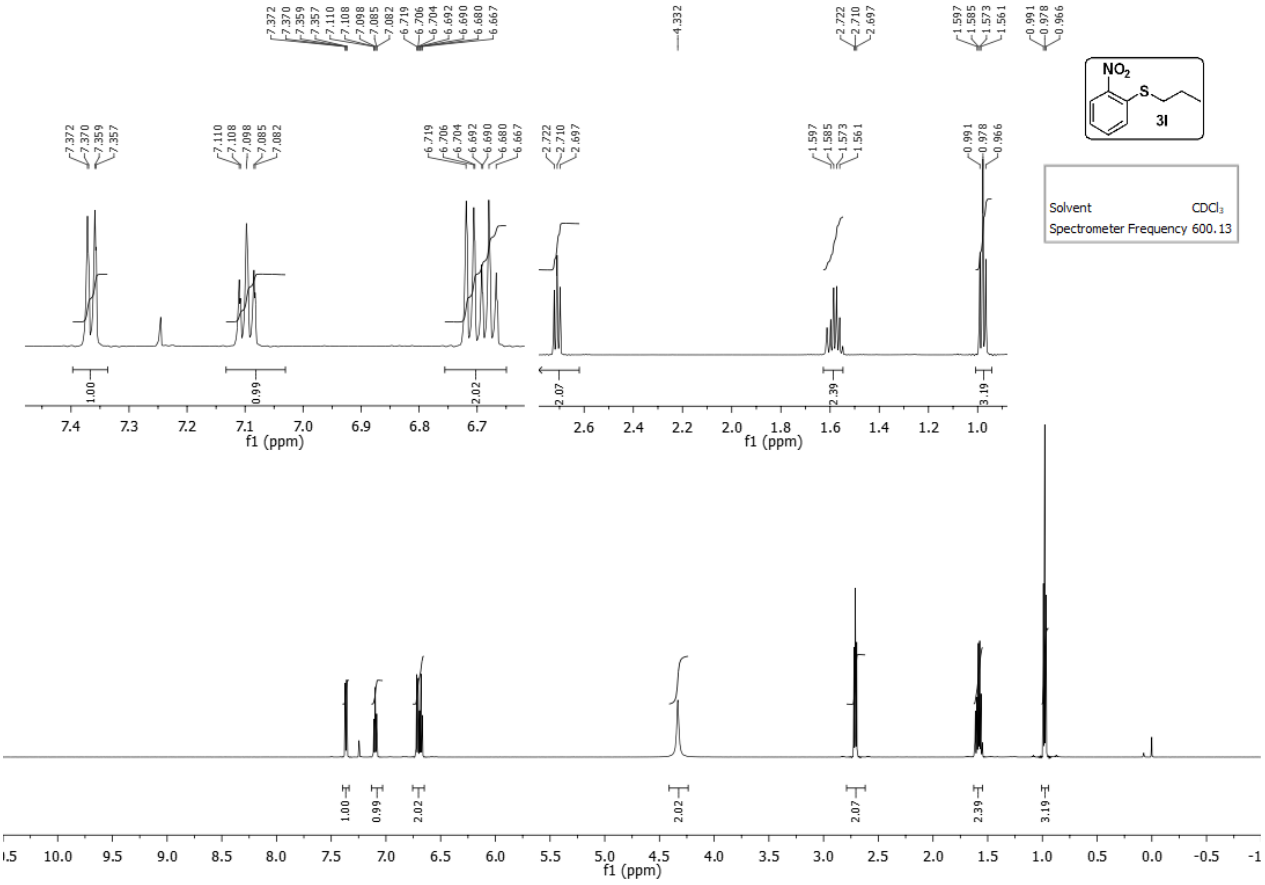
Compound **3i**, ^{13}C-NMR, 150MHz, $CDCl_3$



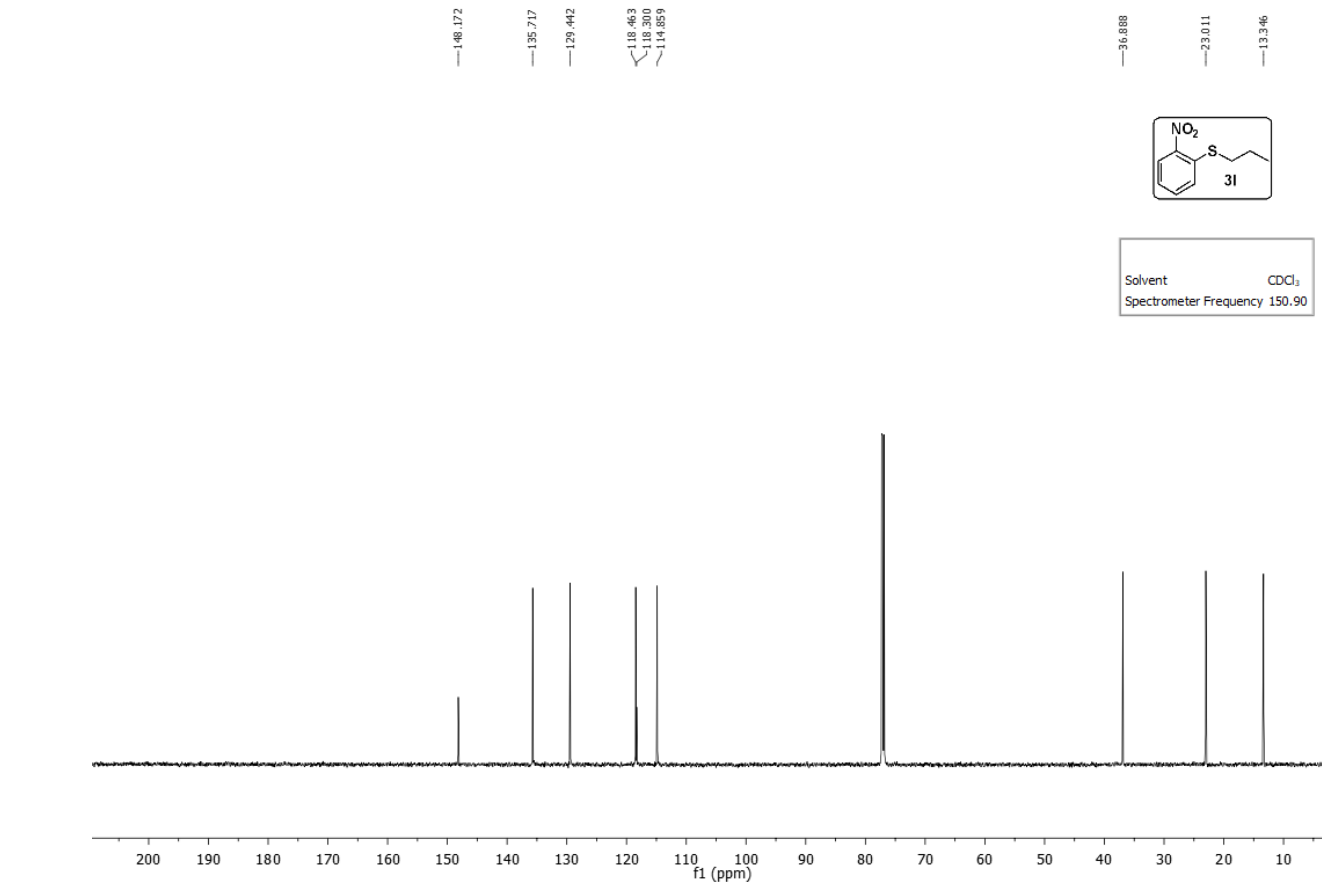
Compound **2l**, ^{1}H-NMR, 600MHz, $CDCl_3$



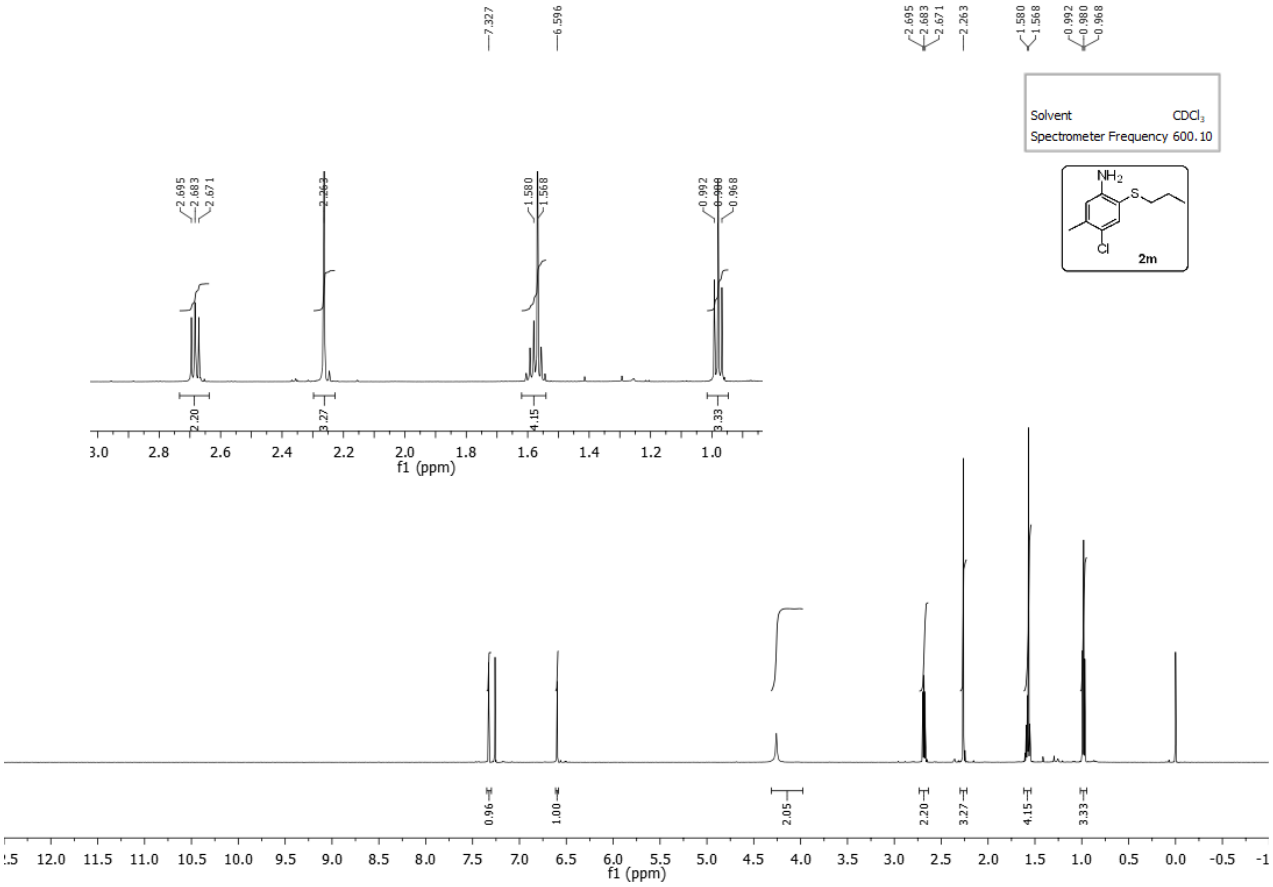
Compound **2l**, ^{13}C-NMR, 150MHz, $CDCl_3$



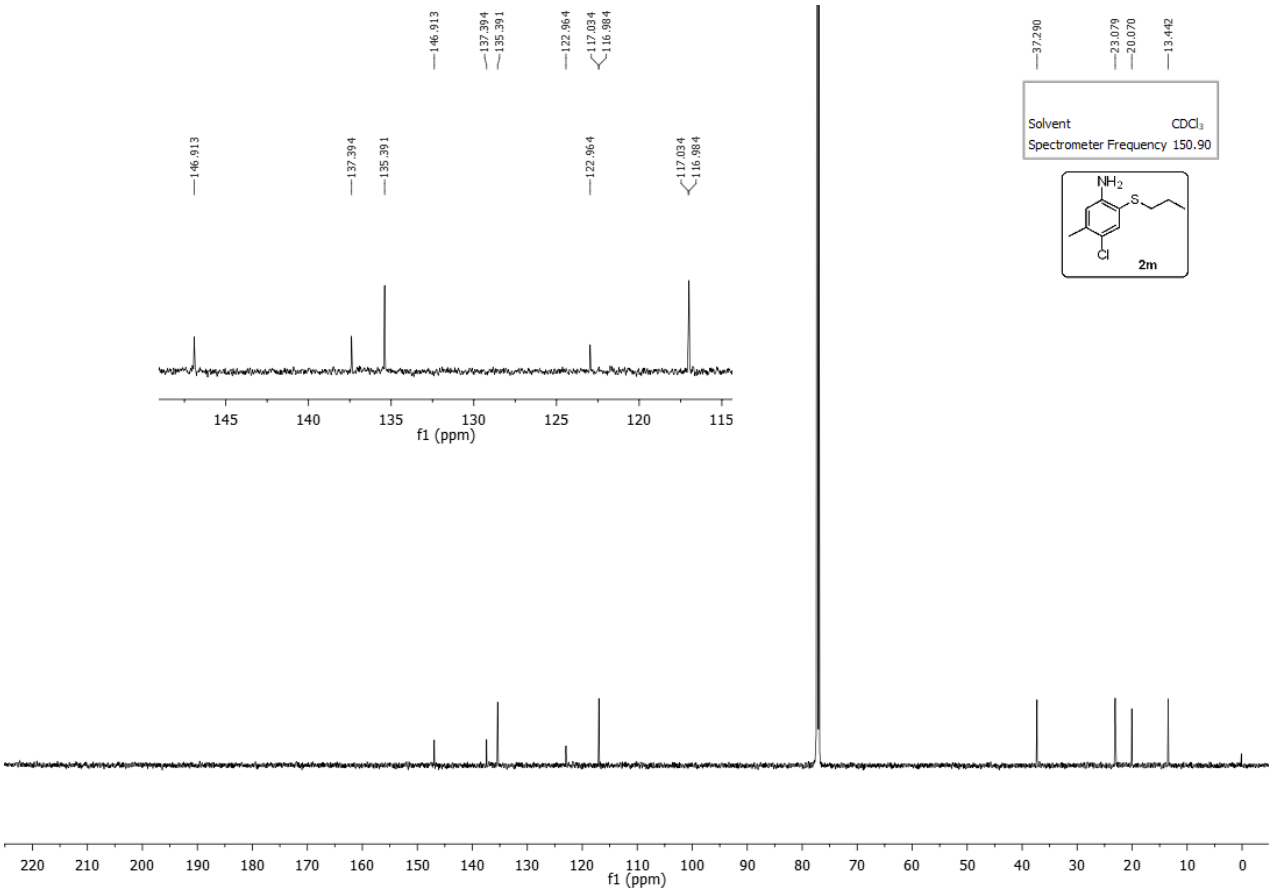
Compound **3l**, ^{1}H-NMR, 600MHz, $CDCl_3$



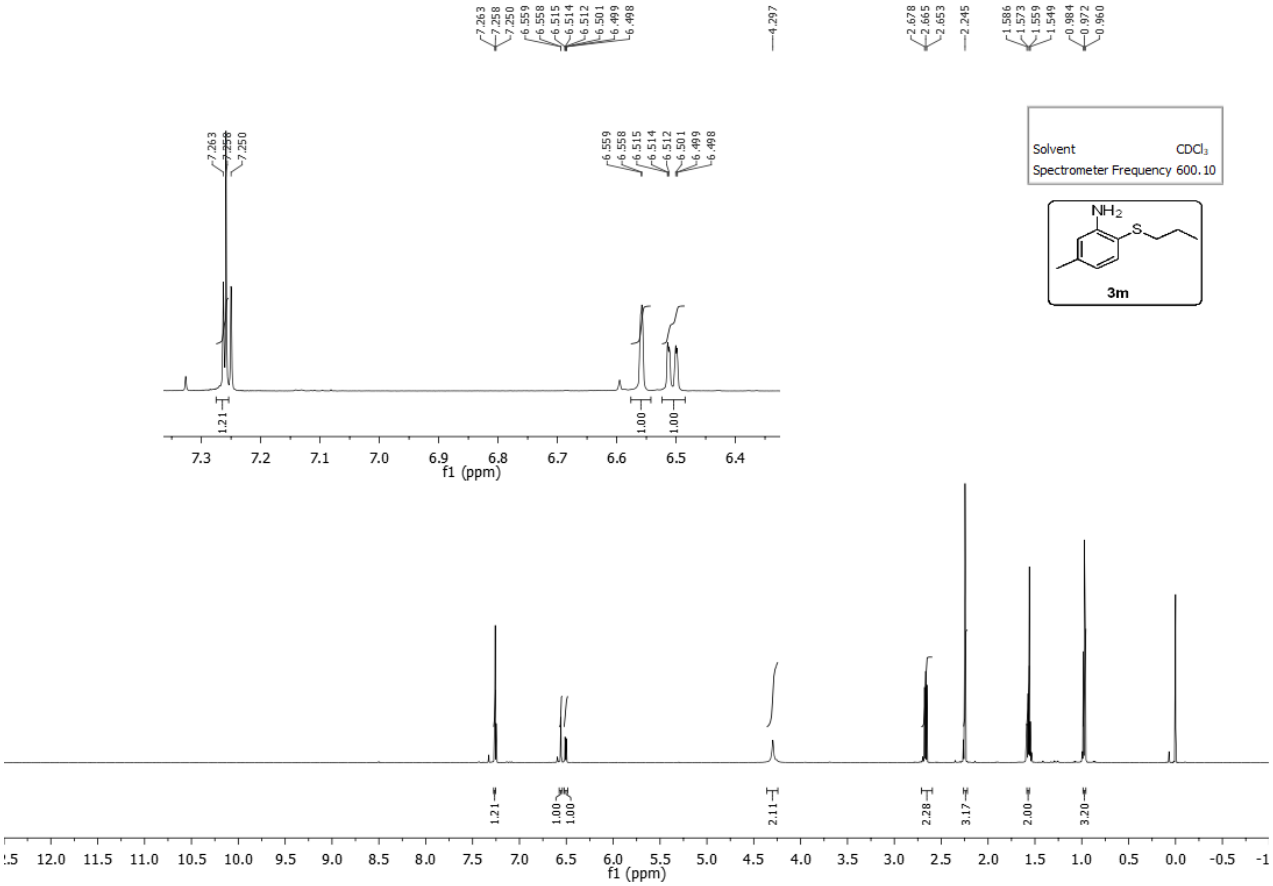
Compound **3l**, ^{13}C-NMR, 150MHz, $CDCl_3$



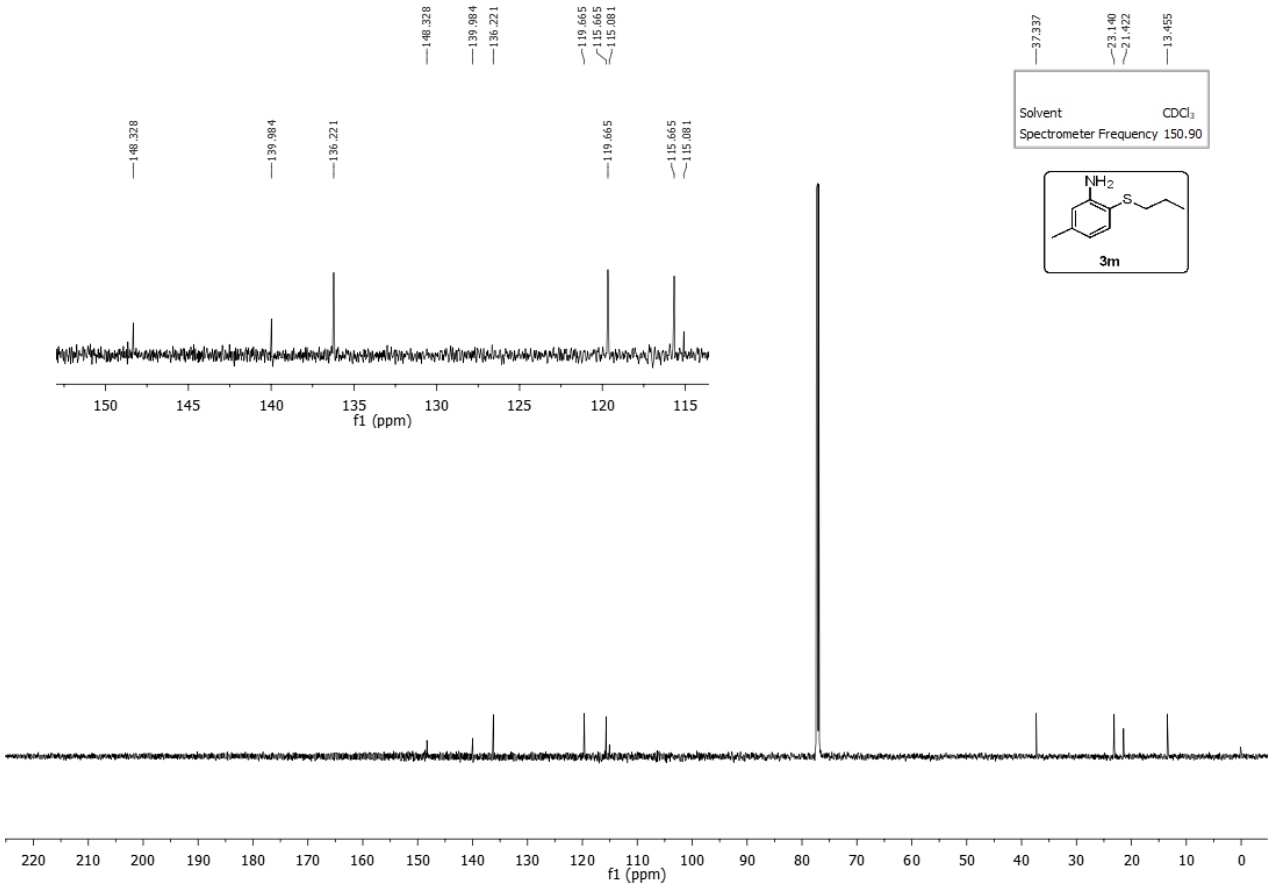
Compound **2m**, ^{1}H-NMR, 600MHz, $CDCl_3$



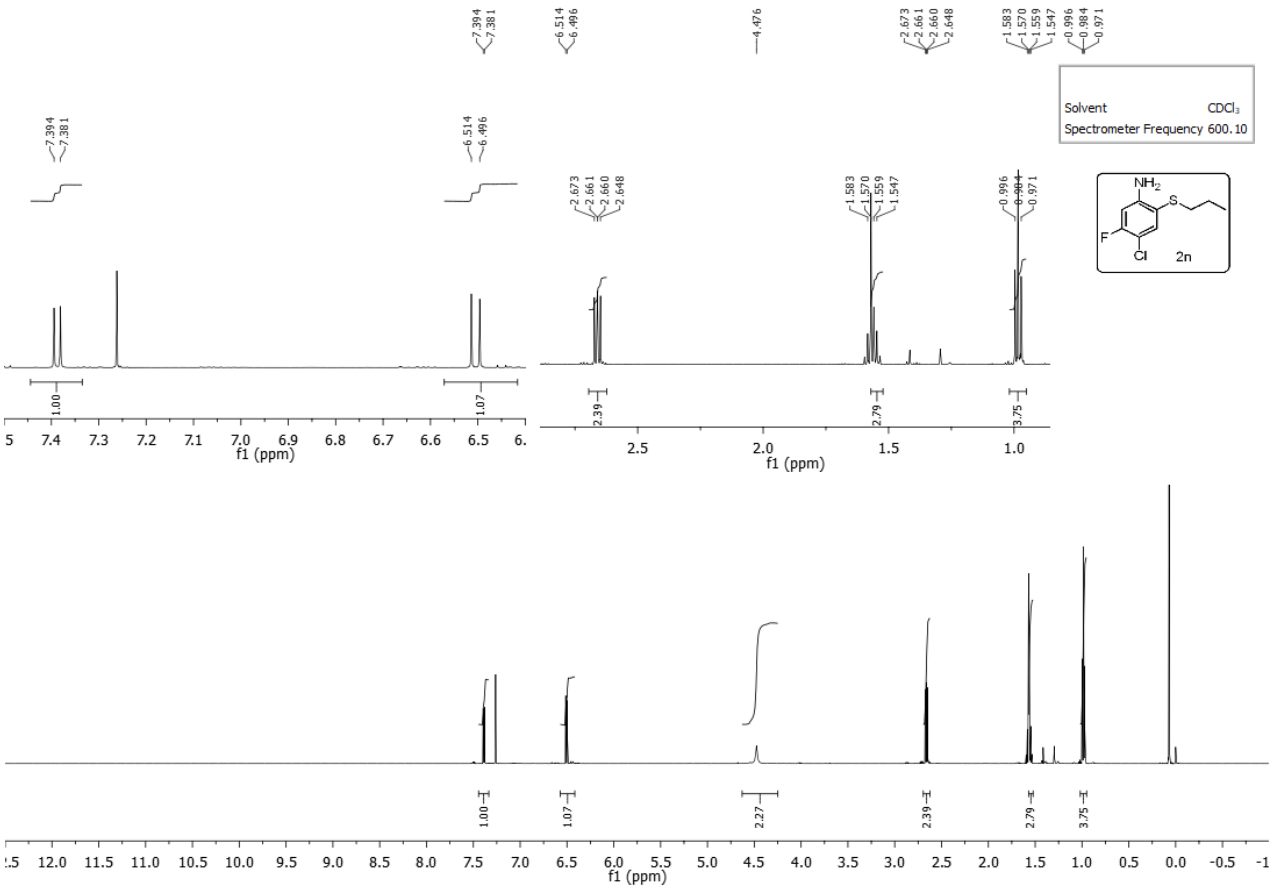
Compound **2m**, ^{13}C-NMR, 150MHz, $CDCl_3$



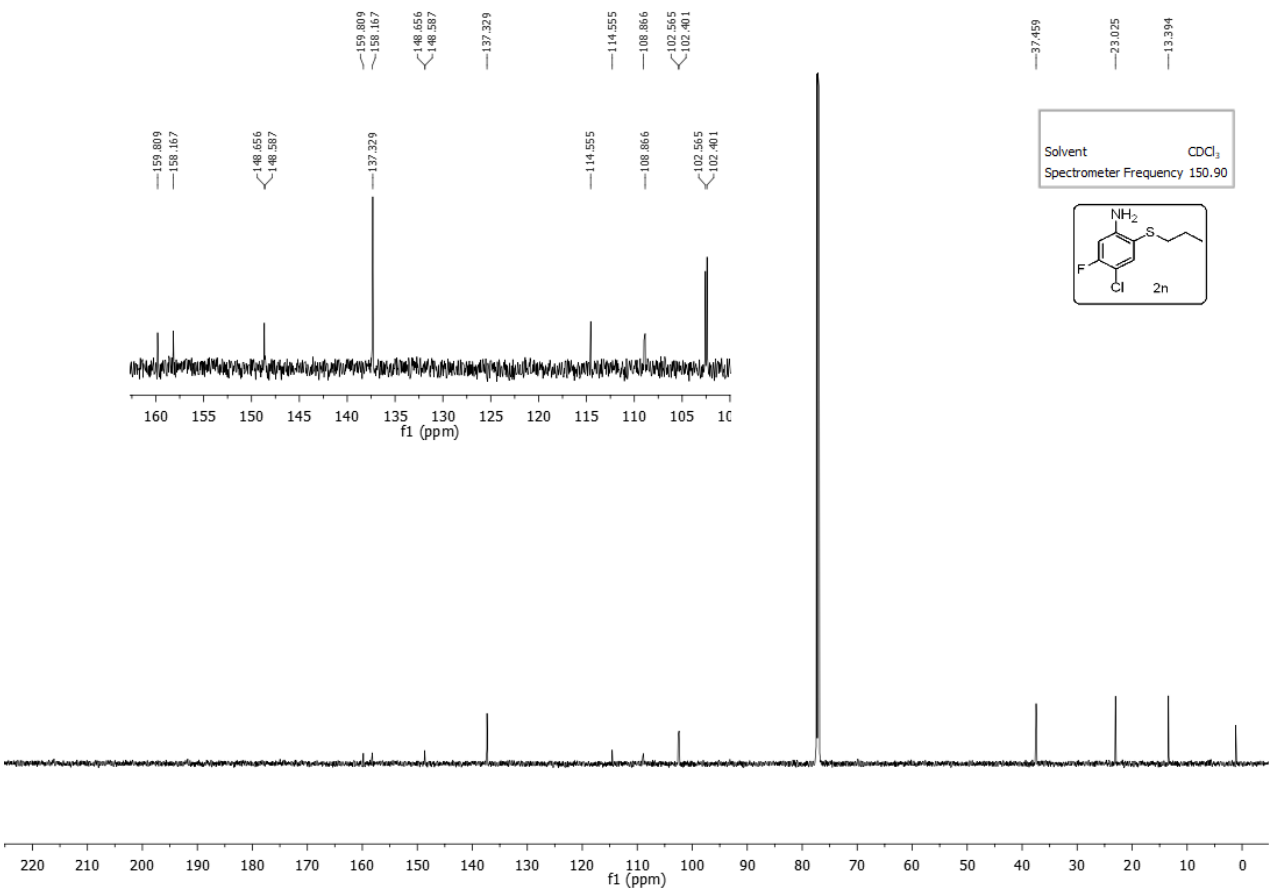
Compound **3m**, ^{1}H-NMR, 600MHz, $CDCl_3$



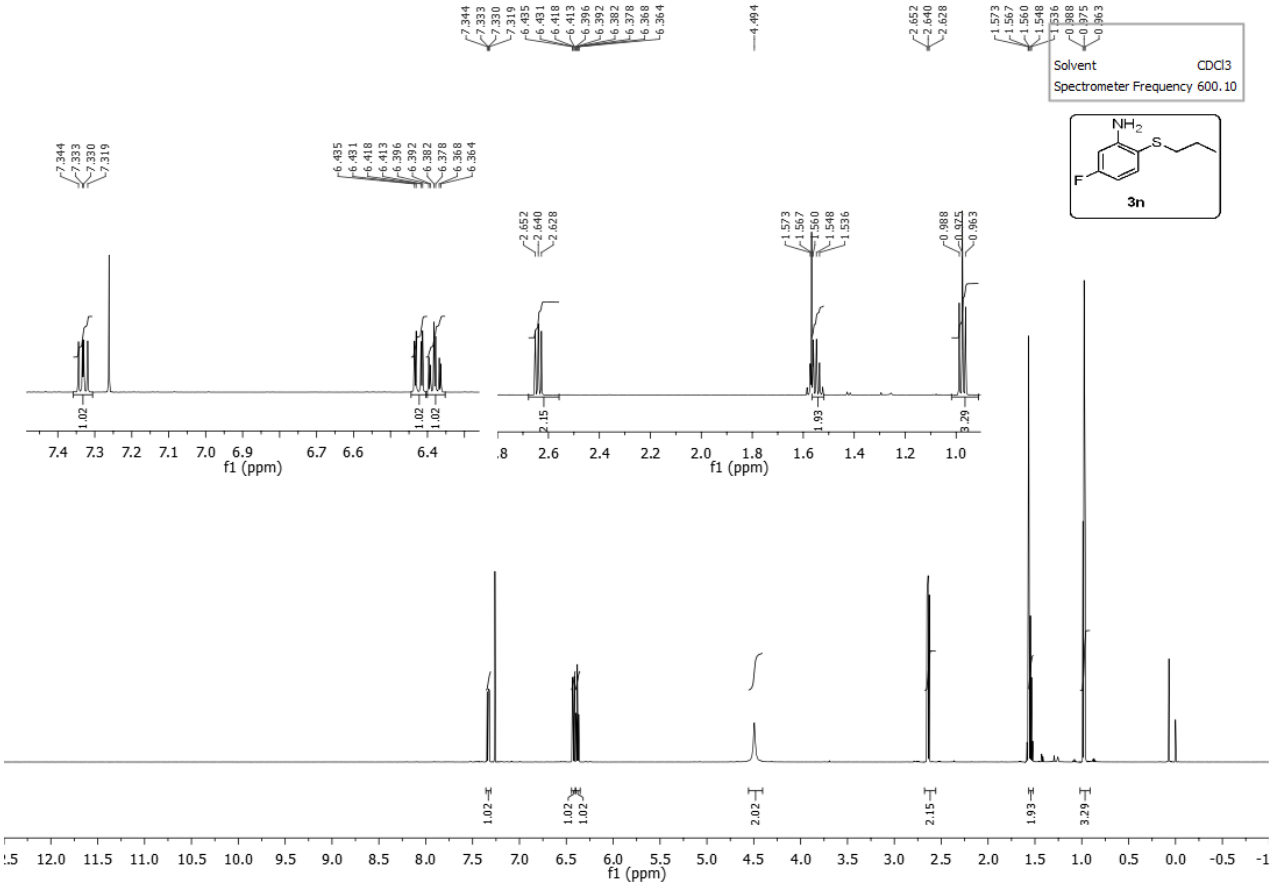
Compound **3m**, ^{13}C-NMR, 150MHz, $CDCl_3$



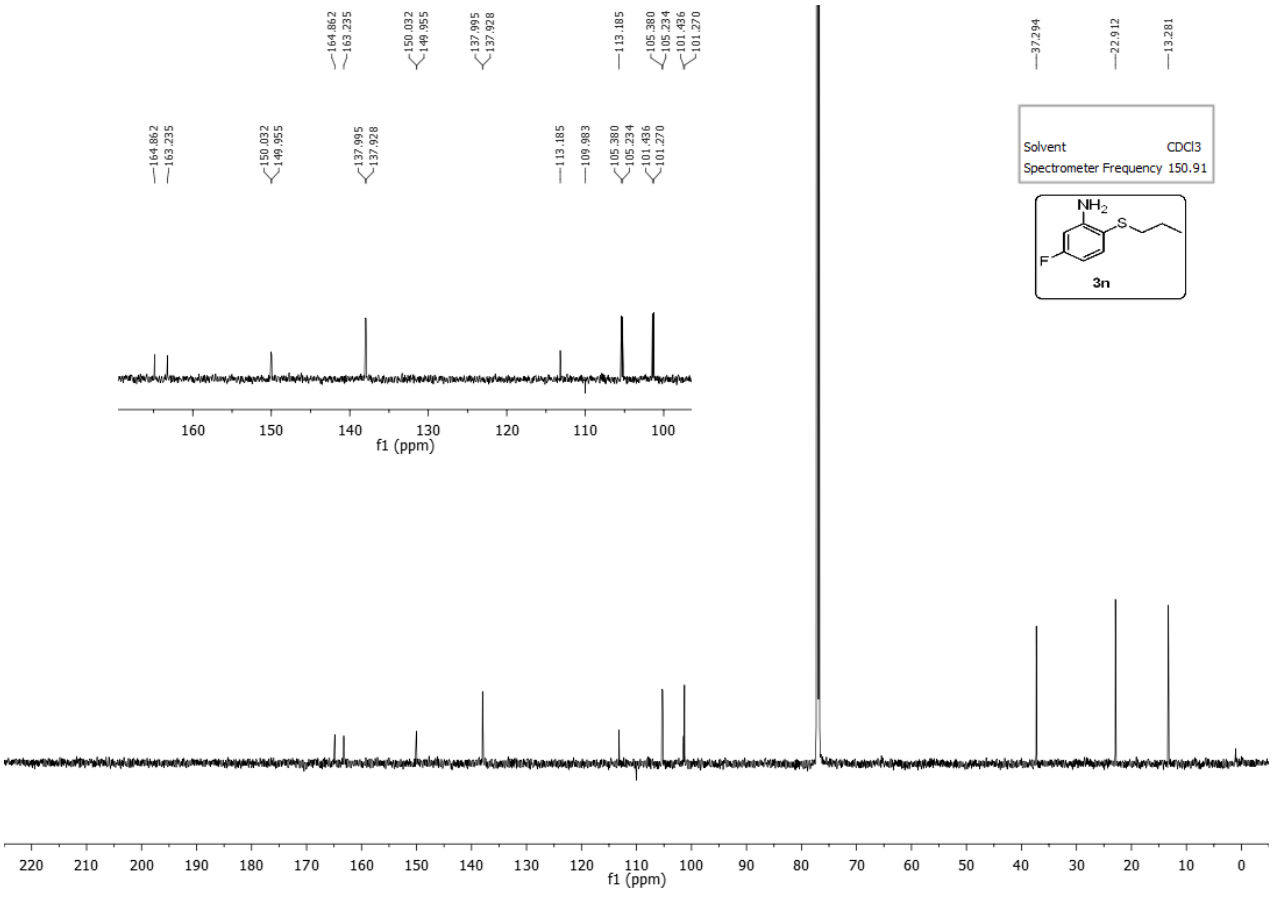
Compound **2n**, ^{1}H-NMR, 600MHz, $CDCl_3$



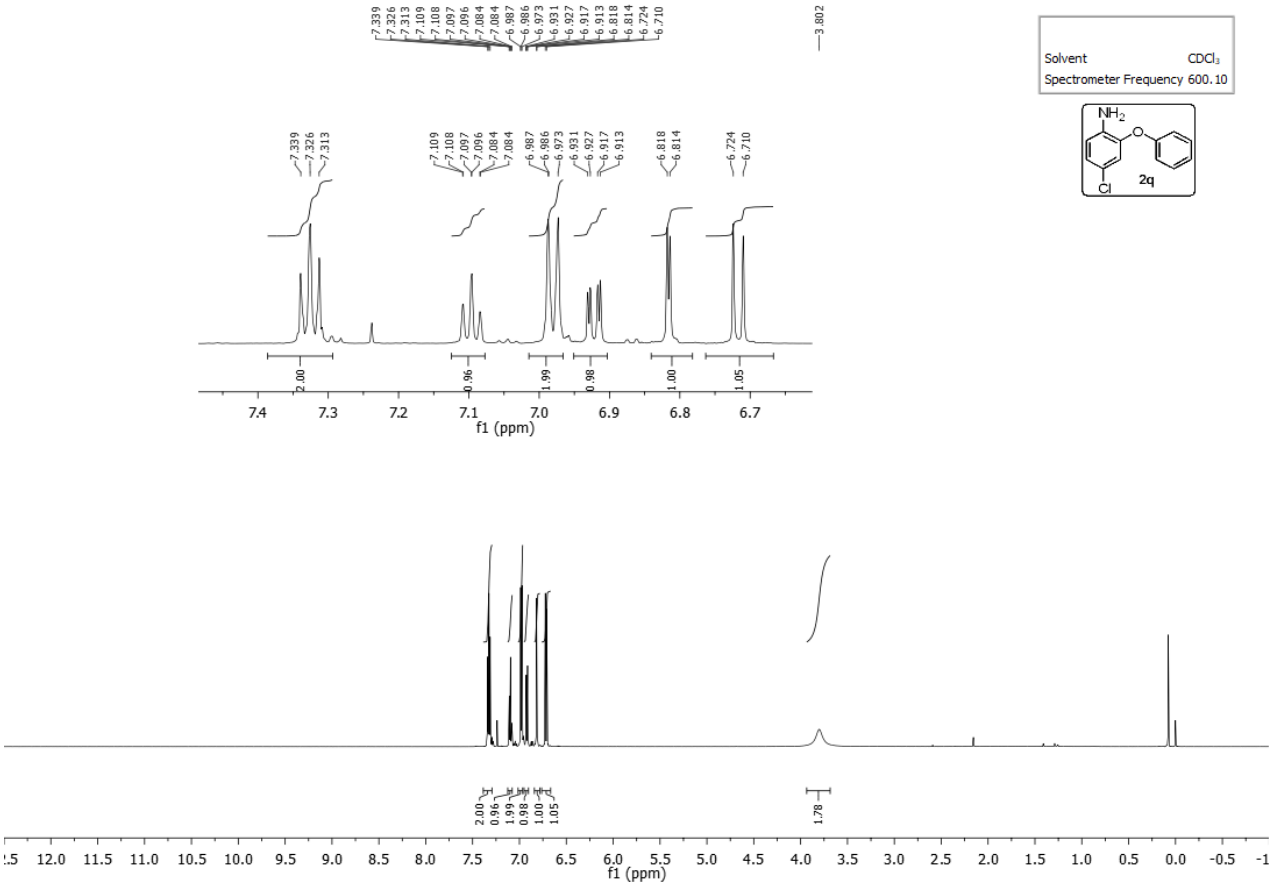
Compound **2n**, ^{13}C-NMR, 150MHz, $CDCl_3$



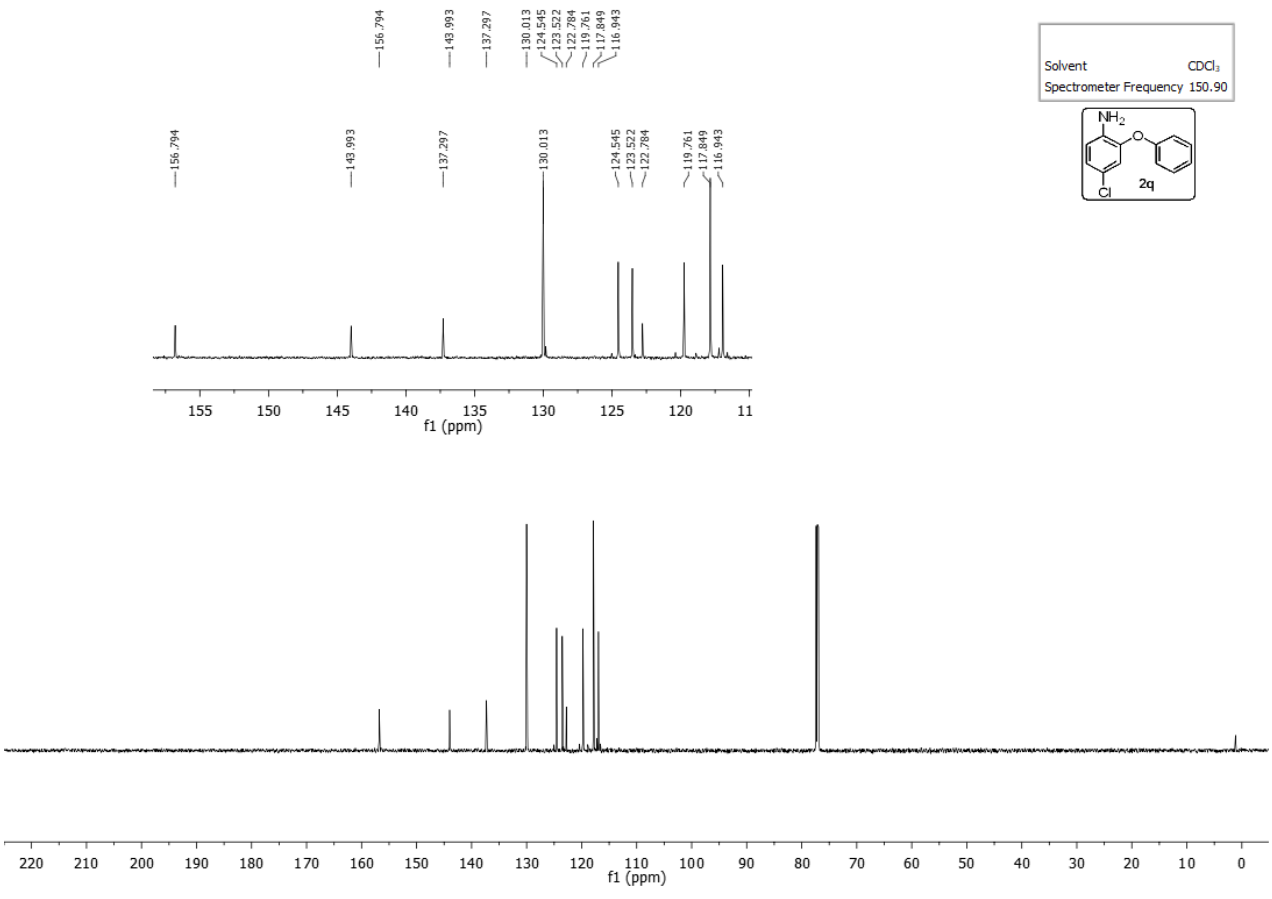
Compound **3n**, ^{1}H-NMR, 600MHz, $CDCl_3$



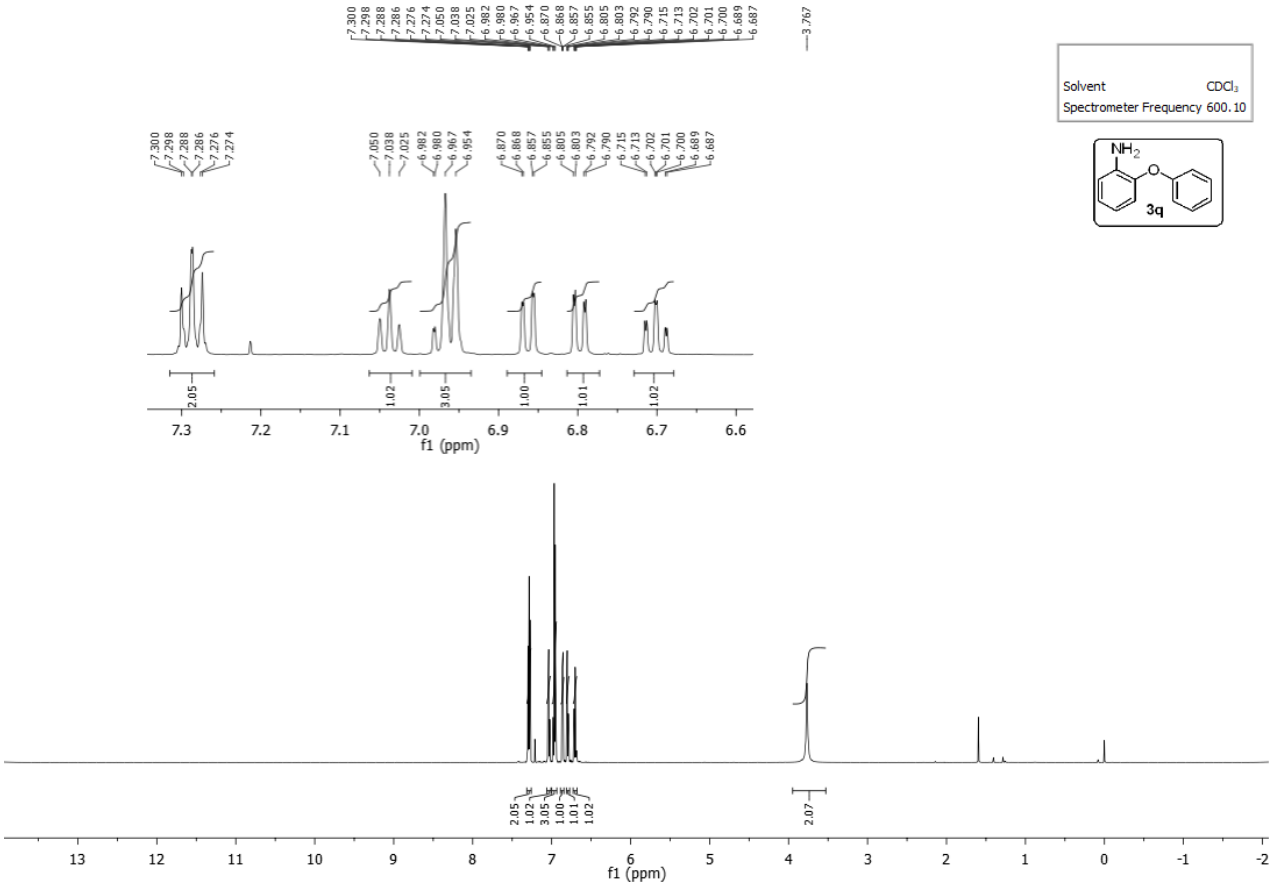
Compound **3n**, ^{13}C-NMR, 150MHz, $CDCl_3$



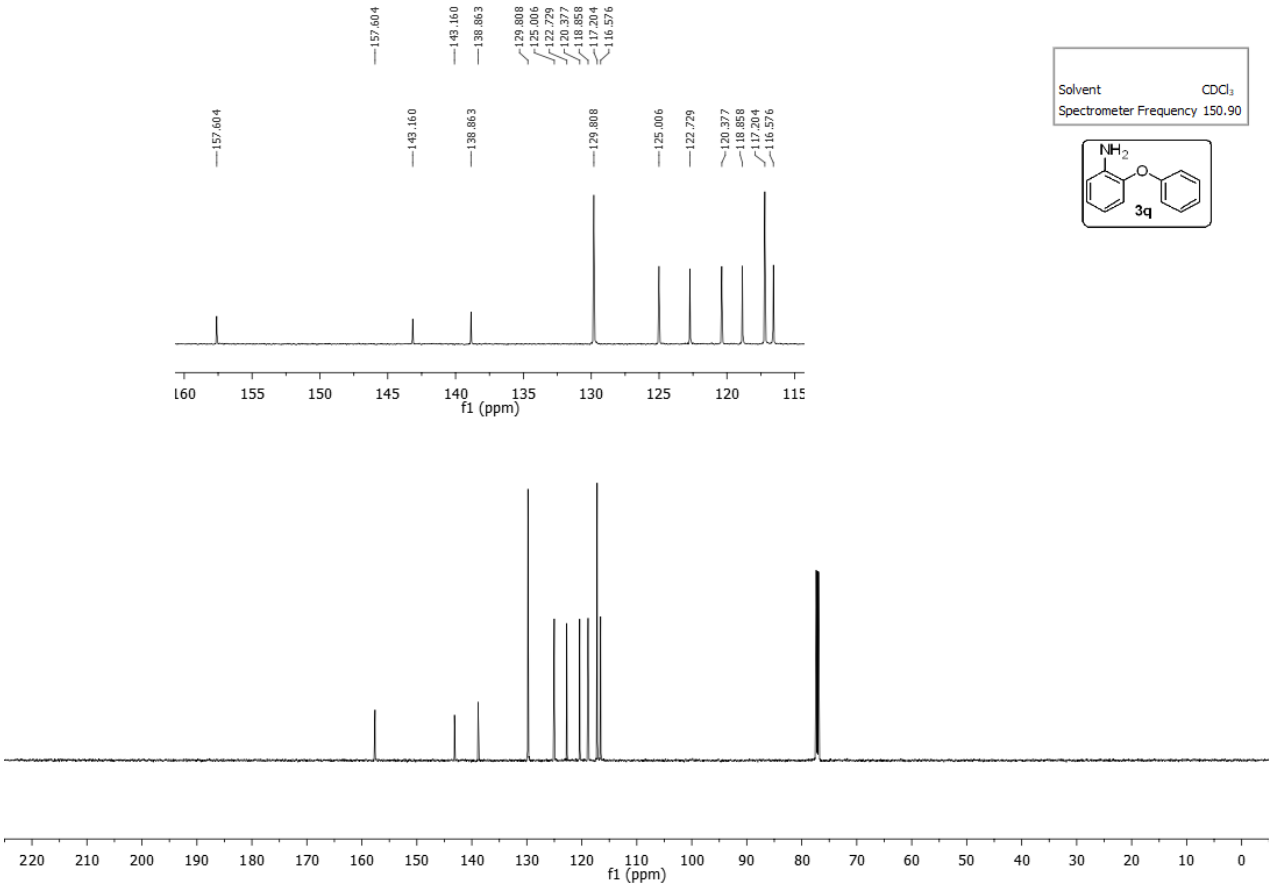
Compound **2q**, ^{1}H-NMR, 600MHz, $CDCl_3$



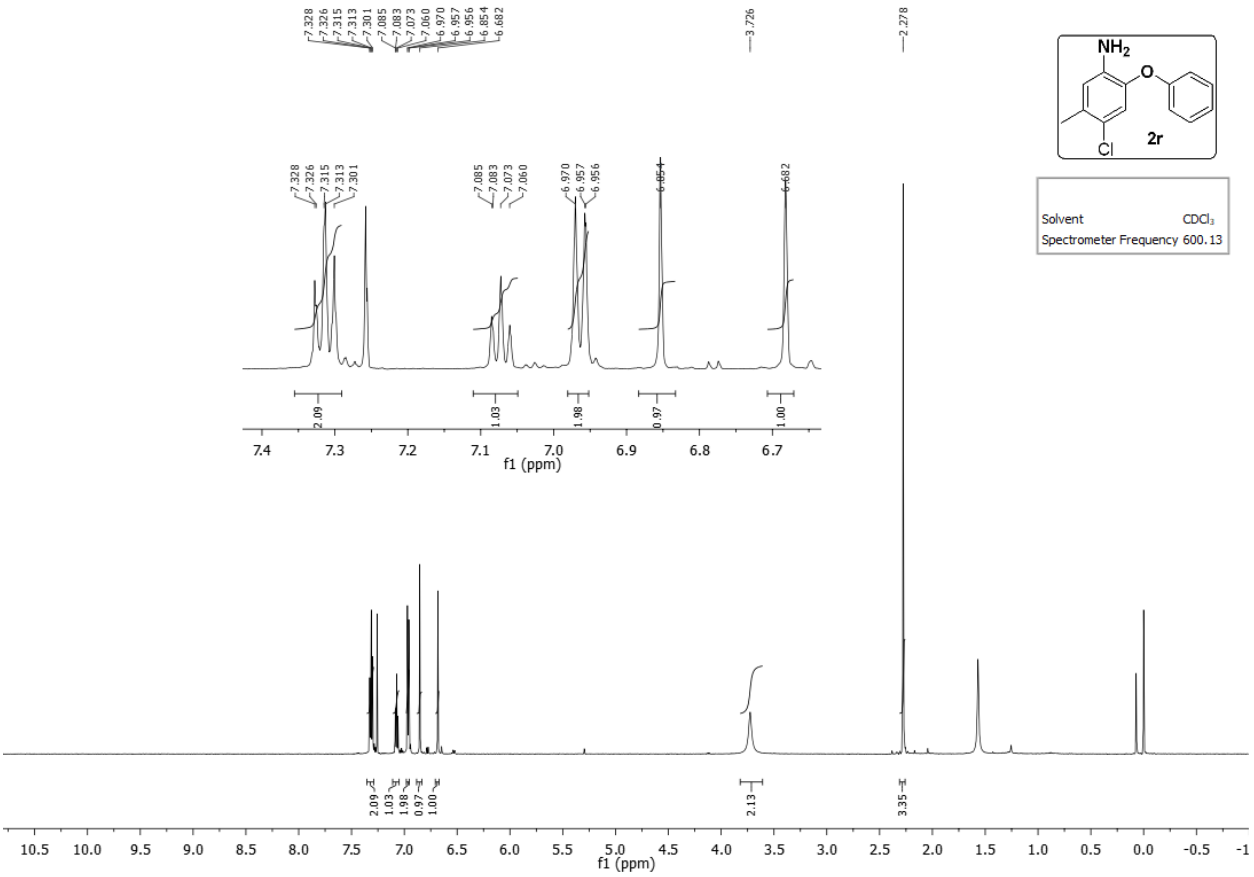
Compound **2q**, ^{13}C-NMR, 150MHz, $CDCl_3$



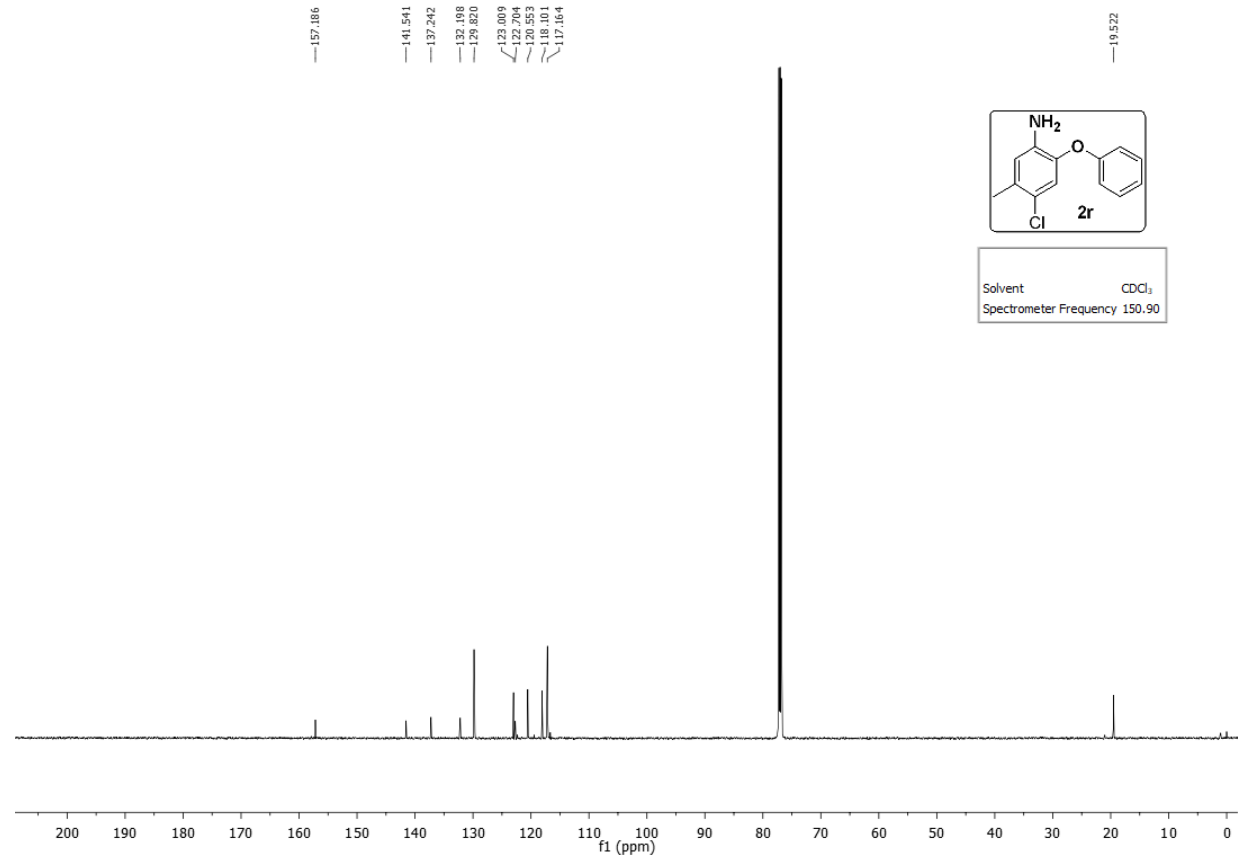
Compound **3q**, ^{1}H-NMR, 600MHz, $CDCl_3$



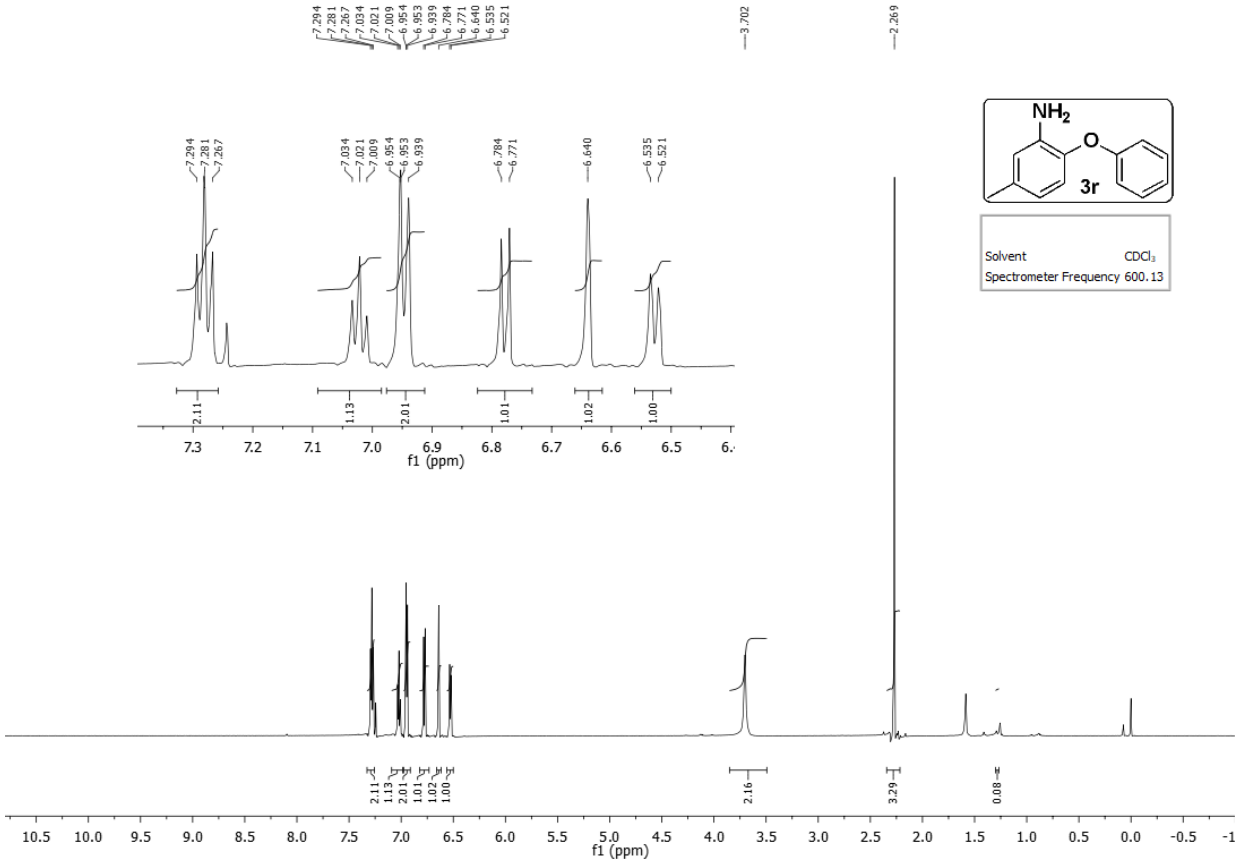
Compound **3q**, ^{13}C-NMR, 150MHz, $CDCl_3$



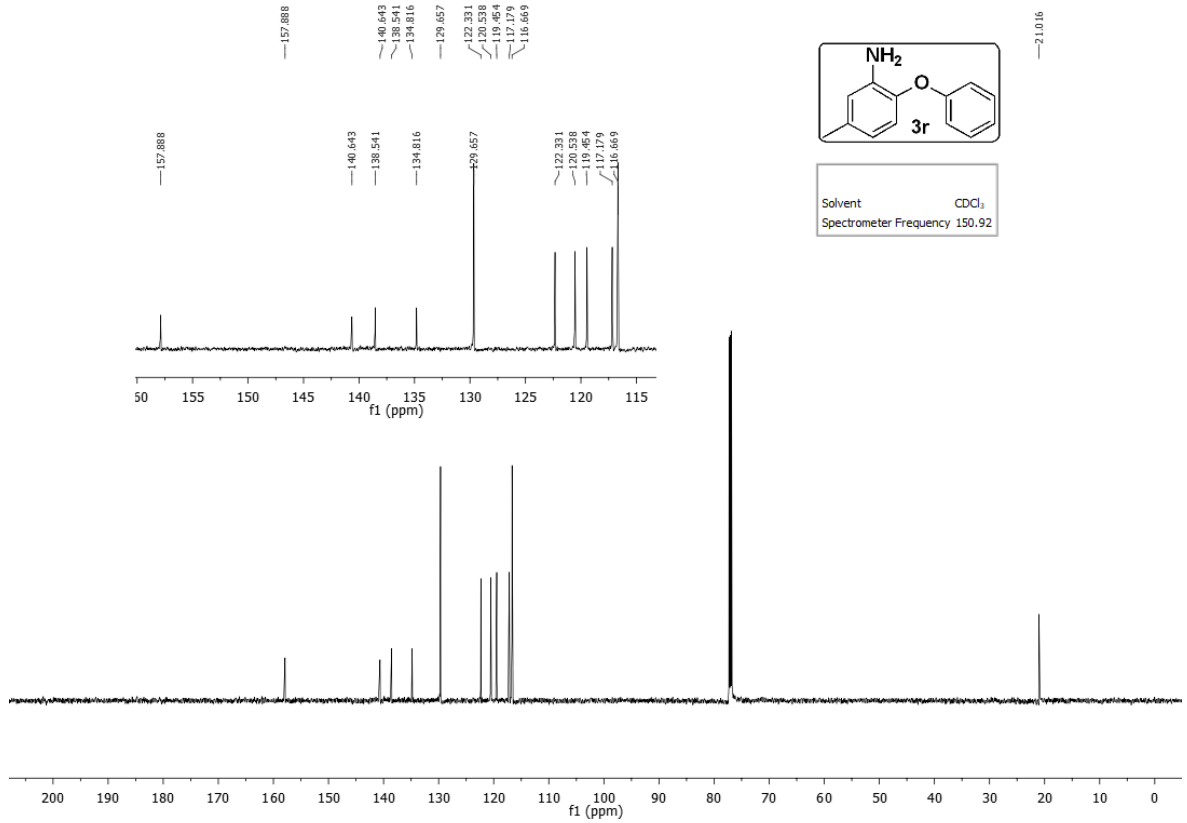
Compound **2r**, ^{1}H-NMR, 600MHz, $CDCl_3$



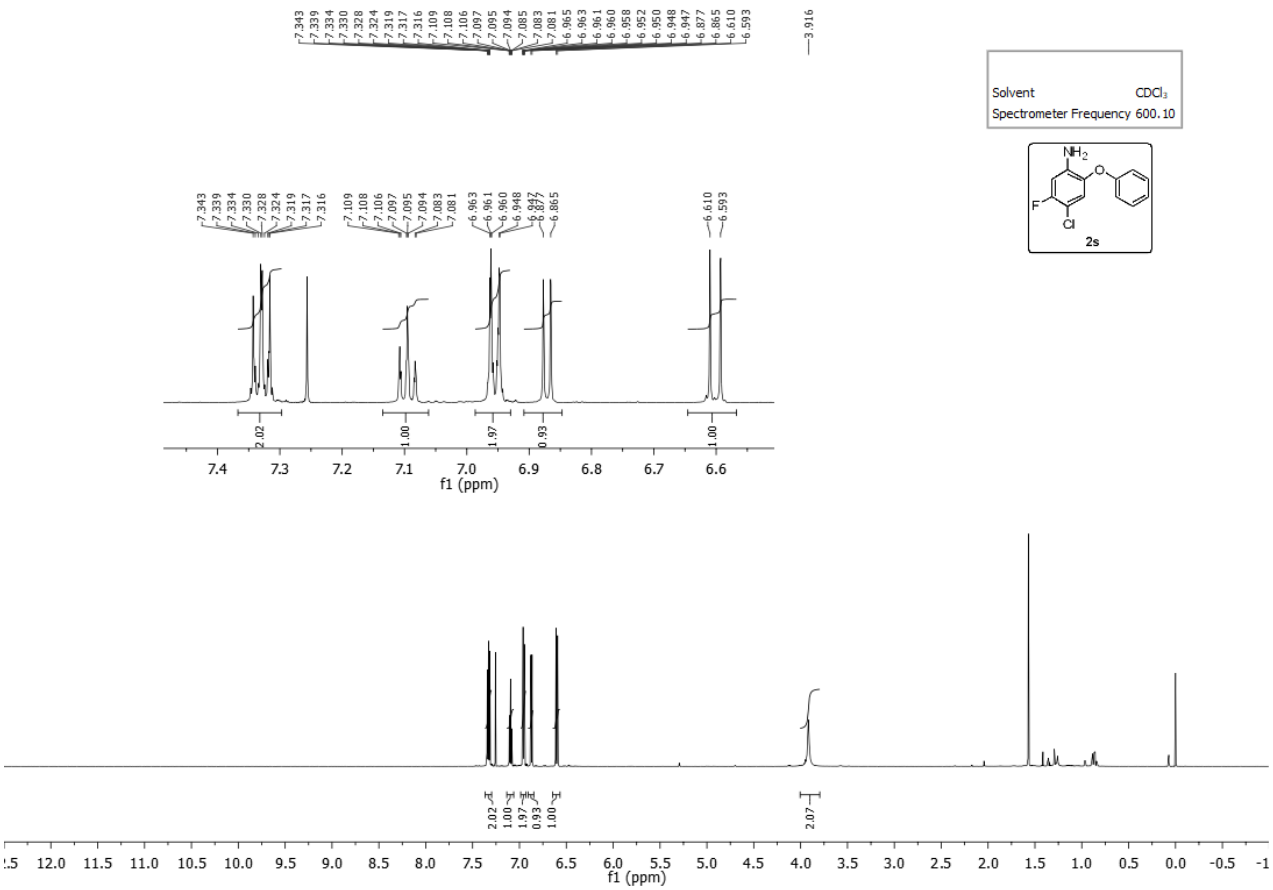
Compound **2r**, ^{13}C-NMR, 150MHz, $CDCl_3$



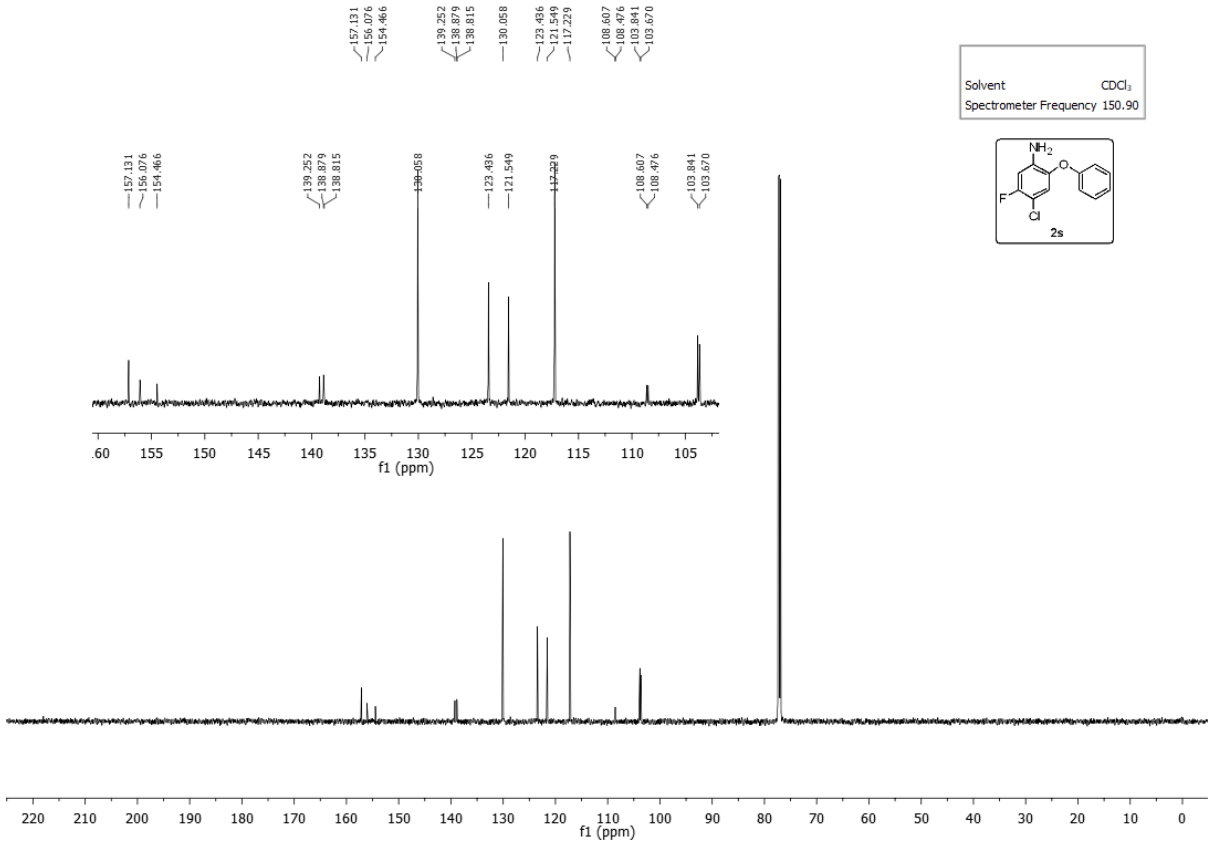
Compound **3r**, ^{1}H-NMR, 600MHz, $CDCl_3$



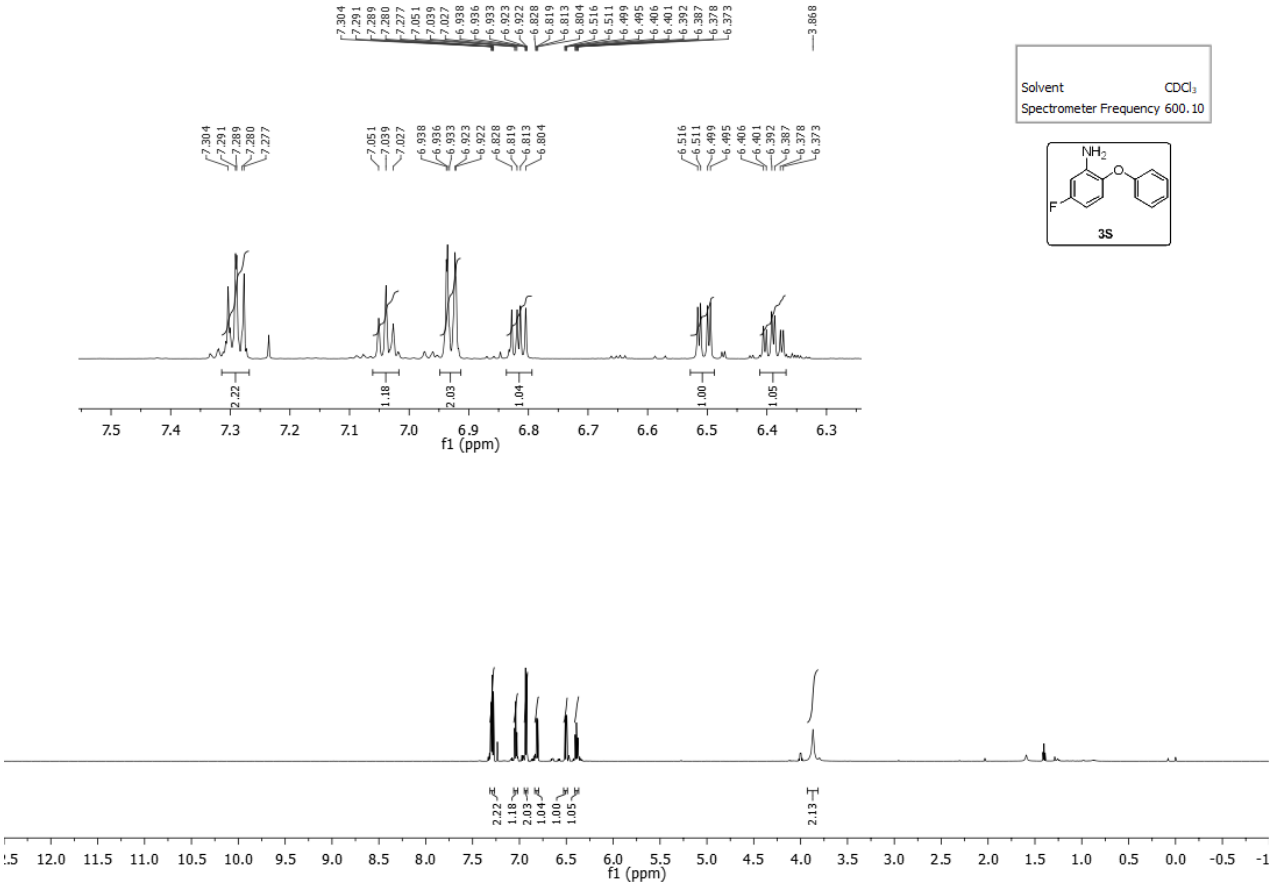
Compound **3r**, ^{13}C-NMR, 150MHz, $CDCl_3$



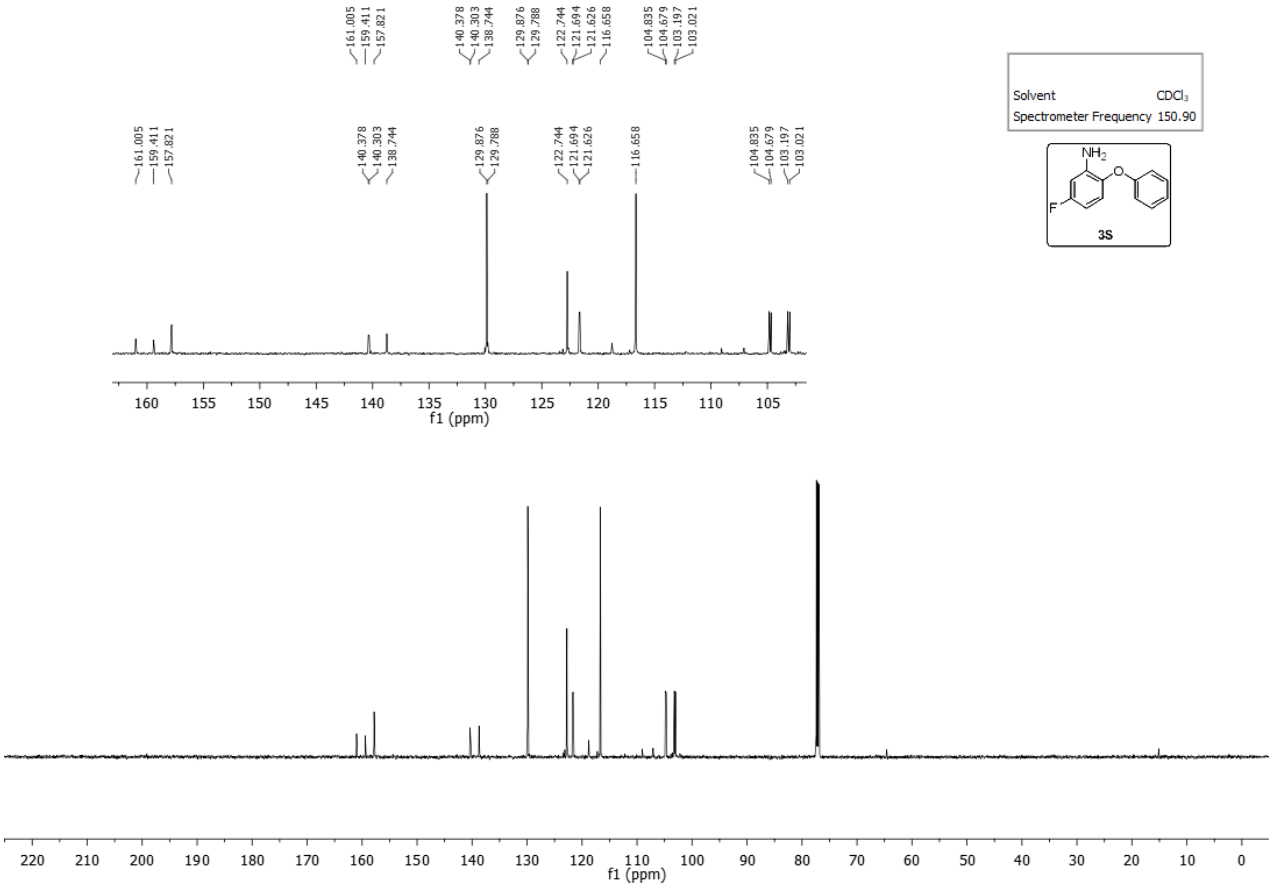
Compound **2s**, ^{1}H-NMR, 600MHz, $CDCl_3$



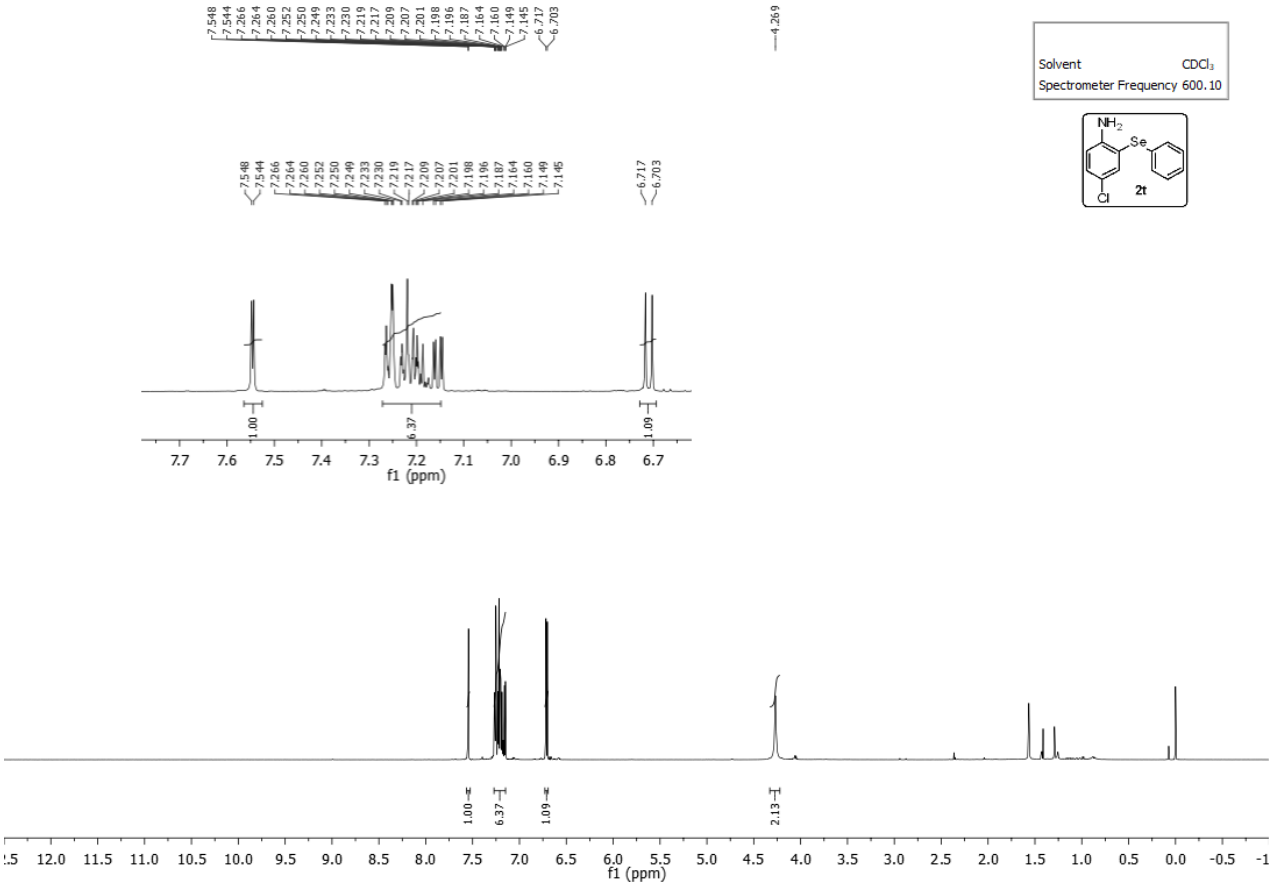
Compound **2s**, ^{13}C-NMR, 150MHz, $CDCl_3$



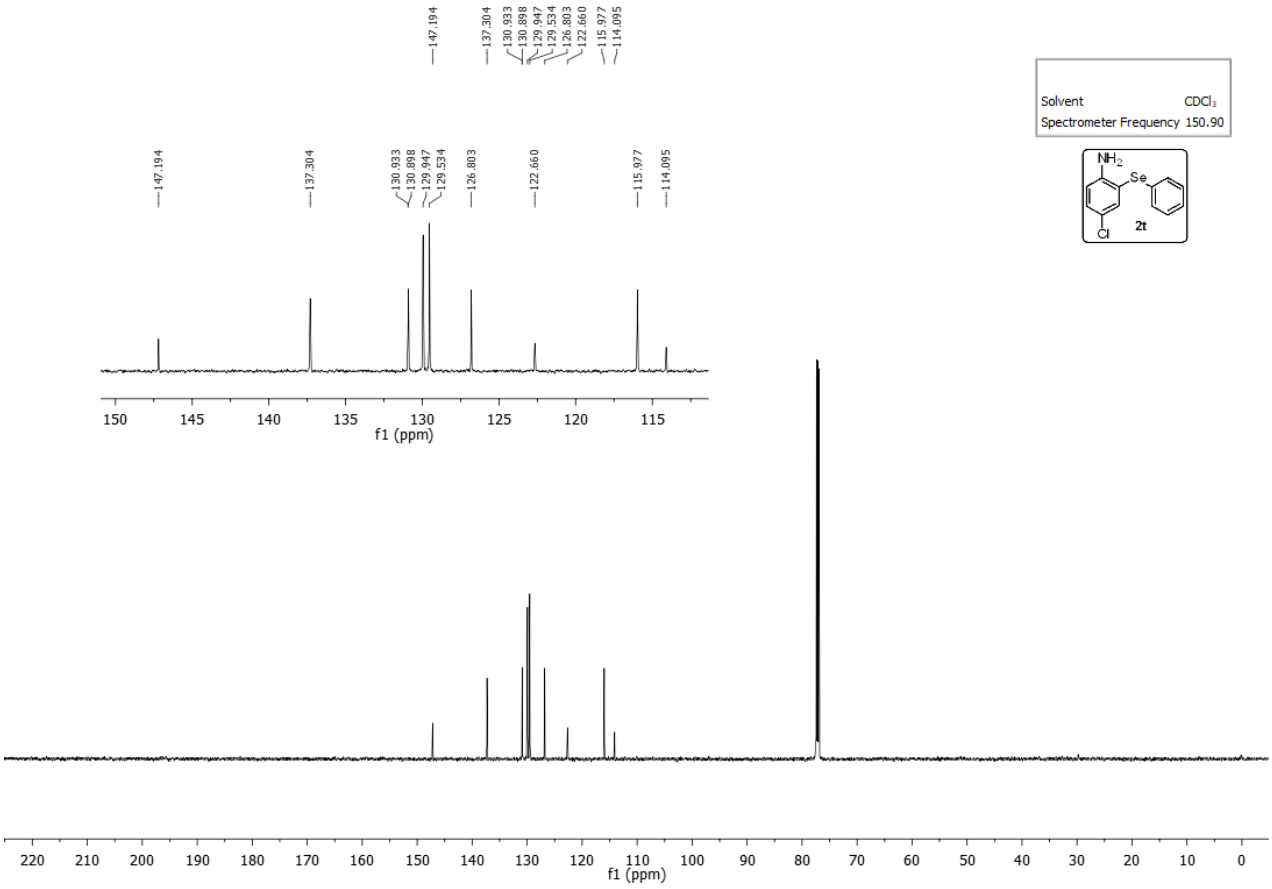
Compound **3s**, ^{1}H-NMR, 600MHz, $CDCl_3$



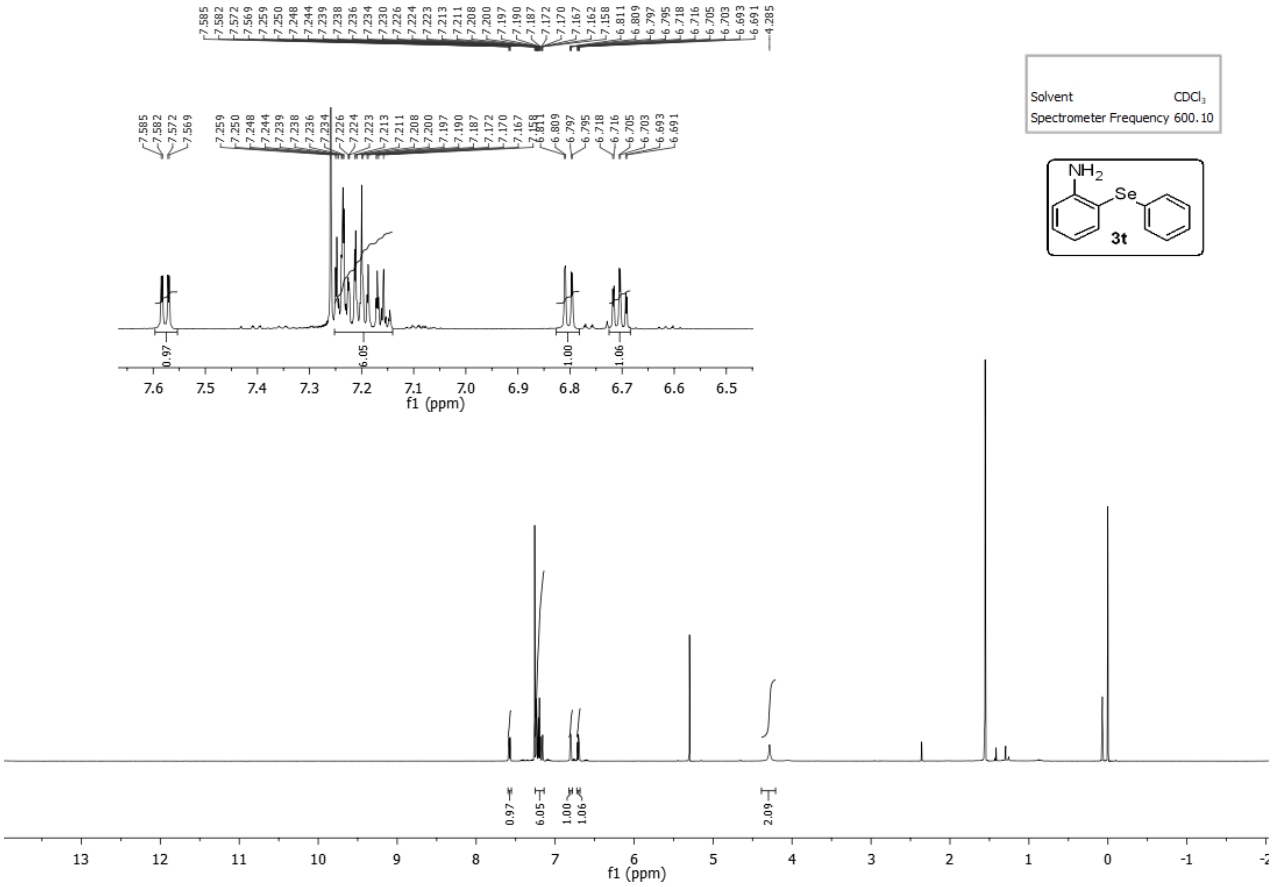
Compound **3s**, ^{13}C-NMR, 150MHz, $CDCl_3$



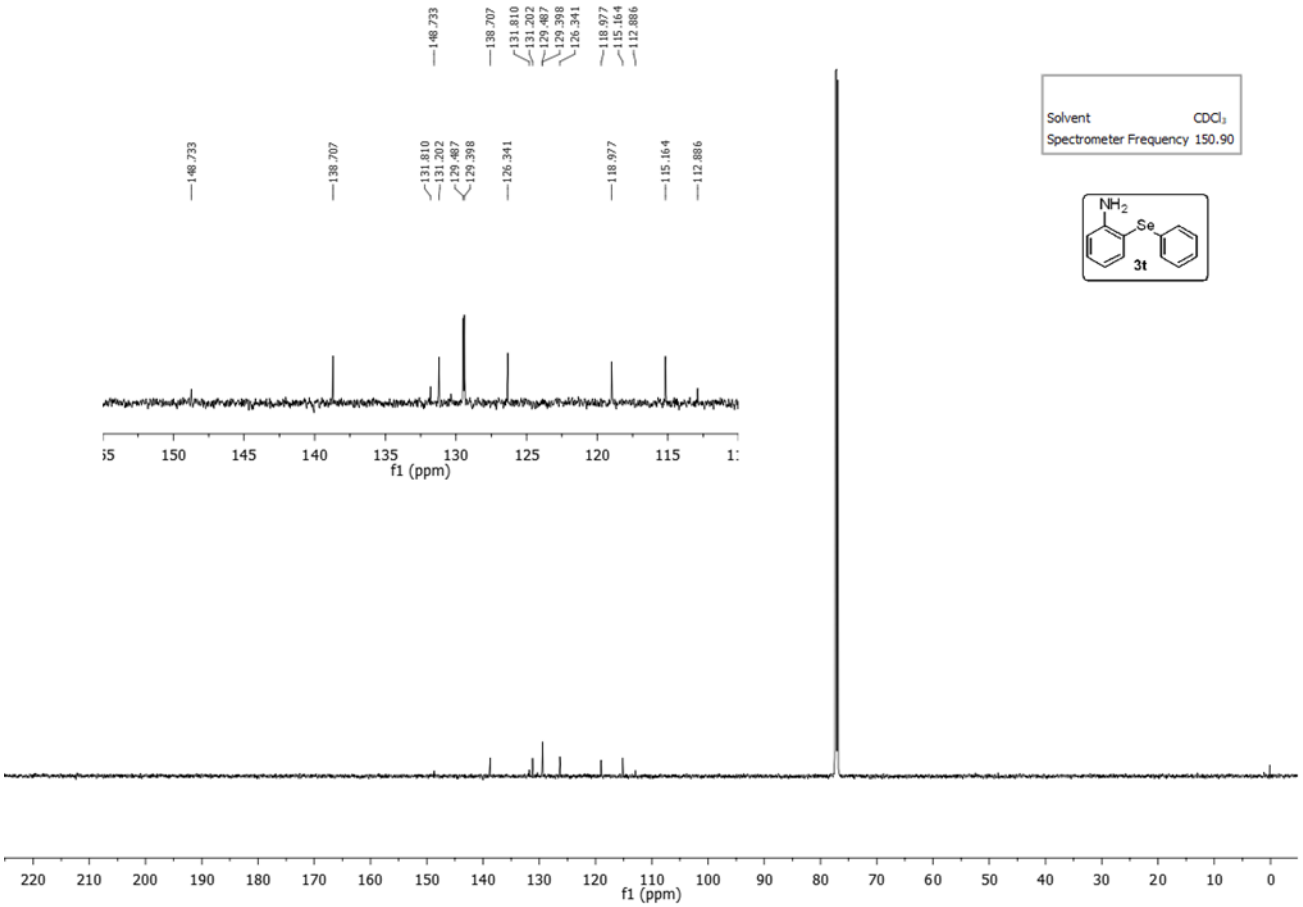
Compound **2t**, ^{1}H-NMR, 600MHz, $CDCl_3$



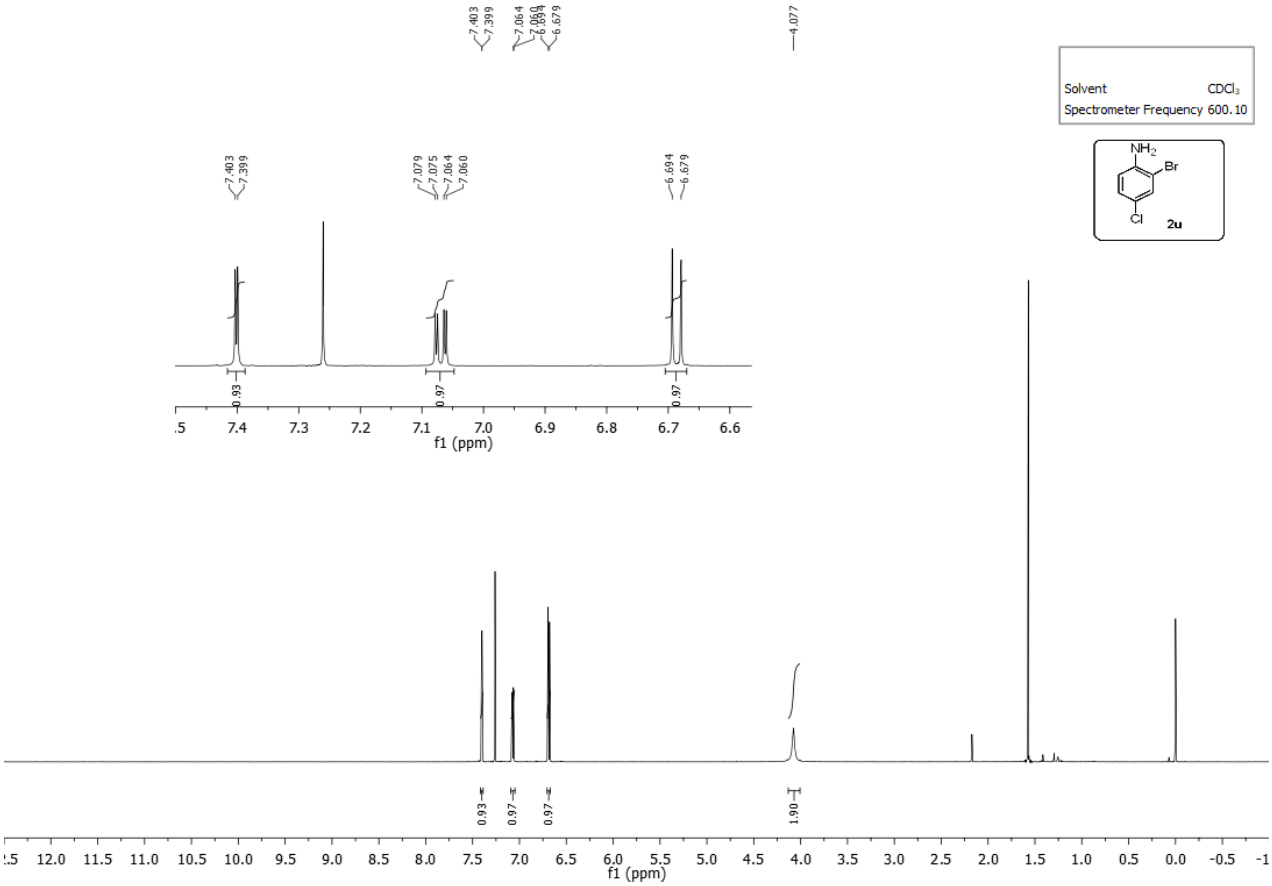
Compound **2t**, ^{13}C-NMR, 150MHz, $CDCl_3$



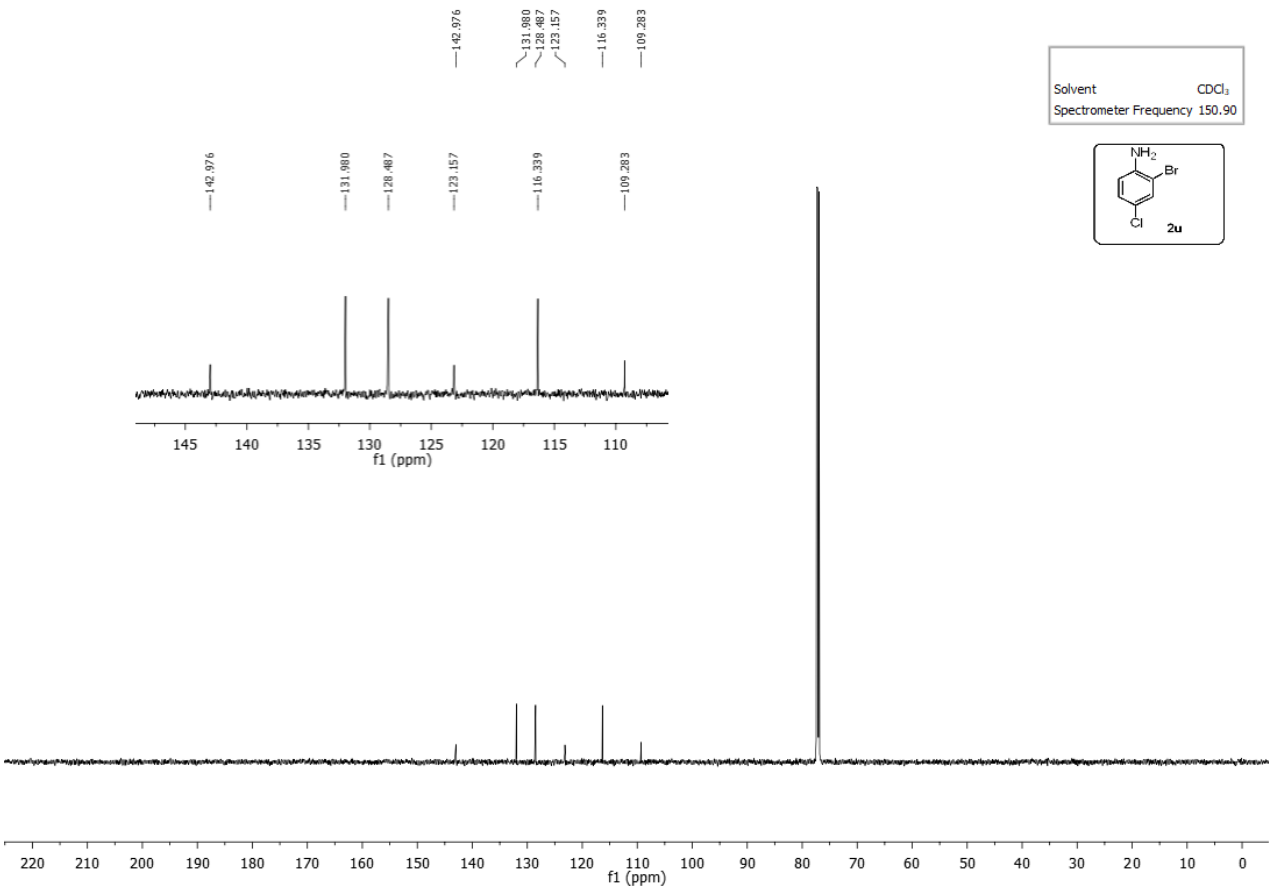
Compound **3t**, ^{1}H-NMR, 600MHz, $CDCl_3$



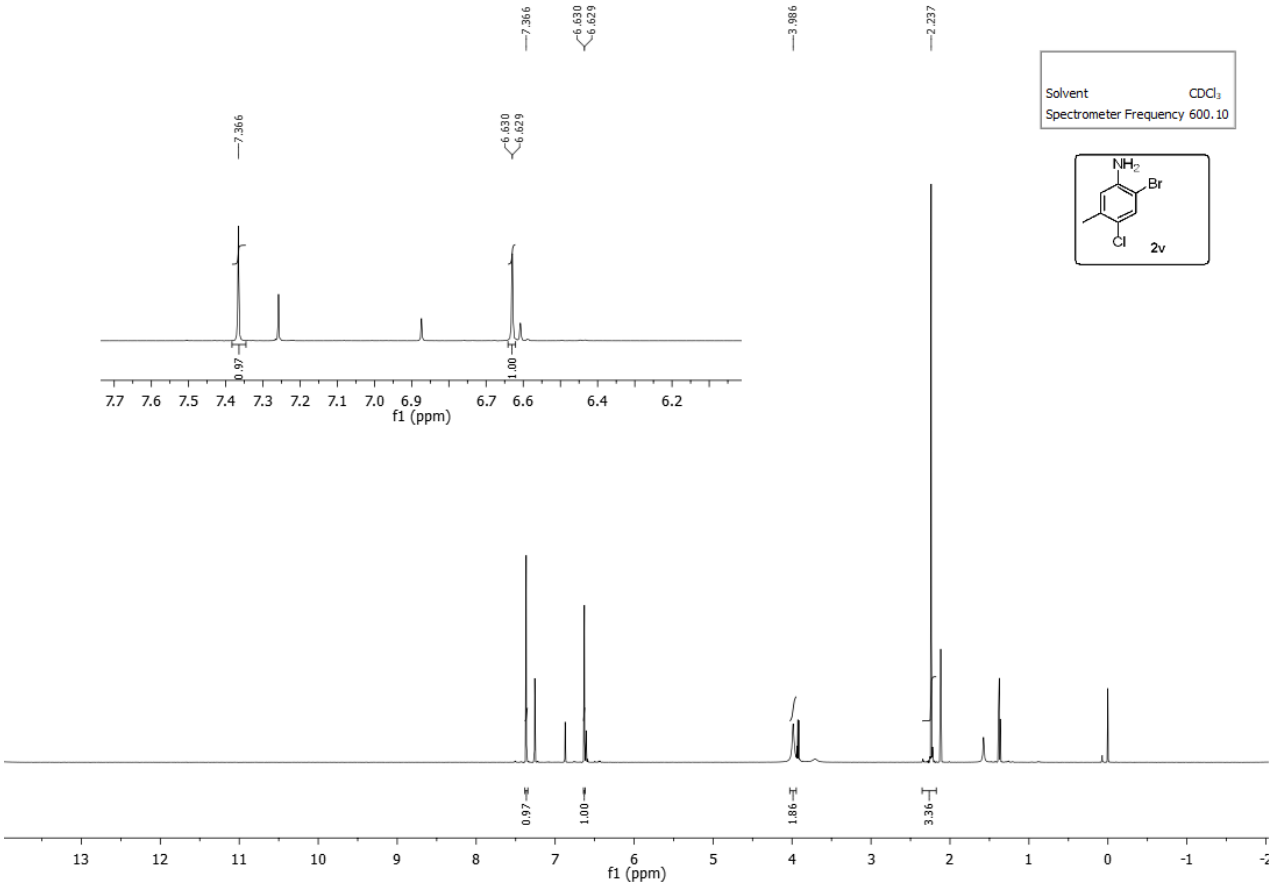
Compound **3t**, ^{13}C-NMR, 150MHz, $CDCl_3$



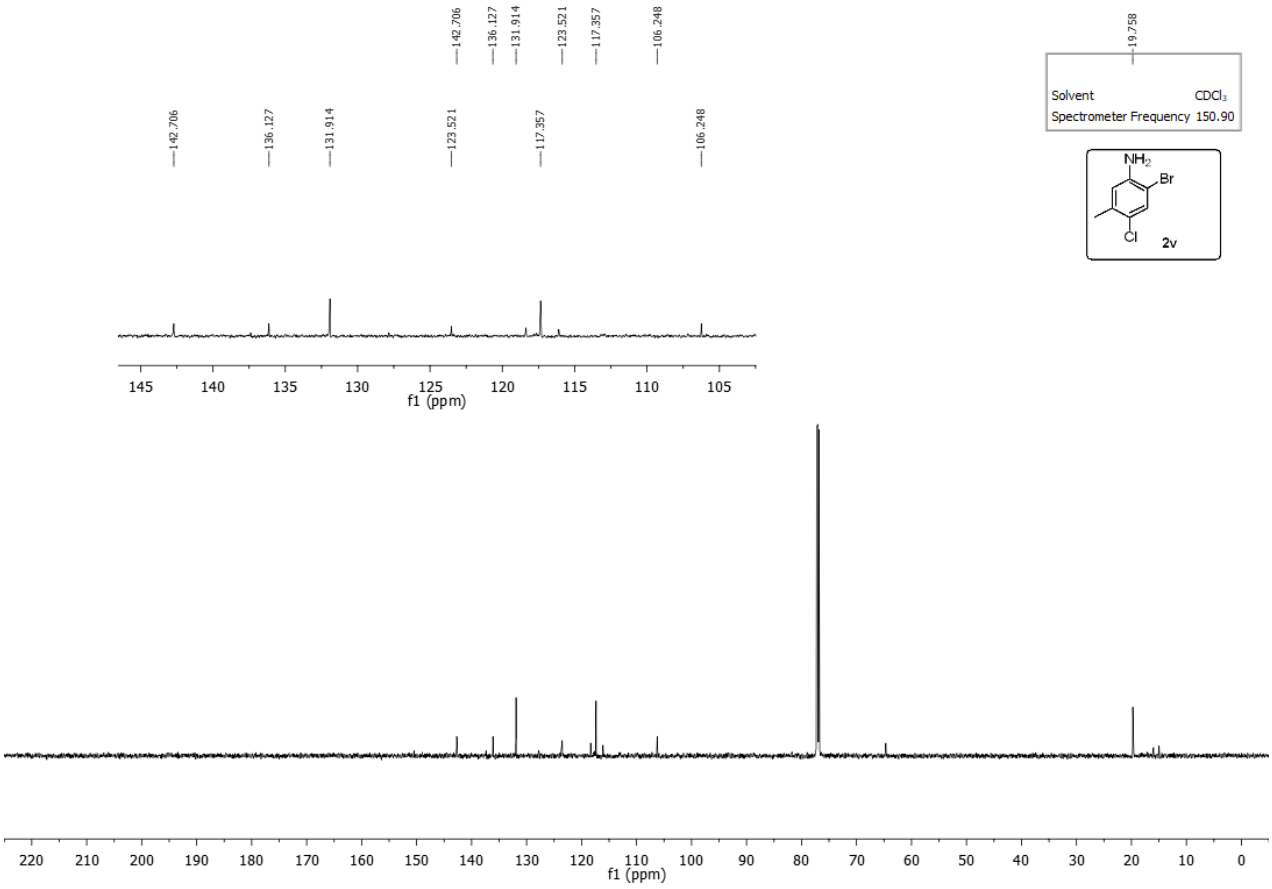
Compound **2u**, ^{1}H-NMR, 600MHz, $CDCl_3$



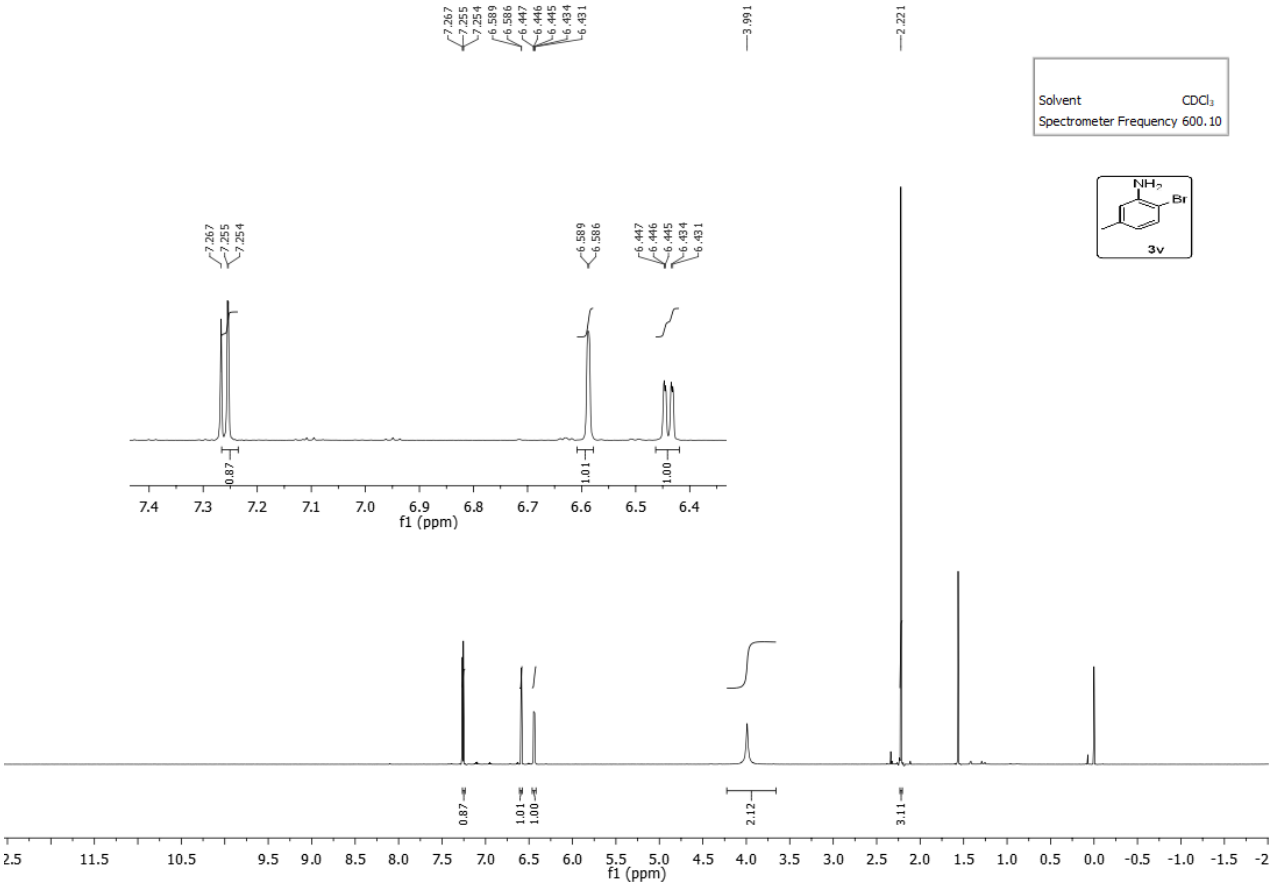
Compound **2u**, ^{13}C-NMR, 150MHz, $CDCl_3$



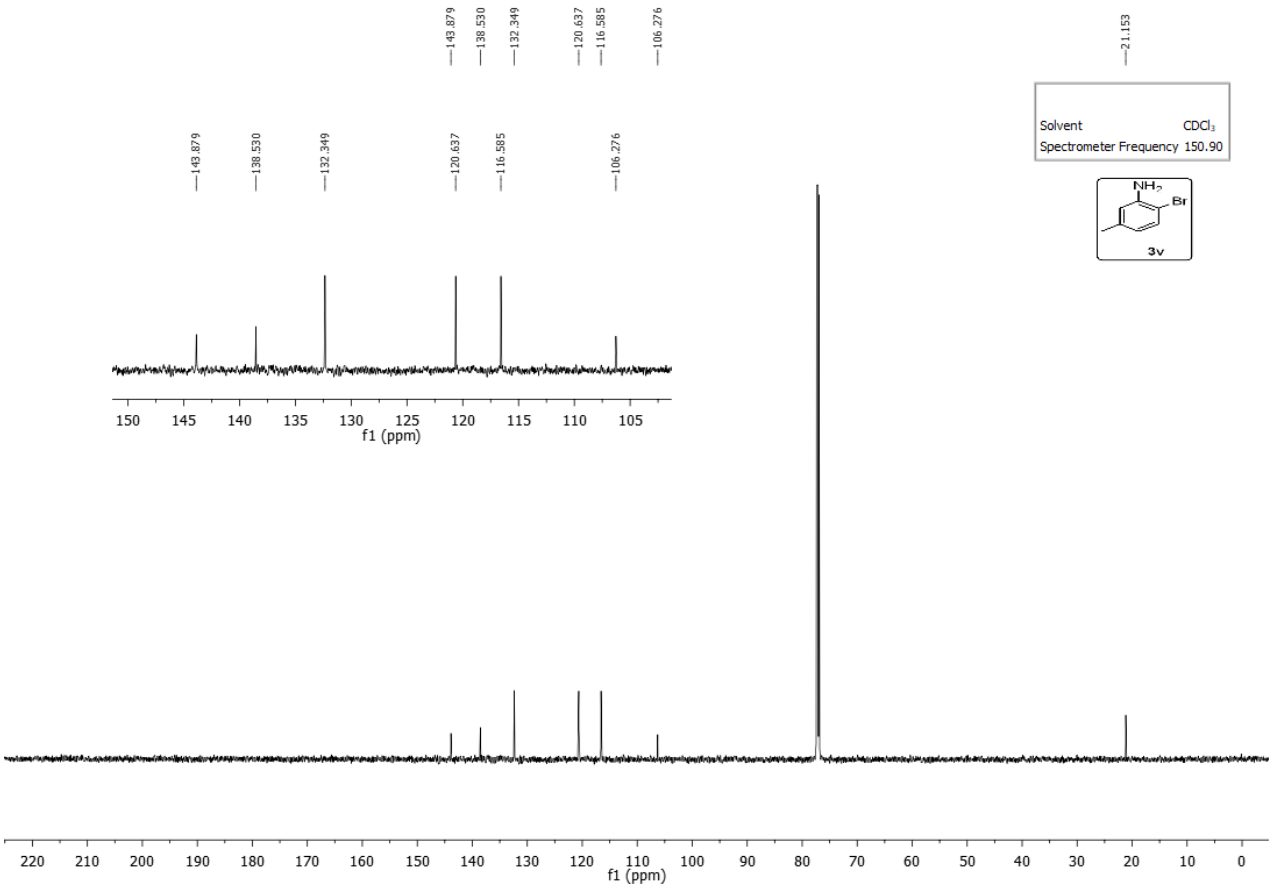
Compound **2v**, ^{1}H-NMR, 600MHz, $CDCl_3$



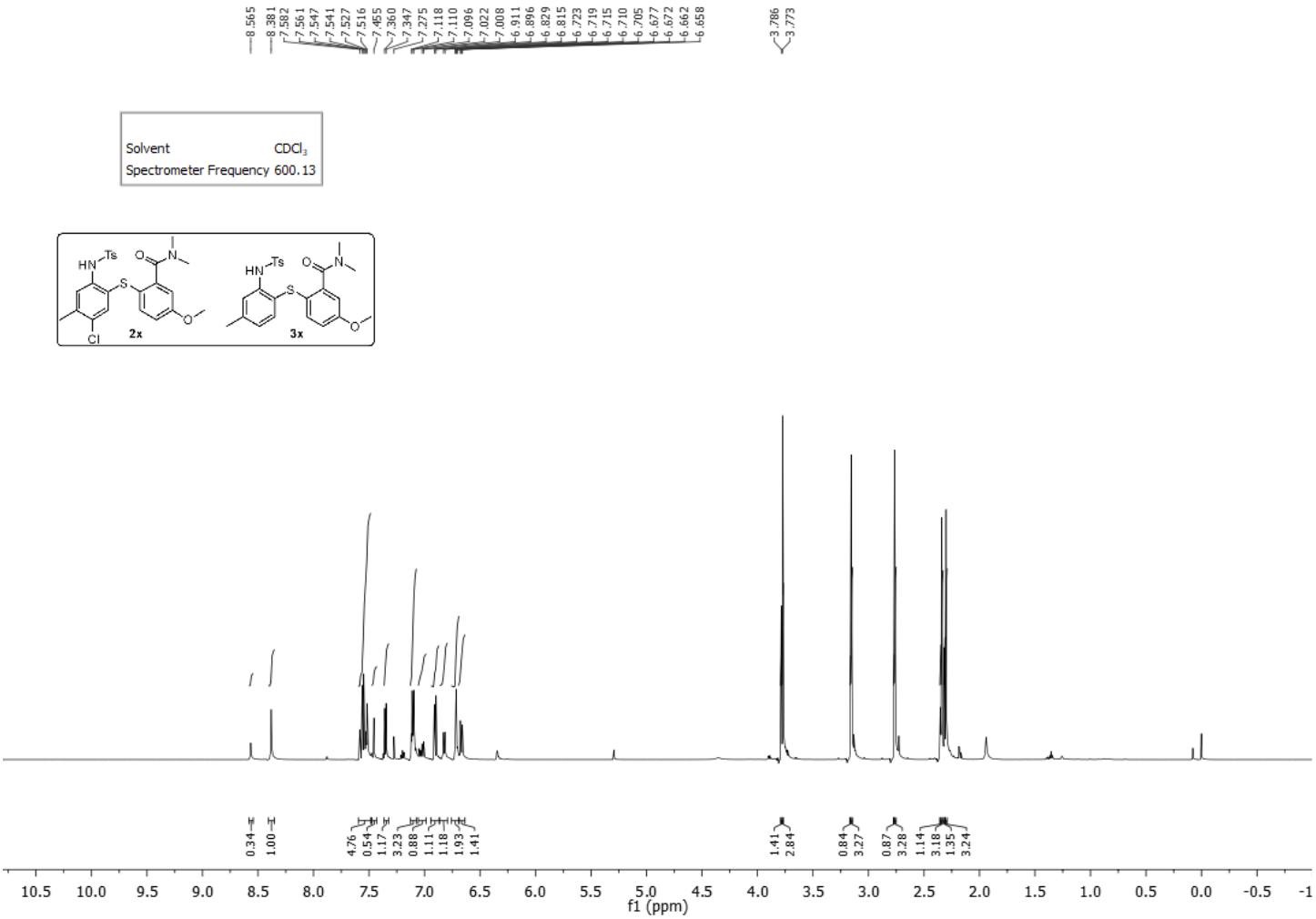
Compound **2v**, ^{13}C-NMR, 150MHz, $CDCl_3$



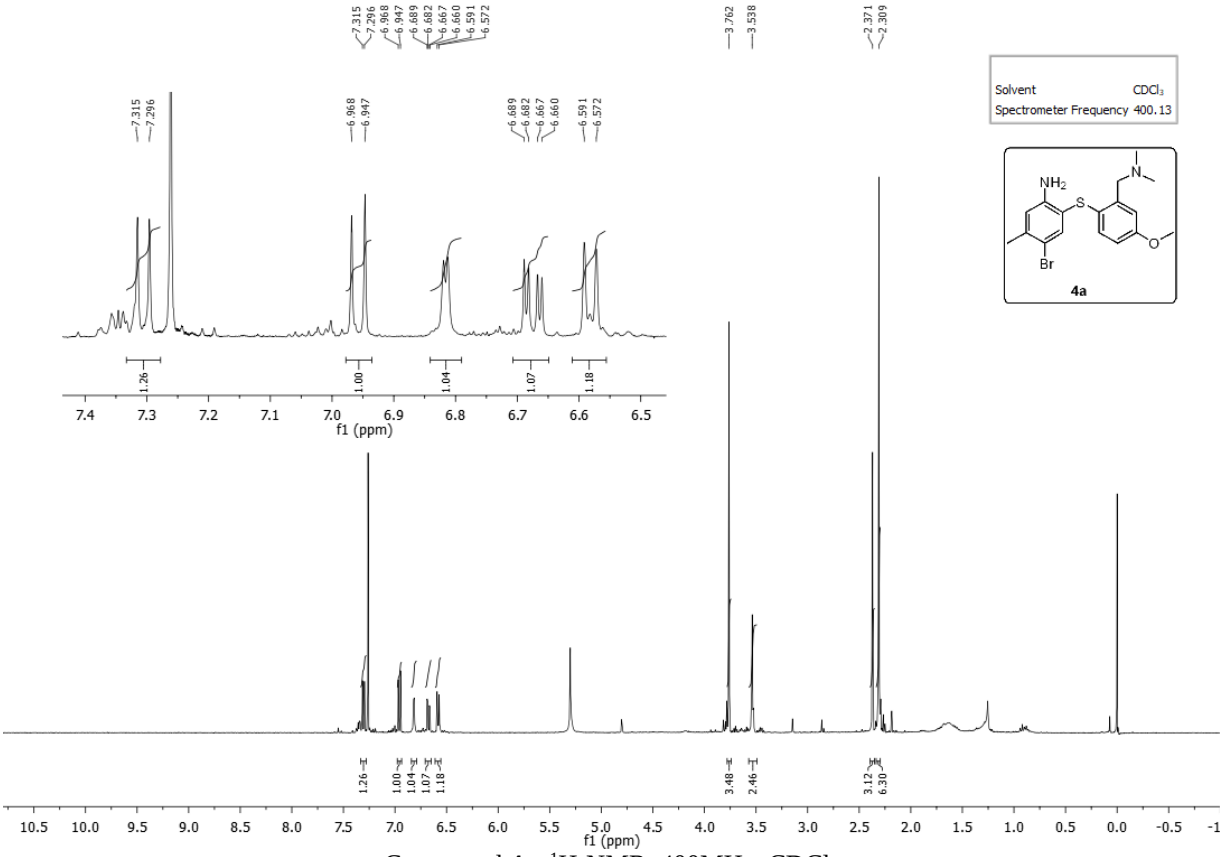
Compound **3v**, ^{1}H-NMR, 600MHz, $CDCl_3$



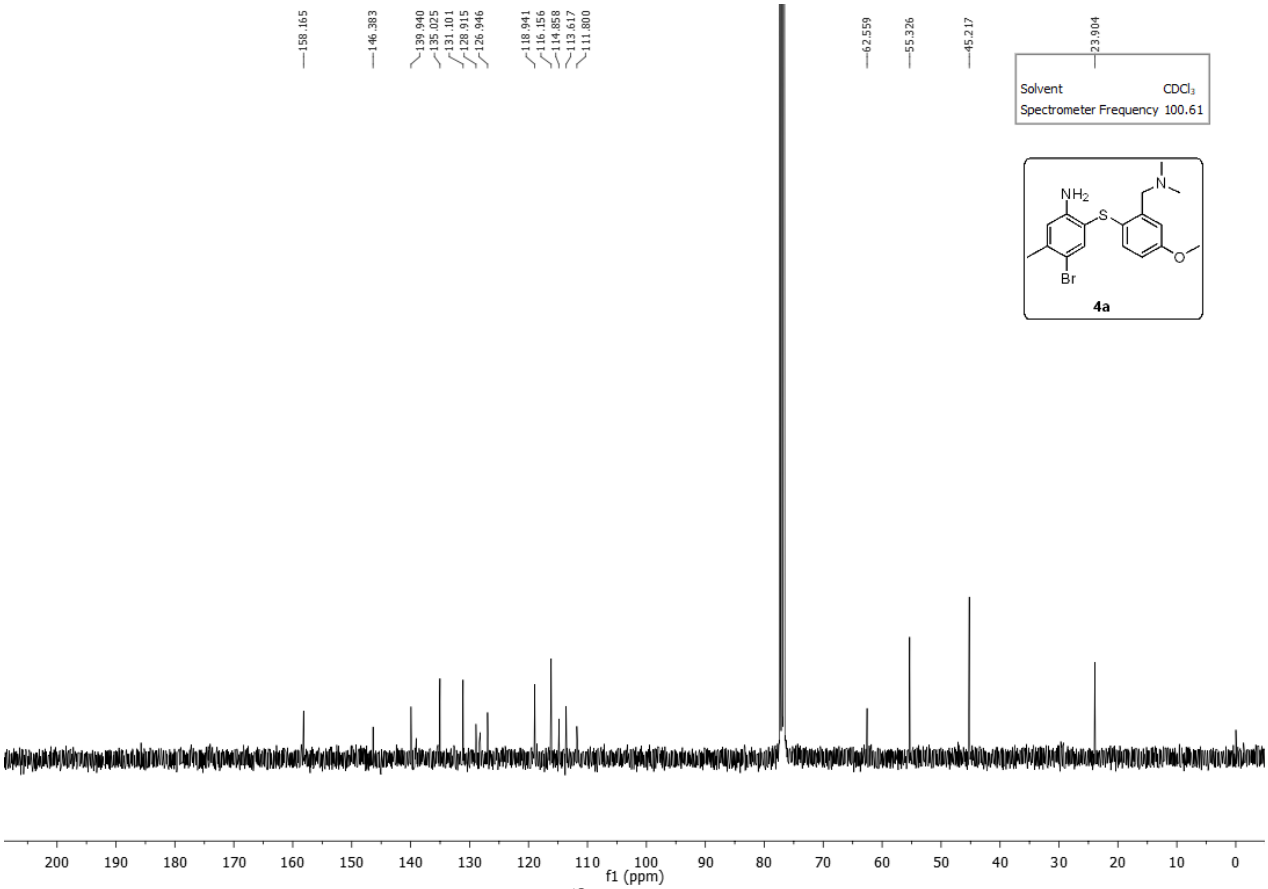
Compound **3v**, ^{13}C-NMR, 150MHz, $CDCl_3$



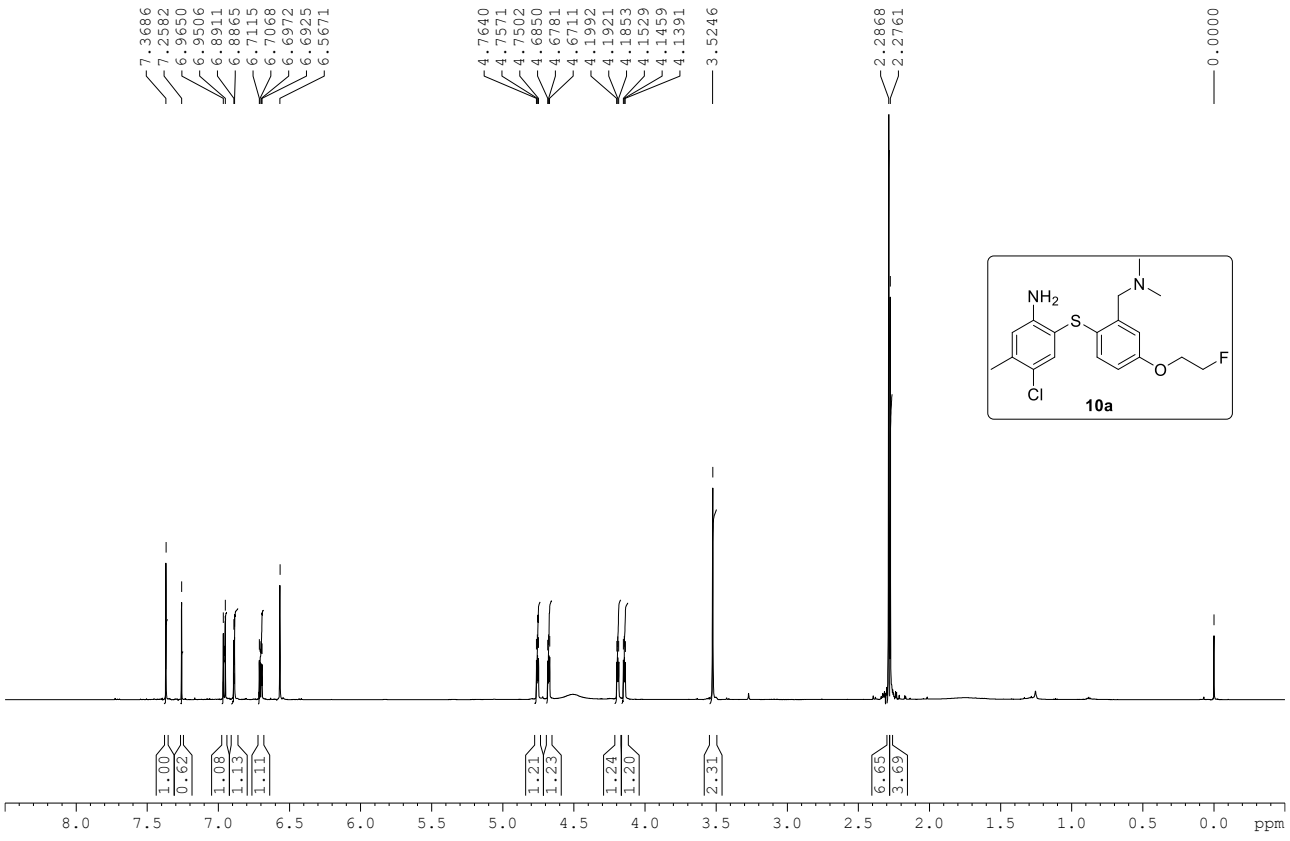
Compound **2x** and **3x**, ^{1}H-NMR, 600MHz, $CDCl_3$



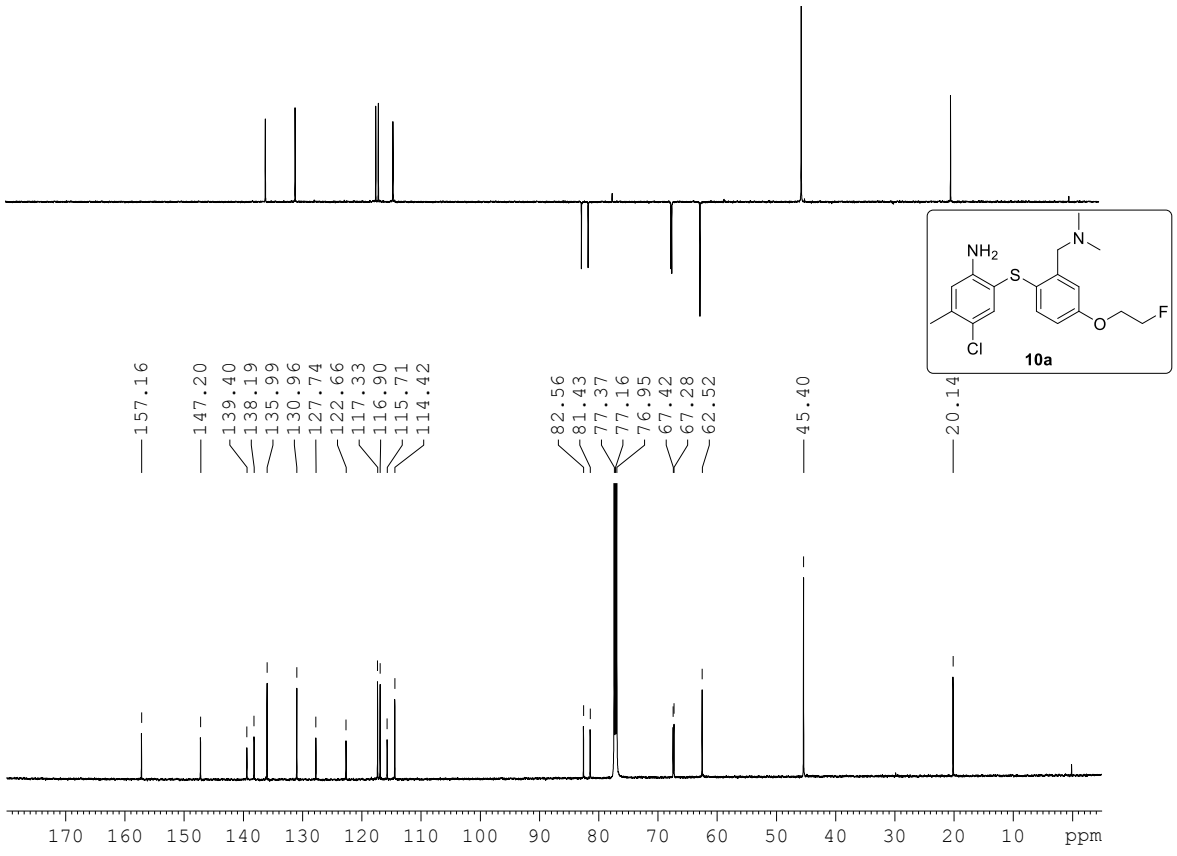
Compound **4a**, ^{1}H-NMR, 400MHz, $CDCl_3$



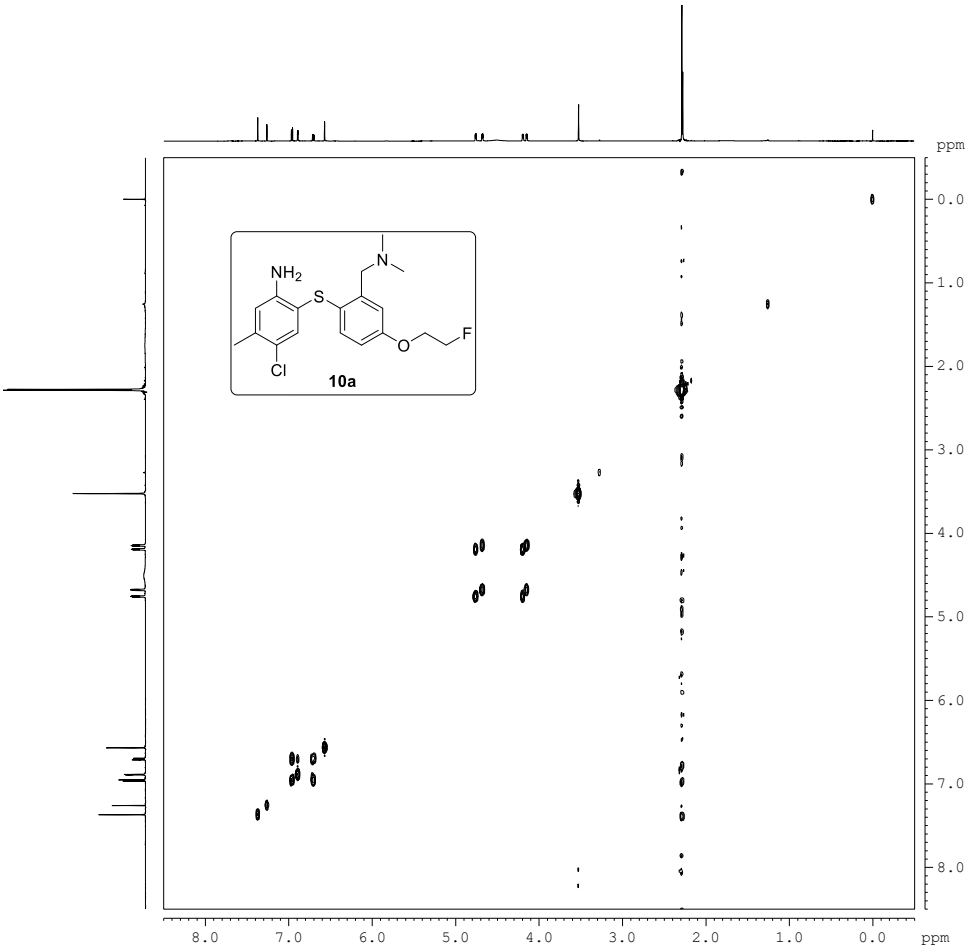
Compound **4a**, ^{13}C-NMR, 100MHz, $CDCl_3$



Compound **10a**, ^{1}H-NMR, 600MHz, $CDCl_3$



Compound **10a**, ^{13}C-NMR, Dept135, 150MHz, $CDCl_3$



Current Data Parameters
NAME lwh-xys-20130730
EXPNO 5
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130730
Time 11.46
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG hsqcetgpsisp2.2
TD 2048
SOLVENT CDCl3
NS 1
DS 16
SWH 8012.820 Hz
FIDRES 3.912510 Hz
AQ 0.1278452 sec
RG 1030
DW 62.400 usec
DE 20.00 usec
TE 300.1 K
CNST2 145.0000000
CNST17 -0.5000000
D0 0.00000300 sec
D1 1.50000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D16 0.00020000 sec
D24 0.00086207 sec
IN0 0.00001540 sec

======== CHANNEL f1 ========
NUC1 1H
P1 10.00 usec
P2 20.00 usec
P28 0 usec
PL1 0 dB
PL1W 16.10119247 W
SFO1 600.0736004 MHz

======== CHANNEL f2 ========
CPDPRG2 garp
NUC2 13C
P3 11.20 usec
P14 500.00 usec
P24 2000.00 usec
PCPD2 60.00 usec
PL0 120.00 dB
PL2 6.00 dB
PL12 19.70 dB
PL0W 0 W
PL2W 23.02994347 W
PL12W 0.98241001 W
SFO2 150.9013014 MHz
SP3 13.41 dB
SP7 13.41 dB
SPNAM3 Crp60,0.5,20.1
SPNAM7 Crp60comp.4
SPOAL3 0.500
SPOAL7 0.500
SPOFFS3 0 Hz
SPOFFS7 0 Hz

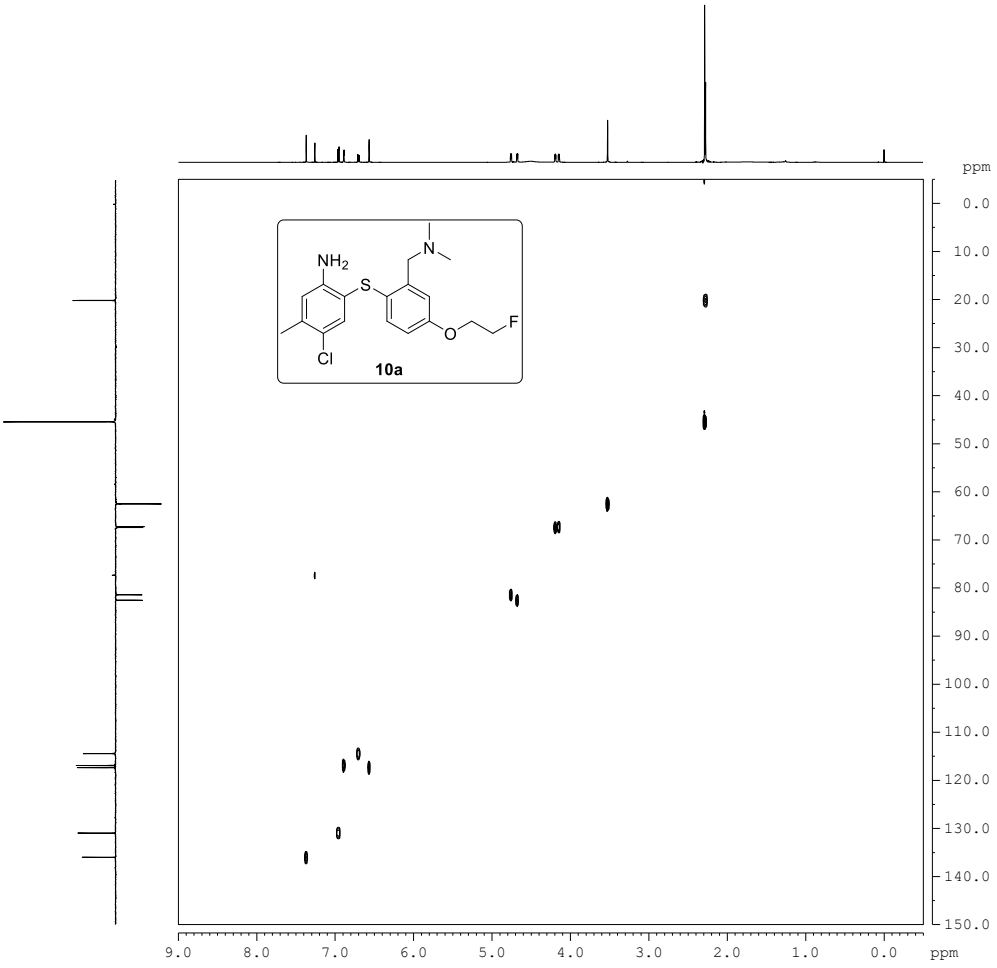
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPNAM3 SINE.100
GPNAM4 SINE.100
GPZ1 80.00 %
GPZ2 20.10 %
GPZ3 11.00 %
GPZ4 -5.00 %
P16 1000.00 usec
P19 600.00 usec

F1 - Acquisition parameters
TD 256
SFO1 150.9013 MHz
FIDRES 126.733513 Hz
SW 215.000 ppm
FnMODE Echo-Antiecho

F2 - Processing parameters
SI 1024
SF 600.0700159 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40

F1 - Processing parameters
SI 1024
MC2 echo-antiecho
SF 150.8876921 MHz
WDW SIN
SSB 2
LB 0 Hz
GB 0

Compound **10a**, ^{1}H-^{1}H COSY, $CDCl_3$.



Current Data Parameters
NAME lwh-xys-20130730
EXPNO 5
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130730
Time 11.46
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG hsqcetgpsisp2.2
TD 2048
SOLVENT CDCl3
NS 1
DS 16
SWH 8012.820 Hz
FIDRES 3.912510 Hz
AQ 0.1278452 sec
RG 1030
DW 62.400 usec
DE 20.00 usec
TE 300.1 K
CNST2 145.0000000
CNST17 -0.5000000
D0 0.00000300 sec
D1 1.50000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D16 0.00020000 sec
D24 0.00086207 sec
IN0 0.00001540 sec

======== CHANNEL f1 ========
NUC1 1H
P1 10.00 usec
P2 20.00 usec
PL1 0 dB
PL1W 16.10119247 W
SFO1 600.0736004 MHz

======== CHANNEL f2 ========
CPDPRG2 garp
NUC2 13C
P3 11.20 usec
P14 500.00 usec
P24 2000.00 usec
PCPD2 60.00 usec
PL0 120.00 dB
PL2 6.00 dB
PL12 19.70 dB
PL0W 0 W
PL2W 23.02994347 W
PL12W 0.98241001 W
SFO2 150.9013014 MHz
SP3 13.41 dB
SP7 13.41 dB
SPNAM3 Crp60,0.5,20.1
SPNAM7 Crp60comp.4
SPOAL3 0.500
SPOAL7 0.500
SPOFFS3 0 Hz
SPOFFS7 0 Hz

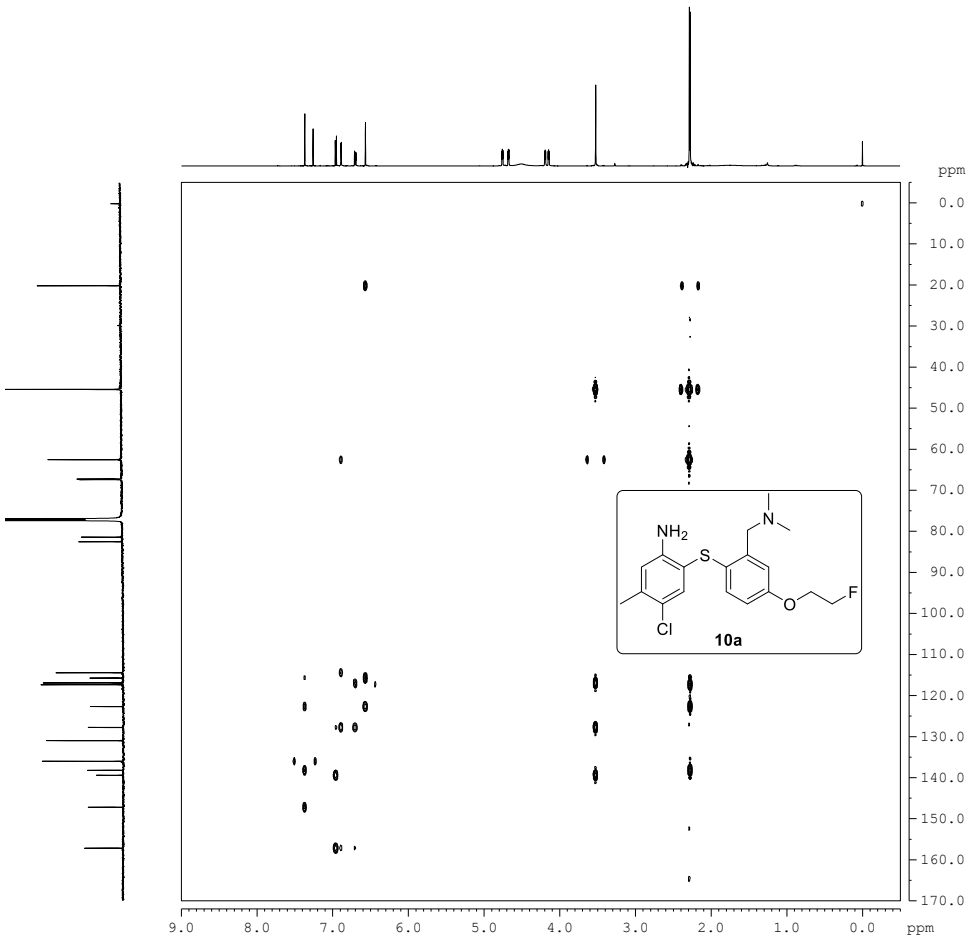
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPNAM3 SINE.100
GPNAM4 SINE.100
GPZ1 80.00 %
GPZ2 20.10 %
GPZ3 11.00 %
GPZ4 -5.00 %
P16 1000.00 usec
P19 600.00 usec

F1 - Acquisition parameters
TD 256
SFO1 150.9013 MHz
FIDRES 126.733513 Hz
SW 215.000 ppm
FnMODE Echo-Antiecho

F2 - Processing parameters
SI 1024
SF 600.0700159 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40

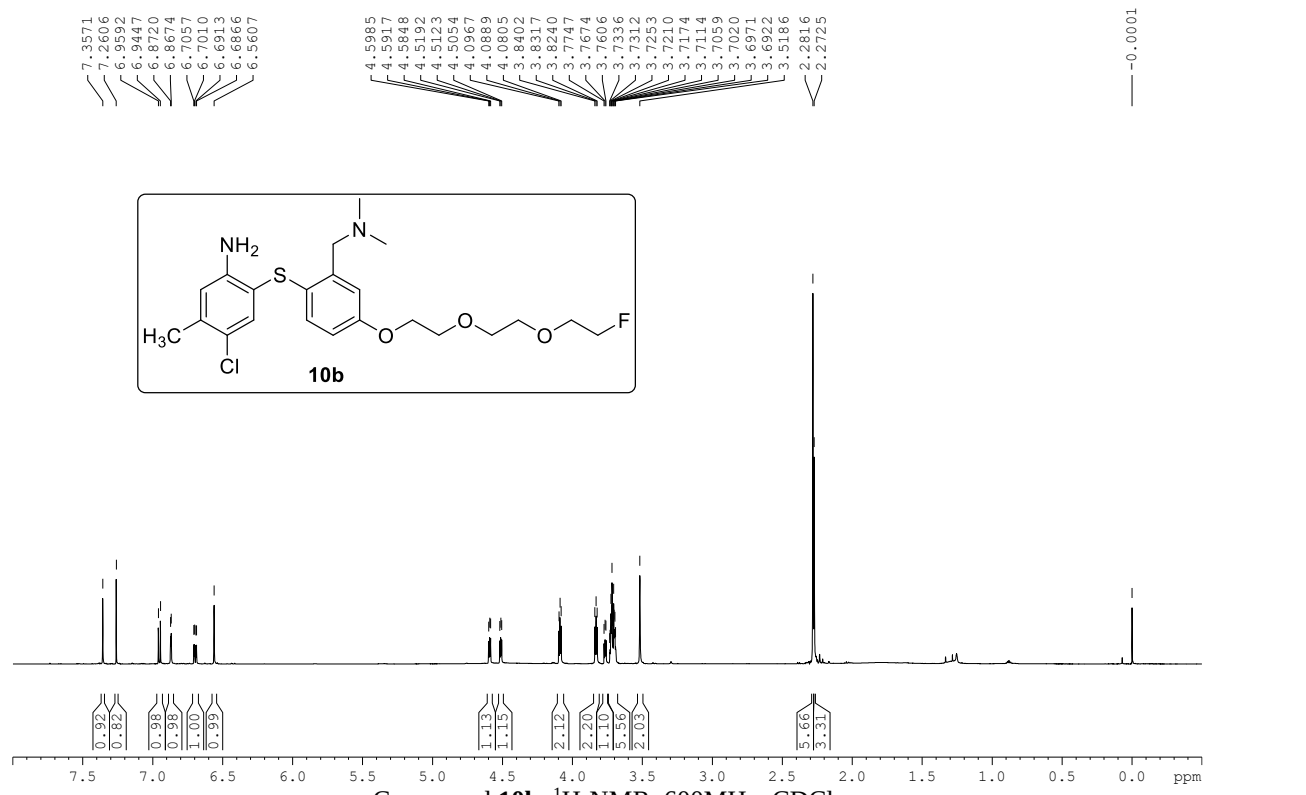
F1 - Processing parameters
SI 1024
MC2 echo-antiecho
SF 150.8876921 MHz
WDW SIN
SSB 2
LB 0 Hz
GB 0

Compound **10a**, ^{1}H-^{13}C HSQC, $CDCl_3$.

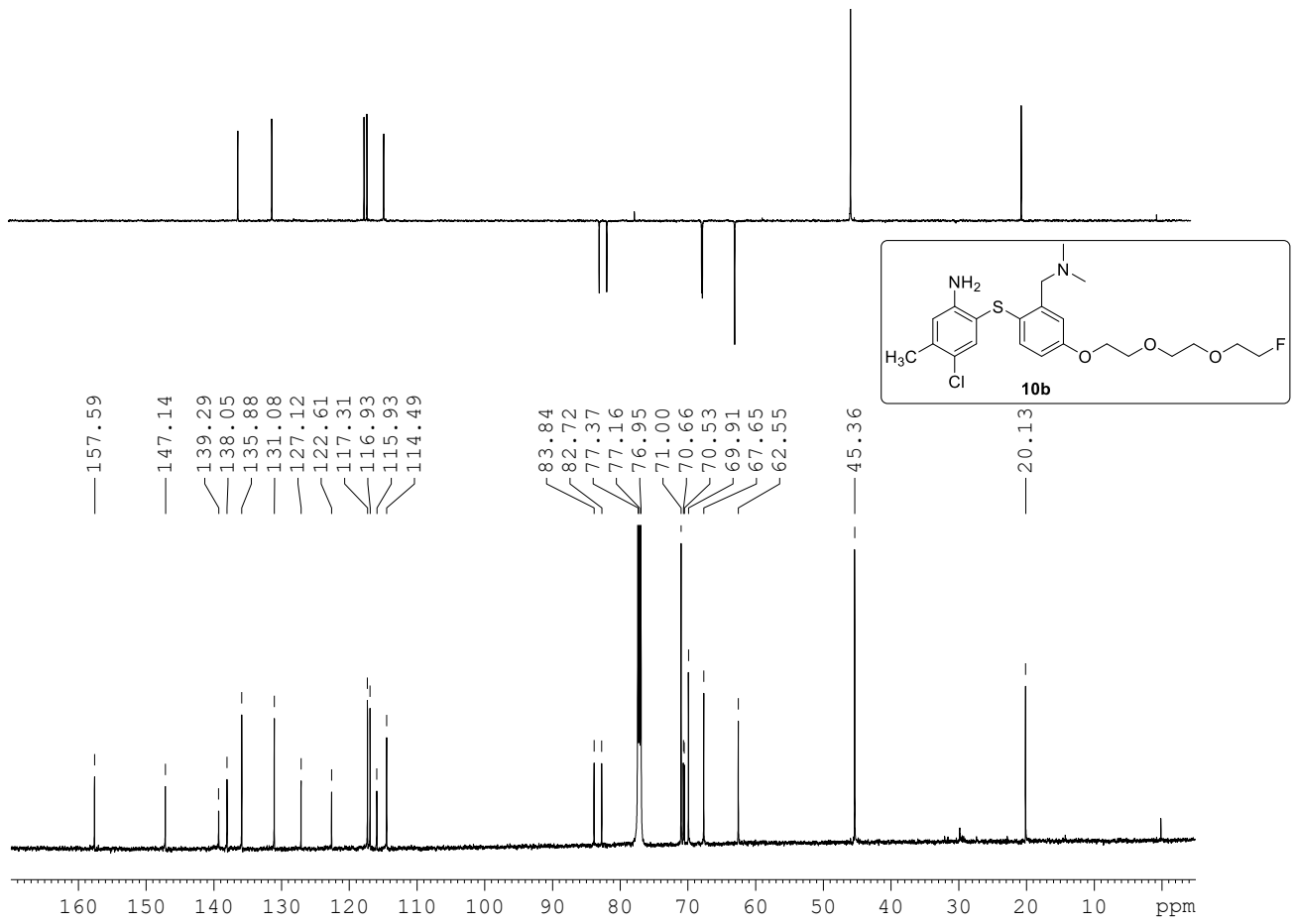



```
Current Data Parameters
NAME      lwh-xys-20130730
EXPNO                    6
PROCNO                   1

F2 - Acquisition Parameters
Date_            20130730
Time                11.53
INSTRUM             spect
PROBHD   5 mm CPDCH 13C
PULPROG    hmbcgplpndqf
TD                  2048
SOLVENT             CDCl3
NS                     2
DS                    16
SWH              8012.820 Hz
FIDRES           3.912510 Hz
AQ               0.1278452 sec
RG                  2050
DW                62.400 usec
DE                20.00 usec
TE                300.0 K
CNST2        145.0000000
CNST13         8.0000000
D0            0.00000300 sec
D1            1.50000000 sec
D2            0.00344828 sec
D6            0.06250000 sec
D16           0.00020000 sec
IN0           0.00001325 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.00 usec
P2                 20.00 usec
PL1        0 dB
PL1W         16.10119247 W
SFO1        600.0736004 MHz

======== CHANNEL f2 ========
NUC2                 13C
P3                 11.20 usec
PL2                 6.00 dB
PL2W         23.02994347 W
SFO2        150.9058280 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPNAM3           SINE.100
GPZ1                50.00 %
GPZ2                30.00 %
GPZ3                40.10 %
P16               1000.00 usec

F1 - Acquisition parameters
TD                   256
SFO1            150.9058 MHz
FIDRES        147.368973 Hz
SW                250.000 ppm
FnMODE                QF

F2 - Processing parameters
SI                   1024
SF           600.0700160 MHz
WDW                  SINE
SSB       0
LB        0 Hz
GB        0
PC                   1.40

F1 - Processing parameters
SI                   1024
MC2                    QF
SF           150.8876821 MHz
WDW                  TPPI
SSB       0
LB        0 Hz
GB        0
```

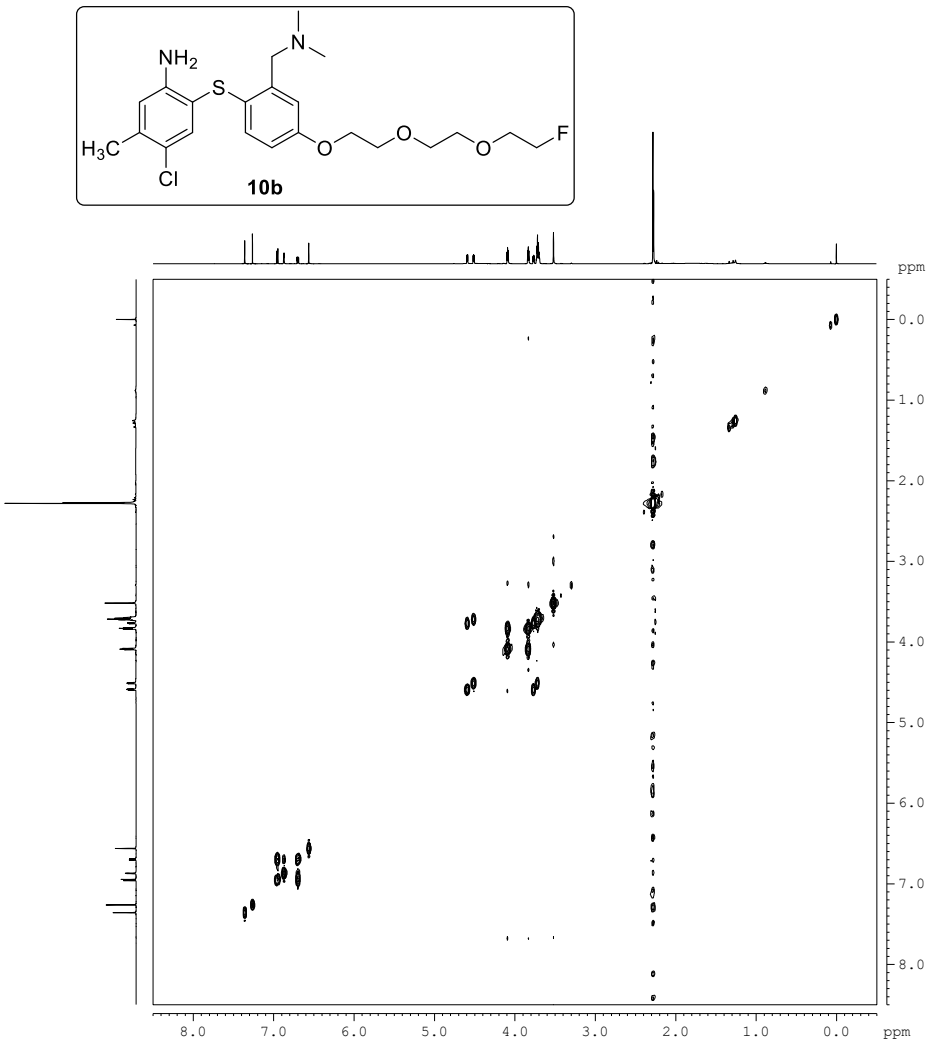
Compound **10a**, ^{1}H-^{13}C HMBC, $CDCl_3$.



Compound **10b**, ^{1}H-NMR, 600MHz, $CDCl_3$

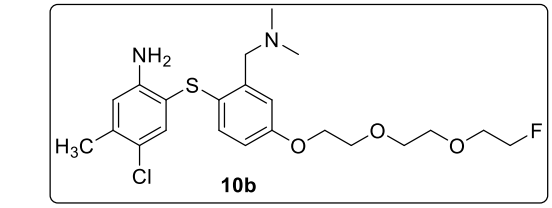


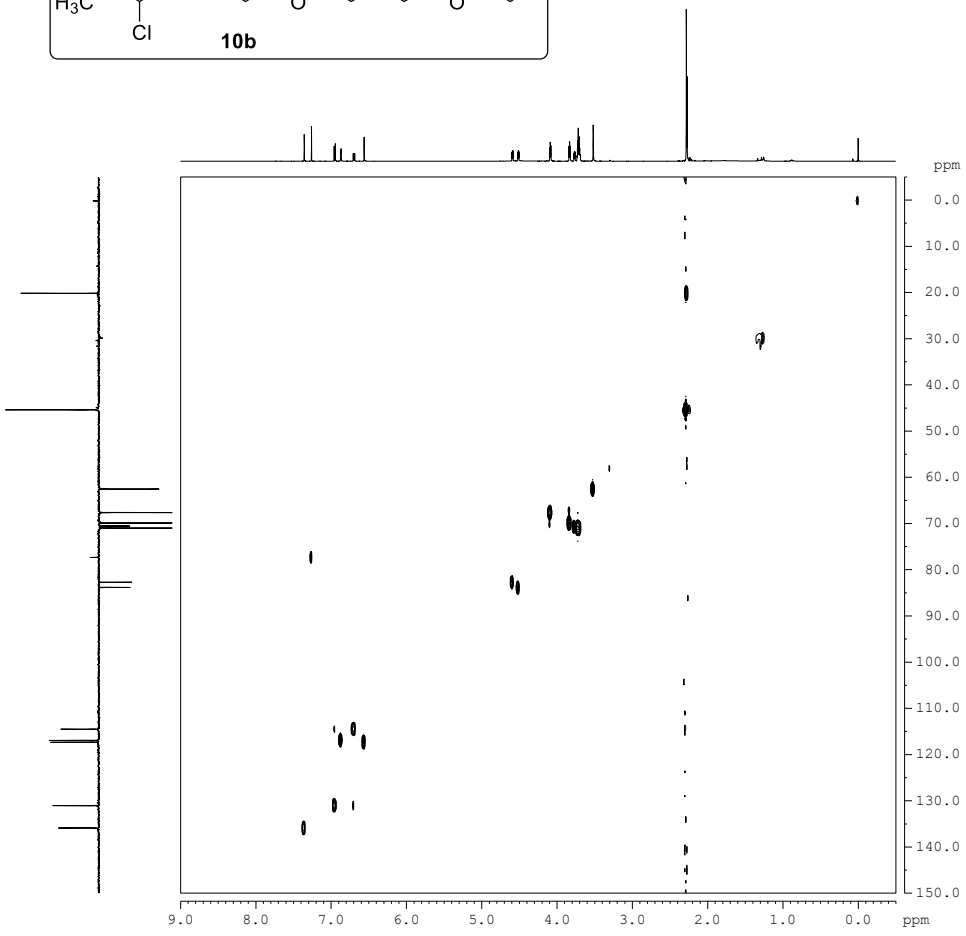
Compound **10b**, ^{13}C-NMR, Dept135, 150MHz, $CDCl_3$




```
Current Data Parameters
NAME      lwh-xys-20130730
EXPNO                   11
PROCNO                   1

F2 - Acquisition Parameters
Date_           20130730
Time               12.54
INSTRUM            spect
PROBHD   5 mm CPDCH 13C
PULPROG       cosygpqf45
TD                  2048
SOLVENT            CDCl3
NS                     1
DS                    16
SWH             8012.820 Hz
FIDRES          3.912510 Hz
AQ              0.1278452 sec
RG                    64
DW                62.400 usec
DE                20.00 usec
TE                299.9 K
D0             0.00000300 sec
D1             2.00000000 sec
D13            0.00000400 sec
D16            0.00020000 sec
IN0            0.00012485 sec

======== CHANNEL f1 ========
NUC1                  1H
P0                  5.00 usec
P1                 10.00 usec
PL1                -0.10 dB
PL1W         16.47623634 W
SFO1         600.0736004 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPZ1                10.00 %
P16               1000.00 usec

F1 - Acquisition parameters
TD                    256
SFO1             600.0736 MHz
FIDRES          31.293562 Hz
SW                 13.350 ppm
FnMODE                  QF

F2 - Processing parameters
SI                    1024
SF           600.0700158 MHz
WDW                   SINE
SSB       0
LB        0 Hz
GB        0
PC                    1.40

F1 - Processing parameters
SI                    1024
MC2                     QF
SF           600.0700159 MHz
WDW
SSB       0
LB        0 Hz
GB        0
```

Compound **10b**, ^{1}H-^{1}H COSY, $CDCl_3$.





Current Data Parameters
NAME lwh-xys-20130730
EXPNO 12
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130730
Time 13.04
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG hsqcetgpsisp2.2
TD 2048
SOLVENT CDCl3
NS 1
DS 16
SWH 8012.820 Hz
FIDRES 3.912510 Hz
AQ 0.1278452 sec
RG 1030
DW 62.400 usec
DE 20.00 usec
TE 299.8 K
CNST2 145.0000000
CNST17 -0.5000000
D0 0.00000300 sec
D1 1.50000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D16 0.00020000 sec
D24 0.00086207 sec
IN0 0.00001540 sec

======== CHANNEL f1 ========
NUC1 1H
P1 10.00 usec
P2 20.00 usec
P28 0 usec
PL1 -0.10 dB
PL1W 16.47623634 W
SFO1 600.0736004 MHz

======== CHANNEL f2 ========
CPDPRG2 garp
NUC2 13C
P3 12.00 usec
P14 500.00 usec
P24 2000.00 usec
PCPD2 55.00 usec
PL0 120.00 dB
PL2 6.00 dB
PL12 19.60 dB
PL0W 0 W
PL2W 23.02994347 W
PL12W 1.00529337 W
SFO2 150.9013014 MHz
SP3 13.41 dB
SP7 13.41 dB
SPNAM3 Crp60,0.5,20.1
SPNAM7 Crp60comp.4
SPOAL3 0.500
SPOAL7 0.500
SPOFFS3 0 Hz
SPOFFS7 0 Hz

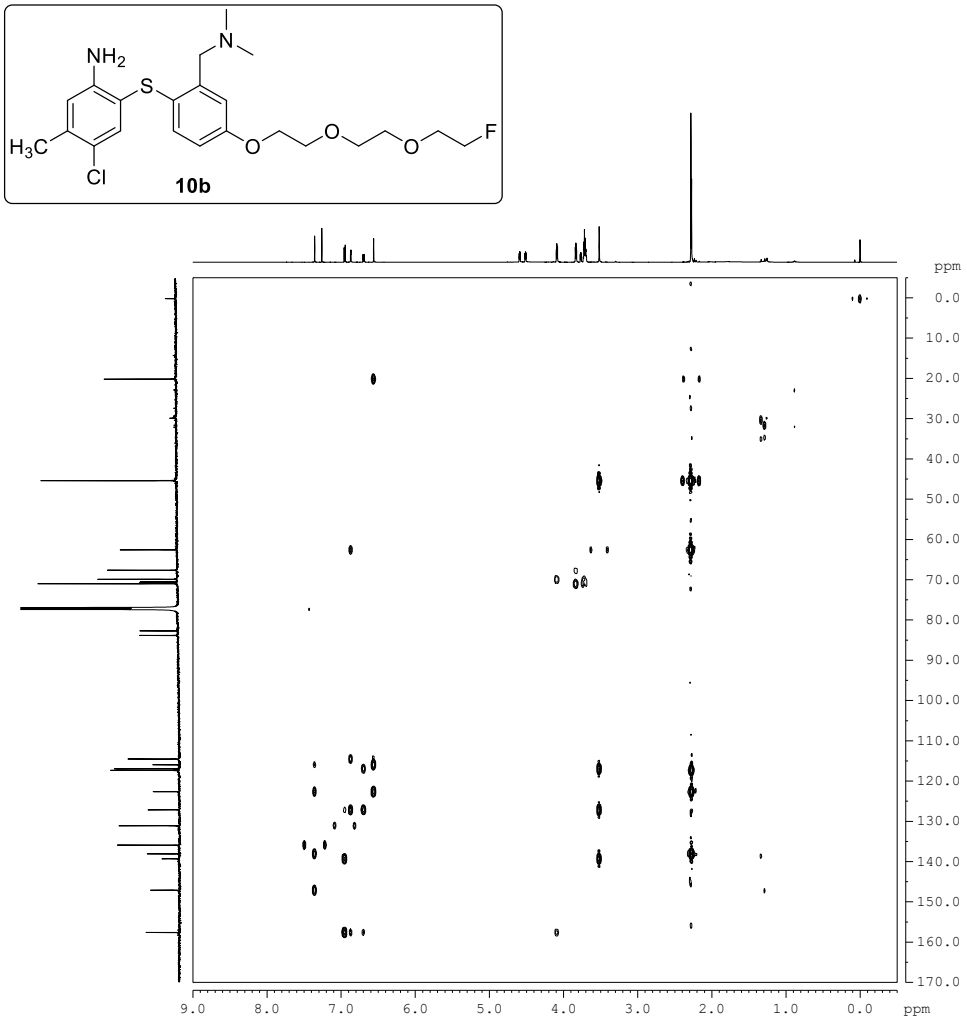
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPNAM3 SINE.100
GPNAM4 SINE.100
GPZ1 80.00 %
GPZ2 20.10 %
GPZ3 11.00 %
GPZ4 -5.00 %
P16 1000.00 usec
P19 600.00 usec

F1 - Acquisition parameters
TD 256
SFO1 150.9013 MHz
FIDRES 126.733513 Hz
SW 215.000 ppm
FnMODE Echo-Antiecho

F2 - Processing parameters
SI 1024
SF 600.0700122 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40

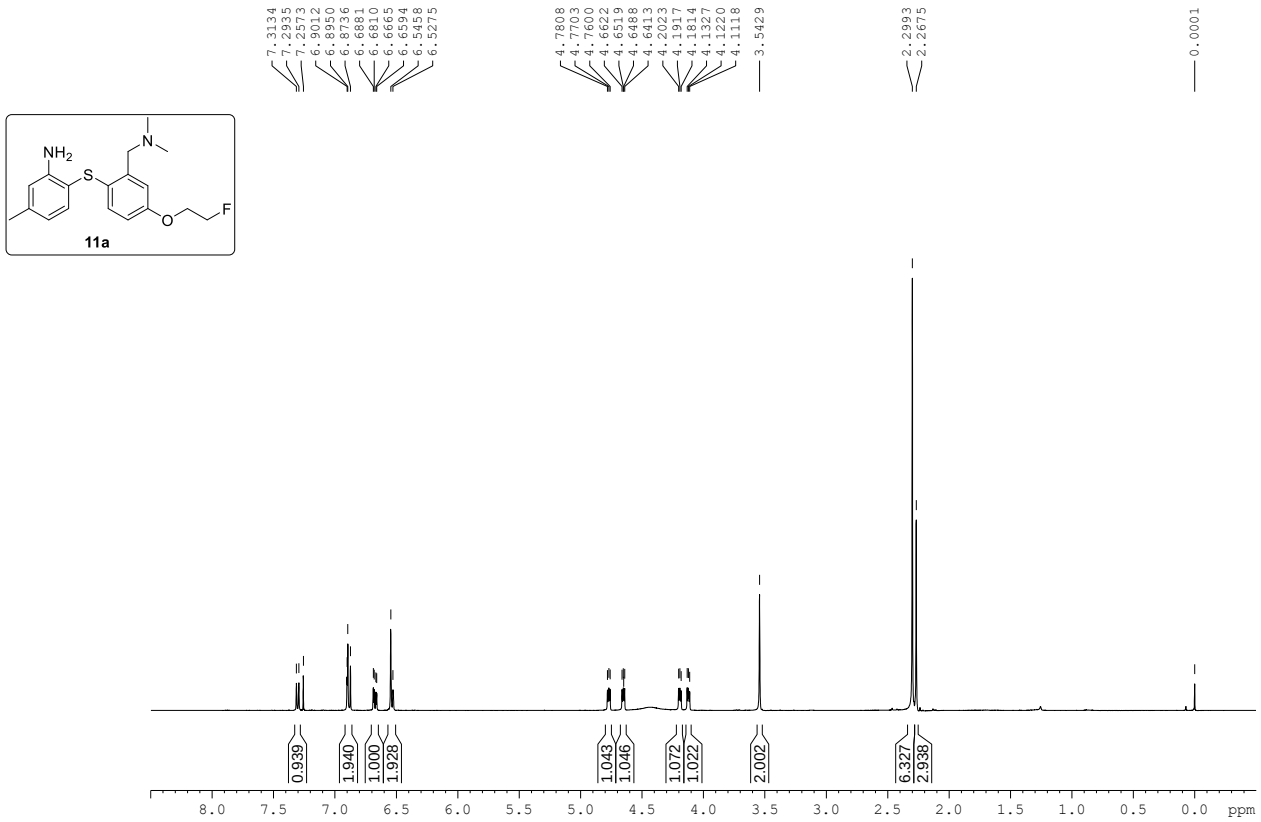
F1 - Processing parameters
SI 1024
MC2 echo-antiecho
SF 150.8876897 MHz
WDW SIN
SSB 2
LB 0 Hz
GB 0

Compound **10b**, ^{1}H-^{13}C HSQC, $CDCl_3$.

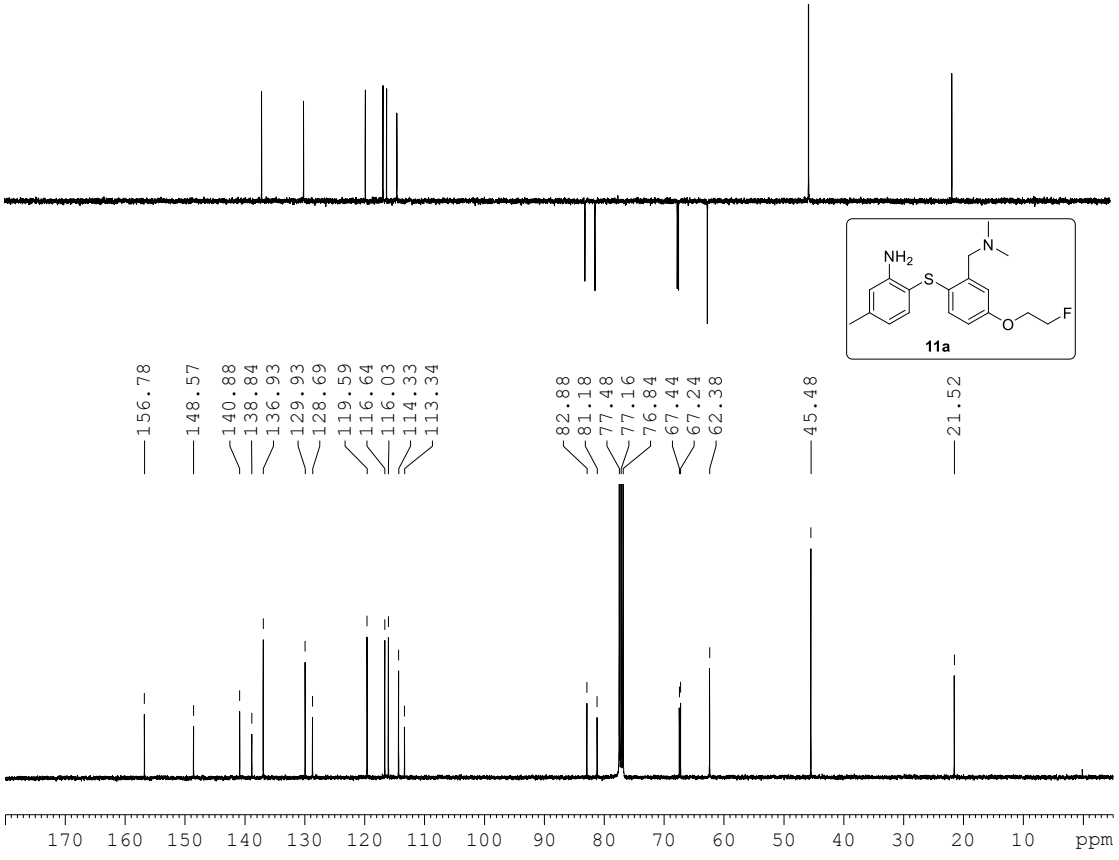



```
Current Data Parameters
NAME      lwh-xys-20130730
EXPNO                   13
PROCNO                   1

F2 - Acquisition Parameters
Date_           20130730
Time_               13.12
INSTRUM             spect
PROBHD   5 mm CPDCH 13C
PULPROG    hmbcgplpndqf
TD                  2048
SOLVENT             CDCl3
NS                     2
DS                    16
SWH              8012.820 Hz
FIDRES           3.912510 Hz
AQ              0.1278452 sec
RG                   2050
DW                 62.400 usec
DE                 20.00 usec
TE                 300.1 K
CNST2        145.0000000
CNST13         8.0000000
D0            0.00000300 sec
D1            1.50000000 sec
D2            0.00344828 sec
D6            0.06250000 sec
D16           0.00020000 sec
IN0           0.00001325 sec

======== CHANNEL f1 ========
NUC1                 1H
P1                10.00 usec
P2                20.00 usec
PL1                -0.10 dB
PL1W         16.47623634 W
SFO1         600.0736004 MHz

======== CHANNEL f2 ========
NUC2                13C
P3                12.00 usec
PL2                6.00 dB
PL2W         23.02994347 W
SFO2         150.9058280 MHz

======= GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPNAM3          SINE.100
GPZ1               50.00 %
GPZ2               30.00 %
GPZ3               40.10 %
P16              1000.00 usec

F1 - Acquisition parameters
TD                   256
SFO1          150.9058 MHz
FIDRES        147.368973 Hz
SW               250.000 ppm
FnMODE              QF

F2 - Processing parameters
SI                  1024
SF           600.0700155 MHz
WDW                 SINE
SSB       0
LB        0 Hz
GB        0
PC                  1.40

F1 - Processing parameters
SI                  1024
MC2                 QF
SF           150.8876867 MHz
WDW         States-TPPI
SSB       0
LB        0 Hz
GB        0
```

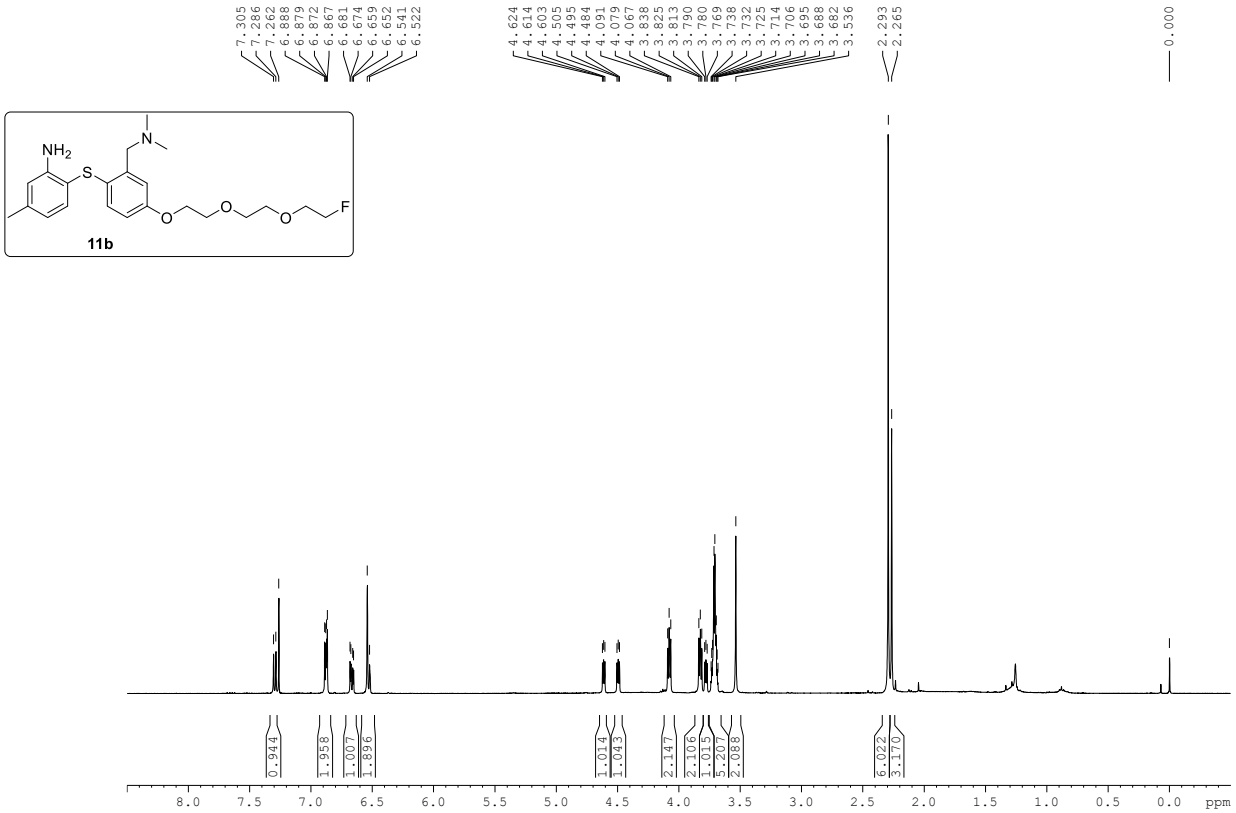
Compound **10b**, ^{1}H-^{13}C HMBC, $CDCl_3$.



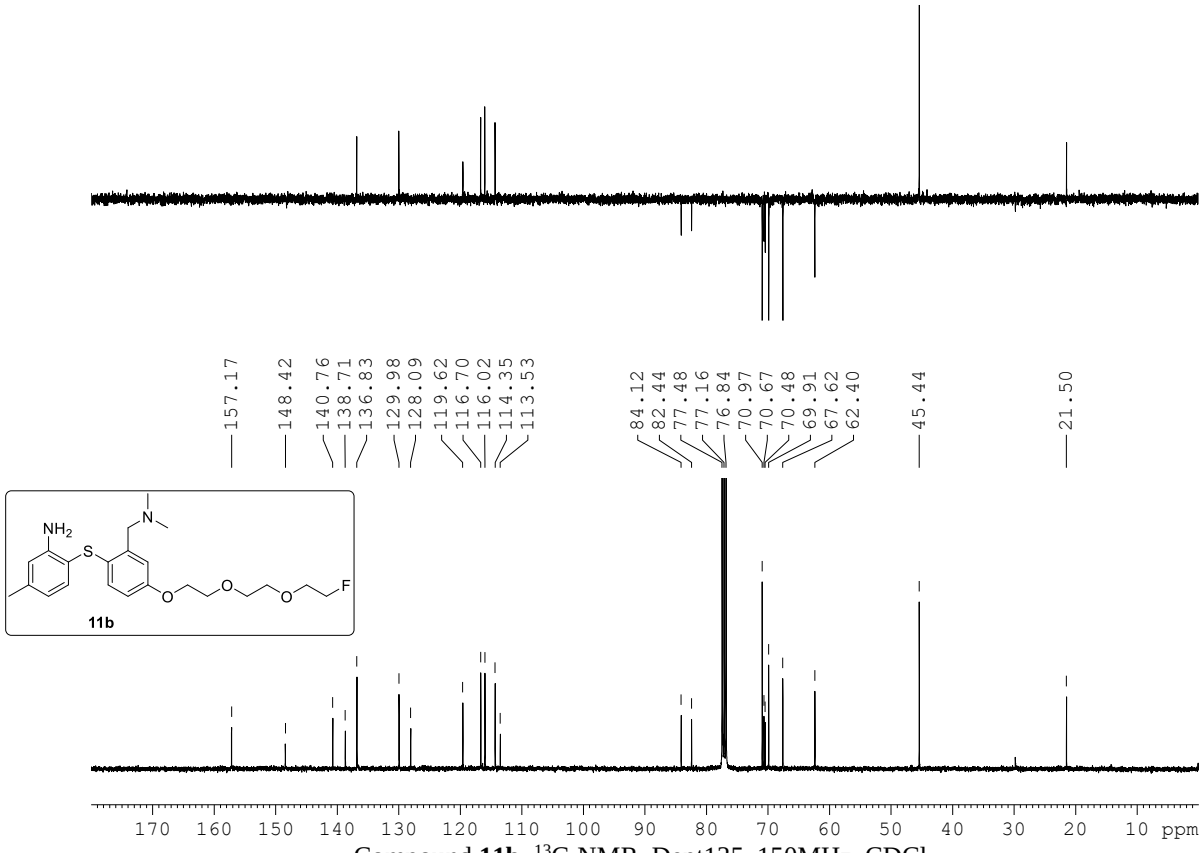
Compound **11a**, ^{1}H-NMR, 200MHz, $CDCl_3$



Compound **11a**, ^{13}C-NMR, Dept135, 50MHz, $CDCl_3$



Compound **11b**, ^{1}H-NMR, 400MHz, $CDCl_3$



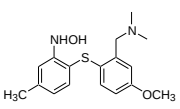
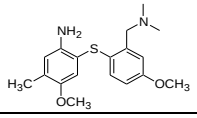
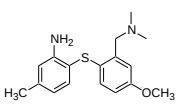
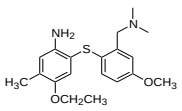
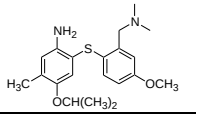
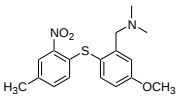
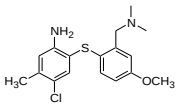
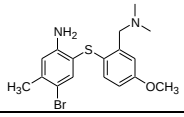
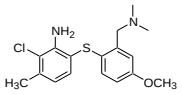
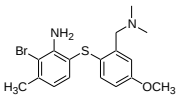
Compound **11b**, ^{13}C-NMR, Dept135, 150MHz, $CDCl_3$

Instrumentation

GC studies were conducted using a Shimadzu® 2014 gas chromatograph. The GC was operated in split less mode with a carrier gas (N_2 gas) flow rate of 1.0 ml/min. The GC injector was maintained at 250°C. The FID detector was maintained at 300°C. The column temperature program consisted of an initial temperature of 100°C for 3 min, ramped up to 300°C at a rate of 20°C/min, and hold at 300°C for 10 min. The total GC run time was 23 min. The crude samples were extracted into ethyl acetate with 10% sodium hydroxide aqueous solution and the samples in ethyl acetate were introduced via the injector. The chromatographic separations of the chlorination test samples were carried out on a 30 m × 0.25 mm i.d. column coated with 0.25 µm 5% phenyl-95% dimethylpolysiloxane (DB-5) using the above-mentioned time program.

LC-MS studies were performed on an Agilent 1100 system consisting of an Agilent G1313A autosampler, an Agilent G1311A quaternary pump, and an Agilent DAD G1315B and an Esquire 2000 mass spectrometer. The mass spectrometer was operated on electron spray ionization (ESI) mode. Sampled 100µL of reaction mixture, evaporated to dryness and partitioned with 10%NaOH and EA. The EA layer was separated, filtered with $MgSO_4$ and dried. The crude sample was then dissolved with HPLC grade ACN. The sample solution (10µL) was eluted using 80%ACN in 10 mM ammonium formate (pH = 7.0 with ammonium hydroxide) as the mobile phase with the flow rate of 1.0 mL/min on the Gemini C18 column (250 × 4.6 mm, 5ml, Phenomenex). The LC-MS system was controlled by HyStar software and the area% value of chemical constitutes P$[M+1]^+$, *p*-Cl-BP$[M+Cl]^+$, and *p*-EtO-BP $[M+OEt]^+$ were calculated based on the UV absorption areas according to MS signals at the wave length of 254 nm in all reaction.

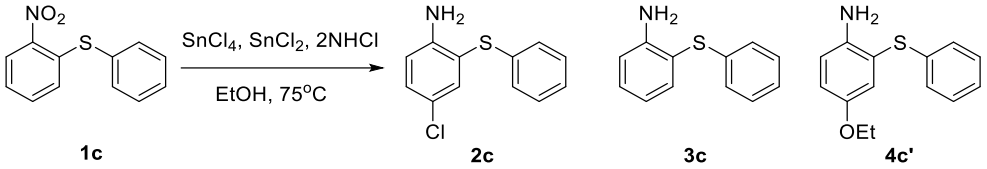
Table 6 Retention time and low-resolution mass results of products in reductive halogenation[a]

Products	**NHOHP**	***p*-MeOP**	**P**	***p*-EtOP**	***p*-*i*-PrOP**
Structure					
Rt (min)	3.2	3.9	4.4	4.6	5.0
Mass, *m/z*	319/274	333/288	303/258	347/302	361
Products	**SM**	***p*-ClP**	***p*-BrP**	***o*-ClP**	***o*-BrP**
Structure					
Rt (min)	5.4	5.8	6.2	7.0	7.7
Mass, *m/z*	333	337/292	381/336	337/292	381/336

[a]NHOHP, *o*-ClP were neglected due to <5 (area %) under 254 nm in LC, *p*-*i*-PrOP related experiment was not shown in the paper.

LC and GC Report of compound 1c under reductive-halogenation condition.

1c Scheme



1c 2c 3c 4c'

Name	2c	3c	4c’
Extract mass	235.0222	201.0612	245.0874
LC-RT	5.83 min	4.87 min	5.02 min
GC-RT	11.7 min	10.5 min	12.0 min

Chromatogram

Report for "H-S-Ph_32_01_5673"
Printed: 15:25:47 08/19/14 Computer:1AP05 User:default

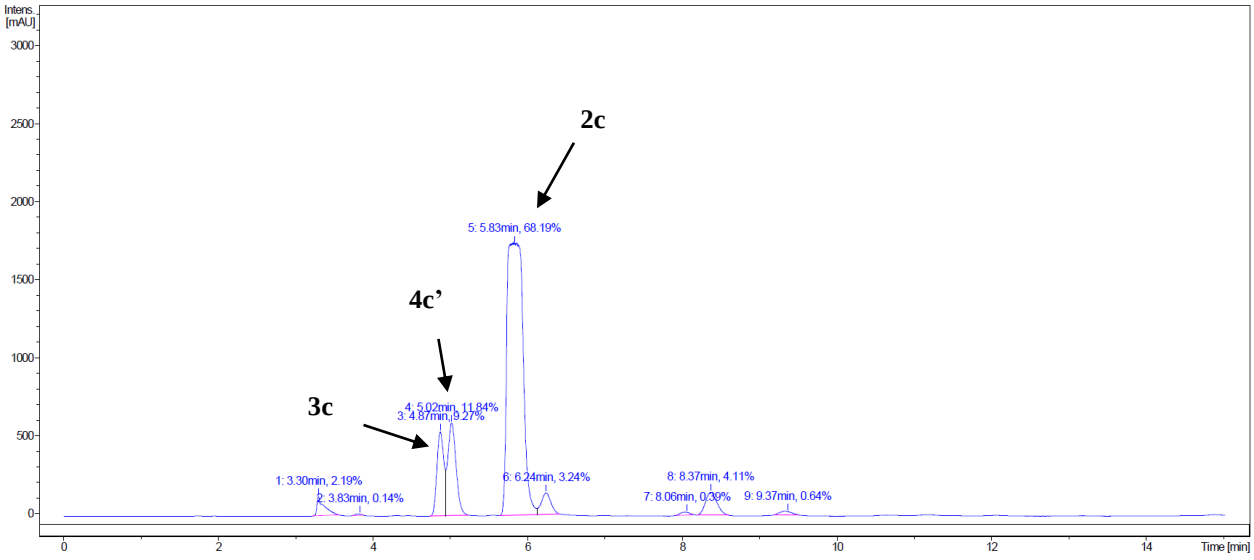
Report for "H-S-Ph_32_01_5673"

Chromatogram File:
D:\CHEM32\1\DATA\H-S-Ph_32_01_5673.d\H-S-Ph_32_01_5673.unt

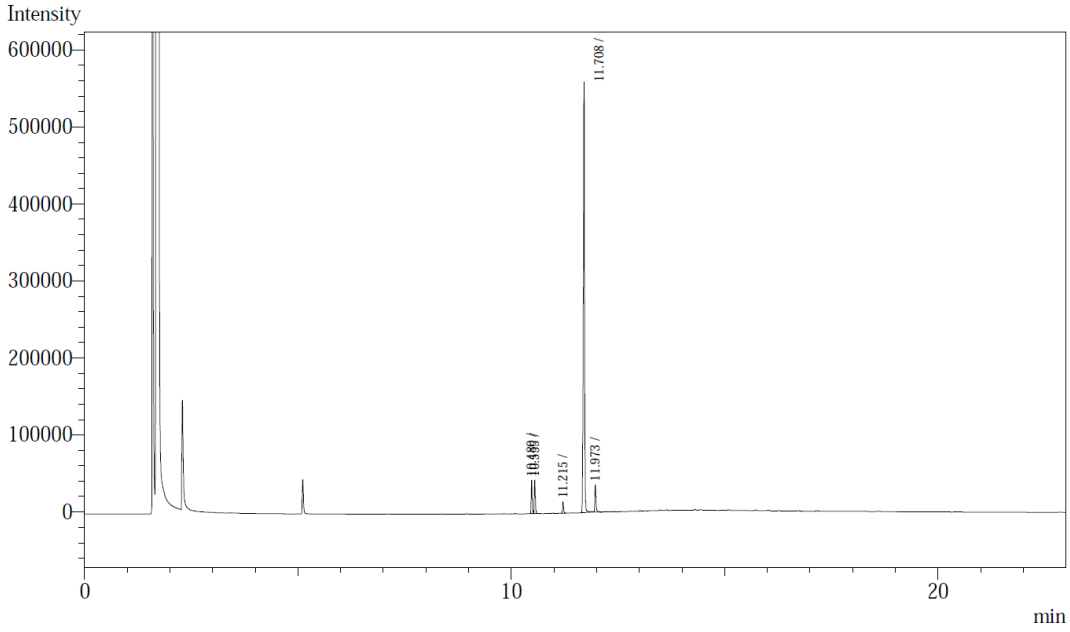
Created on: 8/19/2014 at: 03:14:51 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 15.02 min

Signal 1: DAD (254)



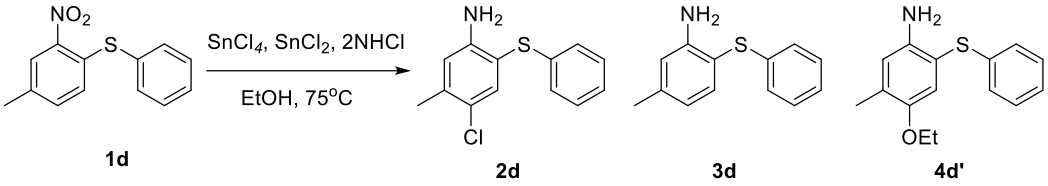
Analysis Date & Time : 2014/8/12 上午 11:57:58
User Name : Lab 1336
Vial# : 1
Sample Name : H-S-Ph
Sample ID : H-S-Ph
Injection Volume : 1 uL
Data Name : D:\1336\HYH\HYH-20140812\H-S-Ph.gcd
Method Name : D:\1336\HYH\HYH-20140401 test-1.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%	
1	10.480	71009	43612	5.3260	3c
2	10.555	72273	42932	5.4207	
3	11.215	24804	15080	1.8604	
4	11.708	1101351	557296	82.6055	2c
5	11.973	63829	35194	4.7874	4c’
Total		1333266	694114	100.0000	

LC Report of compound 1d under reduction-halogenation condition.

1d Scheme



1d 2d 3d 4d'

Name	2d	3d	4d’
Extract mass	249.0379	215.0769	259.1031
LC-RT	7.04 min	5.66 min	6.34 min
GC-RT	ND	ND	ND

Chromatogram

Report for "Me re 5eq_25_01_5316"
Printed: 13:37:42 12/01/14 Computer:1AP05 User:default

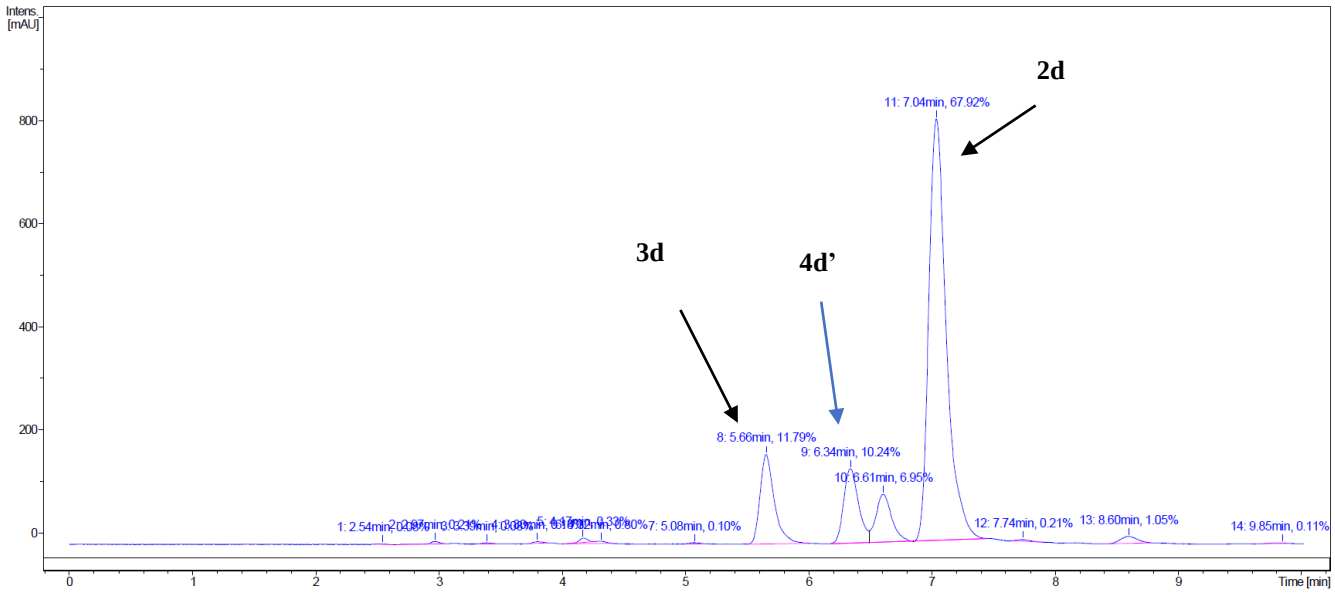
Report for "Me re 5eq_25_01_5316"

Chromatogram File:
D:\CHEM32\1\DATA\Me re 5eq_25_01_5316.d\Me re 5eq_25_01_5316.unt

Created on: 5/20/2014 at: 02:54:20 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

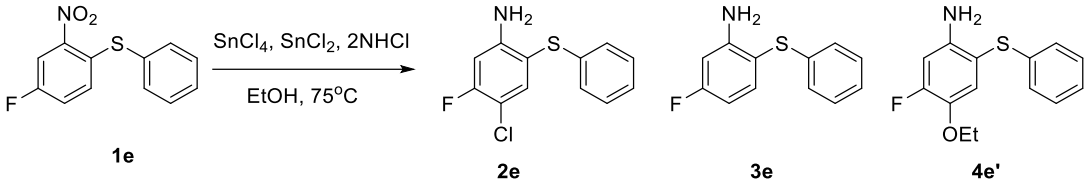
Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



LC Report of compound 1e under reduction-halogenation condition.

1e Scheme



1e 2e 3e 4e'

Name	2e	3e	4e’
Extract mass	253.0128	219.0518	263.0780
LC-RT	6.61 min	5.37 min	5.55 min
GC-RT	ND	ND	ND

Chromatogram

Report for "F reduction_12_01_5365"
Printed: 13:48:09 12/01/14 Computer:1AP05 User:default

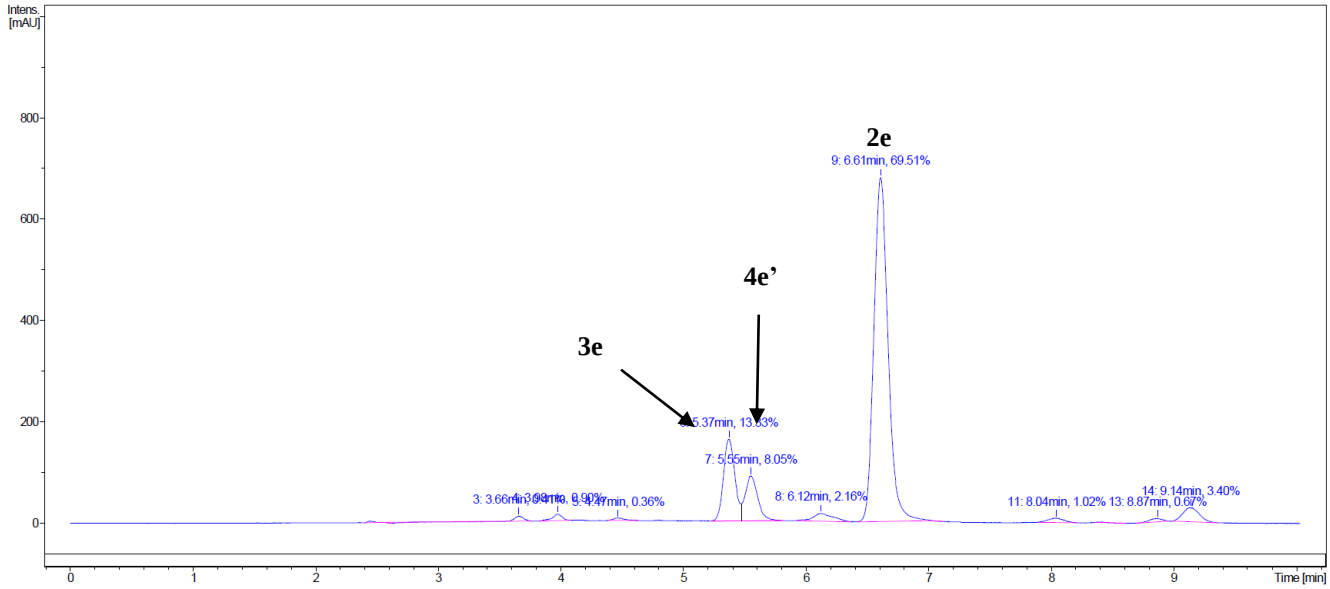
Report for "F reduction_12_01_5365"

Chromatogram File:
D:\CHEM32\1\DATA\lab1336\hyh\HYH-20140523 LC-MS\F reduction_12_01_5365.d\F reduction_12_01_5365.unt

Created on: 5/23/2014 at: 06:55:17 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

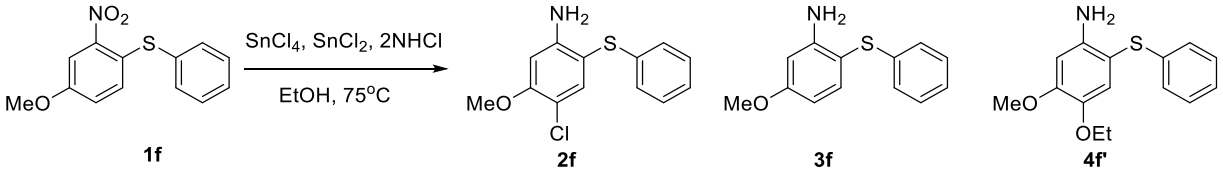
Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



LC and GC Report of compound 1f under reduction-halogenation condition.

1f Scheme



1f 2f 3f 4f'

Name	2f	3f	4f’
Extract mass	265.0328	231.0718	275.0980
LC-RT	5.32 min	3.54 min	4.61 min
GC-RT	14.45 min	13.12 min	14.22 min

Chromatogram

Report for "OMe_22_01_5529"
Printed: 14:41:23 07/17/14 Computer:1AP05 User:default

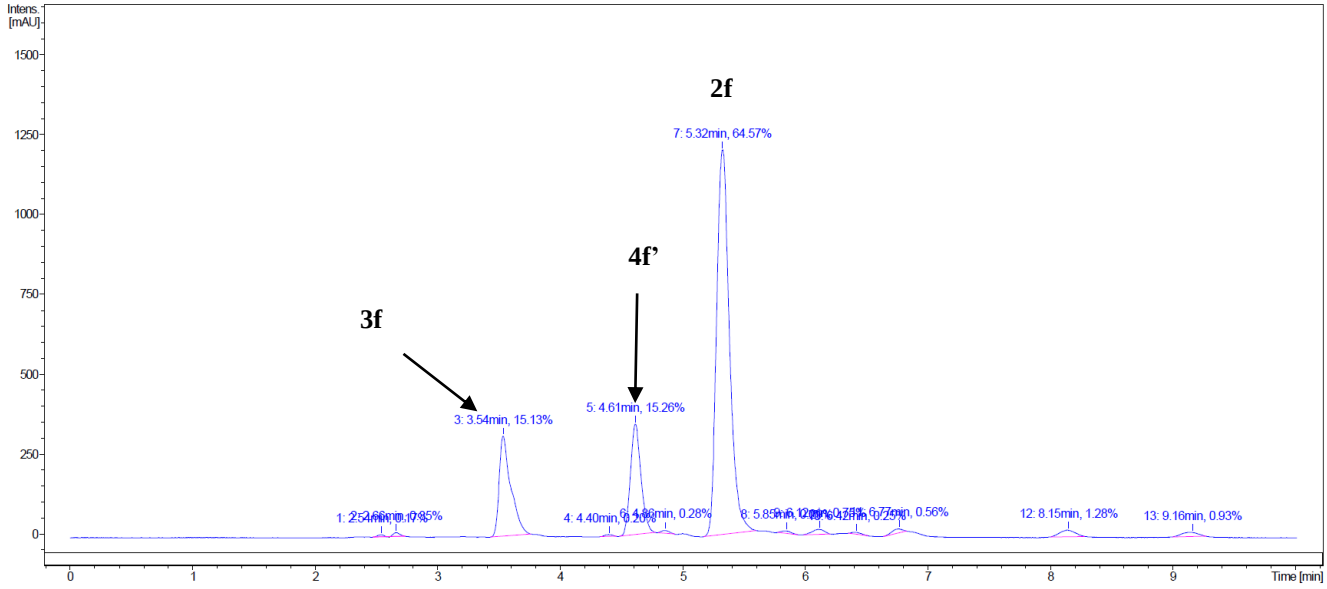
Report for "OMe_22_01_5529"

Chromatogram File:
D:\CHEM32\1\DATA\lab1336\hyh\HYH 20140717 LC-MS\OMe_22_01_5529.d\OMe_22_01_5529.unt

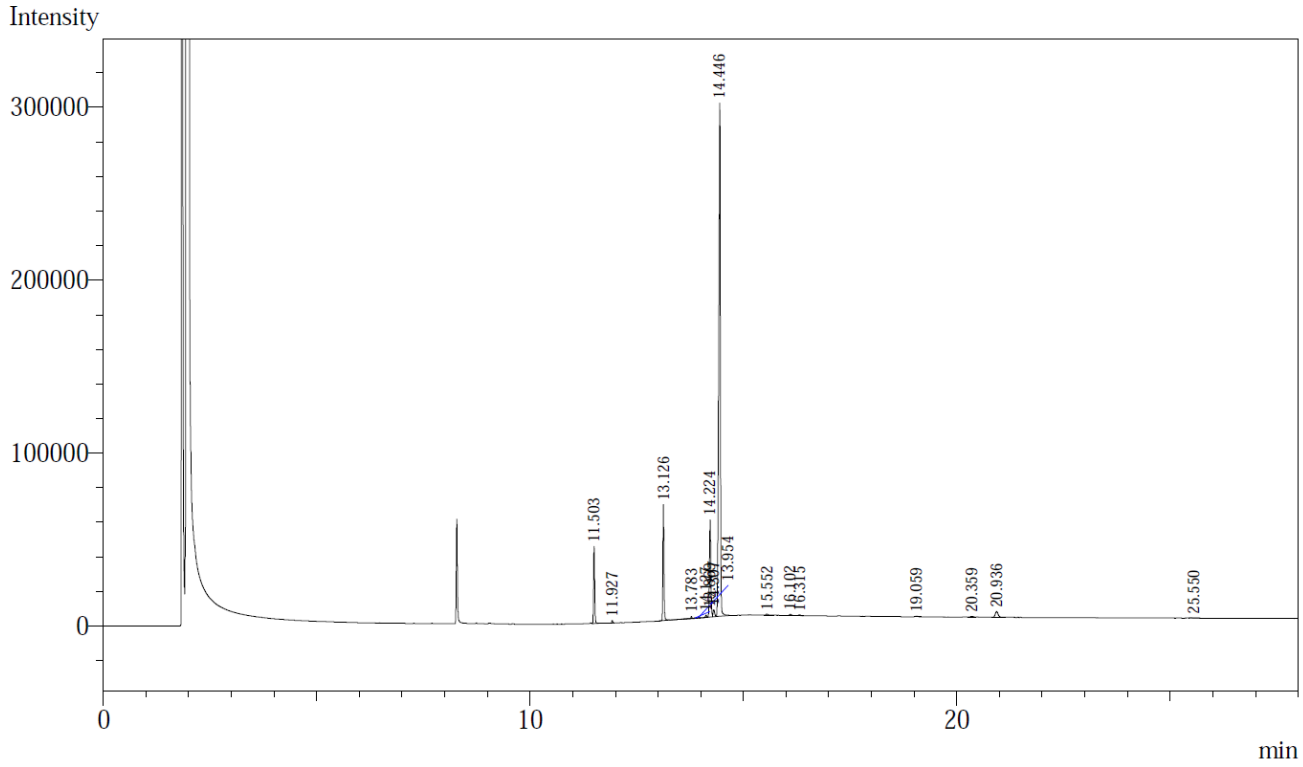
Created on: 7/17/2014 at: 02:16:51 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



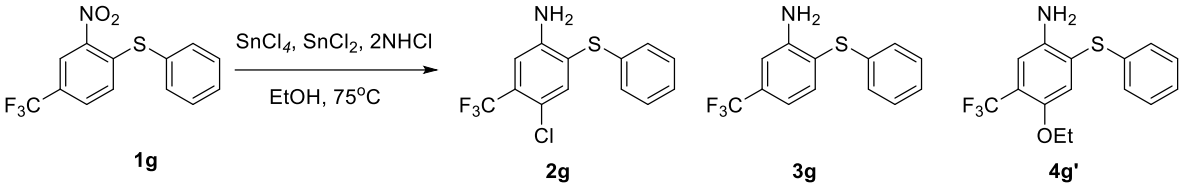
Analysis Date & Time : 2014/7/24 下午 02:01:35
User Name : Lab 1336
Vial# : 1
Sample Name : OMe red
Sample ID : OMe red
Injection Volume : 1 uL
Data Name : D:\1336\HYH\20140724\OMe red.gcd
Method Name : D:\1336\HYH\HYH-20140401.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%	
1	11.503	76765	43901	6.6628	
2	11.927	2675	1534	0.2322	
3	13.126	117539	66705	10.2018	**3f**
4	13.783	2798	1146	0.2429	
5	13.869	1168	352	0.1014	
6	13.954	1174	523	0.1019	
7	14.127	2663	1284	0.2311	
8	14.224	126900	55886	11.0142	**4f'**
9	14.307	10480	4104	0.9096	
10	14.446	784557	295259	68.0954	**2f**
11	15.552	1952	669	0.1694	
12	16.102	1971	651	0.1711	
13	16.315	1394	518	0.1210	
14	19.059	1404	346	0.1219	
15	20.359	2266	430	0.1967	
16	20.936	15403	3389	1.3369	
17	25.550	1034	124	0.0898	
Total		1152143	476821	100.0000	

LC and GC Report of compound 1g under reduction-halogenation condition.

1g Scheme



1g **2g** **3g** **4g'**

Name	**2g**	**3g**	**4g'**
Extract mass	303.0096	269.0486	313.0748
LC-RT	6.94 min	5.82 min	5.56 min
GC-RT	12.8 min	11.5 min	12.3 min

Chromatogram

Report for "CF3_23_01_5530"
Printed: 17:12:36 07/17/14 Computer:1AP05 User:default

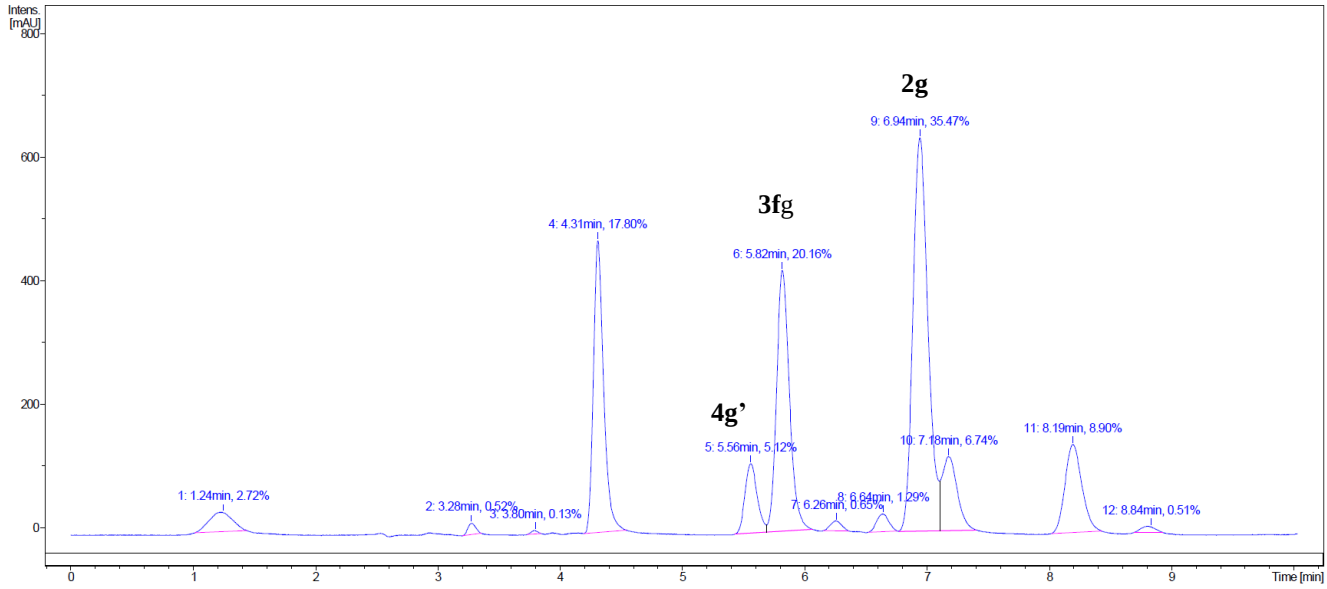
Report for "CF3_23_01_5530"

Chromatogram File:
D:\CHEM32\1\DATA\lab1336\hyh\HYH 20140717 LC-MS\CF3_23_01_5530.d\CF3_23_01_5530.unt

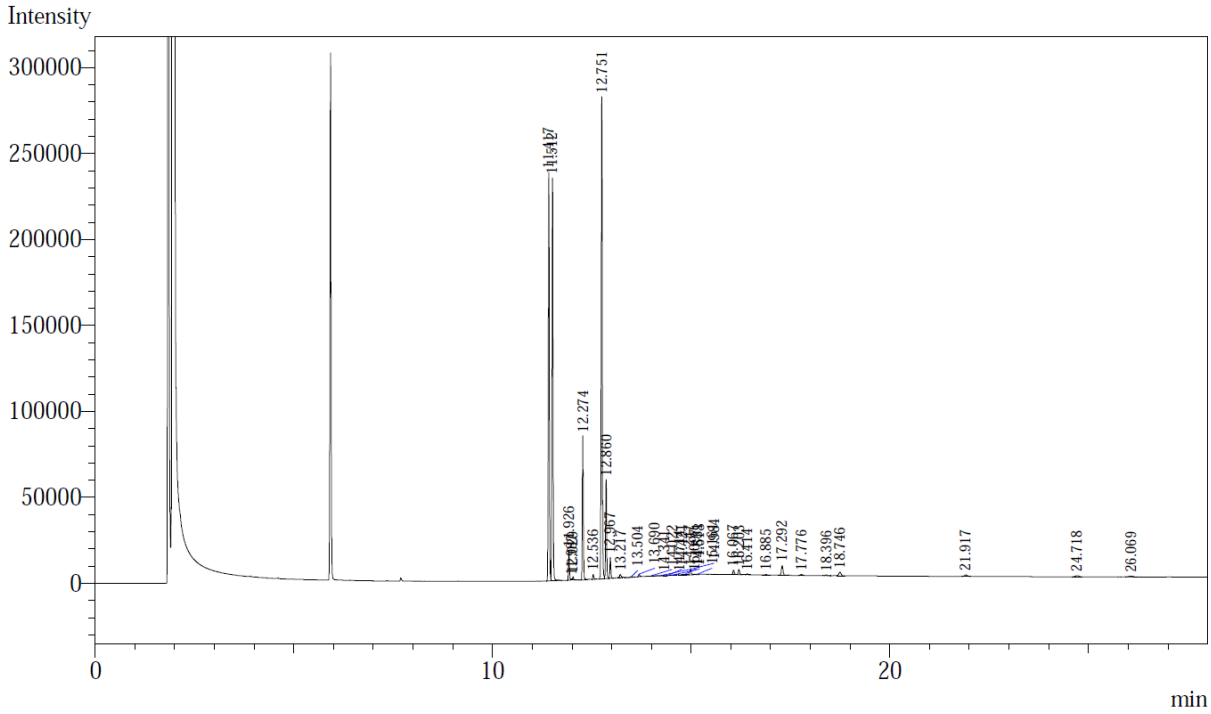
Created on: 7/17/2014 at: 02:28:26 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



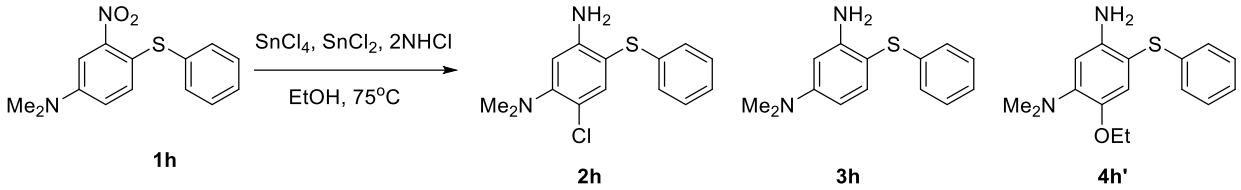
Analysis Date & Time : 2014/7/24 下午 03:17:03
User Name : Lab 1336
Vial# : 1
Sample Name : CF3 red
Sample ID : CF3 red
Injection Volume : 1 uL
Data Name : D:\1336\HYH\20140724\CF3 red.gcd
Method Name : D:\1336\HYH\HYH-20140401.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%	
1	11.417	412300	234967	23.4100	
2	11.512	426186	230945	24.1985	**3**g
3	11.926	28440	17004	1.6148	
4	11.987	1437	811	0.0816	
5	12.029	3580	1972	0.2032	
6	12.274	144288	81902	8.1926	**4g'**
7	12.536	5363	2798	0.3045	
8	12.751	529052	276154	30.0391	**2g**
9	12.860	98826	57066	5.6113	
10	12.967	21577	12137	1.2251	
11	13.217	5938	2005	0.3371	
12	13.504	1496	487	0.0850	
13	13.690	2976	1474	0.1690	
14	14.022	1361	361	0.0773	
15	14.247	2812	238	0.1596	
16	14.341	1286	290	0.0730	
17	14.421	1059	293	0.0601	
18	14.518	2998	290	0.1702	
19	14.714	2212	331	0.1256	
20	14.831	1295	300	0.0735	
21	14.984	9629	3289	0.5468	
22	15.097	1052	268	0.0598	
23	15.161	1003	292	0.0569	
24	16.067	6036	2458	0.3427	
25	16.203	7738	3054	0.4393	
26	16.414	1503	578	0.0853	
27	16.885	1035	335	0.0587	
28	17.292	15998	5513	0.9083	
29	17.776	1658	562	0.0942	
30	18.396	1414	412	0.0803	
31	18.746	7445	2117	0.4227	

LC Report of compound 1h under reduction-halogenation condition.

1h Scheme



1h 2h 3h 4h'

Name	2h	3h	4h’
Extract mass	278.0644	244.1034	288.1296
LC-RT	5.64 min	6.66 min	5.95 min
GC-RT	ND	ND	ND

Chromatogram

Report for "Me2N reduction_11_01_5364"
Printed: 13:45:56 12/01/14 Computer:1AP05 User:default

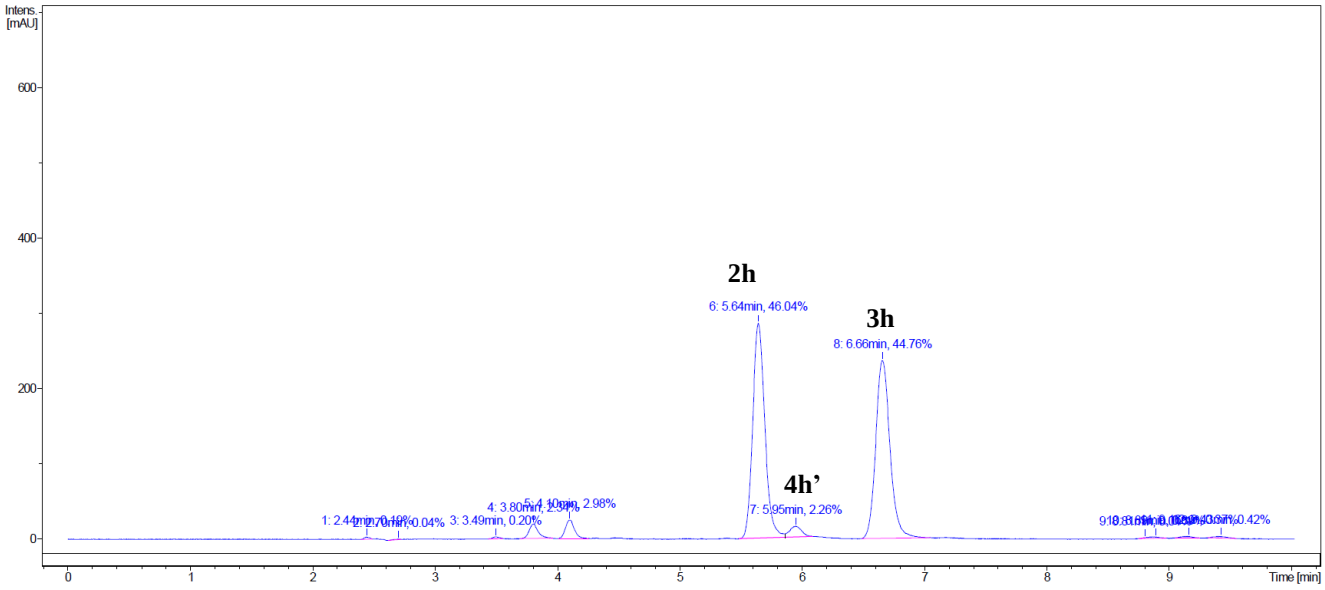
Report for "Me2N reduction_11_01_5364"

Chromatogram File:
D:\CHEM32\1\DATA\lab1336\hyh\HYH-20140523 LC-MS\Me2N reduction_11_01_5364.d\Me2N reduction_11_01_5364.unt

Created on: 5/23/2014 at: 06:42:40 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

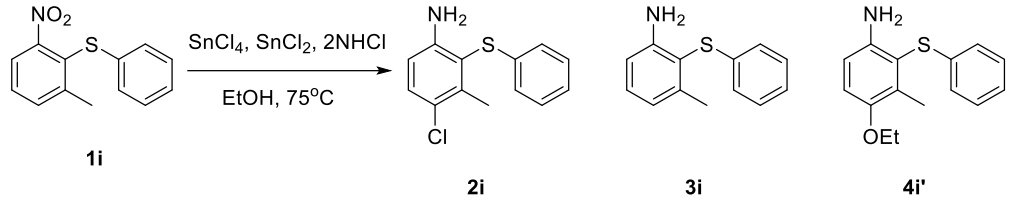
Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



GC Report of compound 1i under reduction-halogenation condition.

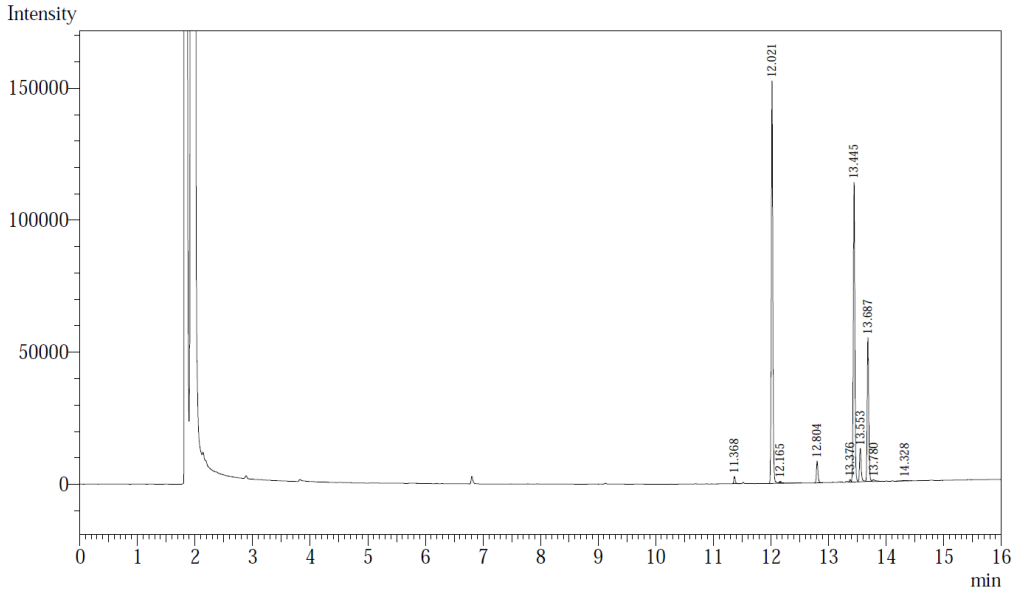
1i Scheme



1i 2i 3i 4i'

Name	2i	3i	4i’
Extract mass	249.0379	215.0769	259.1031
LC-RT	ND	ND	ND
GC-RT	13.69 min	12.02 min	13.45 min

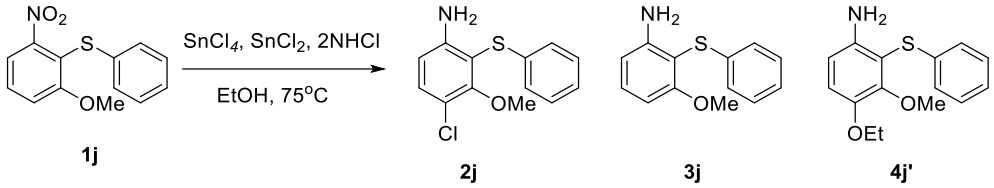
Analysis Date & Time : 2014/9/9 下午 06:29:42
User Name : Lab 1336
Vial# : 1
Sample Name : 3-Me 2-S 1NO2 coupling reaction
Sample ID : 3-Me 2-S 1NO2 coupling reaction
Injection Volume : 1 uL
Data Name : D:\1336\HYH\20140909\3-Me 2-S 1NO2 coupling reaction.gcd
Method Name : D:\1336\HYH\HYH-20140818 for chlorination.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%	
1	11.368	4886	2759	0.7629	
2	12.021	274339	150521	42.8350	**3i**
3	12.165	1019	597	0.1592	
4	12.804	15299	8180	2.3888	
5	13.376	1675	978	0.2615	
6	13.445	212539	111537	33.1856	**4i’**
7	13.553	25525	12419	3.9854	
8	13.687	100831	54053	15.7436	**2i**
9	13.780	2340	636	0.3653	
10	14.328	2002	232	0.3126	
Total		640455	341912	100.0000	

GC Report of compound 1j under reduction-halogenation condition.

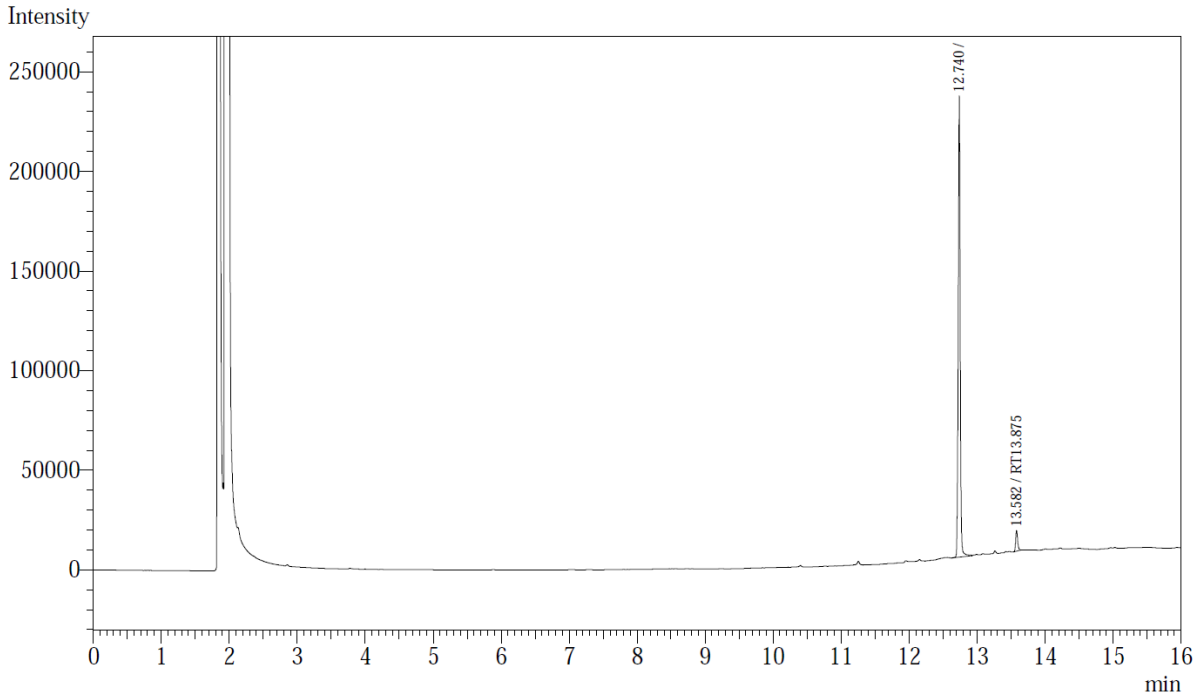
1j Scheme



1j 2j 3j 4j'

Name	2j	3j	4j’
Extract mass	265.0328	231.0718	275.0980
LC-RT	ND	ND	ND
GC-RT	ND	12.74 min	ND

Analysis Date & Time : 2014/9/30 上午 10:59:59
User Name : Lab 1336
Vial# : 1
Sample Name : HYH-2-S-3MeO cl
Sample ID : HYH-2-S-3MeO cl
Injection Volume : 1 uL
Data Name : D:\1336\HYH\HYH 20140928\HYH-2-S-3MeO cl.gcd
Method Name : D:\1336\HYH\HYH-20140928 for chlorination.gcm
$EndIf$

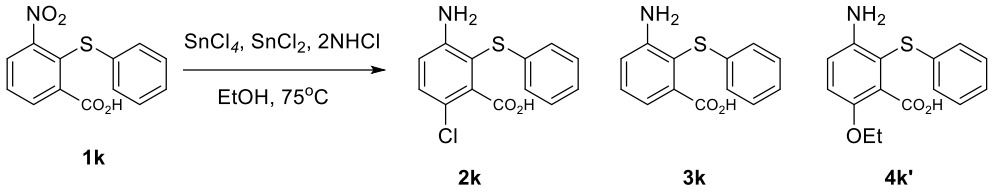


Peak#	Ret.Time	Area	Height	Area%
1	12.740	464804	228046	95.5742
2	13.582	21524	10267	4.4258
Total		486328	238313	100.0000

3j

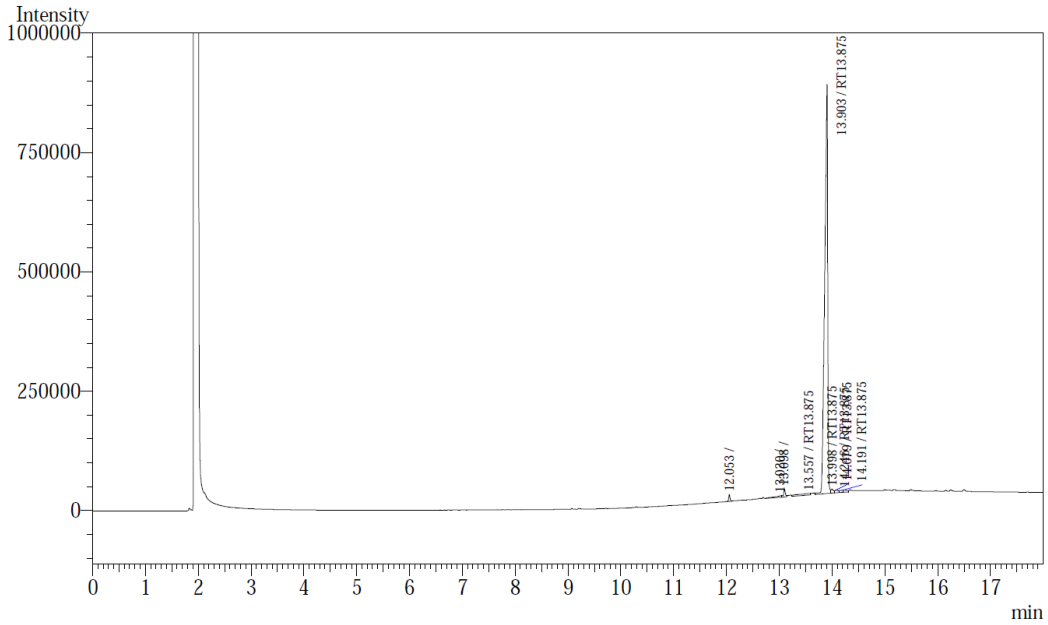
GC Report of compound 1k under reduction-halogenation condition.

1k Scheme



Name	2k	3k	4k’
Extract mass	279.0121	245.0510	289.0773
LC-RT	ND	ND	ND
GC-RT	ND	13.90 min	ND

Analysis Date & Time : 2014/10/17 下午 06:04:02
User Name : Lab 1336
Vial# : 1
Sample Name : 2SPh 3CO2H reduction
Sample ID : 2SPh 3CO2H reduction
Injection Volume : 1 uL
Data Name : D:\1336\HYH\20141017\2SPh 3CO2H reduction -1.gcd
Method Name : D:\1336\HYH\HYH-20140928 for chlorination.gcm
$EndIf$

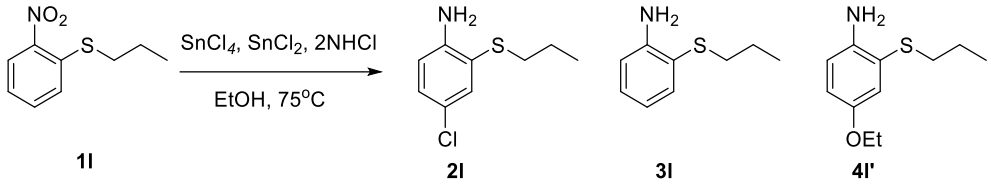


3k

Peak#	Ret.Time	Area	Height	Area%
1	12.053	24255	14020	0.6805
2	13.020	29489	3037	0.8274
3	13.098	40979	16500	1.1497
4	13.557	63727	3500	1.7880
5	13.903	3314108	853032	92.9848
6	13.998	27128	8406	0.7612
7	14.079	23567	5860	0.6612
8	14.191	20631	4243	0.5788
9	14.246	20255	4001	0.5683
Total		3564139	912599	100.0000

LC and GC Report of compound 1l under reduction-halogenation condition.

1l Scheme



1l 2l 3l 4l'

Name	2l	3l	4l'
Extract mass	201.0379	167.0769	211.1031
LC-RT	6.55 min	4.90 min	4.67 min
GC-RT	10.46 min	8.87 min	10.90 min

Chromatogram

Report for "prop-H 4.5eq re_21_01_5395"
Printed: 20:36:14 05/30/14 Computer:1AP05 User:default

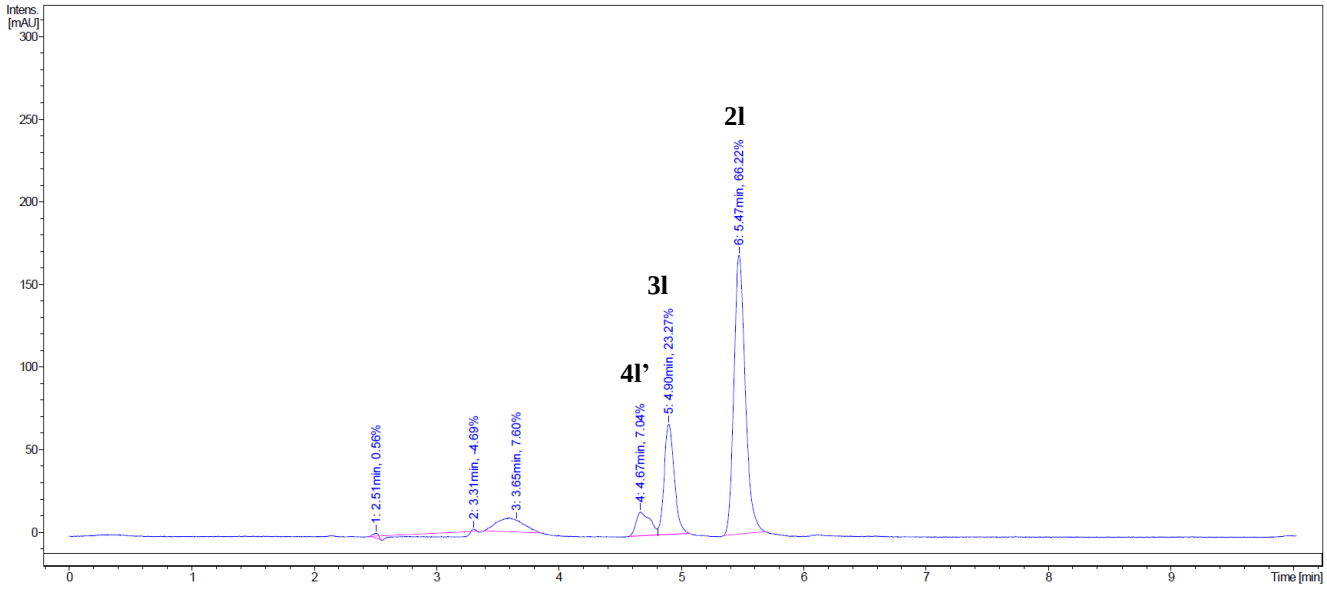
Report for "prop-H 4.5eq re_21_01_5395"

Chromatogram File:
D:\CHEM32\1\DATA\prop-H 4.5eq re_21_01_5395.d\prop-H 4.5eq re_21_01_5395.unt

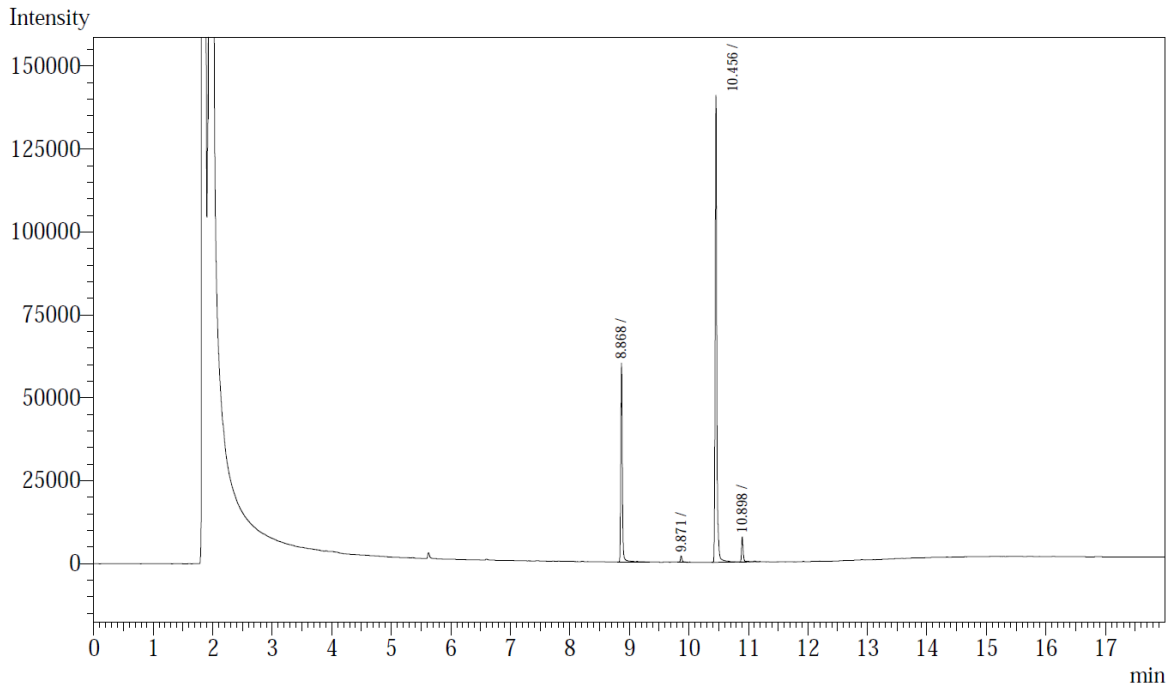
Created on: 5/30/2014 at: 08:26:14 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



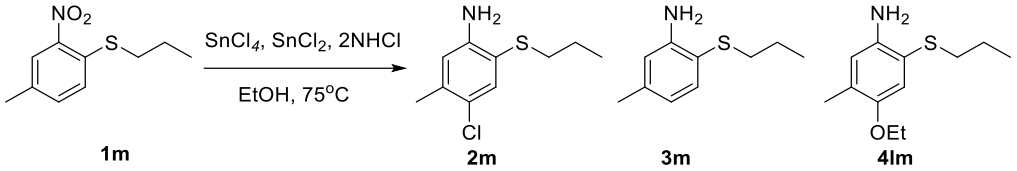
Analysis Date & Time : 2014/6/5 下午 05:05:21
User Name : Lab 1336
Vial# : 1
Sample Name : prop H red
Sample ID : prop H red
Injection Volume : 1 uL
Data Name : D:\1336\HYH\HHY 20140605\prop H red.gcd
Method Name : D:\1336\HYH\HYH-20140401.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%	
1	8.868	109598	58846	28.0339	**3l**
2	9.871	3810	1877	0.9744	
3	10.456	264122	139166	67.5593	**2l**
4	10.898	13419	7343	3.4324	**4l'**
Total		390949	207232	100.0000	

LC and GC Report of compound 1m under reduction-halogenation condition.

1m Scheme



1m 2m 3m 4Im

Name	2m	3m	4m’
Extract mass	215.0535	181.0925	225.1187
LC-RT	6.01 min	4.04 min	2.47 min
GC-RT	11.12 min	9.64 min	11.27 min

Chromatogram

Report for "prop-Me 4.5eq_22_01_5393"
Printed: 20:33:24 05/30/14 Computer:1AP05 User:default

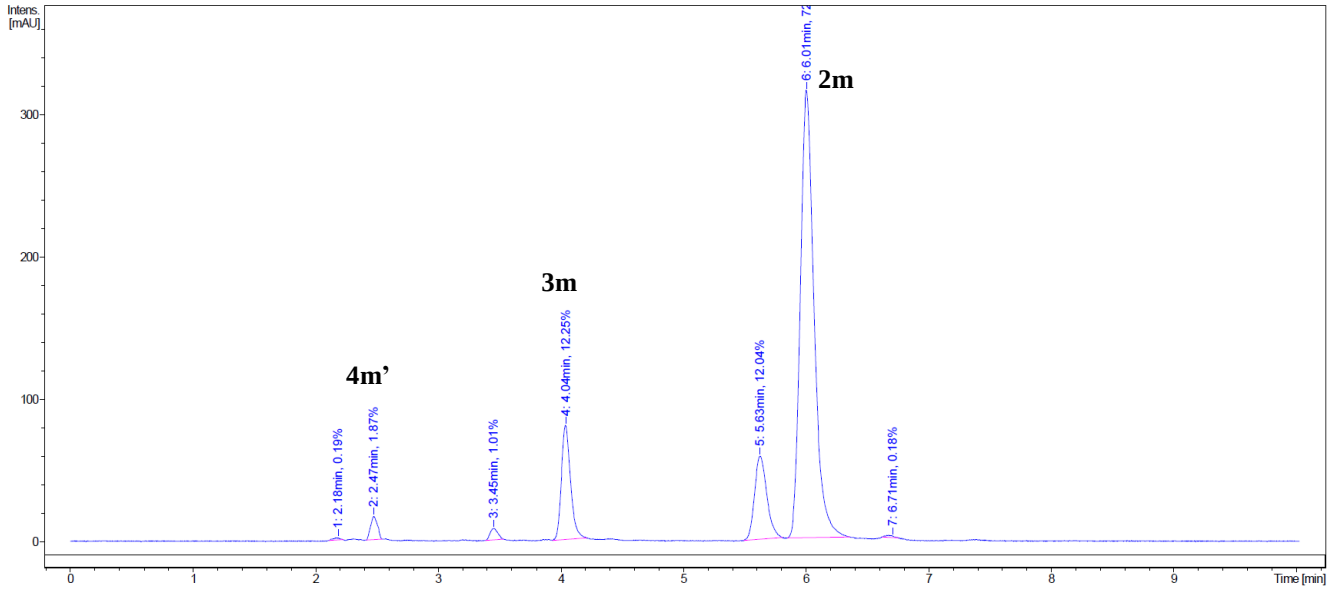
Report for "prop-Me 4.5eq_22_01_5393"

Chromatogram File:
D:\CHEM32\1\DATA\prop-Me 4.5eq_22_01_5393.d\prop-Me 4.5eq_22_01_5393.unt

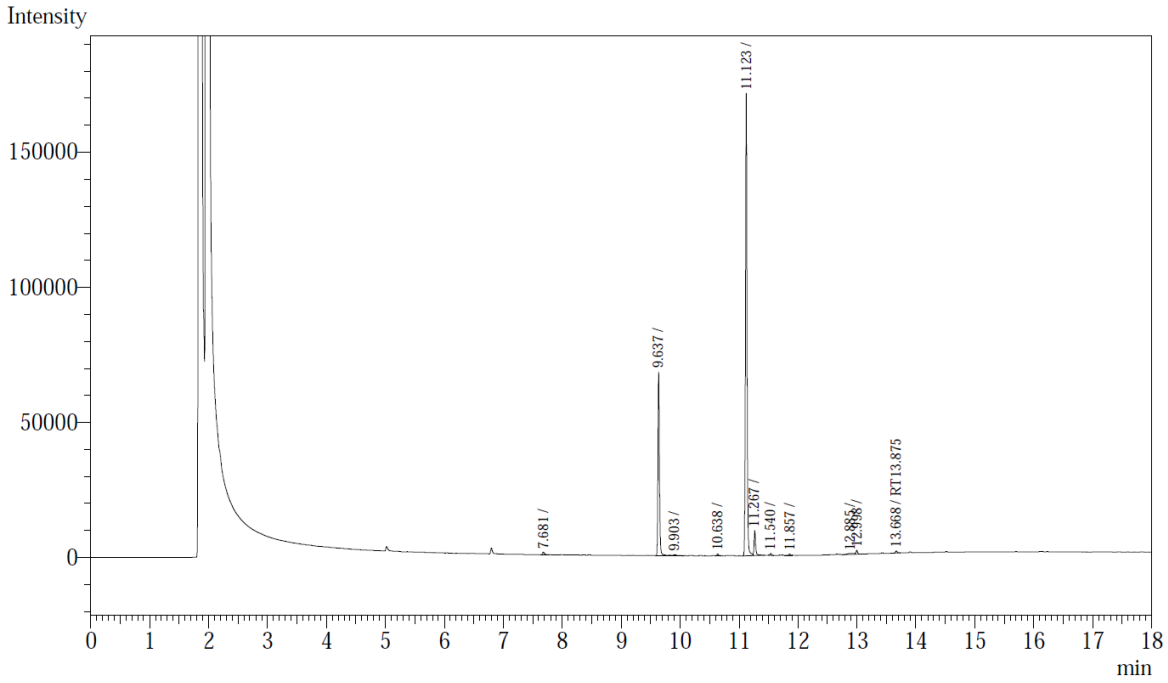
Created on: 5/30/2014 at: 08:01:16 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



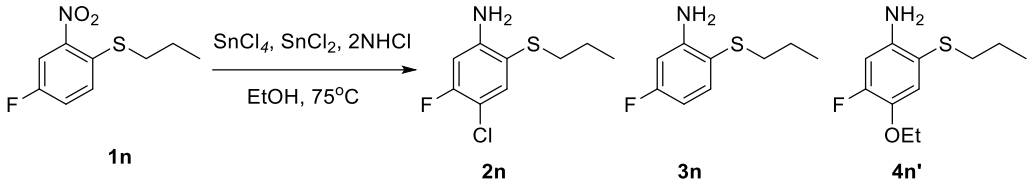
Analysis Date & Time : 2014/6/5 下午 04:00:01
User Name : Lab 1336
Vial# : 1
Sample Name : prop Me red
Sample ID : prop Me red
Injection Volume : 1 uL
Data Name : D:\1336\HYH\HHY 20140605\prop Me red.gcd
Method Name : D:\1336\HYH\HYH-20140401.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%	
1	7.681	2126	986	0.4629	
2	9.637	119484	66992	26.0131	**3m**
3	9.903	1928	379	0.4198	
4	10.638	1338	720	0.2914	
5	11.123	307158	168955	66.8720	**2m**
6	11.267	17836	9086	3.8832	**4m'**
7	11.540	1210	715	0.2634	
8	11.857	1241	594	0.2702	
9	12.885	2717	336	0.5916	
10	12.998	2804	1418	0.6106	
11	13.668	1478	742	0.3217	
Total		459320	250923	100.0000	

LC and GC Report of compound 1n under reduction-halogenation condition.

1n Scheme



Name	2n	3n	4n’
Extract mass	219.0285	185.0674	229.0937
LC-RT	5.85 min	4.84 min	4.31 min
GC-RT	10.46 min	8.87 min	10.90 min

Chromatogram

Report for "prop-F 4.5eq_23_01_5394"
Printed: 20:35:12 05/30/14 Computer:1AP05 User:default

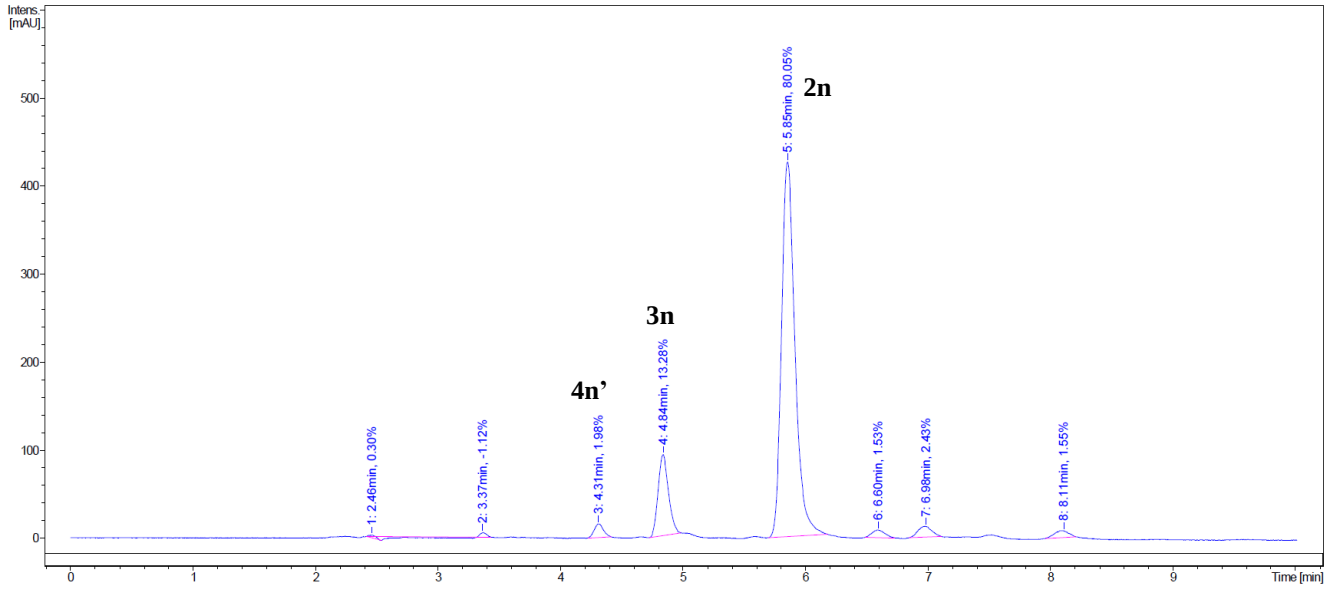
Report for "prop-F 4.5eq_23_01_5394"

Chromatogram File:
D:\CHEM32\1\DATA\prop-F 4.5eq_23_01_5394.d\prop-F 4.5eq_23_01_5394.unt

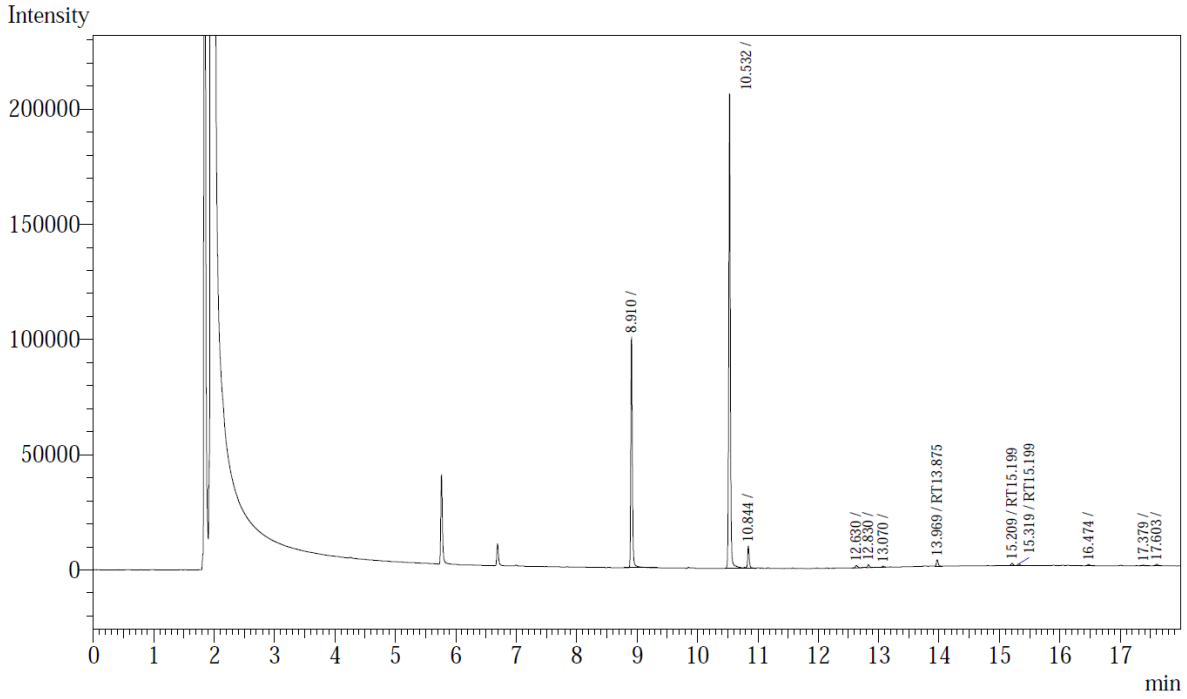
Created on: 5/30/2014 at: 08:13:44 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



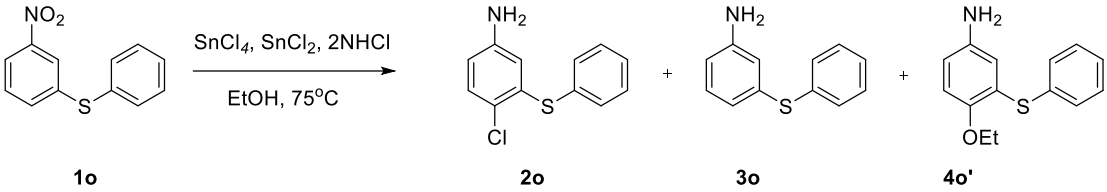
Analysis Date & Time : 2014/6/5 下午 03:13:11
User Name : Lab 1336
Vial# : 1
Sample Name : prop F red
Sample ID : prop F red
Injection Volume : 1 uL
Data Name : D:\1336\HYH\HHY 20140605\prop F red.gcd
Method Name : D:\1336\HYH\HYH-20140401.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%	
1	8.910	180084	98039	29.8751	**3n**
2	10.532	381937	202793	63.3616	**2n**
3	10.844	19462	9698	3.2287	**4n'**
4	12.630	2629	1065	0.4362	
5	12.830	2714	1285	0.4503	
6	13.070	1217	569	0.2019	
7	13.969	5743	2853	0.9527	
8	15.209	2507	1025	0.4160	
9	15.319	1686	767	0.2797	
10	16.474	1326	494	0.2200	
11	17.379	1126	348	0.1868	
12	17.603	2358	767	0.3912	
Total		602789	319703	100.0000	

GC Report of compound 1o under reduction-halogenation condition.

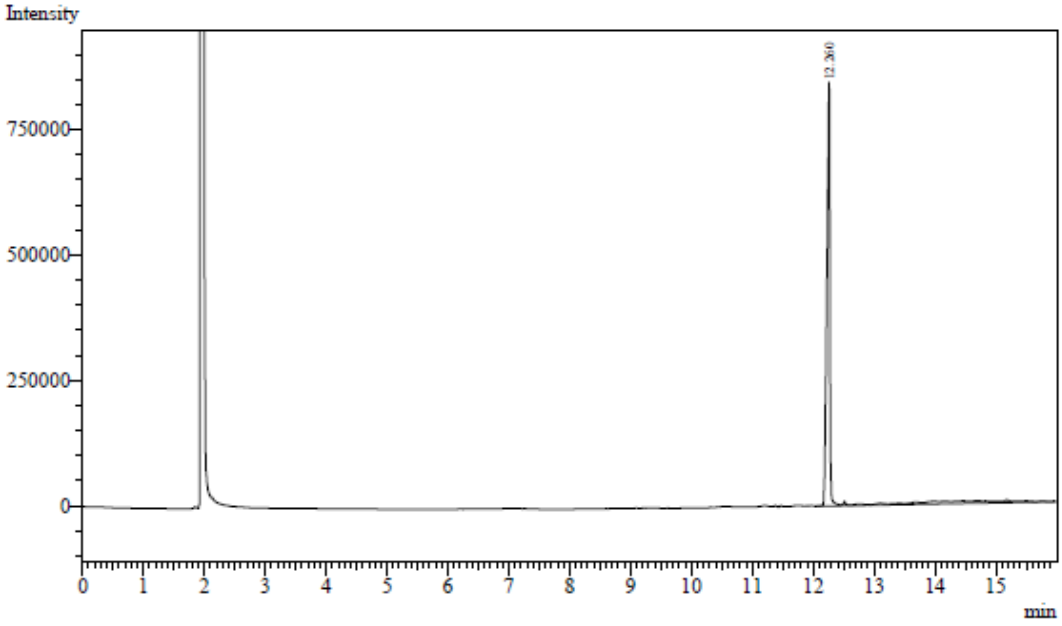
1o Scheme



1o 2o 3o 4o'

Name	2o	3o	4o’
Extract mass	235.0222	201.0612	245.0874
LC-RT	ND	ND	ND
GC-RT	ND	12.26 min	ND

Analysis Date & Time : 2014/9/29 下午 12:05:36
User Name : Lab 1336
Vial# : 1
Sample Name : HYH-20140928-3-S cl-2
Sample ID : HYH-3-S cl -2
Injection Volume : 1 uL
Data Name : D:\1336\HYH\HYH 20140928\HYH-3-S cl -2.gcd
Method Name : D:\1336\HYH\HYH-20140928 for chlorination.gcm
$EndIf$

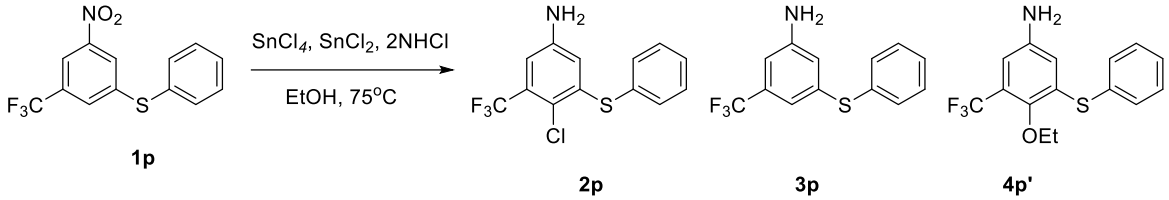


Peak#	Ret.Time	Area	Height	Area%
1	12.260	2917174	831333	100.0000
Total		2917174	831333	100.0000

3o

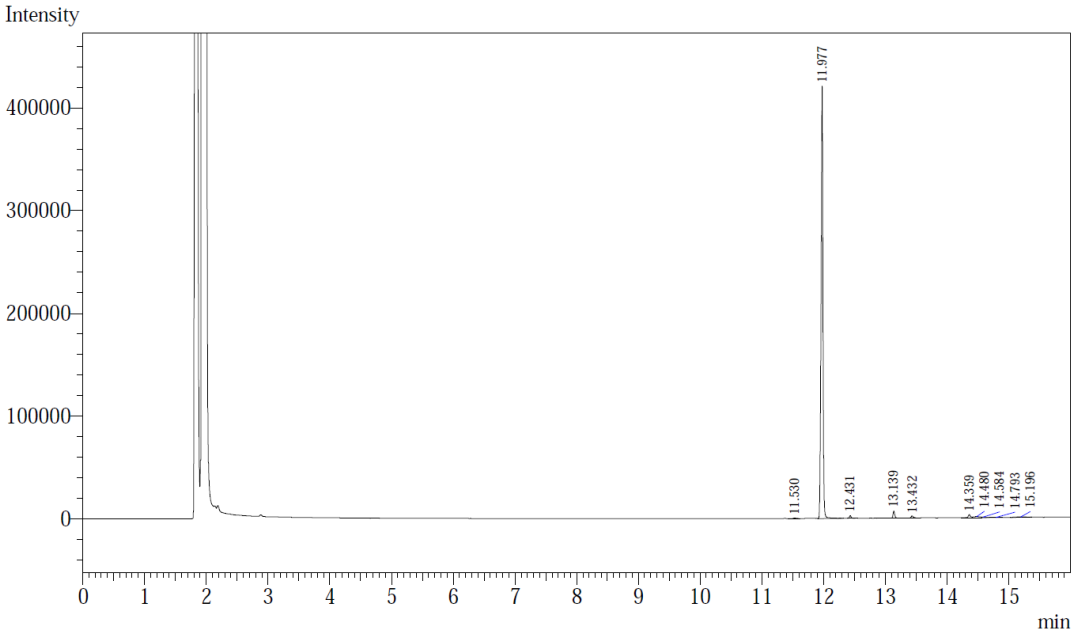
LC and GC Report of compound 1p under reduction-halogenation condition.

1p Scheme



Name	2p	3p	4p’
Extract mass	303.0096	269.0486	313.0748
LC-RT	ND	ND	ND
GC-RT	ND	11.98 min	ND

Analysis Date & Time : 2014/9/9 下午 06:52:28
User Name : Lab 1336
Vial# : 1
Sample Name : 5-CF3 3-S 1NO2 coupling reaction
Sample ID : 5-CF3 3-S 1NO2 coupling reactio
Injection Volume : 1 uL
Data Name : D:\1336\HYH\20140909\5-CF3 3-S 1NO2 coupling reaction.gcd
Method Name : D:\1336\HYH\HYH-20140818 for chlorination.gcm
$EndIf$

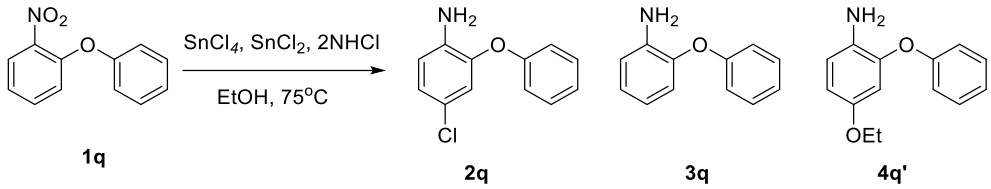


3p

Peak#	Ret.Time	Area	Height	Area%
1	11.530	1405	518	0.1504
2	11.977	885497	418200	94.7819
3	12.431	4571	2584	0.4892
4	13.139	13412	6758	1.4355
5	13.432	5046	2094	0.5401
6	14.359	7775	2977	0.8322
7	14.480	7598	1000	0.8133
8	14.584	2093	590	0.2240
9	14.793	1060	157	0.1134
10	15.196	5791	554	0.6199
Total		934248	435432	100.0000

LC and GC Report of compound 1q under reduction-halogenation condition.

1q Scheme



1q 2q 3q 4q'

Name	2q	3q	4q’
Extract mass	219.0451	185.0841	229.1103
LC-RT	4.84 min	4.16 min	3.83 min
GC-RT	10.64 min	9.40 min	11.00 min

Chromatogram

Report for "H-O-Ph_31_01_5672"
Printed: 15:24:01 08/19/14 Computer:1AP05 User:default

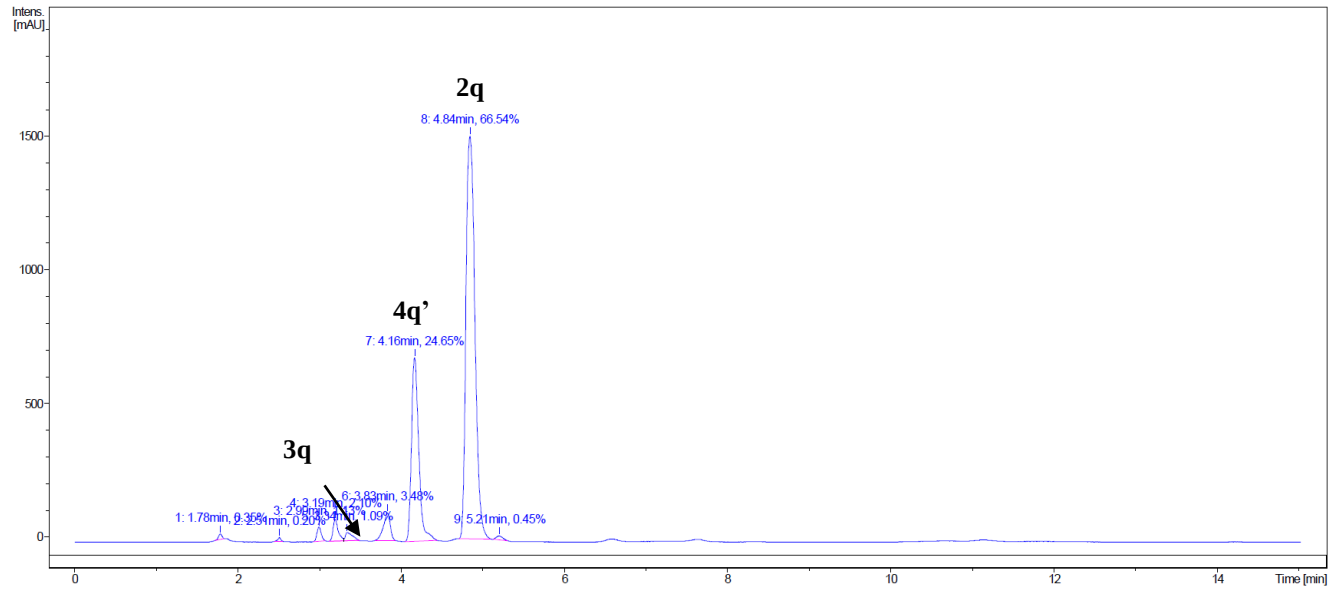
Report for "H-O-Ph_31_01_5672"

Chromatogram File:
D:\CHEM32\1\DATA\H-O-Ph_31_01_5672.d\H-O-Ph_31_01_5672.unt

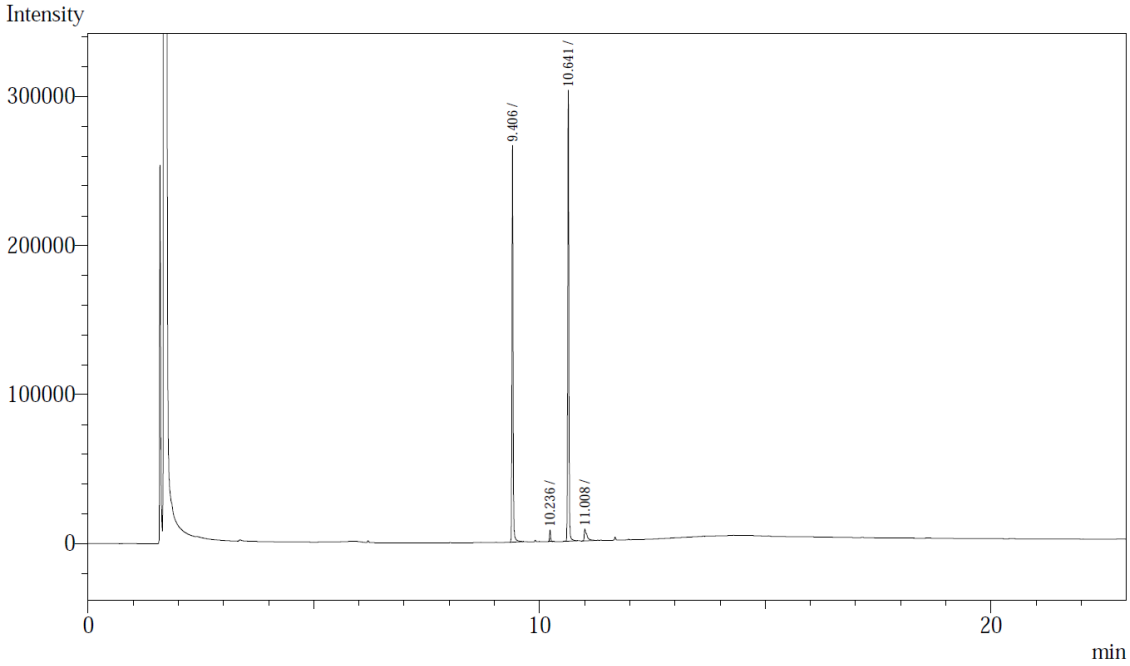
Created on: 8/19/2014 at: 02:57:15 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 15.02 min

Signal 1: DAD (254)



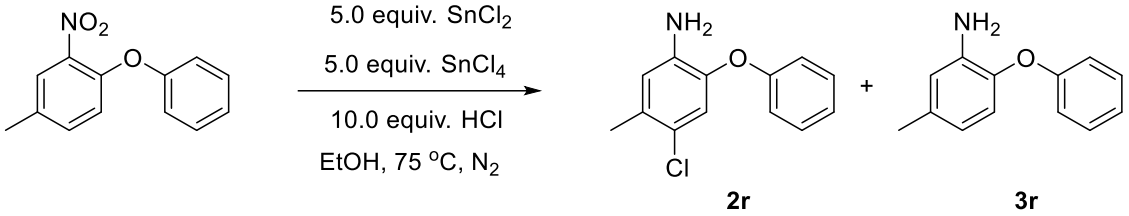
Analysis Date & Time : 2014/8/12 下午 12:26:17
User Name : Lab 1336
Vial# : 1
Sample Name : H-O-Ph
Sample ID : H-O-Ph
Injection Volume : 1 uL
Data Name : D:\1336\HYH\HYH-20140812\H-O-Ph.gcd
Method Name : D:\1336\HYH\HYH-20140401 test-1.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%	
1	9.406	465112	262223	45.0113	**3q**
2	10.236	12820	7841	1.2407	
3	10.641	523174	298395	50.6302	**2q**
4	11.008	32217	8015	3.1178	**4q'**
Total		1033323	576474	100.0000	

LC and GC Report of compound 1r under reduction-halogenation condition.

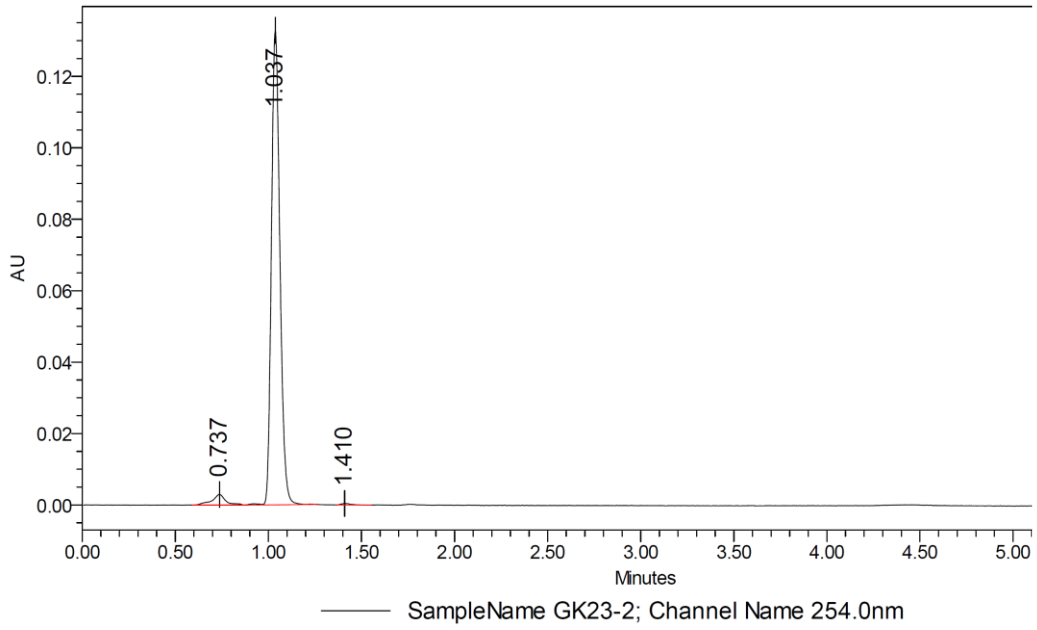
1r Scheme



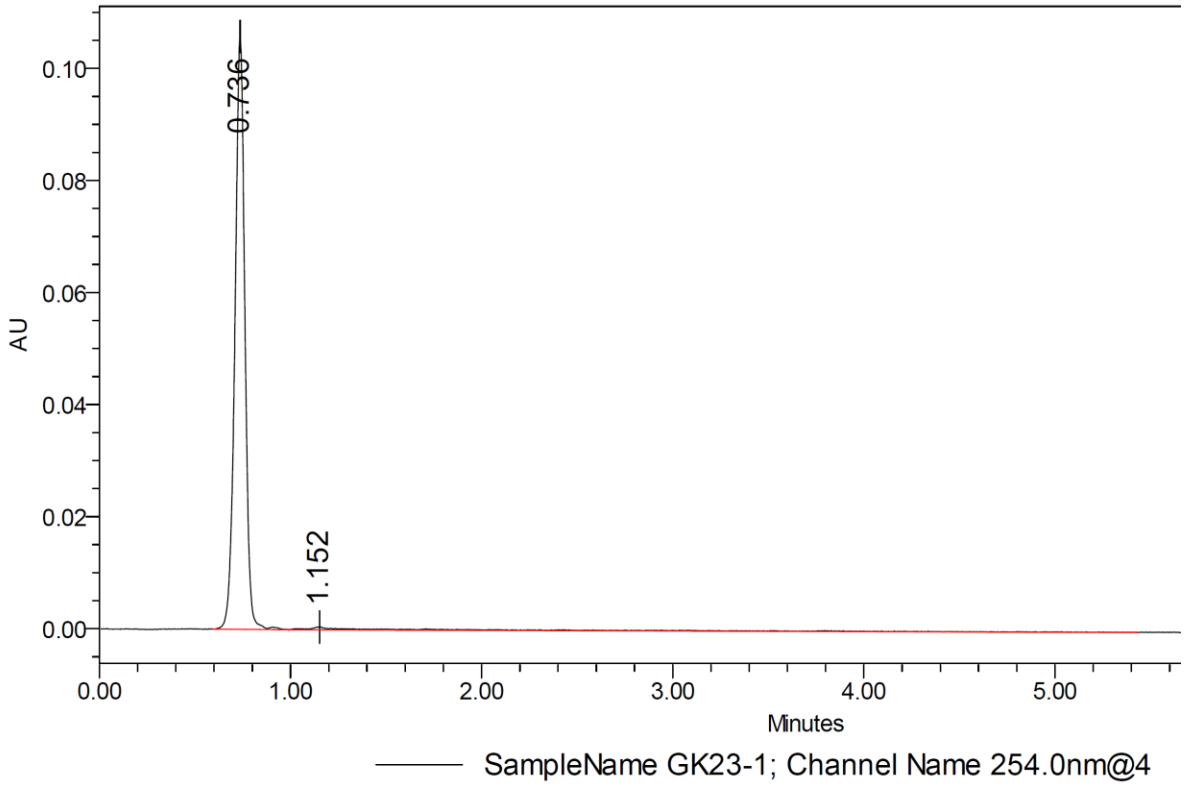
2r **3r**

Name	**2r**	**3r**
LC-RT	1.04 min	0.74 min
MH^+(m/z)	234, 236	200

Mobile phase: 60% ACN in 0.5% TFA
Column: Phenyl-Hexyl



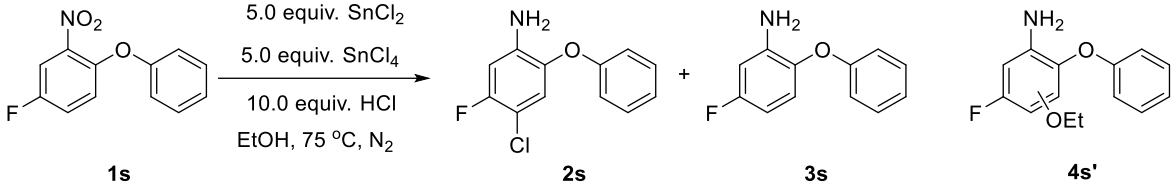
Purified **2r**: $[M+H]^+$ = 234, 236



Purified **3r**: $[M+H]^+ = 200$

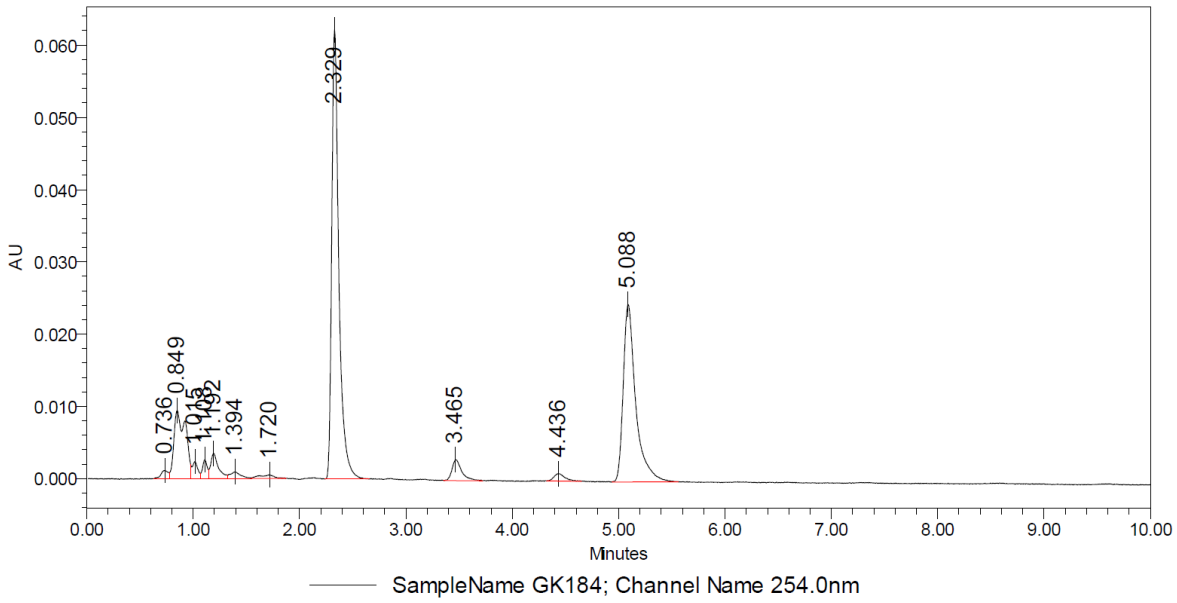
LC and GC Report of compound 1s under reduction-halogenation condition.

1s Scheme

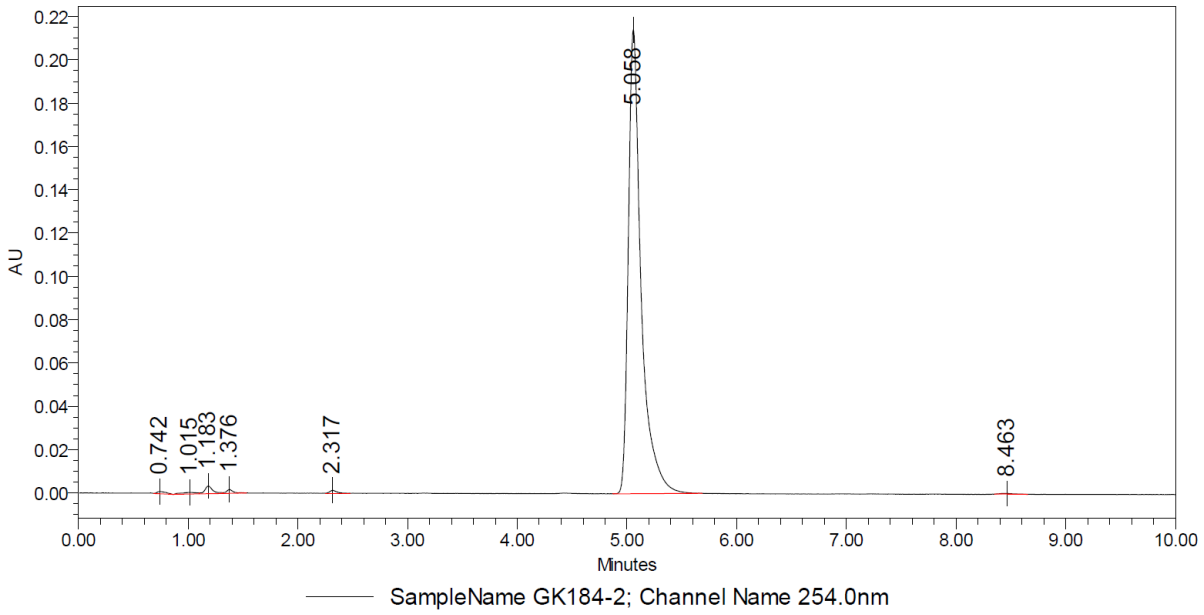


Name	**2s**	**3s**	**4s'**
MH^+(m/z)	238, 240	204	248
LC-RT	5.09 min	2.33 min	1.19, 3.47 min
Peal area %	32	45	2.8, 2.9

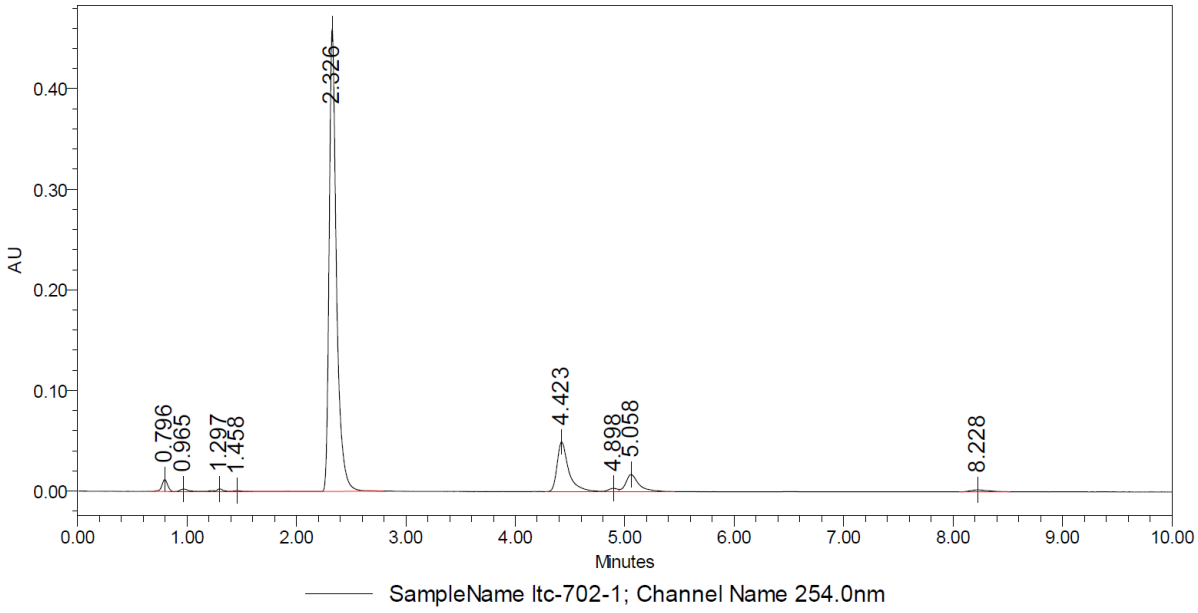
Mobile phase: 40% ACN in 0.5% TFA
Column: Phenyl-Hexyl, 2.1 × 100 mm
Flow rate: 0.4 mL/min
UV: 254 nm



Crude reaction mixture contained compounds **2s** and **3s**.



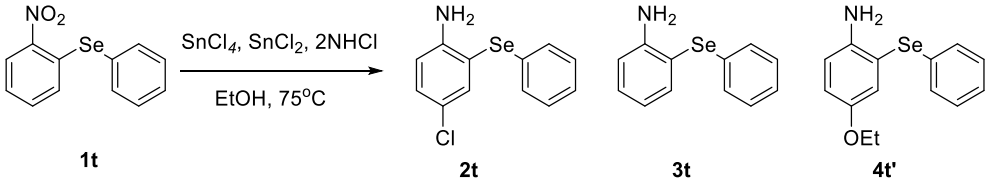
Purified **2s**: $[M+H]^+$ = 238, 240



Purified **3s**: $[M+H]^+$ = 204

LC and GC Report of compound 1s under reduction-halogenation condition.

1t Scheme



1t 2t 3t 4t'

Name	2t	3t	4t’
Extract mass	282.9667	249.0057	293.0319
LC-RT	5.87 min	4.58 min	2.99 min
GC-RT	13.24 min	11.99 min	12.44 min

Chromatogram

Report for "Se_21_01_5528"
Printed: 14:36:33 07/17/14 Computer:1AP05 User:default

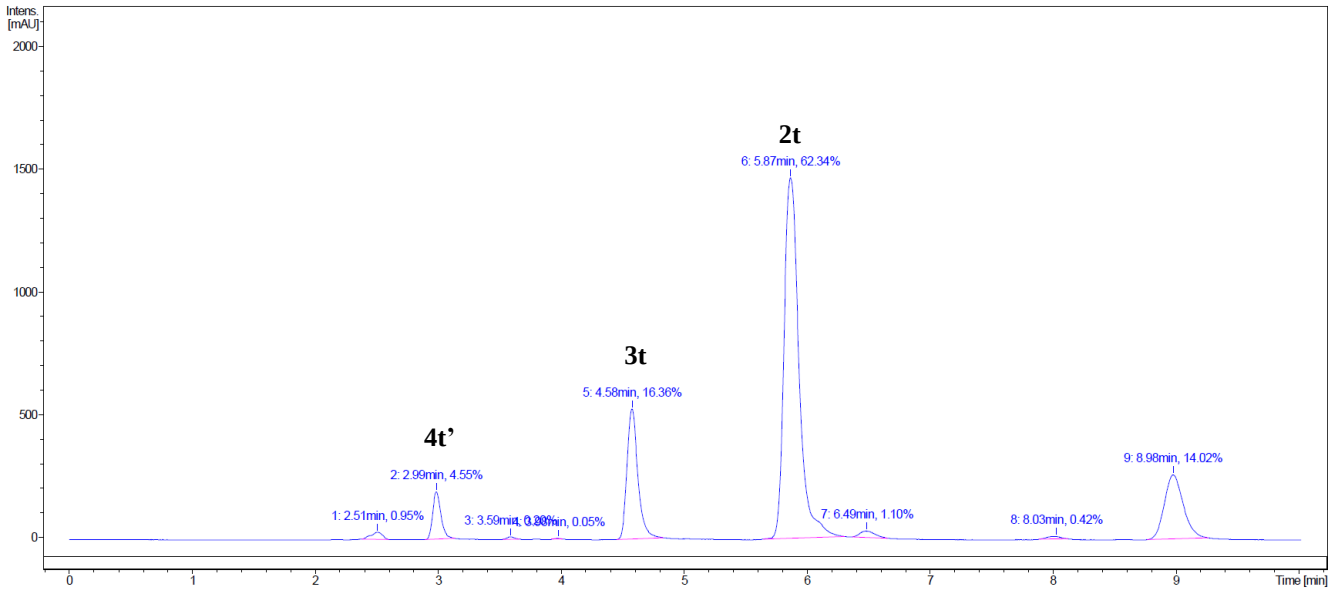
Report for "Se_21_01_5528"

Chromatogram File:
D:\CHEM32\1\DATA\lab1336\hyh\hyh 20140717 lc-ms\Se_21_01_5528.d\Se_21_01_5528.unt

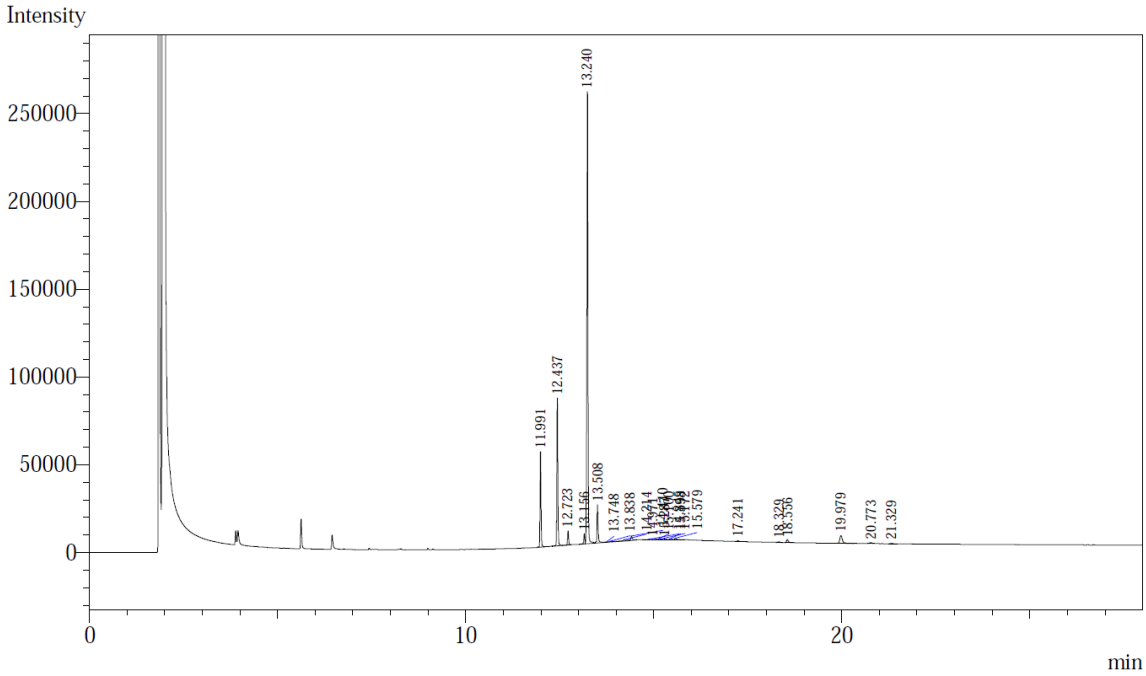
Created on: 7/17/2014 at: 02:05:19 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



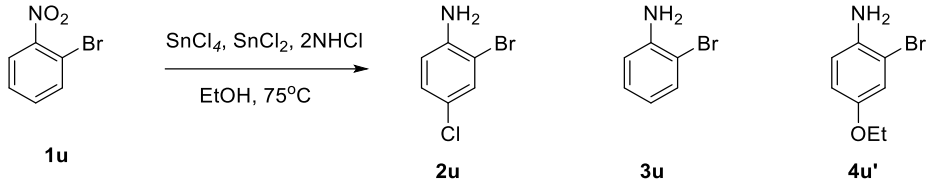
Analysis Date & Time : 2014/7/24 下午 02:42:44
User Name : Lab 1336
Vial# : 1
Sample Name : Se red
Sample ID : Se red
Injection Volume : 1 uL
Data Name : D:\1336\HYH\20140724\Se red.gcd
Method Name : D:\1336\HYH\HYH-20140401.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%	
1	11.991	95823	53819	10.6307	**3t**
2	12.437	152701	81974	16.9407	**4t'**
3	12.723	15217	7900	1.6882	
4	13.156	12084	5783	1.3406	
5	13.240	514317	251199	57.0585	**2t**
6	13.508	45884	21573	5.0904	
7	13.748	1796	225	0.1993	
8	13.838	1877	488	0.2082	
9	14.214	4915	681	0.5453	
10	14.410	9541	2556	1.0585	
11	14.845	1065	143	0.1182	
12	14.971	1457	226	0.1616	
13	15.100	1307	316	0.1450	
14	15.172	1847	360	0.2050	
15	15.287	1868	325	0.2073	
16	15.398	2243	299	0.2489	
17	15.579	4508	1006	0.5002	
18	17.241	1346	458	0.1493	
19	18.329	1231	396	0.1365	
20	18.556	5757	1605	0.6386	
21	19.979	20985	4424	2.3281	
22	20.773	2392	581	0.2654	
23	21.329	1224	244	0.1358	
Total		901385	436581	100.0000	

LC and GC Report of compound 1u under reduction-halogenation condition.

1u Scheme



1u 2u 3u 4u'

Name	2u	3u	4u’
Extract mass	204.9294	170.9684	214.9946
LC-RT	ND	ND	4.04
GC-RT	ND	ND	6.61

Chromatogram

Report for "5H-2Br_12_01_5812"
Printed: 13:27:18 12/01/14 Computer:1AP05 User:default

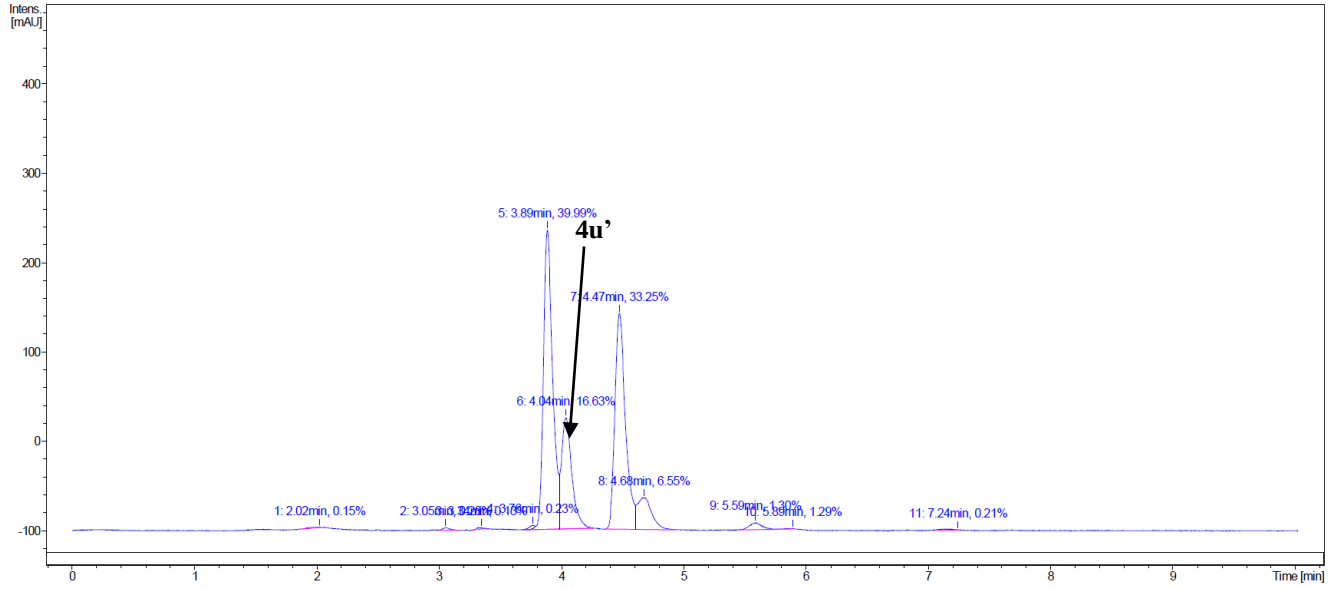
Report for "5H-2Br_12_01_5812"

Chromatogram File:
D:\CHEM32\1\DATA\5H-2Br_12_01_5812.d\5H-2Br_12_01_5812.unt

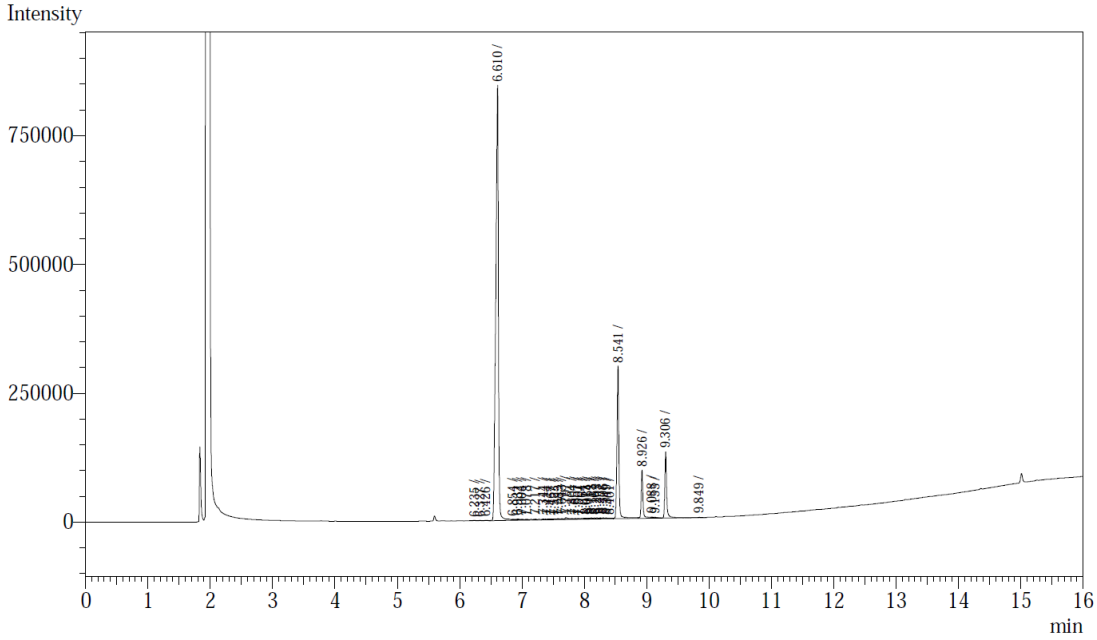
Created on: 10/14/2014 at: 02:26:47 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



Analysis Date & Time : 2014/10/8 下午 04:28:00
User Name : Lab 1336
Vial# : 1
Sample Name : HYH-5-H,2-Br
Sample ID : HYH-5-H,2-Br
Injection Volume : 1 uL
Data Name : D:\1336\HYH\20141008\HYH-5-H,2-Br.gcd
Method Name : D:\1336\HYH\HYH-20140928 for chlorination.gcm
$EndIf$



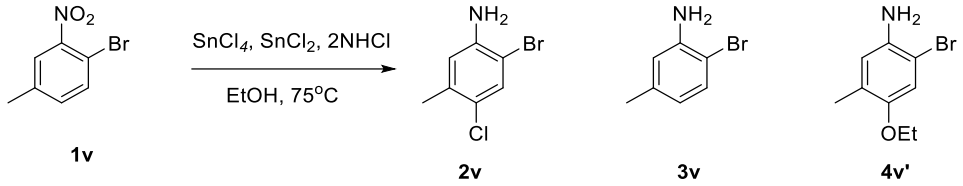
Peak#	Ret.Time	Area	Height	Area%
1	6.235	2434	669	0.0659
2	6.327	1233	457	0.0334
3	6.426	2102	664	0.0569
4	6.610	2535986	835480	68.6652
5	6.854	1050	488	0.0284
6	6.932	2762	846	0.0748
7	7.004	1106	562	0.0299
8	7.078	1500	682	0.0406
9	7.217	2100	844	0.0569
10	7.344	1879	819	0.0509
11	7.414	1464	597	0.0396
12	7.467	2202	951	0.0596
13	7.523	1281	700	0.0347
14	7.583	2424	892	0.0656
15	7.643	1962	984	0.0531
16	7.707	8838	3030	0.2393
17	7.804	1987	902	0.0538
18	7.857	1851	986	0.0501
19	7.907	2182	955	0.0591
20	7.964	2381	1100	0.0645
21	8.017	2776	1181	0.0752
22	8.064	3304	1309	0.0895
23	8.113	3585	1427	0.0971
24	8.161	2767	1312	0.0749
25	8.203	3159	1326	0.0855
26	8.257	2473	1165	0.0670
27	8.306	2541	1103	0.0688
28	8.349	1892	952	0.0512
29	8.401	1557	763	0.0422
30	8.541	633379	289278	17.1496
31	8.926	196226	92900	5.3131

4u'

Peak#	Ret.Time	Area	Height	Area%
32	9.088	1221	704	0.0331
33	9.133	1447	533	0.0392
34	9.306	257126	125229	6.9620
35	9.849	1089	341	0.0295
Total		3693266	1372131	100.0000

LC and GC Report of compound 1v under reduction-halogenation condition.

1v Scheme



1v 2v 3v 4v'

Name	2v	3v	4v’
Extract mass	218.9450	184.9840	229.0102
LC-RT	ND	4.24 min	4.62 min
GC-RT	ND	7.68 min	9.42 min

Chromatogram

Report for "5Me-2Br_13_01_5813"
Printed: 14:47:37 10/14/14 Computer:1AP05 User:default

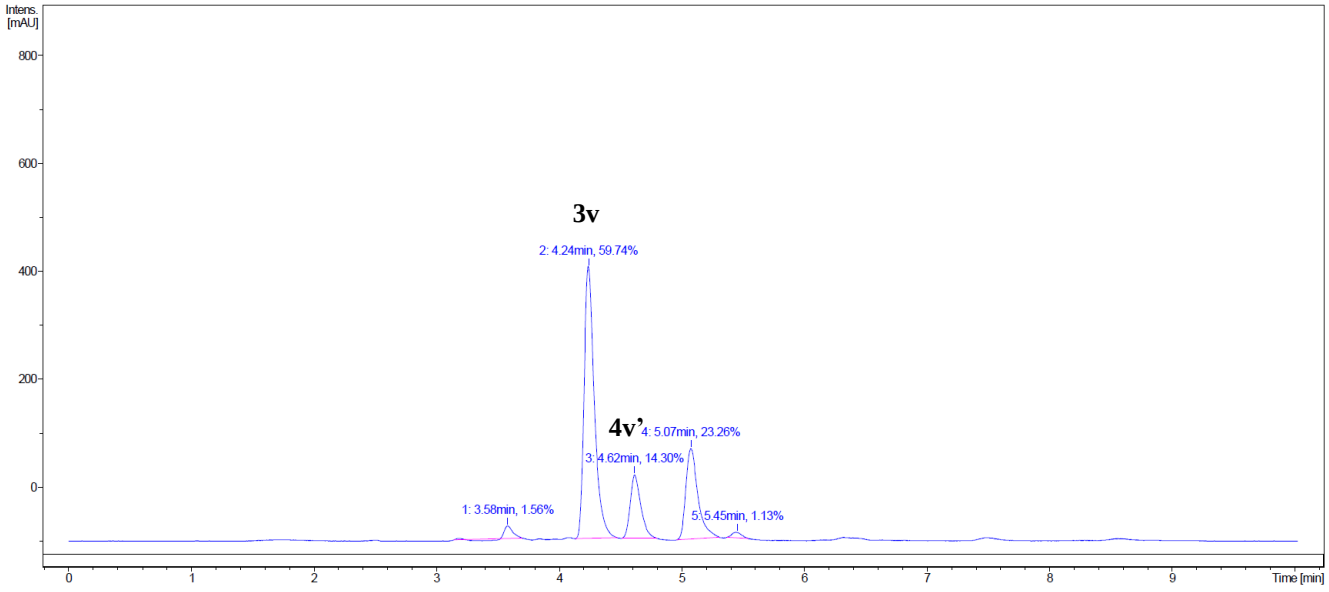
Report for "5Me-2Br_13_01_5813"

Chromatogram File:
D:\CHEM32\1\DATA\5Me-2Br_13_01_5813.d\5Me-2Br_13_01_5813.unt

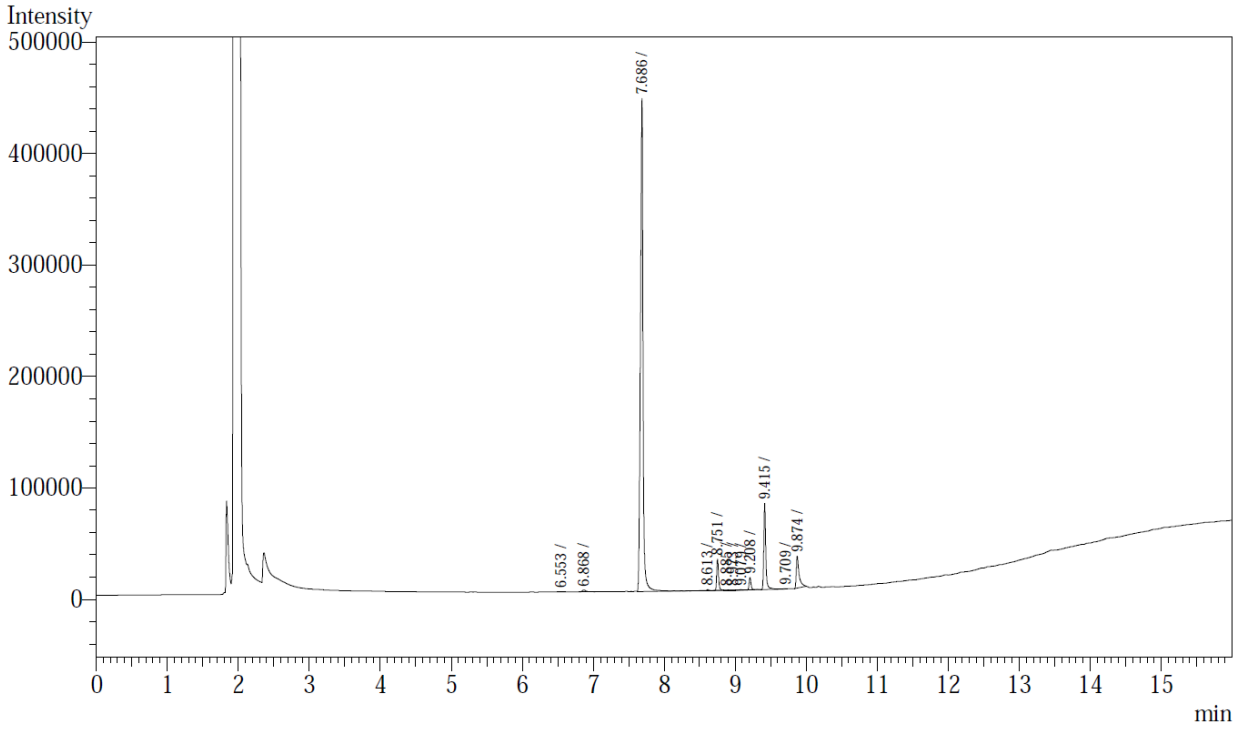
Created on: 10/14/2014 at: 02:39:19 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



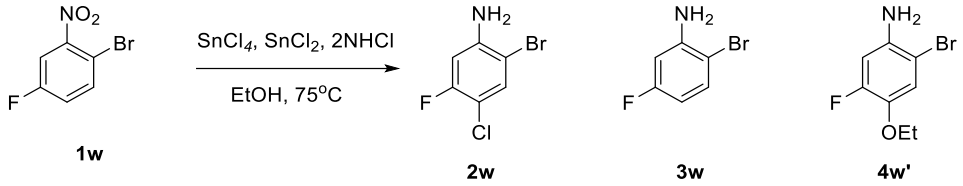
Analysis Date & Time : 2014/10/8 下午 04:01:39
User Name : Lab 1336
Vial# : 1
Sample Name : HYH-5-Me,2-Br
Sample ID : HYH-5-Me,2-Br
Injection Volume : 1 uL
Data Name : D:\1336\HYH\20141008\HYH-5-Me,2-Br2.gcd
Method Name : D:\1336\HYH\HYH-20140928 for chlorination.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%	
1	6.553	1079	188	0.0760	
2	6.868	6684	1876	0.4709	
3	7.686	1104114	435914	77.7893	**3v**
4	8.613	1769	902	0.1246	
5	8.751	50762	27525	3.5764	
6	8.885	1072	307	0.0755	
7	8.973	1351	297	0.0952	
8	9.079	1339	245	0.0943	
9	9.208	20140	10805	1.4189	
10	9.415	151810	76579	10.6956	**4v'**
11	9.709	1117	230	0.0787	
12	9.874	78129	28419	5.5045	
Total		1419366	583287	100.0000	

LC and GC Report of compound 1w under reduction-halogenation condition.

1w Scheme



1w 2w 3w 4w'

Name	2w	3w	4w’
Extract mass	222.9200	188.9589	232.9852
LC-RT	ND	ND	3.88 min
GC-RT	ND	ND	6.64 min

Chromatogram

Report for "5F-2Br_11_01_5807"
Printed: 13:27:33 10/16/14 Computer:1AP05 User:default

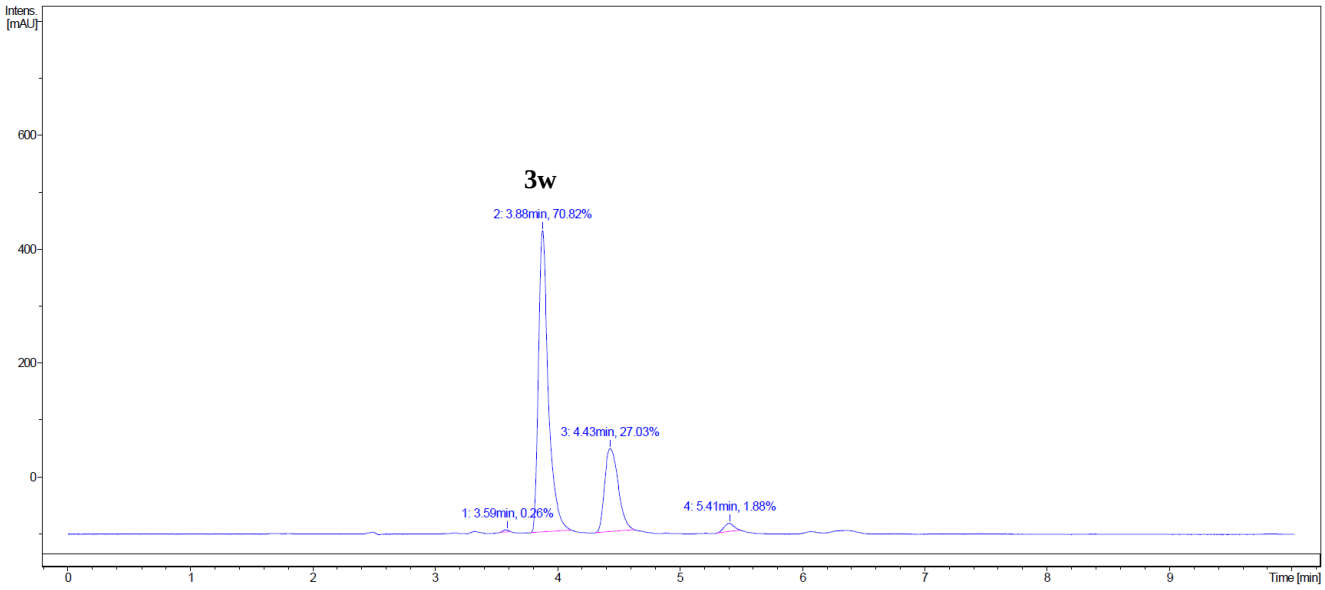
Report for "5F-2Br_11_01_5807"

Chromatogram File:
D:\CHEM32\1\DATA\5F-2Br_11_01_5807.d\5F-2Br_11_01_5807.unt

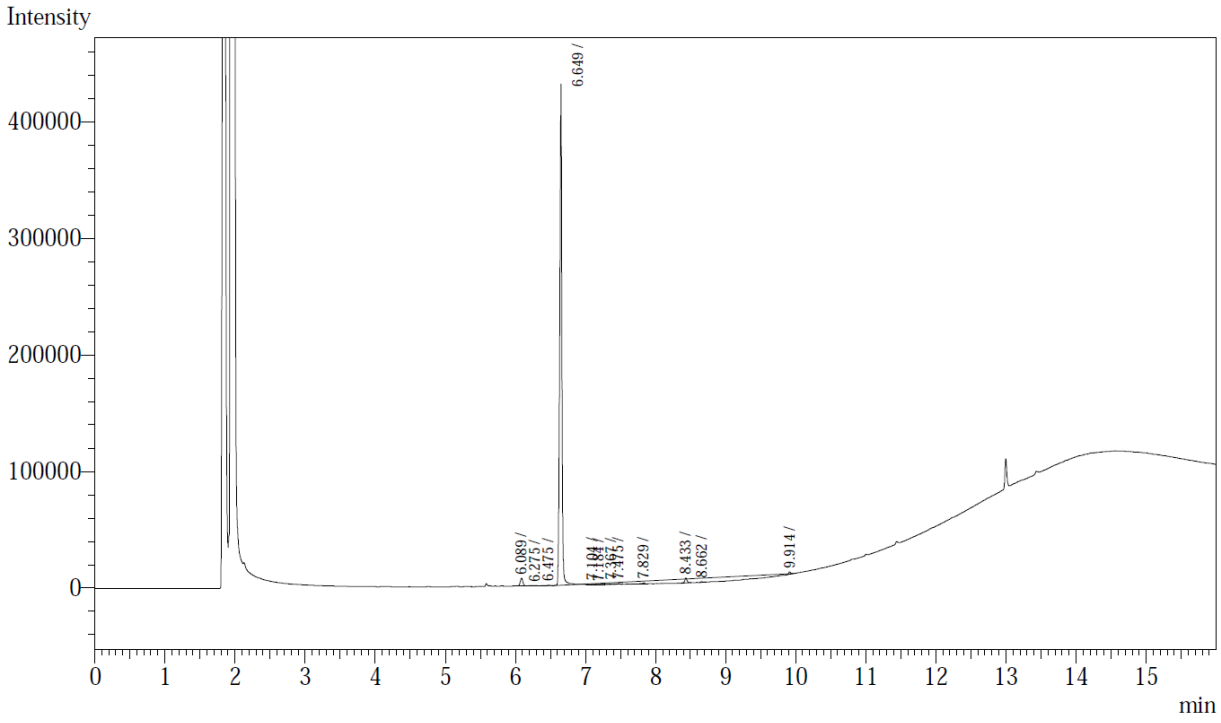
Created on: 10/14/2014 at: 01:23:26 pm
on Windows system: 1AP05 by user: TOF-User
with HyStar Version 3.2.44.0
Operator: default, Laboratory:

Total Chromatogram Runtime: 10.02 min

Signal 1: DAD (254)



Analysis Date & Time : 2014/10/9 下午 04:33:08
User Name : Lab 1336
Vial# : 1
Sample Name : HYH-20141009 5-F-2-Br red
Sample ID : HYH-20141009 5-F-2-Br red
Injection Volume : 1 uL
Data Name : D:\1336\HYH\20141008\HYH-20141009 5-F-2-Br red.gcd
Method Name : D:\1336\HYH\HYH-20140928 for chlorination.gcm
$EndIf$



Peak#	Ret.Time	Area	Height	Area%
1	6.089	17653	6263	3.2813
2	6.275	1411	192	0.2624
3	6.475	1848	378	0.3435
4	6.649	493577	341489	91.7467
5	7.104	1491	316	0.2771
6	7.184	1218	221	0.2265
7	7.367	1493	355	0.2775
8	7.475	1653	524	0.3073
9	7.829	2584	714	0.4803
10	8.433	9137	3418	1.6984
11	8.662	1467	524	0.2727
12	9.914	4446	1879	0.8264
Total		537978	356273	100.0000

3w