

## **Supporting Information**

# **Dual Ligand Enabled Non-Directed C–H Chalcogenation of Arenes and Heteroarenes**

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## **Experimental Section- Part I**

## **1. General information:**

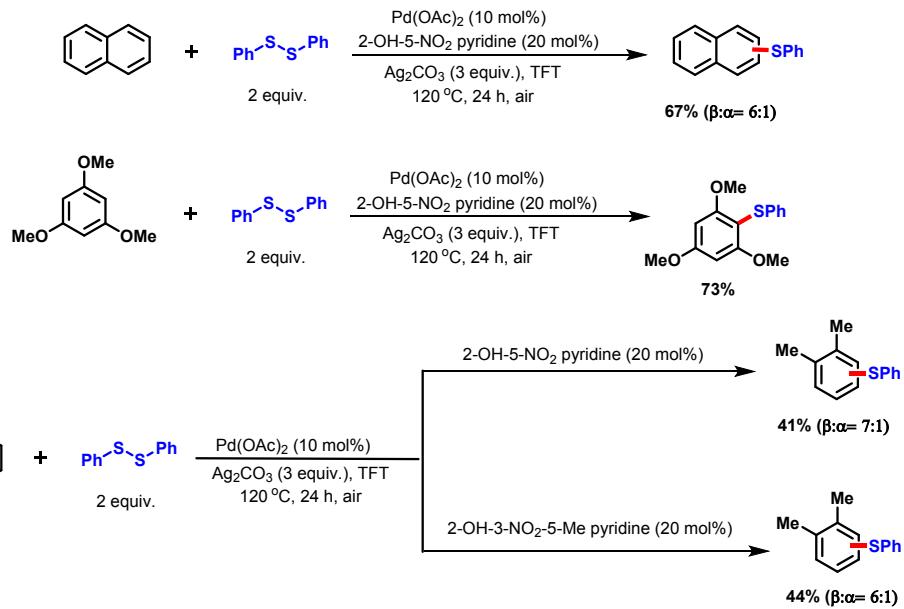
**1.1. Reagent information:** Unless otherwise stated, all the reactions were carried out in screw cap reaction tube with magnetic stirring under air atmosphere. All the palladium salts were purchased from Alfa Aesar and used directly for the reaction. Diaryl dichalcogenide derivatives were mostly purchased from TCI chemicals or prepared independently by the standard procedure<sup>1</sup> and silver carbonate was brought from Sigma-Aldrich Co. Dichloroethane or Chlorobenzene was brought from Spectrochem and used directly. *N*-Acetyl glycine and 3,5-dichloro-2-pyridone were purchased from Sigma-Aldrich Co. and used without further purification. All the other reagents were purchased from commercial source and used as received. For column chromatography silica gel (60-120 mesh and 100-200 mesh) was supplied from SRL Co. During elution petroleum ether and ethyl acetate mixture was used. Thin layer chromatography was performed on EMD Chemicals Si 60 F<sub>254</sub>. TLC plates (silica gel 60F<sub>254</sub>) were supplied from MERCK.

**1.2. Analytical information:** <sup>1</sup>H NMR, <sup>13</sup>C NMR, <sup>19</sup>F spectroscopy and HRMS were used to characterize all the isolated compounds. Copies of the <sup>1</sup>H NMR, <sup>13</sup>C NMR, <sup>19</sup>F NMR spectra were attached in this supporting information. All the NMR spectra were recorded on a BRUKER 400 MHz or BRUKER 500 MHz instrument. All <sup>1</sup>H NMR spectra are reported in parts per million (ppm) downfield of TMS and were measured relative to residual CHCl<sub>3</sub> (7.26 ppm). All <sup>13</sup>C NMR spectra were reported in ppm relative to CDCl<sub>3</sub> (77.16 ppm) and were obtained with proton decoupling. Coupling constants, J are reported in Hertz.

## **2. Experimental section:**

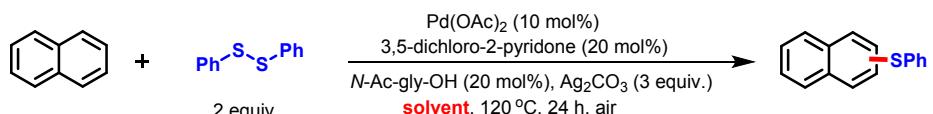
### **2.1. Optimization details**

#### ***Initial reaction condition:***



**Table S1:** Ligand optimization.

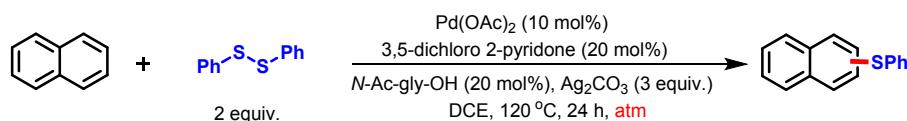
		Pd(OAc) <sub>2</sub> (10 mol%)		
		ligand (20 mol%), N-Ac-gly-OH (20 mol%)		
		Ag <sub>2</sub> CO <sub>3</sub> (3 equiv.), TFT		
		120 °C, 24 h		
L1	61% ( $\beta:\alpha$ 8:1)			
L2	65% ( $\beta:\alpha$ 8:1)			
L3	57% ( $\beta:\alpha$ 2:1)			
L4	n.p.			
L5	38% ( $\beta:\alpha$ >20:1)			
L6	61% ( $\beta:\alpha$ >20:1)			
L7	trace			
L8	trace			
L9	trace			
L10	trace			
L11	20% ( $\beta:\alpha$ 1:1)			
L12	67% ( $\beta:\alpha$ 1:1)			
L13	70% ( $\beta:\alpha$ 1:1)			
L14	60% ( $\beta:\alpha$ 1:1)			
L15	20% ( $\beta:\alpha$ 1:1)			
L16	trace			
L17	trace			
L18	n.p.			
L19	n.p.			
L20	trace			
L21	trace			
L22	57% ( $\beta:\alpha$ >20:1)			
L23	37% ( $\beta:\alpha$ 2:1)			
L24	59% ( $\beta:\alpha$ 4:1)			
L25	50% ( $\beta:\alpha$ 1:1)			
L26	70% ( $\beta:\alpha$ 6:1)			
L27	47% ( $\beta:\alpha$ 10:1)			
L28	33% ( $\beta:\alpha$ 12:1)			
L29	43% ( $\beta:\alpha$ 12:1)			
L30	15% ( $\beta:\alpha$ 1:1)			

**Table S2:** Solvent optimization.

Entry	Solvent	Yield (%)	Selectivity ( $\beta:\alpha$ )
1	THF	trace	-
2	Fluorobenzene	69	12:1
3	TFT	61	>20:1
4	TFE	trace	-
<b>5</b>	<b>Chlorobenzene</b>	<b>80</b>	<b>&gt;20:1</b>
6	Toluene	20	1:1
<b>7</b>	<b>DCE</b>	<b>85</b>	<b>&gt;20:1</b>
8	1,4 dioxane	15	2:1
9	MeOH	trace	-
10	EtOH	trace	-
11	HFIP	35	7:1
12	HFIP: DCE (1:1)	76	14:1
13	Chloroform	n.p	-
14	<i>tert</i> -butanol	trace	-
15	DMF	10	-
16	Mesitylene	trace	-
17	DCM	trace	-
18	Acetone	n.p	-
19	Bromobenzene	78	11:1
20	1,2,3 trichloro propane	40	10:1
21	2,2,2 trifluoro ethanol	45	7:1

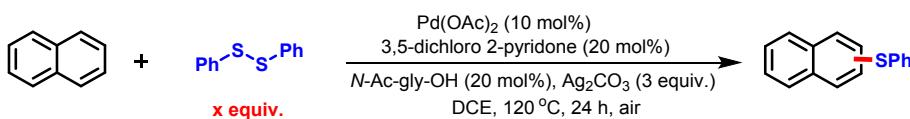
22	Bromoform	58	9:1
23	1,2 dibromoethane	Not conclusive	-
24	Hexafluorobenzene	65	11:1
25	CH <sub>3</sub> CN	trace	-
26	DCE: TFT (1:1)	78	13:1
27	DCE: Chlorobenzene (1:1)	67	3:1
28	DCE: Bromobenzene (1:1)	55	4:1
29	DCE: Hexafluorobenzene (1:1)	59	1:1
30	DCE:1,2 dibromoethane (1:1)	87	9:1
31	DCE: TFE (1:1)	70	2:1
32	DCE: Fluorobenzene (1:1)	42	11:1

**Table S3:** Atmosphere optimization.



Entry	Atmosphere	Yield (%)	Selectivity ( $\beta:\alpha$ )
1	N <sub>2</sub>	54	12:1
2	O <sub>2</sub>	37	3:1
3	Air	85	>20:1

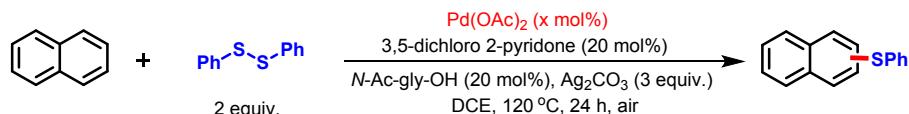
**Table S4:** Disulphide amount optimization.



Entry	Ph <sub>2</sub> S <sub>2</sub> amount (equiv.)	Yield (%)	Selectivity ( $\beta:\alpha$ )
1	1	20	1:1

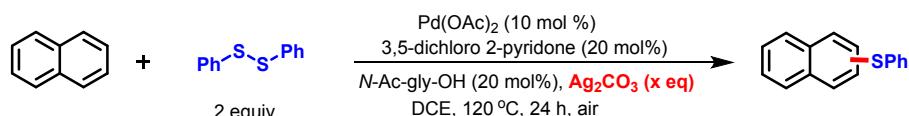
2	1.2	28	3:1
3	1.4	31	10:1
4	1.6	64	18:1
5	1.8	71	>20:1
<b>6</b>	<b>2</b>	<b>85</b>	<b>&gt;20:1</b>
7	3	82	15:1
8	4	80	8:1
9	5	79	6:1

**Table S5:** Pd(OAc)<sub>2</sub> amount optimization



Entry	Pd amount (mol%)	Yield (%)	Selectivity ( $\beta:\alpha$ )
1	5	trace	-
2	7	79	>20:1
3	8	82	>20:1
<b>4</b>	<b>10</b>	<b>85</b>	<b>&gt;20:1</b>
5	12	70	12:1
6	15	30	8:1
7	20	20	4:1

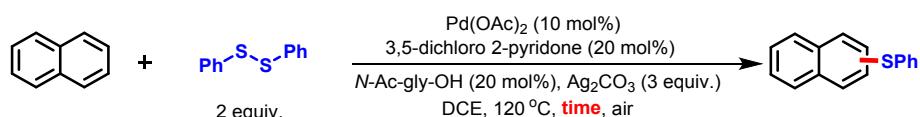
**Table S6:** Oxidant amount optimization.



Entry	Ag <sub>2</sub> CO <sub>3</sub> amount (equiv.)	Yield (%)	Selectivity ( $\beta:\alpha$ )

1	No oxidant	trace	-
2	1	20	2:1
3	2	24	13:1
4	2.2	62	18:1
5	2.4	76	20:1
6	2.6	81	>20:1
7	2.8	80	>20:1
<b>8</b>	<b>3</b>	<b>85</b>	<b>&gt;20:1</b>
9	4	78	18:1
10	5	61	10:1

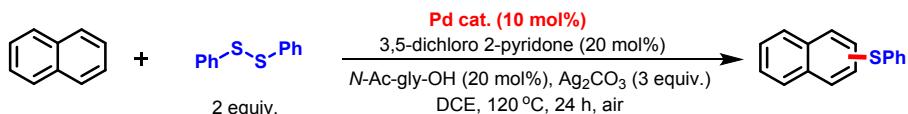
**Table S7:** Time optimization.



Entry	Time (h)	Yield (%)	Selectivity ( $\beta:\alpha$ )
1	4	16	-
2	8	21	-
3	12	40	7:1
4	16	42	8:1
5	20	64	14:1
<b>6</b>	<b>24</b>	<b>85</b>	<b>&gt;20:1</b>
7	28	79	20:1
8	32	76	20:1
9	36	84	16:1
10	40	87	14:1

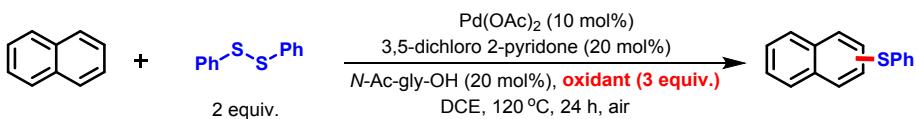
11	44	70	10:1
12	48	50	5:1
13	52	44	3:1

**Table S8:** Pd catalyst optimization.



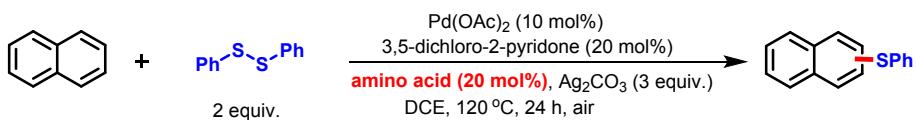
Entry	Pd cat (10 mol%)	Yield (%)	Selectivity ( $\beta:\alpha$ )
1	Pd(CH <sub>3</sub> CN) <sub>2</sub> Cl <sub>2</sub>	n.r.	-
2	tris(dibenzylidene acetone)dipalladium	n.r.	-
3	[1,1'-bis(diphenyl phosphino)ferrocene]dichloro palladium	n.r.	-
4	Pd(OPiv) <sub>2</sub>	n.r.	-
5	Pd(PPh <sub>3</sub> ) <sub>4</sub>	n.r.	-
6	Pd(PPh <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub>	n.r.	-
7	Pd(OTf) <sub>2</sub>	n.r.	-
8	Pd(acac) <sub>2</sub>	n.r.	-
9	Pd(PhCN) <sub>2</sub> Cl <sub>2</sub>	n.r.	-
10	Pd(pi-cinamyl)chloride dimer	n.r.	-
11	PdCl <sub>2</sub>	n.r.	-
12	Tetrakis(acetonitrile)Pd(II)tetrafluoroborate	n.r.	-
13	Dichloro(1,5-cyclooctadiene)Pd(II)	n.r.	-
14	Pd(II)(OCOCMe <sub>3</sub> ) <sub>2</sub>	n.r.	-
15	<b>Pd(OAc)<sub>2</sub></b>	<b>85</b>	<b>&gt;20:1</b>

**Table S9:** Oxidant optimization.



Entry	Oxidant	Yield (%)	Selectivity ( $\beta:\alpha$ )
1	No oxidant	trace	-
2	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	trace	-
3	Na <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	trace	-
4	AgOAc	78	16:1
5	<b>Ag<sub>2</sub>CO<sub>3</sub></b>	<b>85</b>	<b>&gt;20:1</b>
6	Cu(I)OAc	n.r.	-
7	Cu(OAc) <sub>2</sub>	54	3:1
8	CuO	trace	-
9	Cu(I)O	n.r.	-
10	Benzoquinone	trace	-
11	Ag <sub>2</sub> CO <sub>3</sub> + O <sub>2</sub>	78	18:1
12	(NH <sub>4</sub> ) <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	trace	-
13	Oxone	trace	-
14	TBHP in H <sub>2</sub> O	n.r.	-
15	AgNO <sub>3</sub>	12	-
16	Ag <sub>2</sub> SO <sub>4</sub>	trace	-
17	Ag <sub>2</sub> O	59	10:1
18	MnO <sub>2</sub>	n.r.	-

**Table S10:** Amino acid ligand optimization.



Entry	Amino acid (20 mol%)	Yield (%)	Selectivity ( $\beta:\alpha$ )
1	<i>N</i> -Cbz-DL-Val	n.r.	-
2	<i>N</i> -Bn-carbonyl-PheAla	n.r.	-
3	<i>N</i> -Ac-DL-Trp	trace	-
4	<i>N</i> -Boc-Tle-OH	n.r.	-
5	<i>N</i> -Ac-DL-Val	20	2:1
6	<i>N</i> -Boc-Alb-OH	n.r.	-
7	<i>N</i> -Fmoc-DL-Leu	n.r.	-
8	<i>N</i> -Ac-DL-NorLeu	14	1:1
9	<i>N</i> -Ac-DL-aminobutyric acid	trace	-
10	<i>N</i> -Ac-DL-Met	12	1:1
11	<i>N</i> -Boc-Gly-OH	15	4:1
12	<i>N</i> -Boc-Ile	n.r.	-
13	Glycine	n.r.	-
14	<i>N</i> -Boc-L-Tyr	n.r.	-
15	<b><i>N</i>-Ac-Gly-OH</b>	<b>85</b>	<b>&gt;20:1</b>

## 2.2. General procedures

### General procedure A: Non-directed chalcogenation of arenes and heteroarenes:

In a clean, oven-dried screw cap reaction tube containing magnetic stir-bar, arene or heteroarene (0.1 mmol), Pd(OAc)<sub>2</sub> (10 mol%, 0.01 mmol), *N*-Acetyl glycine (20 mol%, 0.02 mmol), 3,5-dichloro-2-pyridone (20 mol%, 0.02 mmol), corresponding diaryl disulfides or diselenides (2 eq, 0.2 mmol) and silver carbonate (3 eq, 0.3 mmol) were weighed. Common laboratory syringe was used to introduce DCE (2 ml) into the reaction mixture. Then the tube was placed in a preheated oil bath at 120 °C and the reaction were stirred (at 1000 rpm) vigorously for 24 h. After detaching the reaction, it was cooled to room temperature and filtered through celite pad using ethyl acetate (30 ml). Solvent was removed in rotatory evaporator. Desired compound was extracted using EtOAc and combined organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>. Finally, it was concentrated in reduced pressure and was purified by column chromatography through silica gel (100-200 mesh size) using PET-ether / ethyl acetate as eluent.

### **General procedure B: Chalcogenation of 2-hydroxy pyridines:**

In a clean, oven-dried screw cap reaction tube containing magnetic stir-bar, corresponding pyridone moiety (0.1 mmol), Pd(OAc)<sub>2</sub> (10 mol%, 0.01 mmol), corresponding disulphide or diselenide (2 eq, 0.2 mmol) and silver carbonate (3 eq, 0.3 mmol) were weighed. Common laboratory syringe was used to introduce chlorobenzene (2 ml) into the reaction mixture. Then the tube was placed in a preheated oil bath at 120 °C and the reaction were stirred (at 1000 rpm) vigorously for 24 h. After detaching the reaction, it was cooled to room temperature and filtered through celite pad using ethyl acetate (30 ml). Solvent was removed in rotatory evaporator. Desired compound was extracted using EtOAc and combined organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>. Finally, it was concentrated in reduced pressure and was purified by column chromatography through silica gel (100-200 mesh size) using PET-ether / ethyl acetate as eluent.

### **General procedure C: Amination of (2-chlorophenyl)(2-nitrophenyl)sulfane:<sup>2</sup>**

2-((2-chlorophenyl)thio)aniline (1 mmol, 235 mg) was dissolved in HCl (1 ml) and granulated tin (1.5 eq) were subsequently added and boiled in a water bath for 30-60 min. After cooling, the reaction mixture was diluted with saturated solution of NaOH. The resultant residue was further diluted with ether, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. Purification by column chromatography through silica gel (100-200 mesh size) afforded the brown semi-liquid in 68% yield.

### **General procedure D: Cyclization of 2-((2-chlorophenyl)thio)aniline:<sup>3</sup>**

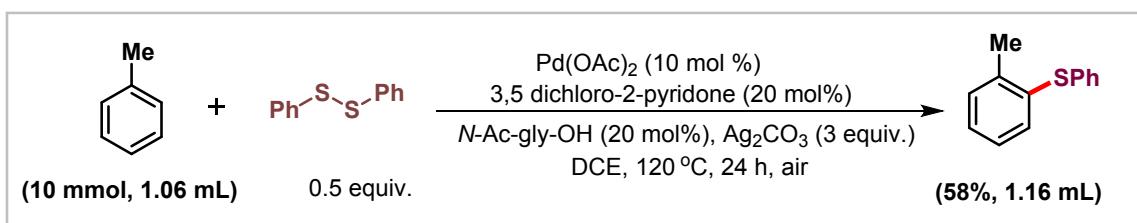
2-((2-chlorophenyl)thio)aniline (1 mmol, 235 mg) was dissolved in DMF (1 ml) and Na<sub>2</sub>CO<sub>3</sub> (1 eq), freshly generated copper (20 mol%) and freshly purified CuI (20 mol%) were subsequently added and heated at reflux for 24 h. After cooling, the crude product was isolated by precipitation from cold brine solution and filtration. The resultant residue was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. Purification by column chromatography through silica gel (100-200 mesh size) using PET-ether afforded the off-white solid in 15% yield.

## **2.3. Synthetic applications of non-directed thioarylation protocol**

### **Gram scale synthesis of phenyl(o-tolyl)sulfane:**

A clean, oven-dried 50 ml round bottle flask with previously placed magnetic stir-bar was charged with toluene (10 mmol, 1.06 ml), palladium(II) acetate (10 mol%, 1 mmol, 224 mg),

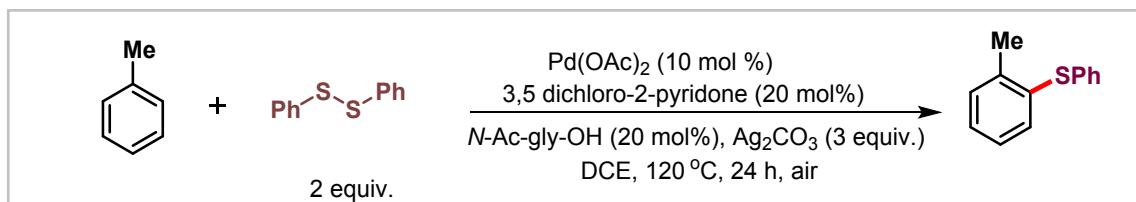
*N*-acetyl glycine (20 mol%, 2 mmol, 234.2 mg), 3,5-dichloro-2-pyridone (20 mol%, 2 mmol, 295.98 mg) and  $\text{Ag}_2\text{CO}_3$  (3 equiv., 30 mmol, 8.27 g) and diphenyl disulfide (0.5 equiv., 5 mmol, 1.09 g) were introduced in this reaction mixture in air atmosphere. DCE (20 ml) was added to this mixture by syringe. The reaction mixture was vigorously stirred for 24 h in a preheated oil bath at 120 °C. After the stipulated time, the reaction mixture was cooled to room temperature and filtered through a celite bed using ethyl acetate as the eluent (50 ml). The diluted ethyl acetate solution of the reaction mixture was subsequently washed with saturated brine solution (2 x 15 mL) followed by water (2 x 15 mL). The ethyl acetate layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and the volatiles were removed under vacuum. The crude reaction mixture was purified by column chromatography using silica gel and petroleum ether/ethyl acetate as the eluent (100:0) to give the desired toluene thioarylated product in gram scale (58%, 1.16 mL).



## 2.4. Mechanistic investigations

**$K_H/K_D$  experiments:** To understand the reversibility of the protocol and to learn more about the rate-determining step of the reaction, we tried to perform the kinetic isotope effect experiment. Various substrates such as toluene, pyridine and benzene were treated towards the kinetic isotope experiment to predict the importance of C–H activation step in the overall methodology. The results are as follows-

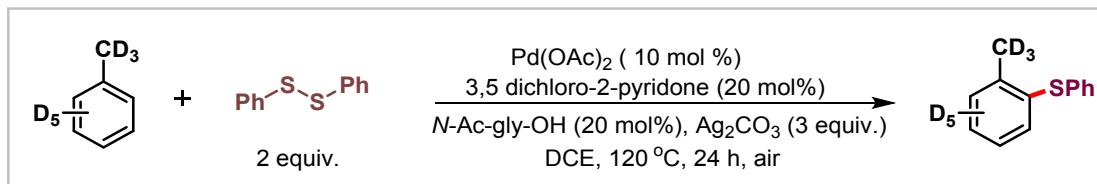
### Substrate- Toluene



**Set I:** Yield with toluene.

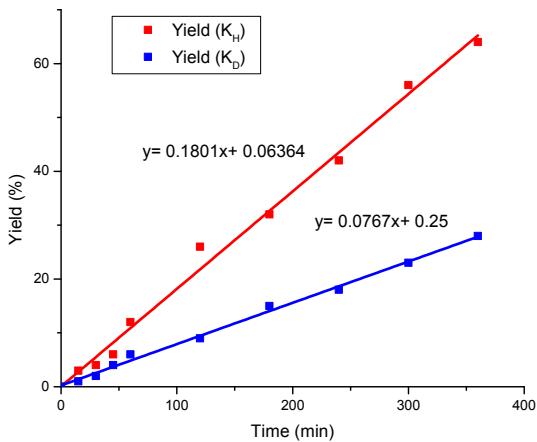
Sl. No.	Time (min)	Yield (%)
---------	------------	-----------

1	0	0
2	15	3
3	30	4
4	45	6
5	60	12
6	120	26
7	180	32
8	240	42
9	300	56
10	360	64



**Set II:** Yield with  $d_8$ -toluene.

Sl. No.	Time (min)	Yield (%)
1	0	0
2	15	1
3	30	2
4	45	4
5	60	6
6	120	9
7	180	15
8	240	18
9	300	23
10	360	28



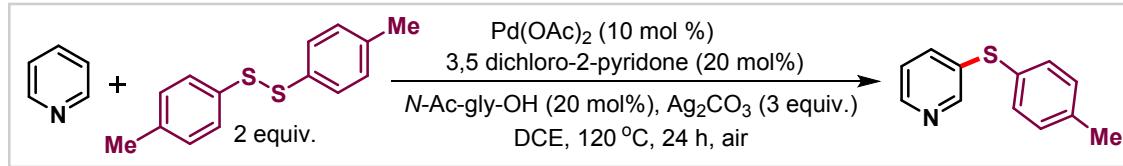
$$K_H/K_D = \text{slope of line 1} / \text{slope of line 2}$$

$$= 0.1801/0.0767$$

$$= 2.35$$

➤  $K_H/K_D : 2.35$

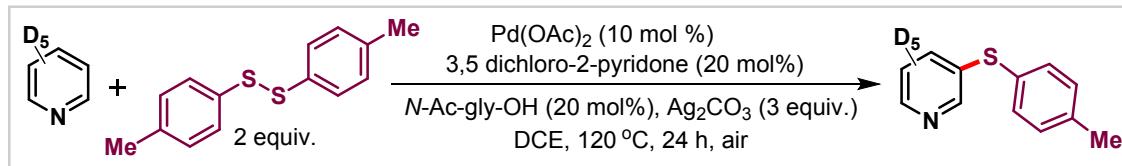
### Substrate- Pyridine



**Set III:** Yield with pyridine.

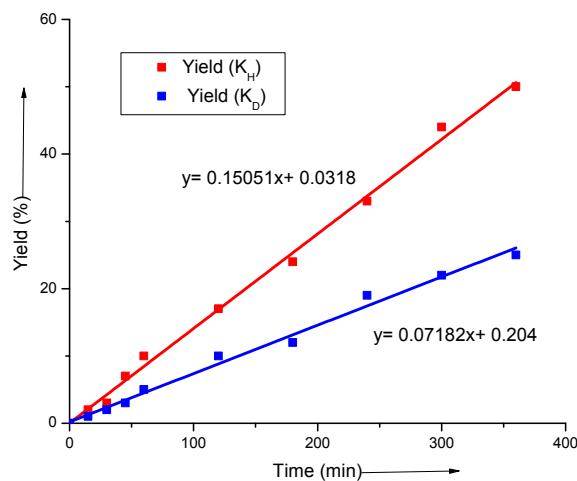
Sl. No.	Time (min)	Yield (%)
1	0	0
2	15	2
3	30	3
4	45	7
5	60	10
6	120	17
7	180	24
8	240	33

9	300	44
10	360	50



**Set IV:** Yield with  $d_5$ -pyridine.

Sl. No.	Time (min)	Yield (%)
1	0	0
2	15	1
3	30	2
4	45	3
5	60	5
6	120	10
7	180	12
8	240	19
9	300	22
10	360	25



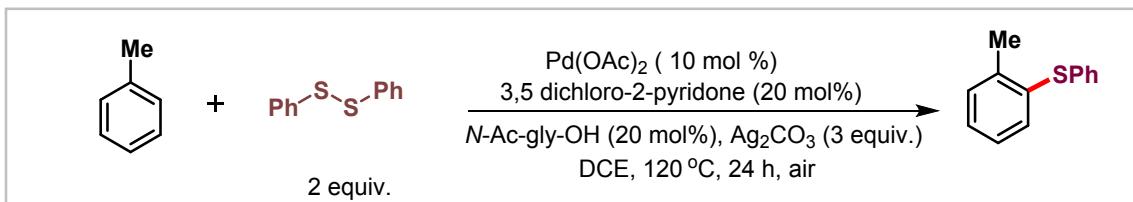
$$K_H/K_D = \text{slope of line 1} / \text{slope of line 2}$$

$$= 0.15051 / 0.07182$$

$$= 2.1$$

➤  $K_H / K_D : 2.1$

**Order determination studies:** To probe more about the mechanistic insight and to get a full proof idea about the components involved in the rate-determining step of the reaction, we carried out the order determination studies using toluene as substrate with respect to substrate, disulphide, partial order with respect to metal catalyst and ligand. The results are as follows-



### Set I: Order with respect to substrate.

Run	Toluene (mmol)	Disulphide (mmol)	Pd(OAc) <sub>2</sub> (mmol)	Ag <sub>2</sub> CO <sub>3</sub> (mmol)	Amino acid ligand (mmol)	DCE (ml)	Pyridone ligand (mmol)
1	0.1	0.2	0.01	0.3	0.02	1	0.02
2	0.05	0.2	0.01	0.3	0.02	1	0.02

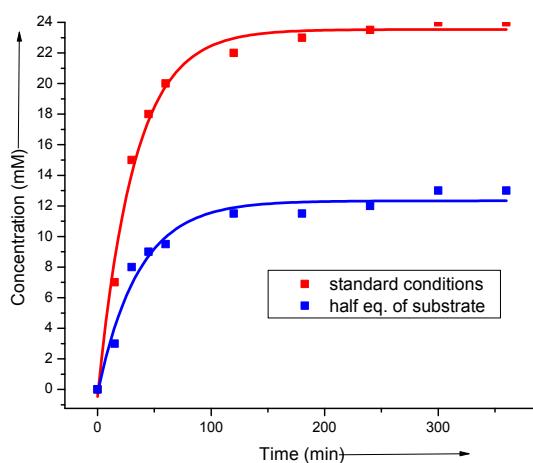
### Run 1.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	7
3	30	15
4	45	18
5	60	20
6	120	22

7	180	23
8	240	23.5
9	300	24
10	360	24

## Run 2.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	3
3	30	8
4	45	9
5	60	9.5
6	120	11.5
7	180	11.5
8	240	12
9	300	13
10	360	13



$$\text{Rate} = [\text{Toluene}]^x[\text{disulphide}]^y$$

For Run 1, initial rate, Rate 1 =  $k \cdot [0.1]^x[0.2]^y$

For Run 2, initial rate, Rate 2 =  $k \cdot [0.05]^x[0.2]^y$

$$1.223 = k \cdot [0.1]^x[0.2]^y$$

$$0.586 = k \cdot [0.05]^x[0.2]^y$$

$$\text{Hence, Rate 2 / Rate 1} = [0.1/0.2]^x$$

$$\log(0.586/1.223) = x \log(0.5)$$

$$x = 1.05 \sim 1$$

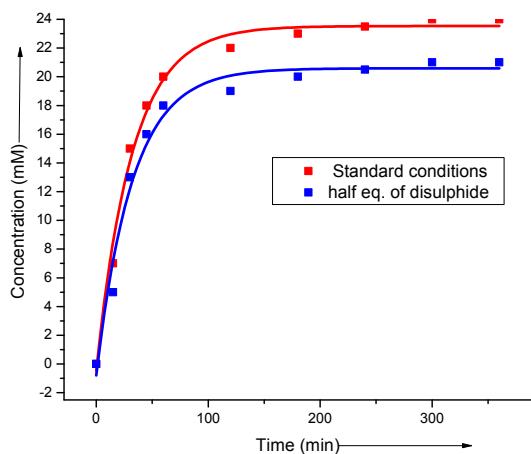
Hence, order with respect to substrate ~ 1

Set II: Order with respect to disulphide.

Run	Toluene (mmol)	Disulphide (mmol)	Pd(OAc) <sub>2</sub> (mmol)	Ag <sub>2</sub> CO <sub>3</sub> (mmol)	Amino acid ligand (mmol)	DCE (mL)	Pyridone ligand (mmol)
1	0.1	0.2	0.01	0.3	0.02	1	0.02
3	0.1	0.1	0.01	0.3	0.02	1	0.02

Run 3.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	5
3	30	13
4	45	16
5	60	18
6	120	19
7	180	20
8	240	20.5
9	300	21
10	360	21



$$\text{Rate} = [\text{Toluene}]^x[\text{disulphide}]^y$$

For Run 1, initial rate, Rate 1 =  $k \cdot [0.1]^x[0.2]^y$

For Run 3, initial rate, Rate 3 =  $k \cdot [0.1]^x[0.1]^y$

$$1.223 = k \cdot [0.1]^x[0.2]^y$$

$$1.113 = k \cdot [0.1]^x[0.1]^y$$

Hence, Rate 3 / Rate 1 =  $[0.1/0.2]^y$

$$\log(1.113/1.223) = y \log(0.5)$$

$$y = 0.16 \sim 0$$

**Hence, order with respect to disulphide  $\sim 0$**

**Set III: Order with respect to metal catalyst.**

Run	Toluene (mmol)	Disulphide (mmol)	Pd(OAc) <sub>2</sub> (mmol)	Ag <sub>2</sub> CO <sub>3</sub> (mmol)	Amino acid ligand (mmol)	DCE (mL)	Pyridone ligand (mmol)
4	0.1	0.2	2.5 mol%	0.3	0.02	1	0.02
5	0.1	0.2	5 mol%	0.3	0.02	1	0.02
6	0.1	0.2	7.5 mol%	0.3	0.02	1	0.02
1	0.1	0.2	10 mol%	0.3	0.02	1	0.02

**Run 4-** With 2.5 mol% of Pd(OAc)<sub>2</sub>.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0

2	15	2
3	30	3
4	45	4
5	60	6
6	120	8
7	180	11
8	240	12
9	300	12.5

**Run 5-** With 5 mol% of Pd(OAc)<sub>2</sub>.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	3.5
3	30	7
4	45	7.5
5	60	8
6	120	10
7	180	11
8	240	14
9	300	15

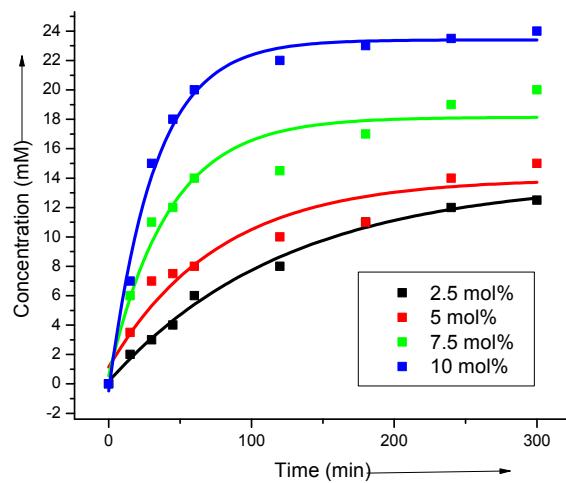
**Run 6-** With 7.5 mol% of Pd(OAc)<sub>2</sub>.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	6
3	30	11
4	45	12
5	60	14
6	120	14.5

7	180	17
8	240	19
9	300	20

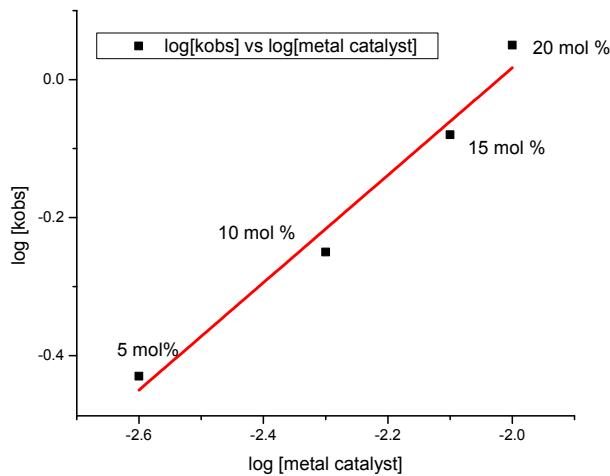
**Run 1-** With 10 mol% of Pd(OAc)<sub>2</sub>.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	7
3	30	15
4	45	18
5	60	20
6	120	22
7	180	23
8	240	23.5
9	300	24



Pd(OAc) <sub>2</sub> loading	Log [Pd(OAc) <sub>2</sub> ]	Log [k <sub>obs</sub> ]
2.5 mol%	-2.6	-0.43
5 mol%	-2.3	-0.25
7.5 mol%	-2.1	-0.08

10 mol%	-2	0.05
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From the plot, slope= 0.92.

**Hence, the order with respect to metal catalyst~ 1**

#### Set IV: Order with respect to amino acid ligand.

Run	Toluene (mmol)	Disulphide (mmol)	Pd(OAc) <sub>2</sub> (mmol)	Ag <sub>2</sub> CO <sub>3</sub> (mmol)	Amino acid ligand (mmol)	DCE (mL)	Pyridone ligand (mmol)
7	0.05	0.1	10 mol%	0.15	10 mol%	1	20 mol%
1	0.05	0.1	10 mol%	0.15	20 mol%	1	20 mol%
8	0.05	0.1	10 mol%	0.15	30 mol%	1	20 mol%
9	0.05	0.1	10 mol%	0.15	40 mol%	1	20 mol%

**Run 7-** With 10 mol% of *N*-Acetyl glycine.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	4
3	30	8

4	45	10
5	60	11
6	120	13
7	180	14
8	240	15
9	300	16

**Run 1-** With 20 mol% of *N*-Acetyl glycine.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	7
3	30	15
4	45	18
5	60	20
6	120	22
7	180	23
8	240	23.5
9	300	24

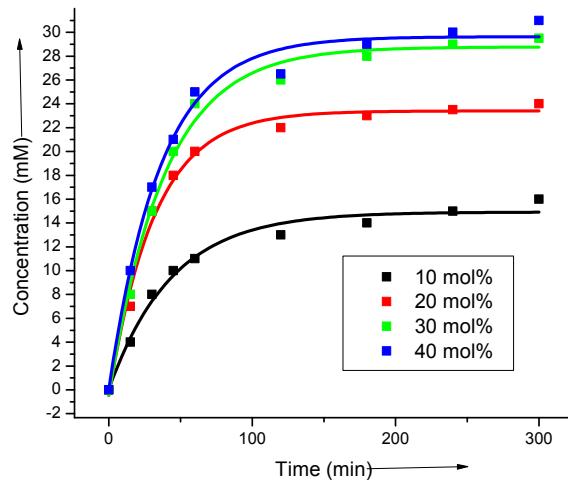
**Run 8-** With 30 mol% of *N*-Acetyl glycine.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	8
3	30	15
4	45	20
5	60	24
6	120	26
7	180	28
8	240	29

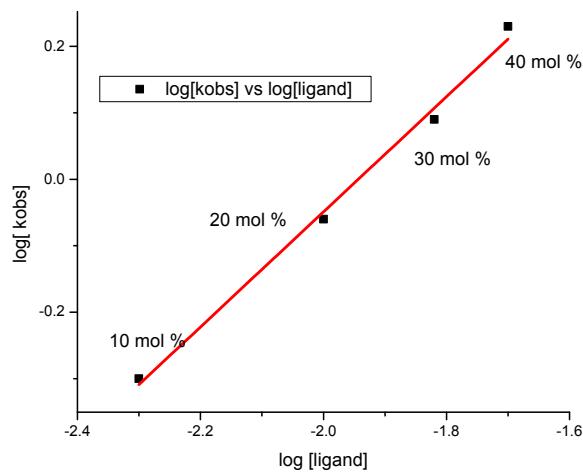
9	300	29.5
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**Run 9- With 40 mol% of *N*-Acetyl glycine.**

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	10
3	30	17
4	45	21
5	60	25
6	120	26.5
7	180	29
8	240	30
9	300	31



Amino acid loading	Log [amino acid]	Log [ $k_{obs}$ ]
10 mol%	-2.3	-0.3
20 mol%	-2	-0.06
30 mol%	-1.82	0.09
40 mol%	-1.7	0.23



From the plot, slope= 0.87.

**Hence, the order with respect to amino acid ligand~ 1**

#### Set V: Order with respect to pyridone ligand.

Run	Toluene (mmol)	Disulphide (mmol)	Pd(OAc) <sub>2</sub> (mmol)	Ag <sub>2</sub> CO <sub>3</sub> (mmol)	Amino acid ligand (mmol)	DCE (mL)	Pyridone ligand (mmol)
10	0.05	0.1	10 mol%	0.15	20 mol%	1	10 mol%
1	0.05	0.1	10 mol%	0.15	20 mol%	1	20 mol%
11	0.05	0.1	10 mol%	0.15	20 mol%	1	30 mol%
12	0.05	0.1	10 mol%	0.15	20 mol%	1	40 mol%

**Run 7-** With 10 mol% of 3,5-dichloro-2-pyridone.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	3
3	30	7
4	45	9

5	60	12
6	120	14
7	180	15
8	240	16
9	300	16.5

**Run 1-** With 20 mol% of 3,5-dichloro-2-pyridone.

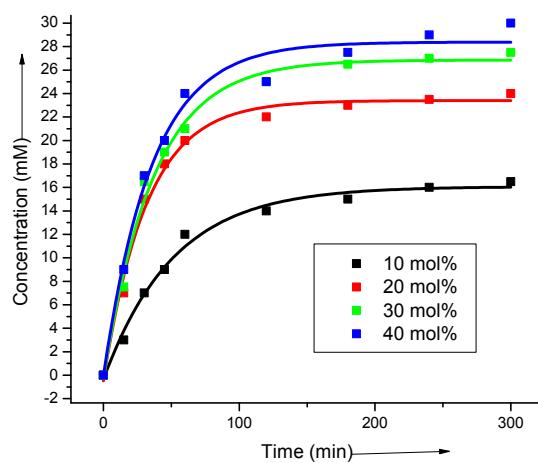
Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	7
3	30	15
4	45	18
5	60	20
6	120	22
7	180	23
8	240	23.5
9	300	24

**Run 8-** With 30 mol% of 3,5-dichloro-2-pyridone.

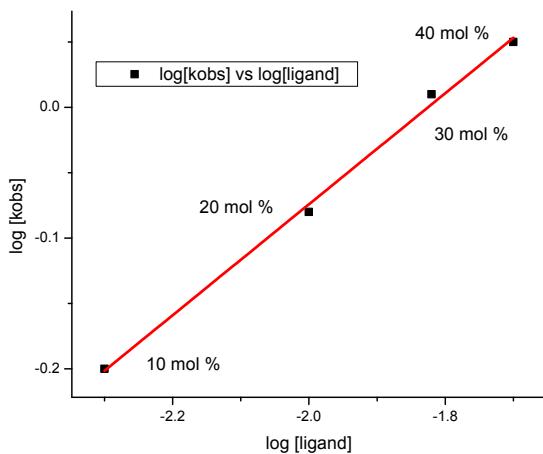
Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	7.5
3	30	16.5
4	45	19
5	60	21
6	120	25
7	180	26.5
8	240	27
9	300	27.5

**Run 9-** With 40 mol% of 3,5-dichloro-2-pyridone.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	9
3	30	17
4	45	20
5	60	24
6	120	25
7	180	27.5
8	240	29
9	300	30



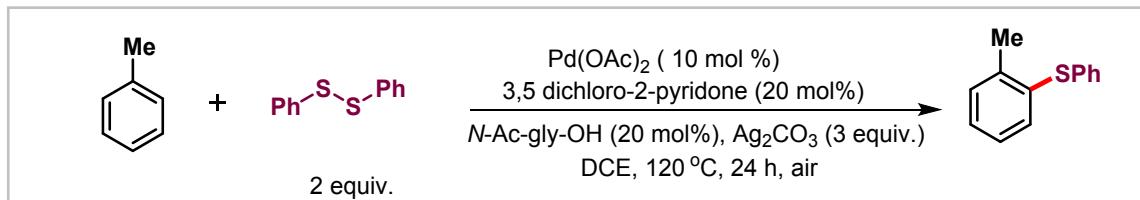
Pyridone loading	Log [pyridone]	Log [ $k_{obs}$ ]
10 mol%	-2.3	-0.2
20 mol%	-2	-0.08
30 mol%	-1.82	0.01
40 mol%	-1.7	0.05



From the plot, slope= 0.506.

**Hence, the order with respect to pyridone ligand~ 0.5**

**Kinetic role of each ligand:** To determine the role of each ligand in the reaction mechanism, we have carried out our methodology in different combinations of ligand. One case involves both the ligands while the other cases involve the reaction in absence of either ligands. Following their results, we have tried to plot the role each ligand plays.



The results are as follows-

**Run 1- Using both ligands.**

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	7
3	30	15
4	45	18
5	60	20
6	120	22

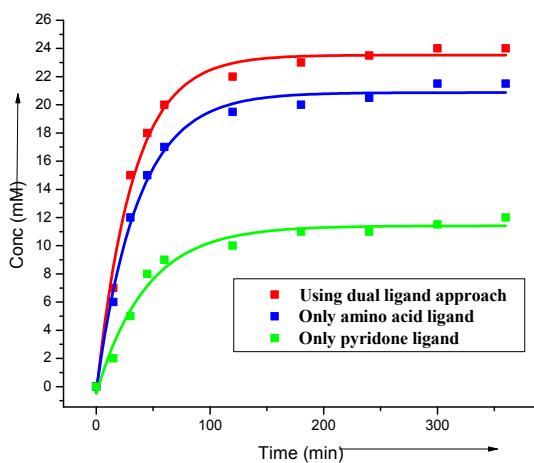
7	180	23
8	240	23.5
9	300	24

**Run 2-** Using only *N*-Acetyl glycine ligand.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	6
3	30	12
4	45	15
5	60	17
6	120	19.5
7	180	20
8	240	20.5
9	300	21.5

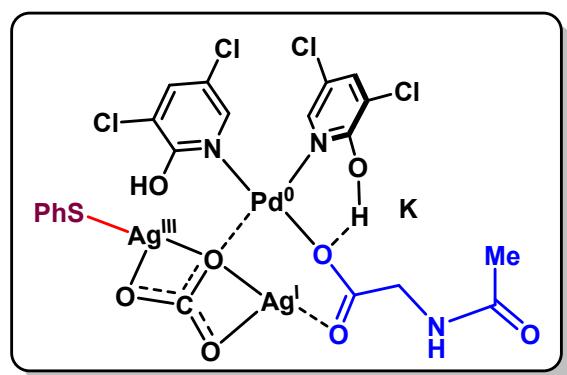
**Run 3-** Using only 3,5-dichloro-2-pyridone ligand.

Sl. No.	Time (min)	Product Concentration (mM)
1	0	0
2	15	2
3	30	5
4	45	8
5	60	9
6	120	10
7	180	11
8	240	11
9	300	11.5

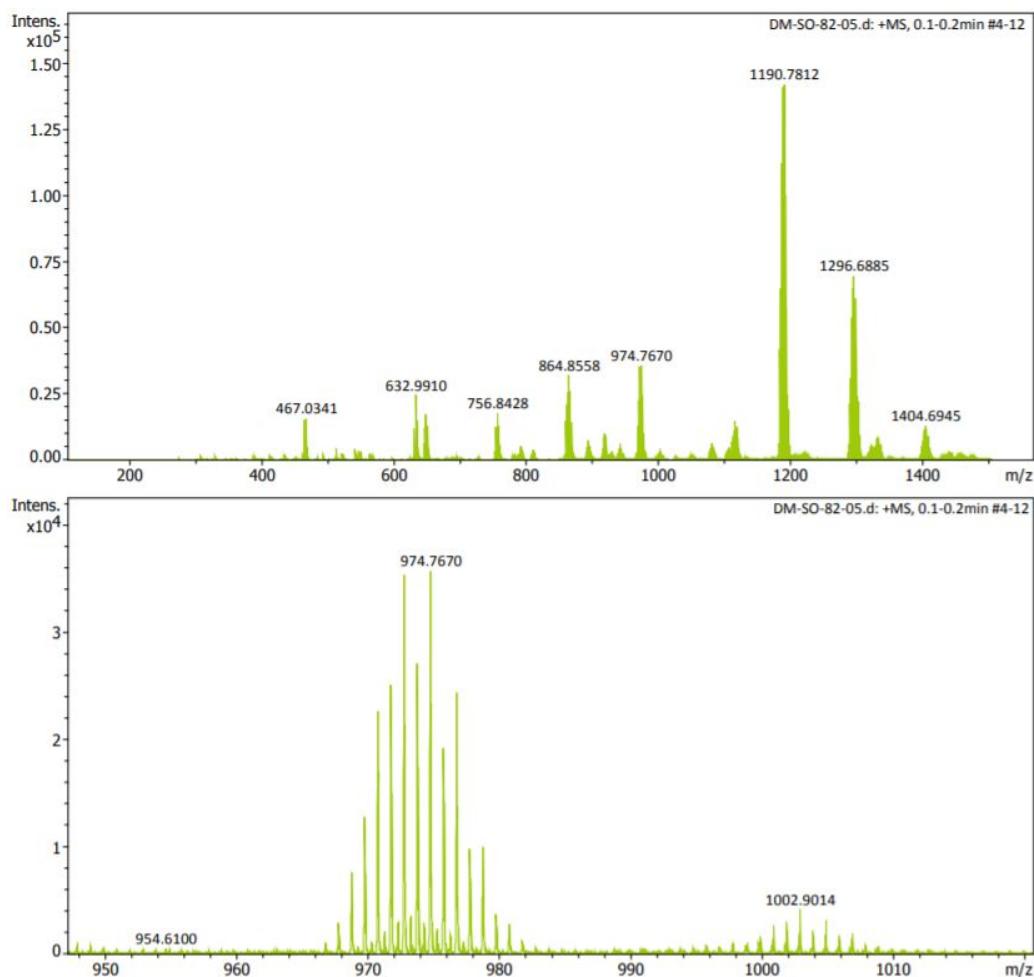


## 2.5 Mass analysis for Pd–Ag heterometallic intermediate:

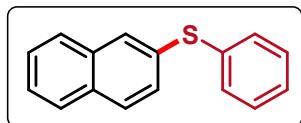
A clean, oven-dried screw cap reaction tube was charged with a magnetic stir-bar,  $\text{Pd}(\text{OAc})_2$  (10 mol%),  $\text{Ph}_2\text{S}_2$  (2 equiv),  $\text{Ag}_2\text{CO}_3$  (3 equiv) and naphthalene (0.05 mmol) and the dual ligands (3,5-dichloro-2-pyridone, 20 mol%; *N*-Acetyl glycine, 20 mol%). Then 1 mL of dichloroethane (DCE) was added. The reaction tube was screwed by a cap fitted with a rubber septum. The reaction mixture was stirred vigorously on a preheated oil bath at 100 °C for 12 h. The crude reaction mixture was subjected to mass analysis. The result is as shown below:



LRMS ( $\text{M} + \text{K}^+$ ): calcd. For  $\text{C}_{21}\text{H}_{18}\text{Ag}_2\text{Cl}_4\text{N}_3\text{O}_8\text{PdSK}$  974.6343. obtained. 974.7670



### 3. Characterization data



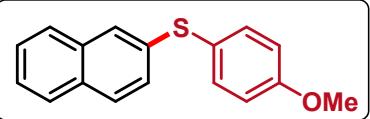
**Naphthalen-2-yl(phenyl)sulfane (Scheme 2A, entry 2a):**

**Yield:** 78%

**Physical state:** Colourless liquid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (100/0, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.90 – 7.87 (m, 1H), 7.86 – 7.73 (m, 3H), 7.53 – 7.48 (m, 2H), 7.45 (dd,  $J = 8.6, 1.7$  Hz, 1H), 7.43 (d,  $J = 1.4$  Hz, 1H), 7.41 (s, 1H), 7.38 – 7.32 (m, 2H), 7.31 – 7.27 (m, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  135.97, 133.92, 133.14, 132.42, 131.09, 130.02, 129.36, 128.99, 128.88, 127.87, 127.56, 127.20, 126.73, 126.34. **HRMS (ESI-TOF)** m/z:  $[\text{M} + \text{K}]^+$  calcd for  $\text{C}_{16}\text{H}_{12}\text{KS}$ : 275.0349, found: 275.0399.



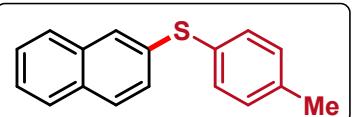
**(4-methoxyphenyl)(naphthalen-2-yl)sulfane (Scheme 2A, entry 2b):<sup>4</sup>**

**Yield:** 85%

**Physical state:** Yellow semi-solid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (98/2, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.44 (d,  $J = 8.6$  Hz, 2H), 7.40 (d,  $J = 8.5$  Hz, 1H), 7.19 (d,  $J = 8.5$  Hz, 1H), 7.14 (t,  $J = 7.8$  Hz, 1H), 7.08 (s, 1H), 7.07 – 7.05 (m, 1H), 7.00 (d,  $J = 7.7$  Hz, 1H), 6.93 (d,  $J = 8.6$  Hz, 2H), 6.90 (d,  $J = 8.8$  Hz, 1H), 3.84 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 160.49, 141.47, 136.27, 135.63, 134.96, 129.98, 129.50, 129.16, 127.23, 125.76, 125.65, 123.77, 122.55, 115.39, 55.54.



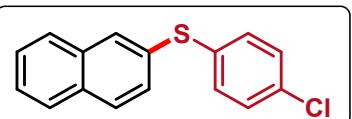
**Naphthalen-2-yl(p-tolyl)sulfane (Scheme 2A, entry 2c):**

**Yield:** 87%

**Physical state:** Yellow liquid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (99.5/0.5, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.81 – 7.78 (m, 1H), 7.74 (d,  $J = 8.7$  Hz, 2H), 7.72 – 7.70 (m, 1H), 7.45 (ddd,  $J = 6.8, 4.3, 1.6$  Hz, 2H), 7.38 – 7.35 (m, 1H), 7.34 (d,  $J = 8.1$  Hz, 2H), 7.16 (d,  $J = 8.0$  Hz, 2H), 2.36 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 137.75, 134.47, 133.91, 132.25, 132.16, 131.52, 130.24, 128.82, 128.52, 128.04, 127.85, 127.43, 126.67, 126.05, 21.29. **HRMS m/z:** [M + H]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>15</sub>S: 251.0889, found: 251.0879.



**(4-chlorophenyl)(naphthalen-2-yl)sulfane (Scheme 2A, entry 2d):**

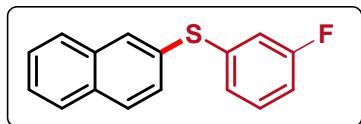
**Yield:** 82%

**Physical state:** Yellowish semi-liquid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (100/0, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.85 (s, 1H), 7.83 – 7.80 (m, 1H), 7.78 (d,  $J = 8.6$  Hz, 1H), 7.77 – 7.74 (m, 1H), 7.51 – 7.47 (m, 2H), 7.39 (dd,  $J = 8.6, 1.8$  Hz, 1H), 7.29 – 7.27 (m, 4H). **<sup>13</sup>C**

**NMR (101 MHz, CDCl<sub>3</sub>)** δ 134.82, 133.90, 132.56, 132.42, 133.15, 132.08, 130.48, 129.50, 129.22, 128.90, 127.90, 127.60, 126.88, 126.59. **LRMS m/z:** [M + Na]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>11</sub>ClS: 293.0168, found: 293.1788.



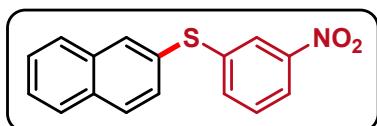
**(3-fluorophenyl)(naphthalen-2-yl)sulfane (Scheme 2A, entry 2e):**

**Yield:** 79%

**Physical state:** Orange semi-liquid.

**TLC:** R<sub>f</sub> = 0.1; petroleum ether/ethyl acetate (100/0, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.96 (s, 1H), 7.85 (d, J = 3.5 Hz, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.79 (dd, J = 6.0, 3.4 Hz, 1H), 7.52 (dd, J = 6.2, 3.2 Hz, 2H), 7.46 (dd, J = 8.5, 1.7 Hz, 1H), 7.24 (dd, J = 8.0, 6.0 Hz, 1H), 7.09 (d, J = 7.9 Hz, 1H), 6.99 (dt, J = 9.3, 2.0 Hz, 1H), 6.91 (td, J = 8.3, 2.0 Hz, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 164.15, 162.18, 139.42, 133.93, 132.83, 131.92, 131.10, 130.49, 130.43, 129.75, 129.35, 127.92, 127.74, 126.89, 126.83, 125.28, 125.26, 116.62, 116.44, 113.74, 113.57. **<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -111.95. **LRMS m/z:** [M + Na]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>11</sub>FS: 254.0565, found: 254.0382.



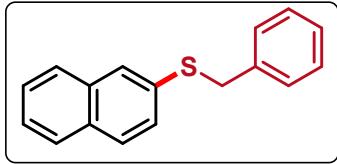
**naphthalen-2-yl(3-nitrophenyl)sulfane (Scheme 2A, entry 2f):**

**Yield:** 82%

**Physical state:** Yellow solid.

**TLC:** R<sub>f</sub> = 0.1; petroleum ether/ethyl acetate (95/5, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 8.10 (t, J = 2.0 Hz, 1H), 8.04 – 8.02 (m, 1H), 8.02 – 7.98 (m, 1H), 7.88 – 7.85 (m, 2H), 7.84 – 7.79 (m, 1H), 7.58 – 7.53 (m, 2H), 7.52 (ddd, J = 7.9, 1.8, 1.0 Hz, 1H), 7.47 (dd, J = 8.6, 1.8 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 148.79, 140.56, 134.43, 133.92, 133.72, 133.09, 129.92, 129.81, 129.80, 129.39, 127.96, 127.82, 127.24, 127.08, 123.33, 121.09. **LRMS m/z:** [M + H]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>12</sub>O<sub>2</sub>NS: 282.0510, found: 282.0522.



**Benzyl(naphthalen-2-yl)sulfane (Scheme 2A, entry 2g):**

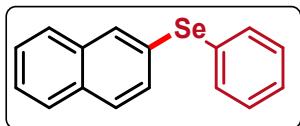
**Yield:** 74%

**Physical state:** Yellow liquid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (100/0, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.78 (d,  $J = 7.6$  Hz, 1H), 7.75 – 7.71 (m, 2H), 7.70 (s, 1H), 7.48 – 7.43 (m, 2H), 7.40 (dd,  $J = 8.7, 1.7$  Hz, 1H), 7.33 (d,  $J = 7.3$  Hz, 2H), 7.29 (t,  $J = 7.3$  Hz, 2H), 7.26 – 7.22 (m, 1H), 4.23 (s, 2H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  137.48, 134.04, 133.84, 132.02, 128.99, 128.68, 128.45, 127.84, 127.83, 127.80, 127.38, 127.29, 126.62, 125.88, 39.06.

**LRMS m/z:** [M + H]<sup>+</sup> calcd. for  $\text{C}_{17}\text{H}_{14}\text{S}$ : 250.0816, found: 250.0802.



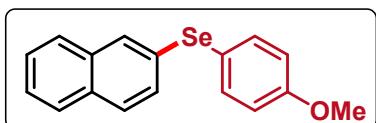
**Naphthalen-2-yl(phenyl)selane (Scheme 2A, entry 2h):<sup>5</sup>**

**Yield:** 80%

**Physical state:** Yellow sticky liquid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (100/0, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.54 (dd,  $J = 6.3, 2.9$  Hz, 3H), 7.34 – 7.31 (m, 5H), 7.21 (dd,  $J = 5.7, 3.5$  Hz, 2H), 7.08 (dd,  $J = 5.8, 3.4$  Hz, 2H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  136.02, 134.92, 134.16, 134.10, 134.05, 133.65, 133.11, 131.11, 130.78, 129.66, 129.54, 128.05, 128.00, 127.81.



**(4-methoxyphenyl)(naphthalen-2-yl)selane (Scheme 2A, entry 2i):**

**Yield:** 72%

**Physical state:** Yellow liquid.

$R_f = 0.1$ ; petroleum ether/ethyl acetate (98/2, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.64 – 7.55 (m, 1H), 7.56 – 7.46 (m, 2H), 7.27 – 7.21 (m, 2H), 7.21 – 7.12 (m, 2H), 7.13 (s, 1H), 6.89 (d,  $J = 2.1$  Hz, 1H), 6.90 – 6.83 (m, 2H), 3.83 (s, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 160.35, 138.75, 137.32, 136.79, 135.59, 135.06, 132.26, 130.18, 130.06, 129.39, 128.46, 126.56, 119.71, 118.92, 55.47. **LRMS m/z:** [M + H]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>15</sub>OSe: 315.0210, found: 315.0070.



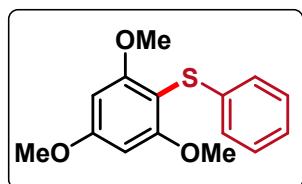
**Diphenylsulfane (Scheme 2A, entry 2j):<sup>6</sup>**

**Yield:** 81%

**Physical state:** Yellowish liquid.

**TLC:** R<sub>f</sub> = 0.6; petroleum ether/ethyl acetate (100/0, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.36 (t, J = 6.4 Hz, 4H), 7.33 (d, J = 7.7 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.13 (q, J = 5.1 Hz, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 131.97, 131.56, 129.49, 127.64.



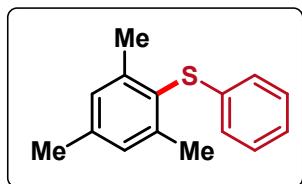
**Phenyl(2,4,6-trimethoxyphenyl)sulfane (Scheme 2A, entry 2k):**

**Yield:** 85%

**Physical state:** Brown semi-liquid.

**TLC:** R<sub>f</sub> = 0.4; petroleum ether/ethyl acetate (98/2, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.15 (t, J = 7.7 Hz, 2H), 7.08 – 6.98 (m, 3H), 6.22 (s, 2H), 3.87 (s, 3H), 3.81 (s, 6H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 163.06, 162.68, 138.80, 131.09, 128.62, 125.74, 124.49, 91.32, 56.44, 55.57. **HRMS (ESI-TOF)** m/z: [M + Na]<sup>+</sup> calcd. for C<sub>15</sub>H<sub>16</sub>NaO<sub>3</sub>S: 299.0761, found: 299.0763.



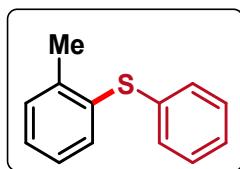
**Mesyl(phenyl)sulfane (Scheme 2A, entry 2l):<sup>7</sup>**

**Yield:** 71%

**Physical state:** Yellow liquid.

**TLC:** R<sub>f</sub> = 0.5; petroleum ether/ethyl acetate (100/0, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.17 (t, *J* = 7.6 Hz, 2H), 7.10 – 7.03 (m, 1H), 7.02 (s, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 2.39 (s, 6H), 2.33 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 143.86, 139.40, 138.53, 129.47, 128.98, 127.08, 125.58, 124.59, 21.89, 21.24.



**Phenyl(o-tolyl)sulfane (Scheme 2A, entry 2m):<sup>4</sup>**

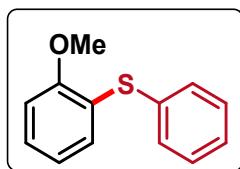
**Yield:** 70%

For isolation purpose, reaction was carried out on 0.05 mmol scale of toluene with 0.5 equiv. of Ph<sub>2</sub>S<sub>2</sub>. Yield and selectivity is determined from the NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene as internal standard.

**Physical state:** Yellow liquid.

**TLC:** R<sub>f</sub> = 0.3; petroleum ether/ethyl acetate (100/0, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.37 – 7.34 (m, 1H), 7.33 – 7.29 (m, 2H), 7.28 – 7.26 (m, 1H), 7.25 – 7.24 (m, 1H), 7.23 – 7.19 (m, 3H), 7.17 – 7.13 (m, 1H), 2.39 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 140.12, 136.29, 133.89, 133.14, 131.17, 130.73, 129.77, 129.26, 128.04, 127.17, 126.85, 126.48, 20.73.



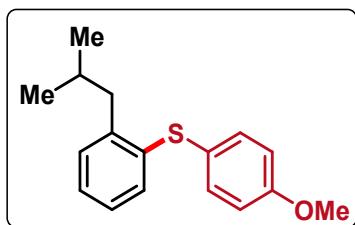
**(2-methoxyphenyl)(phenyl)sulfane (Scheme 2A, entry 2n):<sup>4</sup>**

**Yield:** 60%

**Physical state:** Yellow sticky liquid.

**TLC:** R<sub>f</sub> = 0.1; petroleum ether/ethyl acetate (99/1, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.40 (d, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.28 (q, *J* = 7.8, 7.2 Hz, 2H), 7.14 (d, *J* = 7.7 Hz, 1H), 6.92 (dd, *J* = 17.6, 8.1 Hz, 2H), 3.90 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 157.37, 134.58, 131.69, 131.48, 129.20, 128.42, 127.10, 124.09, 121.30, 110.93, 55.91.



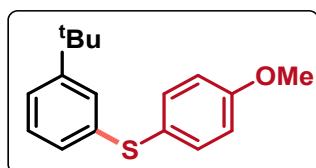
**(3-isobutylphenyl)(4-methoxyphenyl)sulfane (Scheme 2A, entry 2o):**

**Yield:** 61%

**Physical state:** Colourless sticky liquid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (98/2, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.62 – 7.36 (m, 2H), 7.32 (d, *J* = 8.5 Hz, 1H), 7.17 – 7.07 (m, 1H), 7.01 (dd, *J* = 16.5, 10.0 Hz, 2H), 6.92 – 6.85 (m, 2H), 3.82 (s, 3H), 2.47 – 2.35 (m, 2H), 1.81 (dd, *J* = 13.1, 6.6 Hz, 1H), 0.87 (d, *J* = 6.7 Hz, 6H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 159.77, 142.71, 135.03, 129.94, 129.38, 129.03, 128.80, 127.03, 126.03, 115.04, 55.51, 45.36, 29.85, 22.45. **HRMS (ESI-TOF)** m/z: [M + K]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>20</sub>KOS: 311.0866, found: 311.0868.



**(3-(tert-butyl)phenyl)(4-methoxyphenyl)sulfane (Scheme 2A, entry 2p):**

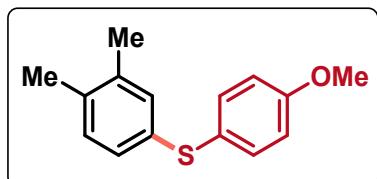
**Yield:** 72%

**Physical state:** Colourless liquid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (98/2, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.40 (dd, *J* = 8.8, 6.8 Hz, 2H), 7.28 (s, 1H), 7.18 – 7.16 (m, 1H), 7.14 (d, *J* = 8.5 Hz, 1H), 6.96 – 6.92 (m, 1H), 6.90 – 6.87 (m, 2H), 3.82 (s, 3H), 1.27 (s, 9H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 159.80, 152.10, 137.94, 135.15, 134.94, 128.68, 126.16, 125.68, 123.17, 115.03, 55.50, 31.35, 29.84. **HRMS (ESI-TOF)** m/z: [M + K]<sup>+</sup> calcd. for C<sub>17</sub>H<sub>20</sub>KOS: 311.0866, found: 311.0866.

For entries 2q-2s, 20 eq. of respective xylene was used.



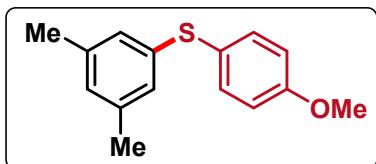
**(3,4-dimethylphenyl)(4-methoxyphenyl)sulfane (Scheme 2A, entry 2q):<sup>8</sup>**

**Yield:** 76%

**Physical state:** Colourless sticky liquid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (98/2, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.39 – 7.30 (m, 2H), 7.07 – 6.94 (m, 3H), 6.87 (s, 2H), 3.81 (s, 3H), 2.26 (dd,  $J = 45.2, 9.6$  Hz, 6H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 159.48, 137.58, 135.09, 134.30, 130.85, 130.42, 127.84, 127.21, 126.00, 114.95, 55.49, 19.86, 19.45.



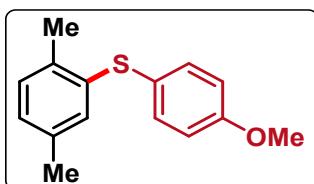
**(3,5-dimethylphenyl)(4-methoxyphenyl)sulfane (Scheme 2A, entry 2r):<sup>8</sup>**

**Yield:** 73%

**Physical state:** Colourless liquid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (98/2, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.38 (s, 1H), 7.23 (s, 1H), 7.02 (s, 1H), 6.93 – 6.85 (m, 2H), 6.85 (d,  $J = 8.9$  Hz, 2H), 3.80 (s, 3H), 2.34 (s, 3H), 2.29 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 159.16, 138.76, 136.89, 135.13, 133.27, 131.40, 128.01, 127.44, 126.38, 115.01, 55.50, 21.35, 20.50.



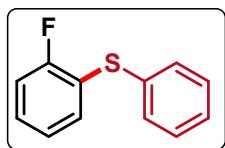
**(2,5-dimethylphenyl)(4-methoxyphenyl)sulfane (Scheme 2A, entry 2s):**

**Yield:** 84%

**Physical state:** Colourless liquid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (98/2, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.32 – 7.28 (m, 2H), 7.07 (d,  $J = 7.6$  Hz, 1H), 6.92 (d,  $J = 7.6$  Hz, 1H), 6.90 – 6.87 (m, 2H), 6.86 (s, 1H), 3.82 (s, 3H), 2.33 (s, 3H), 2.21 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 159.41, 136.30, 136.23, 134.18, 134.11, 130.37, 130.27, 127.39, 125.09, 115.06, 55.49, 21.07, 19.99. **HRMS (ESI-TOF) m/z:** [M + H]<sup>+</sup> calcd. for C<sub>15</sub>H<sub>17</sub>OS: 245.0995, found: 245.0990.



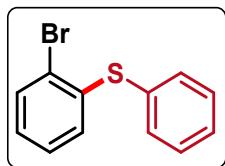
**(2-fluorophenyl)(phenyl)sulfane (Scheme 2A, entry 2t):<sup>9</sup>**

**Yield:** 79%

**Physical state:** Yellowish liquid.

**TLC:**  $R_f = 0.6$ ; petroleum ether/ethyl acetate (99/1, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.36 (t,  $J = 5.9$  Hz, 3H), 7.33 (d,  $J = 7.9$  Hz, 2H), 7.29 (d,  $J = 6.9$  Hz, 2H), 7.12 (q,  $J = 5.1$  Hz, 2H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 137.57, 134.64, 132.19, 131.97, 131.58, 131.56, 131.55, 131.17, 129.50, 127.65. **<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -107.95.



**(2-bromophenyl)(phenyl)sulfane (Scheme 2A, entry 2u):<sup>10</sup>**

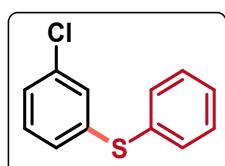
**Yield:** 75%

**Physical state:** Yellow liquid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (100/0, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.57 (d,  $J = 7.5$  Hz, 1H), 7.49 – 7.38 (m, 1H), 7.40 – 7.33 (m, 3H), 7.34 (d,  $J = 1.4$  Hz, 1H), 7.34 – 7.26 (m, 1H), 7.12 (q,  $J = 2.1$  Hz, 2H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 137.56, 136.76, 134.63, 133.77, 131.97, 131.55, 129.50, 128.95, 127.72, 127.65.

For entries 2v-2aa, chlorobenzene was used as solvent.



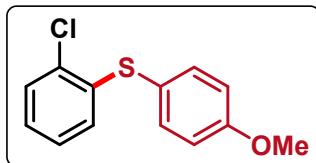
**(3-chlorophenyl)(phenyl)sulfane (Scheme 2A, entry 2v):<sup>4</sup>**

**Yield:** 77%

**Physical state:** Yellow liquid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (97/3, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.79 – 7.74 (m, 1H), 7.66 – 7.59 (m, 1H), 7.46 (d, *J* = 4.4 Hz, 1H), 7.41 – 7.34 (m, 3H), 7.30 (s, 1H), 7.22 (d, *J* = 6.0 Hz, 1H), 7.06 (ddd, *J* = 8.0, 4.9, 1.8 Hz, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 138.98, 137.28, 135.80, 135.21, 134.07, 132.45, 131.08, 130.20, 129.60, 128.10, 128.02, 126.85.



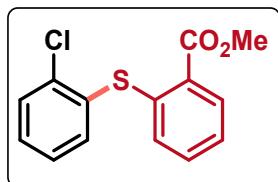
**(2-chlorophenyl)(4-methoxyphenyl)sulfane (Scheme 2A, entry 2w):<sup>11</sup>**

**Yield:** 63%

**Physical state:** Yellow liquid.

**TLC:** R<sub>f</sub> = 0.1; petroleum ether/ethyl acetate (99/1, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.47 (d, *J* = 8.5 Hz, 2H), 7.34 (dd, *J* = 6.0, 3.1 Hz, 1H), 7.07 – 7.02 (m, 2H), 6.96 (d, *J* = 8.5 Hz, 2H), 6.72 (dd, *J* = 6.0, 3.4 Hz, 1H), 3.85 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 160.71, 138.93, 137.02, 131.25, 129.59, 127.75, 127.17, 126.19, 121.89, 115.52, 55.54.



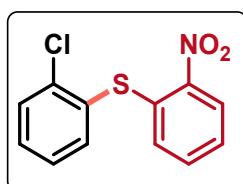
**Methyl 2-((2-chlorophenyl)thio)benzoate (Scheme 2A, entry 2x):**

**Yield:** 78%

**Physical state:** Colourless semi-liquid.

**TLC:** R<sub>f</sub> = 0.4; petroleum ether/ethyl acetate (99/1, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.98 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.56 – 7.45 (m, 1H), 7.43 (d, *J* = 1.7 Hz, 1H), 7.41 (dd, *J* = 3.3, 1.9 Hz, 1H), 7.41 – 7.34 (m, 1H), 7.35 – 7.25 (m, 1H), 7.21 – 7.13 (m, 1H), 6.84 (ddd, *J* = 21.8, 8.1, 0.9 Hz, 1H), 3.95 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 166.97, 141.72, 136.82, 134.82, 133.29, 132.62, 131.21, 130.85, 130.12, 129.29, 128.11, 127.60, 125.05, 52.42. **HRMS (ESI-TOF)** m/z: [M + Na]<sup>+</sup> calcd. for C<sub>14</sub>H<sub>11</sub>ClNaO<sub>2</sub>S: 301.0060, found: 301.0065.



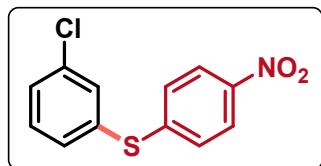
**(2-chlorophenyl)(2-nitrophenyl)sulfane (Scheme 2A, entry 2y):**

**Yield:** 83%

**Physical state:** Yellow solid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (96/4, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  8.26 (dd,  $J = 8.2, 1.4$  Hz, 1H), 7.71 (dd,  $J = 7.6, 1.7$  Hz, 1H), 7.58 (dd,  $J = 8.0, 1.3$  Hz, 1H), 7.46 (td,  $J = 7.7, 1.7$  Hz, 1H), 7.41 – 7.33 (m, 2H), 7.26 – 7.21 (m, 1H), 6.77 (dd,  $J = 8.2, 1.2$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  140.19, 138.18, 137.33, 133.71, 131.83, 131.07, 130.44, 128.82, 128.30, 128.07, 126.10, 125.48. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{12}\text{H}_9\text{ClNO}_2\text{S}$ : 266.0037, found: 266.0033.



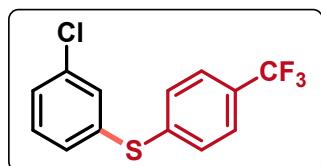
**(3-chlorophenyl)(4-nitrophenyl)sulfane (Scheme 2A, entry 2z):**

**Yield:** 73%

**Physical state:** Yellow semi-solid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (97/3, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  8.21 – 8.15 (m, 1H), 8.10 (dd,  $J = 11.6, 8.9$  Hz, 2H), 7.62 (dd,  $J = 8.7, 6.1$  Hz, 1H), 7.52 (s, 1H), 7.47 (d,  $J = 8.5$  Hz, 1H), 7.42 – 7.36 (m, 1H), 7.19 (d,  $J = 8.9$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  147.76, 146.94, 136.00, 133.91, 132.31, 131.12, 130.43, 129.80, 127.79, 127.11, 126.42, 124.38 **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{12}\text{H}_9\text{ClNO}_2\text{S}$ : 266.0037, found: 266.0035.



**(3-chlorophenyl)(4-(trifluoromethyl)phenyl)sulfane (Scheme 2A, entry 2aa):**

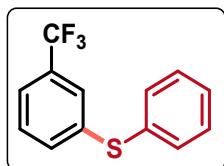
**Yield:** 84%

**Physical state:** Yellow solid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (99/1, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.66 – 7.61 (m, 2H), 7.59 – 7.52 (m, 2H), 7.50 (s, 1H), 7.44 (d,  $J = 8.6$  Hz, 1H), 7.33 (d,  $J = 8.1$  Hz, 1H), 7.22 (d,  $J = 8.1$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  146.62, 140.07, 134.36, 133.00, 129.91, 129.73, 128.07, 126.84, 126.54, 126.07,

125.30, 125.16. **<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -62.51. **LRMS:** (ESI-TOF) m/z: [M + K]<sup>+</sup> calcd. for C<sub>13</sub>H<sub>8</sub>ClF<sub>3</sub>KS: 326.9624, found: 327.2083.



**Phenyl(3-(trifluoromethyl)phenyl)sulfane (Scheme 2A, entry 2ab):<sup>10</sup>**

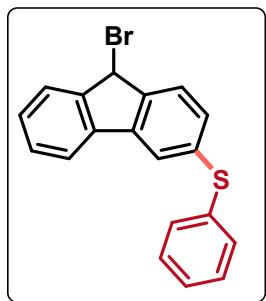
**Yield:** 68%.

TFT was used as solvent.

**Physical state:** Yellow semi-liquid.

**TLC:** R<sub>f</sub> = 0.1; petroleum ether/ethyl acetate (100/0, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.49 (s, 1H), 7.48–7.32 (m, 8H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 137.47, 133.68, 132.64, 129.82, 129.73, 129.60, 128.80, 128.44, 128.34, 125.98, 125.94. **<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>)** δ -62.84.



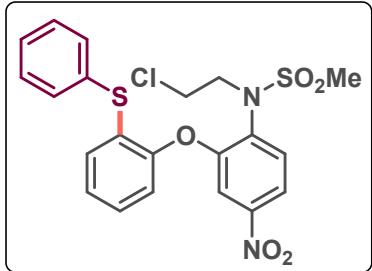
**(9-bromo-9H-fluoren-3-yl)(phenyl)sulfane (Scheme 2A, entry 2ac):**

**Yield:** 71%

**Physical state:** Brown solid.

**TLC:** R<sub>f</sub> = 0.25; petroleum ether/ethyl acetate (98/2, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.63 (d, J = 7.4 Hz, 1H), 7.56 (dd, J = 7.7, 0.9 Hz, 1H), 7.36 (dd, J = 2.3, 1.4 Hz, 2H), 7.34 (d, J = 0.9 Hz, 2H), 7.32 (dd, J = 1.3, 0.5 Hz, 1H), 7.31 – 7.29 (m, 1H), 7.29 – 7.28 (m, 1H), 7.22 (d, J = 1.6 Hz, 1H), 7.13 (s, 1H), 7.13 – 7.12 (m, 1H), 5.27 (s, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 144.47, 140.61, 133.44, 132.87, 131.95, 130.91, 130.69, 130.09, 129.58, 128.90, 128.63, 128.15, 127.83, 127.42, 125.52, 120.01, 51.89. **LRMS:** (ESI-TOF) m/z: [M + K]<sup>+</sup> calcd. for C<sub>19</sub>H<sub>13</sub>BrKS: 390.9558, found: 390.9127.



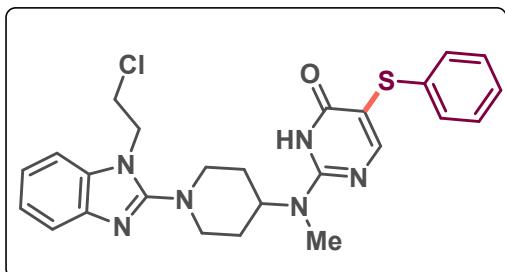
**N-(2-chloroethyl)-N-(4-nitro-2-(phenylthio)phenoxy)phenylmethanesulfonamide  
(Scheme 2A, entry 2ad):**

**Yield:** 84%

**Physical state:** White solid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (95/5, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.95 (dd,  $J = 8.7, 2.5$  Hz, 1H), 7.68 (d,  $J = 8.7$  Hz, 1H), 7.64 (d,  $J = 2.5$  Hz, 1H), 7.48 (td,  $J = 7.6, 1.9$  Hz, 3H), 7.36 – 7.29 (m, 2H), 7.29 (d,  $J = 6.5$  Hz, 1H), 7.15 – 7.06 (m, 3H), 4.05 (t,  $J = 6.3$  Hz, 2H), 3.68 (t,  $J = 6.3$  Hz, 2H), 3.07 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 155.50, 154.10, 148.50, 134.44, 134.16, 131.70, 129.53, 129.07, 127.90, 126.29, 120.16, 118.00, 114.12, 112.36, 52.09, 42.49, 40.14. **HRMS:** (ESI-TOF) m/z: [M + Na]<sup>+</sup> calcd. for C<sub>21</sub>H<sub>19</sub>ClN<sub>2</sub>NaO<sub>5</sub>S<sub>2</sub>: 501.0316, found: 501.0306.



**2-((1-(1-(2-chloroethyl)-1H-benzo[d]imidazol-2-yl)piperidin-4-yl)(methyl)amino)-5-(phenylthio)pyrimidin-4(3H)-one (Scheme 2A, entry 2ae):**

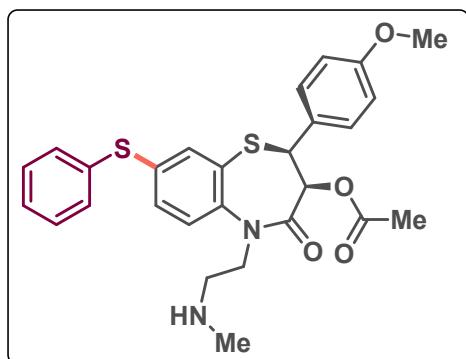
**Yield:** 62%

**Physical state:** Yellow solid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (40/60, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 8.03 (s, 1H), 7.71 (dd,  $J = 5.7, 3.4$  Hz, 1H), 7.52 (dd,  $J = 5.6, 3.3$  Hz, 1H), 7.28 (t,  $J = 1.7$  Hz, 1H), 7.22 (t,  $J = 7.6$  Hz, 4H), 7.16 – 7.08 (m, 2H), 4.30 (t,  $J = 6.7$  Hz, 2H), 4.19 – 4.11 (m, 2H), 4.09 (d,  $J = 6.7$  Hz, 1H), 3.80 – 3.68 (m, 2H), 3.04 (s, 3H), 1.71 (dd,  $J = 14.8, 7.0$  Hz, 2H), 1.43 (dt,  $J = 14.8, 7.3$  Hz, 2H), 0.96 (t,  $J = 7.5$  Hz, 2H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 162.40, 160.71, 158.02, 137.27, 131.04, 128.99, 128.95, 128.05,

127.10, 126.44, 126.00, 107.79, 65.70, 47.59, 41.11, 31.69, 30.73, 22.82, 19.33, 13.85. **HRMS:** (ESI-TOF) m/z: [M + K]<sup>+</sup> calcd. for C<sub>25</sub>H<sub>27</sub>ClKN<sub>6</sub>OS: 533.1293, found: 533.3970.



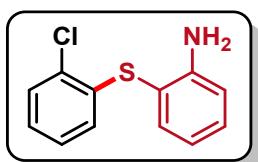
**(2S,3S)-2-(4-methoxyphenyl)-5-(2-(methylamino)ethyl)-4-oxo-8-(phenylthio)-2,3,4,5-tetrahydrobenzo[b][1,4]thiazepin-3-yl acetate (Scheme 2A, entry 2af):**

**Yield:** 64%

**Physical state:** Brown liquid.

**TLC:** R<sub>f</sub> = 0.1; petroleum ether/ethyl acetate (60/40, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.72 – 7.68 (m, 1H), 7.52 – 7.45 (m, 3H), 7.44 – 7.39 (m, 3H), 7.29 (ddd, J = 7.4, 4.1, 2.3 Hz, 2H), 7.24 (d, J = 1.2 Hz, 1H), 6.92 – 6.87 (m, 2H), 5.15 (d, J = 7.5 Hz, 1H), 5.01 (d, J = 7.6 Hz, 1H), 3.81 (d, J = 3.6 Hz, 3H), 3.57 – 3.37 (m, 2H), 2.77 (t, J = 7.0 Hz, 2H), 2.34 (s, 3H), 1.90 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 170.04, 167.11, 159.88, 145.69, 135.49, 132.54, 131.16, 130.92, 129.02, 128.70, 128.07, 127.54, 126.78, 125.96, 124.89, 113.87, 71.24, 59.31, 55.36, 54.53, 48.07, 41.70, 20.63. **LRMS:** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for C<sub>27</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>: 509.1563, found: 509.1382.



**2-((2-chlorophenyl)thio)aniline (Scheme 2C, entry 4):**

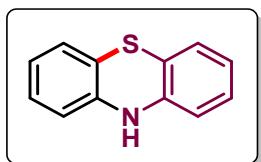
**Yield:** 68%

**Physical state:** Brown semi-liquid.

**TLC:** R<sub>f</sub> = 0.15; petroleum ether/ethyl acetate (90/10, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.46 (dd, J = 7.7, 1.5 Hz, 1H), 7.38 – 7.33 (m, 1H), 7.29 (ddd, J = 8.1, 7.4, 1.6 Hz, 1H), 7.08 – 6.99 (m, 2H), 6.86 – 6.74 (m, 2H), 6.67 – 6.60 (m, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 138.05, 136.12, 131.87, 131.23, 131.03, 129.67, 128.65, 127.32,

126.50, 126.20, 119.41, 115.82. **LRMS** m/z: [M + K]<sup>+</sup> calcd. for C<sub>12</sub>H<sub>10</sub>CINS: 273.9685, found: 274.2394.



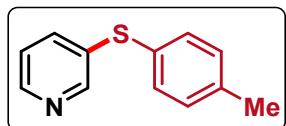
**2-((2-chlorophenyl)thio)aniline (Scheme 2C, entry 5):**

**Yield:** 15%

**Physical state:** White solid.

**TLC:** R<sub>f</sub> = 0.3; petroleum ether/ethyl acetate (90/10, v/v).

**<sup>1</sup>H NMR (500 MHz, DMSO)** δ 8.57 (s, 1H), 6.98 (td, J = 7.7, 1.4 Hz, 2H), 6.90 (dd, J = 7.6, 1.2 Hz, 2H), 6.75 (td, J = 7.5, 1.2 Hz, 2H), 6.68 (dd, J = 7.9, 1.1 Hz, 2H). **<sup>13</sup>C NMR (101 MHz, DMSO)** δ 142.13, 127.57, 126.27, 121.80, 116.36, 114.45. **LRMS** m/z: [M + H]<sup>+</sup> calcd. for C<sub>12</sub>H<sub>10</sub>NS: 199.0456, found: 199.0436.



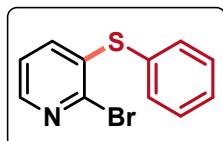
**3-(p-tolylthio)pyridine (Scheme 3, entry 3a):**

**Yield:** 84%

**Physical state:** Reddish semi-solid.

**TLC:** R<sub>f</sub> = 0.3; petroleum ether/ethyl acetate (70/30, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 8.49 (s, 1H), 8.15 (s, 1H), 7.74 – 7.66 (m, 2H), 7.46 (ddd, J = 8.4, 2.6, 1.3 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.29 (dd, J = 8.5, 4.8 Hz, 1H), 2.44 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 148.26, 146.14, 144.06, 135.25, 131.79, 130.32, 130.15, 128.64, 124.36, 21.86. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> : calcd. for C<sub>12</sub>H<sub>12</sub>NS: 202.0685, found: 202.0678.



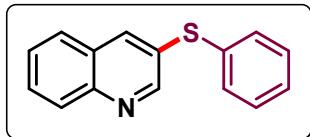
**2-bromo-3-(phenylthio)pyridine (Scheme 3, entry 3b):**

**Yield:** 74%

**Physical state:** Yellow liquid.

**TLC:** R<sub>f</sub> = 0.2; petroleum ether/ethyl acetate (95/5, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.65 (ddd, *J* = 5.7, 3.0, 1.4 Hz, 1H), 7.55 – 7.48 (m, 4H), 7.41 – 7.37 (m, 1H), 7.35 (t, *J* = 2.2 Hz, 1H), 7.13 (dd, *J* = 8.6, 2.5 Hz, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 147.82, 147.23, 138.69, 135.54, 131.70, 130.46, 129.43, 129.10, 124.61, 124.12, 119.25. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>11</sub>H<sub>9</sub>BrNS: 265.9634, found: 265.9633.



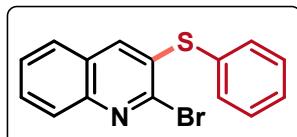
**3-(phenylthio)quinoline (Scheme 3, entry 3c):**

**Yield:** 78%

**Physical state:** Reddish semi-solid.

**TLC:** R<sub>f</sub> = 0.3; petroleum ether/ethyl acetate (70/30, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 88.82 (s, 1H), 8.08 (d, *J* = 9.1 Hz, 2H), 7.69 (t, *J* = 8.1 Hz, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.36 – 7.30 (m, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 152.24, 146.73, 137.20, 136.48, 134.40, 131.49, 129.72, 129.65, 129.40, 128.13, 127.87, 127.41, 127.38. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>15</sub>H<sub>12</sub>NS: 238.0685, found: 238.0681.



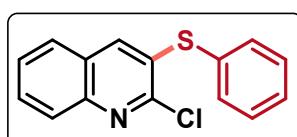
**2-bromo-3-(phenylthio)quinoline (Scheme 3, entry 3d):**

**Yield:** 85%

**Physical state:** Colourless liquid.

**TLC:** R<sub>f</sub> = 0.3; petroleum ether/ethyl acetate (90/10, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.95 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.7 Hz, 1H), 7.71 – 7.64 (m, 4H), 7.50 – 7.43 (m, 3H), 6.98 (d, *J* = 8.7 Hz, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 161.72, 148.16, 136.58, 135.25, 130.97, 130.14, 129.75, 129.34, 128.45, 127.67, 125.95, 125.89, 119.61. **LRMS (ESI-TOF)** m/z: [M + K]<sup>+</sup> calcd. for C<sub>15</sub>H<sub>10</sub>BrNNaS: 337.9615, found: 337.9976.



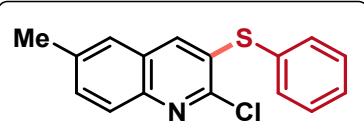
**2-chloro-3-(phenylthio)quinoline (Scheme 3, entry 3e):**

**Yield:** 84%

**Physical state:** Colourless sticky liquid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (90/10, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.95 (d,  $J = 8.6$  Hz, 1H), 7.89 (d,  $J = 8.7$  Hz, 1H), 7.73 – 7.64 (m, 4H), 7.49 – 7.44 (m, 3H), 6.99 (d,  $J = 8.7$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  161.77, 148.20, 136.63, 135.30, 131.03, 130.18, 129.79, 129.38, 128.50, 127.70, 126.01, 125.94, 119.69. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{15}\text{H}_{11}\text{ClNS}$ : 272.0295, found: 272.0295.



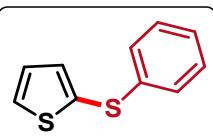
**2-chloro-6-methyl-3-(phenylthio)quinoline (Scheme 3, entry 3f):**

**Yield:** 82%

**Physical state:** Yellow sticky liquid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (90/10, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.85 (d,  $J = 8.6$  Hz, 1H), 7.79 (d,  $J = 8.7$  Hz, 1H), 7.68 – 7.63 (m, 2H), 7.50 – 7.43 (m, 3H), 7.43 (d,  $J = 2.5$  Hz, 1H), 6.96 (d,  $J = 8.7$  Hz, 1H), 2.49 (s, 3H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  160.44, 146.73, 136.02, 135.75, 135.08, 132.28, 131.28, 129.67, 129.16, 128.14, 126.55, 125.98, 119.75, 21.56. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{16}\text{H}_{13}\text{ClNS}$ : 286.0452, found: 286.0452.



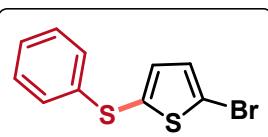
**2-(phenylthio)thiophene (Scheme 3, entry 3g):<sup>9</sup>**

**Yield:** 85%

**Physical state:** Yellowish liquid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (100/0, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.57 – 7.49 (m, 3H), 7.37 – 7.31 (m, 3H), 7.27 (td,  $J = 3.7, 3.2$ , 2.0 Hz, 1H), 7.25 – 7.18 (m, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  137.15, 136.21, 131.42, 129.20, 129.11, 128.07, 127.64, 127.29, 127.25, 126.19.



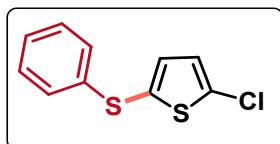
**2-bromo-5-(phenylthio)thiophene (Scheme 3, entry 3h):**

**Yield:** 60%

**Physical state:** Sticky yellow liquid.

**TLC:**  $R_f = 0.5$ ; petroleum ether/ethyl acetate (100/0, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.30 – 7.27 (m, 1H), 7.25 (s, 1H), 7.23 (d,  $J = 1.7$  Hz, 1H), 7.21 – 7.17 (m, 2H), 7.07 (d,  $J = 3.8$  Hz, 1H), 7.03 (d,  $J = 3.8$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  137.84, 136.52, 133.05, 130.96, 129.26, 127.69, 126.69, 116.46. **LRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{10}\text{H}_8\text{BrS}_2$ : 269.9173, found: 269.2526.



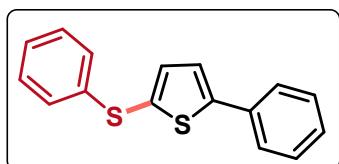
**2-chloro-5-(phenylthio)thiophene (Scheme 3, entry 3i):<sup>6</sup>**

**Yield:** 68%

**Physical state:** Sticky yellow orangish liquid.

**TLC:**  $R_f = 0.5$ ; petroleum ether/ethyl acetate (100/0, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.29 – 7.27 (m, 1H), 7.26 (s, 1H), 7.23 (d,  $J = 1.6$  Hz, 1H), 7.21 – 7.17 (m, 2H), 7.10 (d,  $J = 3.8$  Hz, 1H), 6.88 (d,  $J = 3.8$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  137.92, 135.91, 134.15, 130.23, 129.26, 128.44, 127.58, 126.65.



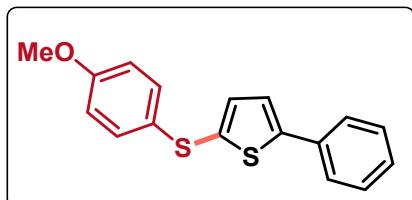
**2-phenyl-5-(phenylthio)thiophene (Scheme 3, entry 3j):<sup>6</sup>**

**Yield:** 86%

**Physical state:** Yellow liquid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (100/0, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.60 – 7.55 (m, 2H), 7.38 (t,  $J = 7.6$  Hz, 2H), 7.33 – 7.30 (m, 1H), 7.30 – 7.27 (m, 6H), 7.20 – 7.15 (m, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  149.98, 138.65, 137.17, 133.96, 130.59, 129.17, 129.12, 128.21, 127.43, 126.32, 125.94, 123.74.



**2-((4-methoxyphenyl)thio)-5-phenylthiophene (Scheme 3, entry 3k):**

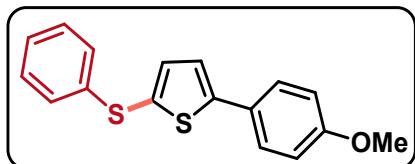
**Yield:** 77%

**Physical state:** Orange solid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (98/2, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.57 – 7.51 (m, 2H), 7.40 – 7.33 (m, 4H), 7.29 (d,  $J = 7.1$  Hz, 1H), 7.20 (d,  $J = 3.7$  Hz, 1H), 7.17 (d,  $J = 3.7$  Hz, 1H), 6.85 (d,  $J = 8.8$  Hz, 2H), 3.79 (s, 3H).

**$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  159.23, 148.68, 134.88, 134.07, 133.91, 131.48, 129.06, 128.30, 127.99, 125.83, 123.50, 114.90, 55.51. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{17}\text{H}_{15}\text{OS}_2$ : 299.0559, found: 299.0553.



**2-(4-methoxyphenyl)-5-(phenylthio)thiophene (Scheme 3, entry 3l):<sup>6</sup>**

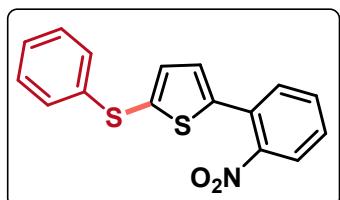
**Yield:** 80%

**Physical state:** Yellow semi-liquid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (99/1, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.50 (d,  $J = 8.9$  Hz, 2H), 7.25 (d,  $J = 3.3$  Hz, 4H), 7.23 (d,  $J = 3.7$  Hz, 1H), 7.18 – 7.16 (m, 1H), 7.15 (d,  $J = 3.7$  Hz, 1H), 6.97 – 6.87 (m, 2H), 3.83 (s, 3H).

**$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  159.79, 150.13, 138.92, 137.39, 129.14, 127.26, 126.88, 126.20, 124.76, 122.70, 120.50, 114.52, 55.53.



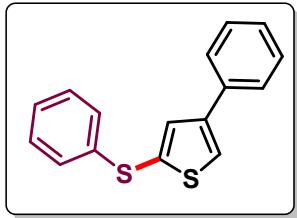
**2-(2-nitrophenyl)-5-(phenylthio)thiophene (Scheme 3, entry 3m):**

**Yield:** 65%

**Physical state:** Yellow sticky solid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (97/3, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.81 – 7.76 (m, 1H), 7.61 – 7.56 (m, 1H), 7.54 – 7.46 (m, 3H), 7.29 (d,  $J = 2.4$  Hz, 1H), 7.28 (s, 2H), 7.23 (d,  $J = 3.7$  Hz, 1H), 7.20 (ddd,  $J = 6.9, 5.5, 3.1$  Hz, 1H), 7.03 (d,  $J = 3.7$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  149.33, 142.41, 137.93, 136.10, 134.03, 132.30, 132.22, 129.29, 129.17, 127.96, 127.93, 126.67, 124.70, 124.24. **LRMS** (ESI-TOF) m/z: [M + K]<sup>+</sup> calcd. for  $\text{C}_{16}\text{H}_{11}\text{KNO}_2\text{S}_2$ : 351.9868, found: 352.0084.



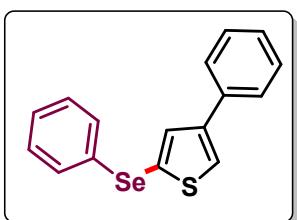
**4-phenyl-2-(phenylthio)thiophene (Scheme 3, entry 3n):**

**Yield:** 76%

**Physical state:** Yellow sticky solid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (98/2, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.60 – 7.55 (m, 2H), 7.53 – 7.48 (m, 1H), 7.40 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.37 – 7.32 (m, 1H), 7.31 – 7.26 (m, 2H), 7.25 (d, *J* = 2.9 Hz, 1H), 7.24 – 7.21 (m, 1H), 7.20 – 7.16 (m, 1H), 7.15 – 7.11 (m, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 143.13, 138.39, 135.36, 135.05, 132.52, 130.07, 129.20, 128.40, 127.60, 126.96, 126.38, 125.79. **HRMS (ESI-TOF)** m/z: [M + K]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>12</sub>S<sub>2</sub>K: 307.0017, found: 307.0022.



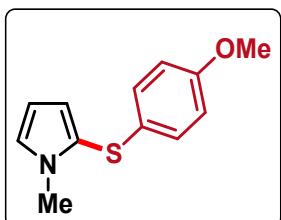
**4-phenyl-2-(phenylselanyl)thiophene (Scheme 3, entry 3o):**

**Yield:** 74%

**Physical state:** Yellow sticky solid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (98/2, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.63 (s, 1H), 7.61 (s, 1H), 7.59 (d, *J* = 4.0 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 4H), 7.34 (d, *J* = 7.3 Hz, 1H), 7.30 – 7.27 (m, 2H), 7.24 (d, *J* = 6.9 Hz, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 143.60, 136.05, 135.12, 132.89, 130.30, 129.43, 129.04, 127.58, 127.04, 126.72, 126.44, 124.38. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>13</sub>SSe: 316.9898, found: 316.9894.



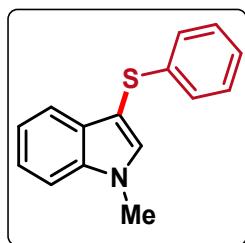
**2-((4-methoxyphenyl)thio)-1-methyl-1H-pyrrole (Scheme 3, entry 3p):**

**Yield:** 89%

**Physical state:** Brownish sticky liquid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (98/2, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.09 – 6.98 (m, 2H), 6.89 – 6.84 (m, 1H), 6.84 – 6.74 (m, 2H), 6.57 (dd,  $J = 3.6, 1.8$  Hz, 1H), 6.22 (dd,  $J = 3.6, 2.9$  Hz, 1H), 3.77 (s, 3H), 3.59 (s, 3H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  158.06, 129.25, 128.20, 125.75, 118.89, 114.80, 108.33, 108.21, 55.47, 34.11. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{12}\text{H}_{14}\text{NOS}$ : 220.0791, found: 220.0787.



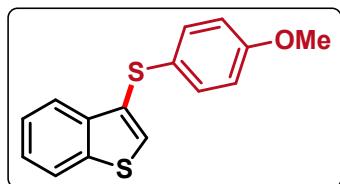
**1-methyl-3-(phenylthio)-1H-indole (Scheme 3, entry 3q):<sup>6</sup>**

**Yield:** 83%

**Physical state:** Yellow semi-solid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (95/5, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.68 – 7.63 (m, 1H), 7.44 – 7.38 (m, 1H), 7.35 (s, 1H), 7.34 – 7.29 (m, 1H), 7.23 – 7.19 (m, 1H), 7.18 (s, 1H), 7.16 (q,  $J = 1.5, 1.0$  Hz, 1H), 7.15 – 7.11 (m, 2H), 7.09 – 7.03 (m, 1H), 3.85 (s, 3H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  139.78, 135.18, 129.31, 128.76, 126.67, 125.80, 124.76, 122.67, 120.60, 119.83, 109.84, 100.55, 33.24.



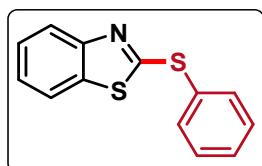
**3-((4-methoxyphenyl)thio)benzo[b]thiophene (Scheme 3, entry 3r):<sup>6</sup>**

**Yield:** 64%

**Physical state:** Yellow semi-liquid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (98/2, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.72 – 7.65 (m, 2H), 7.43 (d,  $J = 8.9$  Hz, 2H), 7.32 (s, 1H), 7.30 – 7.28 (m, 1H), 7.27 (d,  $J = 1.3$  Hz, 1H), 6.87 (d,  $J = 8.9$  Hz, 2H), 3.80 (s, 3H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  159.87, 141.98, 139.92, 133.40, 127.57, 126.10, 124.59, 124.54, 123.28, 122.06, 121.11, 115.00, 55.53.



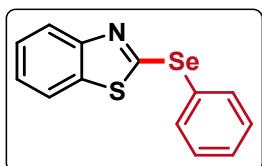
**2-(phenylthio)benzo[d]thiazole (Scheme 3, entry 3s):<sup>10</sup>**

**Yield:** 85%

**Physical state:** Red semi-liquid.

**TLC:**  $R_f = 0.25$ ; petroleum ether/ethyl acetate (90/10, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.89 (ddd,  $J = 8.2, 1.0, 0.6$  Hz, 1H), 7.77 – 7.75 (m, 1H), 7.74 (t,  $J = 1.9$  Hz, 1H), 7.65 (ddd,  $J = 8.0, 1.1, 0.5$  Hz, 1H), 7.54 – 7.45 (m, 3H), 7.41 (ddd,  $J = 8.3, 7.3, 1.2$  Hz, 1H), 7.30 – 7.26 (m, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 169.72, 153.97, 135.59, 135.41, 130.52, 129.98, 126.87, 126.22, 124.39, 121.99, 120.85.



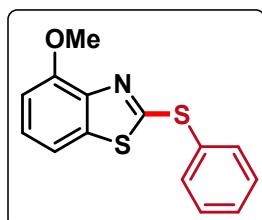
**2-(phenylselanyl)benzo[d]thiazole (Scheme 3, entry 3t):**

**Yield:** 82%

**Physical state:** Red semi-liquid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (90/10, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.93 (d,  $J = 8.1$  Hz, 1H), 7.87 – 7.82 (m, 2H), 7.69 (d,  $J = 7.9$  Hz, 1H), 7.51 (td,  $J = 6.3, 5.1, 3.0$  Hz, 1H), 7.47 – 7.43 (m, 2H), 7.43 – 7.38 (m, 1H), 7.30 – 7.25 (m, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 162.93, 154.70, 136.74, 130.22, 130.08, 129.05, 126.68, 126.17, 124.50, 122.10, 120.92. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>13</sub>H<sub>10</sub>NSSe: 291.9694, found: 291.9690.



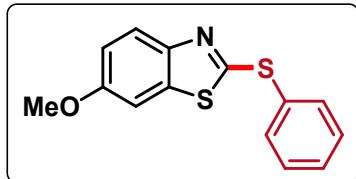
**4-methoxy-2-(phenylthio)benzo[d]thiazole (Scheme 3, entry 3u):**

**Yield:** 88%

**Physical state:** Brown semi-solid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (90/10, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.70 (dd, *J* = 8.0, 1.4 Hz, 2H), 7.49 – 7.40 (m, 3H), 7.20 – 7.16 (m, 2H), 6.88 – 6.77 (m, 1H), 3.99 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 168.47, 152.32, 143.95, 141.57, 137.09, 135.34, 130.40, 129.91, 125.28, 112.85, 106.84, 55.93. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>14</sub>H<sub>12</sub>NOS<sub>2</sub>: 274.0355, found: 274.0357.



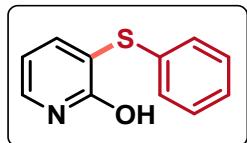
**6-methoxy-2-(phenylthio)benzo[d]thiazole (Scheme 3, entry 3v):**

**Yield:** 90%

**Physical state:** Brownish semi-solid.

**TLC:** R<sub>f</sub> = 0.2; petroleum ether/ethyl acetate (90/10, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.77 (d, *J* = 8.9 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.44 (t, *J* = 7.2 Hz, 3H), 7.10 (d, *J* = 2.4 Hz, 1H), 7.03 – 6.95 (m, 1H), 3.78 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 165.50, 157.17, 148.33, 137.11, 134.80, 130.49, 130.07, 129.79, 122.54, 115.00, 103.90, 55.70. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>14</sub>H<sub>12</sub>NOS<sub>2</sub>: 274.0355, found: 274.0358.



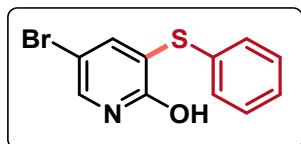
**3-(phenylthio)pyridin-2-ol (Scheme 3, entry 3w):**

**Yield:** 90%

**Physical state:** Yellow liquid.

**TLC:** R<sub>f</sub> = 0.1; petroleum ether/ethyl acetate (40/60, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.57 – 7.50 (m, 2H), 7.41 (q, *J* = 5.1 Hz, 3H), 7.31 – 7.27 (m, 1H), 6.93 (dd, *J* = 7.1, 1.4 Hz, 1H), 6.19 (t, *J* = 6.8 Hz, 1H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 162.37, 136.58, 134.45, 131.62, 131.28, 129.87, 128.96, 127.97, 107.56.



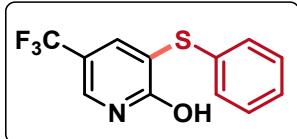
**5-bromo-3-(phenylthio)pyridin-2-ol (Scheme 3, entry 3x):**

**Yield:** 85%

**Physical state:** Orange-brownish semi-solid.

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (40/60, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.56 (dd,  $J = 6.4, 2.9$  Hz, 2H), 7.50 – 7.45 (m, 3H), 7.36 – 7.33 (m, 1H), 6.77 (d,  $J = 1.6$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  137.11, 135.69, 135.18, 132.86, 131.65, 130.52, 130.26, 129.85, 100.19. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{11}\text{H}_9\text{BrNOS}$ : 281.9583, found: 281.9581.



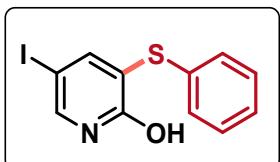
**3-(phenylthio)-5-(trifluoromethyl)pyridin-2-ol (Scheme 3, entry 3y):**

**Yield:** 73%

**Physical state:** Reddish orange solid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (40/60, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  12.92 (s, 1H), 7.62 (s, 1H), 7.56 (dd,  $J = 6.4, 3.0$  Hz, 2H), 7.51 – 7.45 (m, 3H), 6.87 (d,  $J = 2.1$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  162.02, 135.12, 134.93, 134.41, 130.34, 130.02, 129.79, 129.63, 129.59, 129.17.  **$^{19}\text{F NMR}$  (377 MHz,  $\text{CDCl}_3$ )**  $\delta$  -62.69. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{12}\text{H}_9\text{F}_3\text{NOS}$ : 272.0351, found: 272.0347.



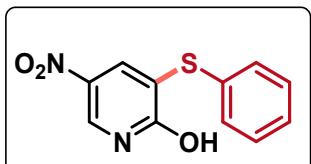
**5-iodo-3-(phenylthio)pyridin-2-ol (Scheme 3, entry 3z):**

**Yield:** 79%

**Physical state:** Brown solid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (30/70, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.54 (dd,  $J = 6.5, 3.0$  Hz, 2H), 7.47 (s, 1H), 7.45 (d,  $J = 2.1$  Hz, 3H), 6.88 (d,  $J = 1.9$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  160.99, 141.90, 135.96, 134.92, 134.83, 130.20, 129.85, 129.70, 66.47. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{11}\text{H}_9\text{INOS}$ : 329.9444, found: 329.9446.



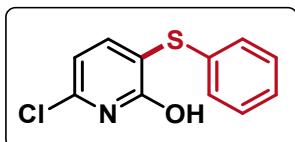
**5-nitro-3-(phenylthio)pyridin-2-ol (Scheme 3, entry 3aa):**

**Yield:** 76%

**Physical state:** Yellow solid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (30/70, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  8.42 (d,  $J = 2.8$  Hz, 1H), 7.59 (dd,  $J = 6.9, 2.8$  Hz, 2H), 7.52 (dd,  $J = 5.1, 1.9$  Hz, 3H), 7.45 (d,  $J = 2.7$  Hz, 1H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  161.63, 135.50, 135.21, 133.06, 130.94, 130.61, 129.94, 128.25, 126.65. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{11}\text{H}_9\text{N}_2\text{O}_3\text{S}$ : 249.0328, found: 249.0324.



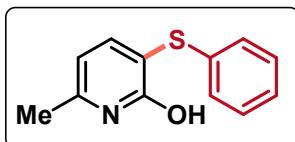
**6-chloro-3-(phenylthio)pyridin-2-ol (Scheme 3, entry 3ab):**

**Yield:** 87%

**Physical state:** Yellow solid

**TLC:**  $R_f = 0.2$ ; petroleum ether/ethyl acetate (30/70, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.54 (t,  $J = 7.8$  Hz, 1H), 7.51 – 7.48 (m, 1H), 7.41 – 7.37 (m, 2H), 7.03 (d,  $J = 7.8$  Hz, 0.5H), 6.69 (dd,  $J = 13.3, 8.0$  Hz, 2H), 6.44 (d,  $J = 7.8$  Hz, 0.5H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  135.76, 133.61, 131.86, 129.19, 128.02, 127.73, 126.56, 125.82, 125.73. **HRMS** (ESI-TOF) m/z: [M + Na]<sup>+</sup> calcd. for  $\text{C}_{11}\text{H}_8\text{ClNNaOS}$ : 259.9961, found: 259.9963.



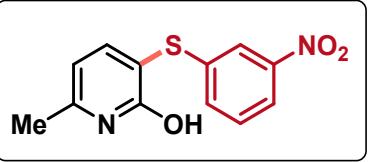
**6-methyl-3-(phenylthio)pyridin-2-ol (Scheme 3, entry 3ac):**

**Yield:** 89%

**Physical state:** Colourless liquid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (40/60, v/v).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**  $\delta$  7.45 (dd,  $J = 8.1, 1.3$  Hz, 2H), 7.38 – 7.29 (m, 3H), 7.08 (d,  $J = 7.3$  Hz, 1H), 5.96 (d,  $J = 7.3$  Hz, 1H), 2.27 (s, 3H).  **$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )**  $\delta$  162.97, 144.00, 140.03, 133.20, 132.80, 132.66, 130.70, 129.45, 127.93, 106.51, 18.89. **HRMS** (ESI-TOF) m/z: [M + H]<sup>+</sup> calcd. for  $\text{C}_{12}\text{H}_{12}\text{NOS}$ : 218.0634, found: 218.0643.



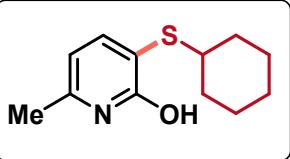
**6-methyl-3-((3-nitrophenyl)thio)pyridin-2-ol (Scheme 3, entry 3ad):**

**Yield:** 88%

**Physical state:** Yellow solid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (30/70, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 12.99 (s, 1H), 8.14 (t, *J* = 1.8 Hz, 1H), 8.05 – 7.97 (m, 1H), 7.64 – 7.56 (m, 2H), 7.44 (t, *J* = 8.0 Hz, 1H), 6.09 (d, *J* = 7.3 Hz, 1H), 2.23 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 163.57, 148.68, 147.93, 146.40, 138.47, 135.31, 129.69, 124.15, 121.41, 119.70, 106.85, 19.03. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>12</sub>H<sub>10</sub>N<sub>2</sub>O<sub>3</sub>S: 262.0412, found: 262.0410.



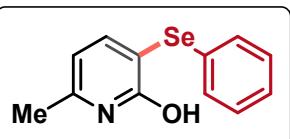
**3-(cyclohexylthio)-6-methylpyridin-2-ol (Scheme 3, entry 3ae):**

**Yield:** 91%

**Physical state:** Brownish black solid.

**TLC:**  $R_f = 0.1$ ; petroleum ether/ethyl acetate (30/70, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 12.72 (s, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 6.08 – 5.96 (m, 1H), 3.30 (dq, *J* = 10.3, 6.7, 5.1 Hz, 1H), 2.35 (s, 3H), 1.97 (d, *J* = 10.8 Hz, 2H), 1.83 – 1.73 (m, 2H), 1.43 – 1.25 (m, 6H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 164.11, 143.90, 141.83, 123.05, 106.27, 43.45, 33.19, 26.13, 25.96, 18.98. **HRMS (ESI-TOF)** m/z: [M + Na]<sup>+</sup> calcd. for C<sub>12</sub>H<sub>17</sub>NNaOS: 246.0923, found: 246.0919.



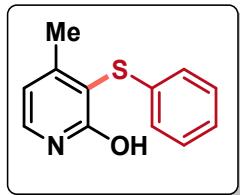
**6-methyl-3-(phenylselanyl)pyridin-2-ol (Scheme 3, entry 3af):**

**Yield:** 83%

**Physical state:** Yellow semi-liquid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (40/60, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.63 (d, *J* = 9.3 Hz, 1H), 7.24 (d, *J* = 3.6 Hz, 4H), 7.22 – 7.18 (m, 1H), 6.39 (d, *J* = 9.3 Hz, 1H), 2.54 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 165.65, 150.82, 150.31, 132.04, 129.92, 129.58, 126.80, 117.88, 105.26, 20.56. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>12</sub>H<sub>12</sub>NOSe: 266.0079, found: 266.0072.



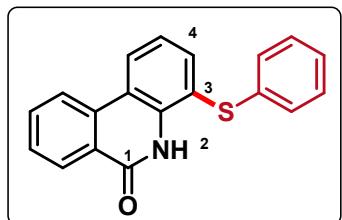
**4-methyl-3-(phenylthio)pyridin-2-ol (Scheme 3, entry 3ag):**

**Yield:** 56%

**Physical state:** Yellow semi-liquid.

**TLC:** R<sub>f</sub> = 0.3; petroleum ether/ethyl acetate (40/60, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.35 (d, *J* = 52.9 Hz, 1H), 7.21 (t, *J* = 7.4 Hz, 2H), 7.17 – 7.04 (m, 3H), 6.30 (s, 1H), 2.41 (s, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 160.77, 136.76, 135.27, 129.91, 129.52, 127.99, 127.65, 126.14, 111.33, 22.80. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>12</sub>H<sub>12</sub>NOS: 218.0634, found: 218.0642.



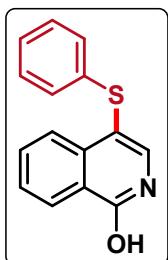
**4-(phenylthio)phenanthridin-6(5H)-one (Scheme 3, entry 3ah):**

**Yield:** 76%

**Physical state:** Yellow solid.

**TLC:** R<sub>f</sub> = 0.3; petroleum ether/ethyl acetate (30/70, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 9.53 (s, 1H), 8.50 (d, *J* = 7.9 Hz, 1H), 8.32 (t, *J* = 8.5 Hz, 2H), 7.80 (td, *J* = 15.7, 7.3 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.37 – 7.28 (m, 2H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.18 – 7.12 (m, 1H), 7.09 (d, *J* = 7.5 Hz, 2H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 162.37, 137.61, 136.58, 136.14, 134.45, 133.77, 131.62, 131.28, 129.87, 128.96, 128.39, 127.94, 127.04, 126.03, 125.70, 113.08, 107.56. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>19</sub>H<sub>14</sub>NOS: 304.0791, found: 304.0785.



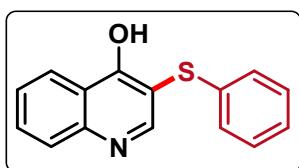
**4-(phenylthio)isoquinolin-1-ol (Scheme 3, entry 3ai):**

**Yield:** 82%

**Physical state:** Yellow sticky liquid.

**TLC:**  $R_f = 0.3$ ; petroleum ether/ethyl acetate (40/60, v/v).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 10.73 (s, 1H), 8.45 (d,  $J = 8.0$  Hz, 1H), 7.97 (d,  $J = 8.2$  Hz, 1H), 7.69 (d,  $J = 7.3$  Hz, 1H), 7.67 (s, 1H), 7.55 (t,  $J = 7.6$  Hz, 1H), 7.21 (t,  $J = 7.7$  Hz, 2H), 7.12 (dd,  $J = 13.5, 7.2$  Hz, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 164.29, 138.38, 137.31, 135.76, 133.68, 129.20, 127.99, 127.76, 126.67, 126.34, 125.86, 125.72, 108.38. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>15</sub>H<sub>12</sub>NOS: 254.0634, found: 254.0636.



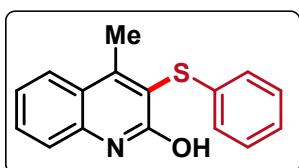
**3-(phenylthio)quinolin-4-ol (Scheme 3, entry 3aj):<sup>12</sup>**

**Yield:** 50%

**Physical state:** Yellow solid.

**TLC:**  $R_f = 0.4$ ; petroleum ether/ethyl acetate (30/70, v/v).

**<sup>1</sup>H NMR (400 MHz, MeOD)** δ 8.19 (d,  $J = 1.3$  Hz, 1H), 8.17 (s, 1H), 7.68 – 7.60 (m, 1H), 7.51 (d,  $J = 8.4$  Hz, 1H), 7.36 (t,  $J = 7.6$  Hz, 1H), 7.12 (d,  $J = 6.4$  Hz, 4H), 7.02 (ddd,  $J = 8.4, 5.6, 2.1$  Hz, 1H). **<sup>13</sup>C NMR (101 MHz, MeOD)** δ 178.79, 146.67, 143.11, 138.43, 133.98, 130.11, 128.68, 126.94, 126.13, 119.75, 113.53, 110.10, 107.54.



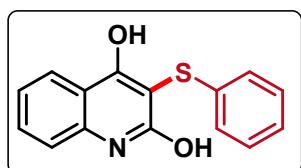
**4-methyl-3-(phenylthio)quinolin-2-ol (Scheme 3, entry 3ak):**

**Yield:** 74%

**Physical state:** Yellow liquid.

**TLC:**  $R_f = 0.35$  (30:70, v/v petroleum ether:EtOAc).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 9.51 (s, 1H), 7.79 (ddd, *J* = 17.6, 7.8, 1.3 Hz, 2H), 7.31 – 7.26 (m, 1H), 7.25 – 7.23 (m, 1H), 7.22 – 7.20 (m, 1H), 7.18 – 7.14 (m, 1H), 7.08 – 7.04 (m, 2H), 6.55 (s, 1H), 2.51 (d, *J* = 1.2 Hz, 3H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 162.03, 148.88, 139.30, 138.89, 135.26, 129.53, 127.53, 126.85, 126.71, 122.72, 121.97, 121.53, 117.83, 19.41. **HRMS (ESI-TOF)** m/z: [M + H]<sup>+</sup> calcd. for C<sub>16</sub>H<sub>14</sub>NOS: 268.0791, found: 268.0797.



**3-(phenylthio)quinoline-2,4-diol (Scheme 3, entry 3al):<sup>13</sup>**

**Yield:** 81%

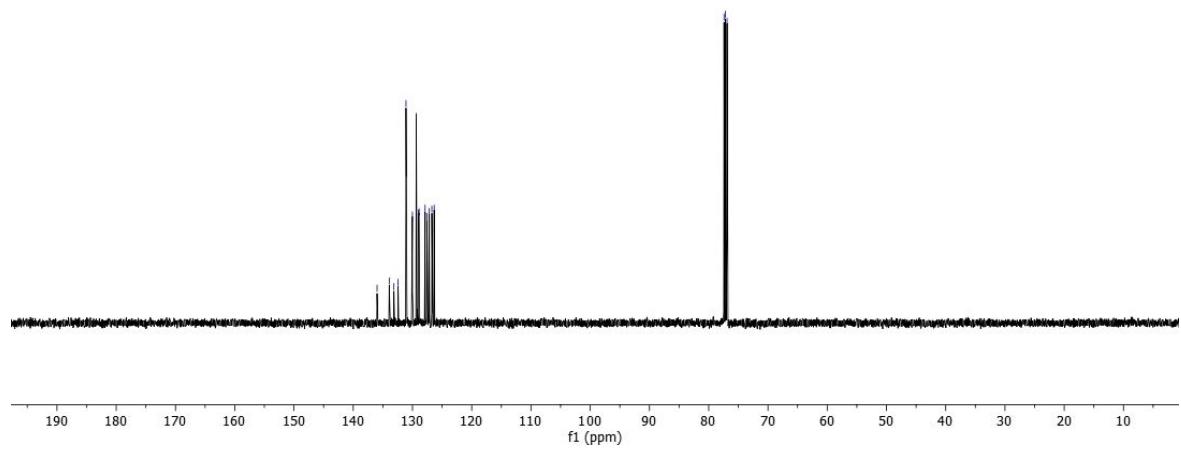
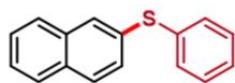
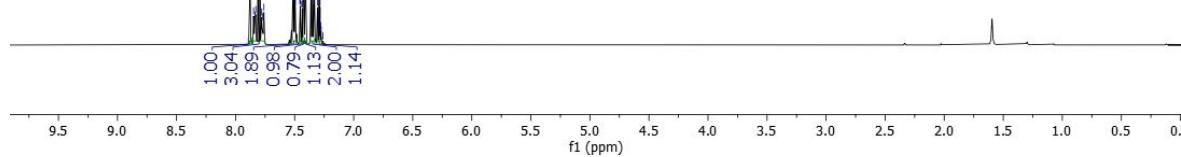
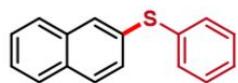
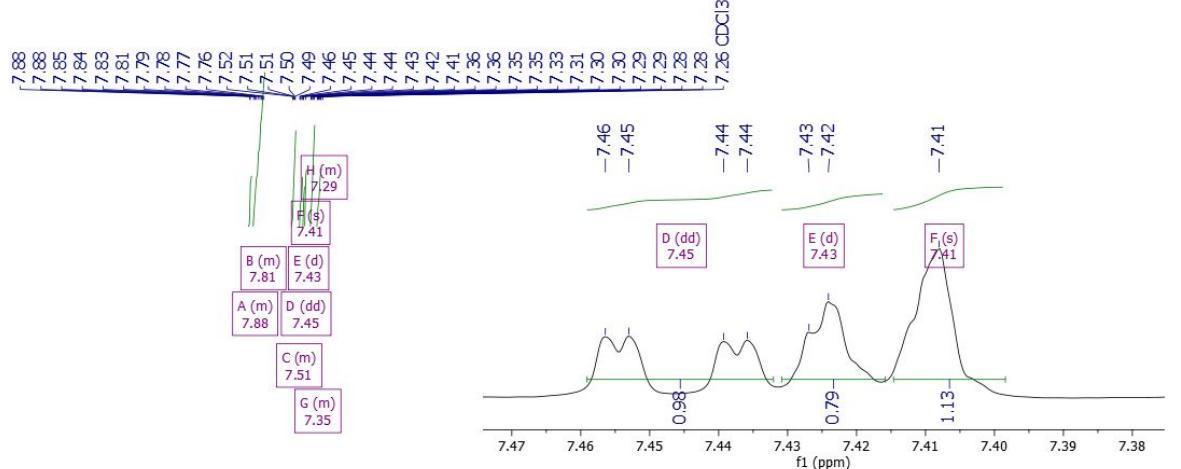
**Physical state:** Orangish semi-solid.

**TLC:** R<sub>f</sub> = 0.2; petroleum ether/ethyl acetate (30/70, v/v).

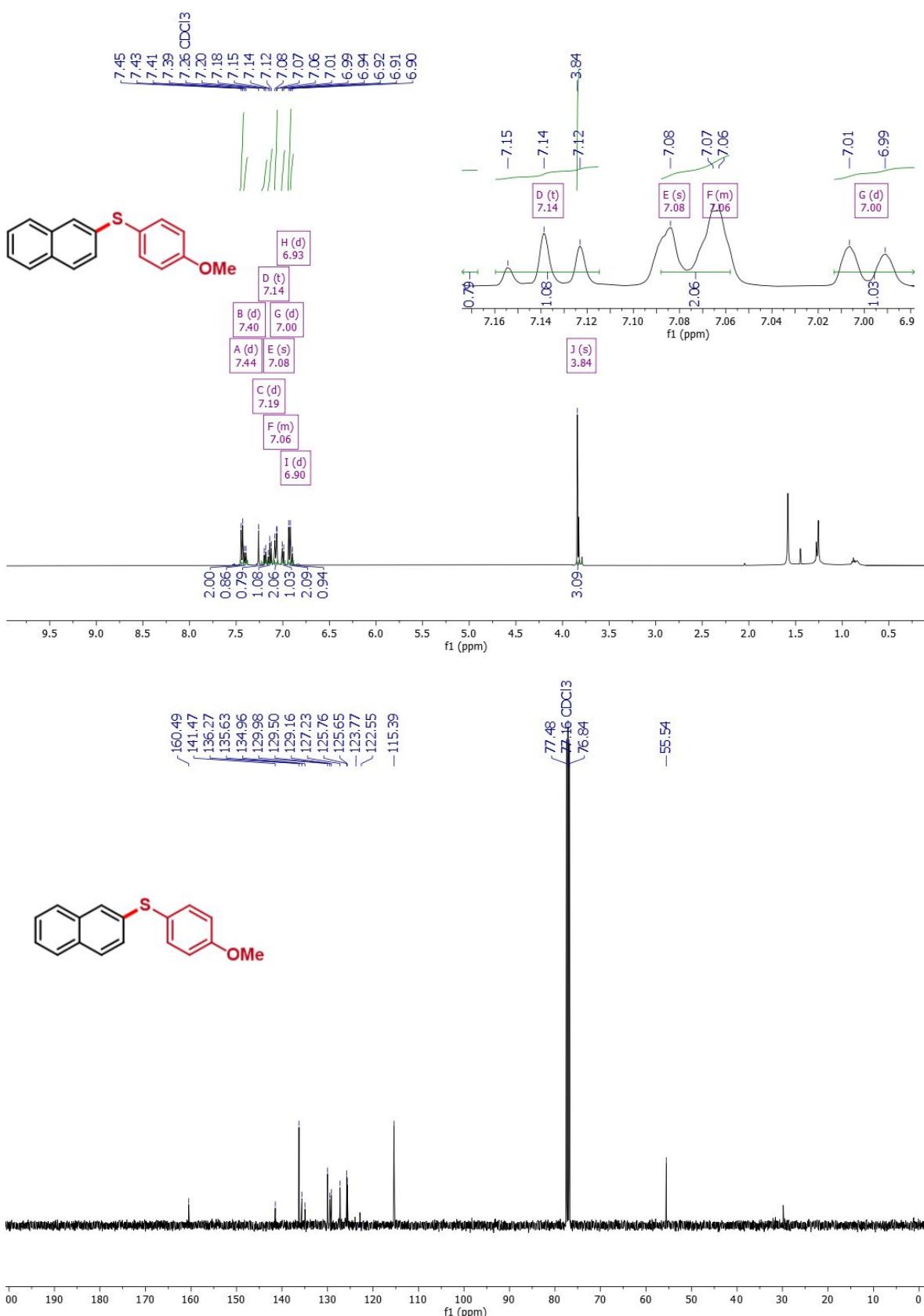
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 10.73 (s, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.72 – 7.62 (m, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 2H), 7.12 (dd, *J* = 13.5, 7.2 Hz, 2H). **<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 175.06, 138.28, 137.08, 135.76, 133.61, 132.40, 131.86, 131.31, 128.02, 127.73, 126.56, 125.82, 125.73.

# **NMR Spectra**

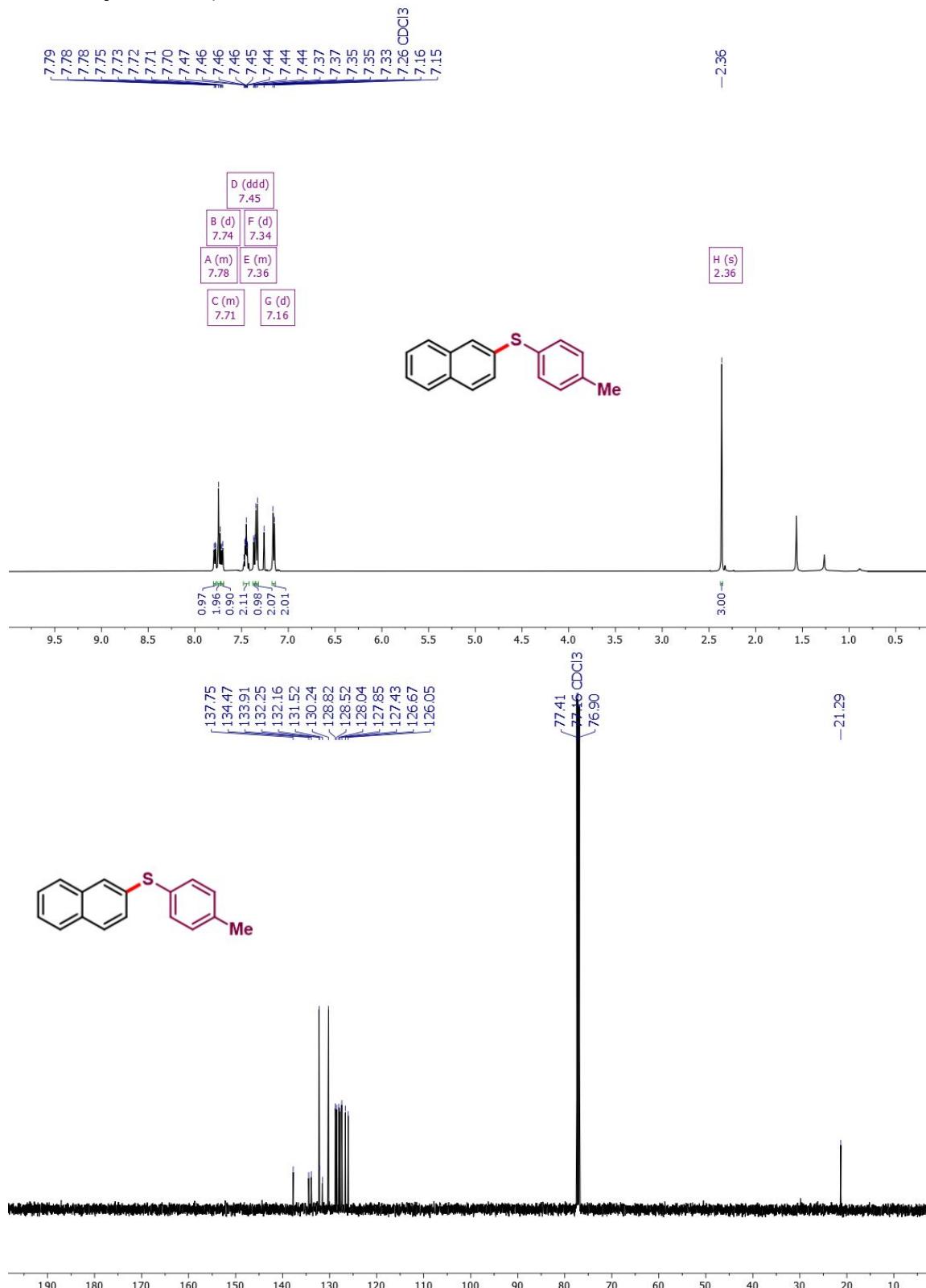
**Scheme 2A, entry 2a**  
**Yield: 78% ( $\beta:\alpha > 30:1$ )<sup>14</sup>**



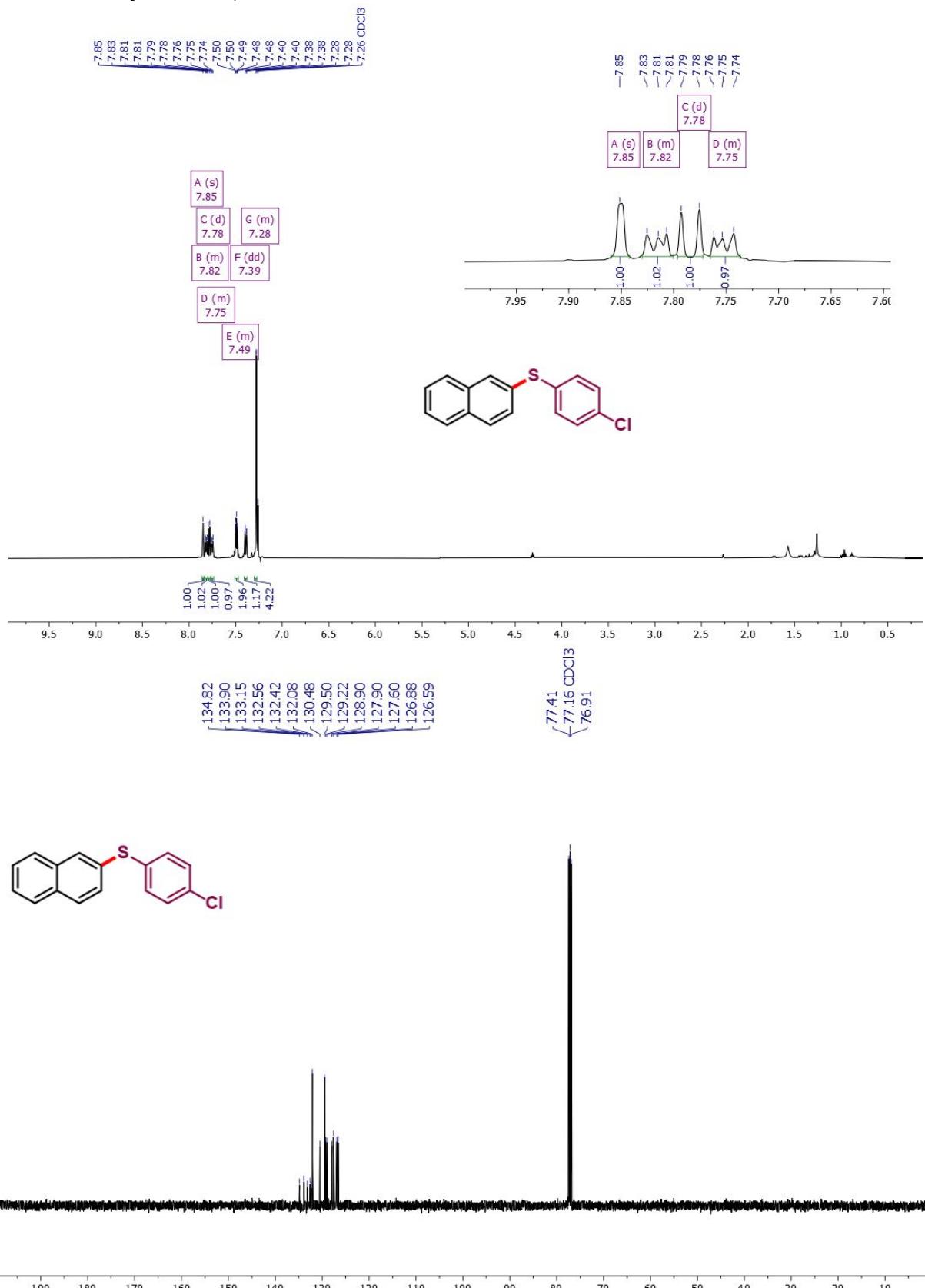
**Scheme 2A, entry 2b**  
**Yield: 85% ( $\beta:\alpha = 17:1$ )<sup>14</sup>**



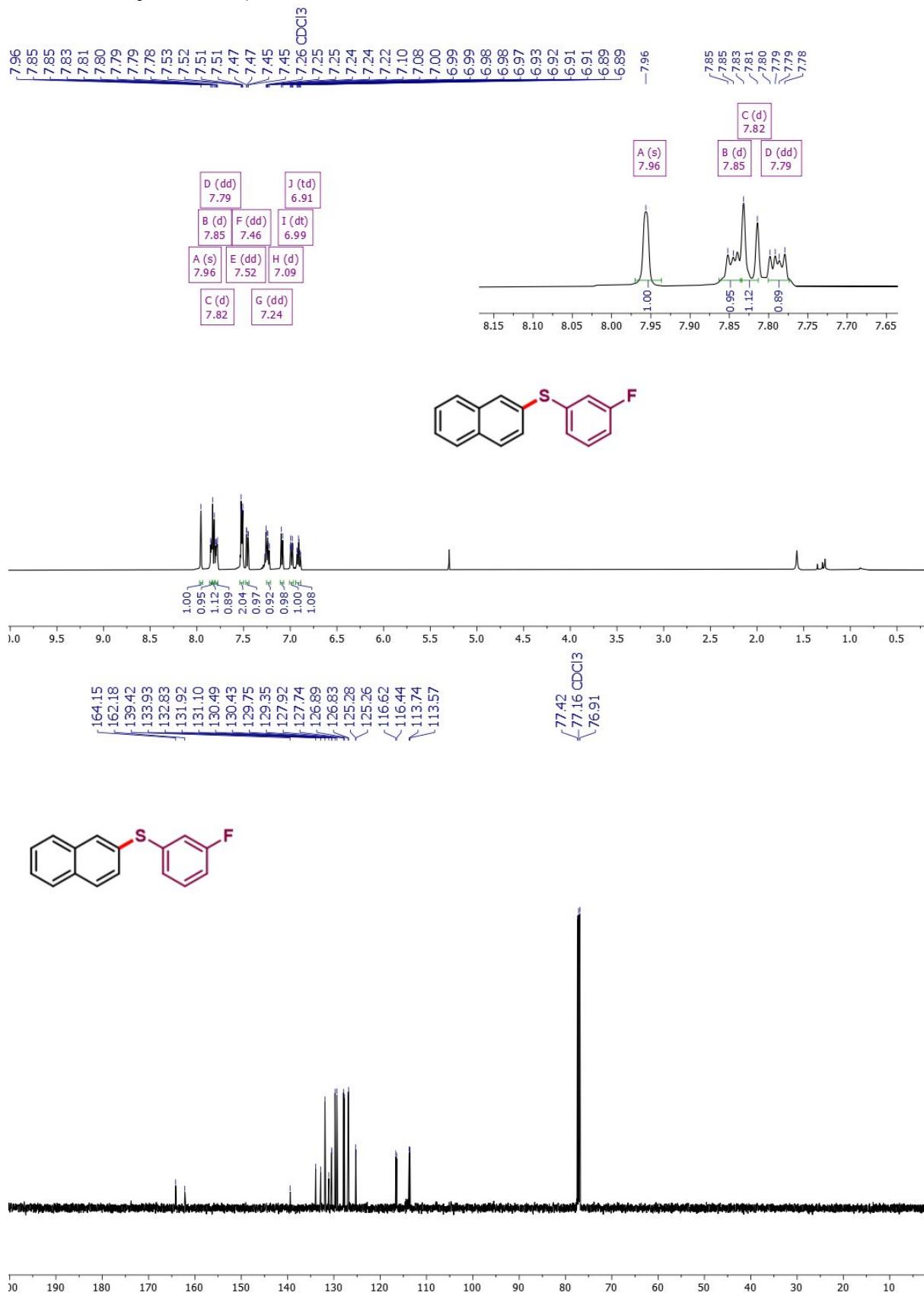
**Scheme 2A, entry 2c**  
**Yield: 87% ( $\beta:\alpha > 20:1$ )<sup>14</sup>**

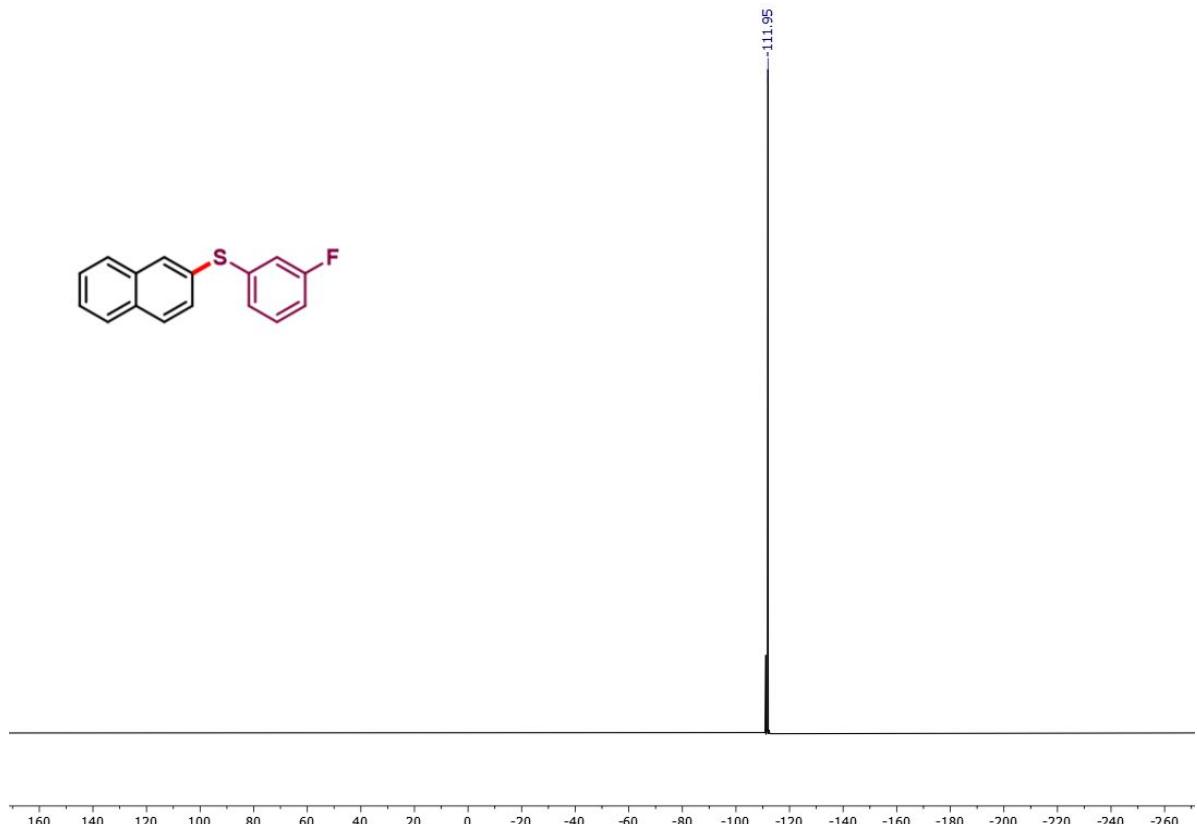
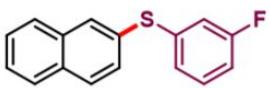


**Scheme 2A, entry 2d**  
**Yield: 82% ( $\beta:\alpha > 20:1$ )<sup>14</sup>**



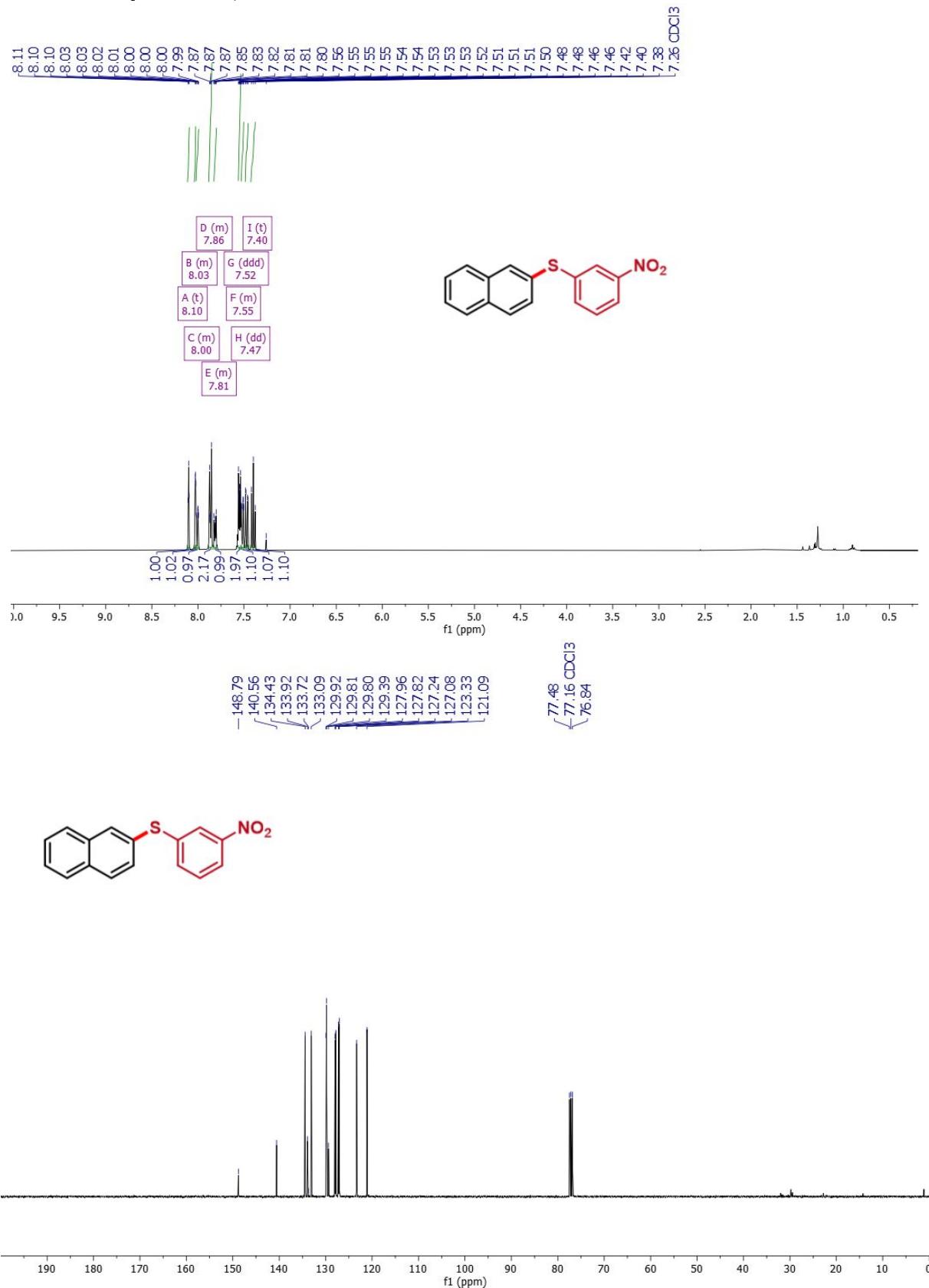
**Scheme 2A, entry 2e**  
**Yield: 79% ( $\beta:\alpha = 18:1$ )<sup>14</sup>**



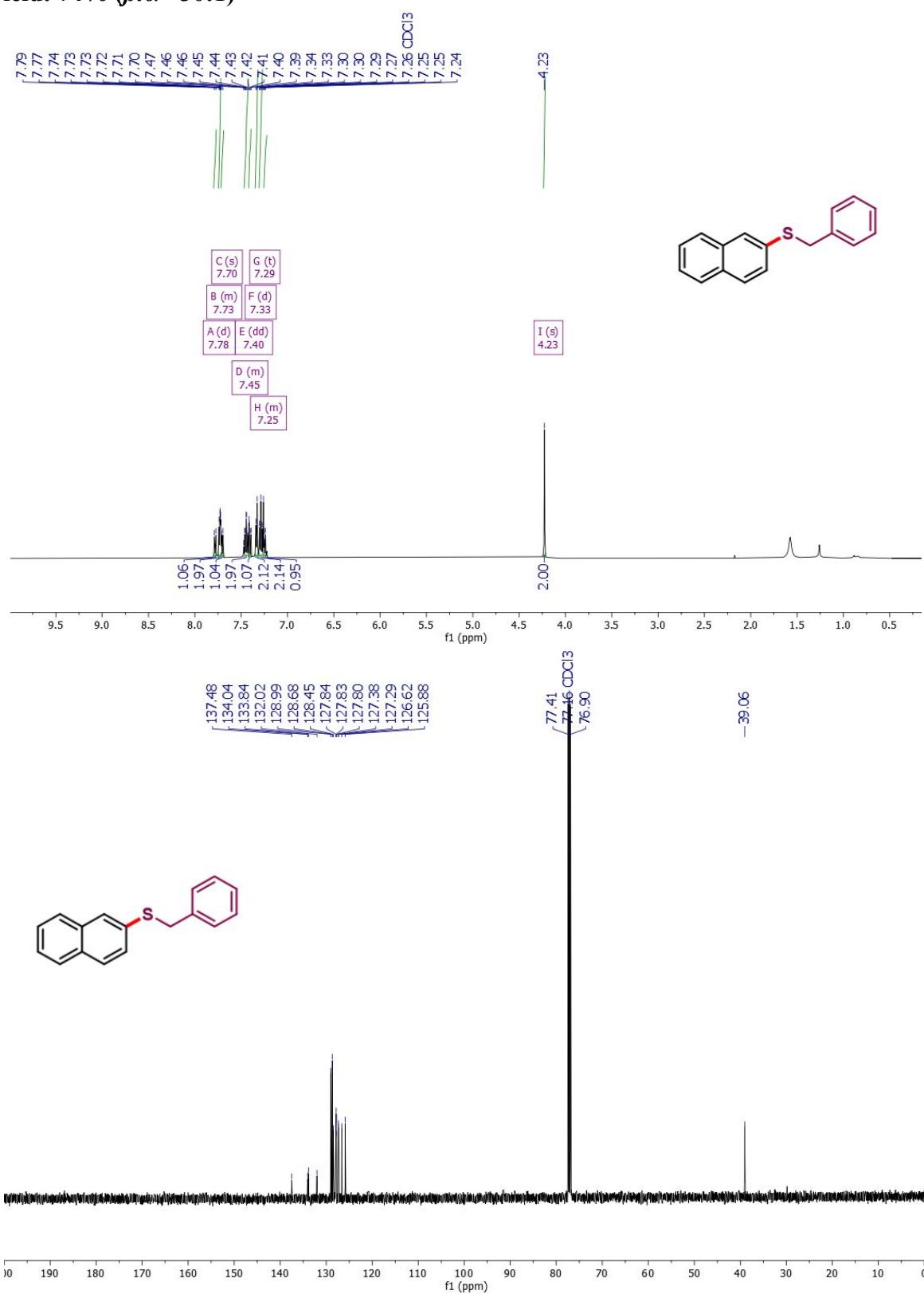


**Scheme 2A, entry 2f**

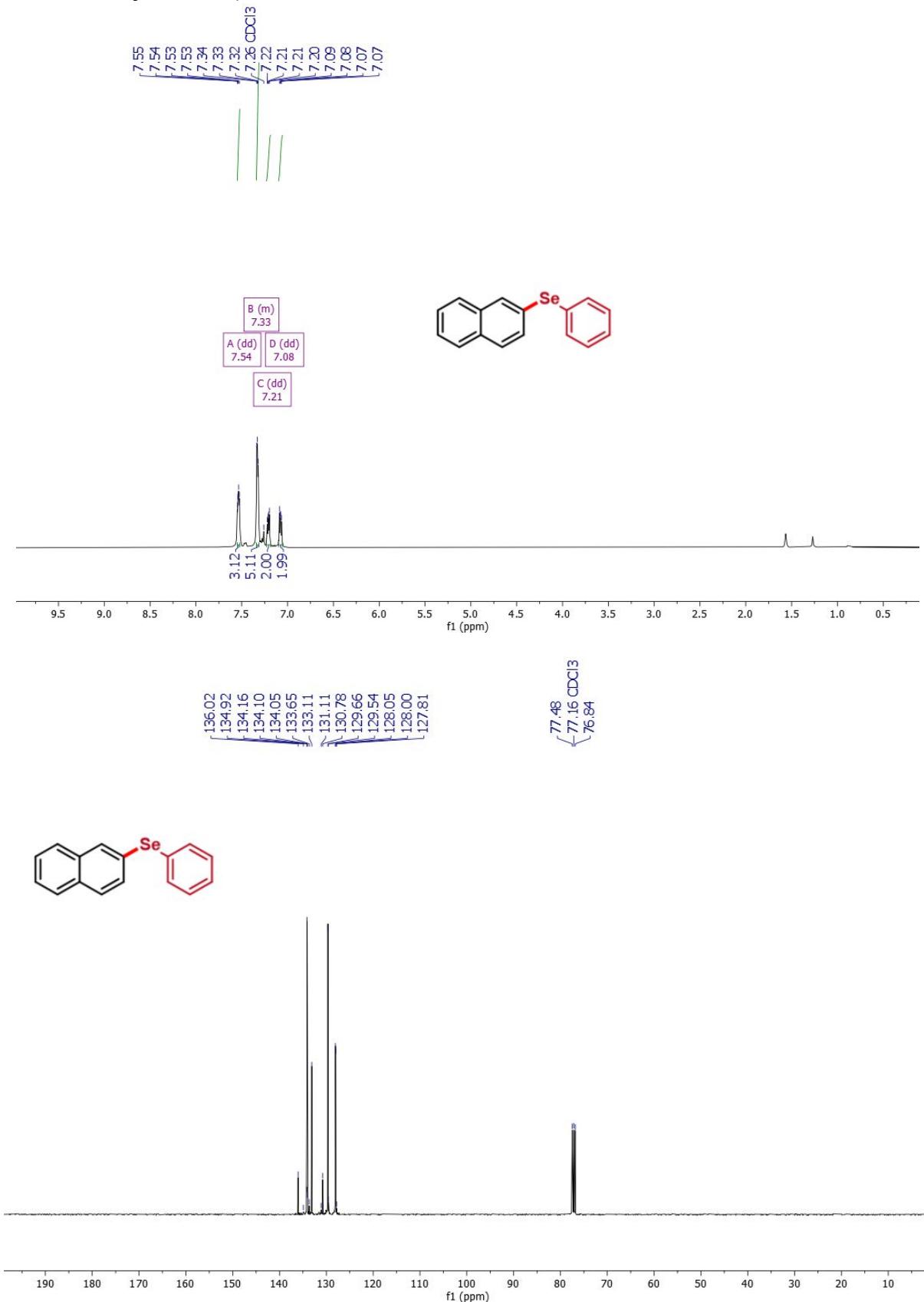
**Yield: 82% ( $\beta:\alpha > 30:1$ )<sup>14</sup>**



**Scheme 2A, entry 2g**  
**Yield: 74% ( $\beta:\alpha > 30:1$ )<sup>14</sup>**

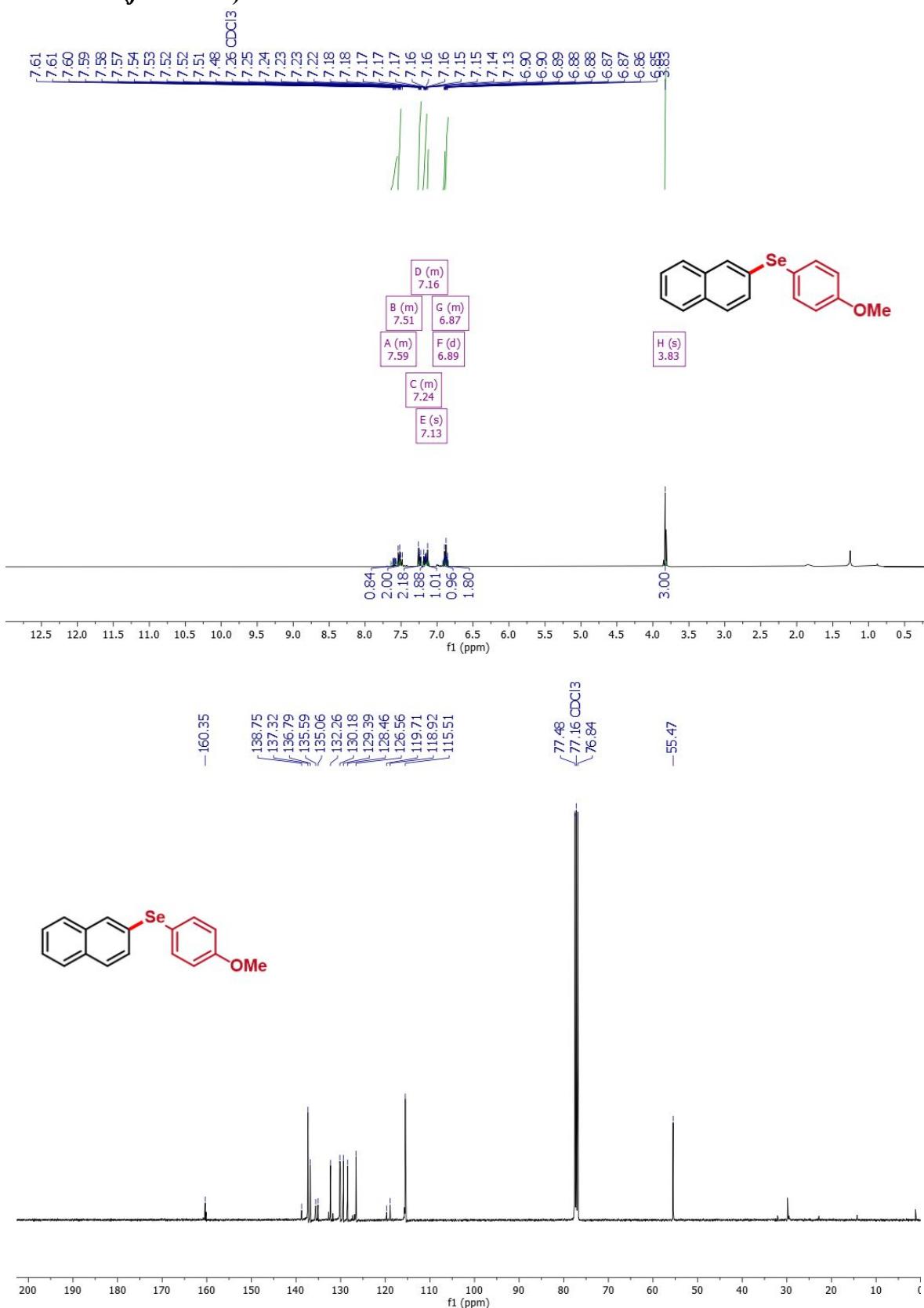


**Scheme 2A, entry 2h**  
**Yield: 80% ( $\beta:\alpha > 30:1$ )<sup>14</sup>**



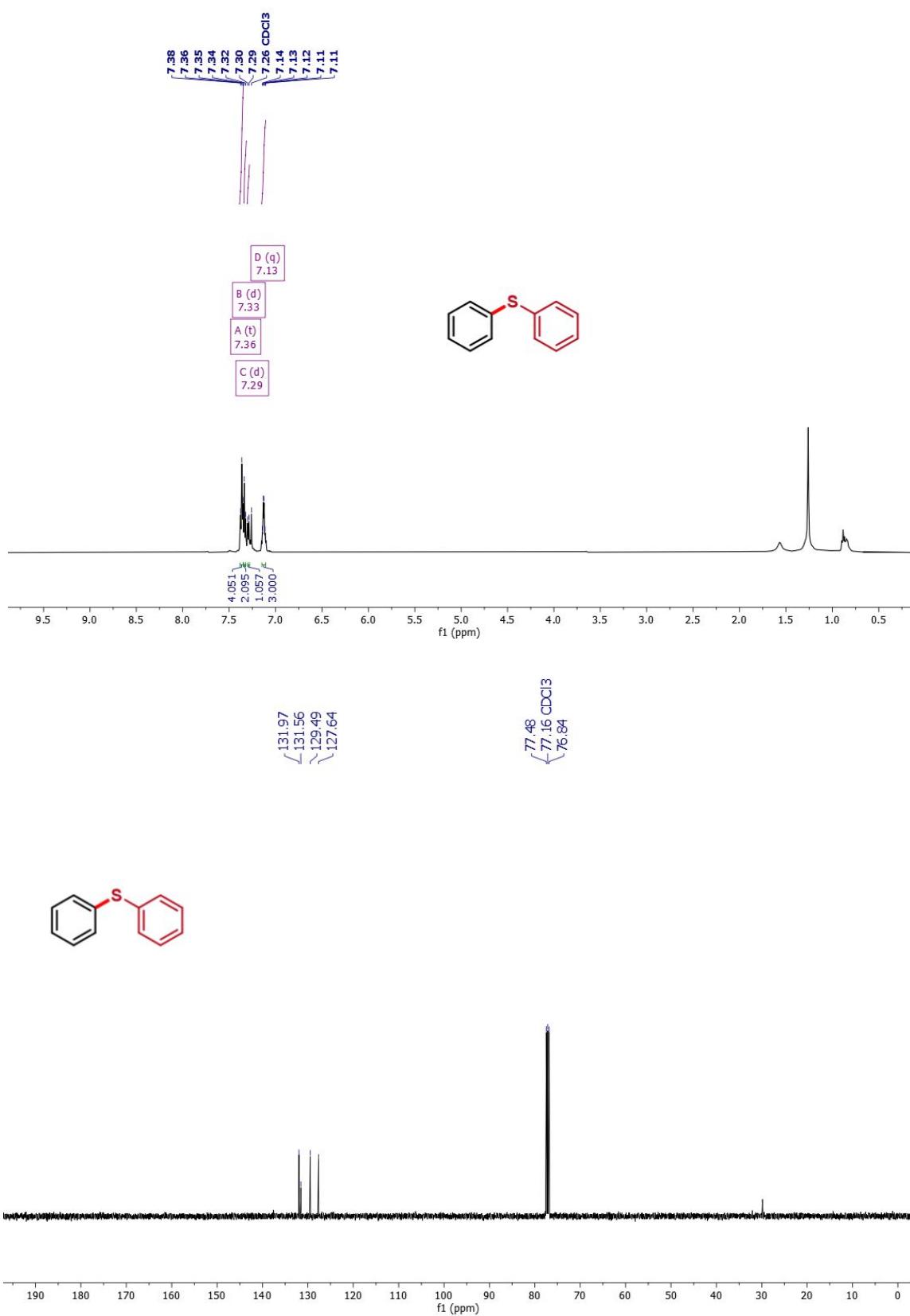
**Scheme 2A, entry 2i**

**Yield: 72% ( $\beta:\alpha > 30:1$ )<sup>14</sup>**



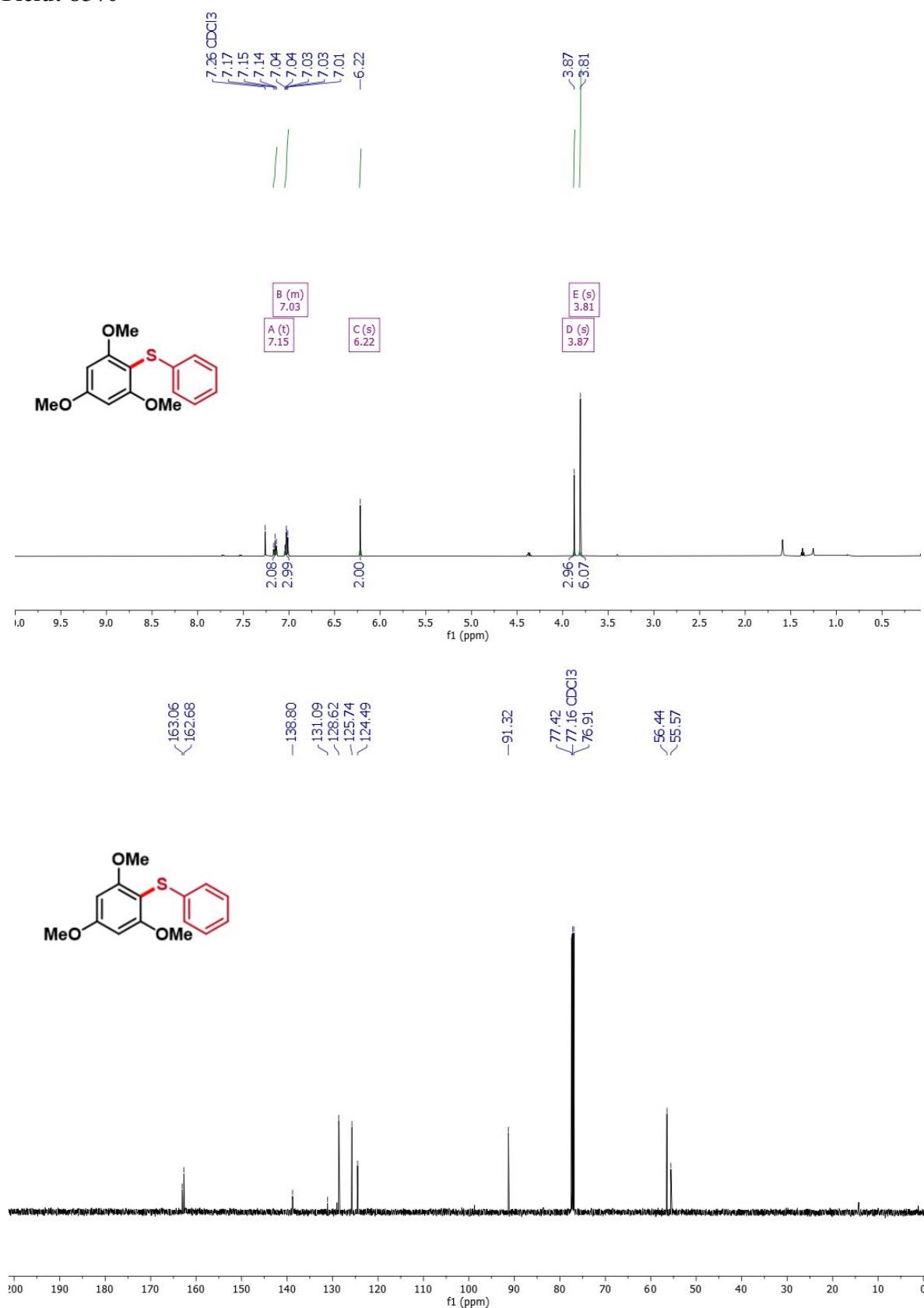
**Scheme 2A, entry 2j**

**Yield: 81%**



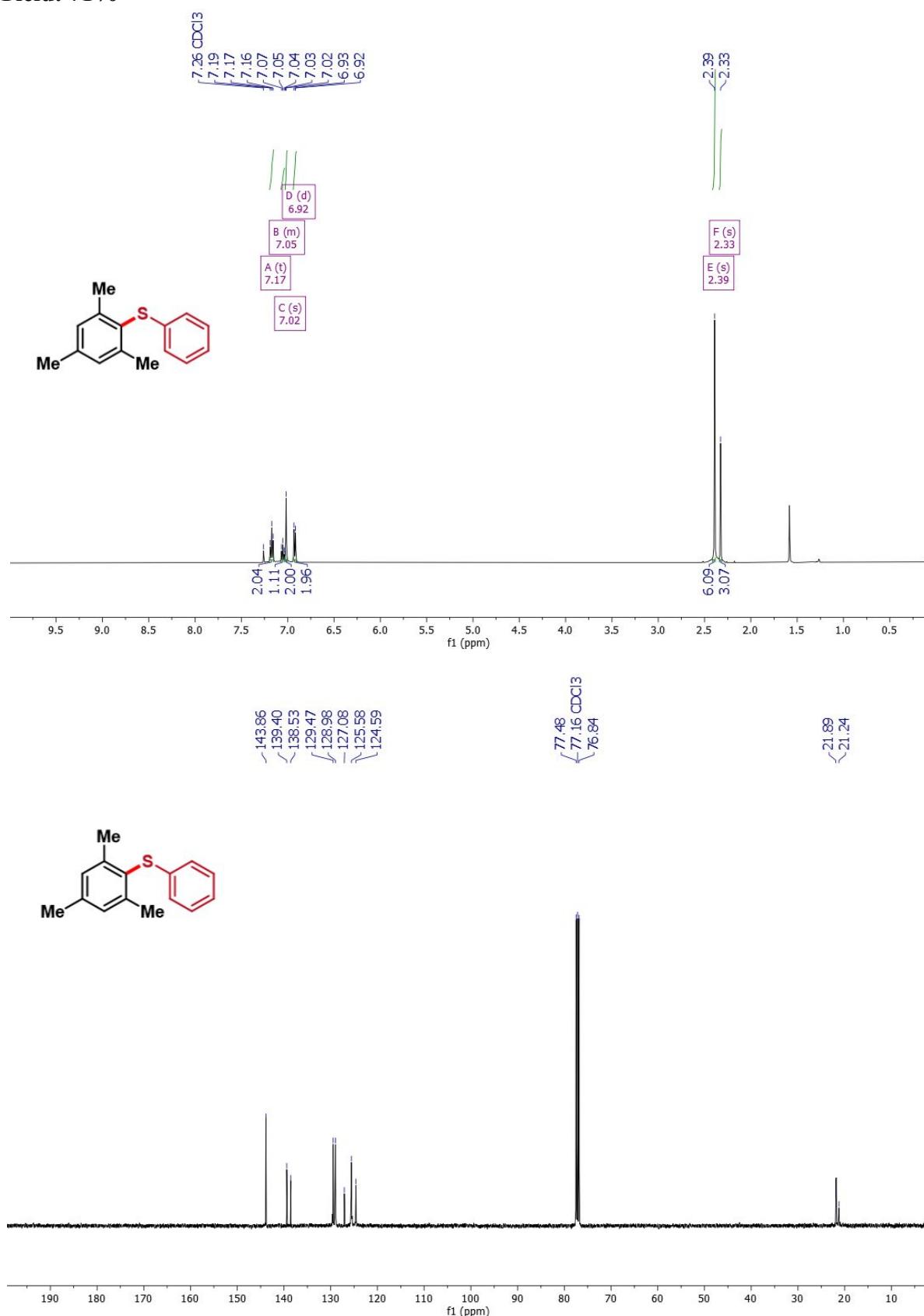
**Scheme 2A, entry 2k**

**Yield: 85%**



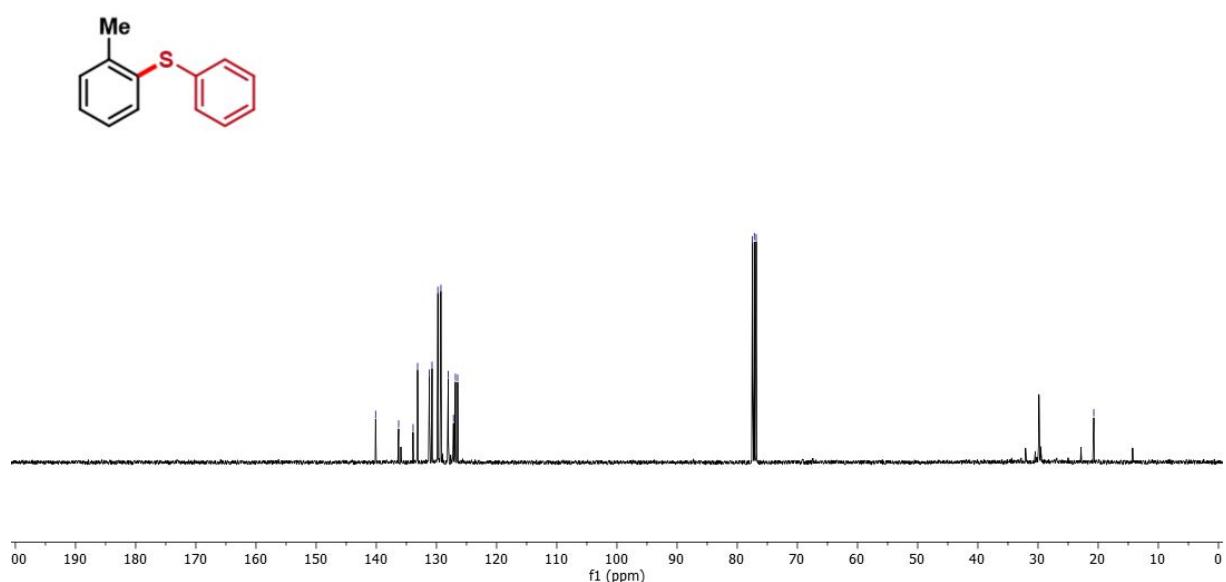
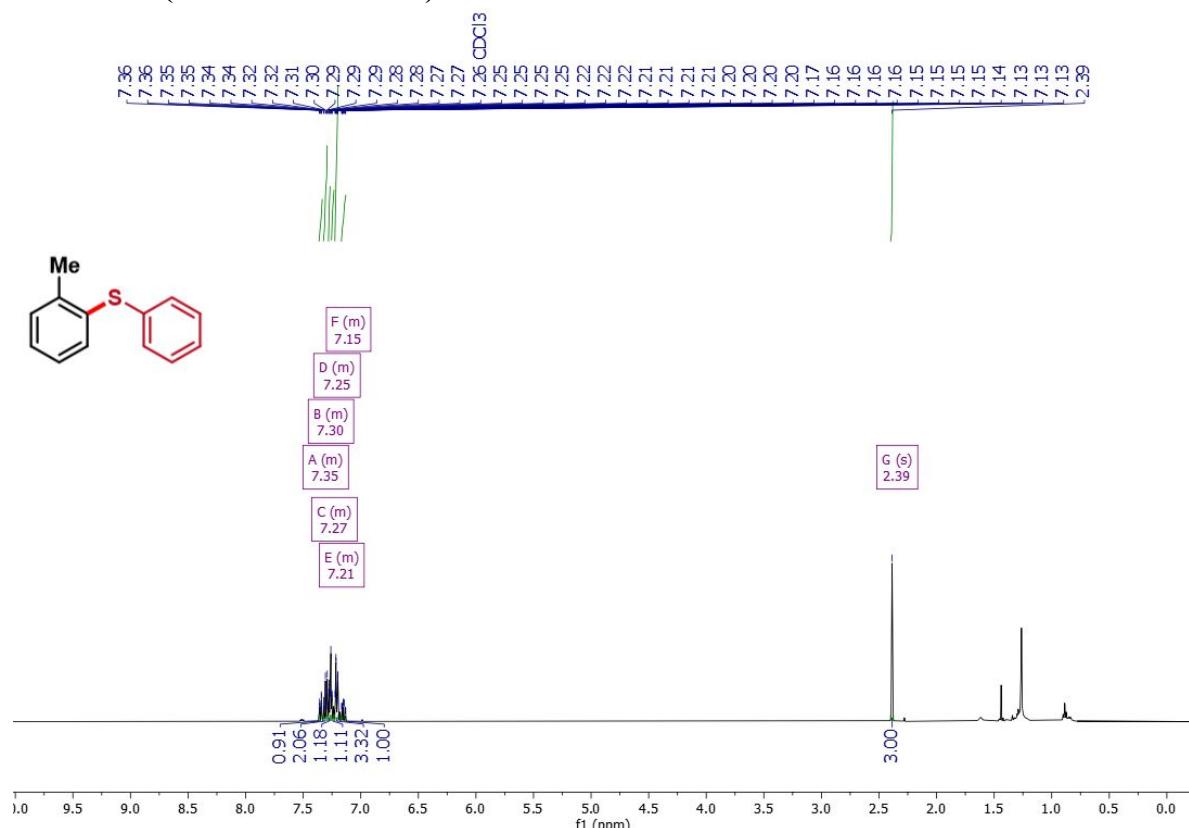
**Scheme 2A, entry 2l**

**Yield: 71%**



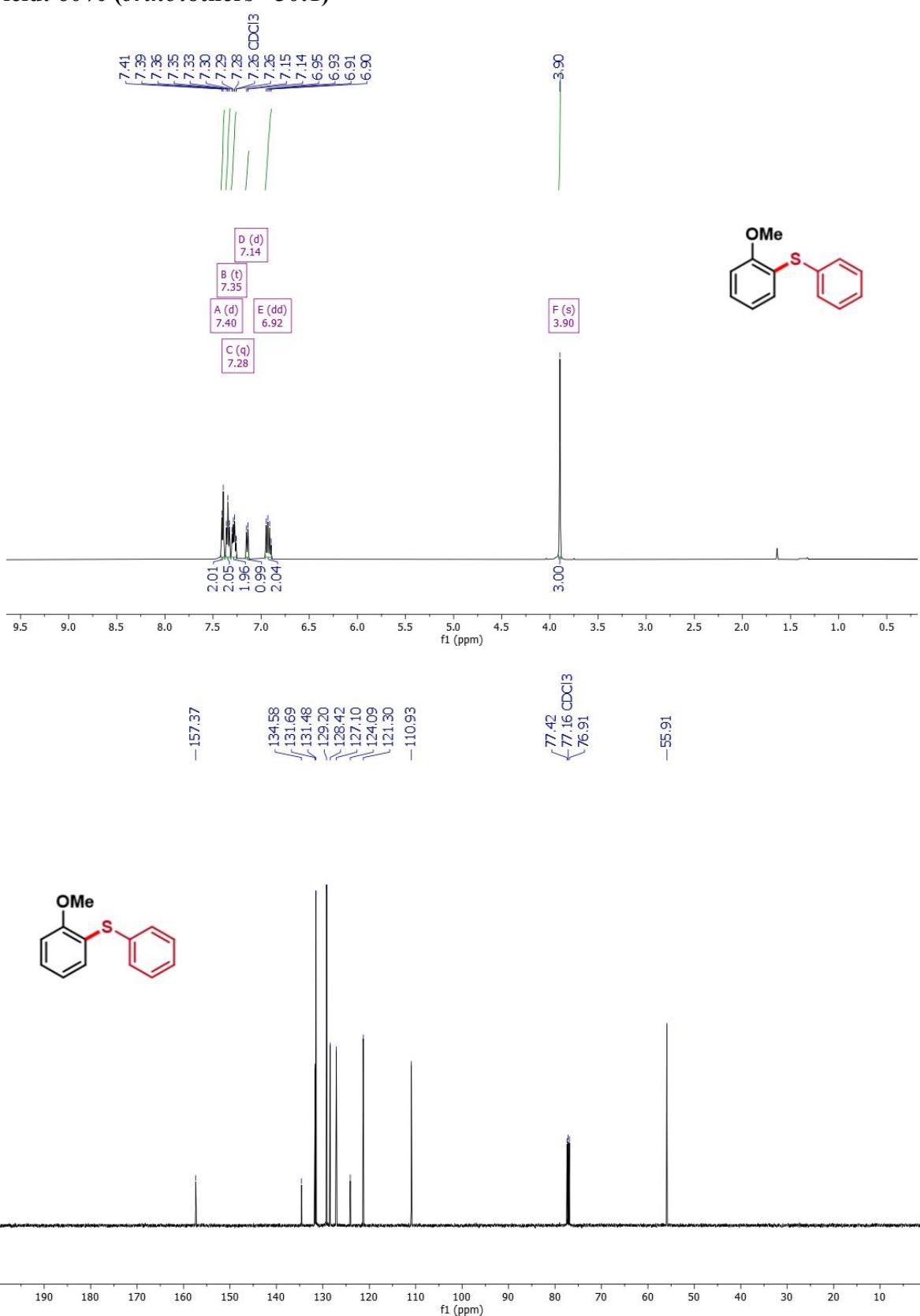
**Scheme 2A, entry 2m**

**Yield: 70% (*ortho*:others >20:1)<sup>14</sup>**



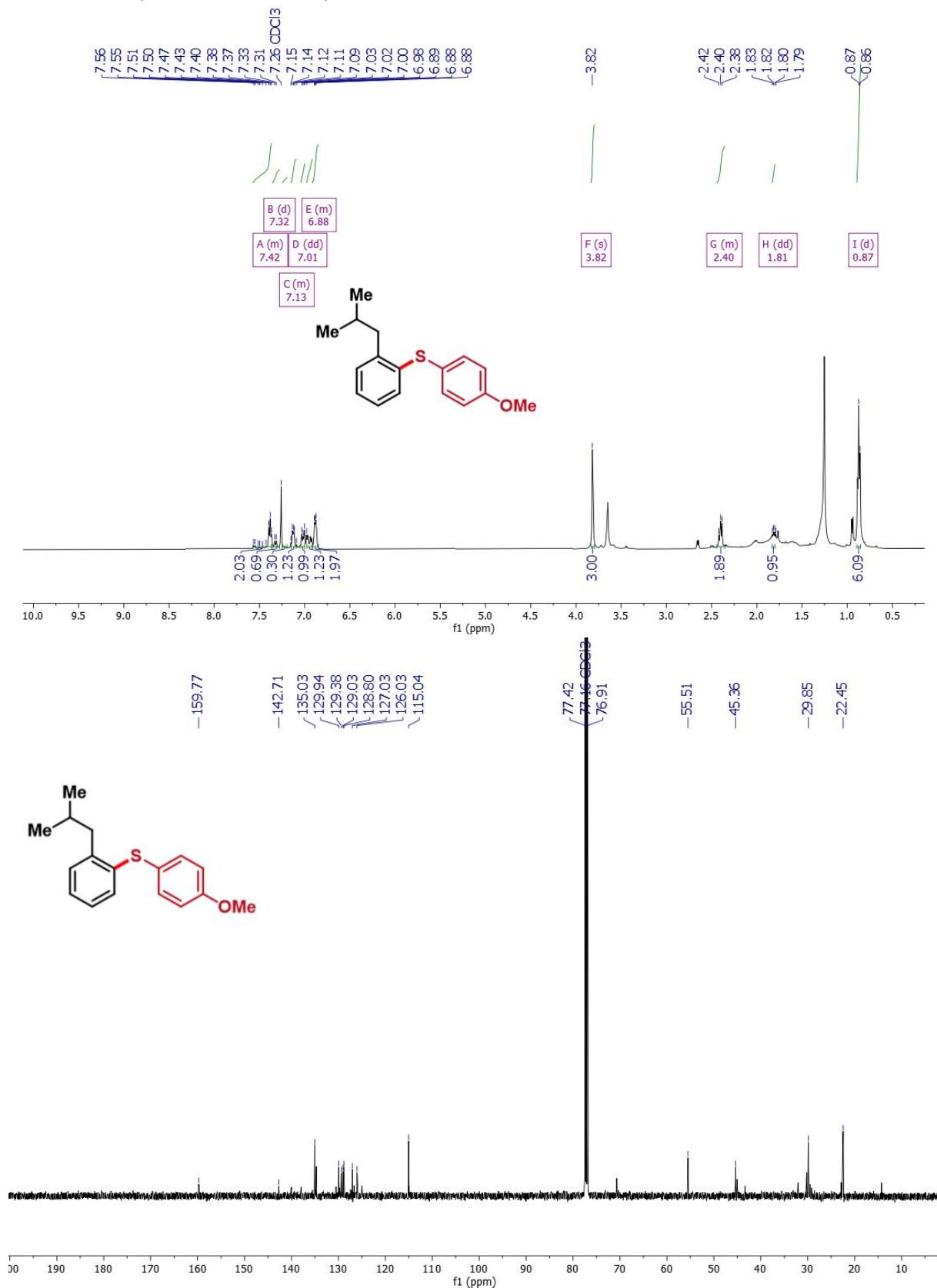
**Scheme 2A, entry 2n**

**Yield: 60% (*ortho*:others >30:1)<sup>14</sup>**

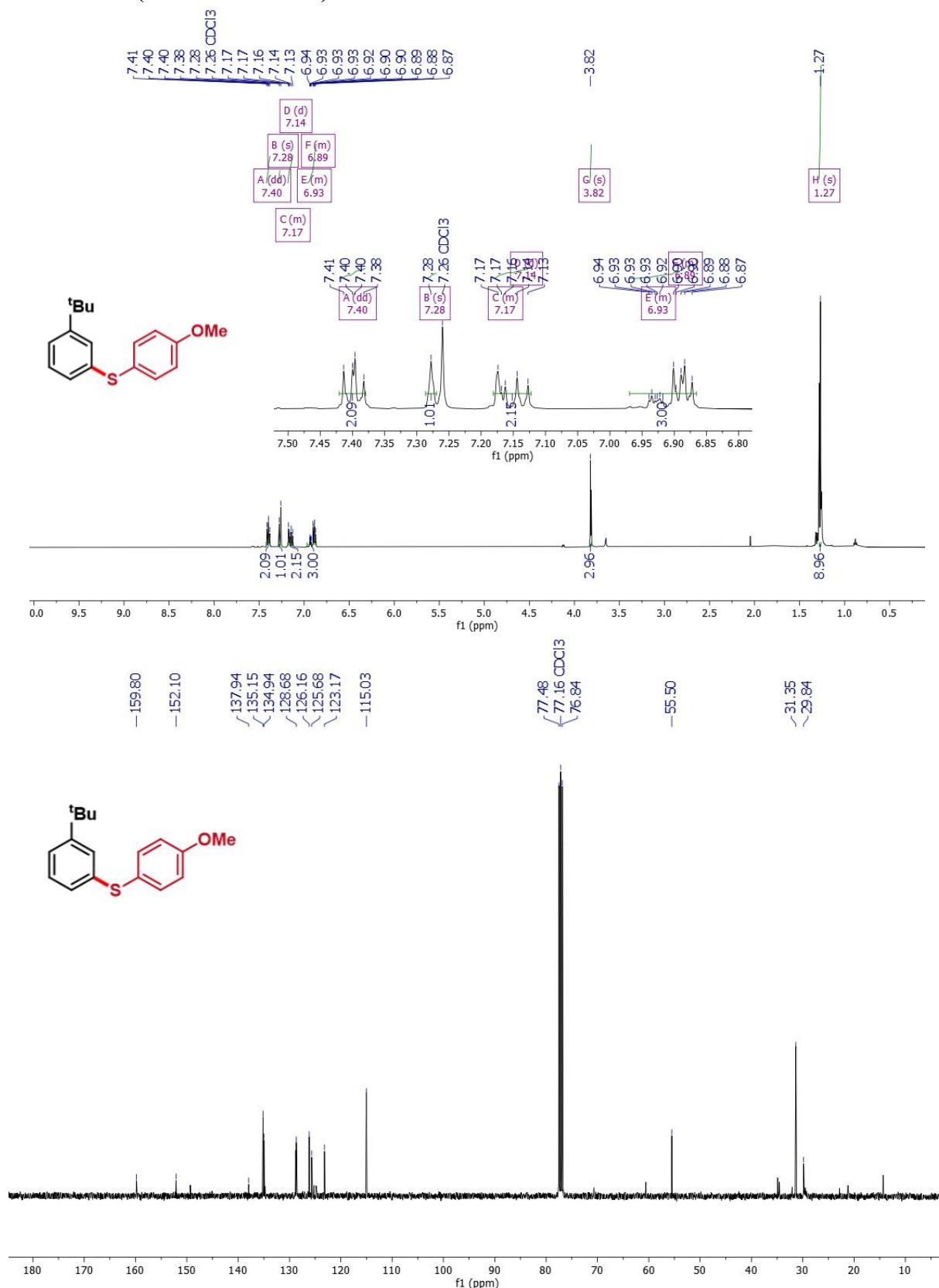


### Scheme 2A, entry 2o

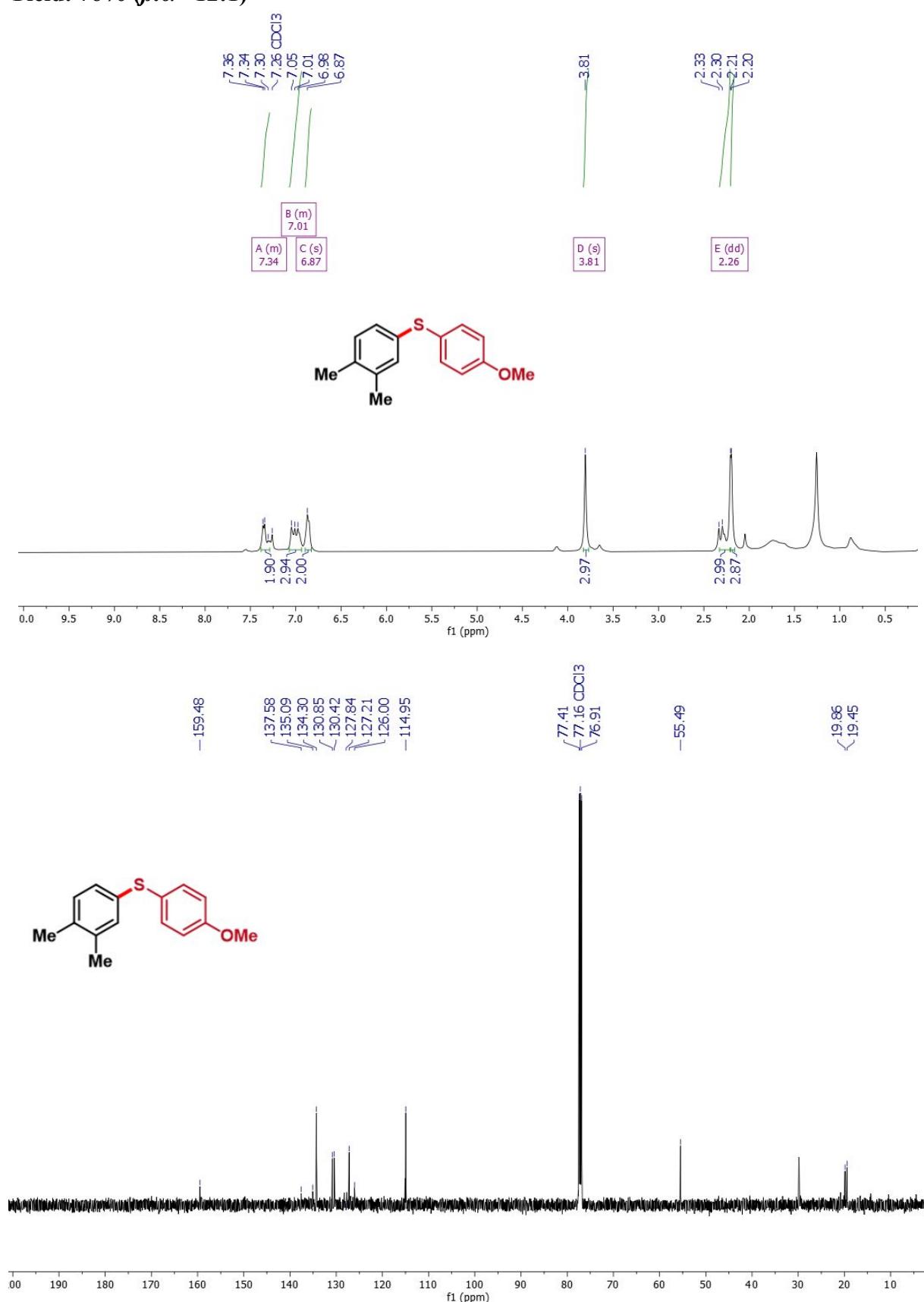
**Yield: 61% (*ortho*:others = 6:1)**<sup>14</sup>



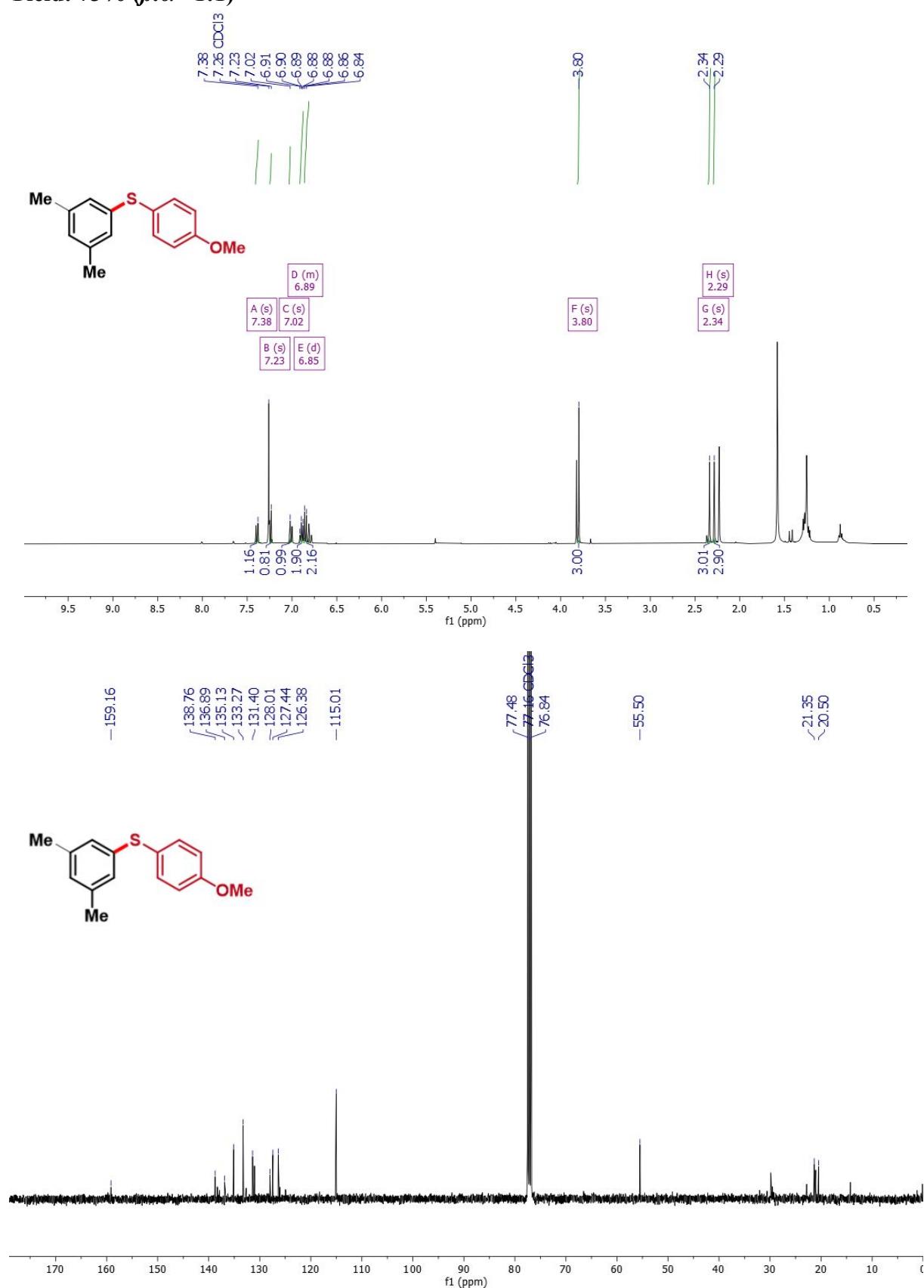
**Scheme 2A, entry 2p**  
**Yield: 72% (*meta*:others = 4:1)**<sup>14</sup>



**Scheme 2A, entry 2q**  
**Yield: 76% ( $\beta:\alpha = 12:1$ )<sup>14</sup>**

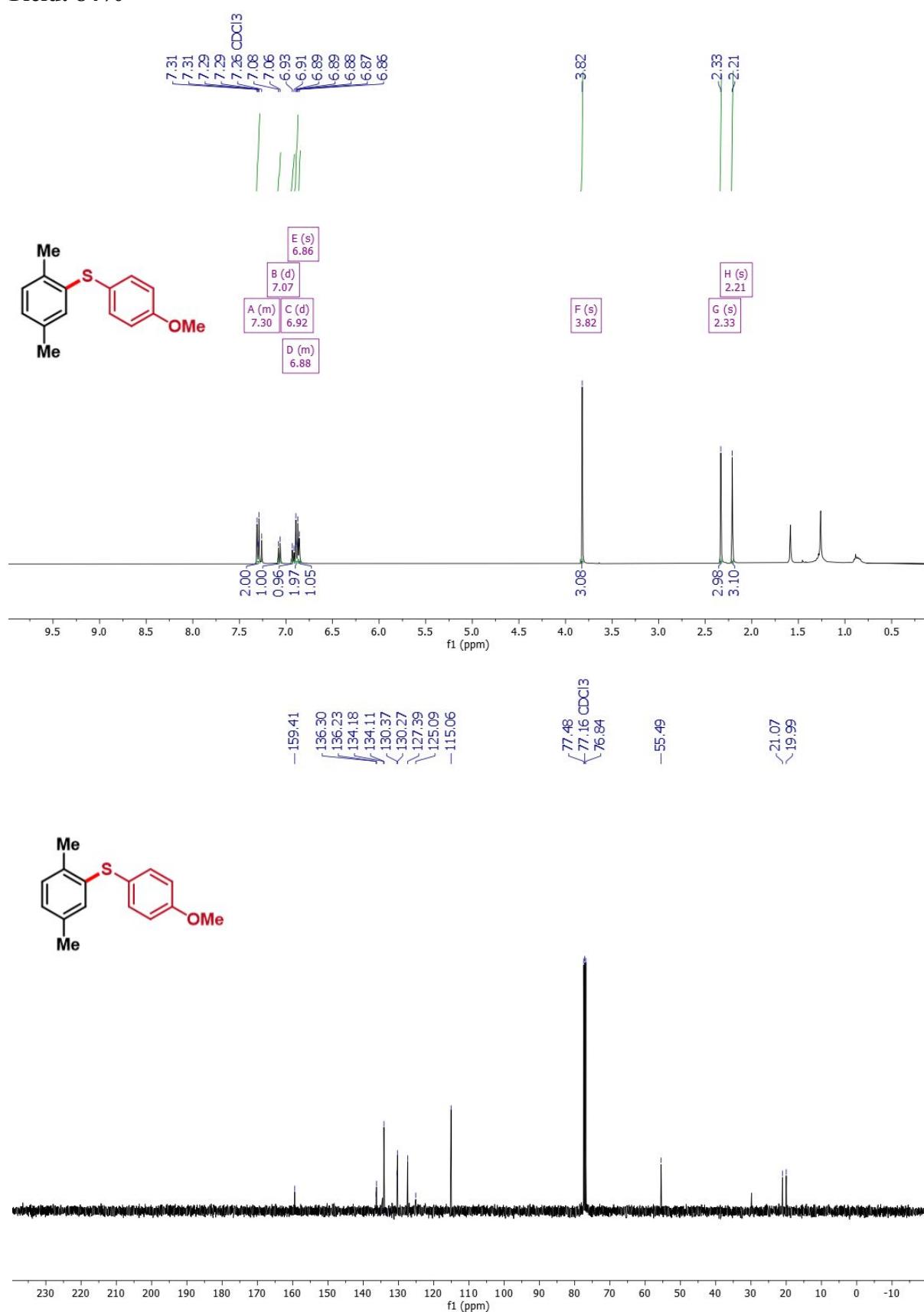


**Scheme 2A, entry 2r**  
**Yield: 73% ( $\beta:\alpha = 1:1$ )<sup>14</sup>**



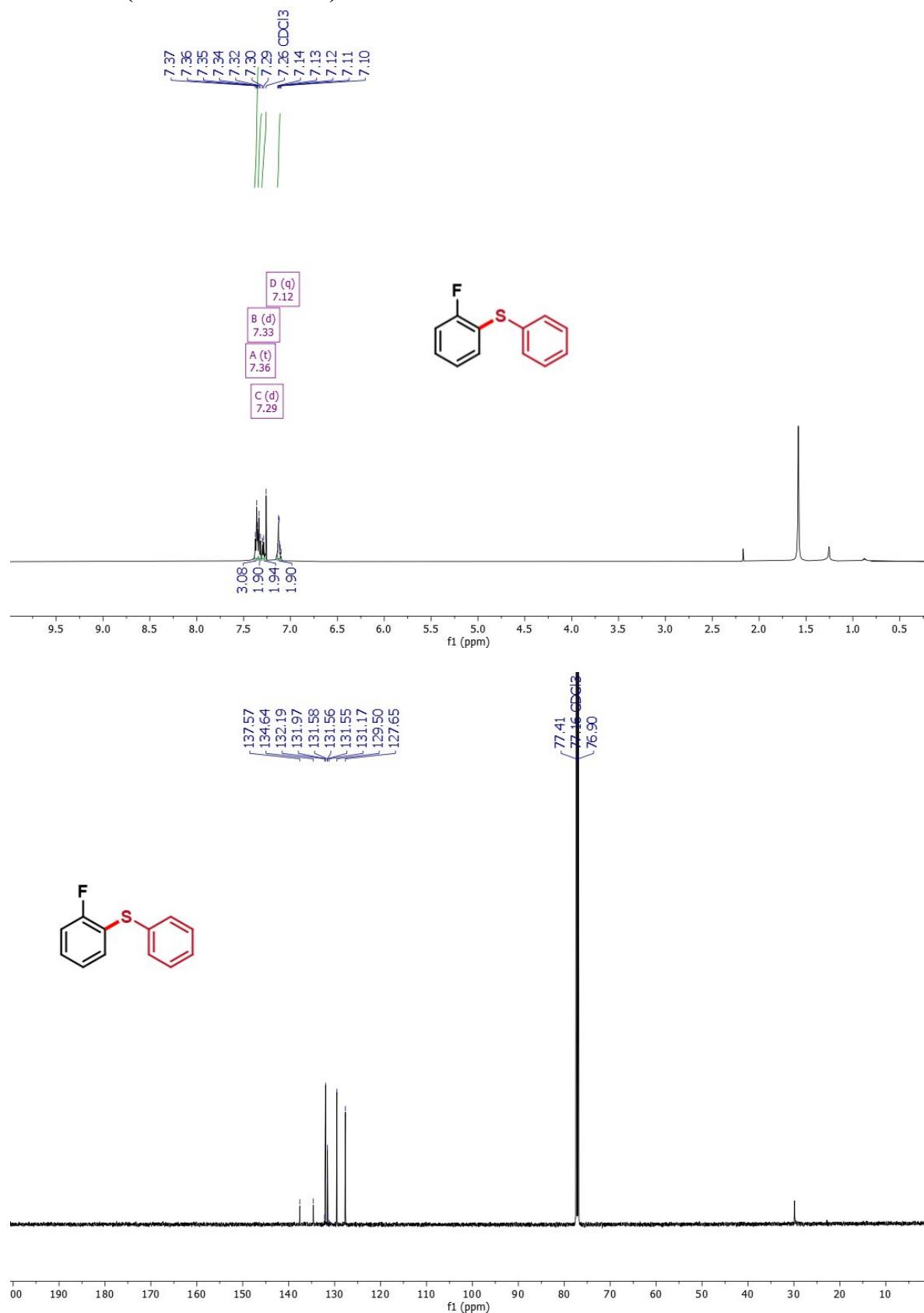
**Scheme 2A, entry 2s**

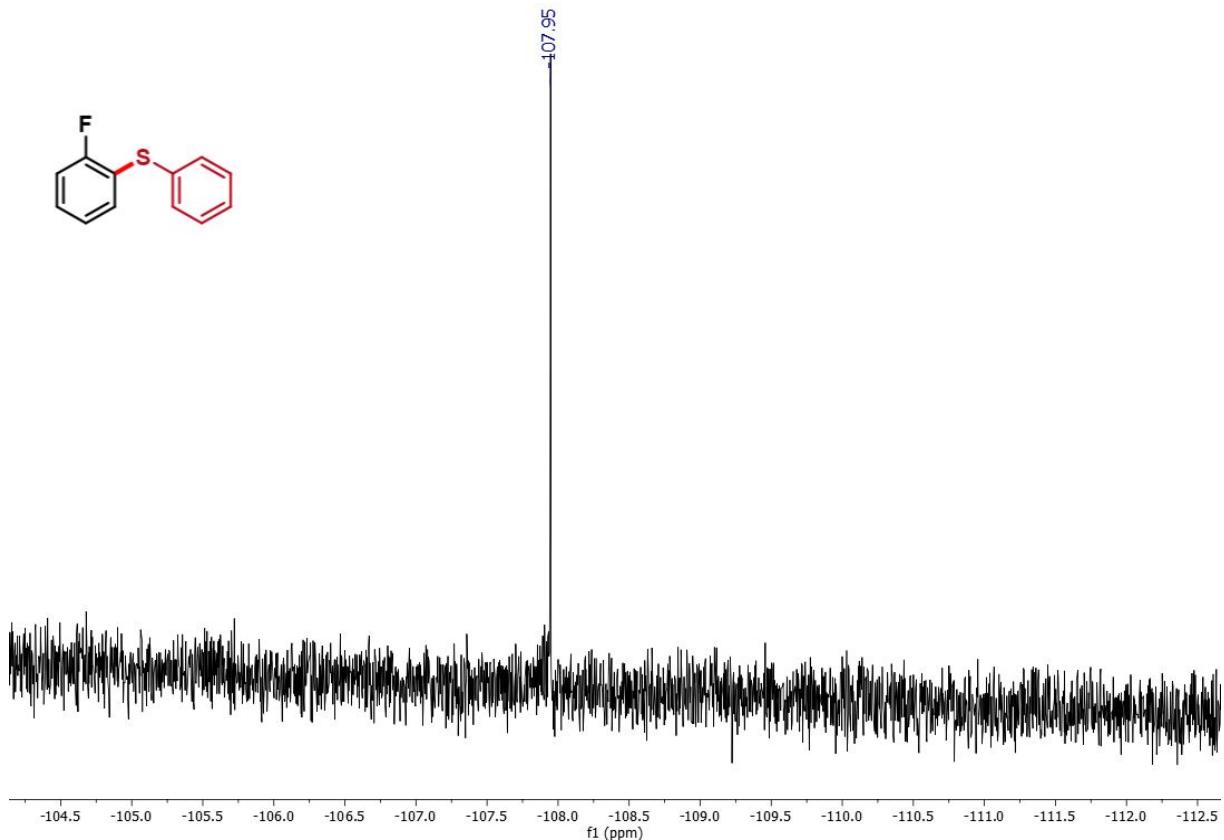
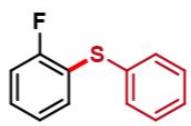
**Yield: 84%**



**Scheme 2A, entry 2t**

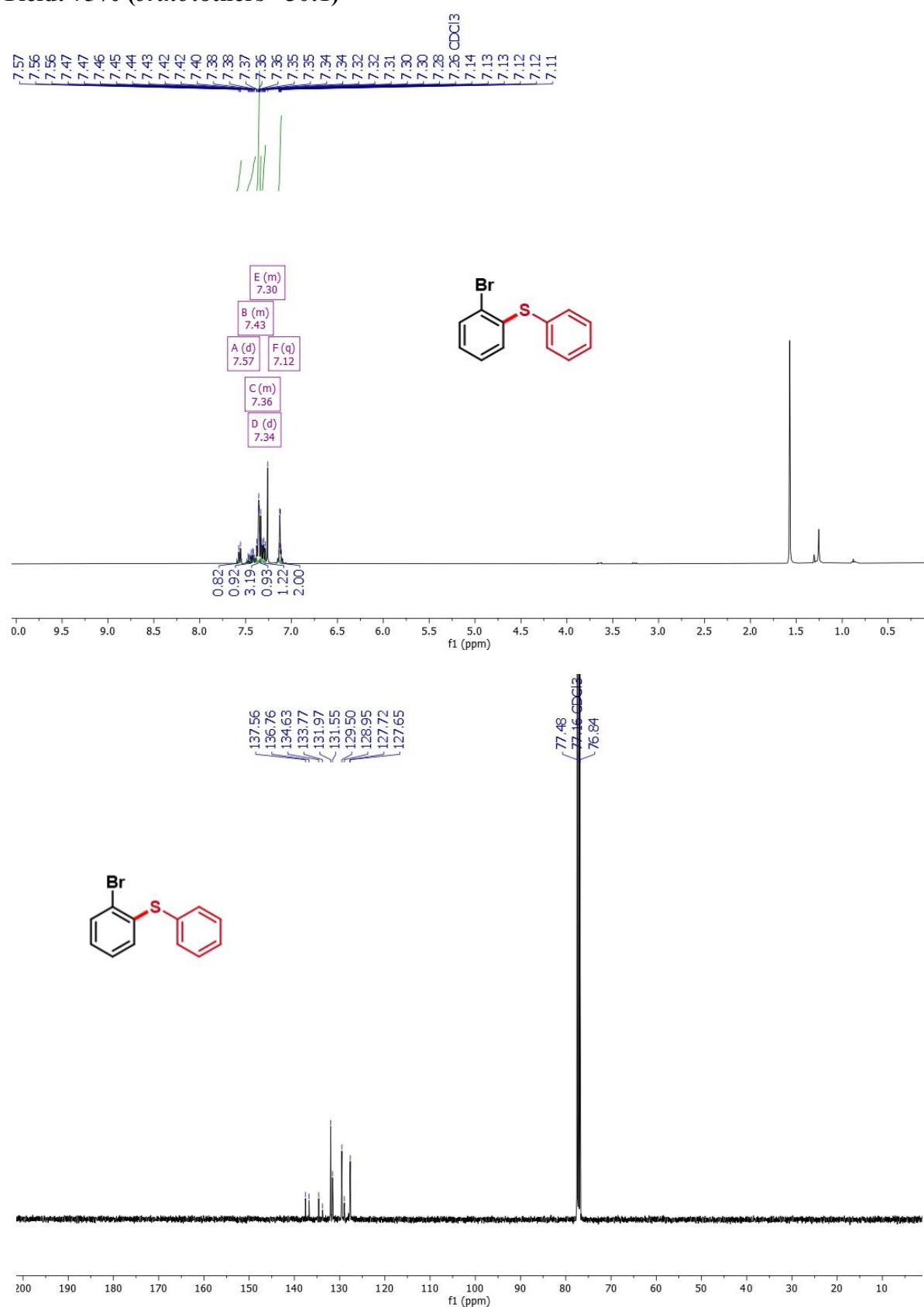
**Yield: 79% (*ortho*:others >30:1)<sup>14</sup>**





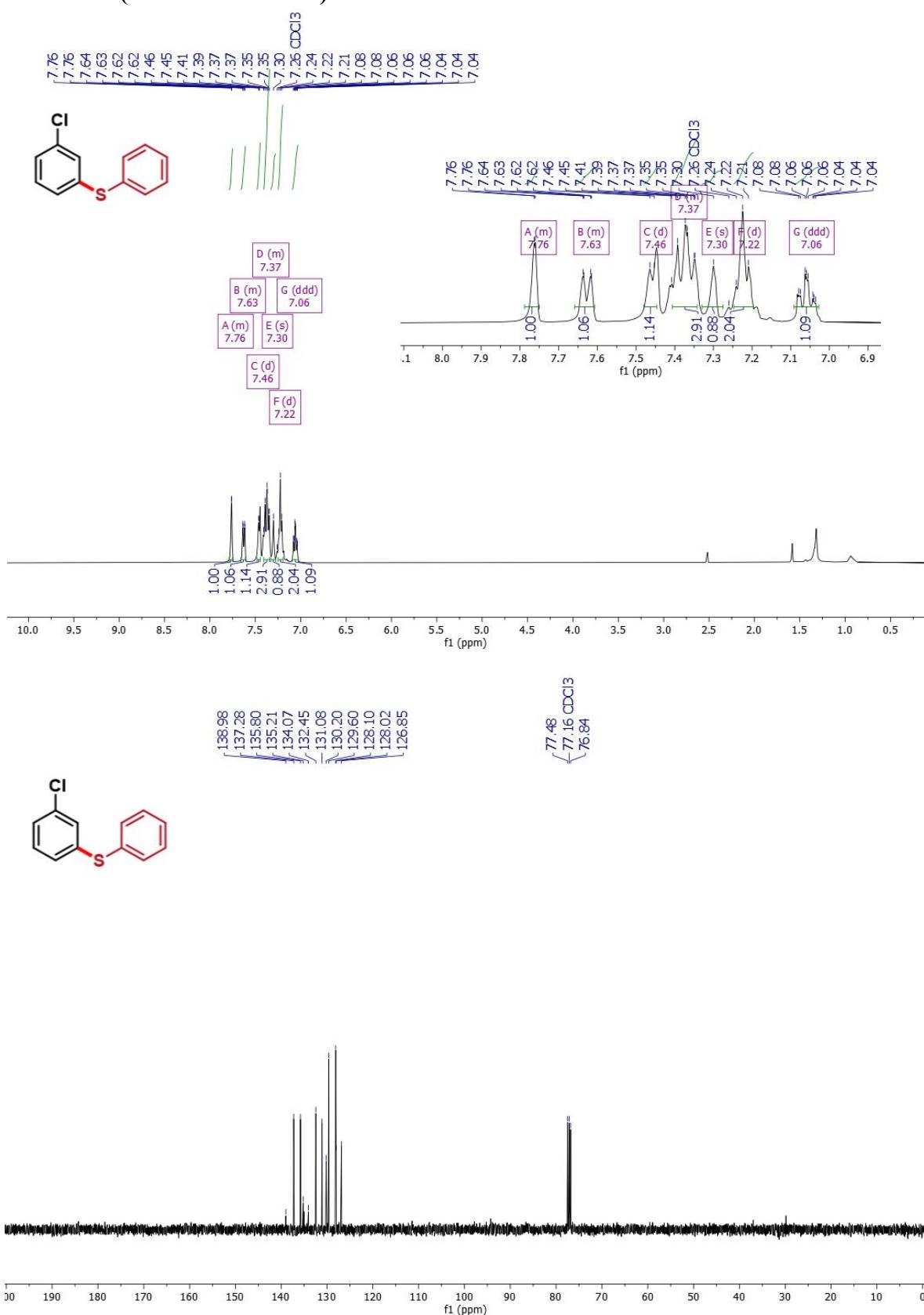
**Scheme 2A, entry 2u**

**Yield: 75% (*ortho*:others >30:1)<sup>14</sup>**



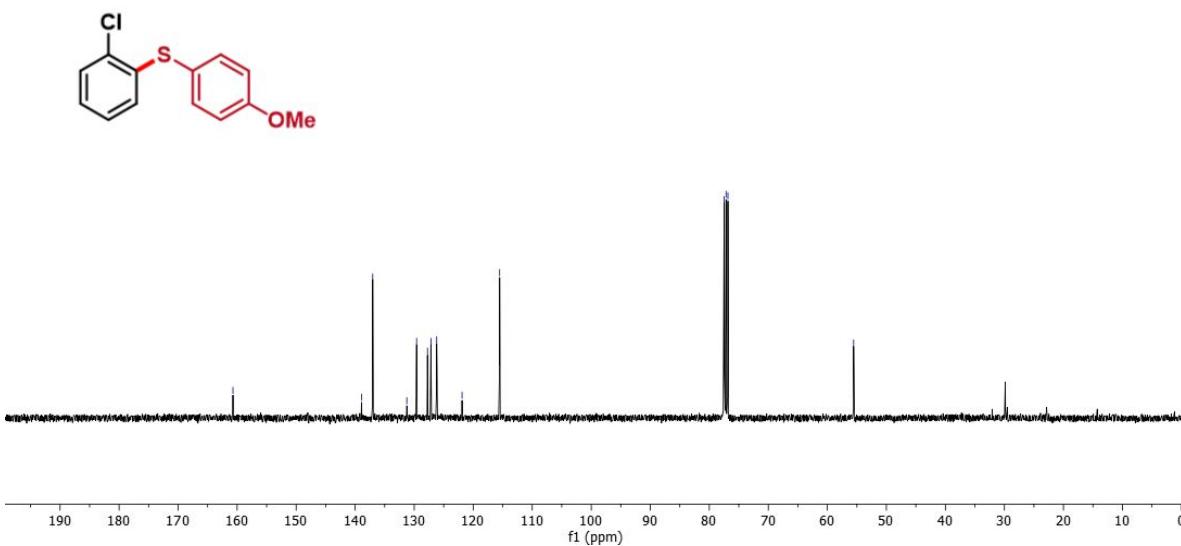
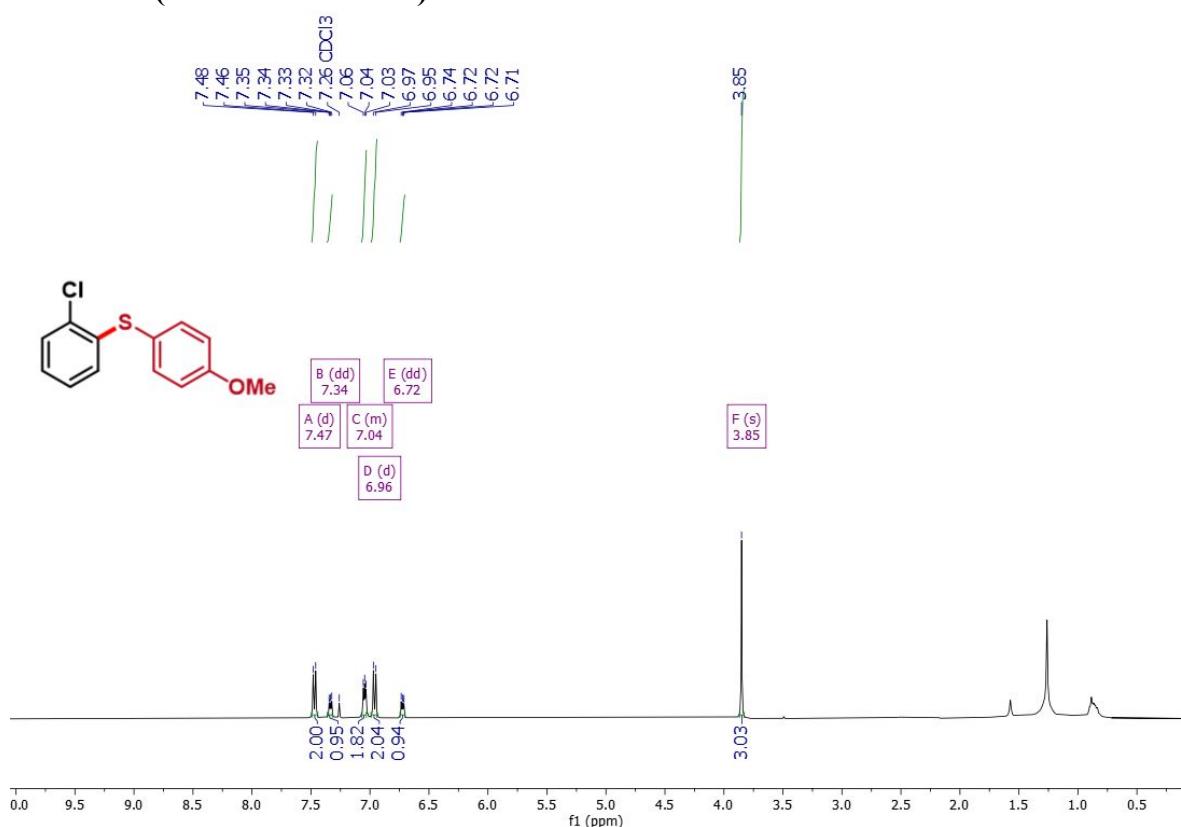
**Scheme 2A, entry 2v**

**Yield: 77% (*meta*:others >20:1)<sup>14</sup>**



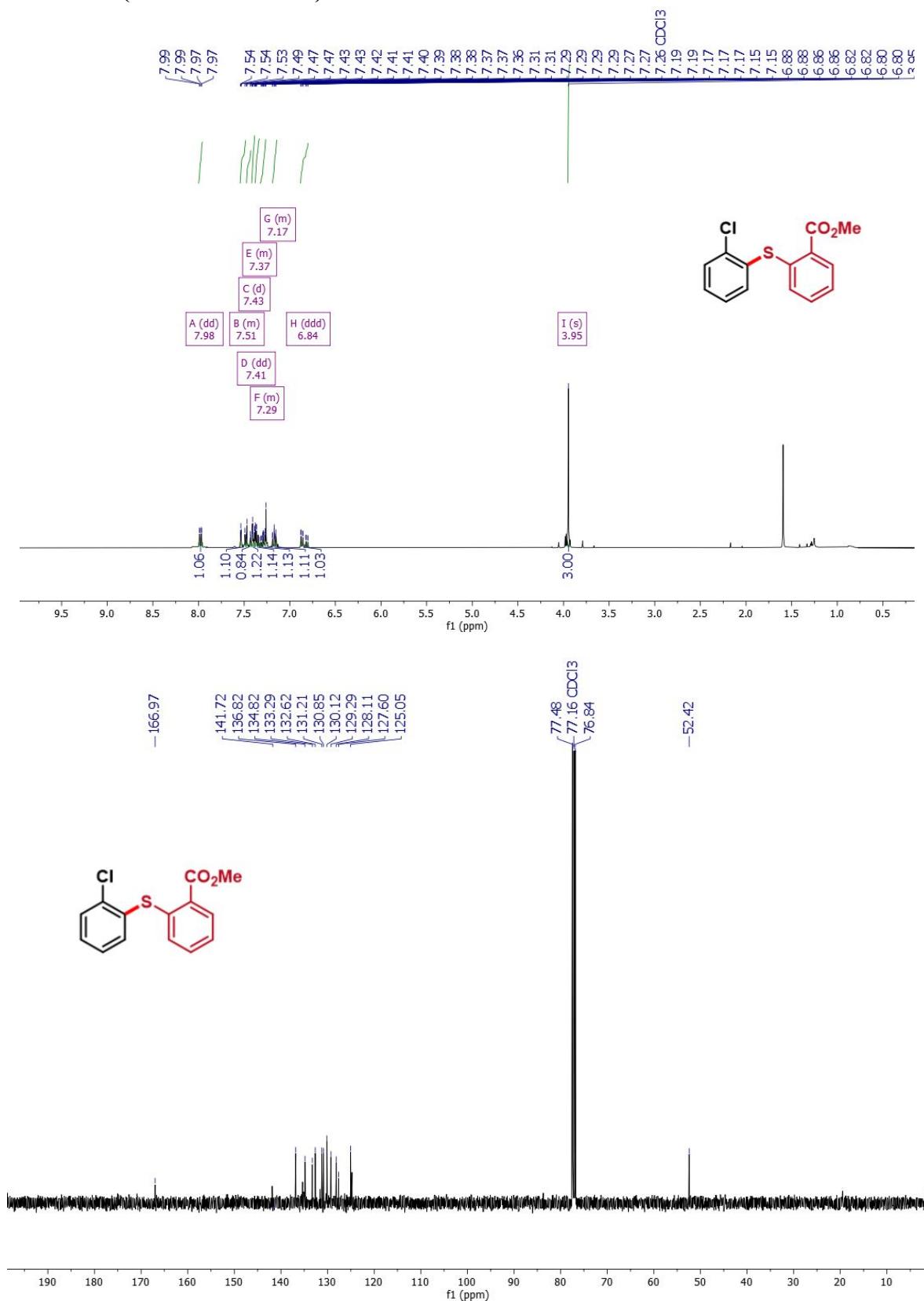
**Scheme 2A, entry 2w**

**Yield: 63% (*ortho*:others >20:1)<sup>14</sup>**



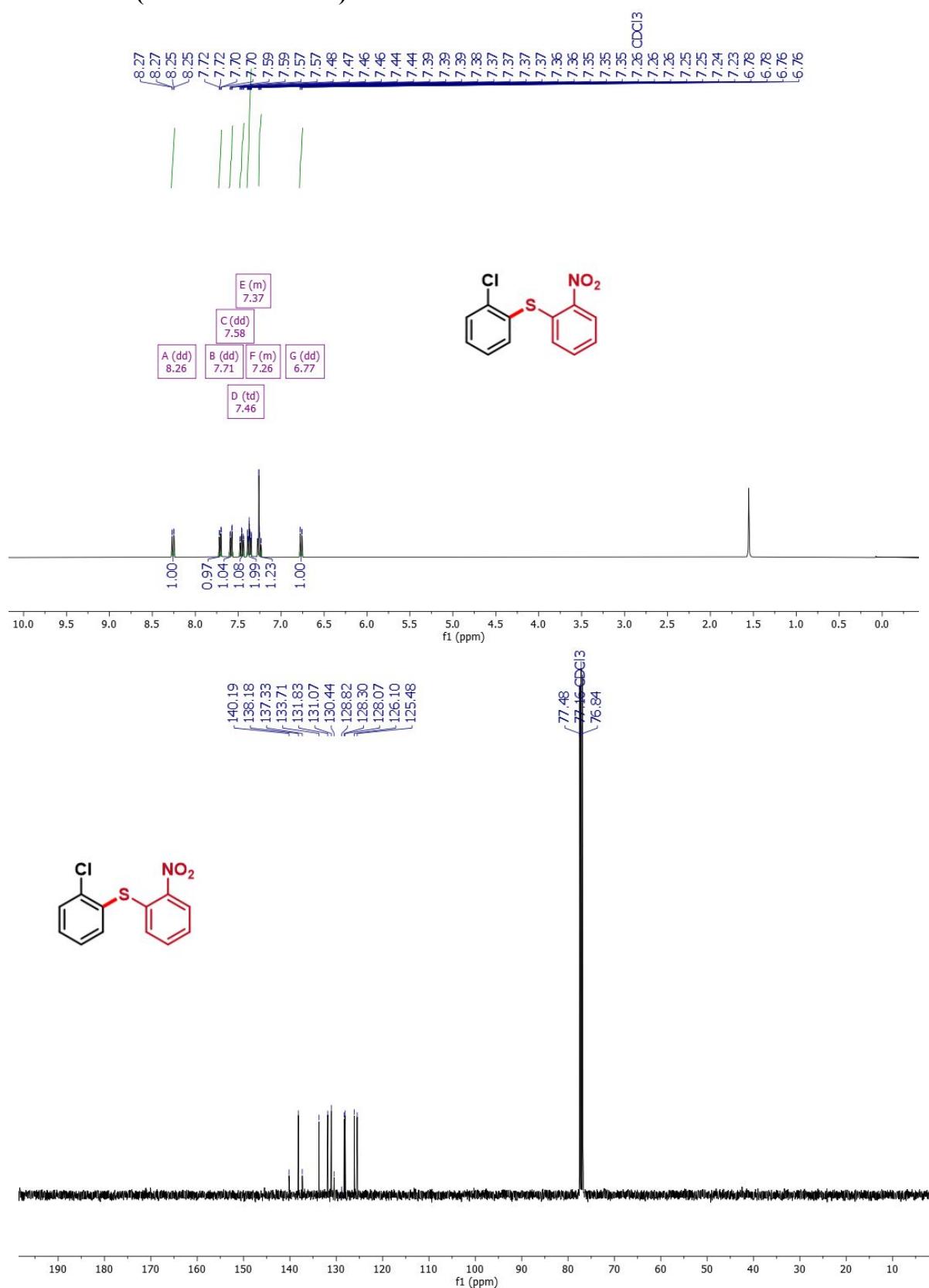
**Scheme 2A, entry 2x**

**Yield: 78% (*ortho*:others = 9:1)<sup>14</sup>**

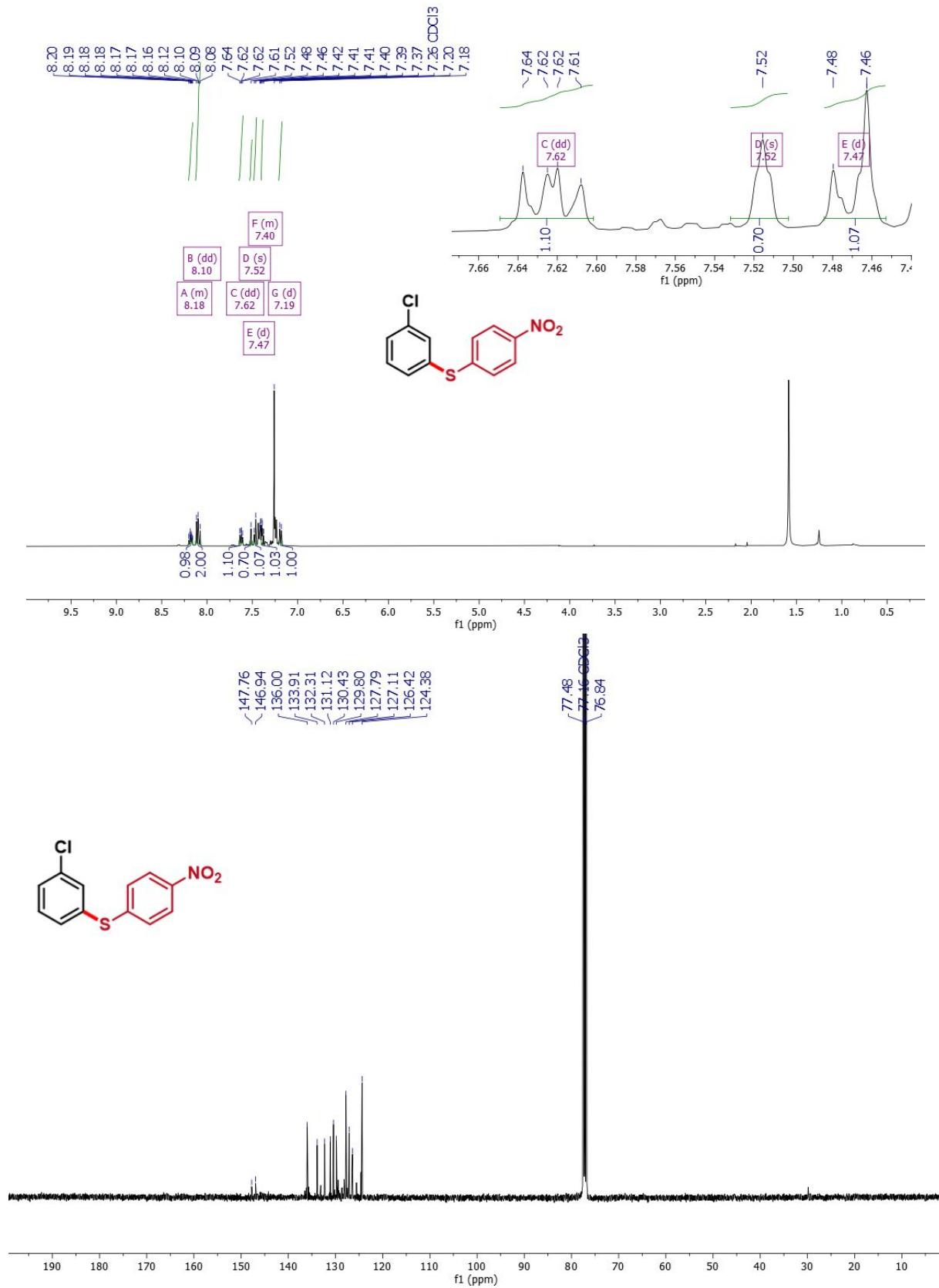


**Scheme 2A, entry 2y**

**Yield: 83% (*ortho*:others = 10:1)<sup>14</sup>**

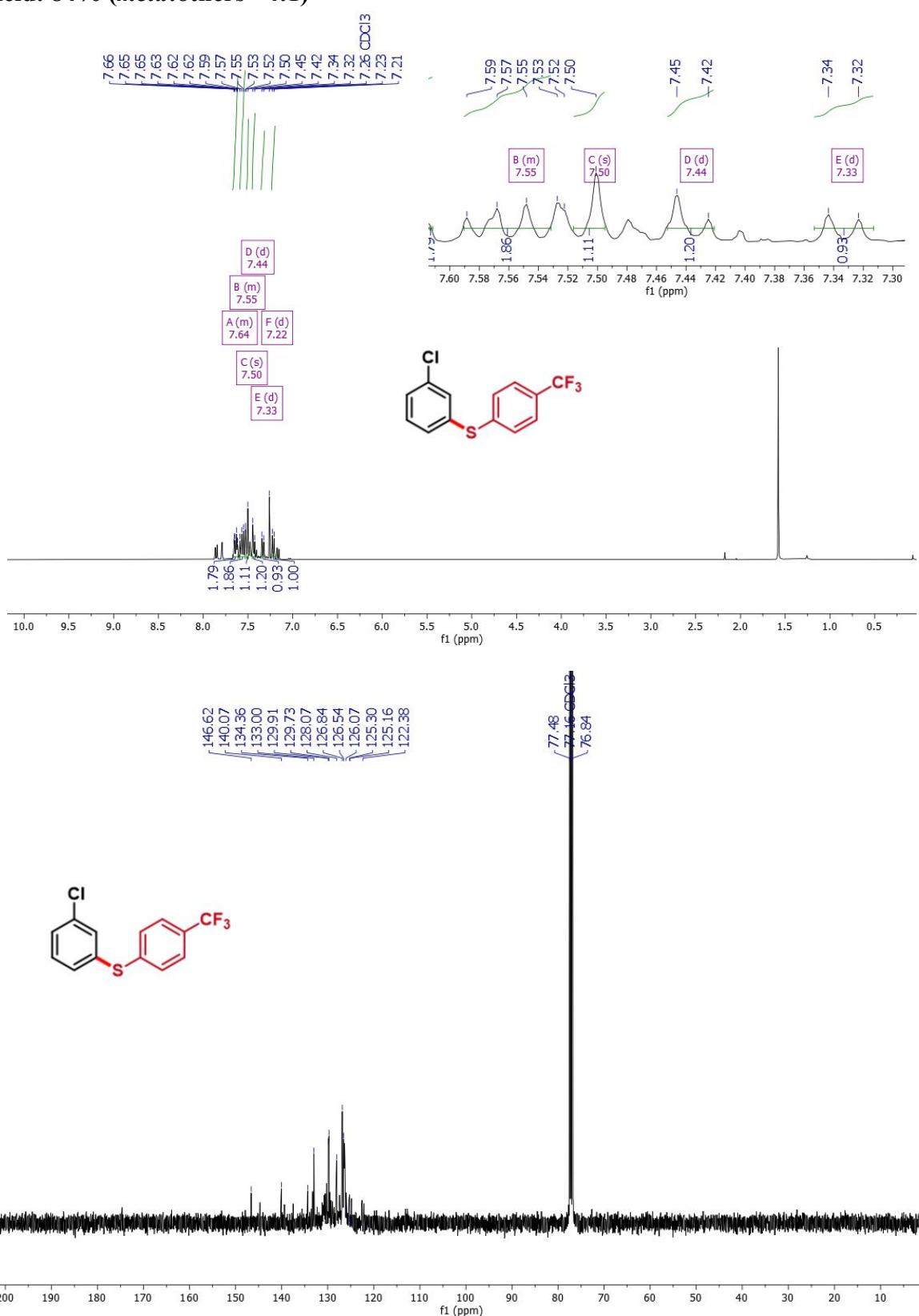


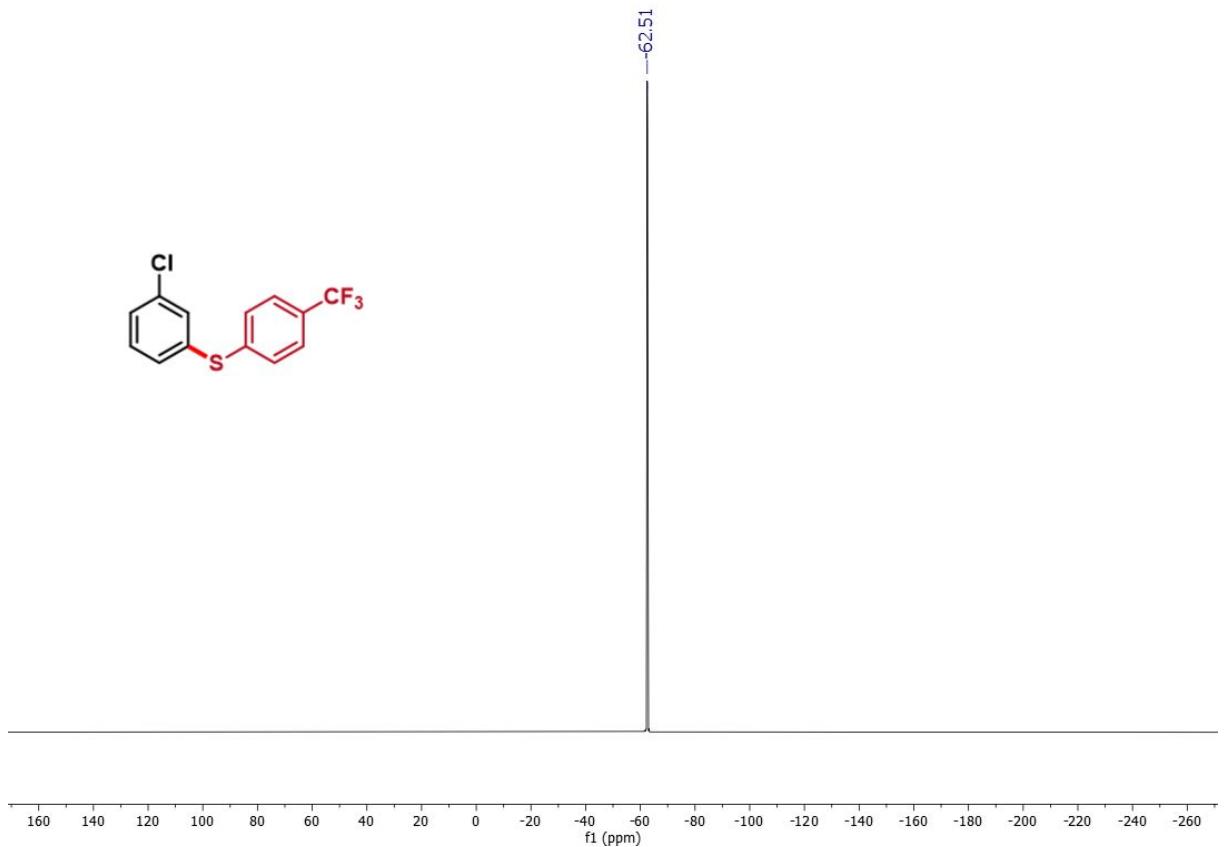
**Scheme 2A, entry 2z**  
**Yield: 73% (*meta*:others = 5:1)**<sup>14</sup>



**Scheme 2A, entry 2aa**

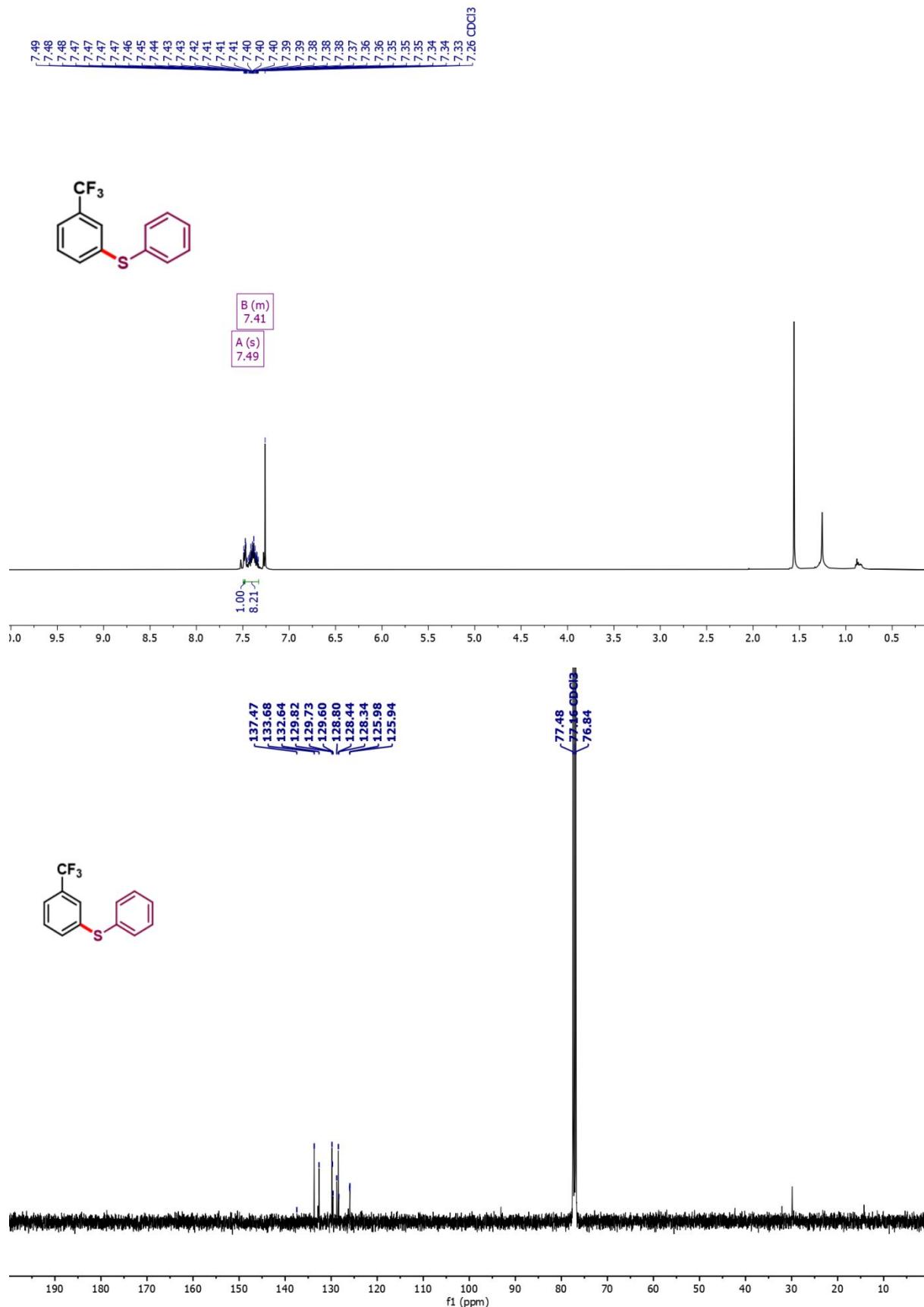
**Yield: 84% (*meta*:others = 4:1)<sup>14</sup>**





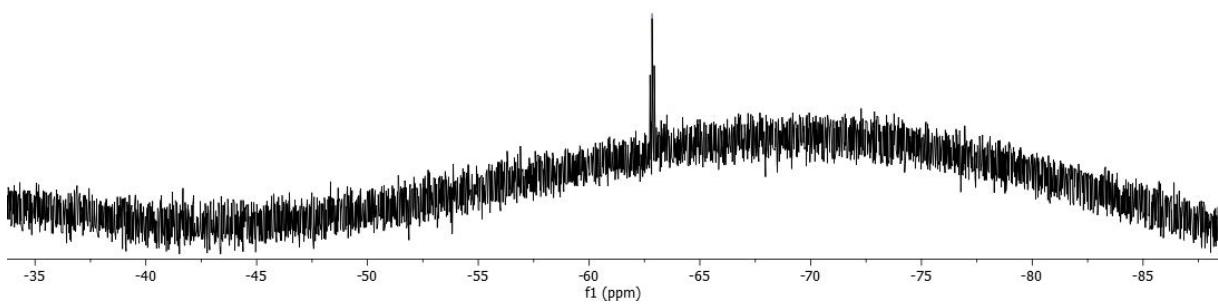
**Scheme 2A, entry 2ab**

**Yield: 68% (*meta*:others >20:1)**



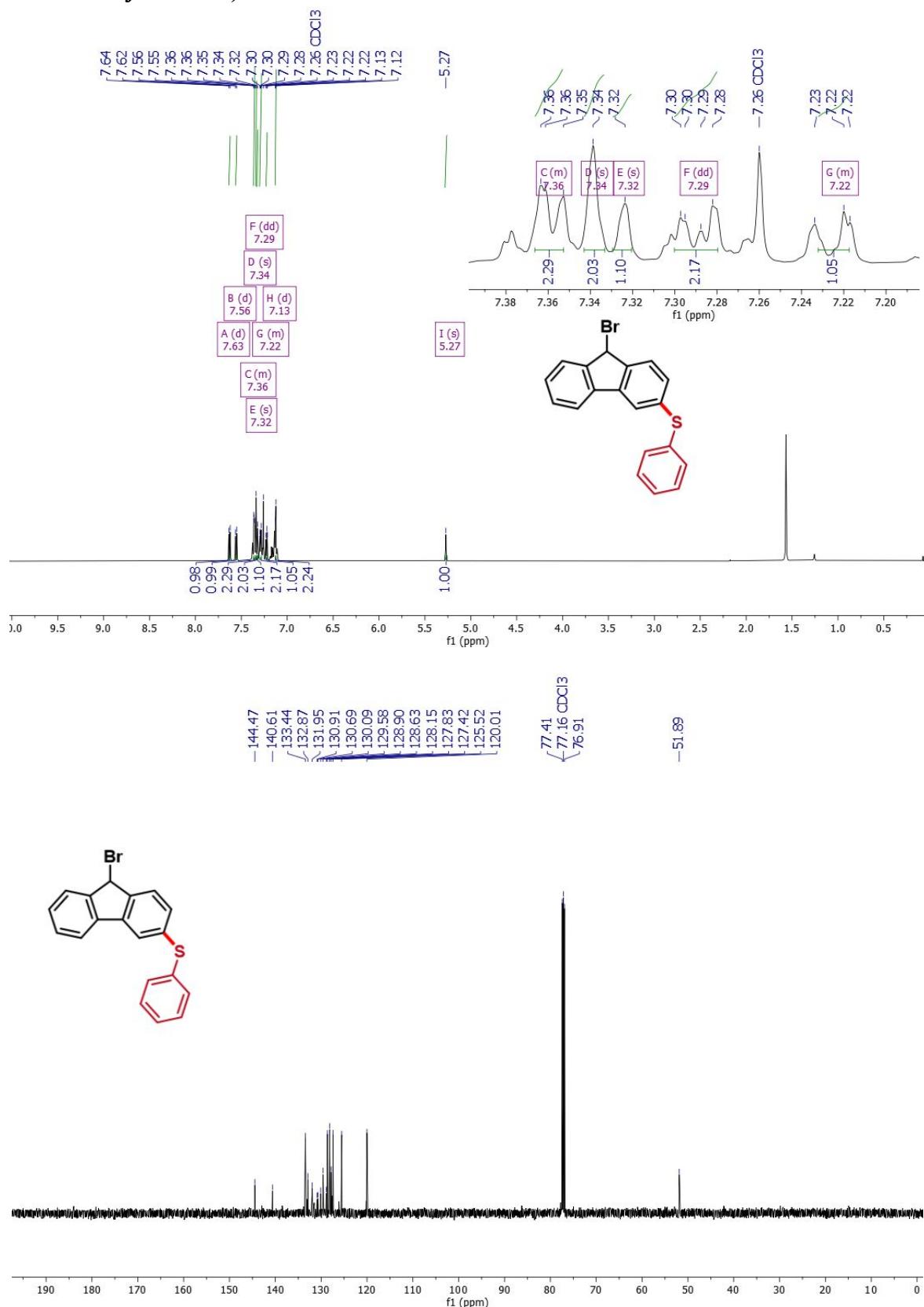


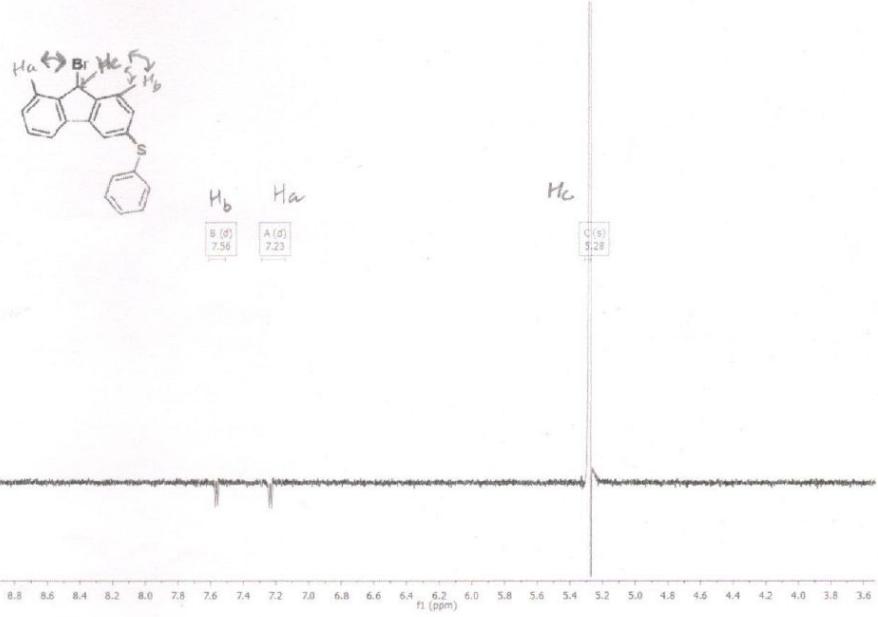
-62.84



**Scheme 2A, entry 2ac**

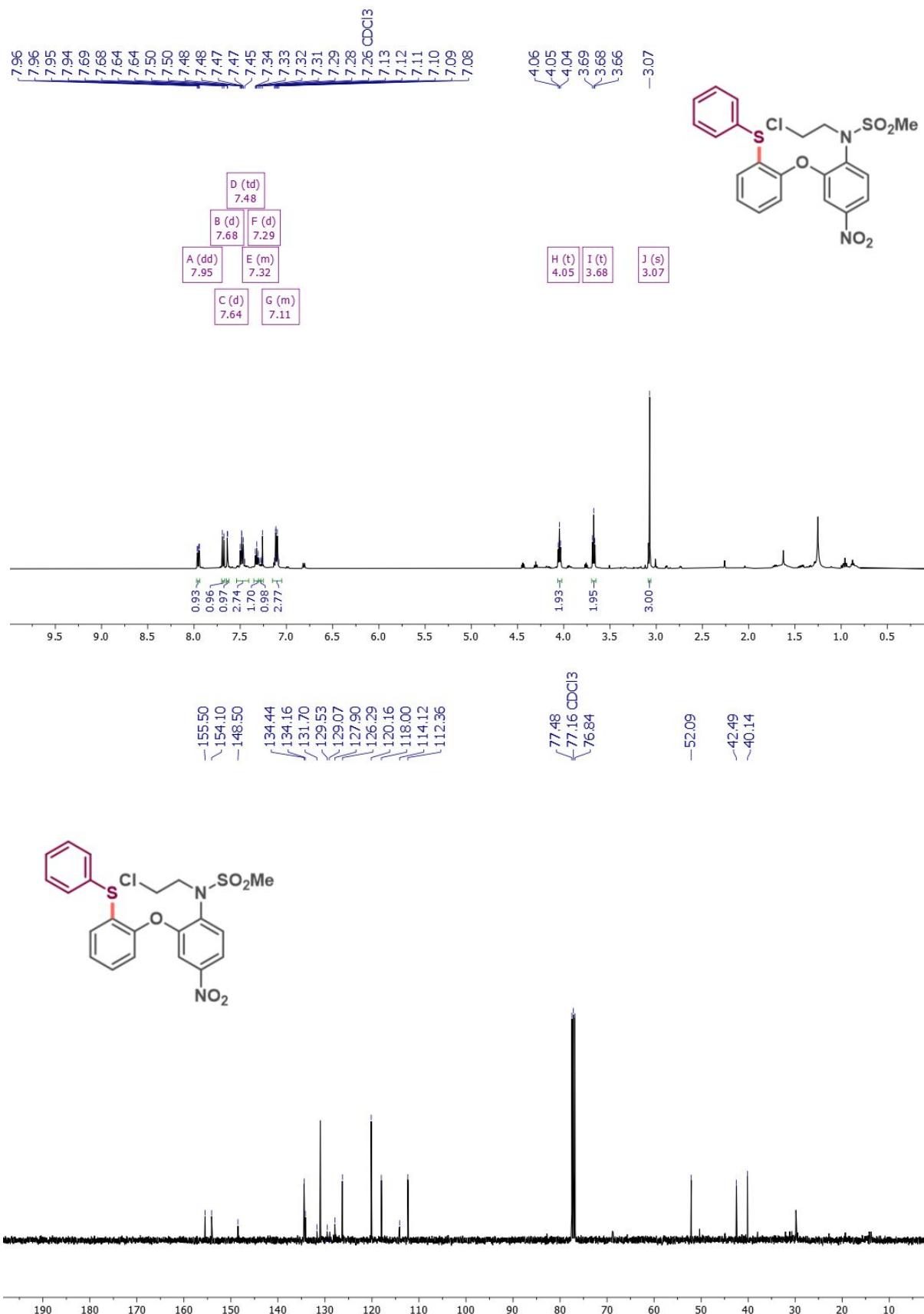
**Yield: 71% ( $\beta:\alpha = 15:1$ )<sup>14</sup>**





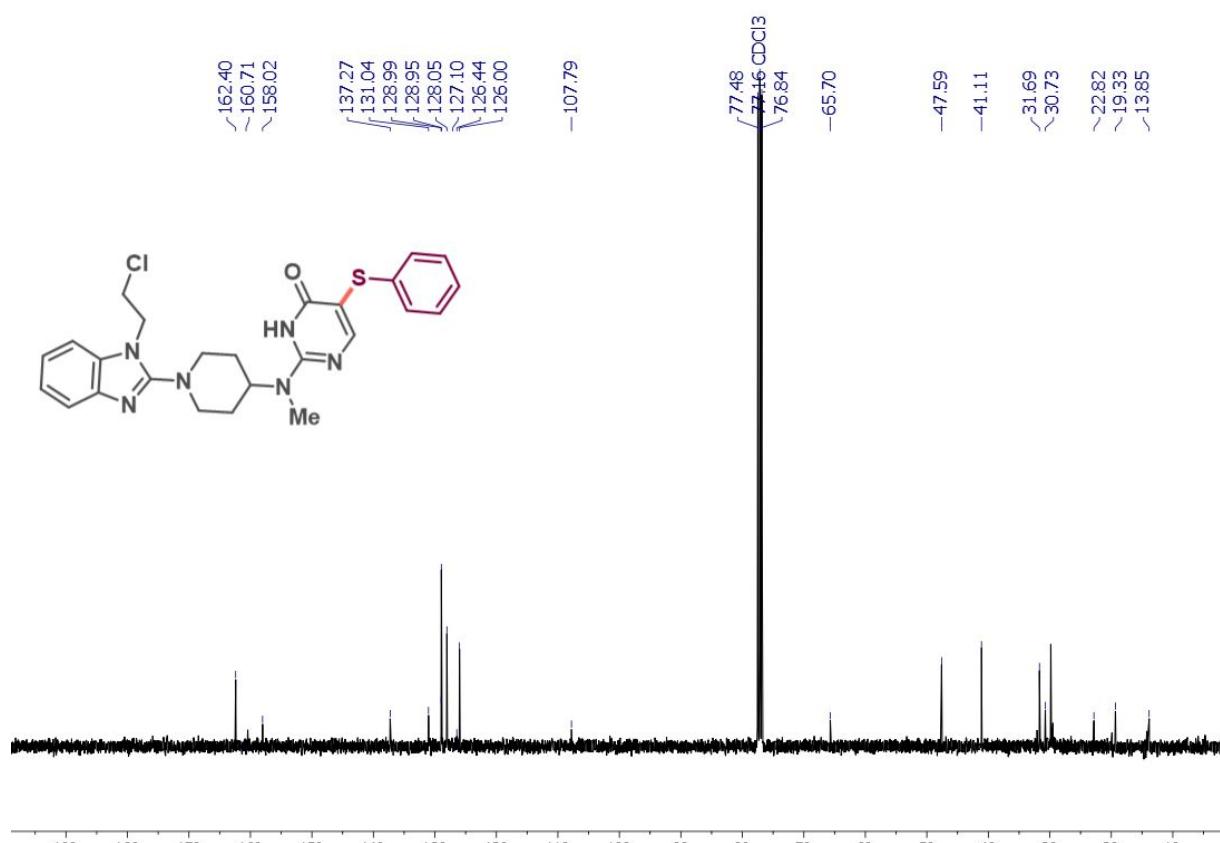
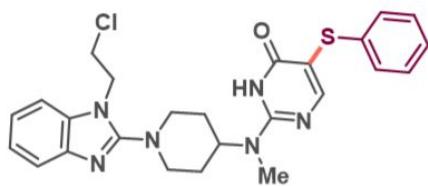
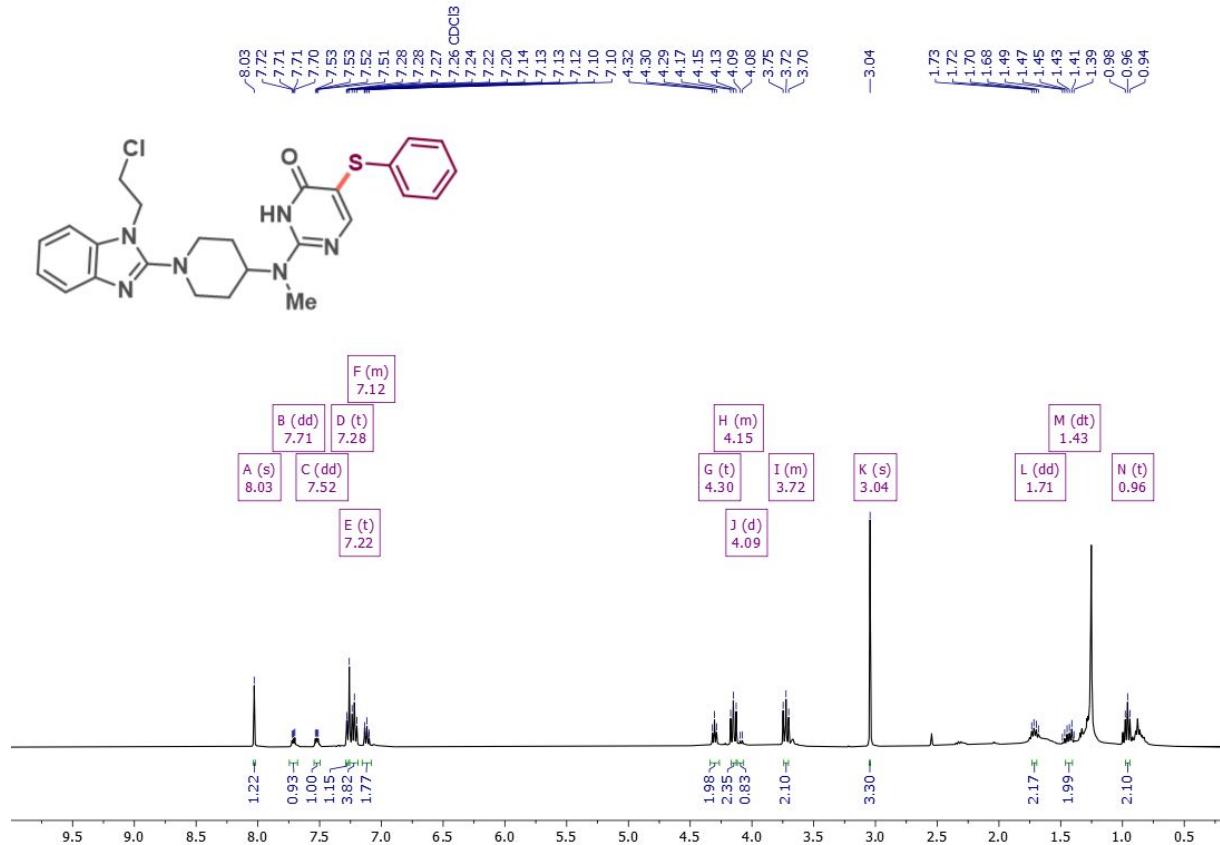
### Scheme 2A, entry 2ad

**Yield: 84%**



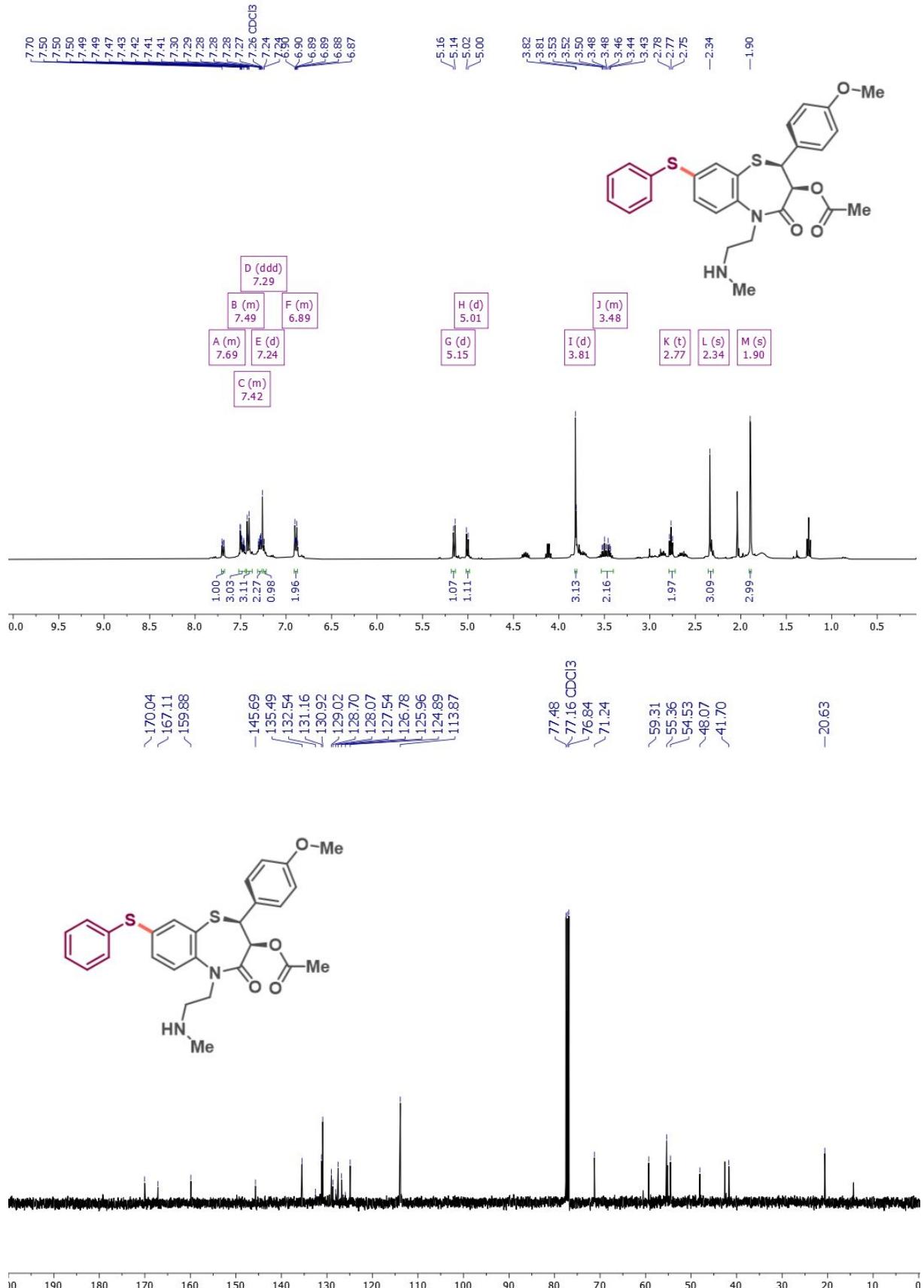
### Scheme 2A, entry 2ae

**Yield: 62%**



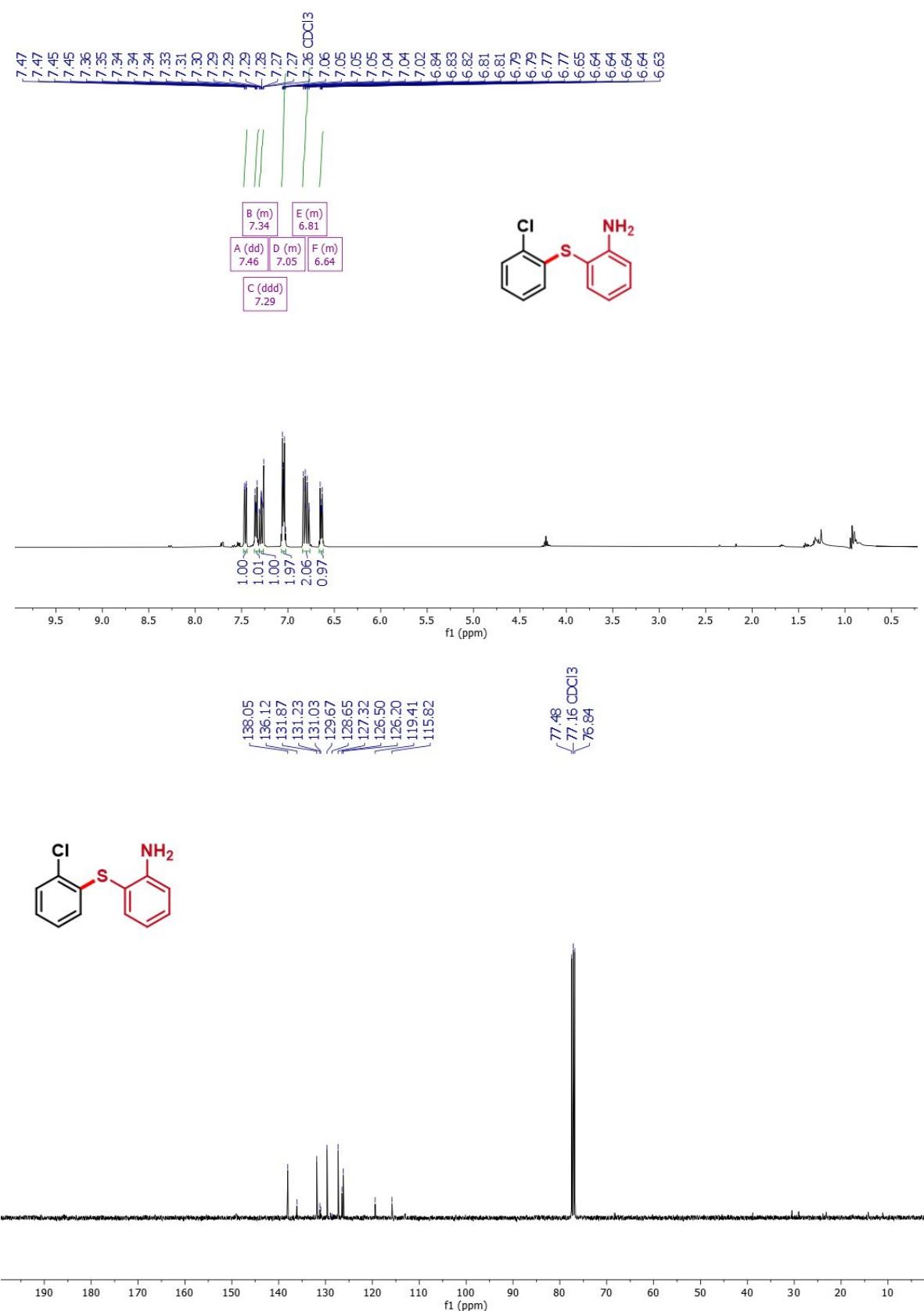
### Scheme 2A, entry 2af

**Yield: 64% ( $\beta:\alpha$  3:1)**<sup>14</sup>



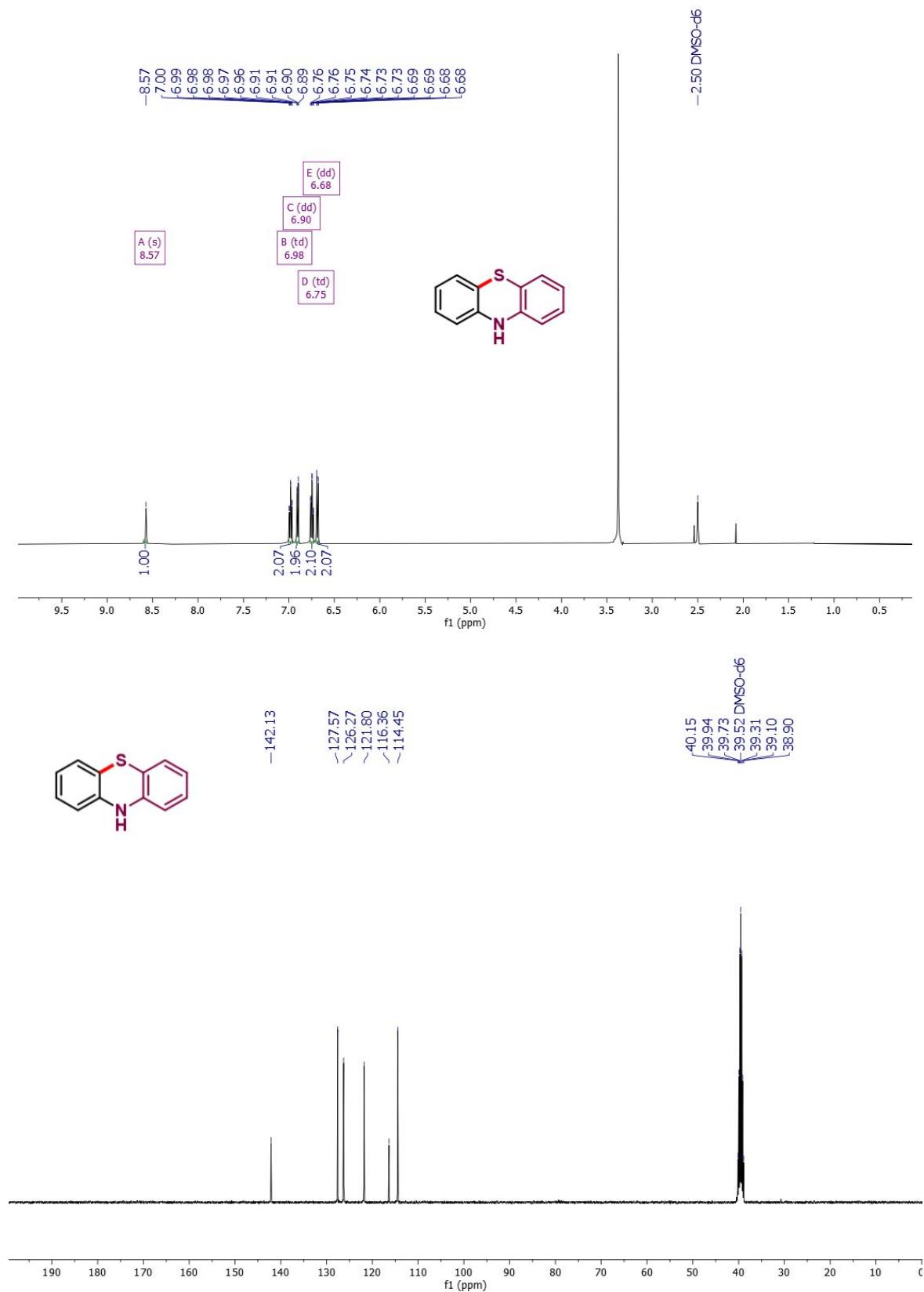
**Scheme 2B, entry 4**

**Yield: 68%**



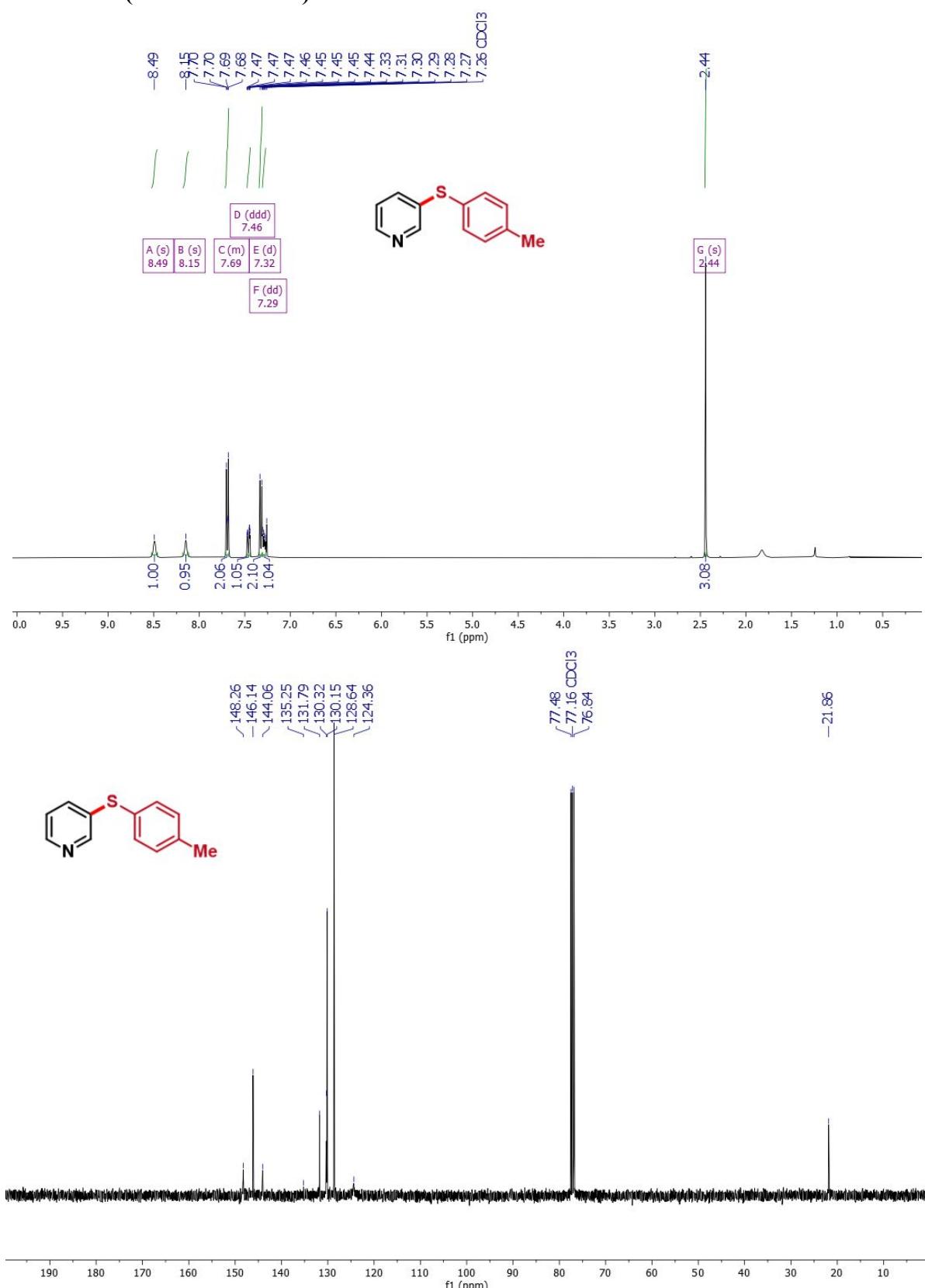
**Scheme 2B, entry 5**

**Yield: 15%**



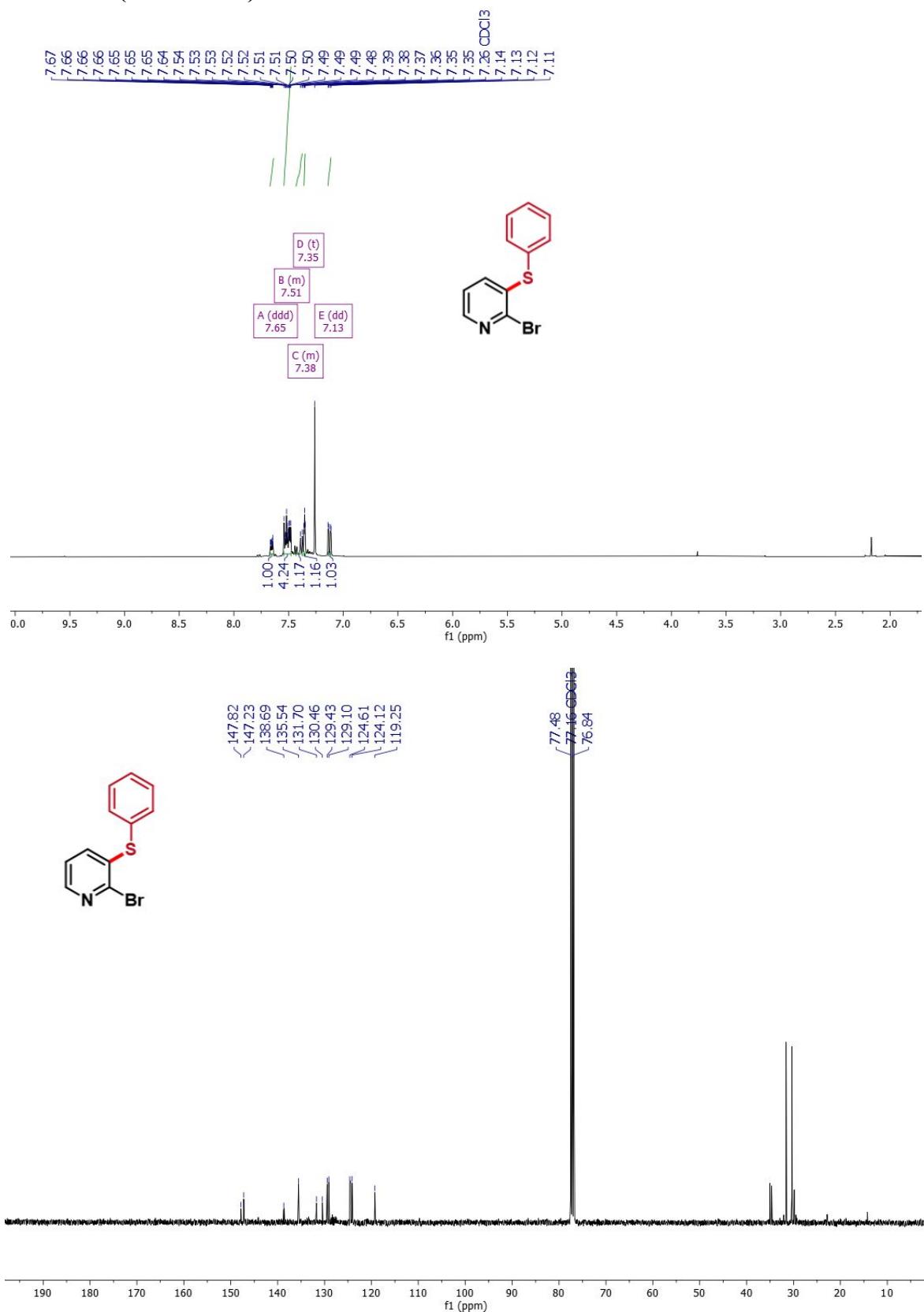
**Scheme 3, entry 3a**

**Yield: 84% (C3:others >30:1)<sup>14</sup>**



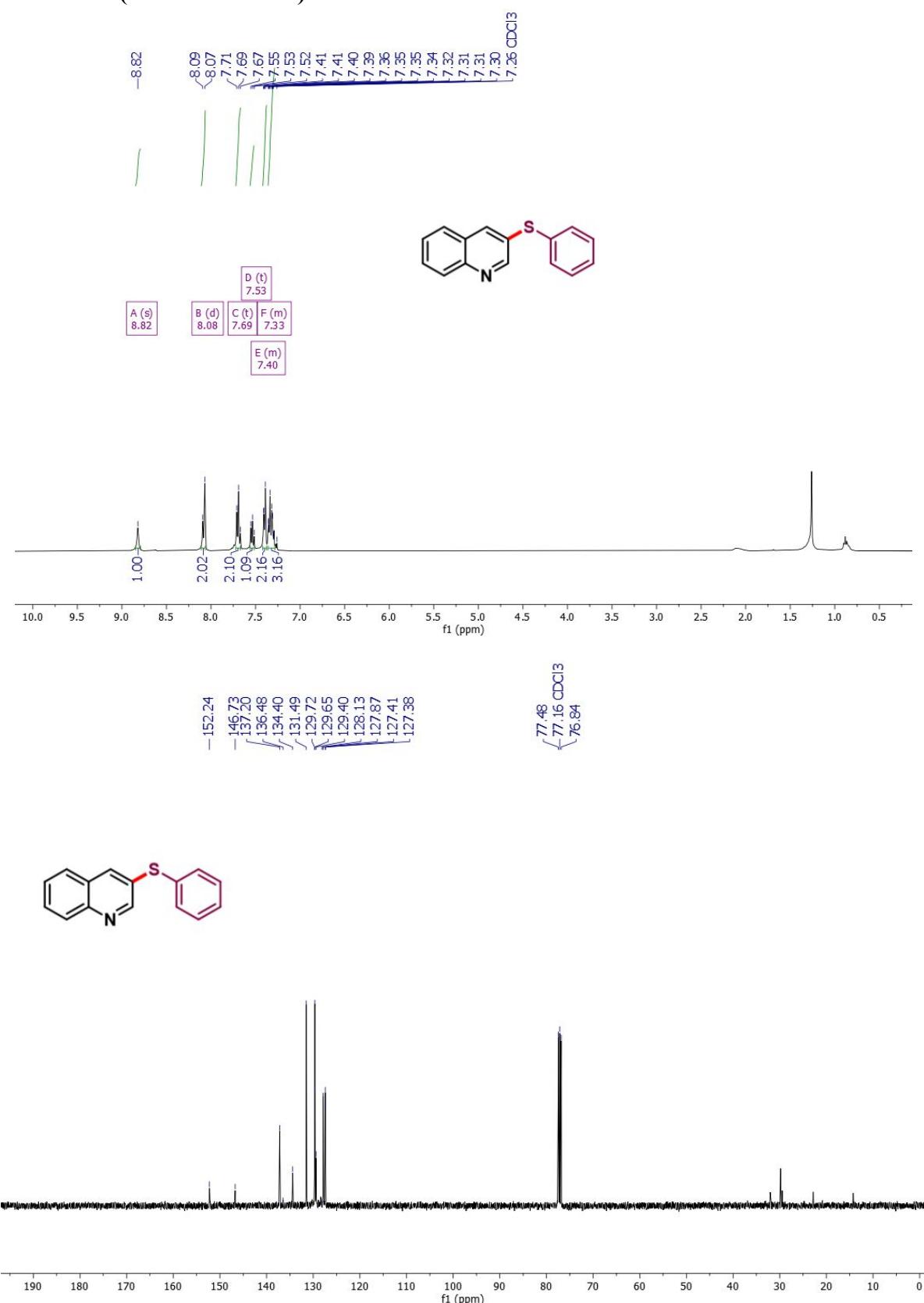
**Scheme 3, entry 3b**

**Yield: 74% (C3:C5= 6:1)<sup>14</sup>**



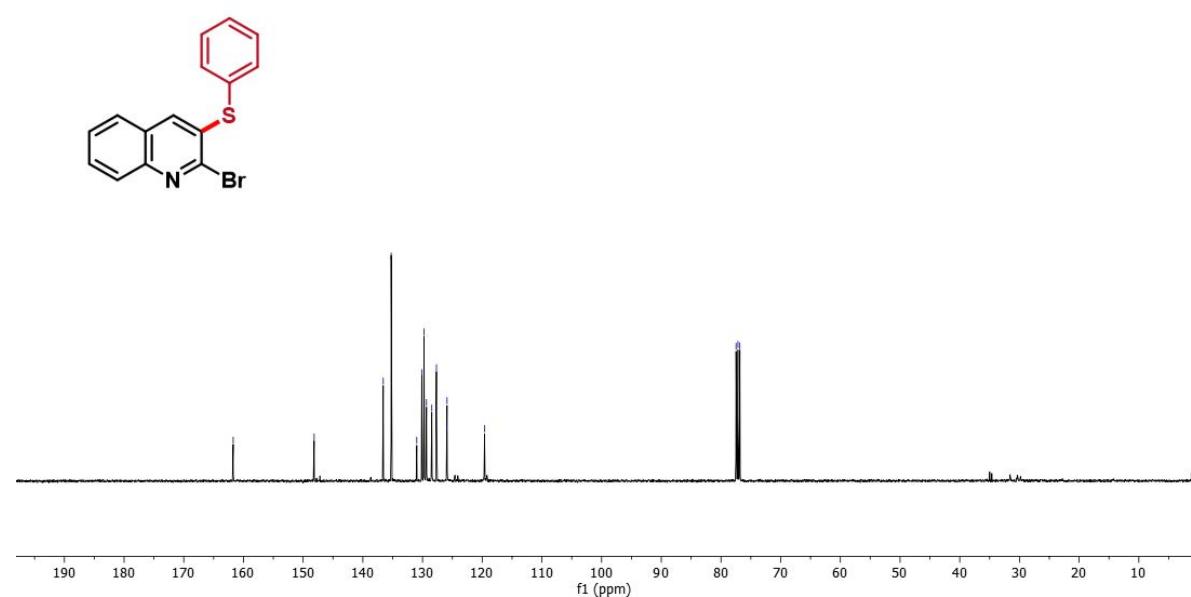
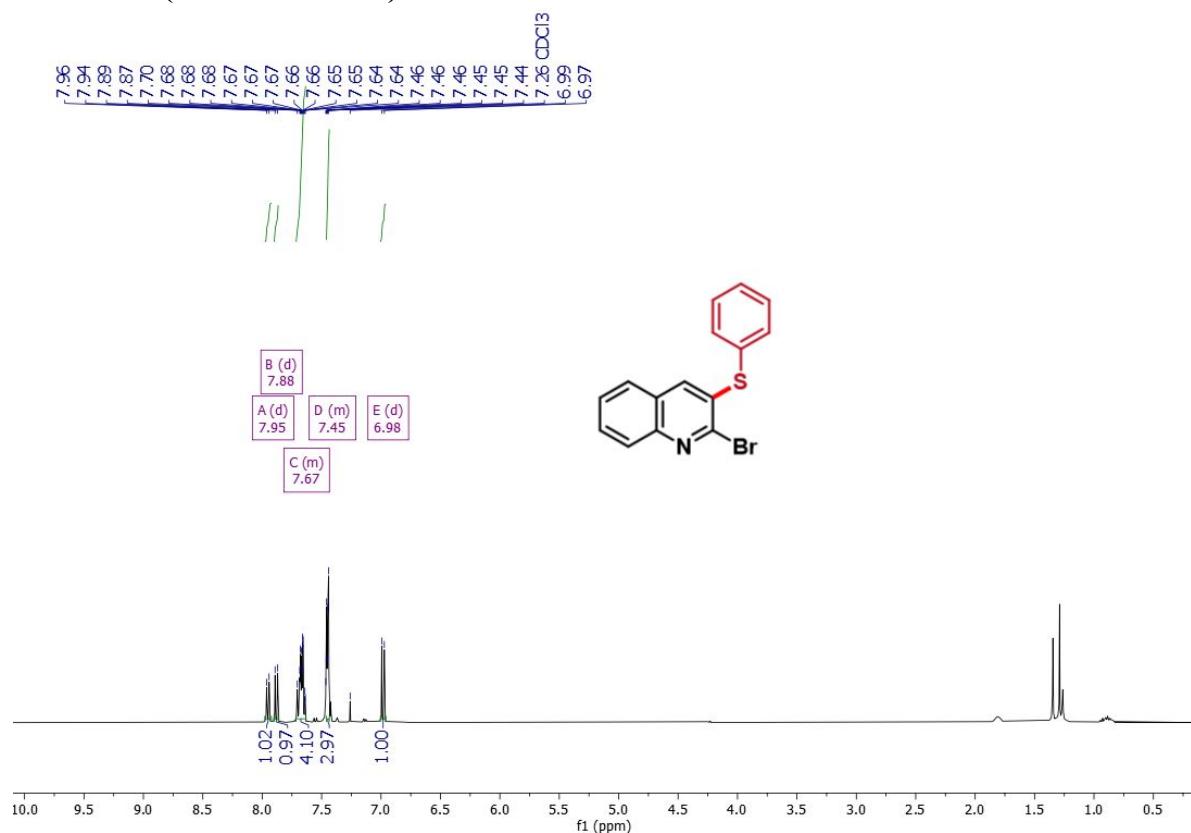
**Scheme 3, entry 3c**

**Yield: 78% (C3:others >20:1)<sup>14</sup>**



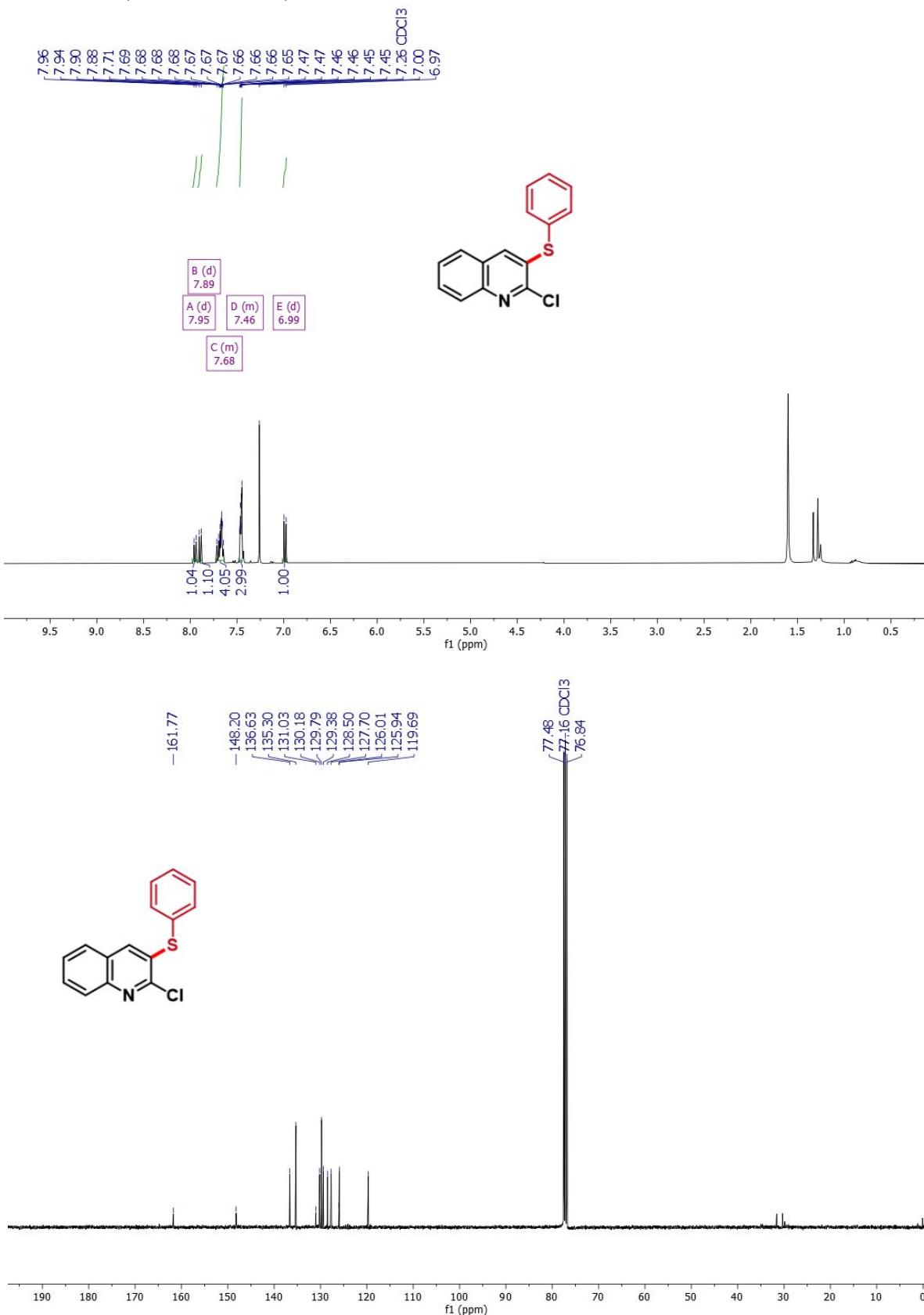
**Scheme 3, entry 3d**

**Yield: 85% (*C3:others*= 10:1)<sup>14</sup>**



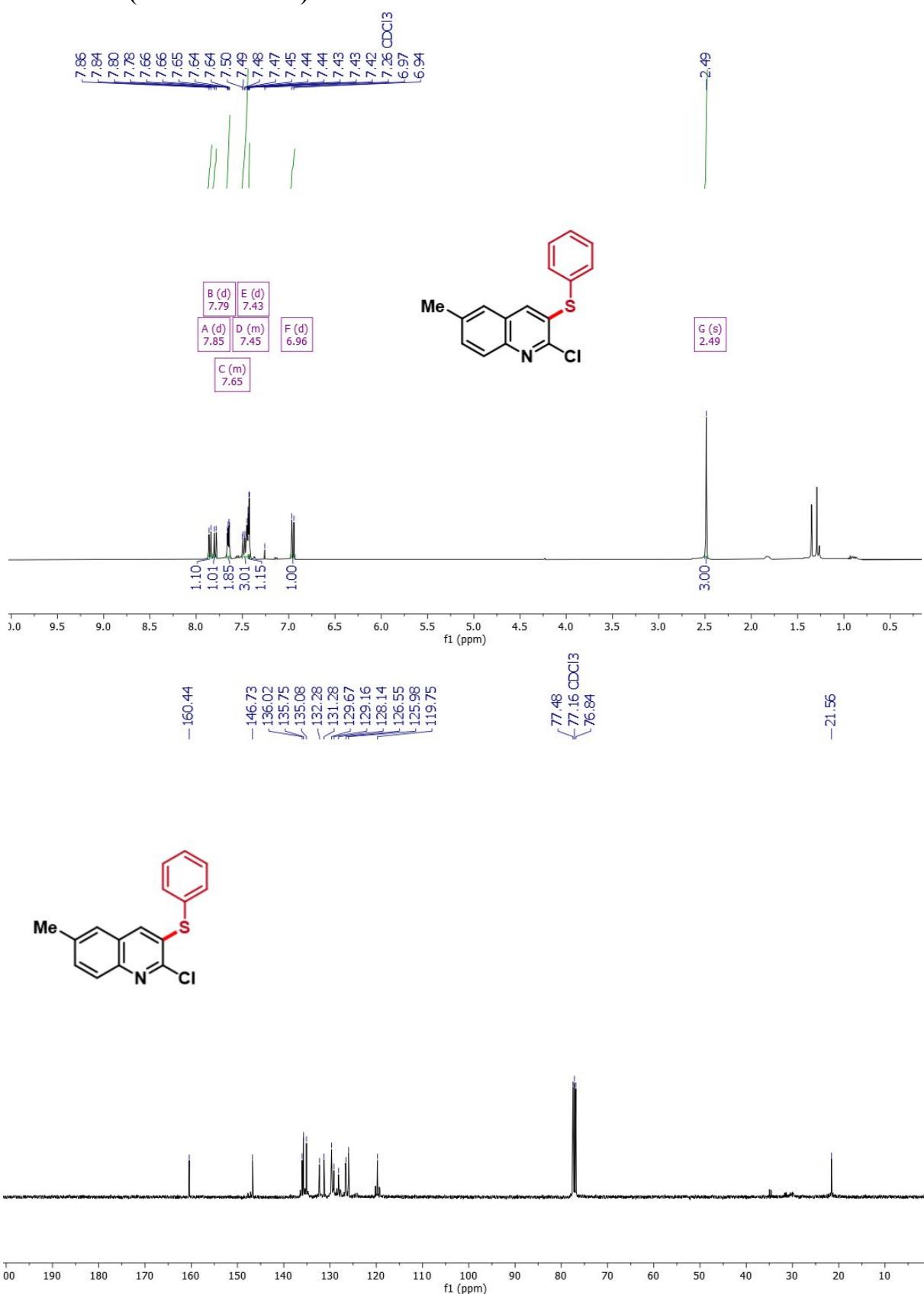
**Scheme 3, entry 3e**

**Yield: 84% (*C3:others*= 8:1)<sup>14</sup>**



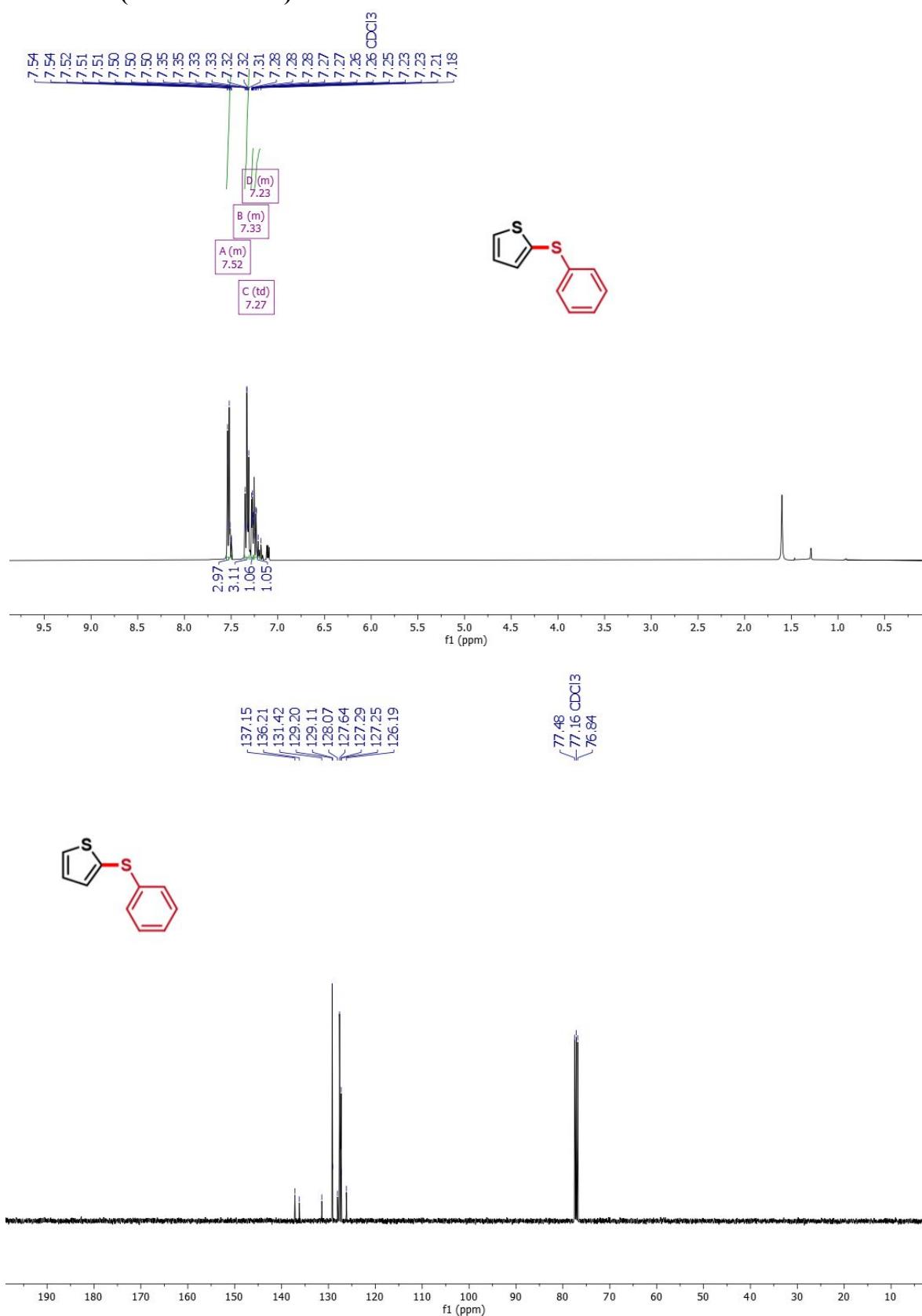
**Scheme 3, entry 3f**

**Yield: 82% (C3:others= 11:1)<sup>14</sup>**



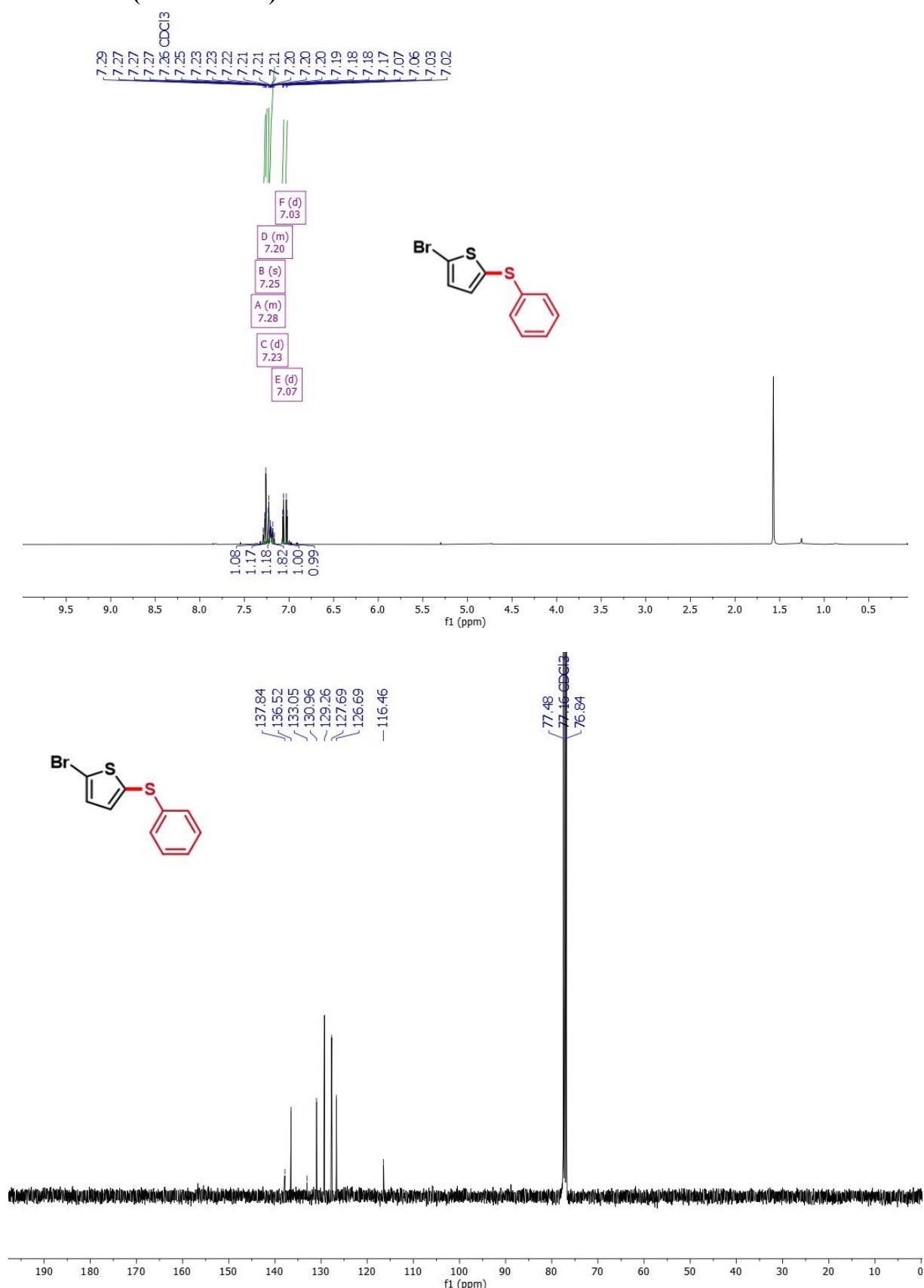
**Scheme 3, entry 3g**

**Yield: 85% (C2:others= 5:1)<sup>14</sup>**



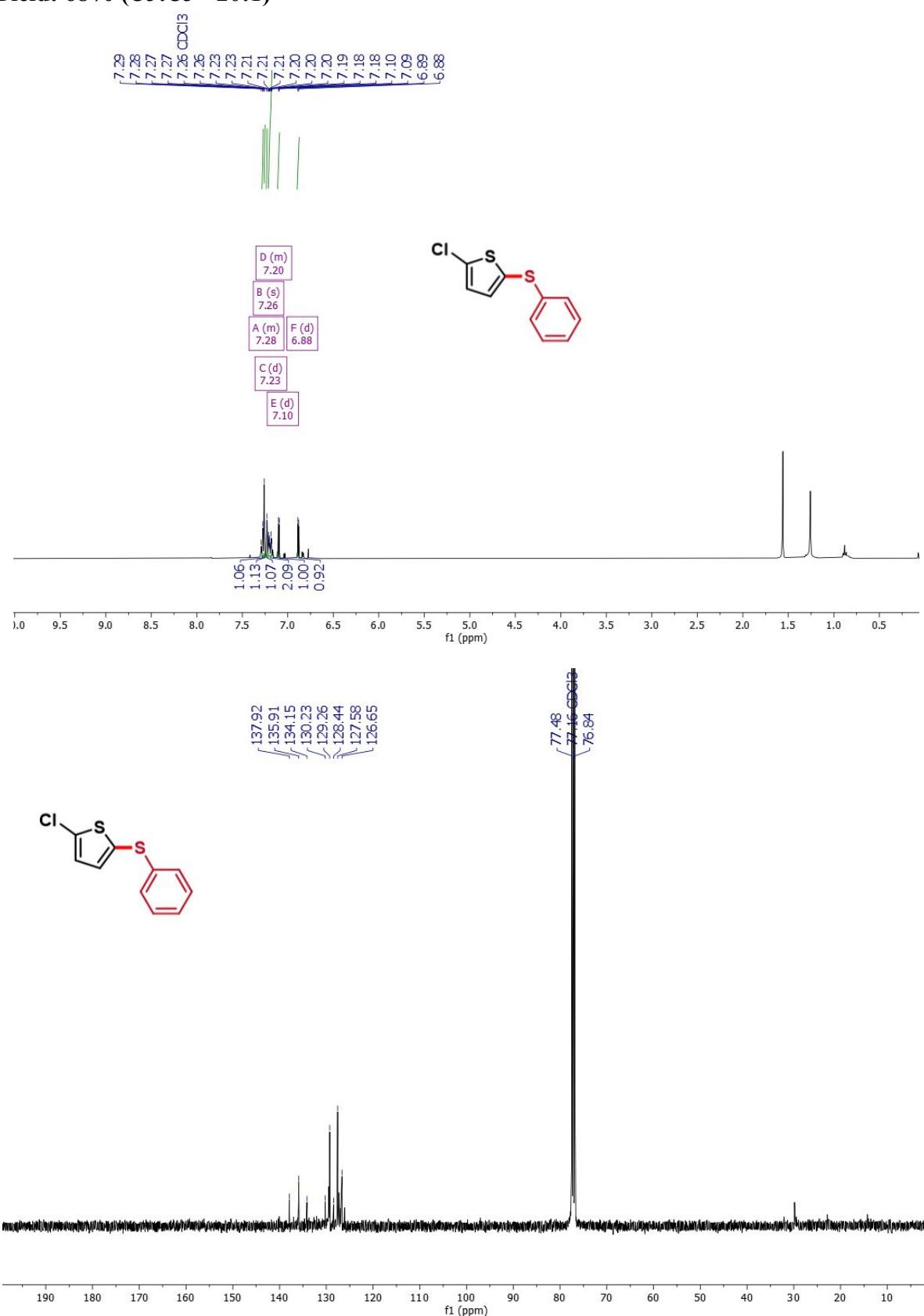
**Scheme 3, entry 3h**

**Yield: 60% ( $C_5:C_3 = 20:1$ )<sup>14</sup>**



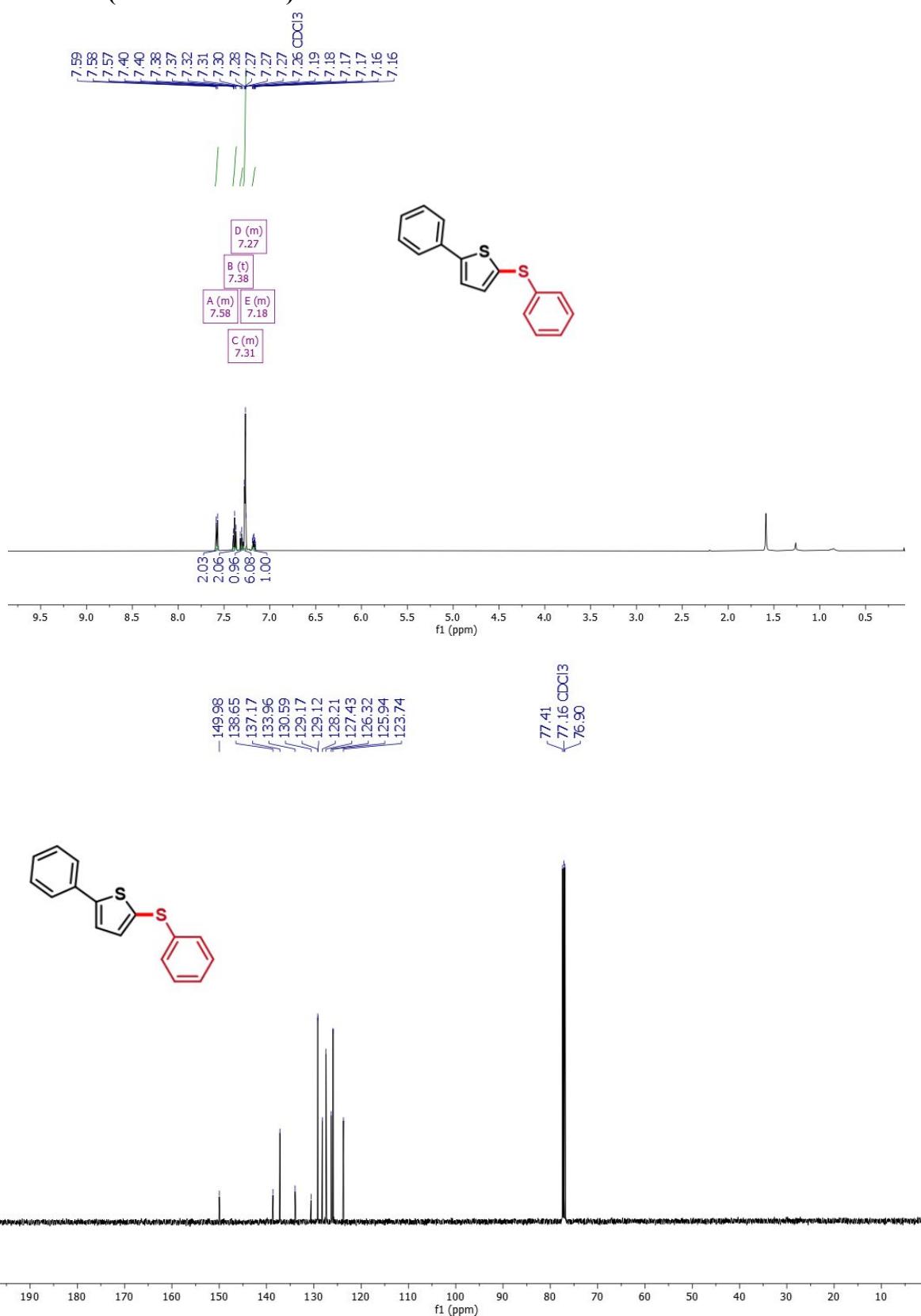
**Scheme 3, entry 3i**

**Yield: 68% ( $C_5:C_3 = 20:1$ )<sup>14</sup>**



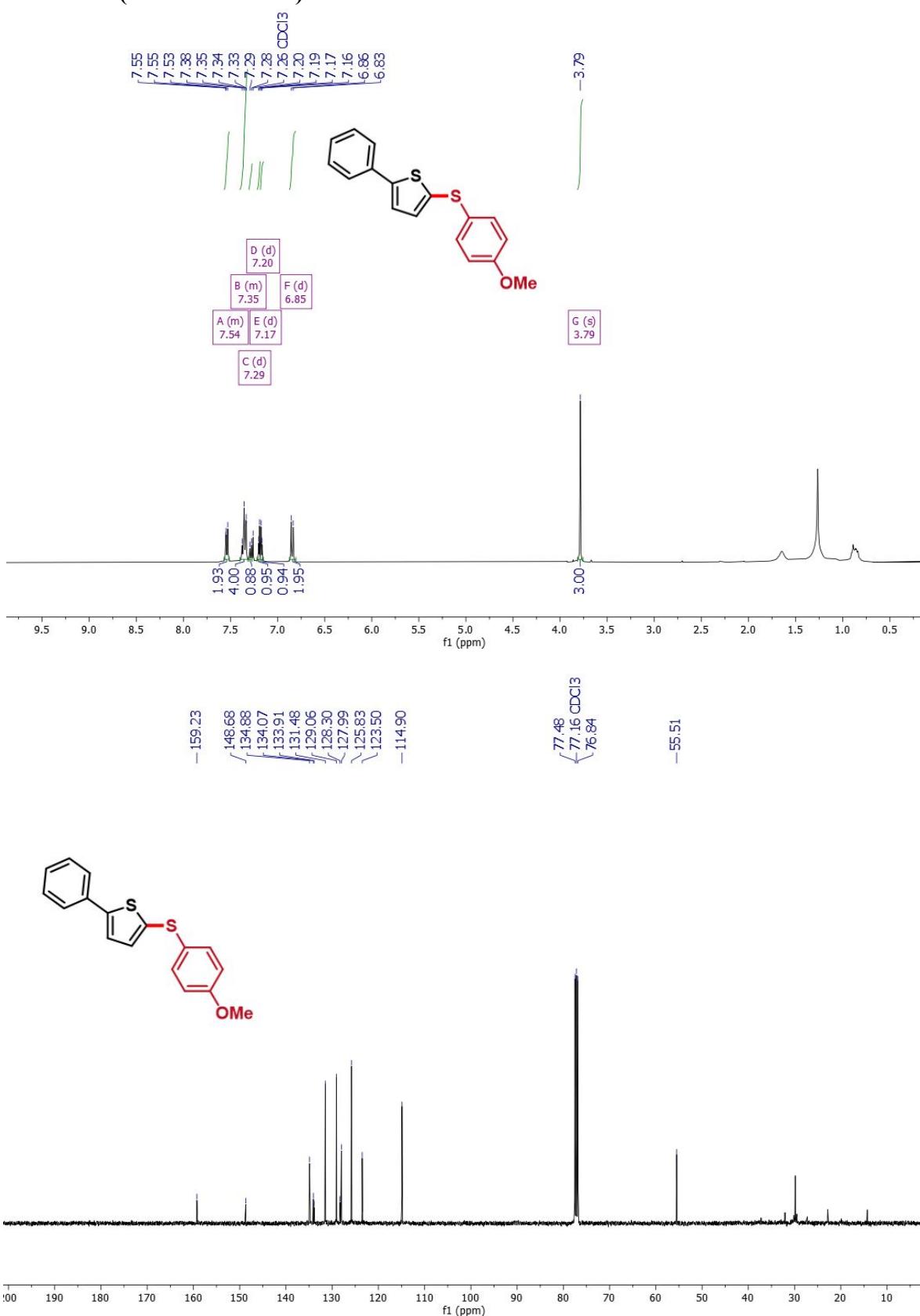
**Scheme 3, entry 3j**

**Yield: 86% (*C5:others >30:1*)<sup>14</sup>**



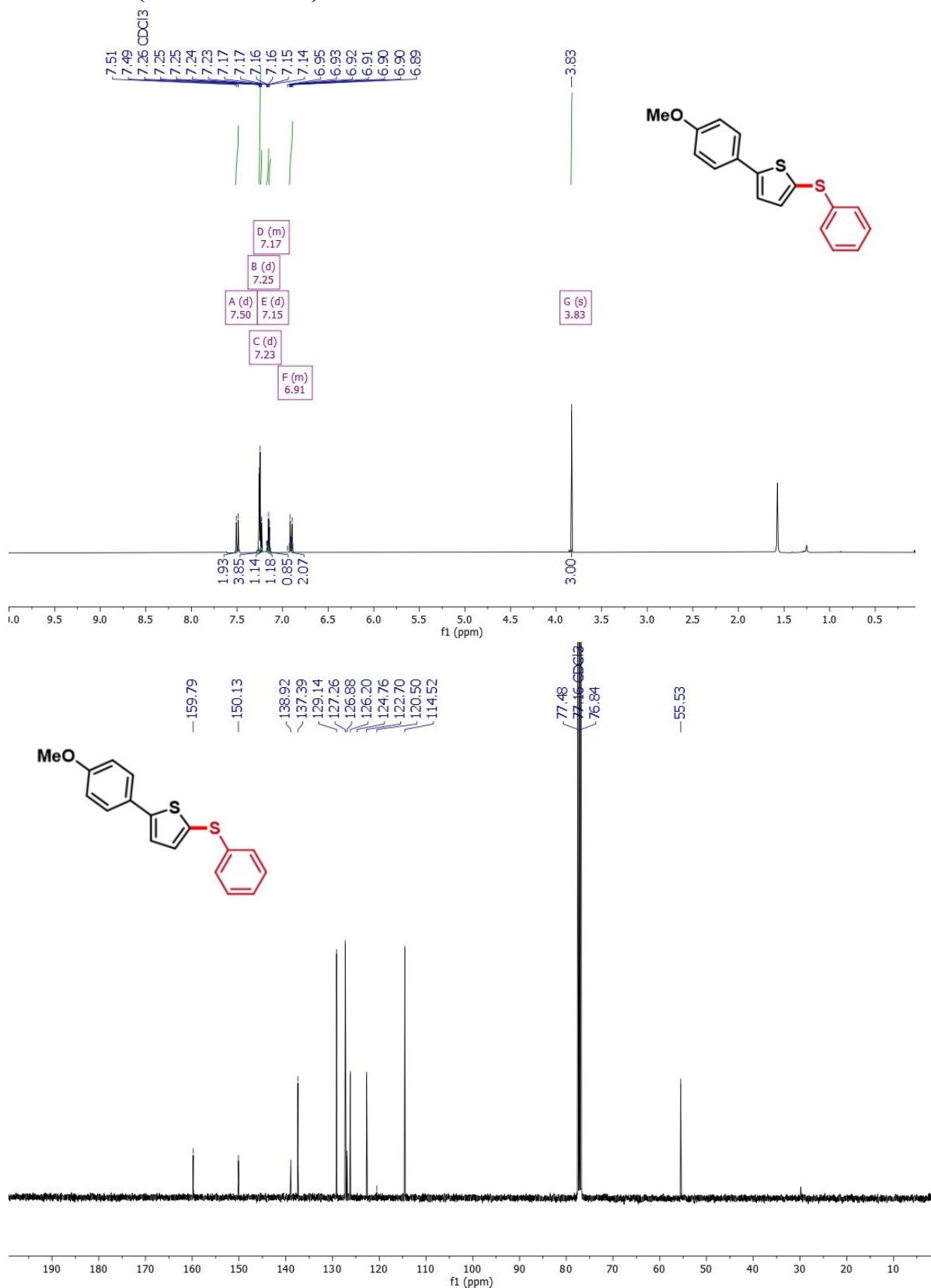
**Scheme 3, entry 3k**

**Yield: 77% (*C5:others* >30:1)<sup>14</sup>**



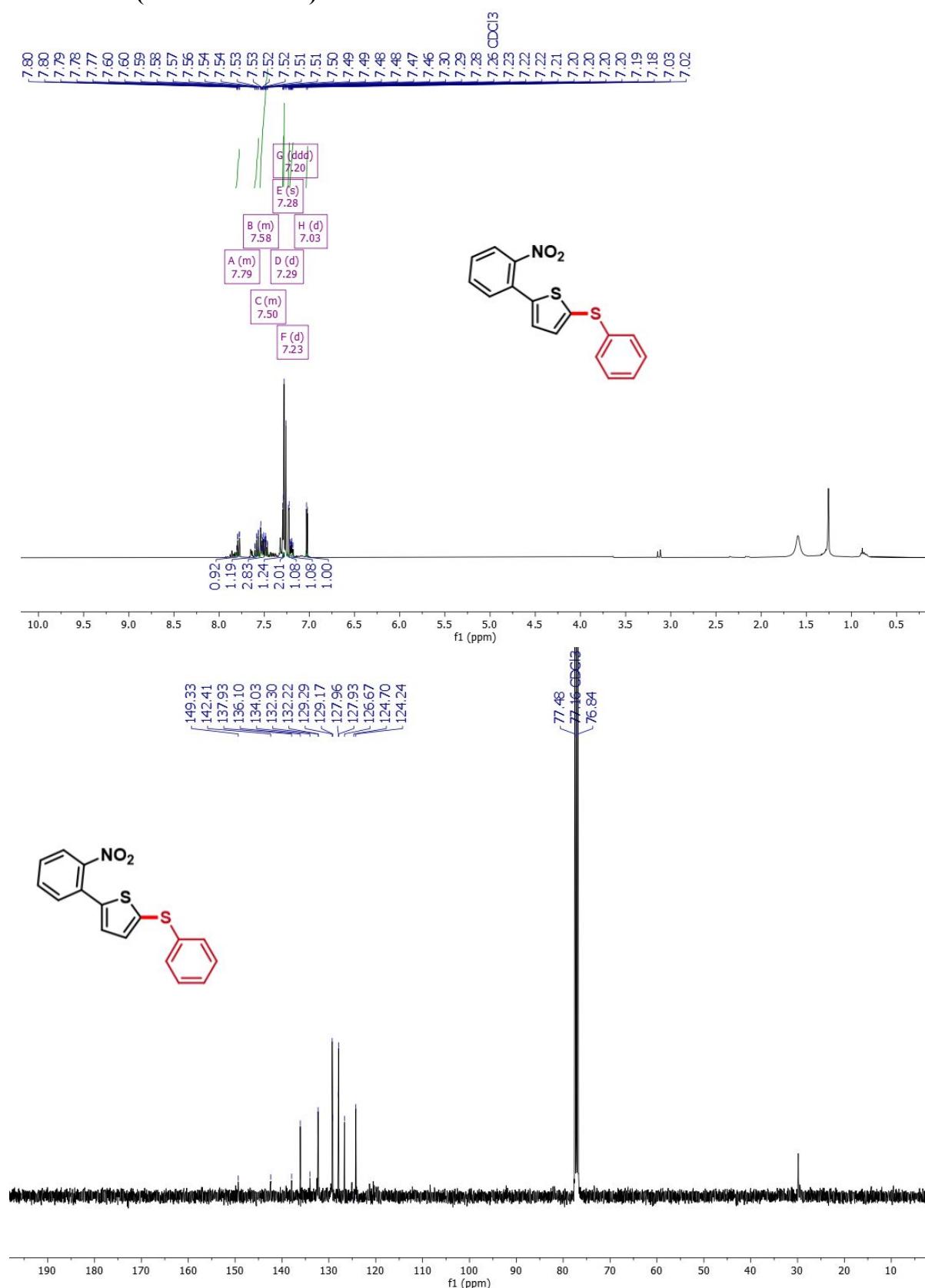
**Scheme 3, entry 3l**

**Yield: 80% (*C5:others* >30:1)<sup>14</sup>**



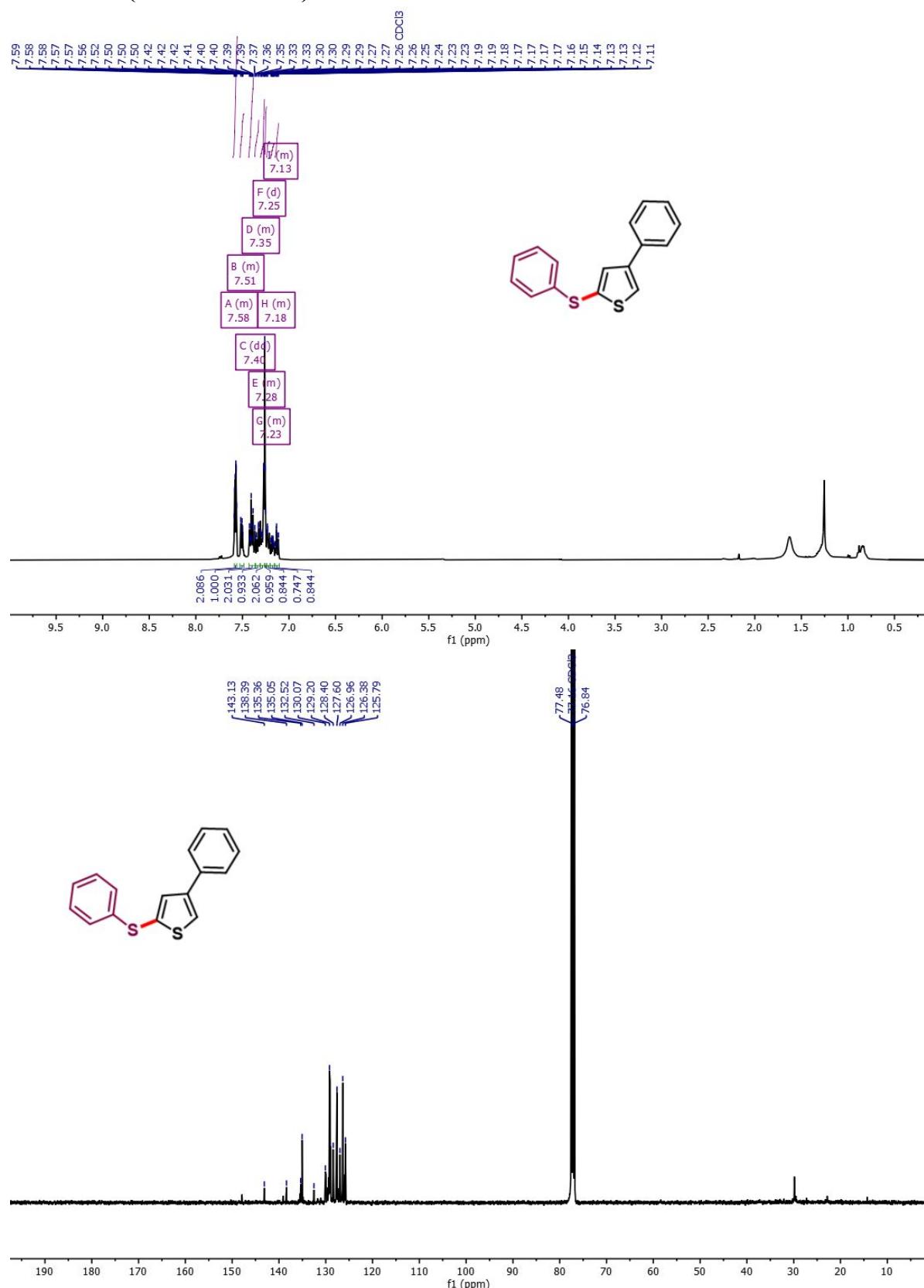
**Scheme 3, entry 3m**

**Yield: 65% (*C5:others >30:1*)<sup>14</sup>**



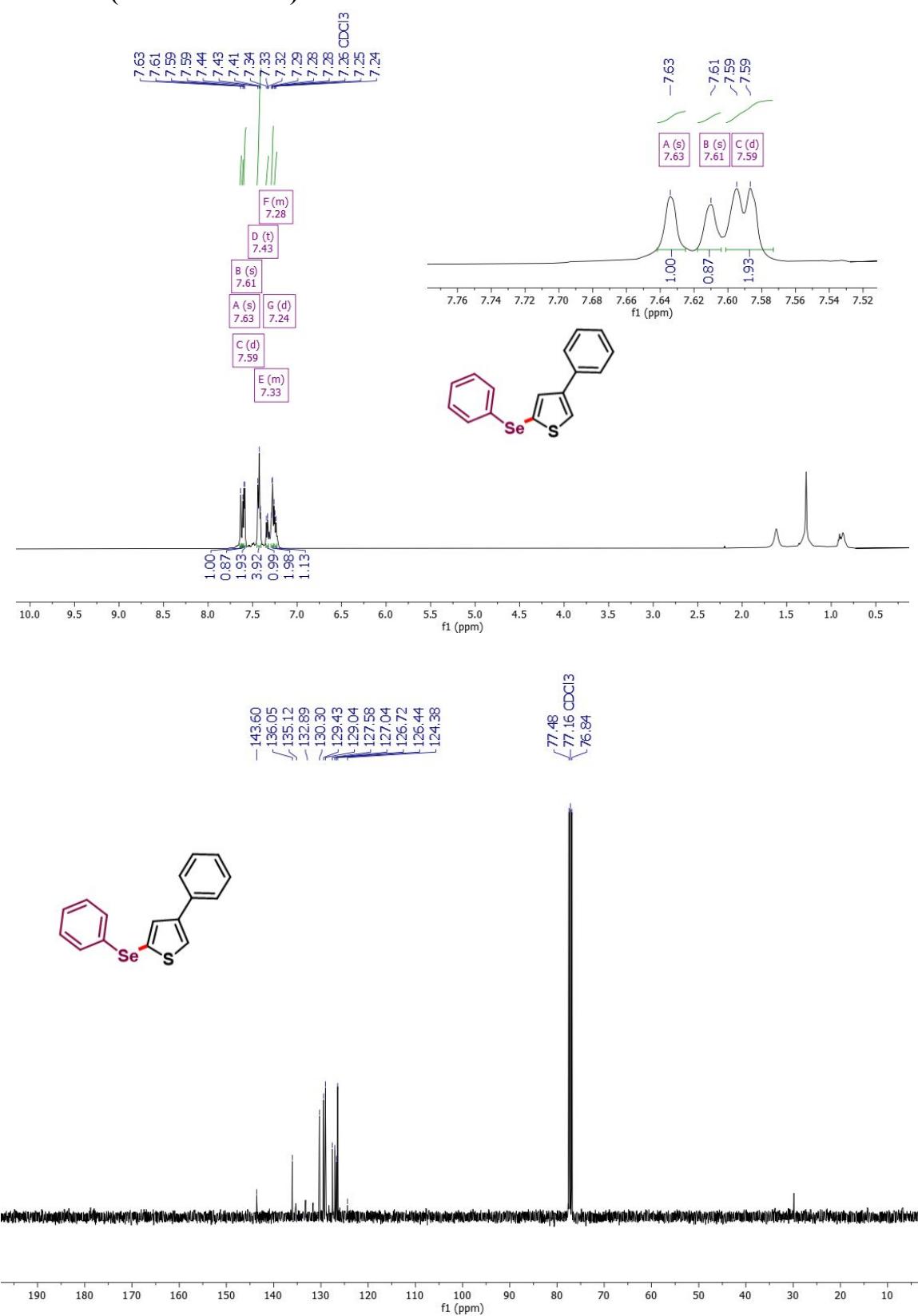
**Scheme 3, entry 3n**

**Yield: 76% (*C5:others* >30:1)<sup>14</sup>**



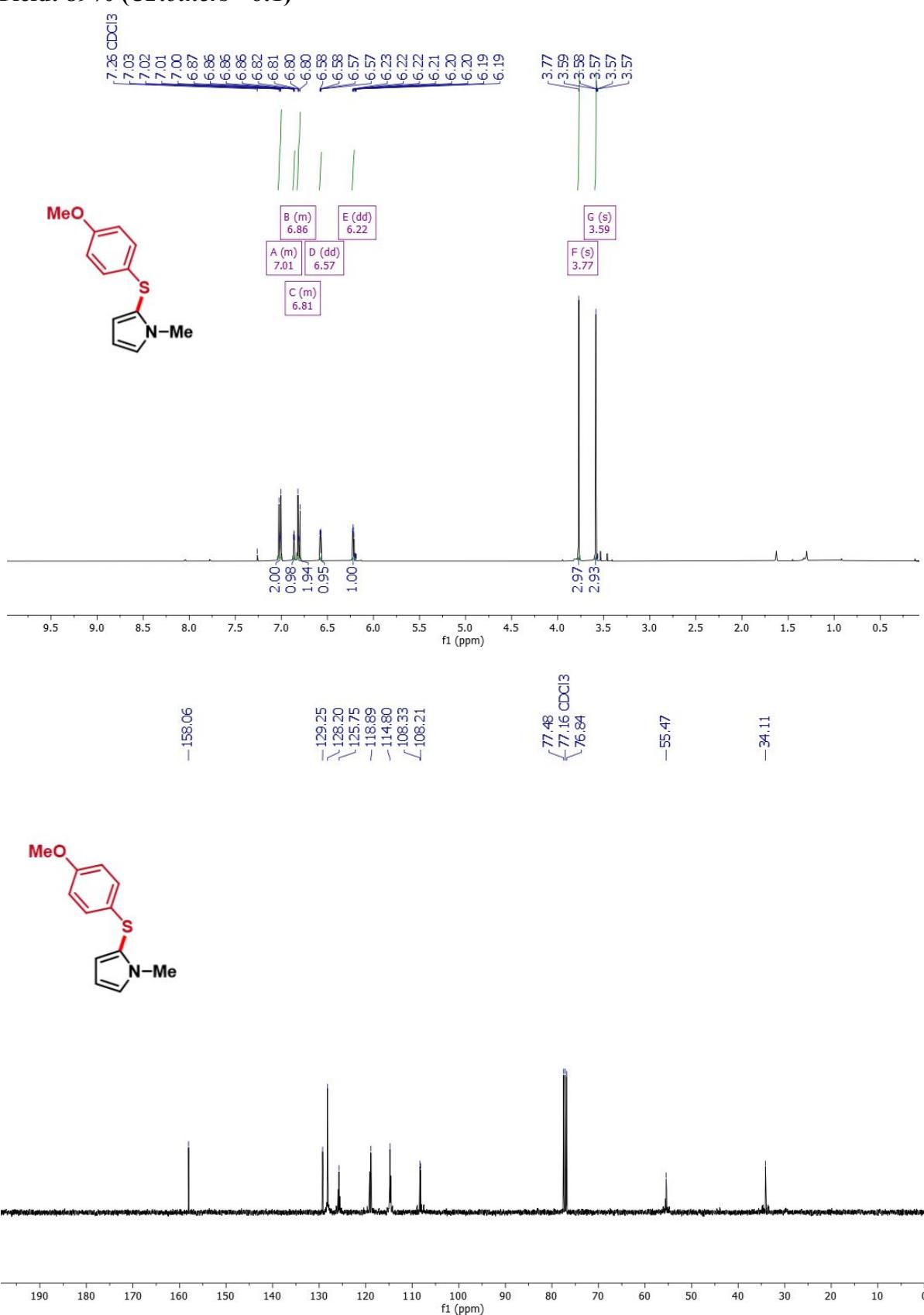
**Scheme 3, entry 3o**

**Yield: 74% (*C5:others >30:1*)<sup>14</sup>**



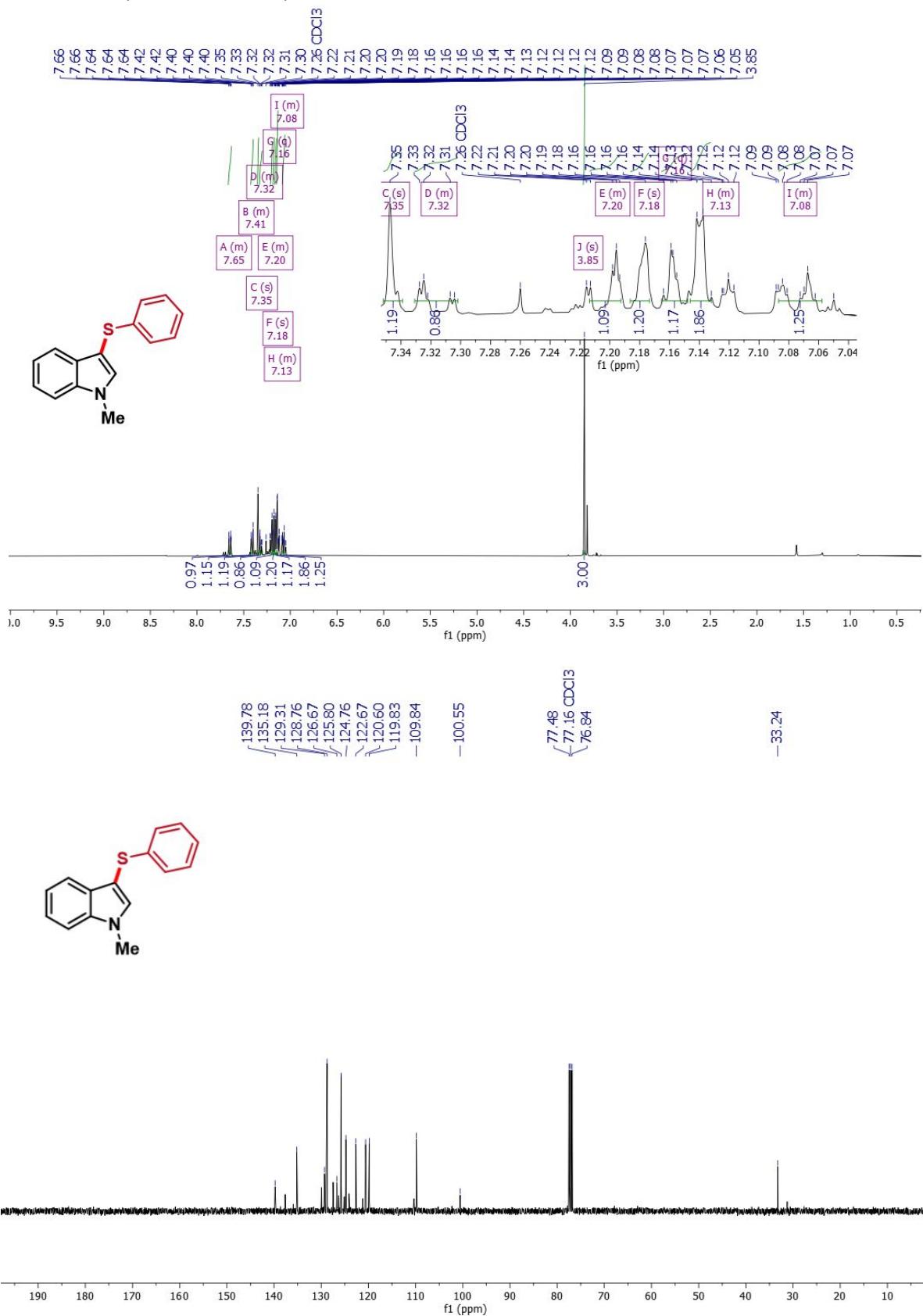
**Scheme 3, entry 3p**

**Yield: 89% (*C<sub>2</sub>:others = 6:1*)<sup>14</sup>**



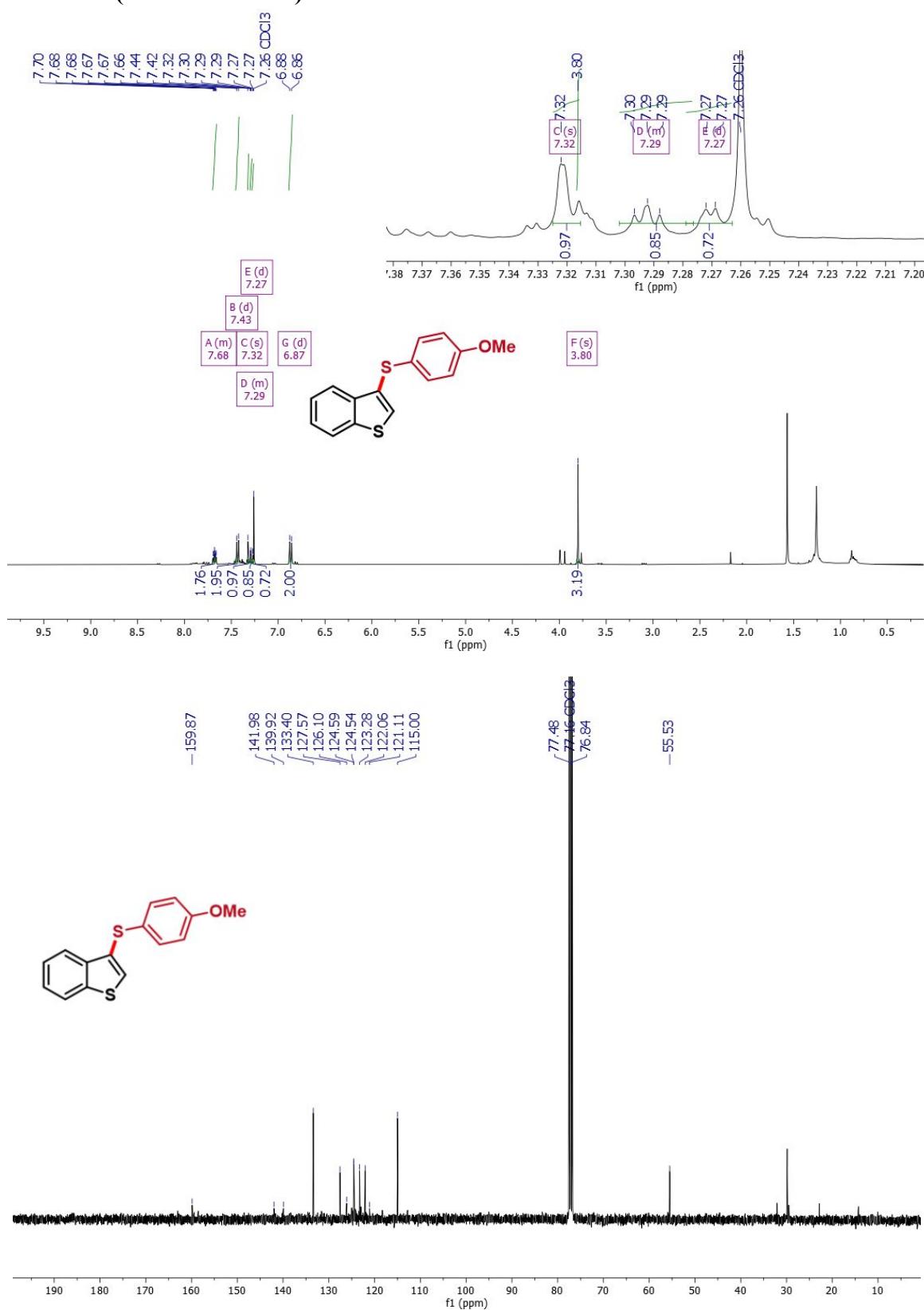
### Scheme 3, entry 3q

**Yield: 83% (*C*3:*others* = 6:1)**<sup>14</sup>



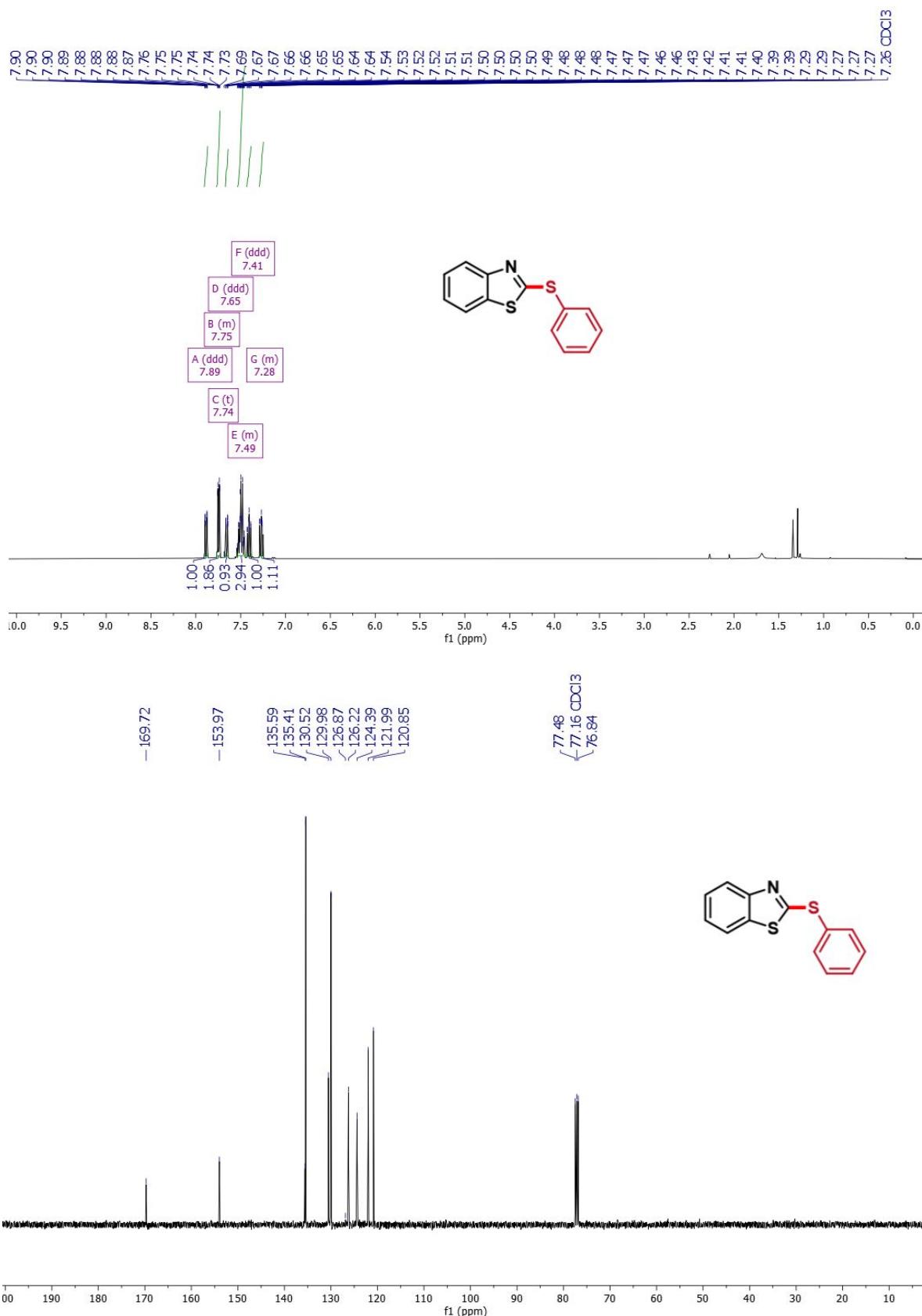
**Scheme 3, entry 3r**

**Yield: 64% (*C3:others*= 12:1)<sup>14</sup>**



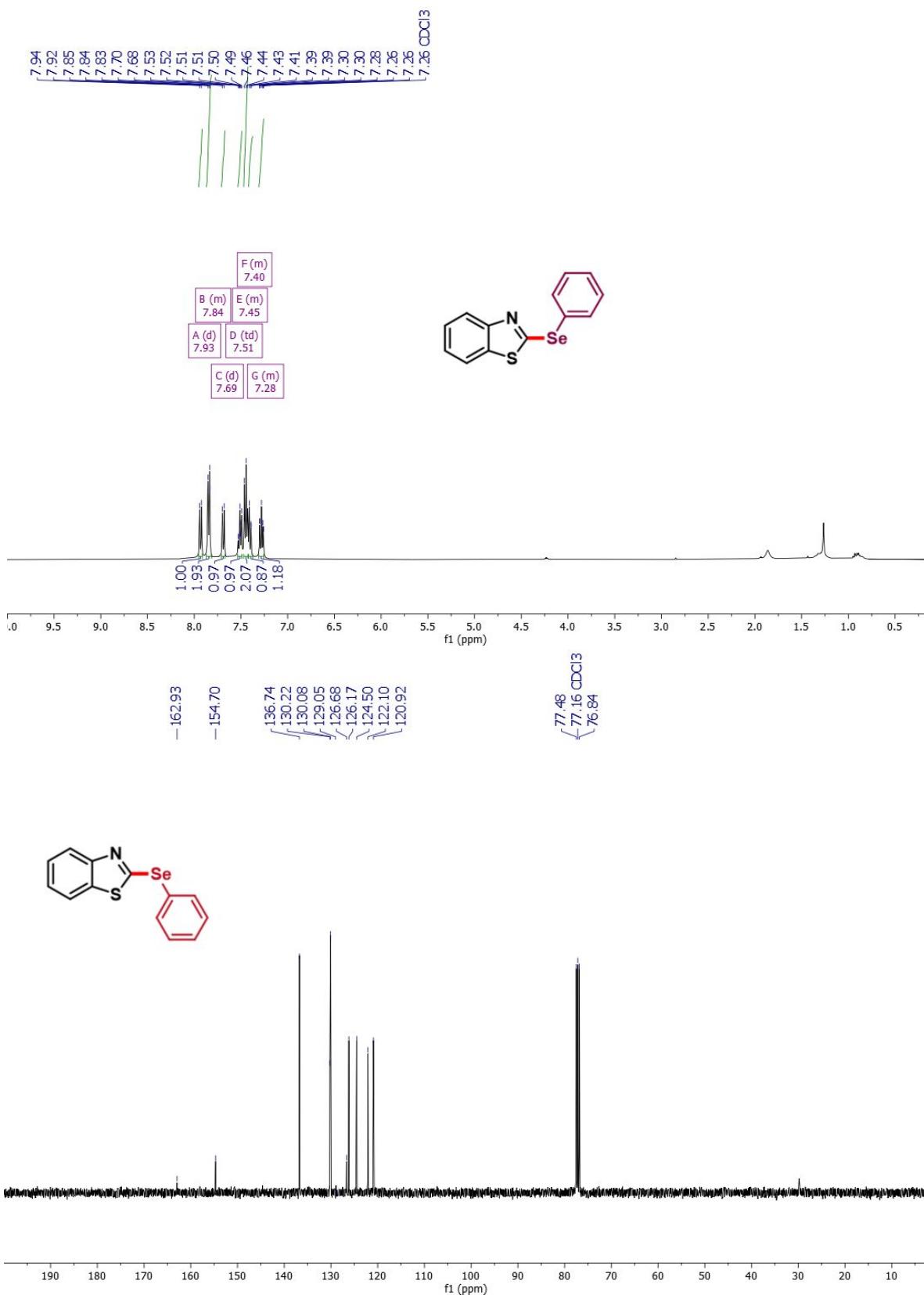
**Scheme 3, entry 3s**

**Yield: 85%**



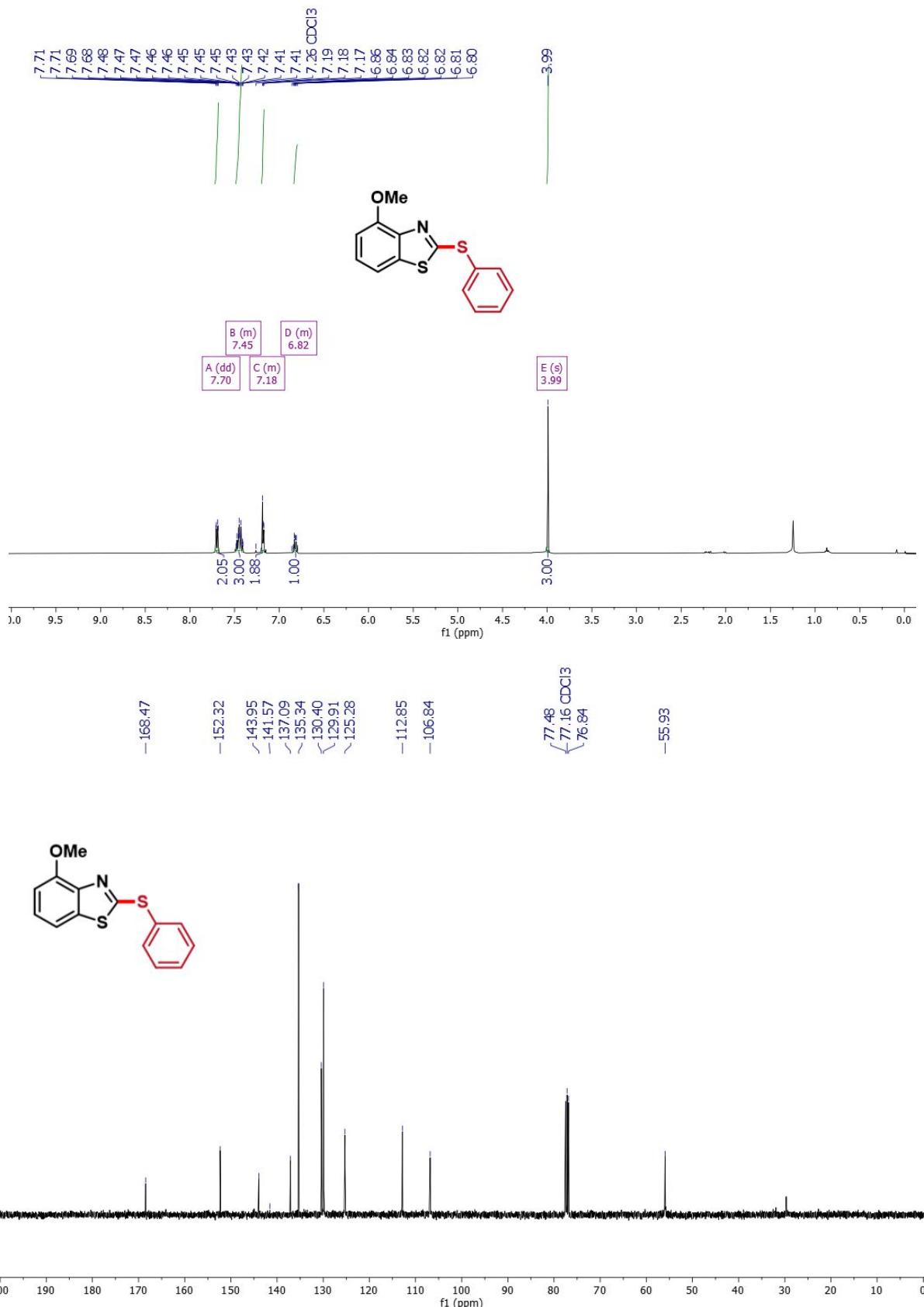
**Scheme 3, entry 3t**

**Yield: 82%**



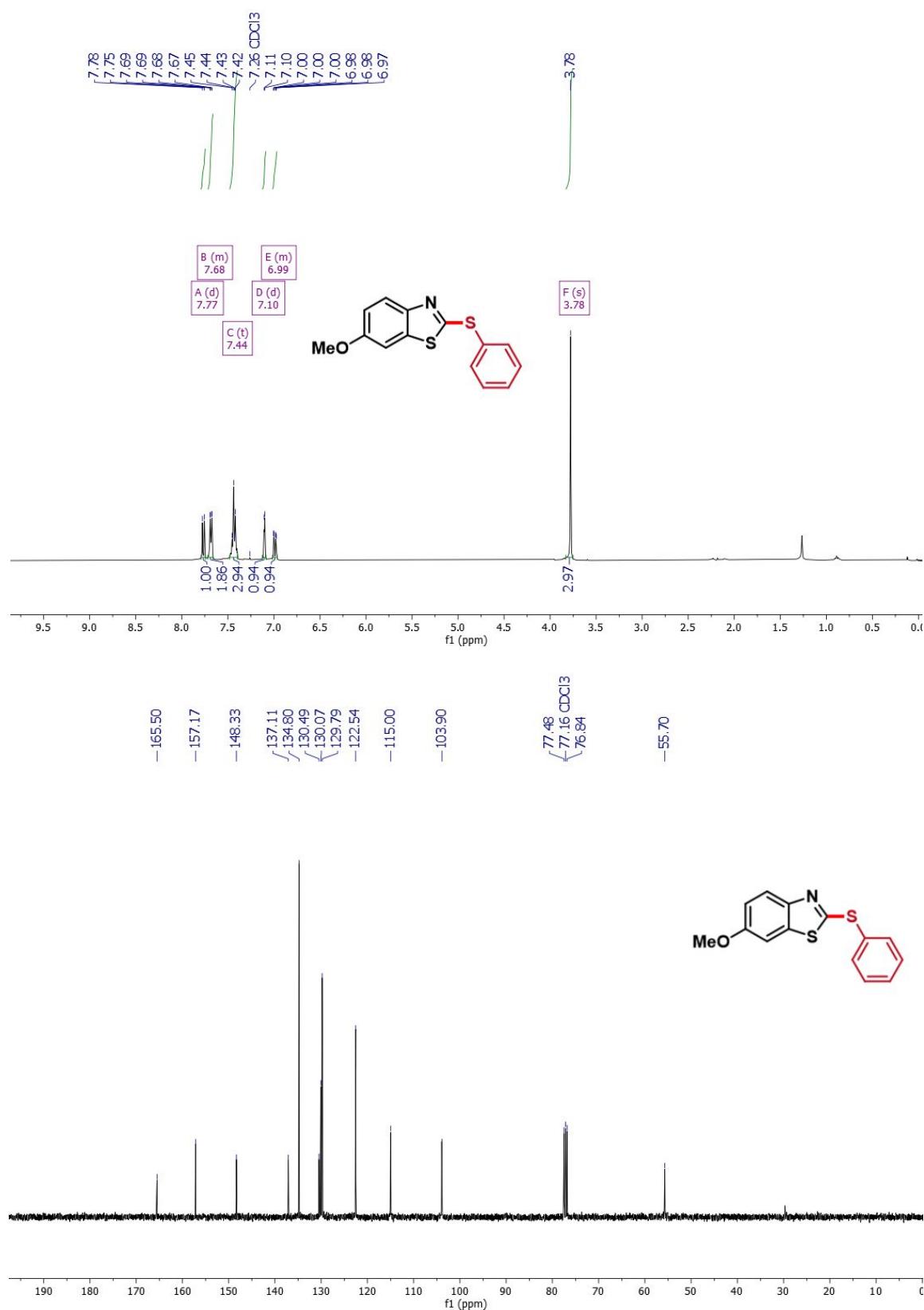
**Scheme 3, entry 3u**

**Yield: 88%**



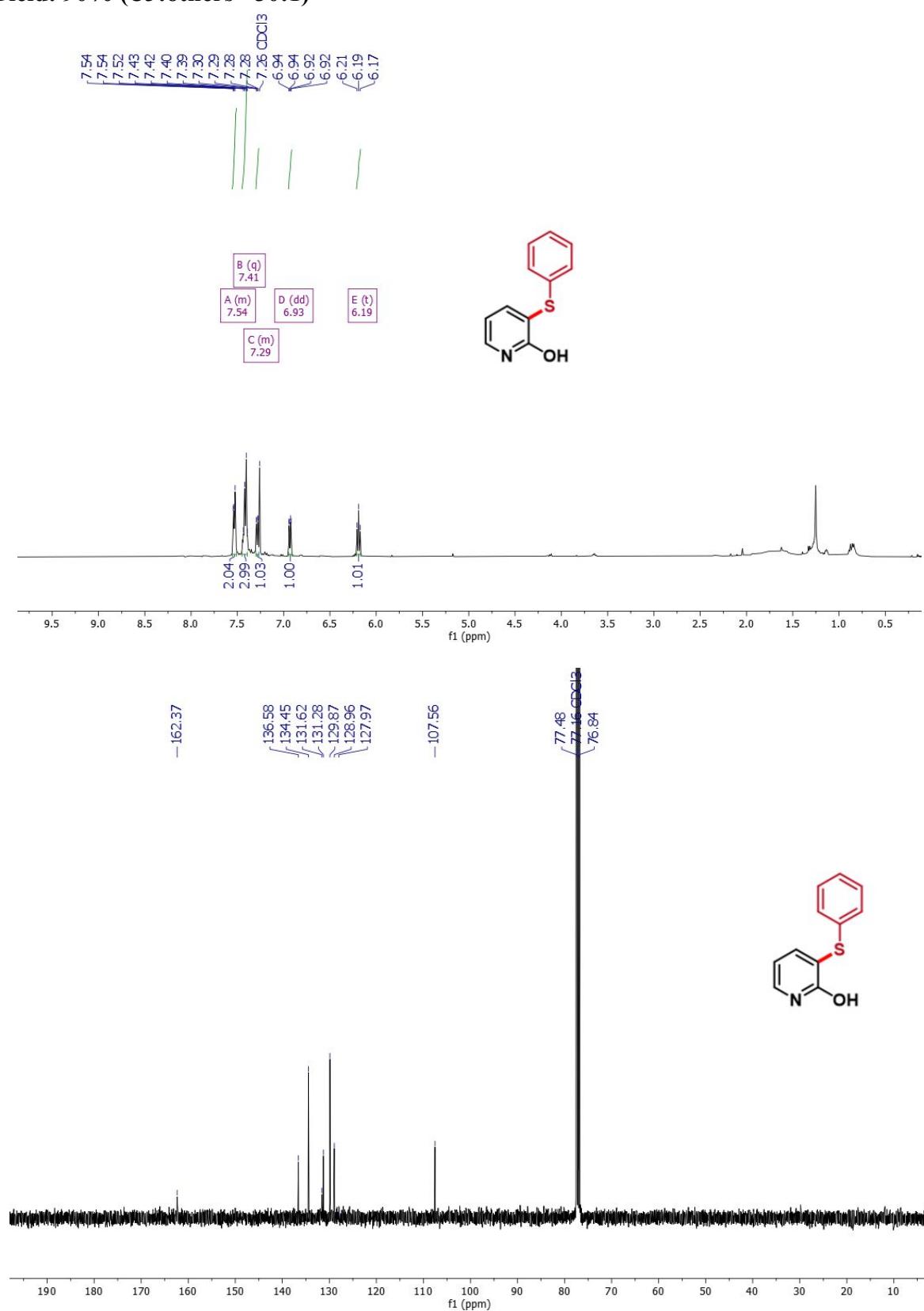
**Scheme 3, entry 3v**

**Yield: 90%**



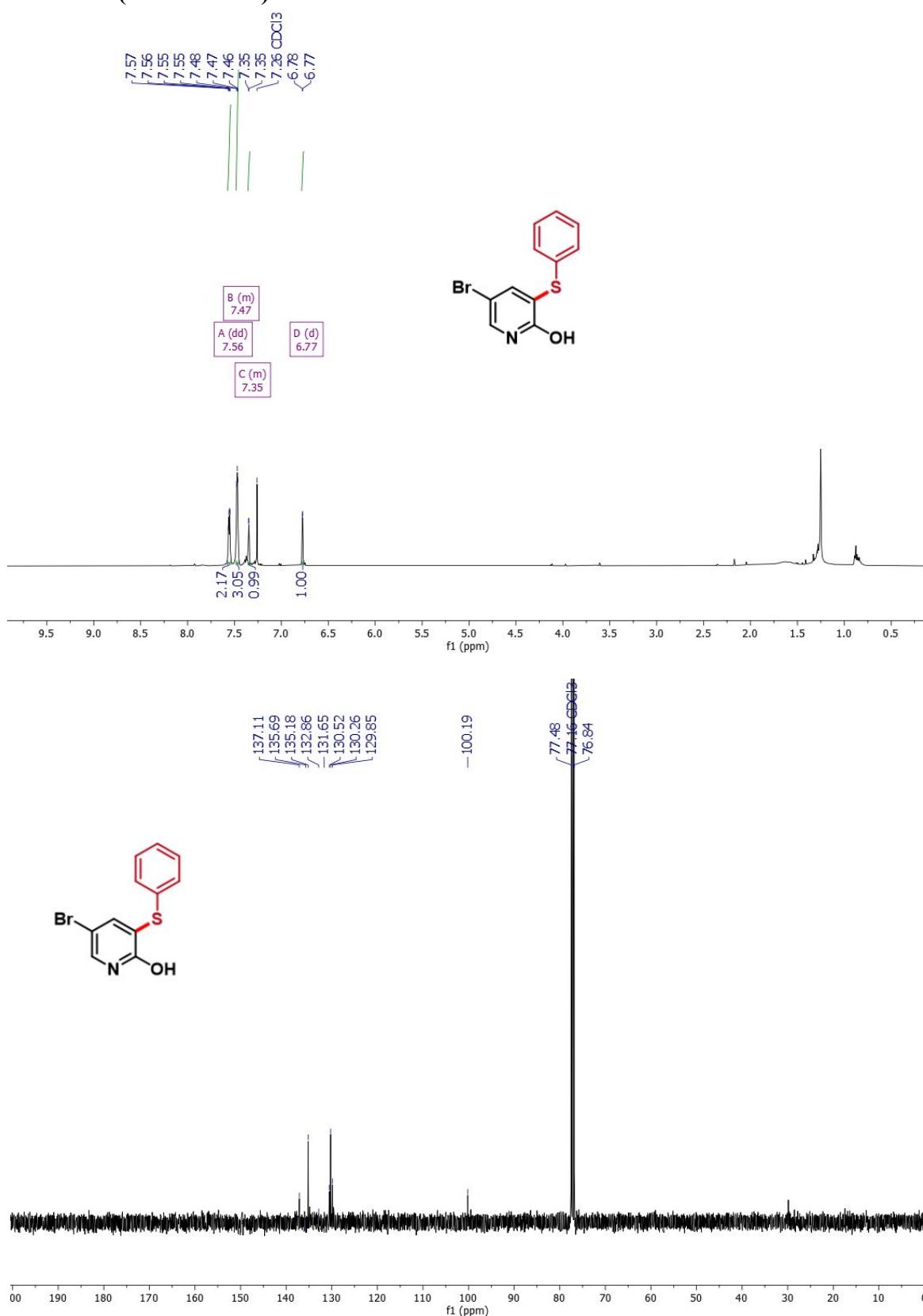
**Scheme 3, entry 3w**

**Yield: 90% (C3:others >30:1)<sup>14</sup>**



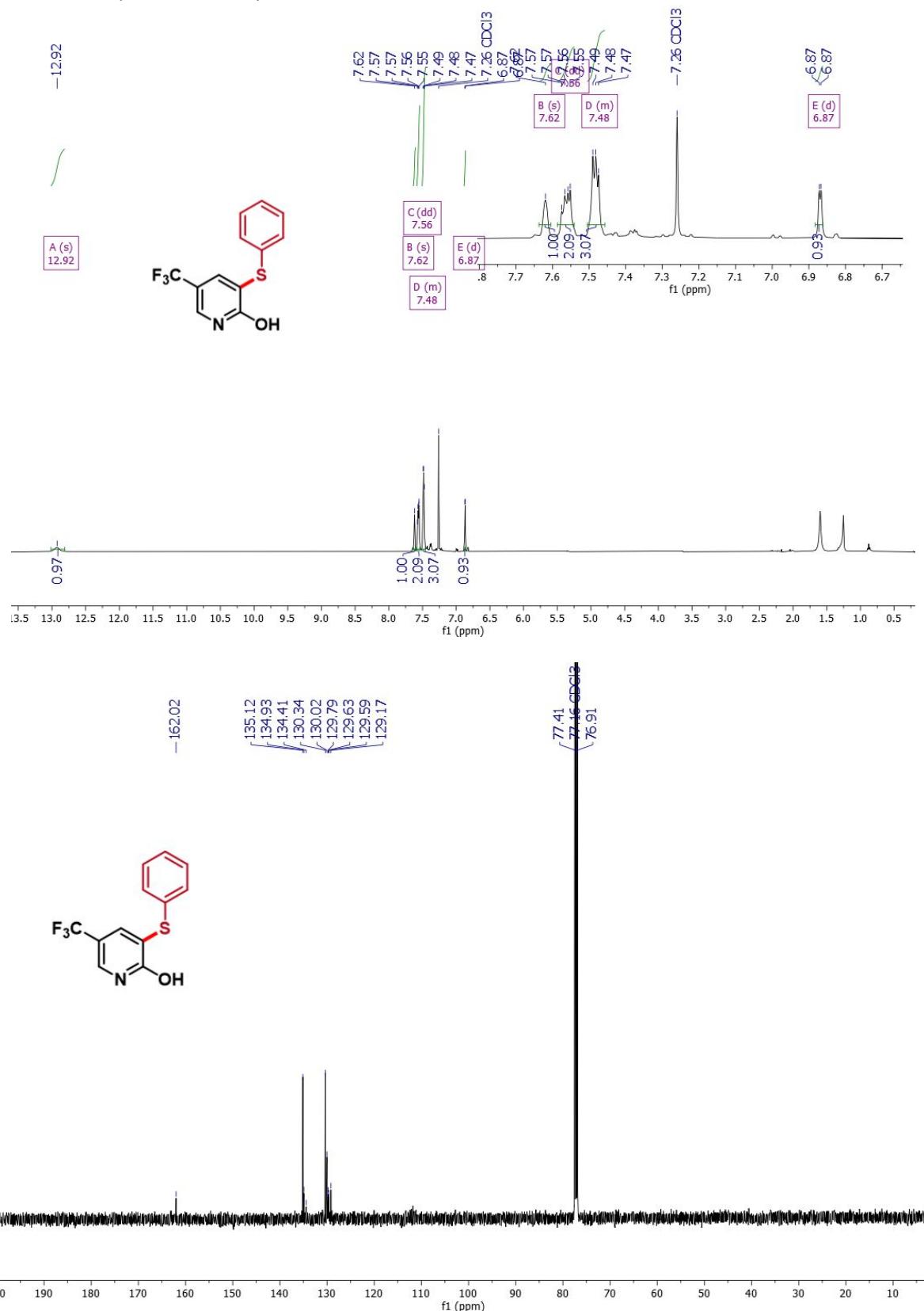
**Scheme 3, entry 3x**

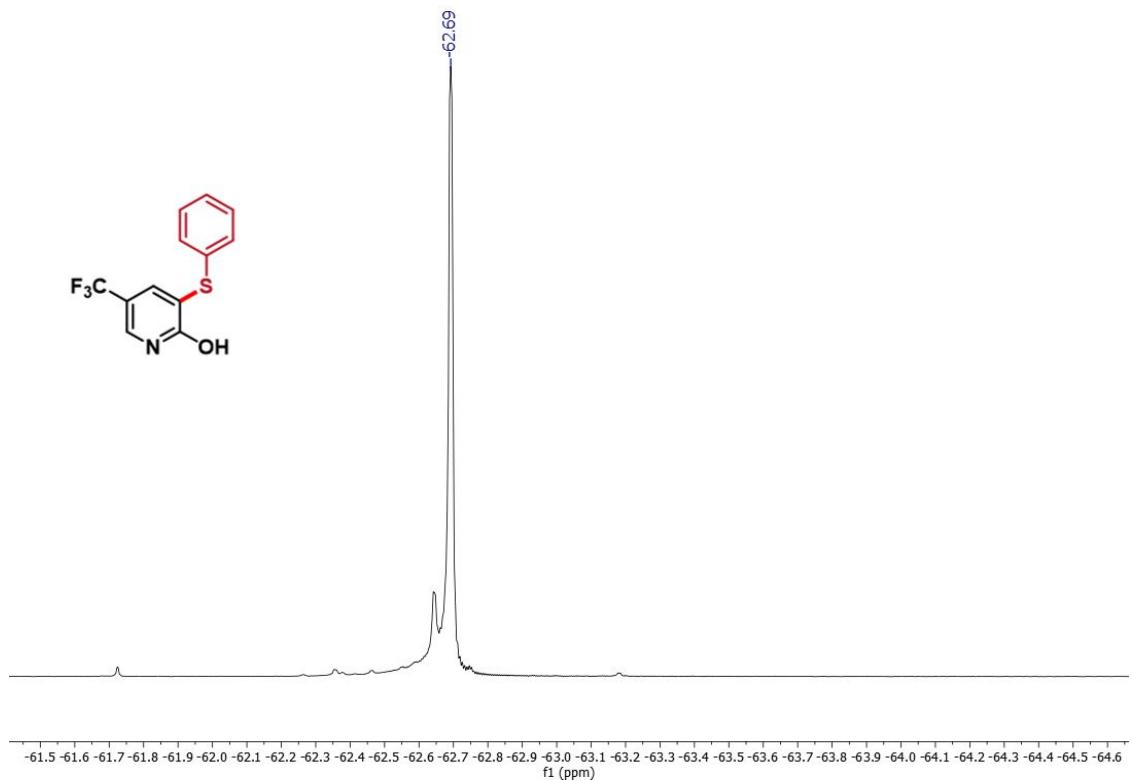
**Yield: 85% ( $C_3:C_4 = 10:1$ )<sup>14</sup>**



### Scheme 3, entry 3y

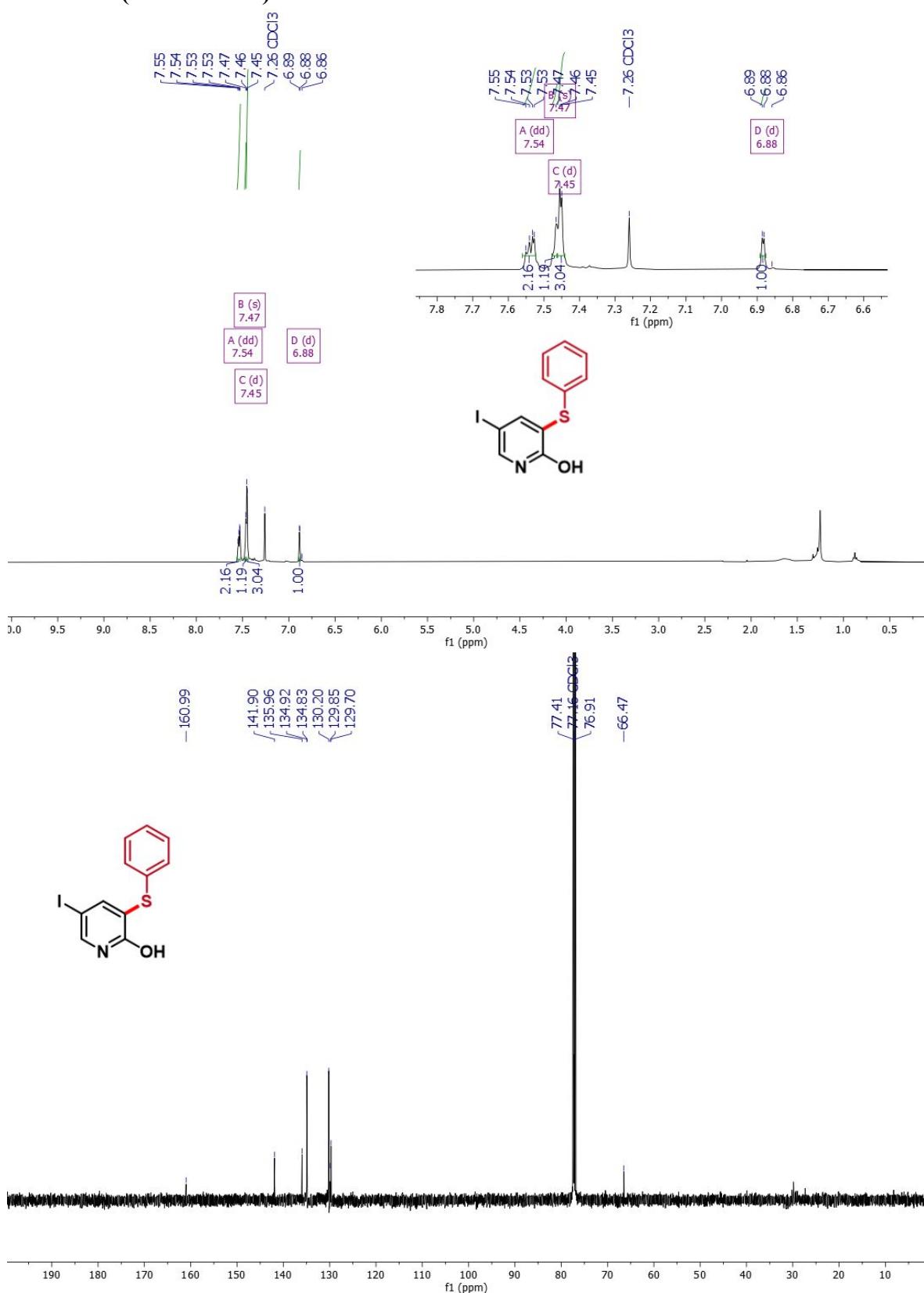
**Yield: 73% ( $C_3:C_4 = 11:1$ )<sup>14</sup>**





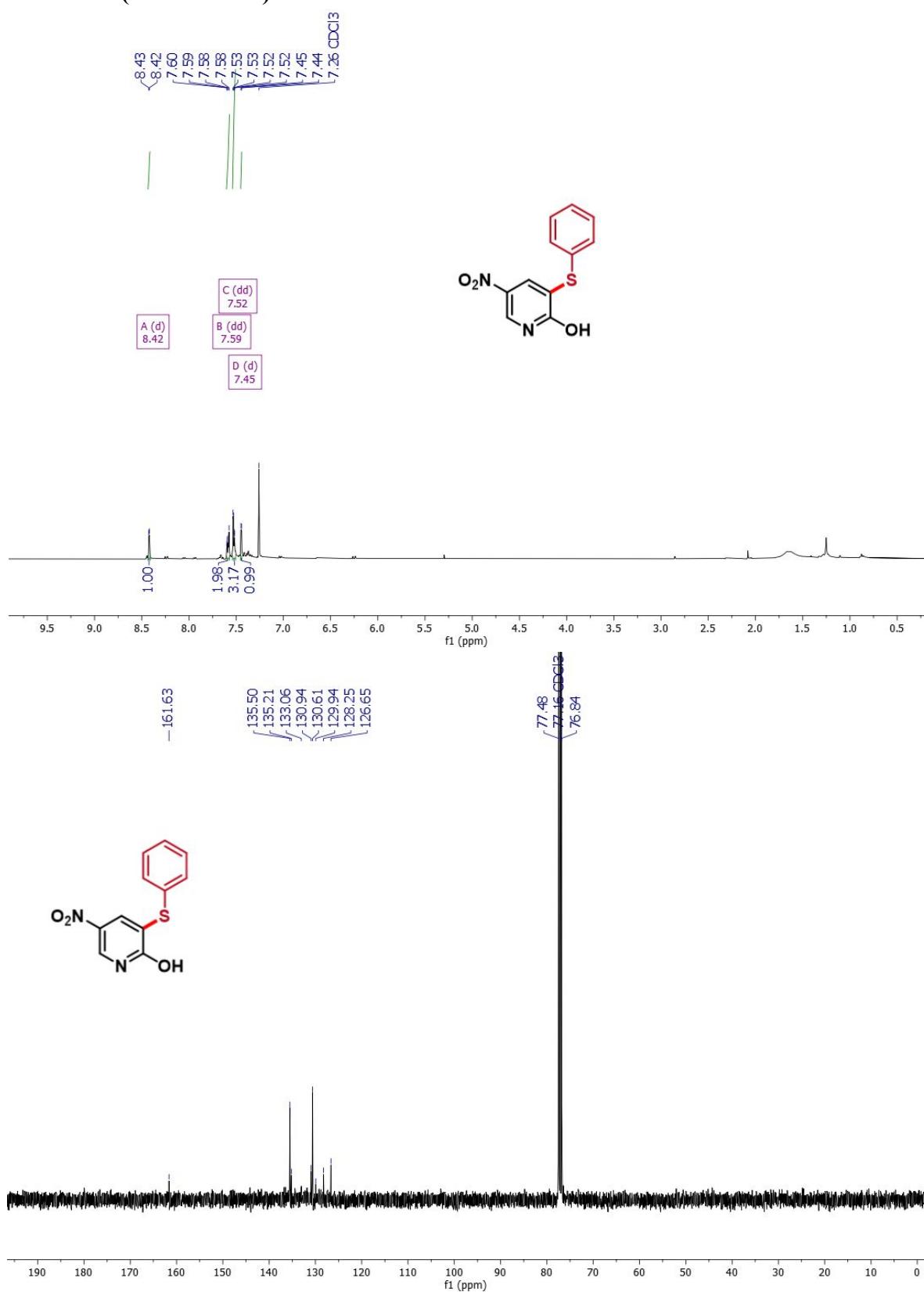
### Scheme 3, entry 3z

**Yield: 79% ( $C_3:C_4 = 15:1$ )<sup>14</sup>**



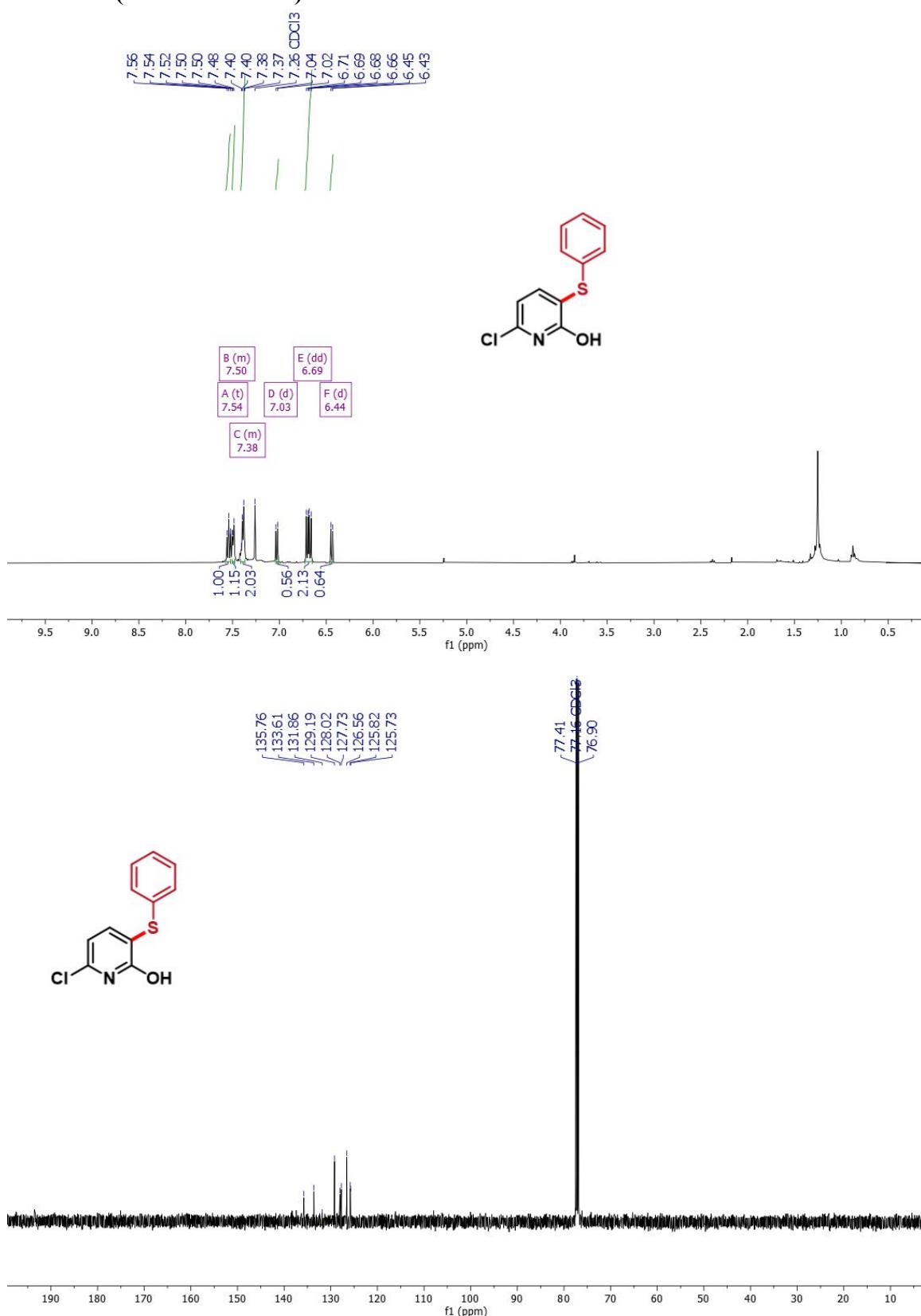
**Scheme 3, entry 3aa**

**Yield: 76% (*C*3:*C*4 = 12:1)<sup>14</sup>**



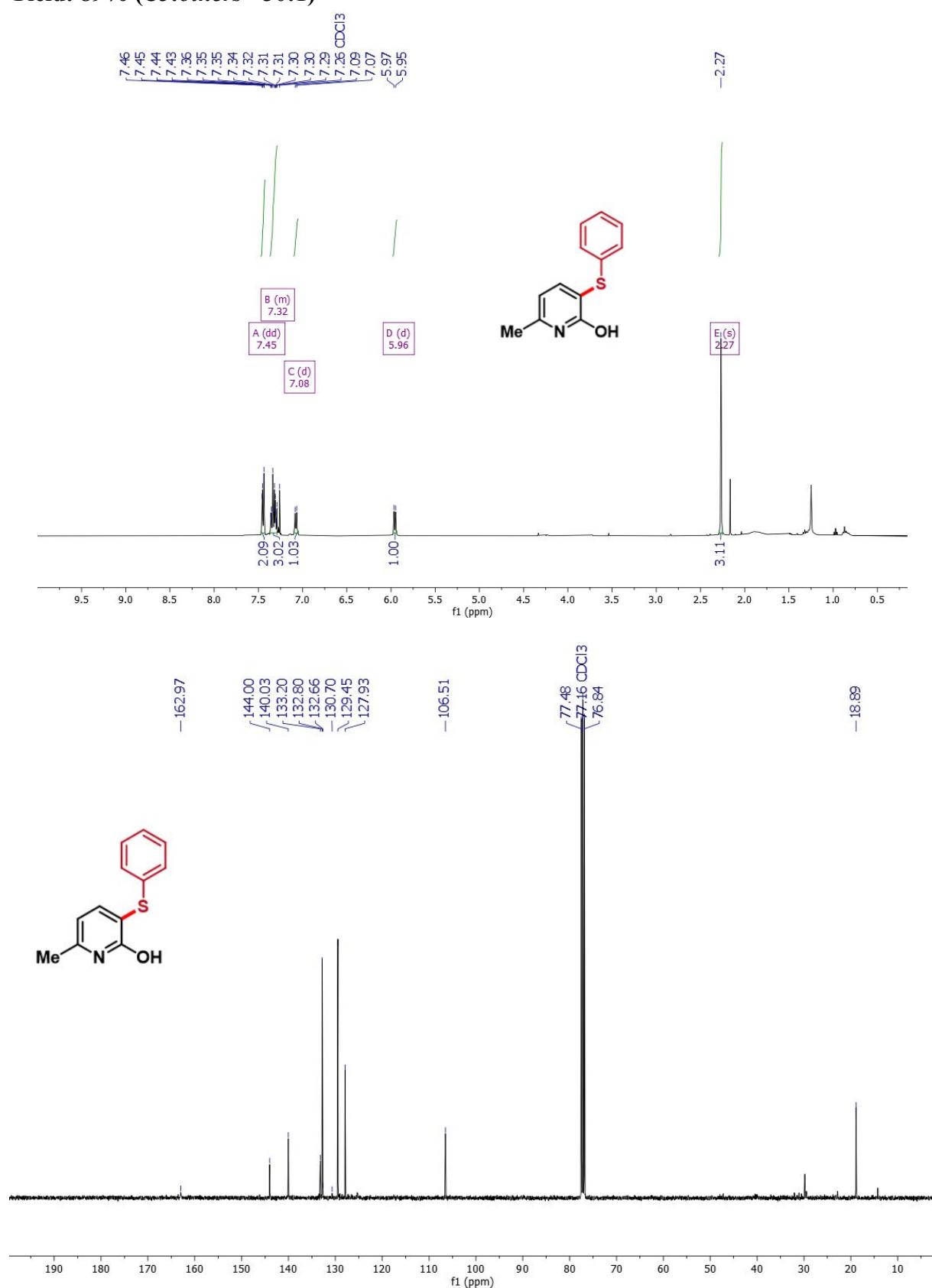
**Scheme 3, entry 3ab**

**Yield: 87% (*C3:others* >30:1)<sup>14</sup>**



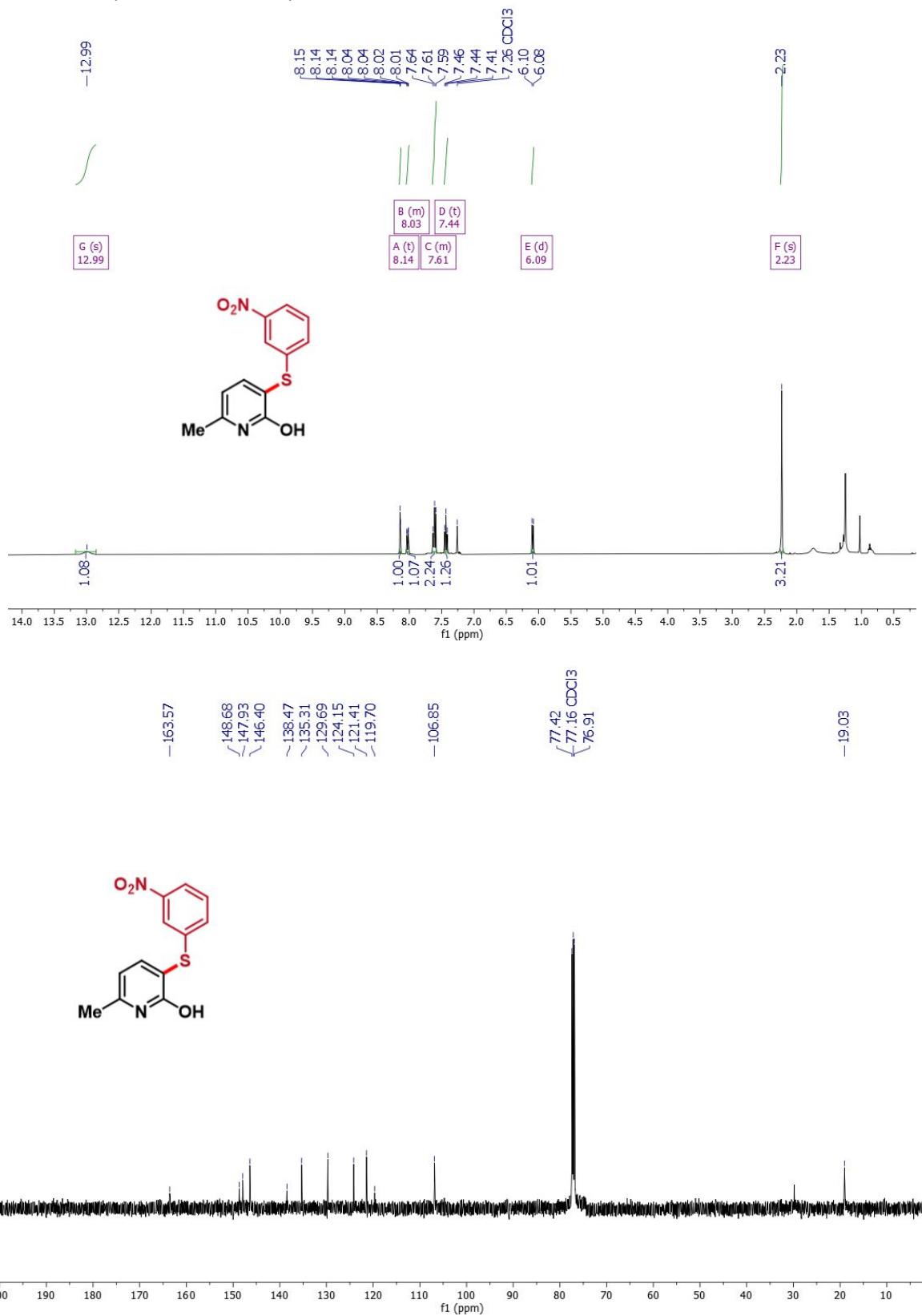
**Scheme 3, entry 3ac**

**Yield: 89% (*C3:others >30:1*)<sup>14</sup>**



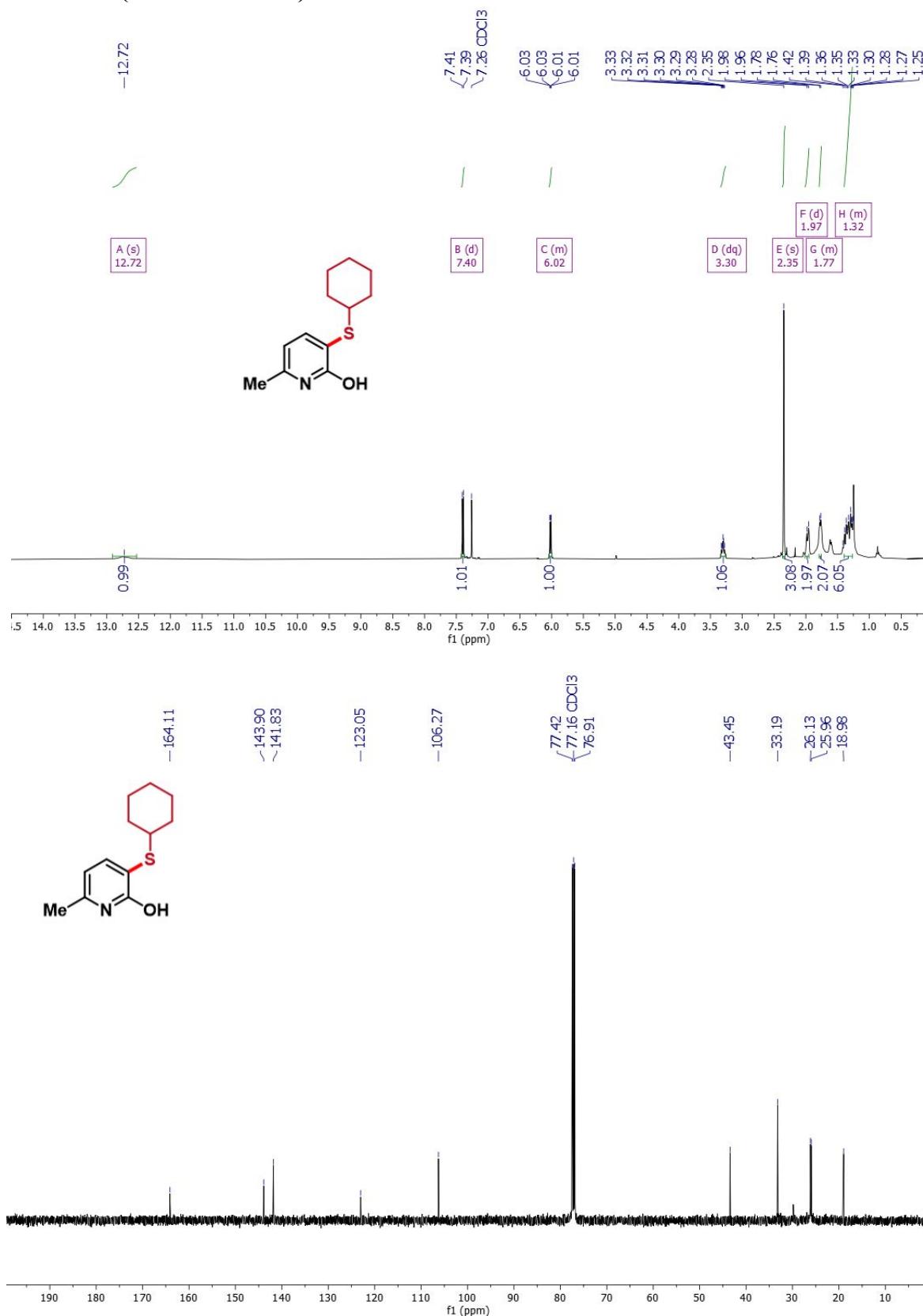
**Scheme 3, entry 3ad**

**Yield: 88% (*C3:others* >30:1)<sup>14</sup>**



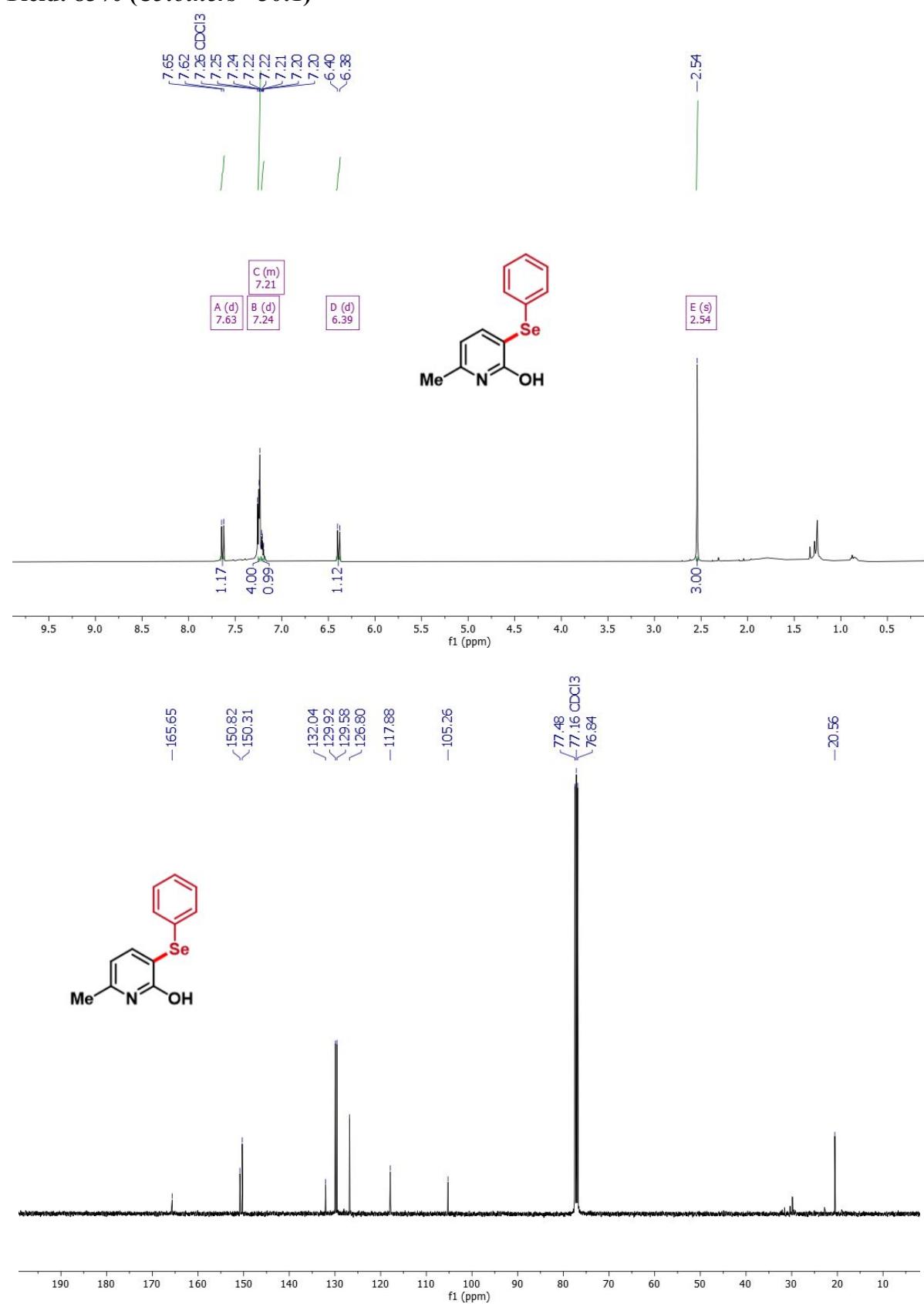
**Scheme 3, entry 3ae**

**Yield: 91% (*C3:others* >30:1)<sup>14</sup>**



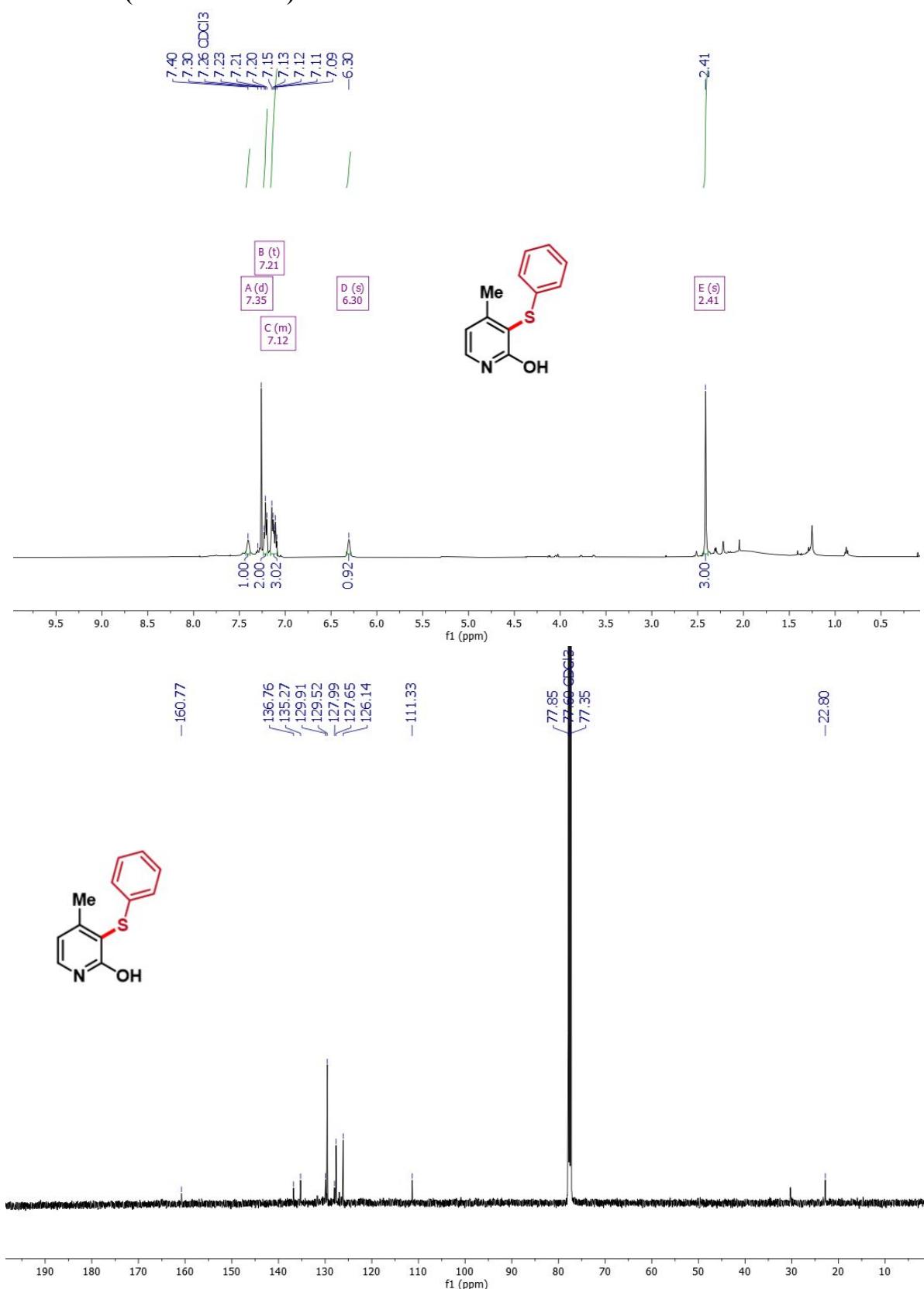
**Scheme 3, entry 3af**

**Yield: 83% (*C3:others* >30:1)<sup>14</sup>**



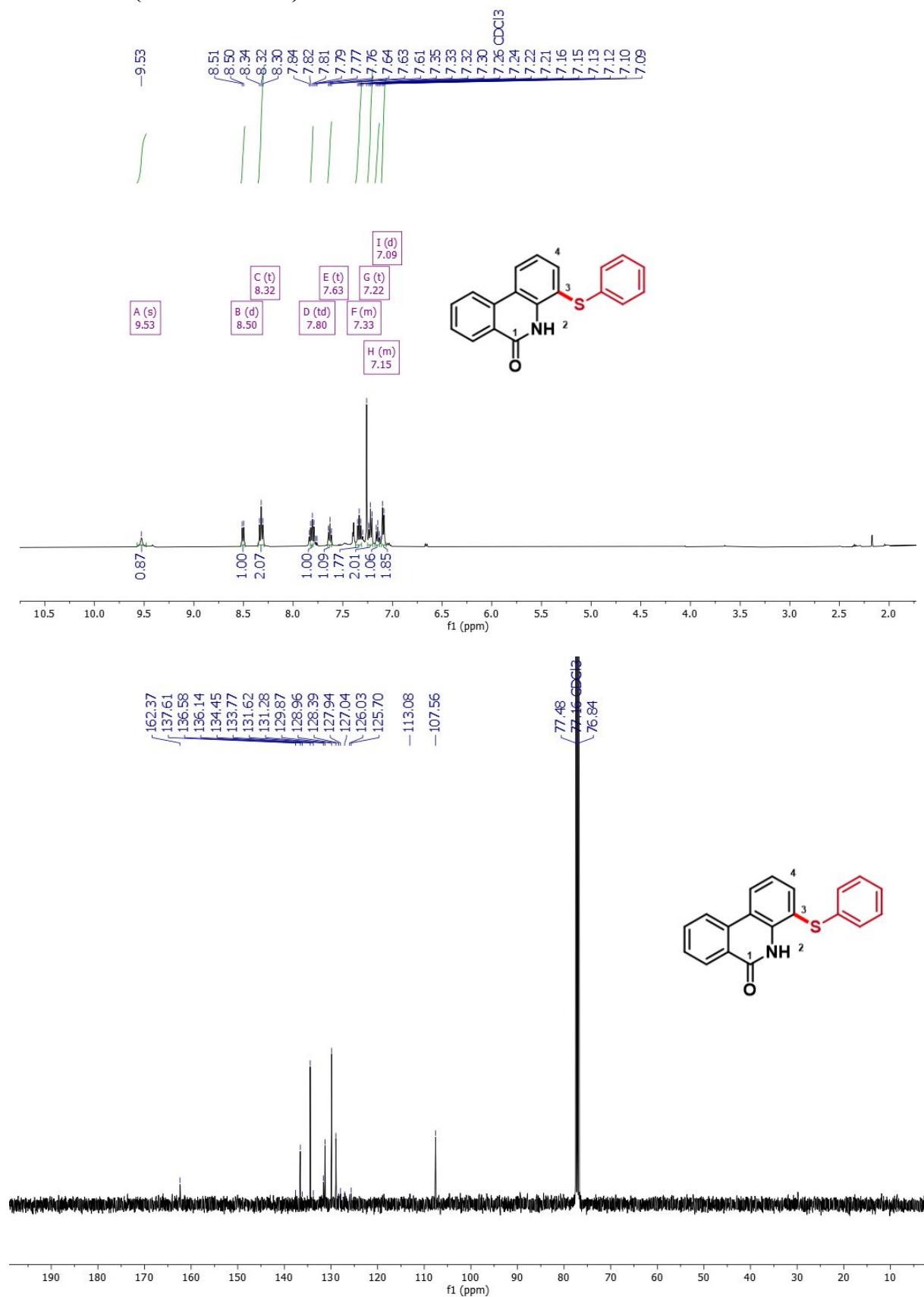
**Scheme 3, entry 3ag**

**Yield: 56% (*C3:others*= 9:1)<sup>14</sup>**



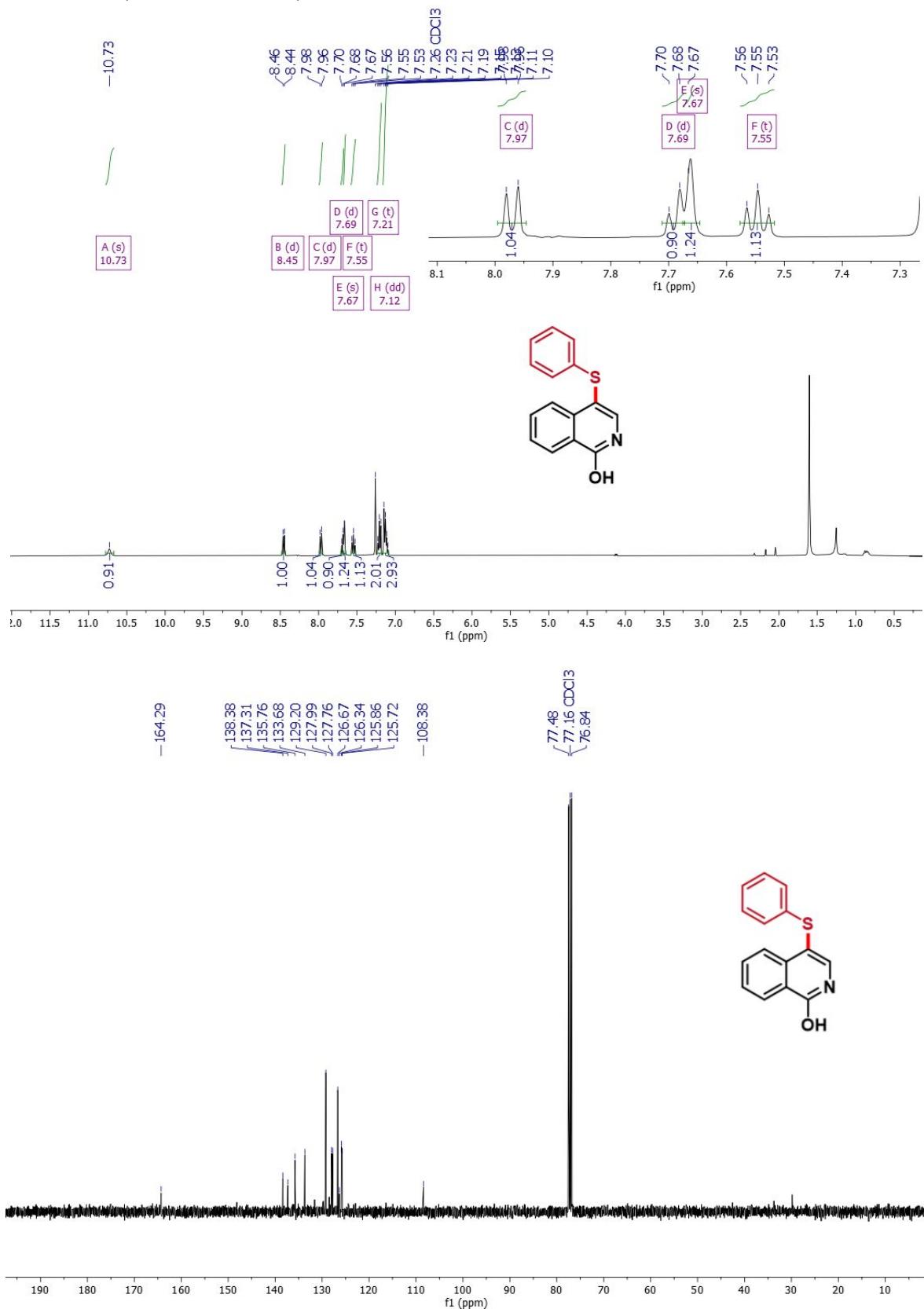
**Scheme 3, entry 3ah**

**Yield: 76% (C3:others= 7:1)<sup>14</sup>**



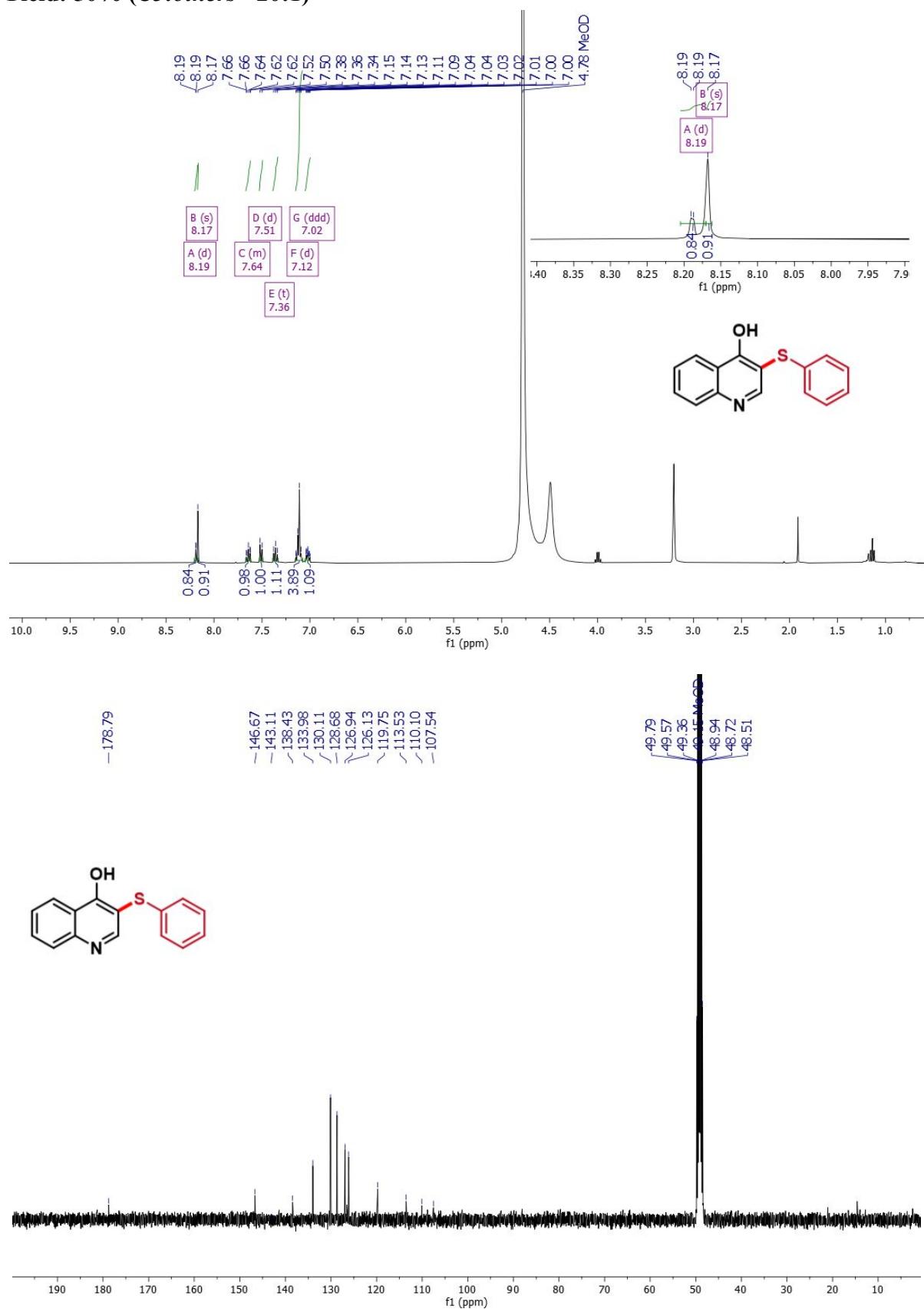
### Scheme 3, entry 3ai

**Yield: 82% (*C4:others*= 17:1)**<sup>14</sup>



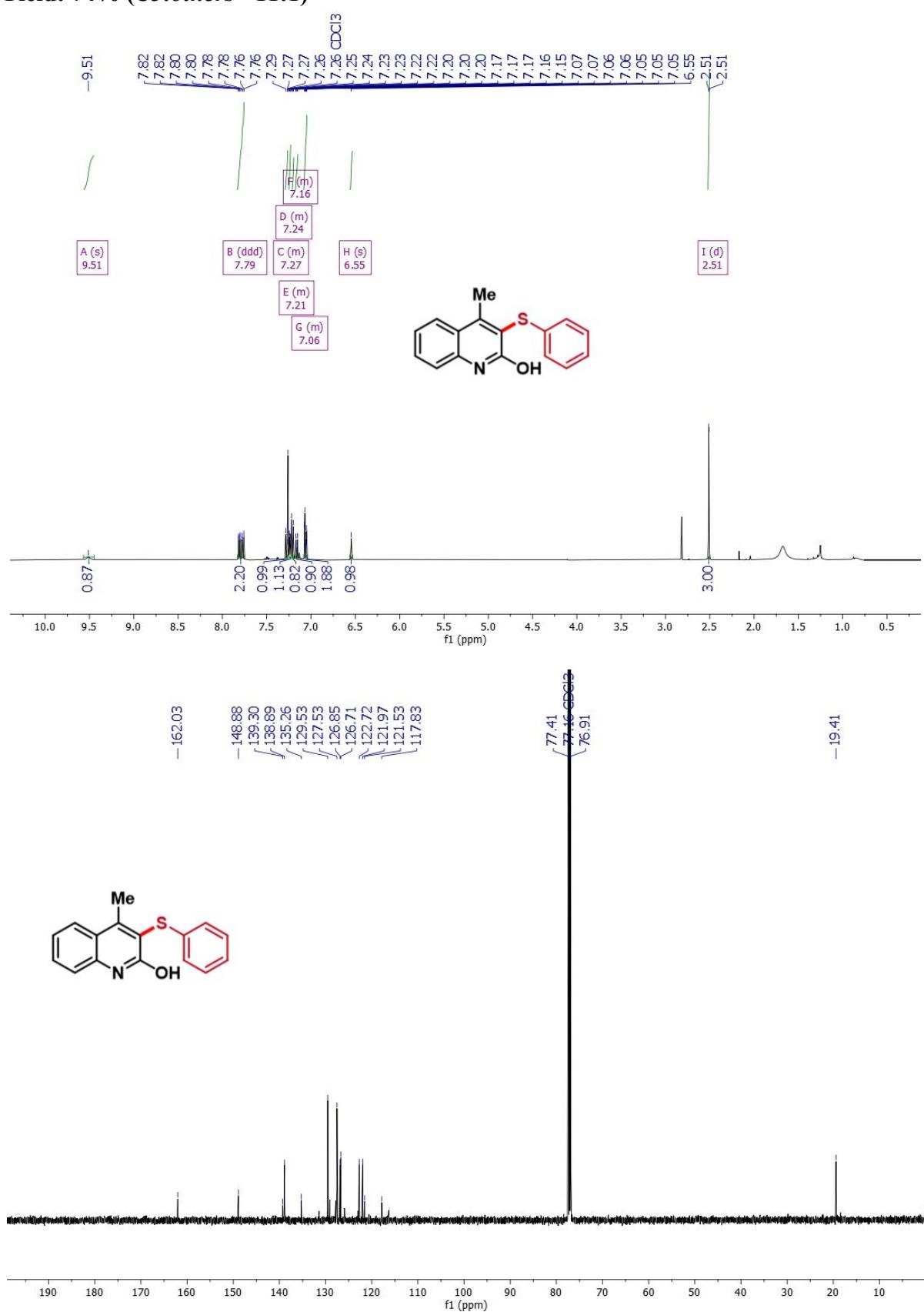
### Scheme 3, entry 3aj

**Yield: 50% (*C<sub>3</sub>:others >20:1*)<sup>14</sup>**



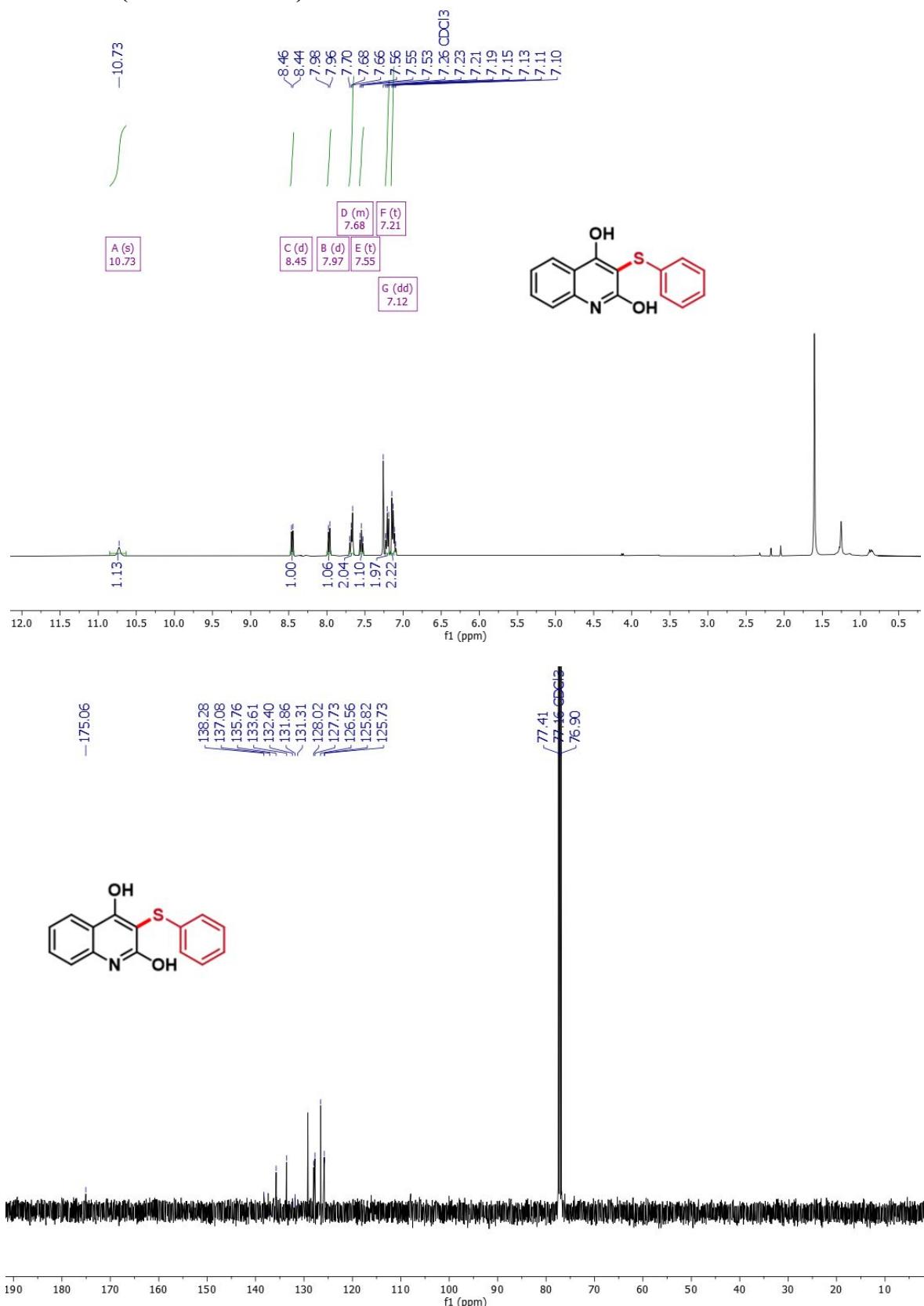
**Scheme 3, entry 3ak**

**Yield: 74% (*C3:others*= 11:1)<sup>14</sup>**

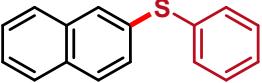
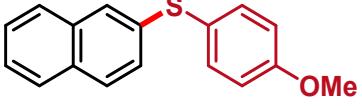
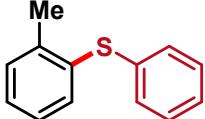
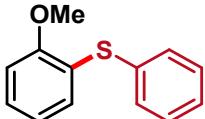
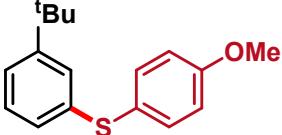
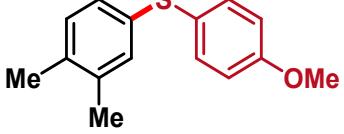
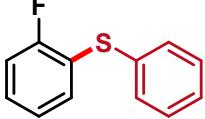
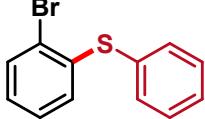
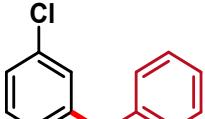


**Scheme 3, entry 3al**

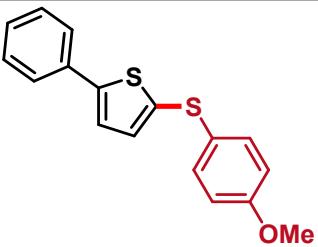
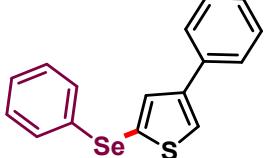
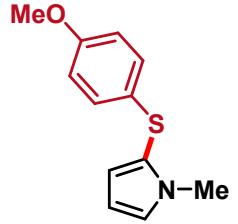
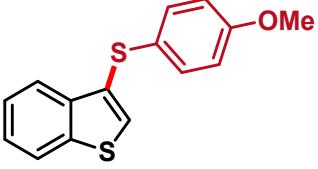
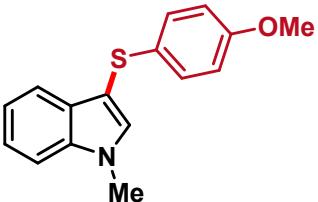
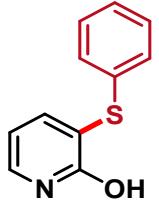
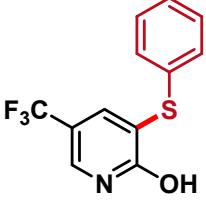
**Yield: 81% (*C3:others*= 17:1)<sup>14</sup>**



### Site-selective product confirmation

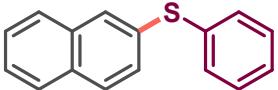
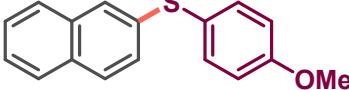
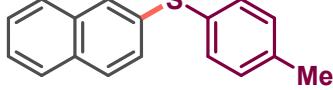
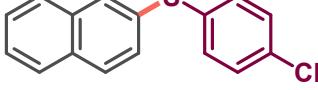
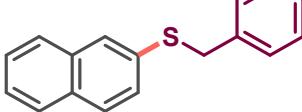
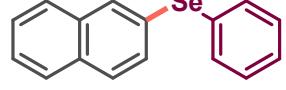
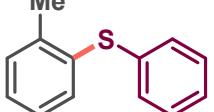
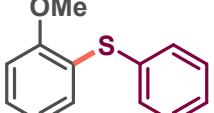
Compounds	Proof of selectivity
	Singlet at 7.41 ppm proves $\beta$ product
	Singlet at 7.08 ppm confirms $\beta$ product
	Absence of any singlet and absence of two distinct doublets rules out the possibility of <i>meta</i> and <i>para</i> product respectively
	Absence of any singlet and absence of two distinct doublets rules out the possibility of <i>meta</i> and <i>para</i> product respectively. Presence of two doublets and a triplet confirms <i>ortho</i> product.
	Singlet at 7.28 ppm confirms <i>meta</i> product
	Singlet at 6.87 ppm confirms $\beta$ product.
	Absence of any singlet and absence of two distinct doublets rules out the possibility of <i>meta</i> and <i>para</i> product respectively. Presence of two doublets and a triplet confirms <i>ortho</i> product.
	Absence of any singlet and absence of two distinct doublets rules out the possibility of <i>meta</i> and <i>para</i> product respectively
	Singlet at 7.30 ppm confirms <i>meta</i> product

	Absence of any singlet removes the possibility of <i>meta</i> product. Presence of two doublets and two triplets merged into multiplet confirms <i>ortho</i> product.
	Presence of singlet at 7.52 ppm confirms <i>meta</i> product
	Presence of singlet at 7.50 ppm confirms <i>meta</i> product
	Absence of any clear singlet and the presence of distinct doublets and triplets indicate <i>ortho</i> product
	Presence of singlet at 7.13 ppm confirms $\beta$ product. 1D NOE further confirms the position of product.
	Singlet at 8.15 ppm proves C-3 selective product.
	Absence of singlet predicts C-3 selective product formation
	Absence of any singlet and presence of a triplet of doublet shows C-2 selective product
	Presence of two distinct doublets at 7.03 ppm and 7.07 ppm proves C-5 selective product to be formed.

	Two distinct doublets at 7.17 ppm and 7.20 ppm confirms the C-2 product
	Two singlets at 7.63 and 7.61 ppm confirm the C-5 functionalized product
	Two doublets at 6.57 ppm and 6.22 ppm confirms C-2 product
	Singlet at 7.32 ppm confirms C-3 product
	Singlet at 7.35 ppm confirms C-3 product
	Doublet of doublet at 6.93 ppm and triplet at 6.19 ppm predicts C-3 functionalized product
	Singlet at 7.62 ppm and <i>meta</i> coupled doublet at 6.87 ppm confirms C-3 selective product

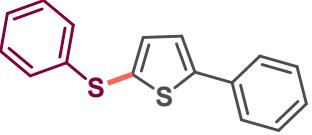
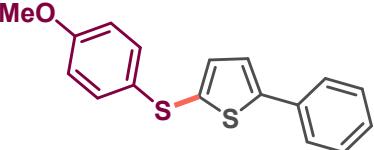
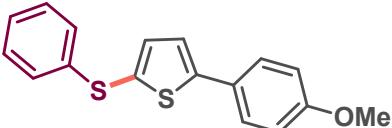
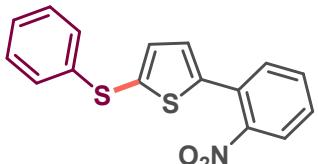
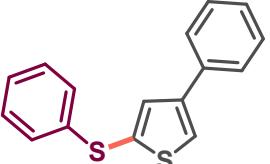
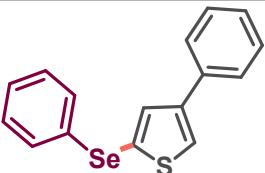
	Singlet at 7.47 ppm and <i>meta</i> coupled doublet at 6.88 ppm confirms C-3 selective product
	Doublet at 7.05 ppm and 5.96 ppm proves C-3 product
	Two doublets at 7.40 ppm and 6.02 ppm proves C-3 product
	Singlet at 7.67 ppm confirms C-4 product
	Singlet at 8.17 ppm proves C-3 product

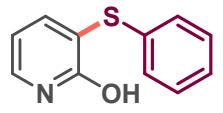
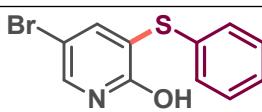
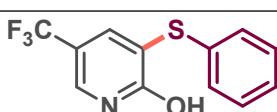
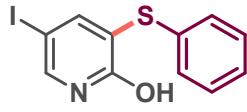
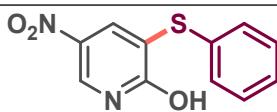
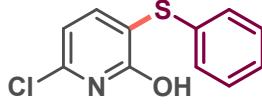
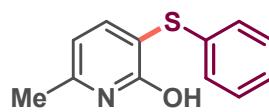
**Comparision of isolated selectivity and selectivity of crude reaction mixture**

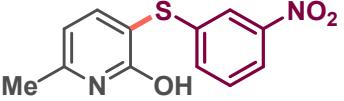
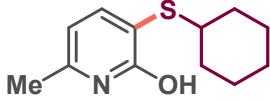
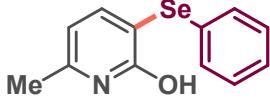
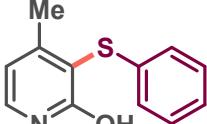
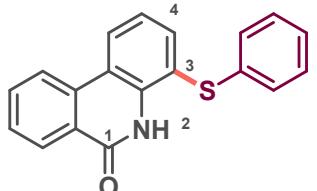
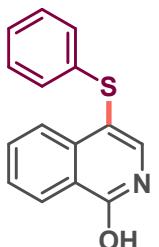
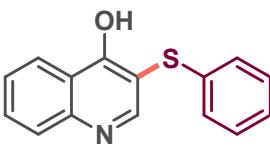
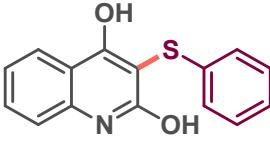
Structure	Code	Selectivity from isolated material	Selectivity from crude reaction mixture (NMR/HPLC)
	<b>2a</b>	$\beta:\alpha > 30:1$	$\beta:\alpha > 30:1$ (HPLC)
	<b>2b</b>	$\beta:\alpha = 17:1$	$\beta:\alpha > 20:1$ (HPLC)
	<b>2c</b>	$\beta:\alpha > 20:1$	$\beta:\alpha > 20:1$ (HPLC)
	<b>2d</b>	$\beta:\alpha > 20:1$	$\beta:\alpha = 18:1$ (HPLC)
	<b>2e</b>	$\beta:\alpha 18:1$	$\beta:\alpha > 20:1$ (HPLC)
	<b>2f</b>	$\beta:\alpha > 30:1$	$\beta:\alpha = 8:1$ (HPLC)
	<b>2g</b>	$\beta:\alpha > 30:1$	isolated selectivity >30:1
	<b>2h</b>	$\beta:\alpha > 30:1$	isolated selectivity >30:1
	<b>2m</b>	o:others >20:1	o:others = 12:1 (NMR)
	<b>2n</b>	o:others >30:1	o:others >30:1 (NMR)

	<b>2o</b>	o:others = 6:1	o:others = 3:1 (NMR)
	<b>2p</b>	m:others = 4:1	m:others = 4:1 (NMR)
	<b>2q</b>	$\beta:\alpha = 12:1$	$\beta:\alpha = 12:1$ (NMR)
	<b>2r</b>	$\beta:\alpha = 1:1$	$\beta:\alpha = 1:1$ (NMR)
	<b>2t</b>	o:others >30:1	o:others >30:1 (NMR) o:others >30:1 (HPLC)
	<b>2u</b>	o:others >30:1	o:others >30:1 (NMR) o:others >30:1 (HPLC)
	<b>2v</b>	m:others >20:1	m:others >20:1 (NMR) m:others >20:1 (HPLC)
	<b>2w</b>	o:others >20:1	isolated selectivity >20:1
	<b>2x</b>	o:others = 9:1	o:others = 6:1 (NMR)
	<b>2y</b>	o:others = 10:1	o:others = 6:1 (NMR)

	<b>2z</b>	m:others = 5:1	m:others = 8:1 (NMR)
	<b>2aa</b>	m:others = 4:1	m:others = 4:1 (NMR) m:others = 4:1 (HPLC)
	<b>2ab</b>	m:others >20:1	m:others >20:1 (HPLC)
	<b>3a</b>	C3:others >30:1	C3:others >30:1 (HPLC)
	<b>3b</b>	C3: C5 = 6:1	C3: C5 = 6:1 (NMR)
	<b>3c</b>	C3:others >20:1	C3:others = 17:1 (HPLC)
	<b>3d</b>	C3:others = 10:1	C3:others = 10:1 (NMR) C3:others = 10:1 (HPLC)
	<b>3e</b>	C3:others = 8:1	C3:others = 15:1 (NMR)
	<b>3g</b>	C2:others = 5:1	C2:others = 5:1 (NMR)
	<b>3h</b>	C5:C3 = 20:1	C5:C3 = 17:1 (NMR)
	<b>3i</b>	C5:C3 = 20:1	C5:C3 = 20:1 (NMR)

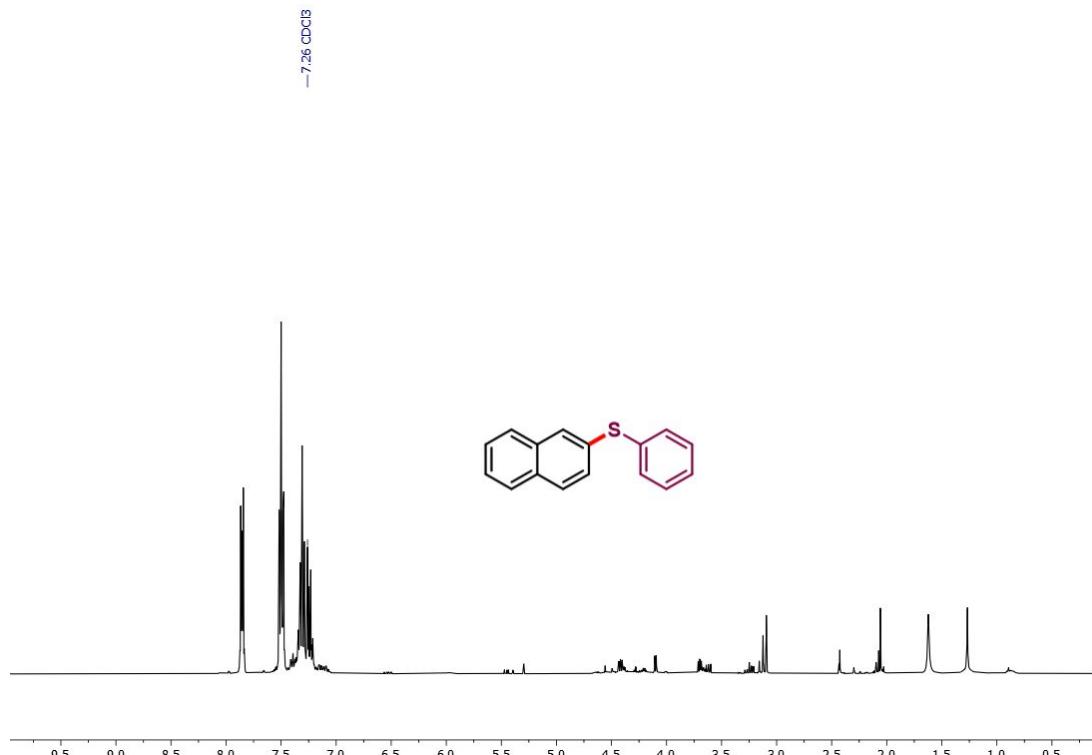
	<b>3j</b>	C5:others >30:1	C5:others >30:1 (NMR) C5:others >30:1 (HPLC)
	<b>3k</b>	C5:others >30:1	C5:others = 18:1 (NMR)
	<b>3l</b>	C5:others >30:1	C5:others = 19:1 (NMR) C5:others >20:1 (HPLC)
	<b>3m</b>	C5:others >30:1	C5:others >30:1 (NMR)
	<b>3n</b>	C5:others >30:1	C5:others >30:1 (NMR)
	<b>3o</b>	C5:others >30:1	C5:others >30:1 (NMR)
	<b>3p</b>	C2:others = 6:1	C2:others = 6:1 (NMR)

	<b>3q</b>	C3:others = 6:1	C3:others = 5:1 (NMR) C3:others = 6:1 (HPLC)
	<b>3r</b>	C3:others = 12:1	C3:others = 16:1 (HPLC)
	<b>3w</b>	C3:others >30:1	C3:others > 30:1 (NMR)
	<b>3x</b>	C3:C4 = 10:1	C3:others = 10:1 (HPLC)
	<b>3y</b>	C3:C4 = 11:1	C3:C4 = 11:1 (NMR)
	<b>3z</b>	C3:C4 = 15:1	C3:C4 >20:1 (NMR)
	<b>3aa</b>	C3:C4 = 12:1	C3:C4 =11:1 (NMR) C3:others = 12:1 (HPLC)
	<b>3ab</b>	C3:others >30:1	C3:others = 17:1 (NMR)
	<b>3ac</b>	C3:others >30:1	C3:others = 9:1 (NMR)

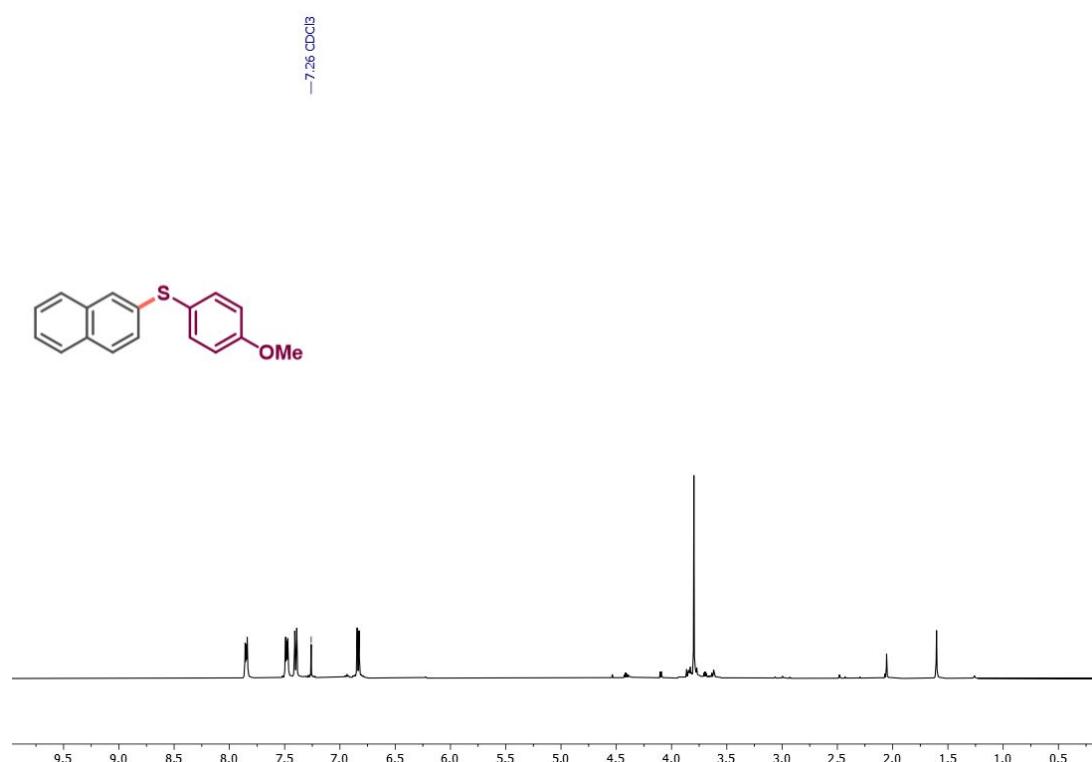
	<b>3ad</b>	C3:others >30:1	C3:others >20:1 (NMR) C3:others >20:1 (HPLC)
	<b>3ae</b>	C3:others >30:1	C3:others = 20:1 (NMR) C3:others >30:1 (HPLC)
	<b>3af</b>	C3:others >30:1	C3:others >20:1 (NMR) C3:others >30:1 (HPLC)
	<b>3ag</b>	C3:others = 9:1	C3:others = 9:1 (NMR) C3:others = 9:1 (HPLC)
	<b>3ah</b>	C3:C4 = 7:1	C3:C4 = 7:1 (NMR)
	<b>3ai</b>	C4:others = 17:1	C4:others >20:1 (HPLC)
	<b>3aj</b>	C3:others >20:1	C3:others >20:1 (NMR)
	<b>3al</b>	C3:others = 17:1	isolated selectivity =17:1

### NMR data of crude reaction mixtures

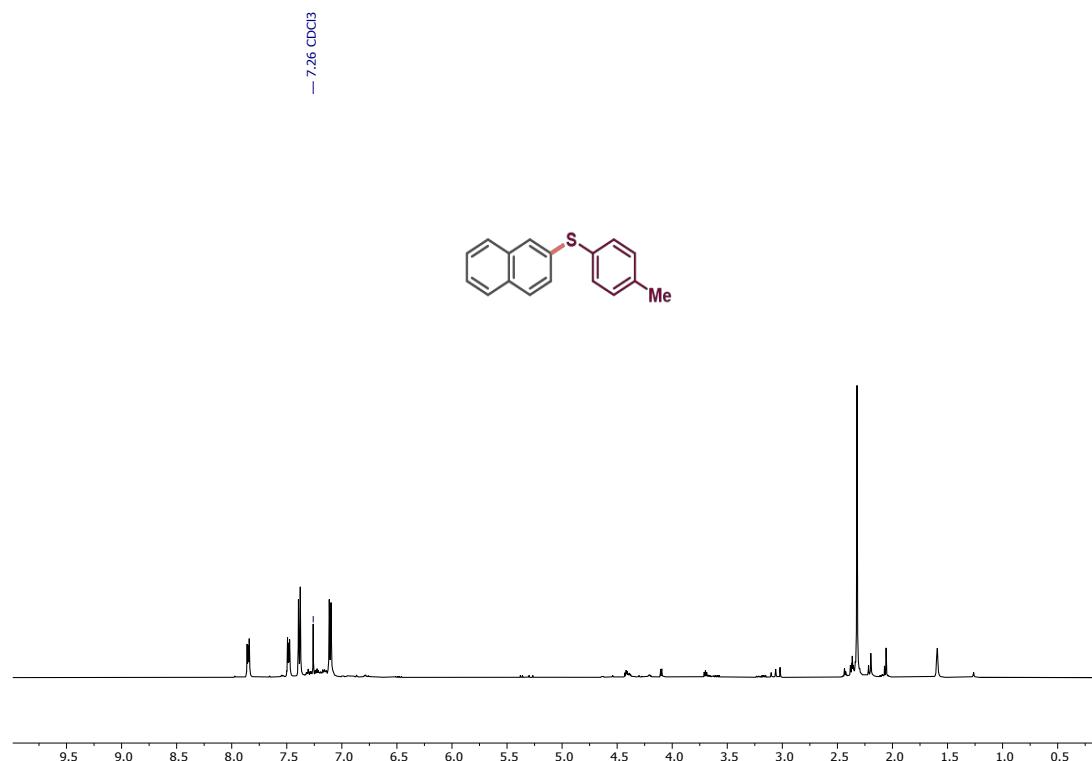
**Naphthalen-2-yl(phenyl)sulfane (2a): NMR data of crude reaction mixture**



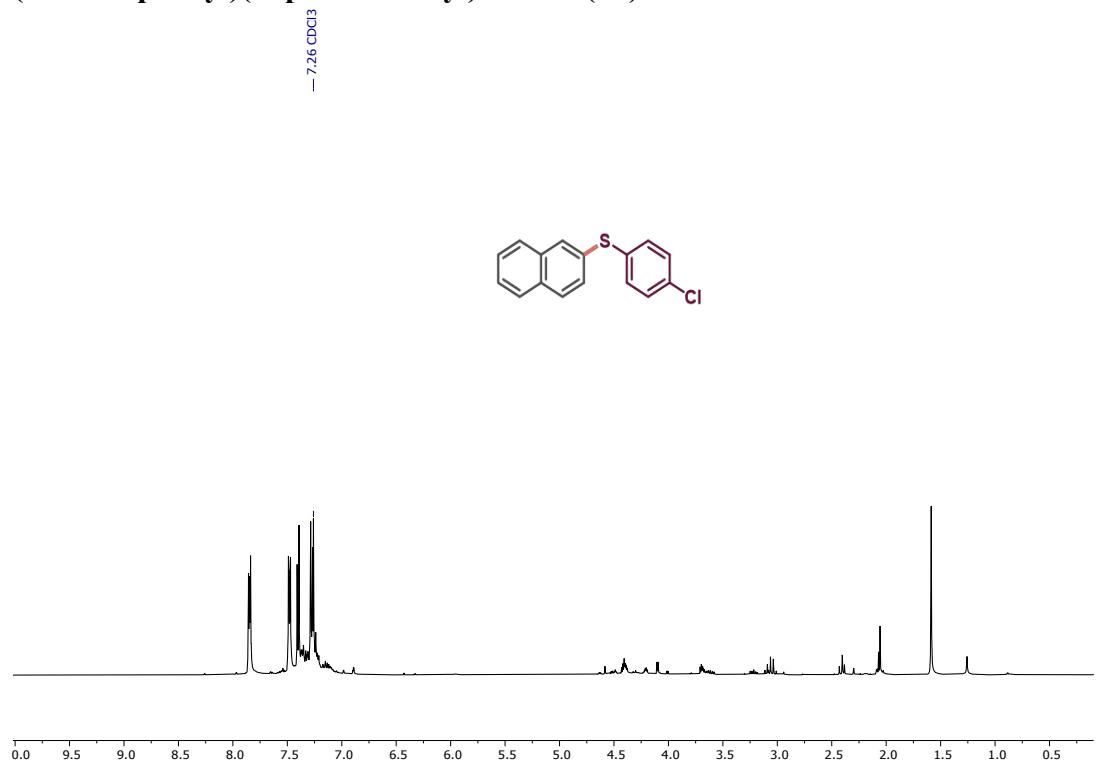
**(4-methoxyphenyl)(naphthalen-2-yl)sulfane (2b): NMR data of crude reaction mixture**



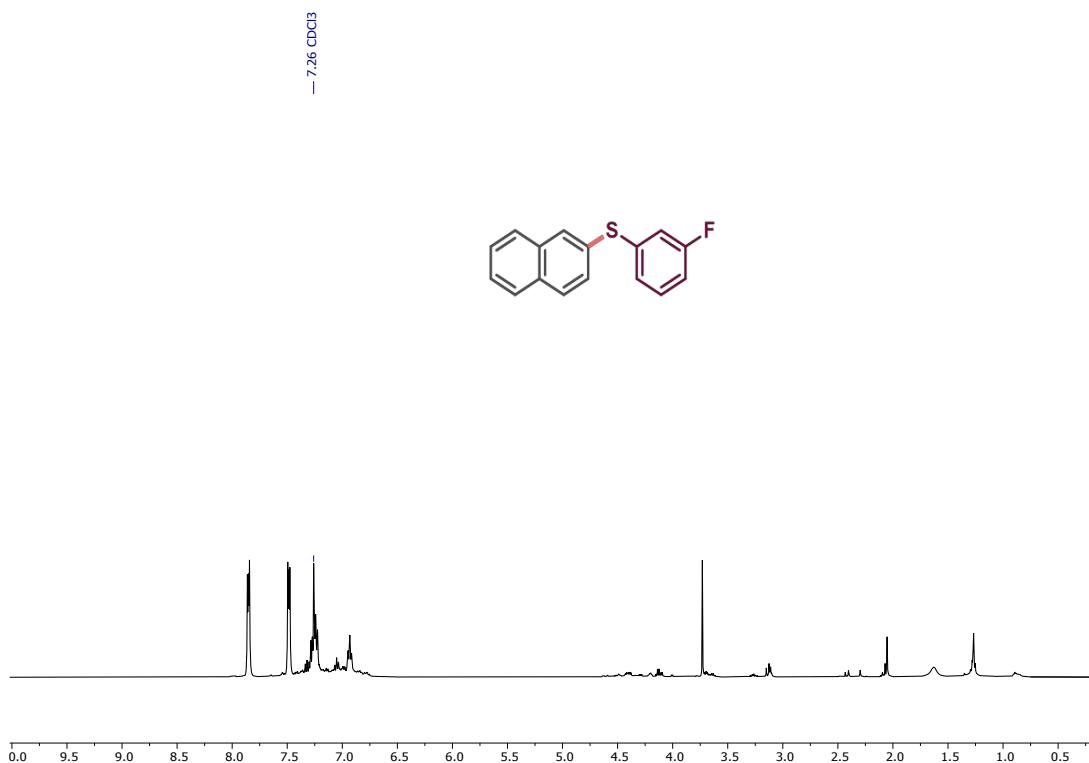
**Naphthalen-2-yl(p-tolyl)sulfane (2c): NMR data of crude reaction mixture**



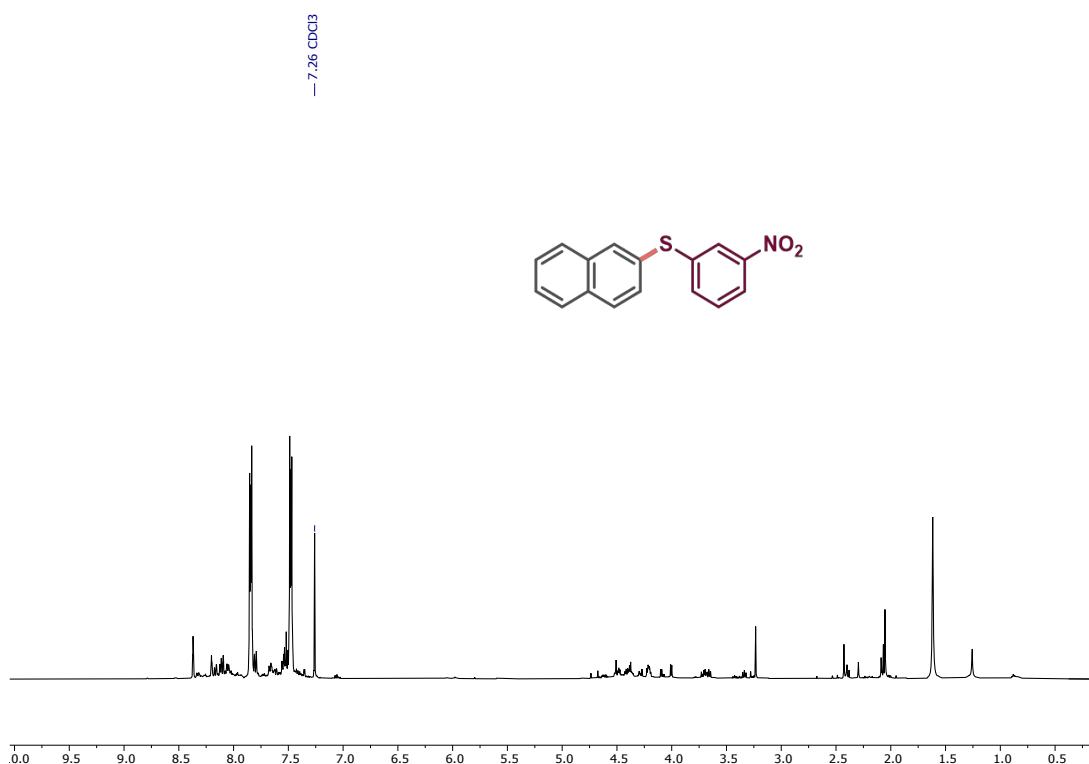
**(4-chlorophenyl)(naphthalen-2-yl)sulfane (2d): NMR data of crude reaction mixture**



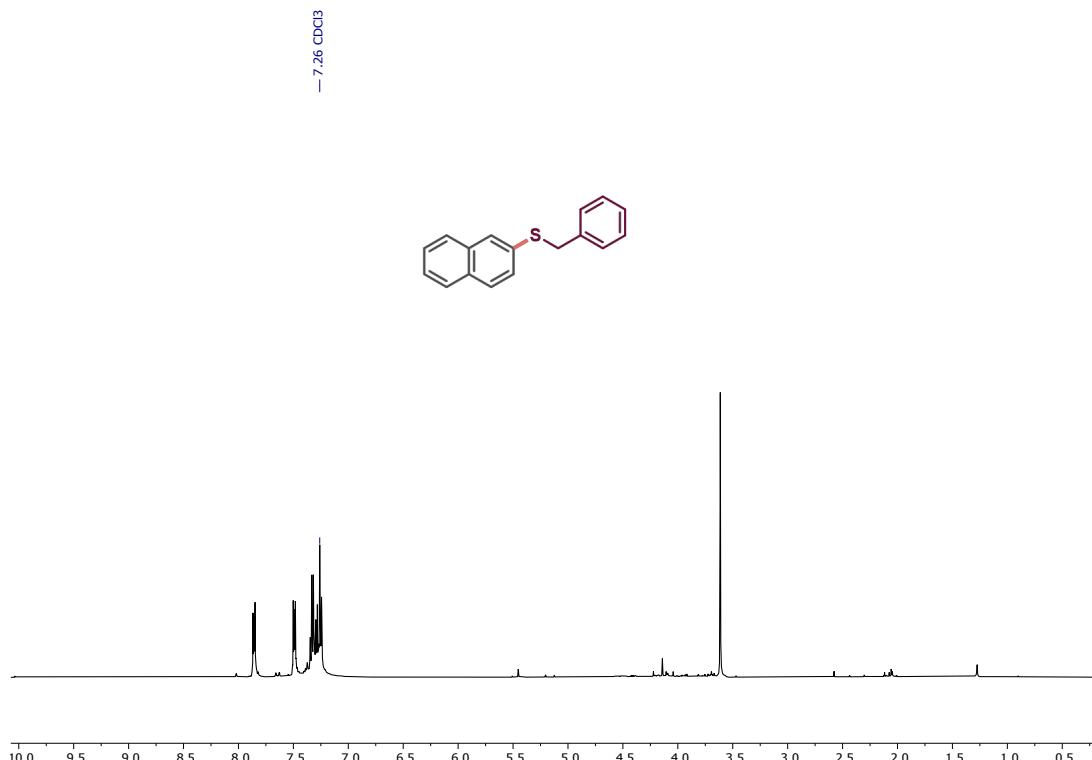
**(3-fluorophenyl)(naphthalen-2-yl)sulfane (2e): NMR data of crude reaction mixture**



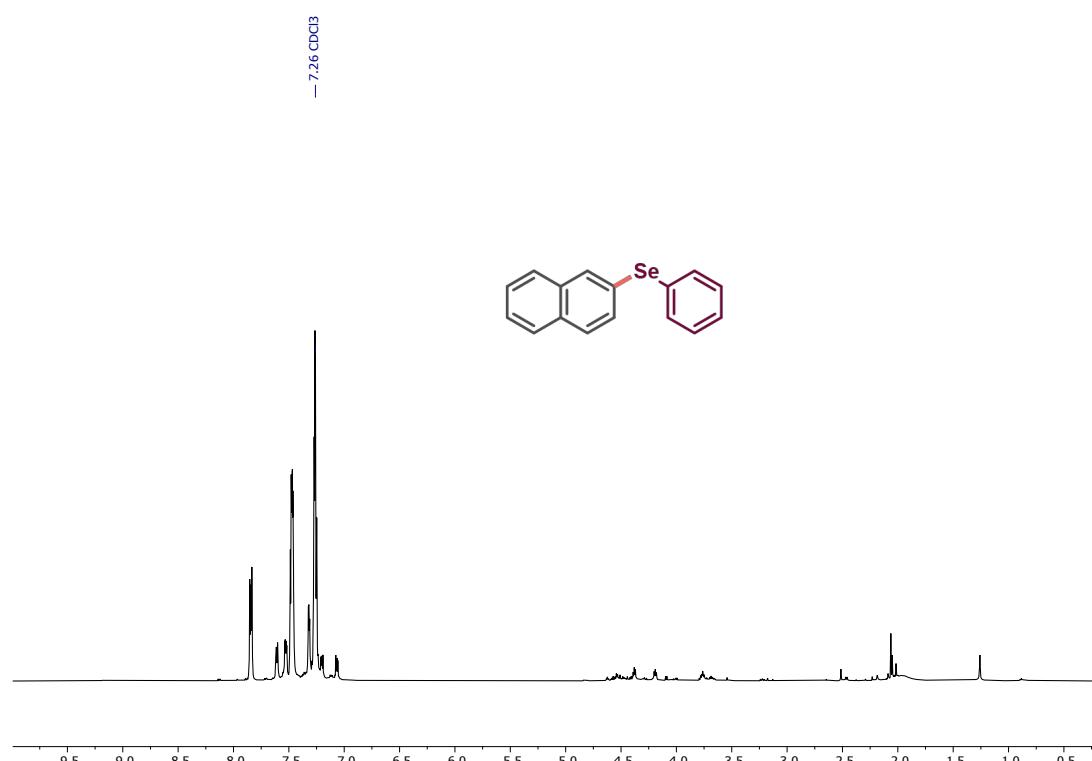
**Naphthalen-2-yl(3-nitrophenyl)sulfane (2f): NMR data of crude reaction mixture**



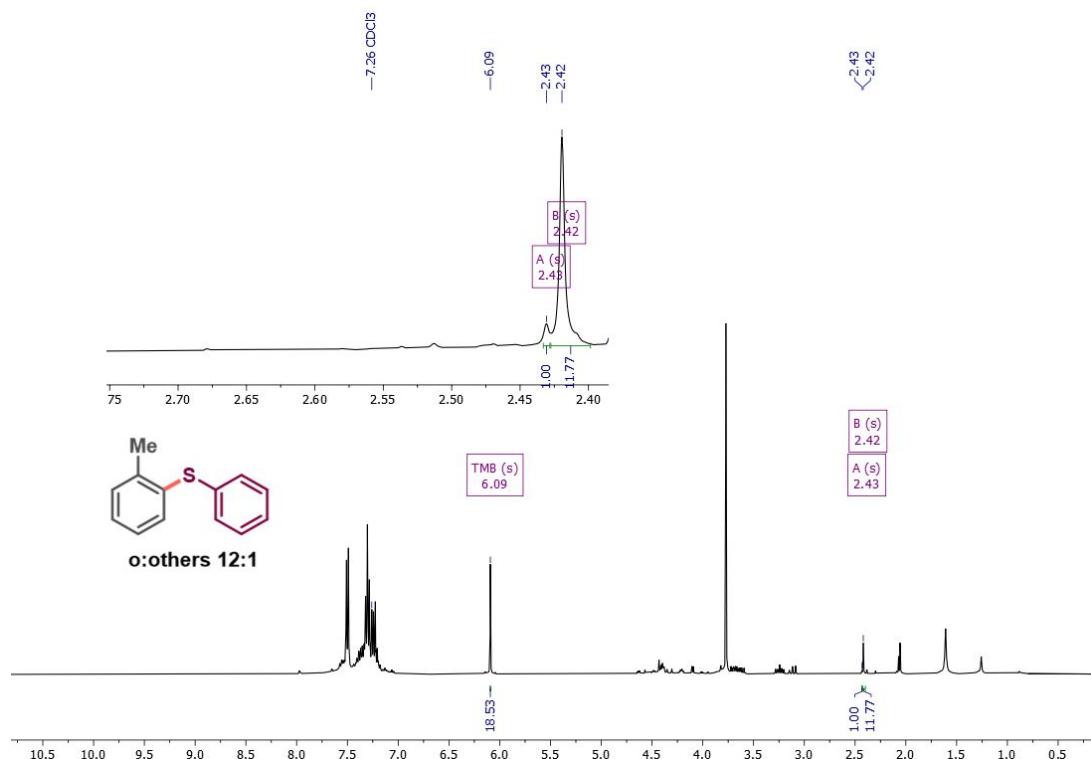
**Benzyl(naphthalen-2-yl)sulfane (2g): NMR data of crude reaction mixture**



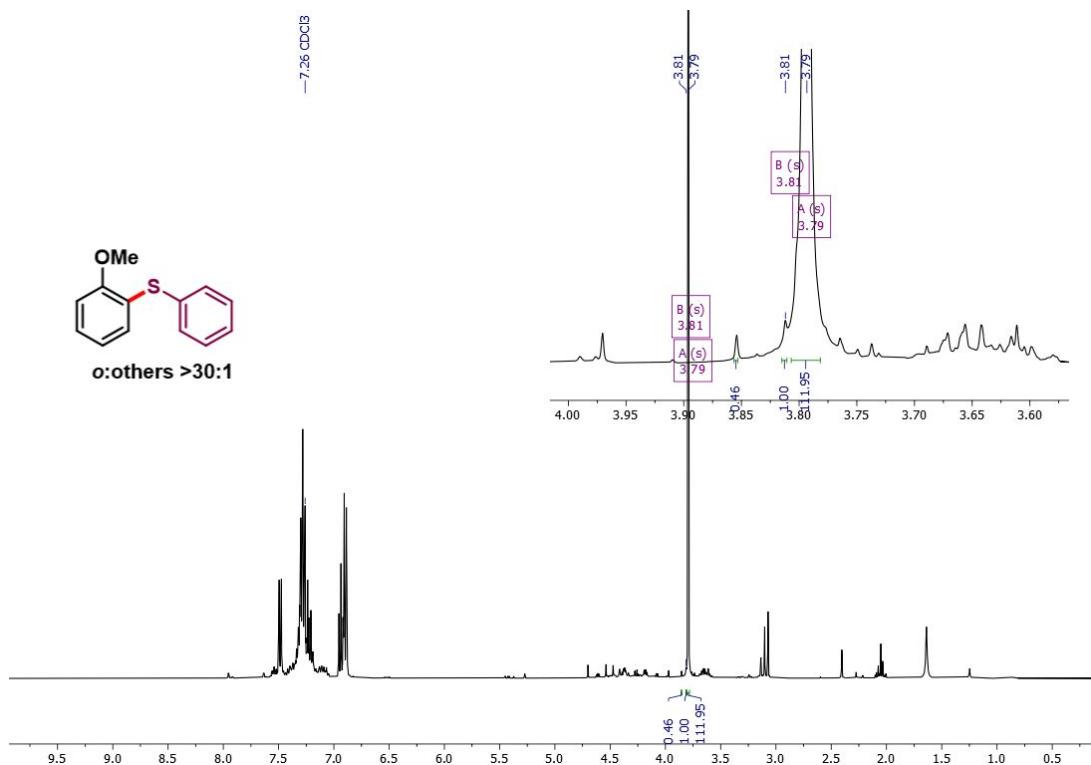
**Naphthalen-2-yl(phenyl)selane (2h): NMR data of crude reaction mixture**



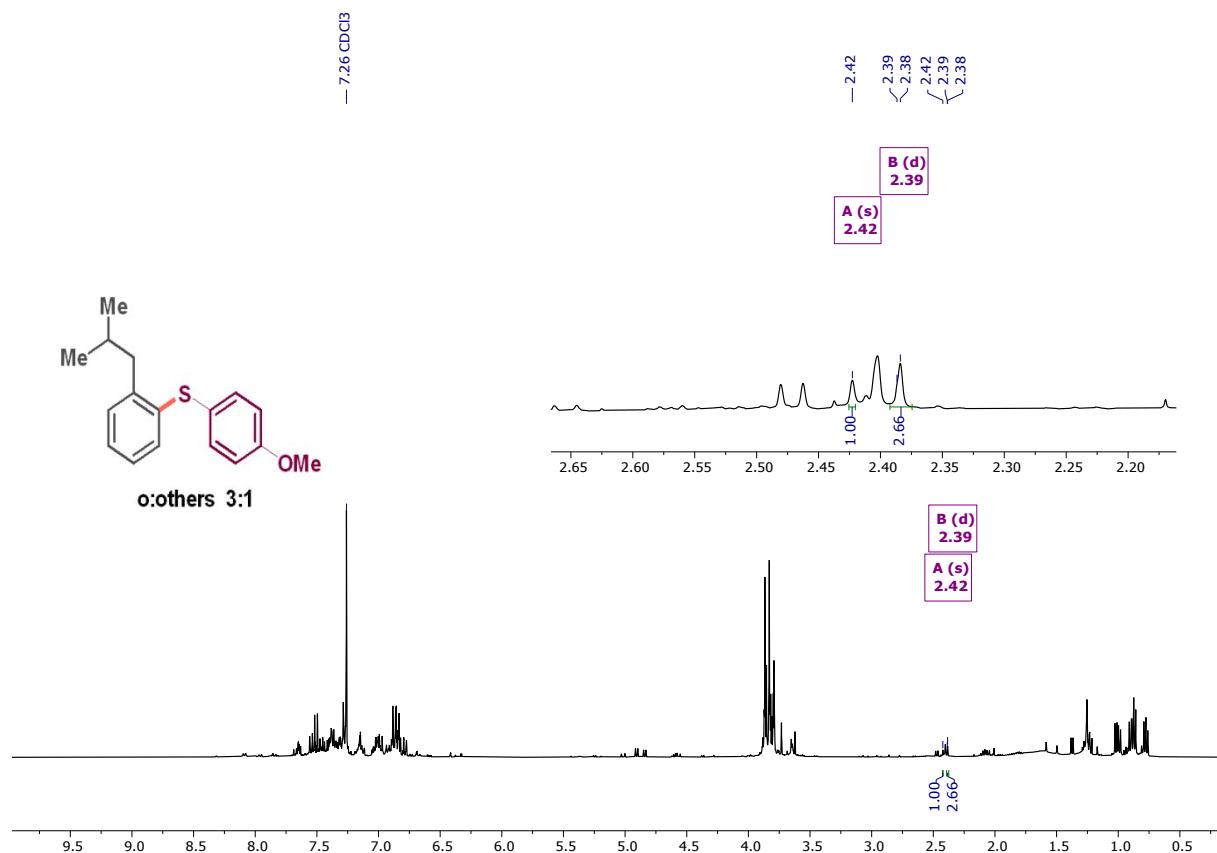
**Phenyl(o-tolyl)sulfane (2m): NMR data of crude reaction mixture**



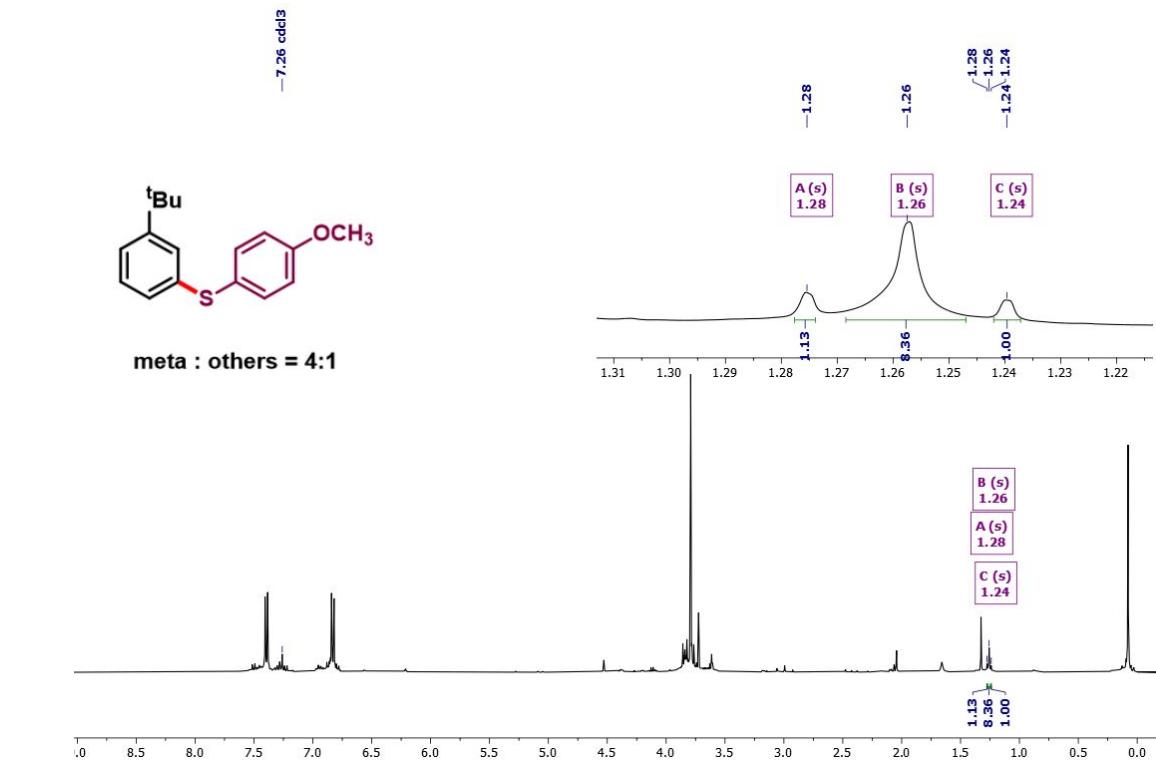
**(2-methoxyphenyl)(phenyl)sulfane (2n): NMR data of crude reaction mixture**



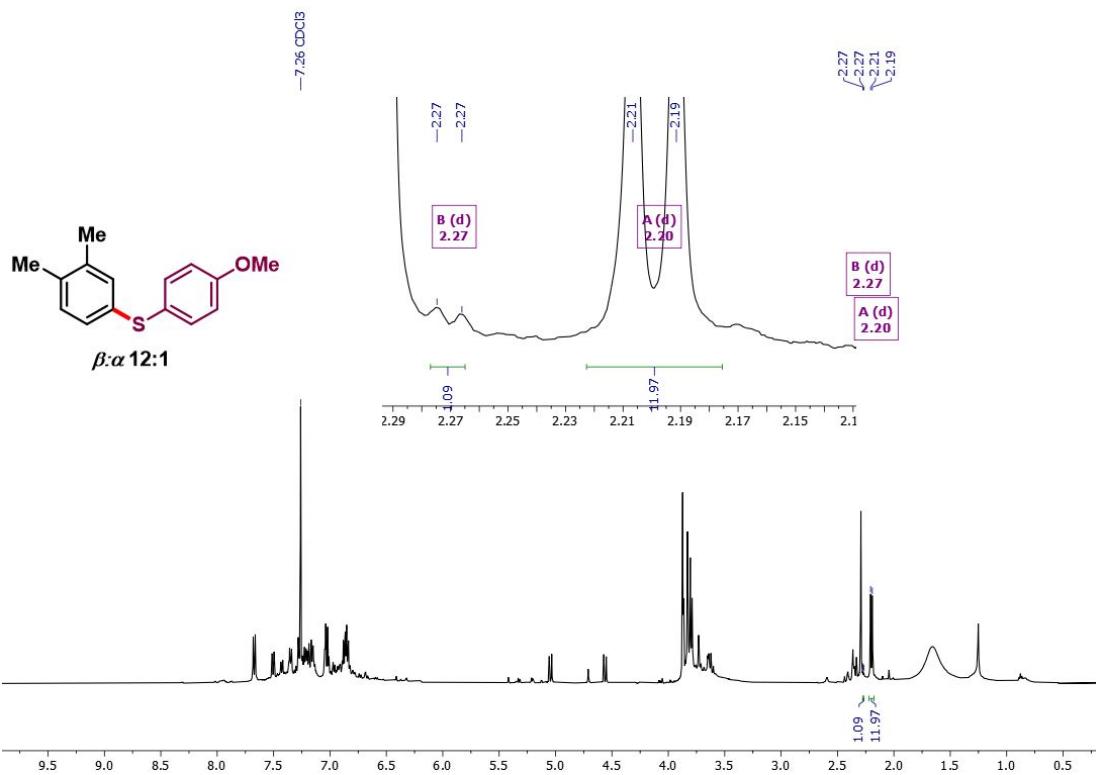
**(2-isobutylphenyl)(4-methoxyphenyl)sulfane (2o): NMR data of crude reaction mixture**



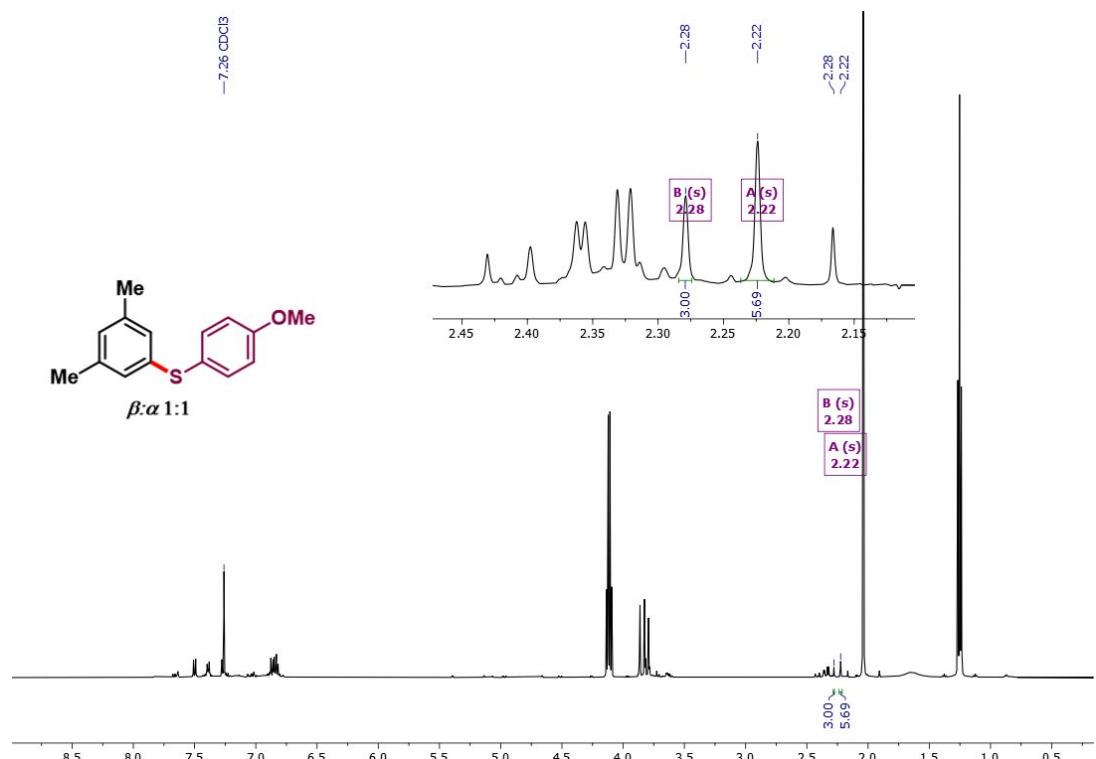
**(3-(tert-butyl)phenyl)(4-methoxyphenyl)sulfane (2p): NMR data of crude reaction mixture**



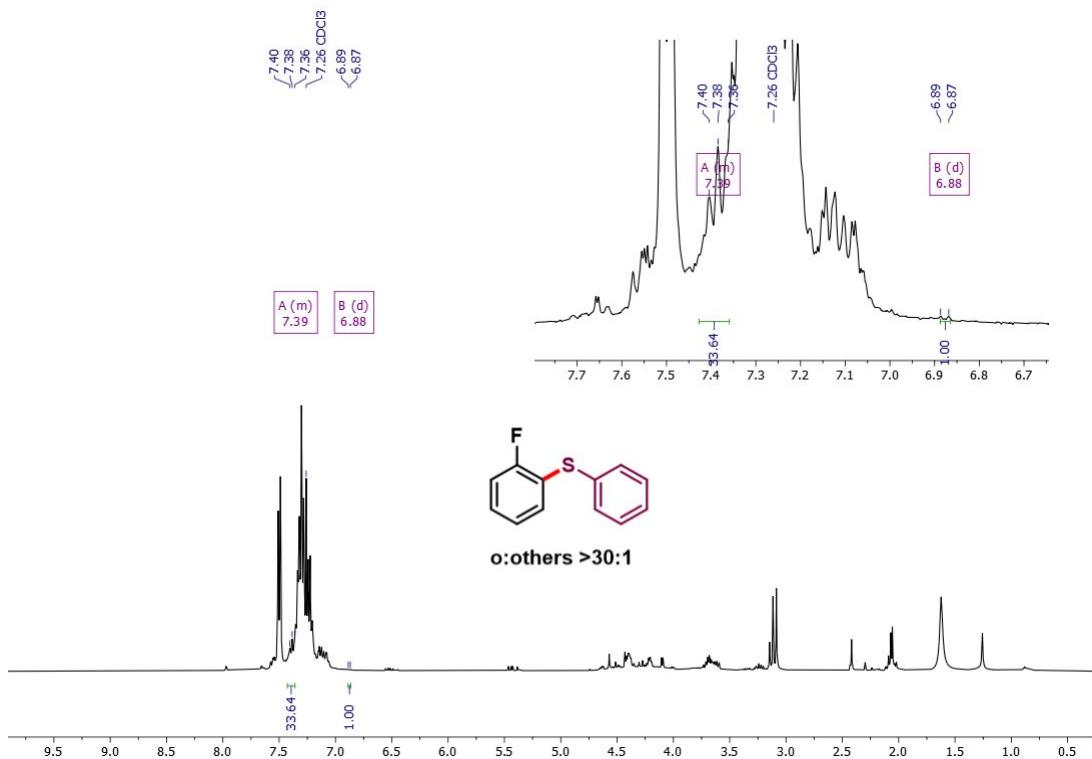
**(3,4-dimethylphenyl)(4-methoxyphenyl)sulfane (2q): NMR data of crude reaction mixture**



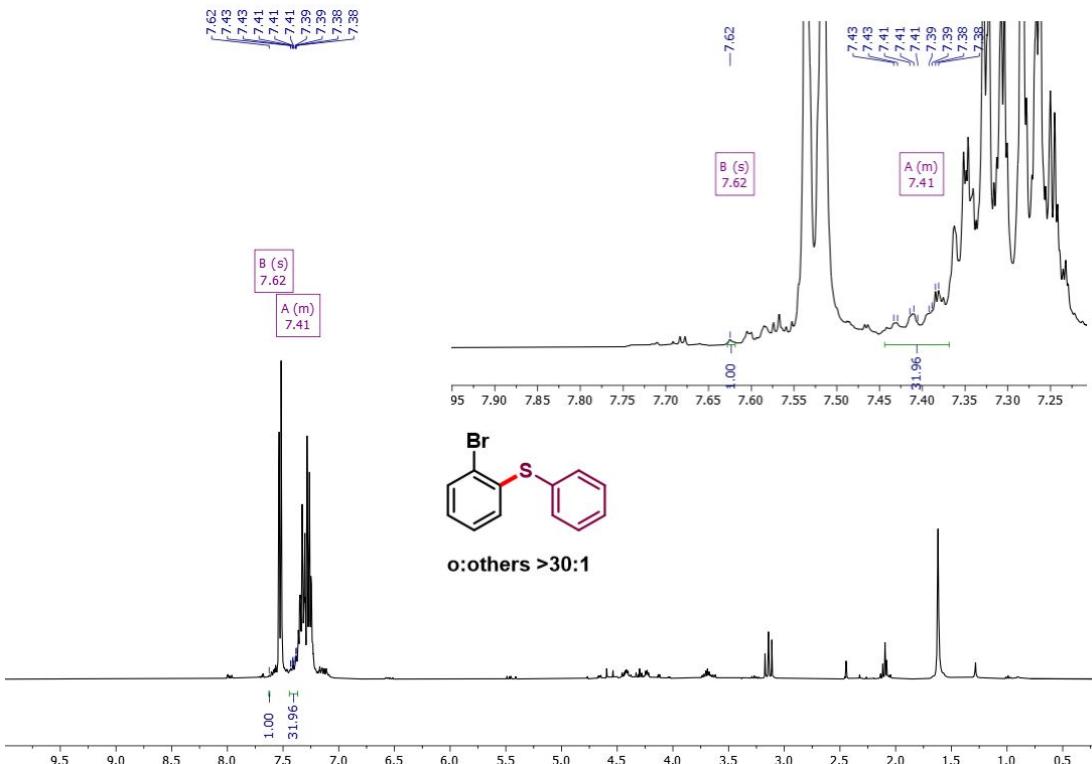
### (3,5-dimethylphenyl)(4-methoxyphenyl)sulfane (2r): NMR data of crude reaction mixture



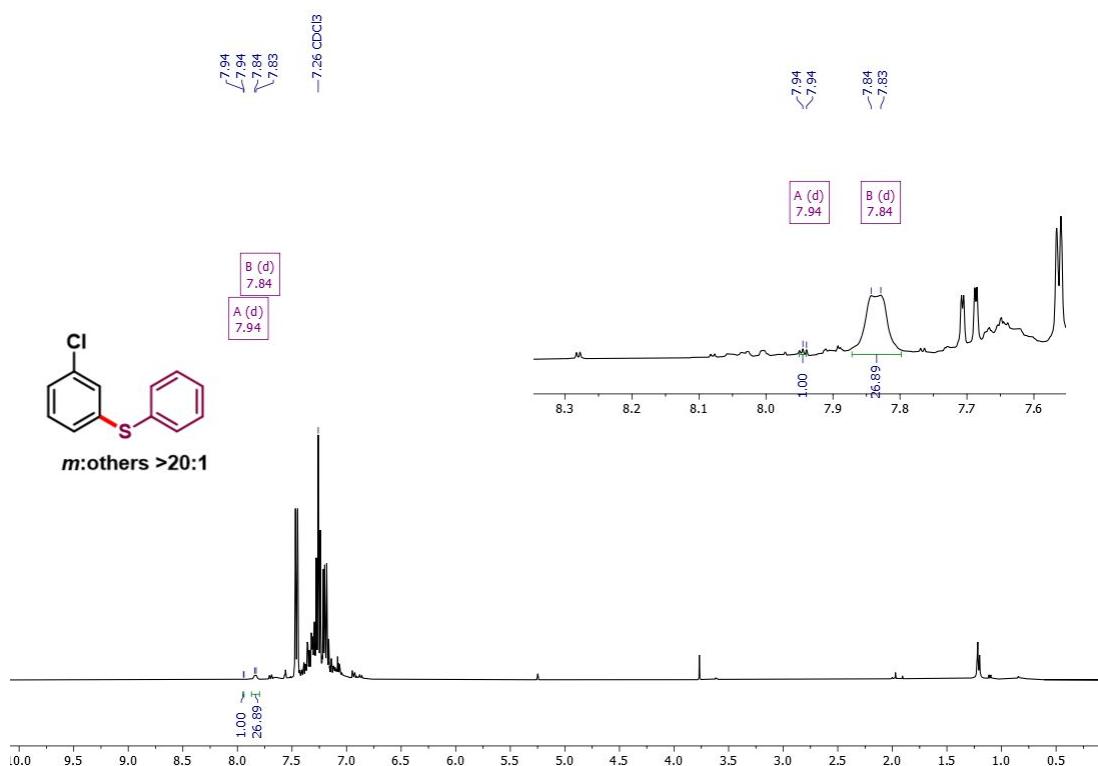
**(2-fluorophenyl)(phenyl)sulfane (2t): NMR data of crude reaction mixture**



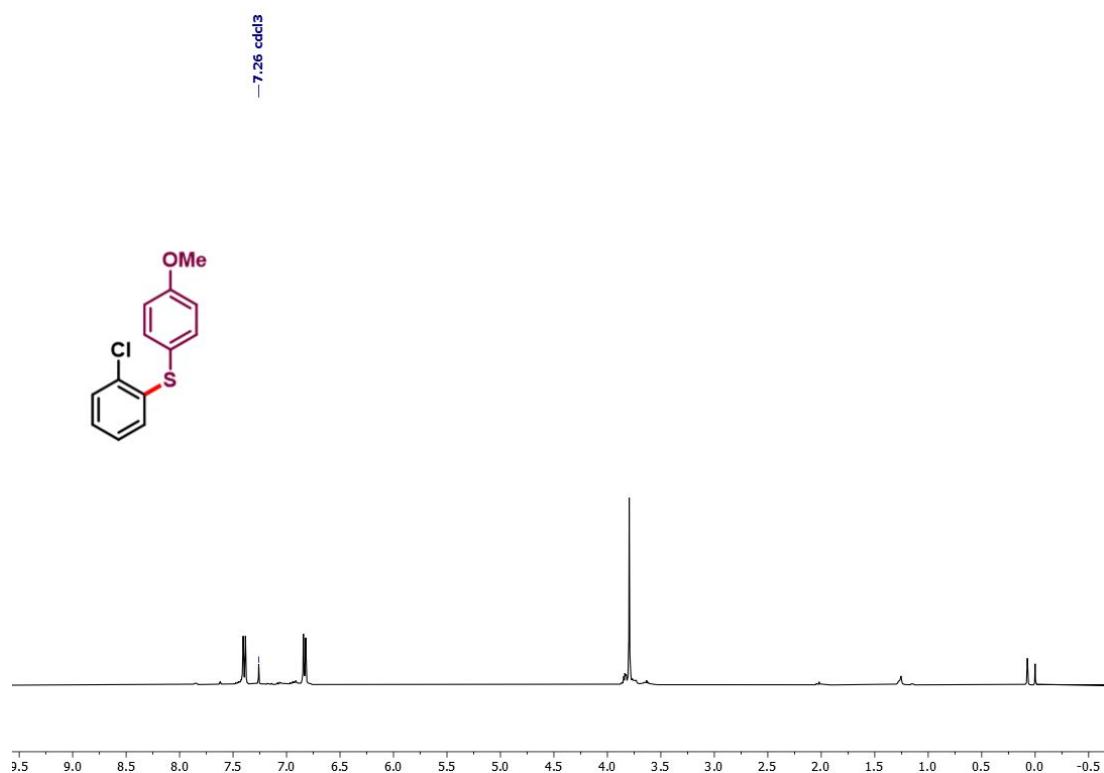
**(2-bromophenyl)(phenyl)sulfane (2u): NMR data of crude reaction mixture**



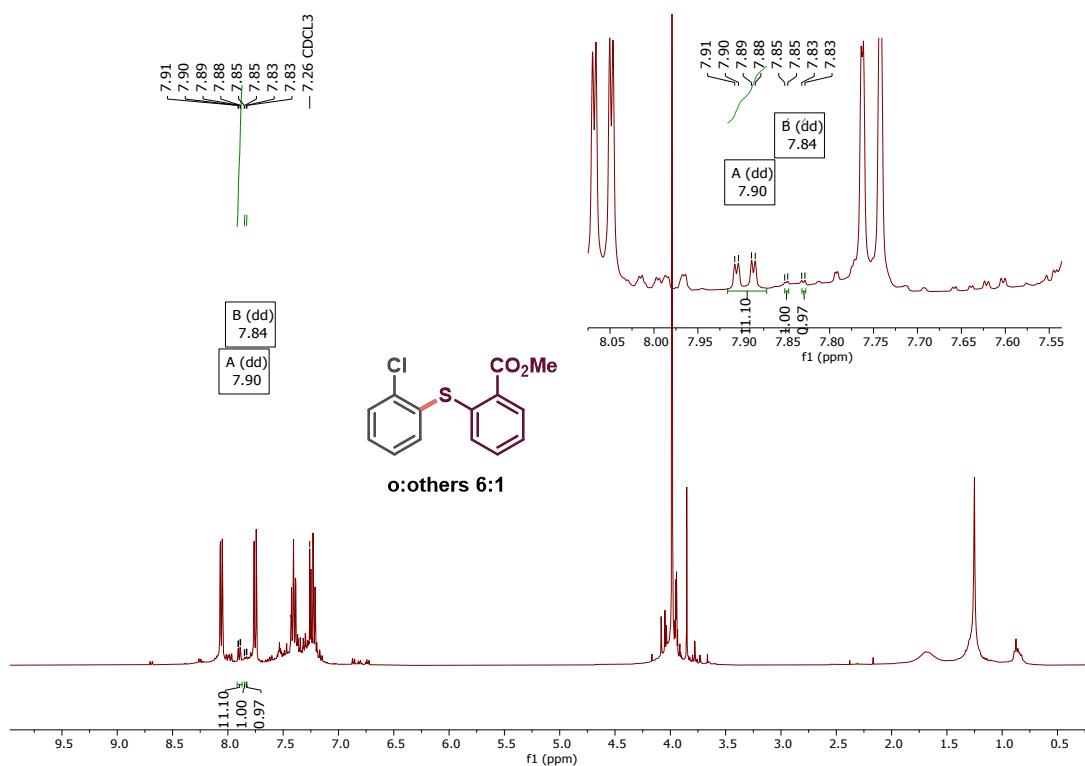
**(3-chlorophenyl)(phenyl)sulfane (2v): NMR data of crude reaction mixture**



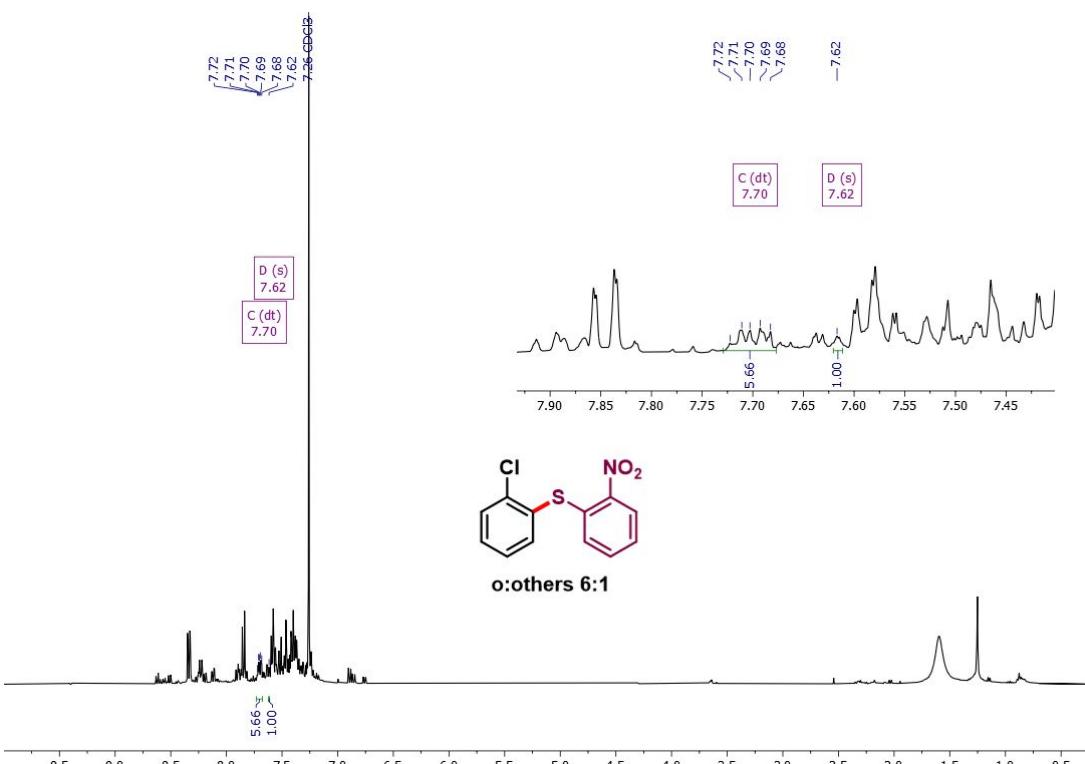
**(2-chlorophenyl)(4-methoxyphenyl)sulfane (2w): NMR data of crude reaction mixture**



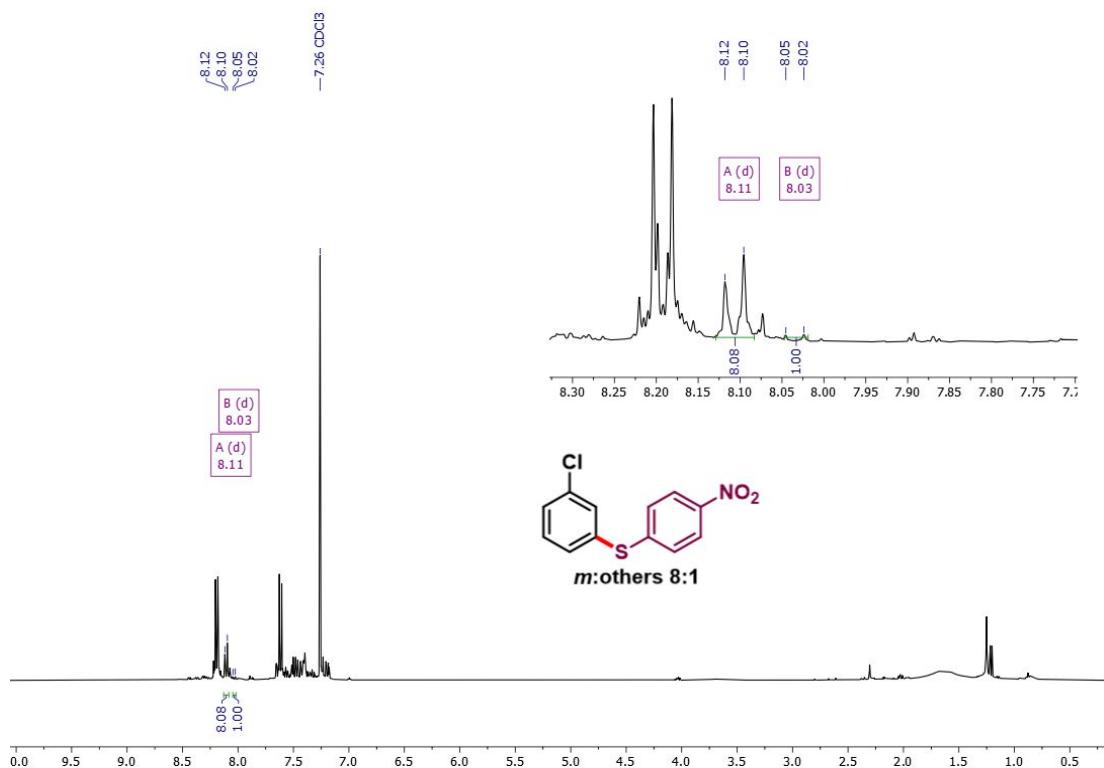
**Methyl 2-((2-chlorophenyl)thio)benzoate (2x): NMR data of crude reaction mixture**



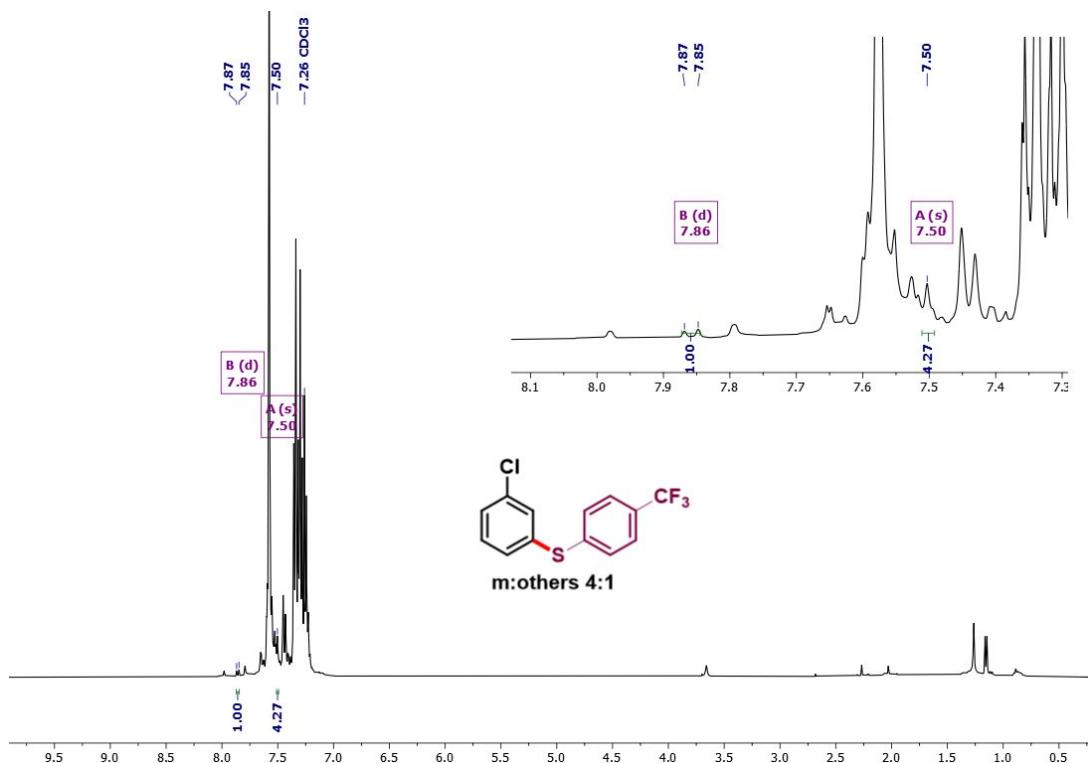
**(2-chlorophenyl)(2-nitrophenyl)sulfane (2y): NMR data of crude reaction mixture**



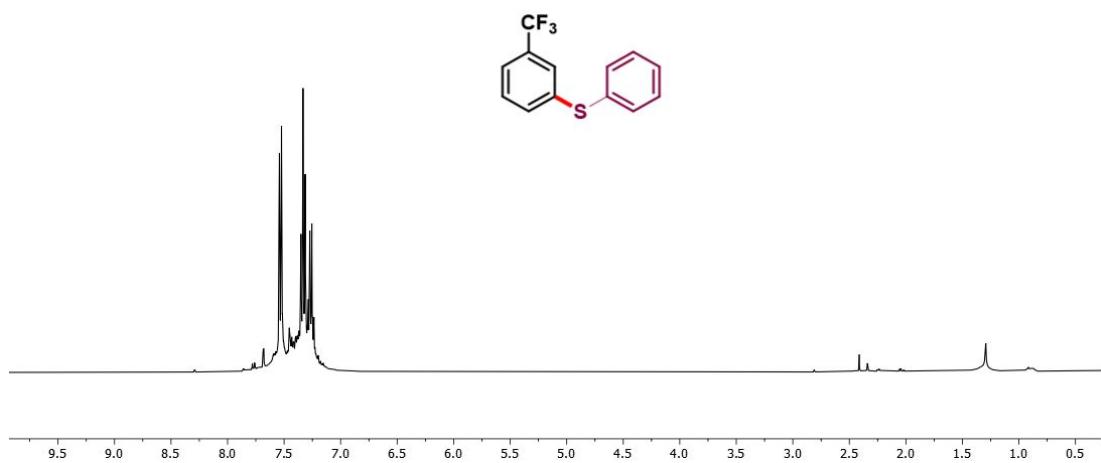
**(3-chlorophenyl)(4-nitrophenyl)sulfane (2z): NMR data of crude reaction mixture**



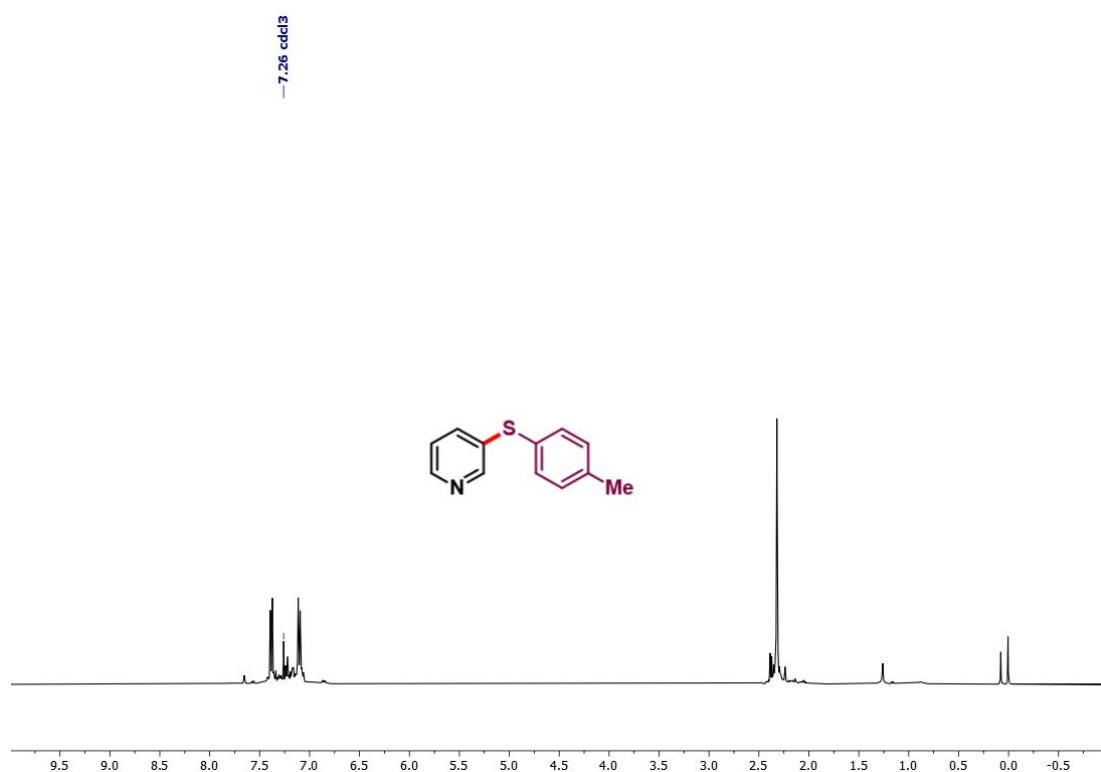
**(3-chlorophenyl)(4-(trifluoromethyl)phenyl)sulfane (2aa): NMR data of crude reaction mixture**



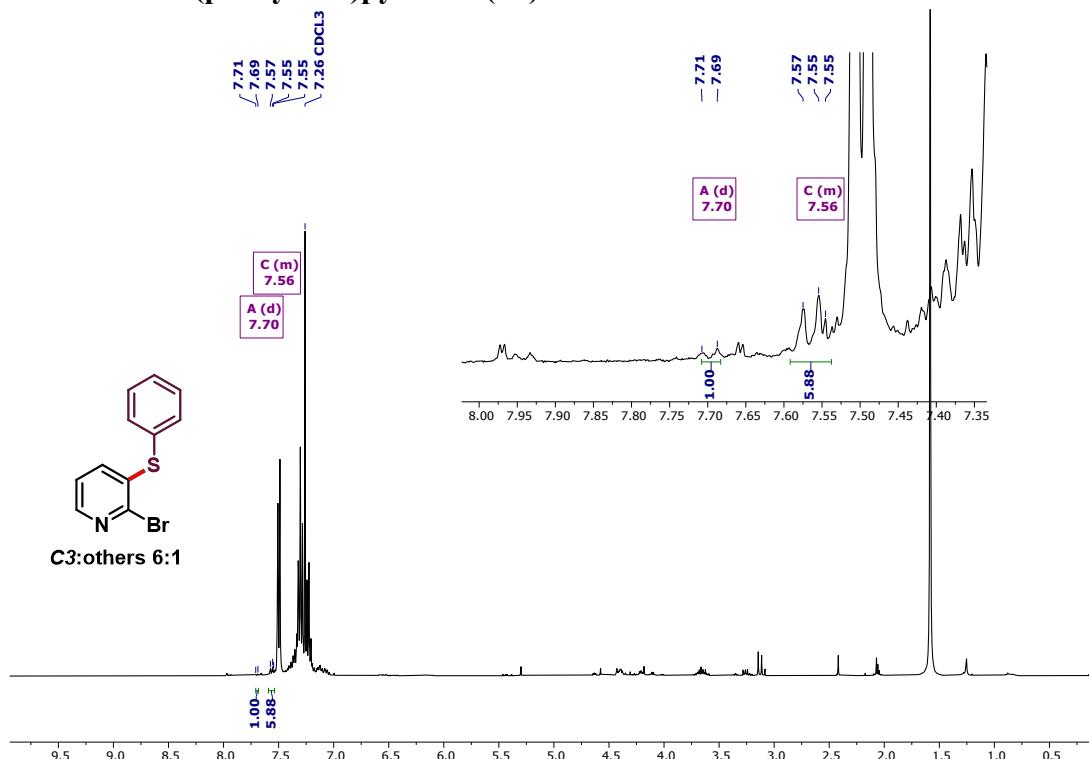
**Phenyl(3-(trifluoromethyl)phenyl)sulfane (2ab): NMR data of crude reaction mixture**



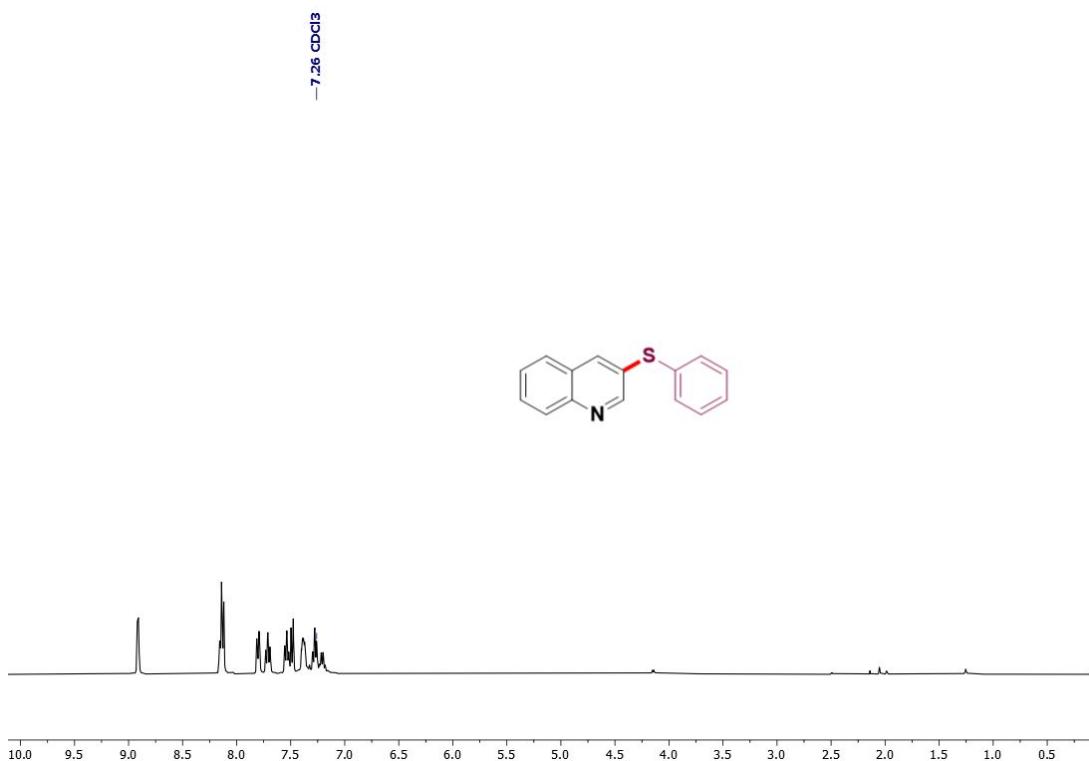
**3-(p-tolylthio)pyridine (3a): NMR data of crude reaction mixture**



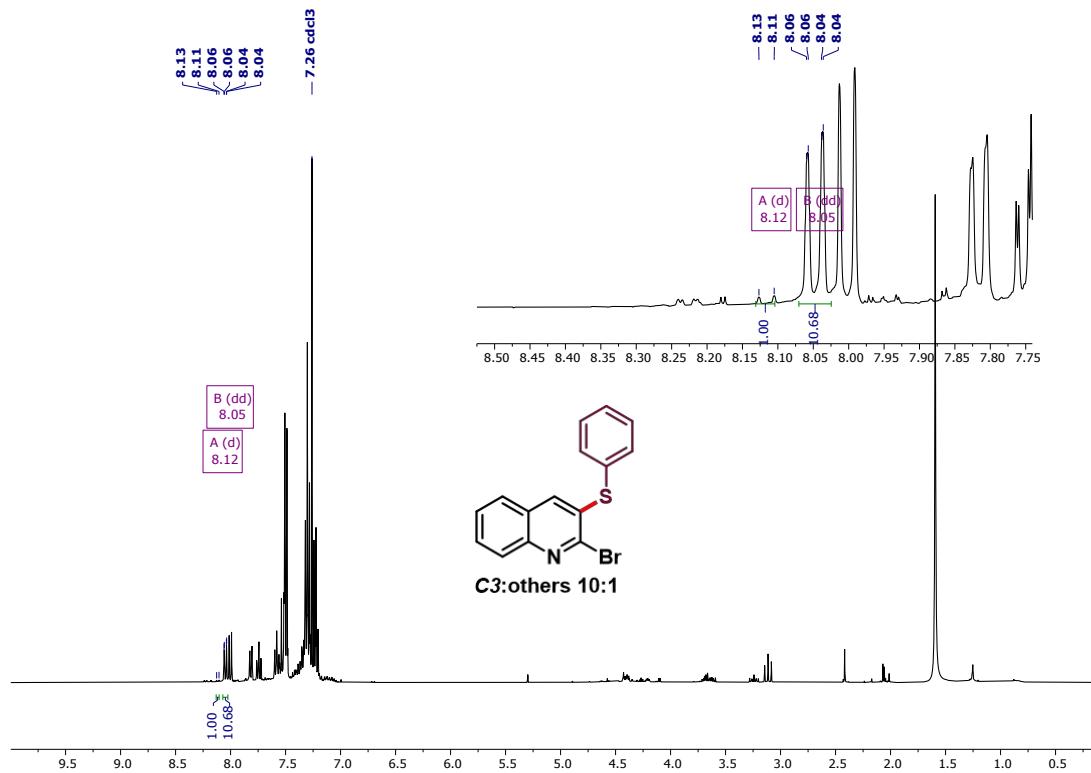
**2-bromo-3-(phenylthio)pyridine (3b): NMR data of crude reaction mixture**



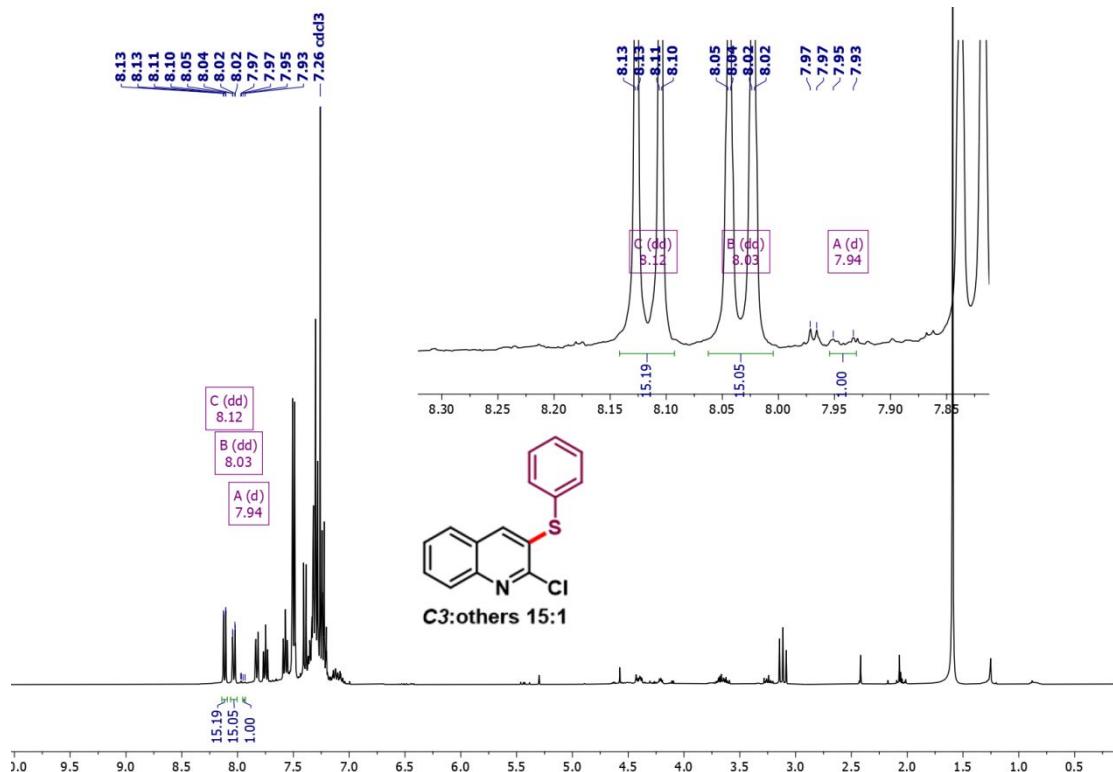
**3-(phenylthio)quinoline (3c): NMR data of crude reaction mixture**



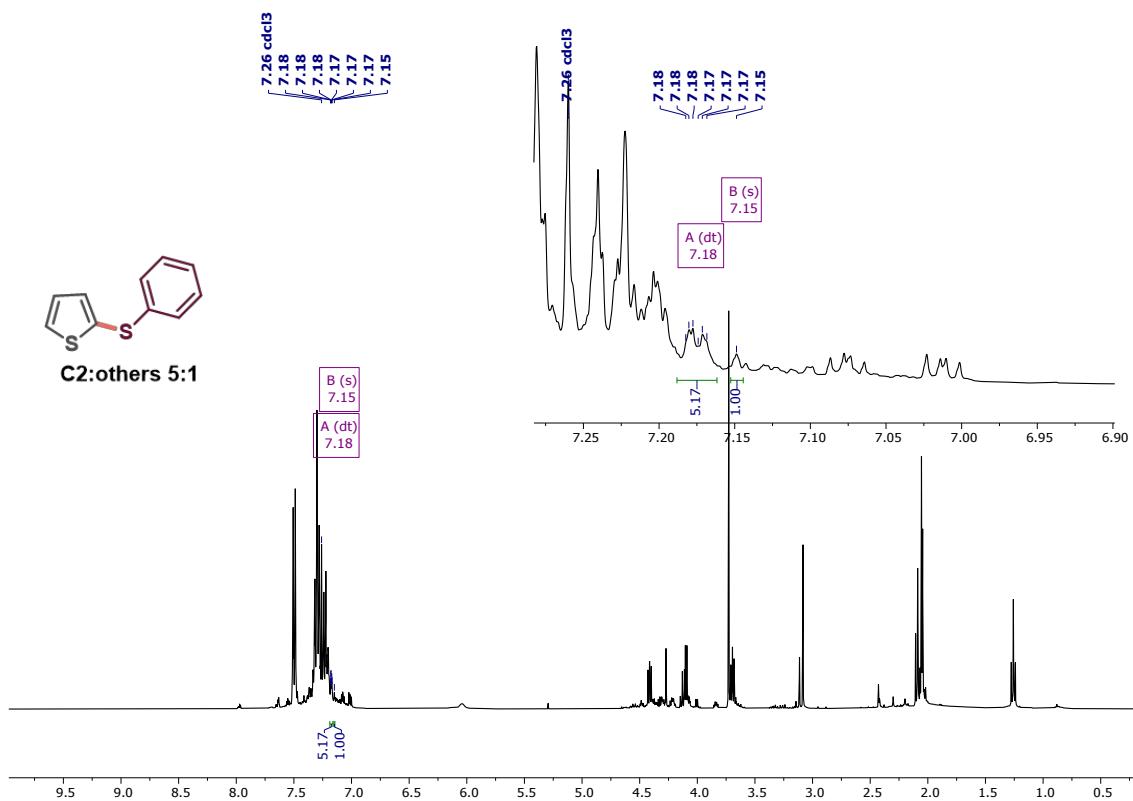
### 2-bromo-3-(phenylthio)quinoline (3d): NMR data of crude reaction mixture



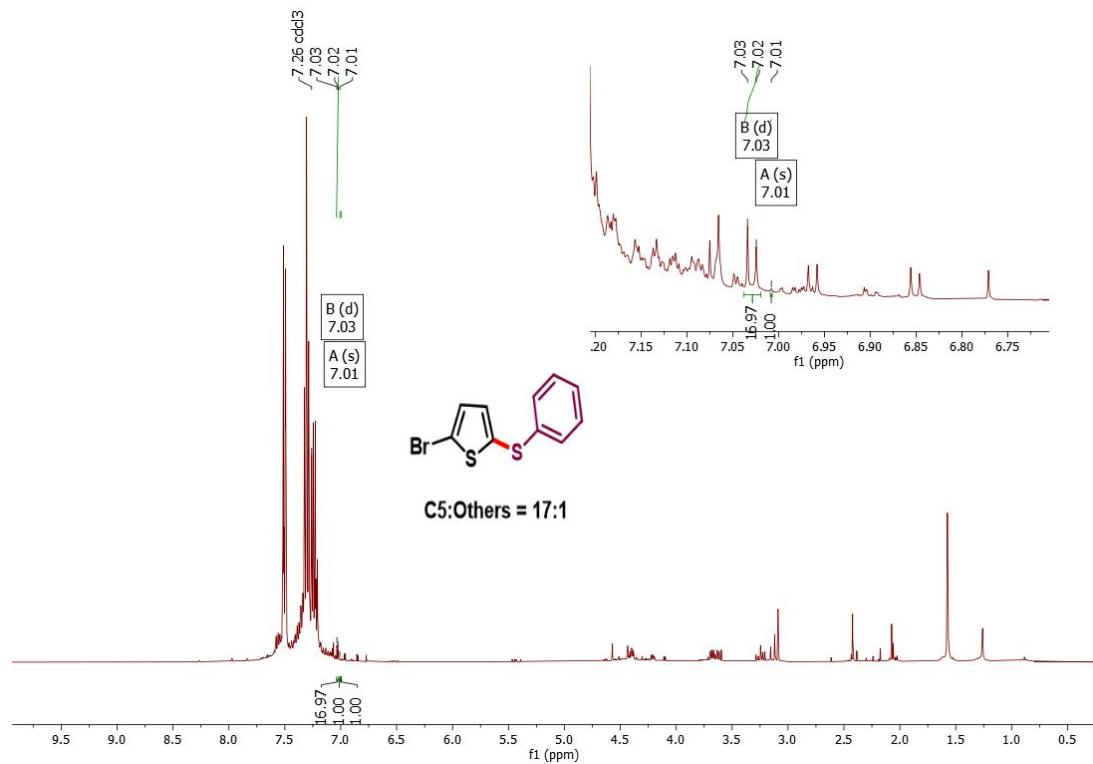
#### 2-chloro-3-(phenylthio)quinoline (3e): NMR data of crude reaction mixture



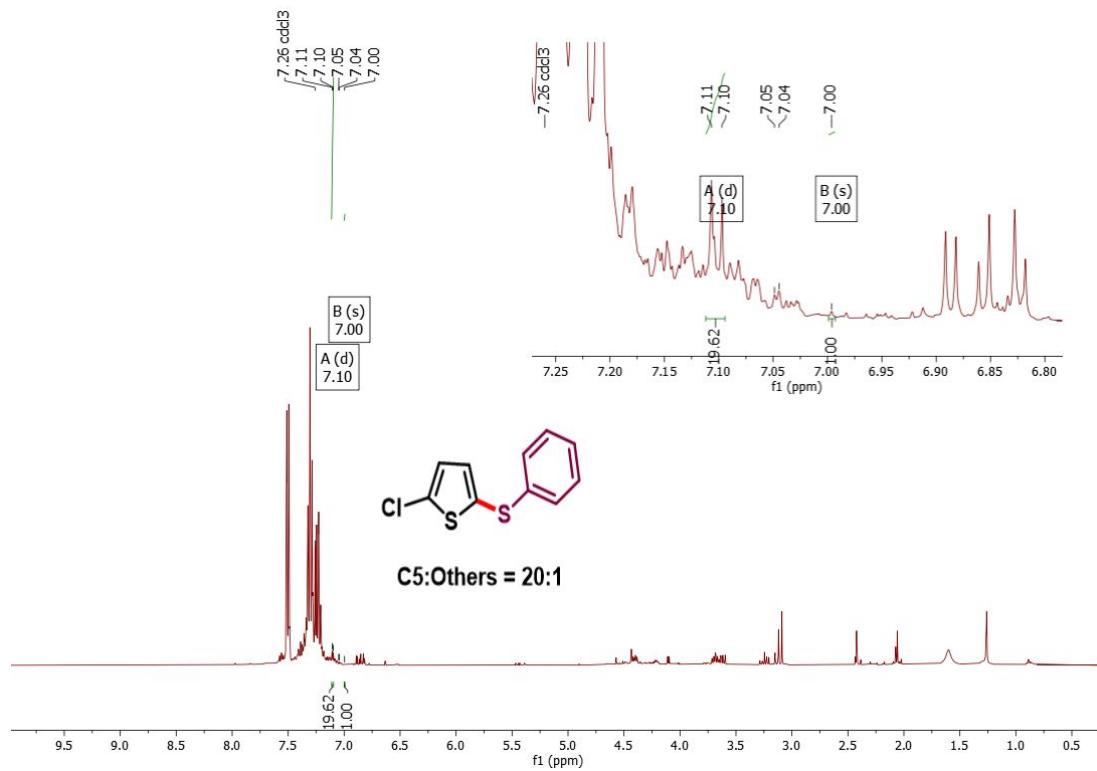
**2-(phenylthio)thiophene (3g): NMR data of crude reaction mixture**



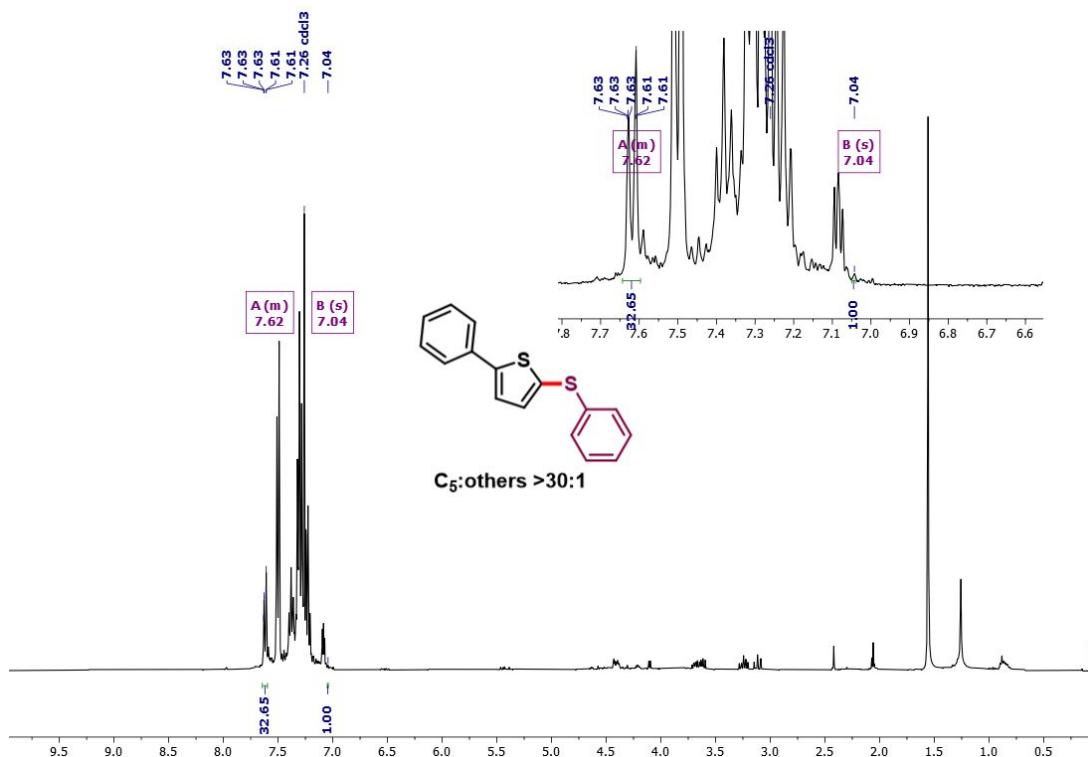
**2-bromo-5-(phenylthio)thiophene (3h): NMR data of crude reaction mixture**



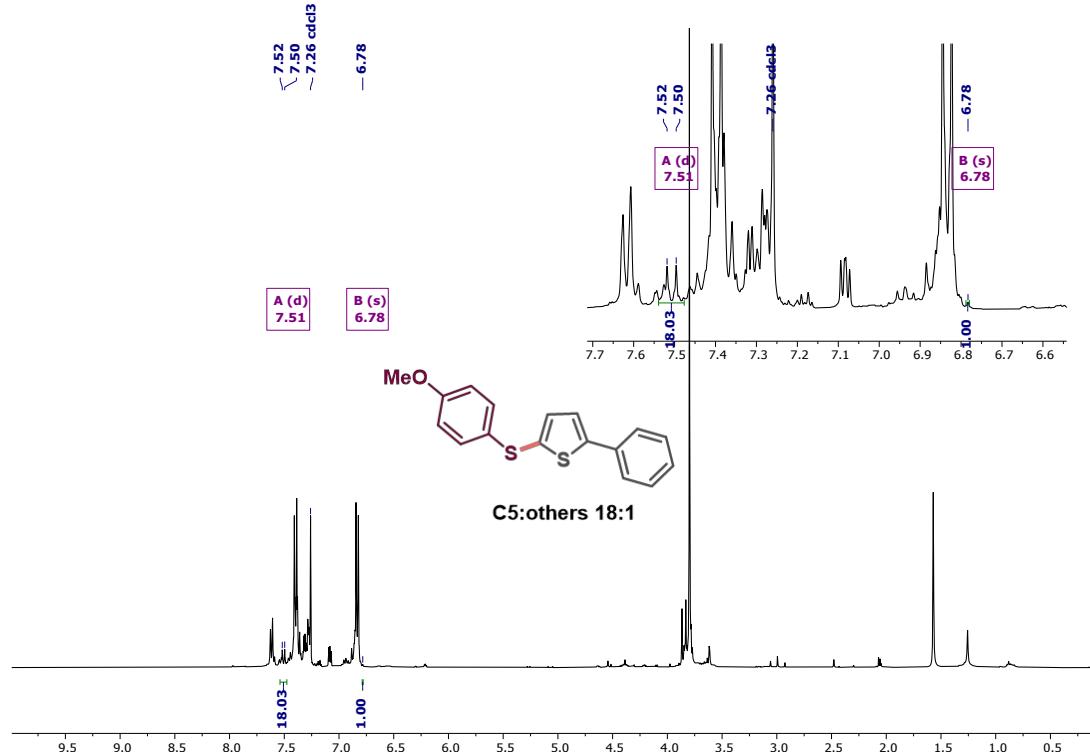
## 2-chloro-5-(phenylthio)thiophene (3i): NMR data of crude reaction mixture



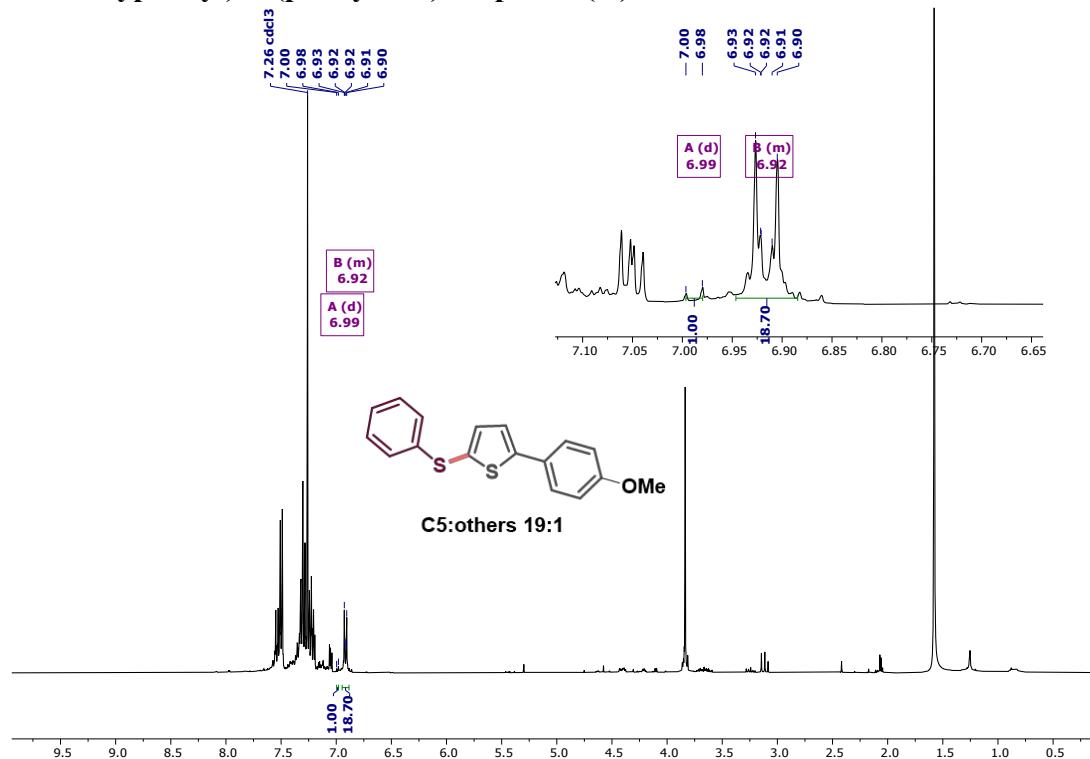
#### 2-phenyl-5-(phenylthio)thiophene (3j): NMR data of crude reaction mixture



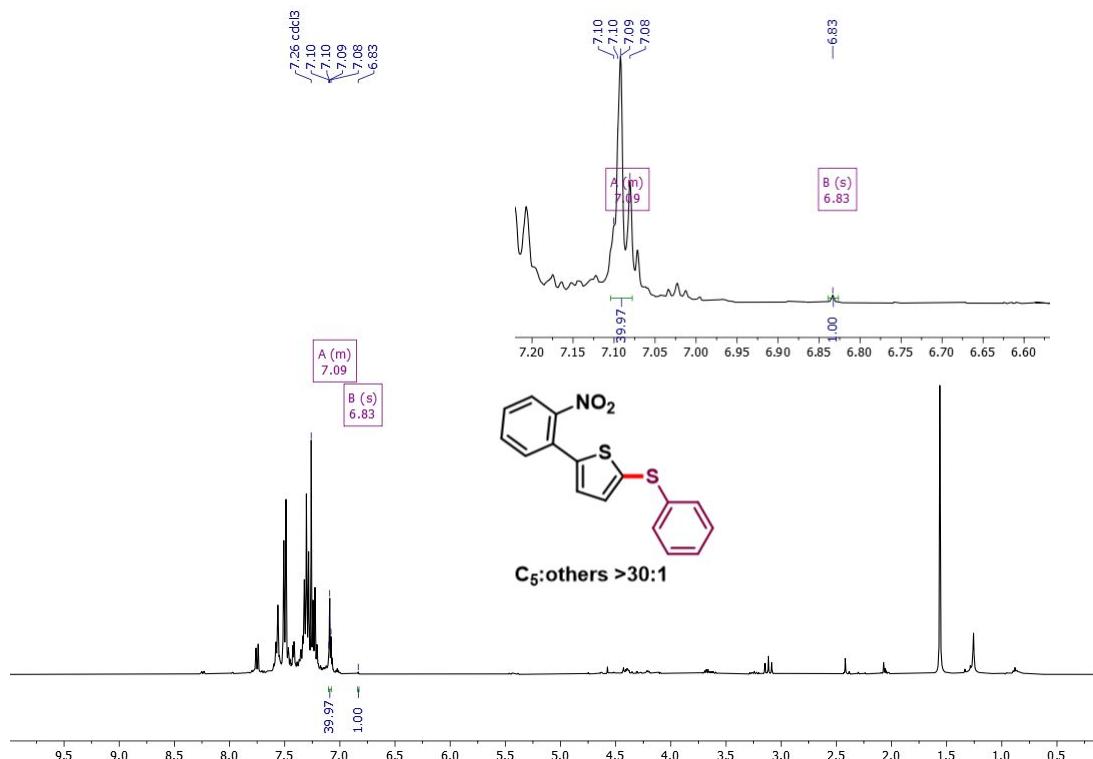
**2-((4-methoxyphenyl)thio)-5-phenylthiophene (3k): NMR data of crude reaction mixture**



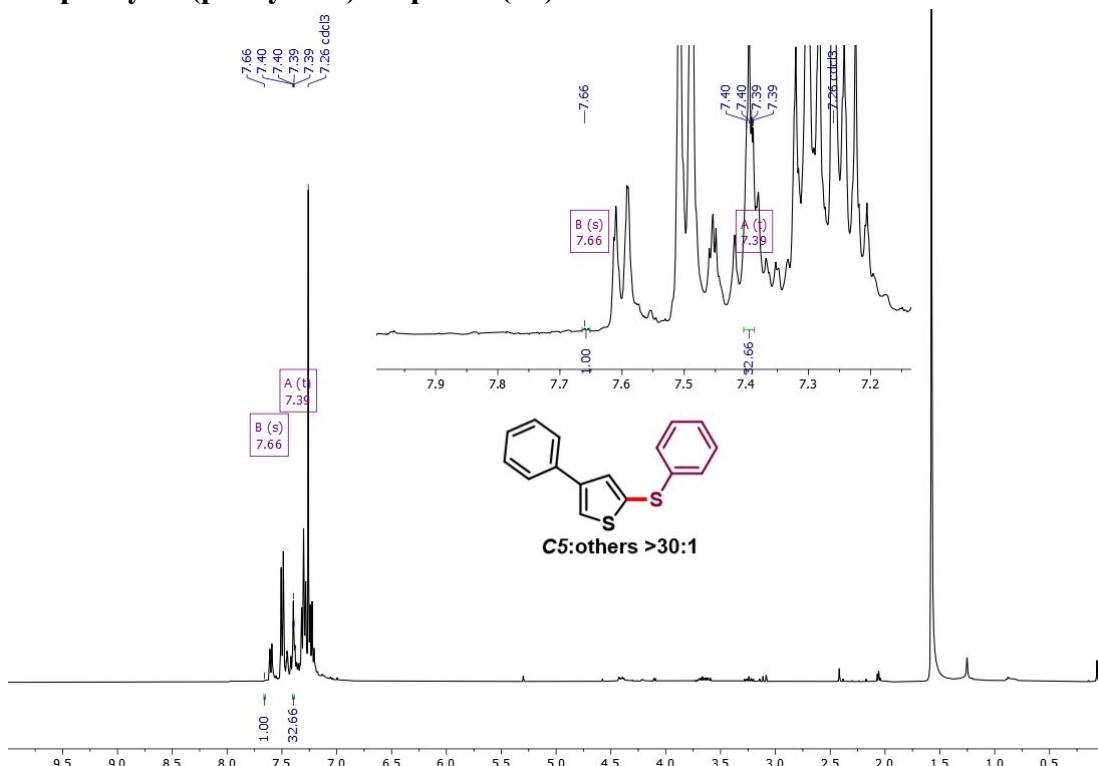
**2-(4-methoxyphenyl)-5-(phenylthio)thiophene (3l): NMR data of crude reaction mixture**



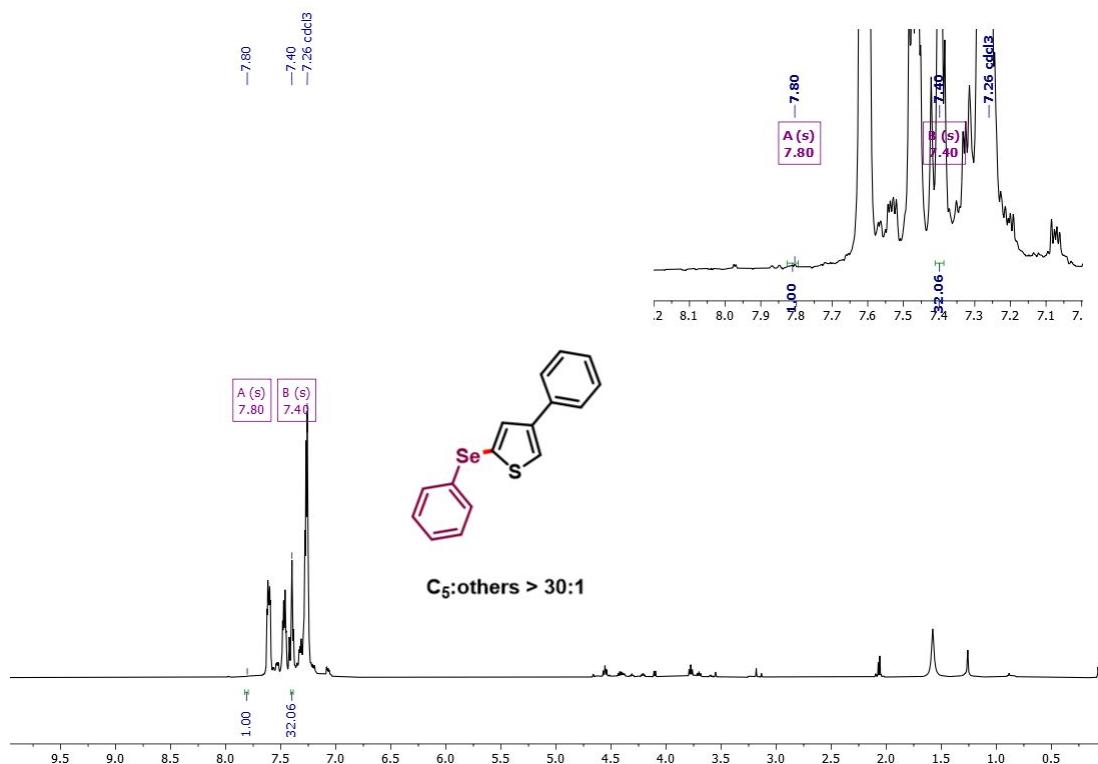
**2-(2-nitrophenyl)-5-(phenylthio)thiophene (3m): NMR data of crude reaction mixture**



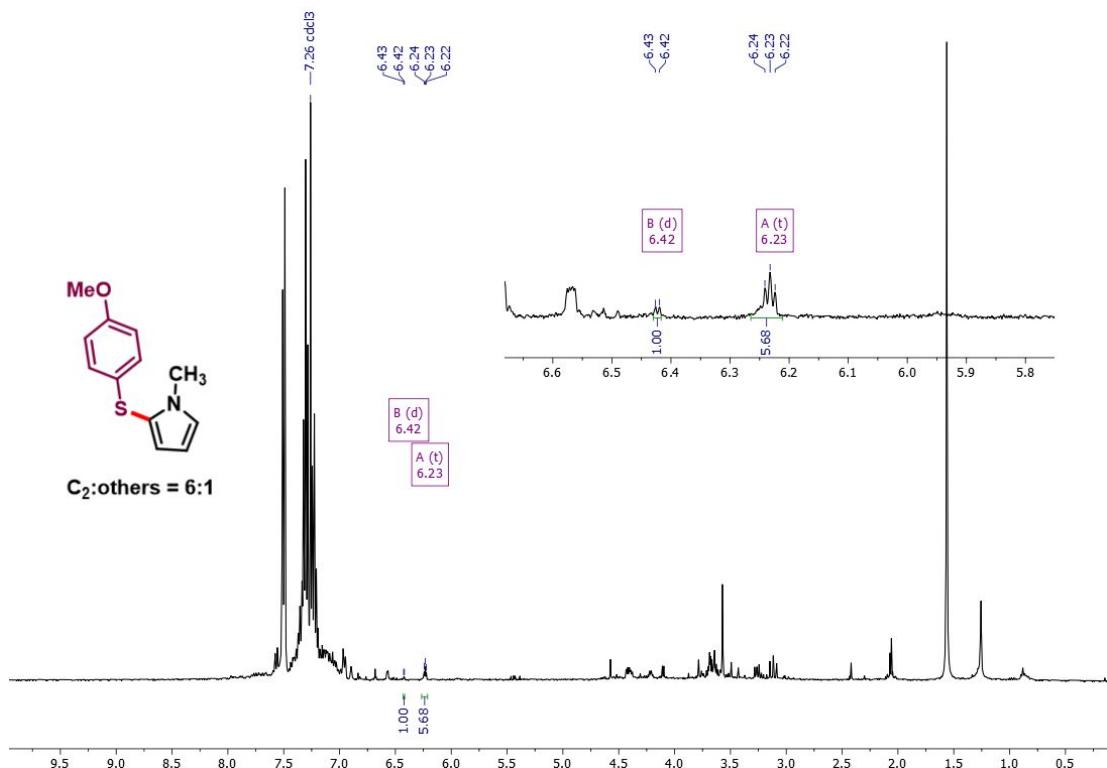
**4-phenyl-2-(phenylthio)thiophene (3n): NMR data of crude reaction mixture**



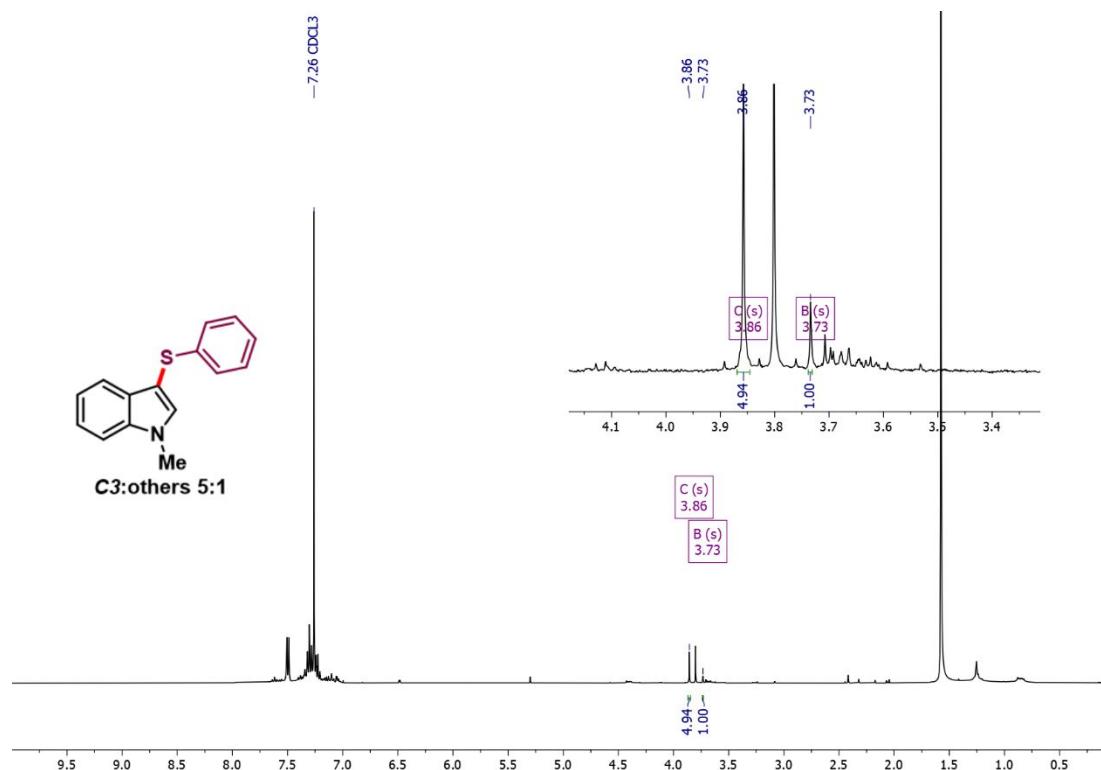
**4-phenyl-2-(phenylselanyl)thiophene (3o): NMR data of crude reaction mixture**



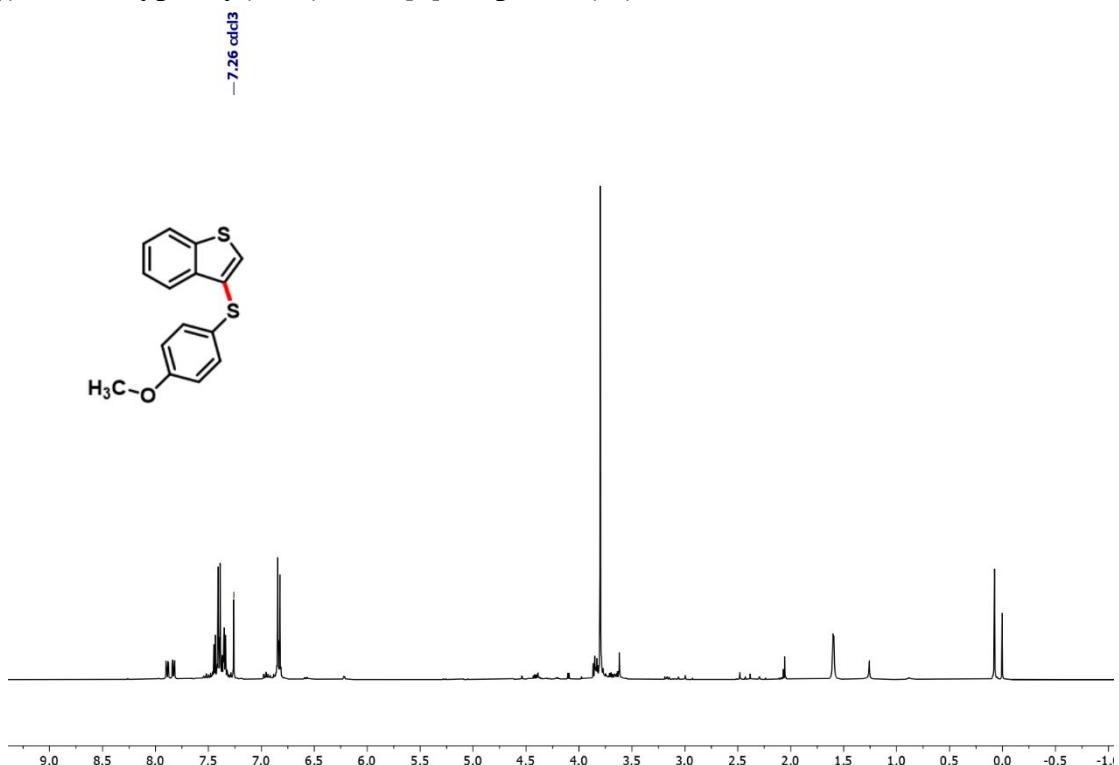
**2-((4-methoxyphenyl)thio)-1-methyl-1H-pyrrole (3p): NMR data of crude reaction mixture**



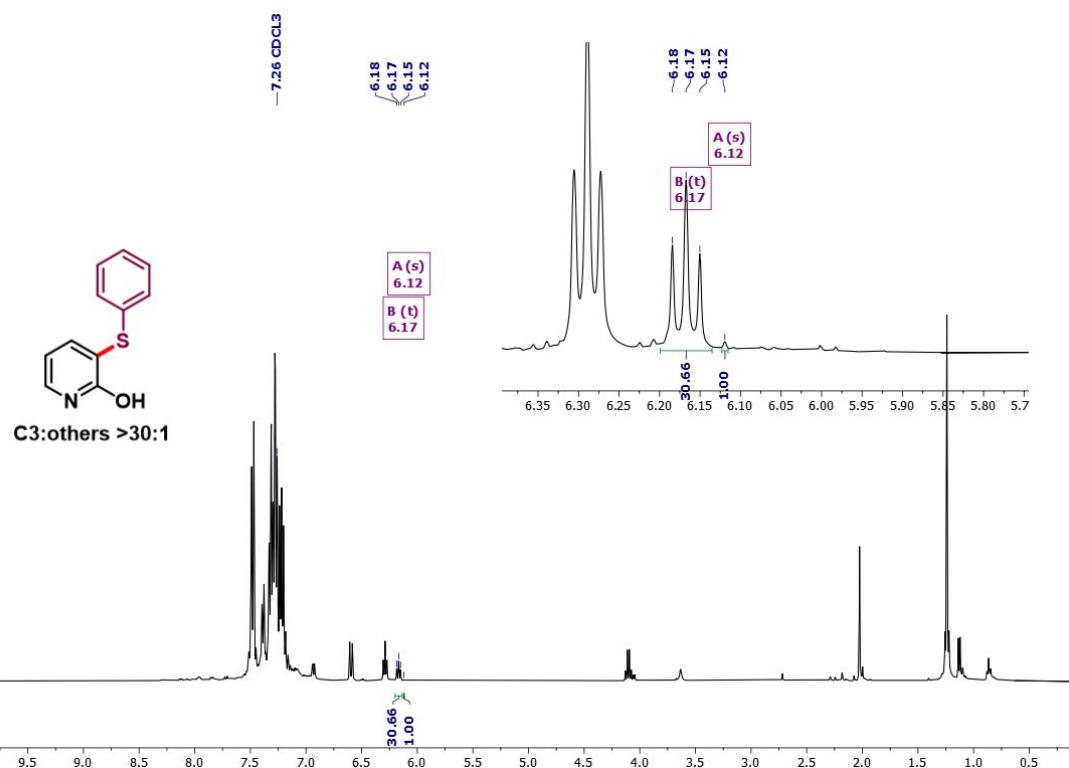
**1-methyl-3-(phenylthio)-1H-indole (3q): NMR data of crude reaction mixture**



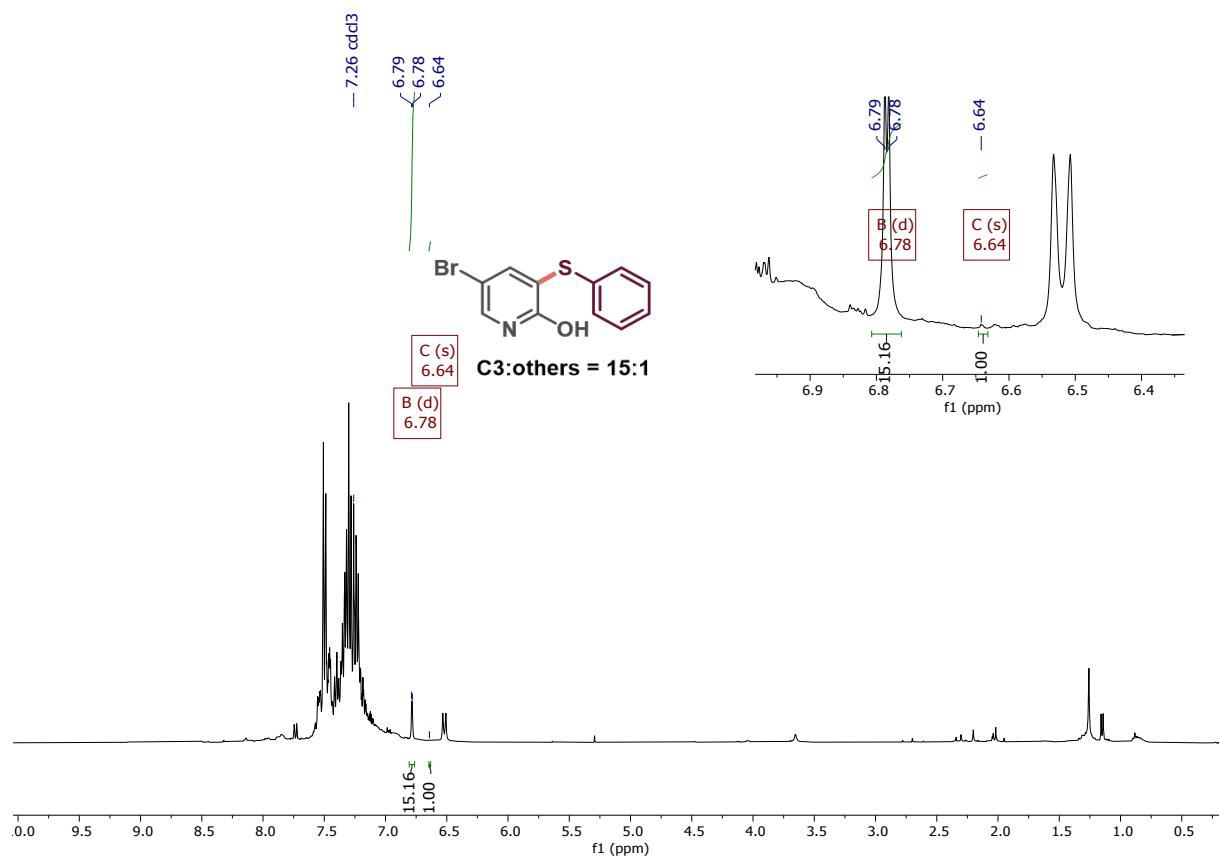
**3-((4-methoxyphenyl)thio)benzo[b]thiophene (3r): NMR data of crude reaction mixture**



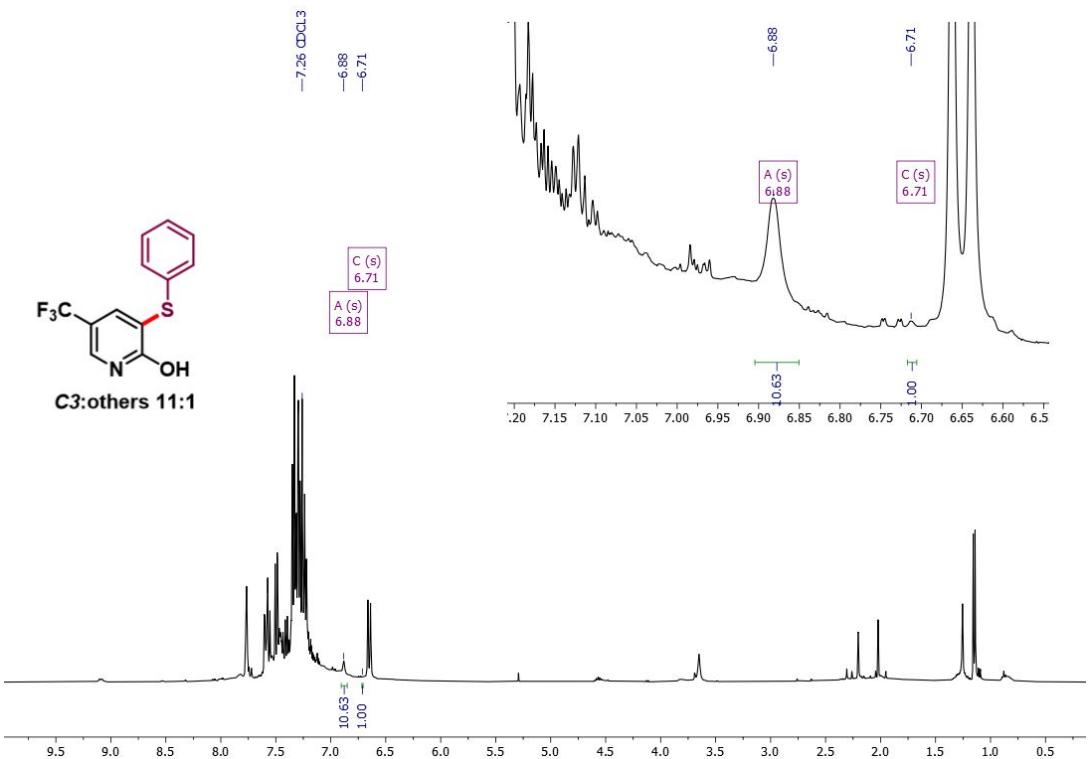
**3-(phenylthio)pyridin-2-ol (3w): NMR data of crude reaction mixture**



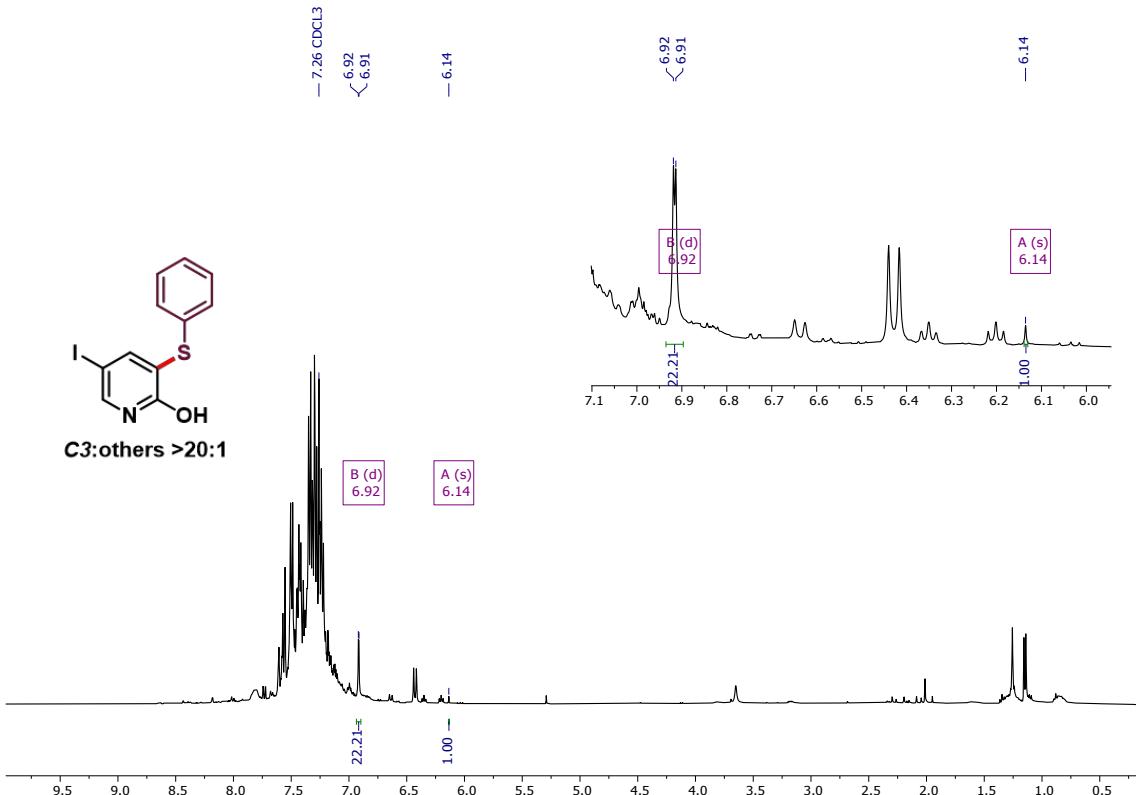
**5-bromo-3-(phenylthio)pyridin-2-ol (3x): NMR data of crude reaction mixture**



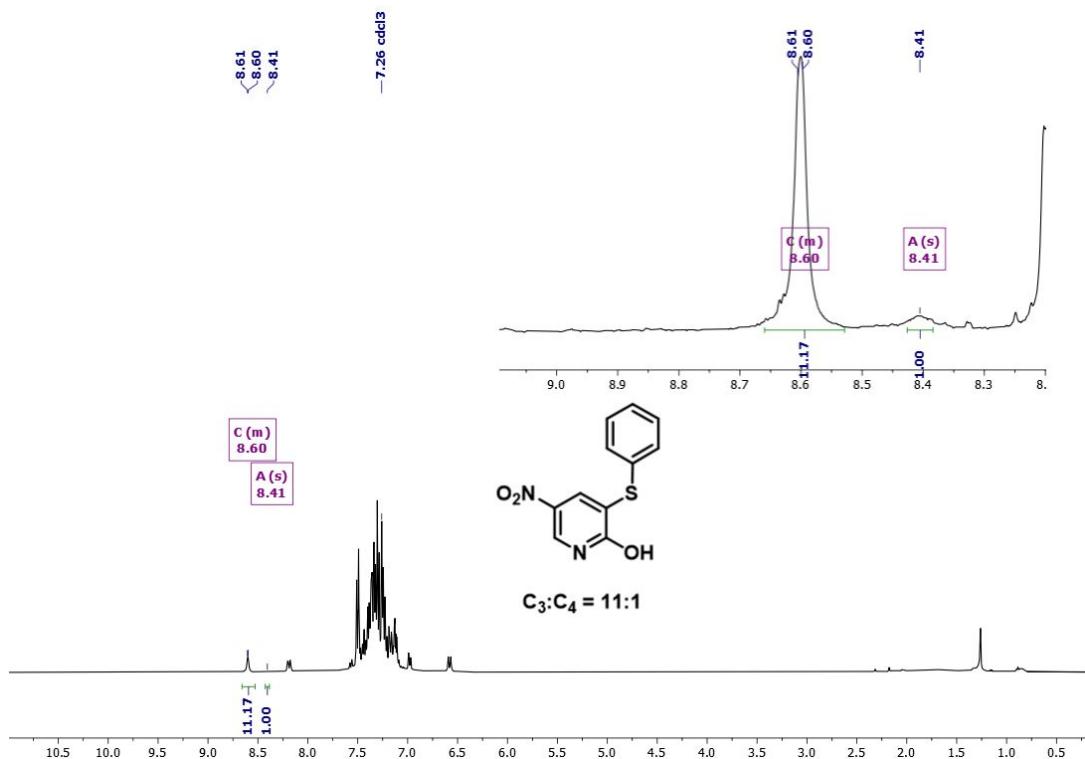
**3-(phenylthio)-5-(trifluoromethyl)pyridin-2-ol (3y): NMR data of crude reaction mixture**



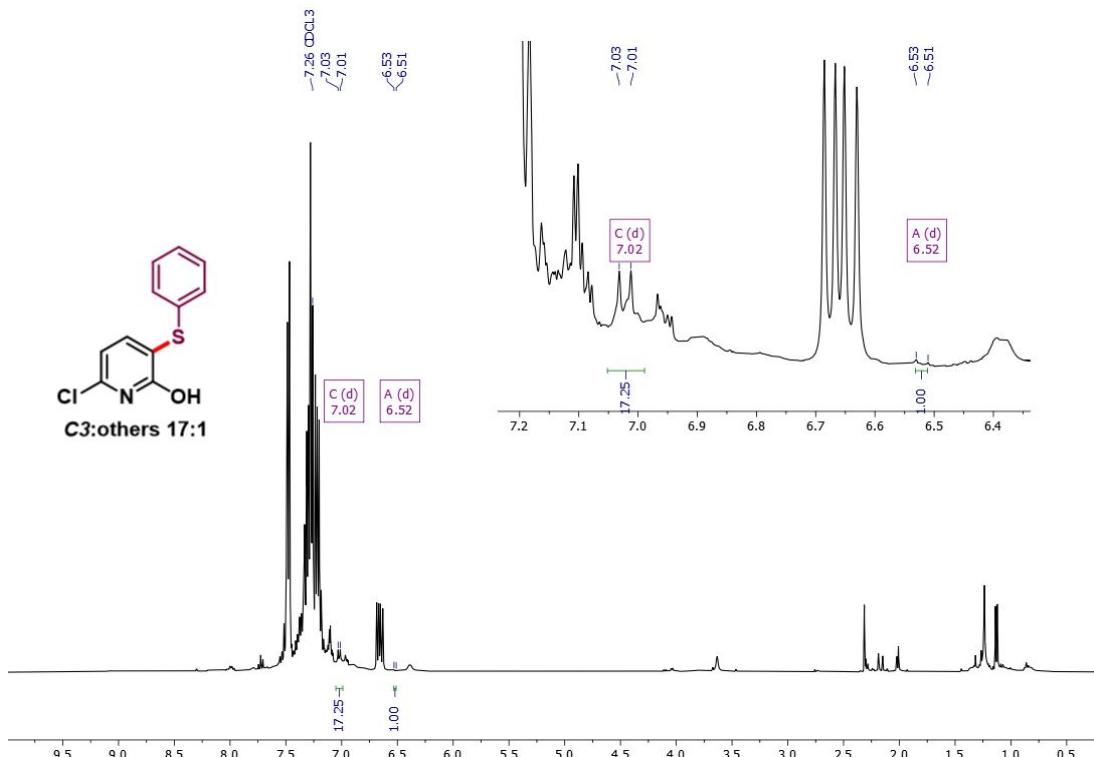
**5-iodo-3-(phenylthio)pyridin-2-ol (3z): NMR data of crude reaction mixture**



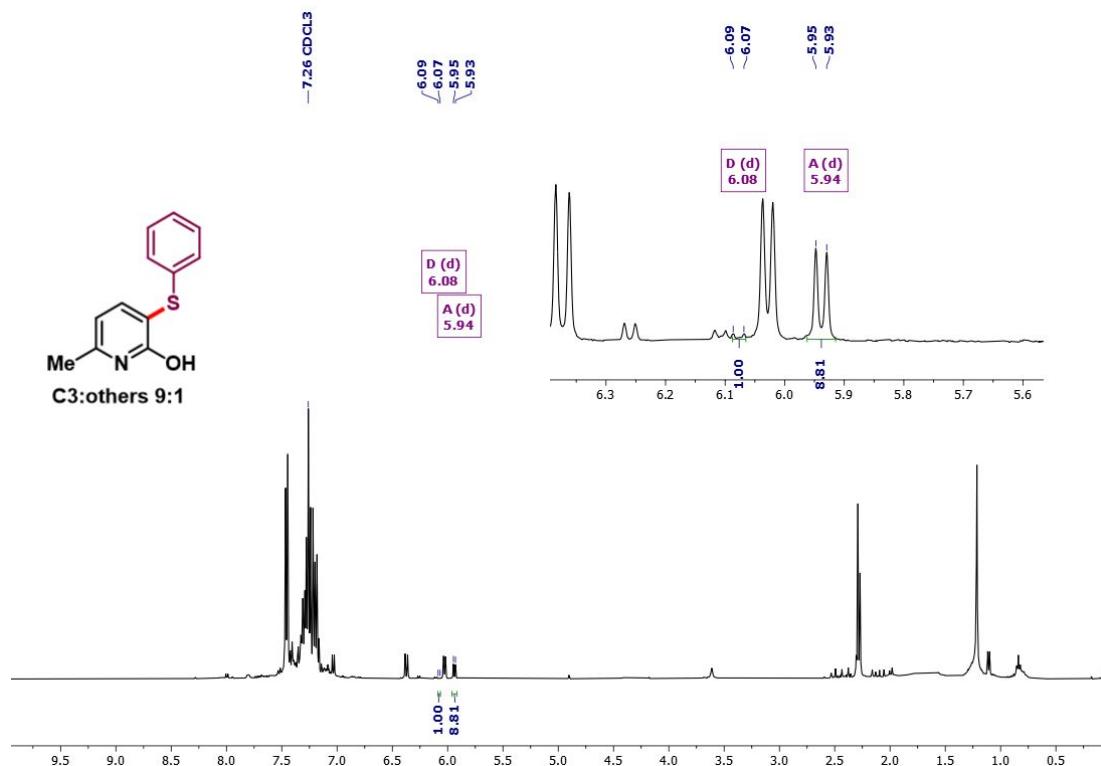
**5-nitro-3-(phenylthio)pyridin-2-ol (3aa): NMR data of crude reaction mixture**



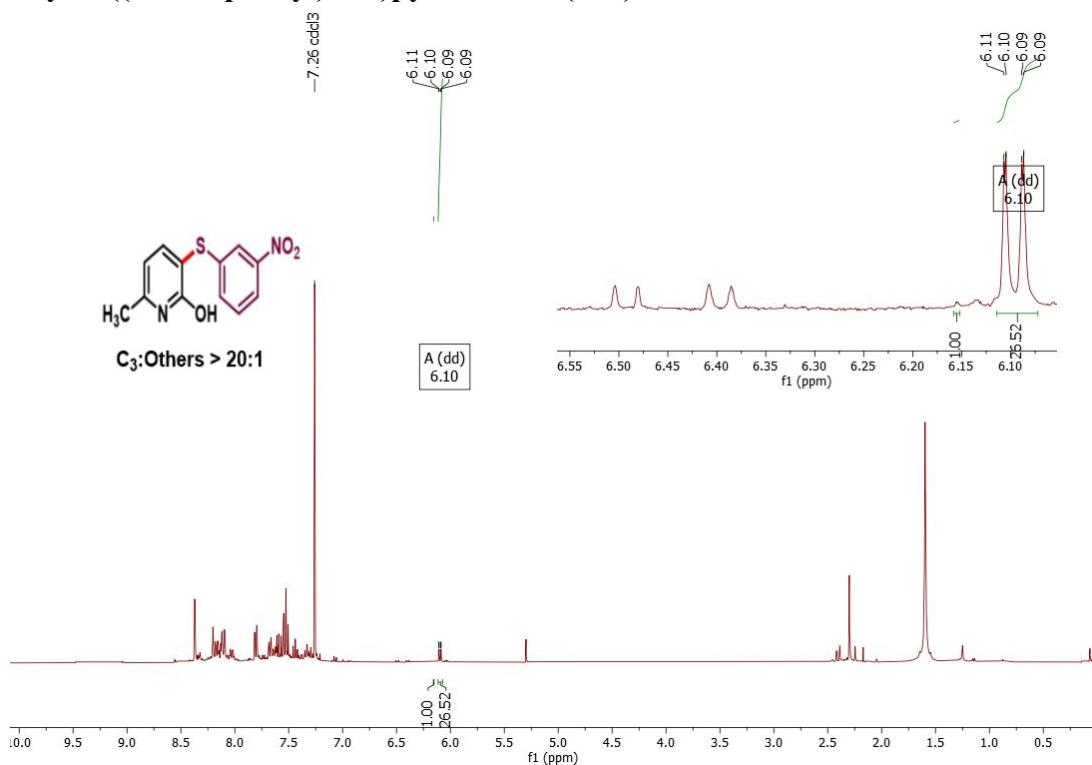
**6-chloro-3-(phenylthio)pyridin-2-ol (3ab): NMR data of crude reaction mixture**



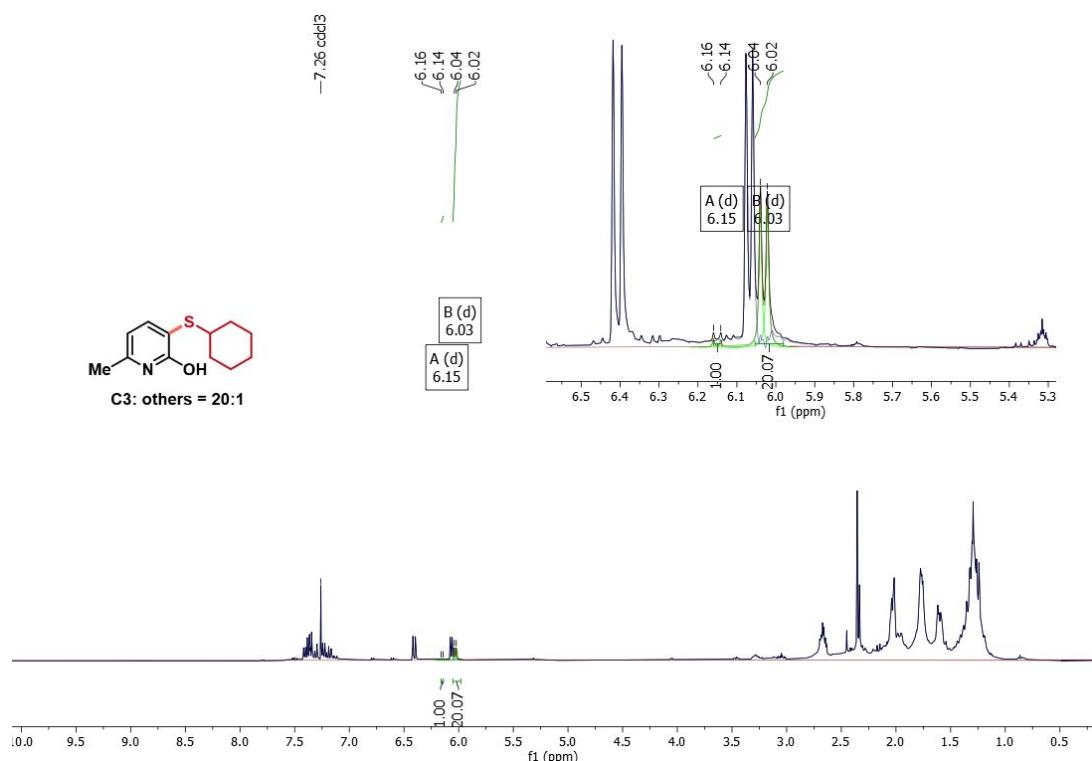
**6-methyl-3-(phenylthio)pyridin-2-ol (3ac): NMR data of crude reaction mixture**



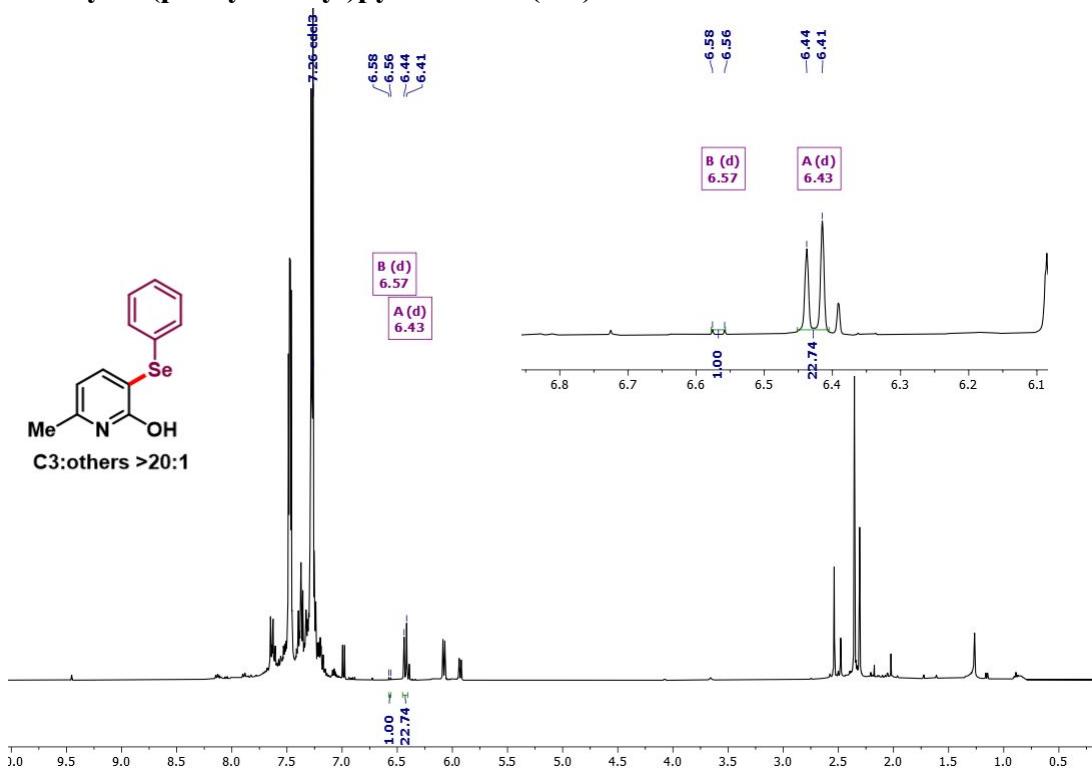
**6-methyl-3-((3-nitrophenyl)thio)pyridin-2-ol (3ad): NMR data of crude reaction mixture**



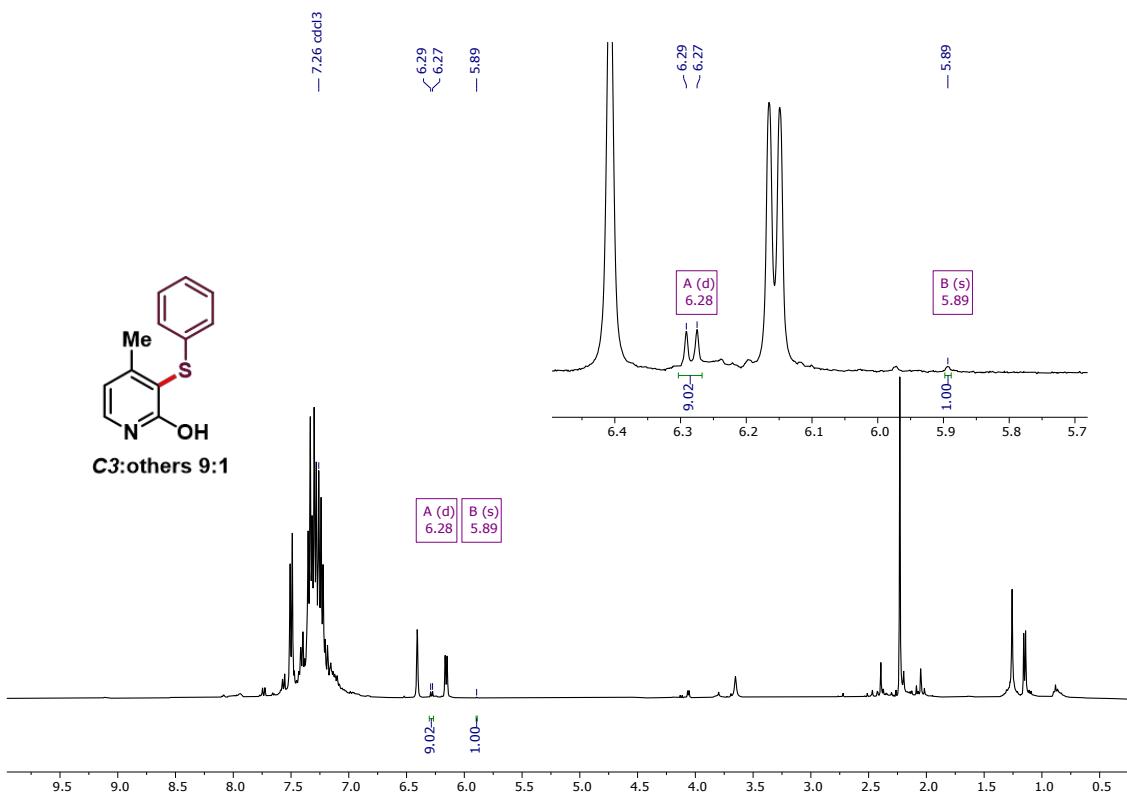
**3-(cyclohexylthio)-6-methylpyridin-2-ol (3ae): NMR data of crude reaction mixture**



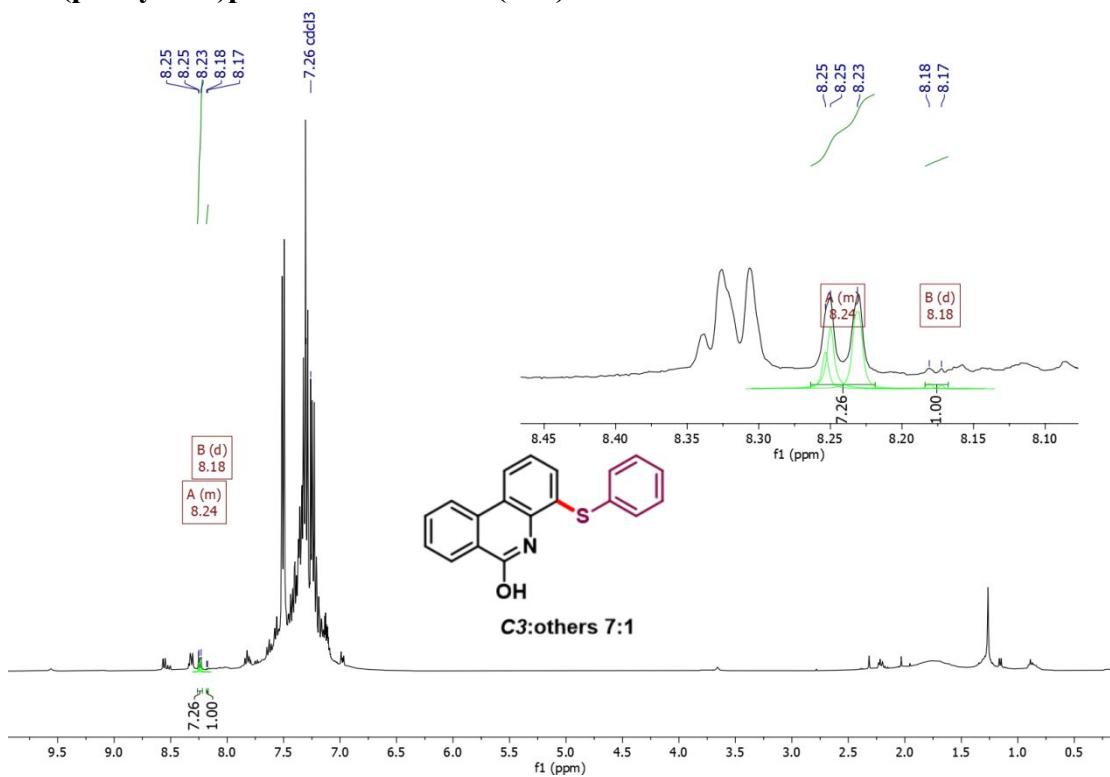
**6-methyl-3-(phenylselanyl)pyridin-2-ol (3af): NMR data of crude reaction mixture**



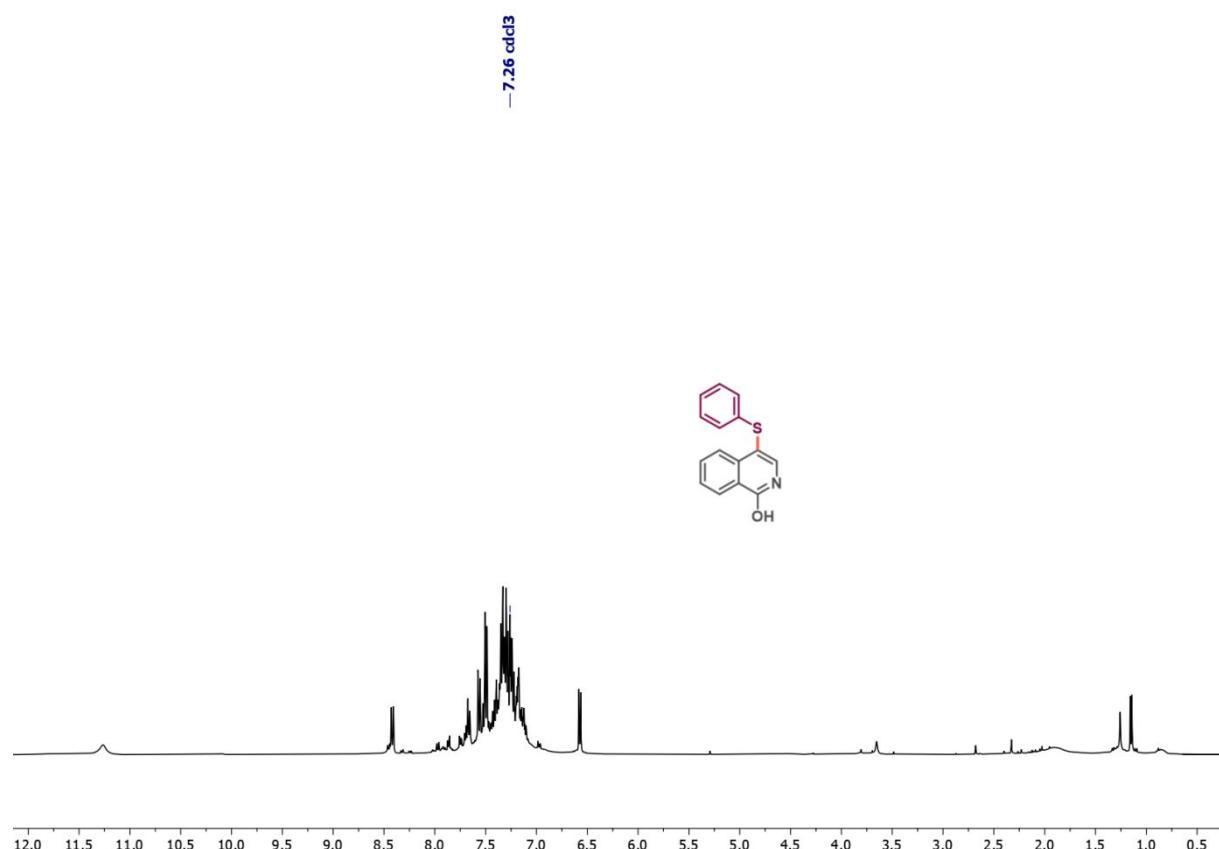
**4-methyl-3-(phenylthio)pyridin-2-ol (3ag): NMR data of crude reaction mixture**



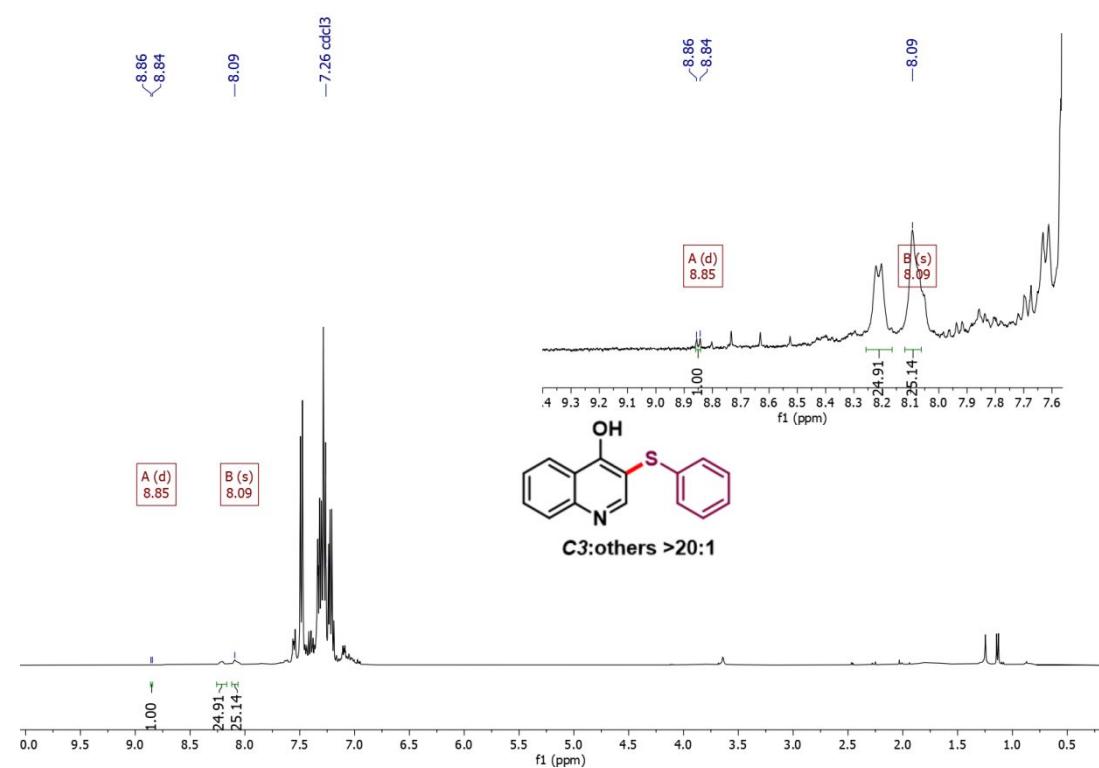
**4-(phenylthio)phenanthridin-6-ol (3ah): NMR data of crude reaction mixture**



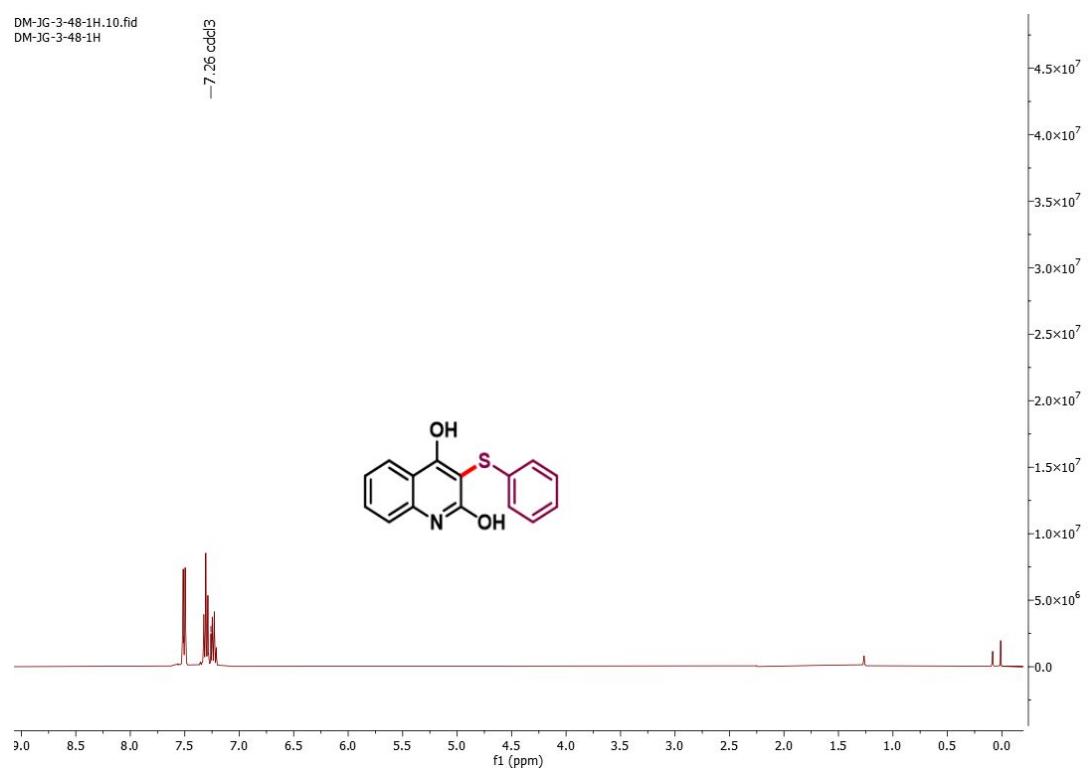
**4-(phenylthio)isoquinolin-1-ol (3ai): NMR data of crude reaction mixture**



**3-(phenylthio)quinolin-4-ol (3aj): NMR data of crude reaction mixture**

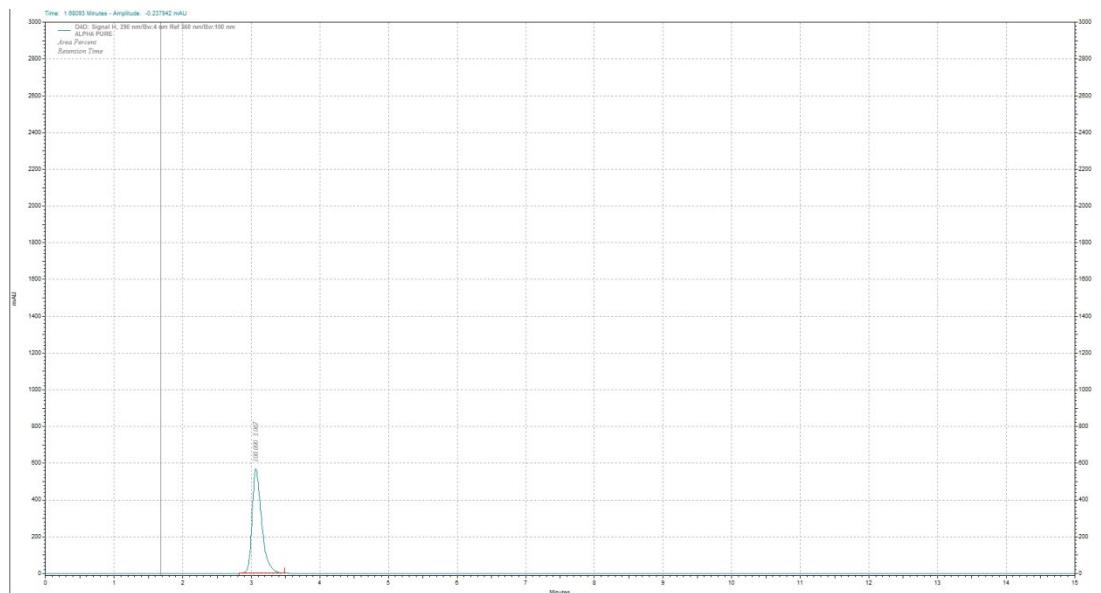


**3-(phenylthio)quinoline-2,4-diol (3al): NMR data of crude reaction mixture**

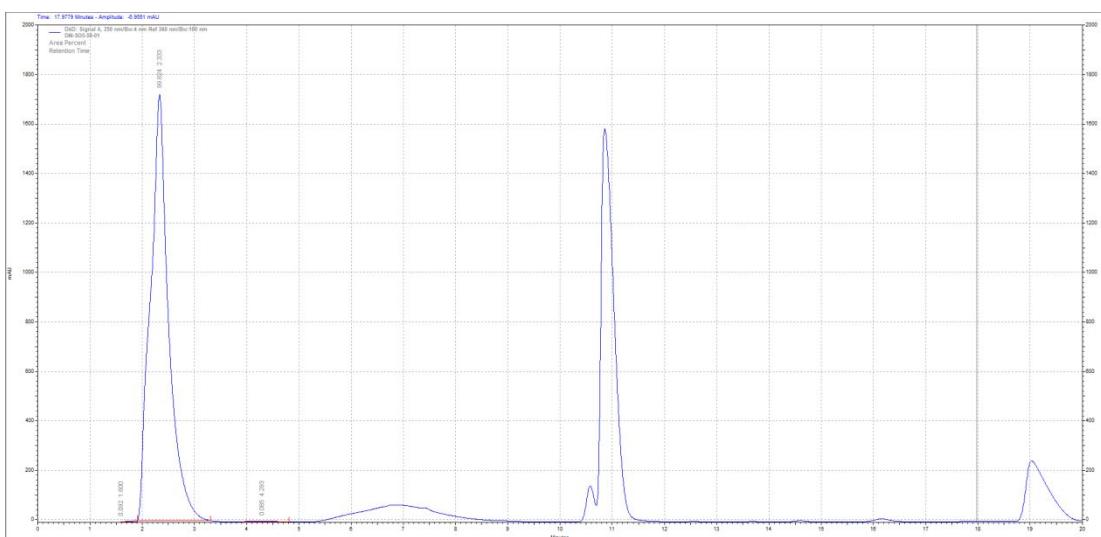


## HPLC data of crude reaction mixtures

### Naphthalen-2-yl(phenyl)sulfane ( $\beta:\alpha > 30:1$ ) (2a): HPLC of isolated material



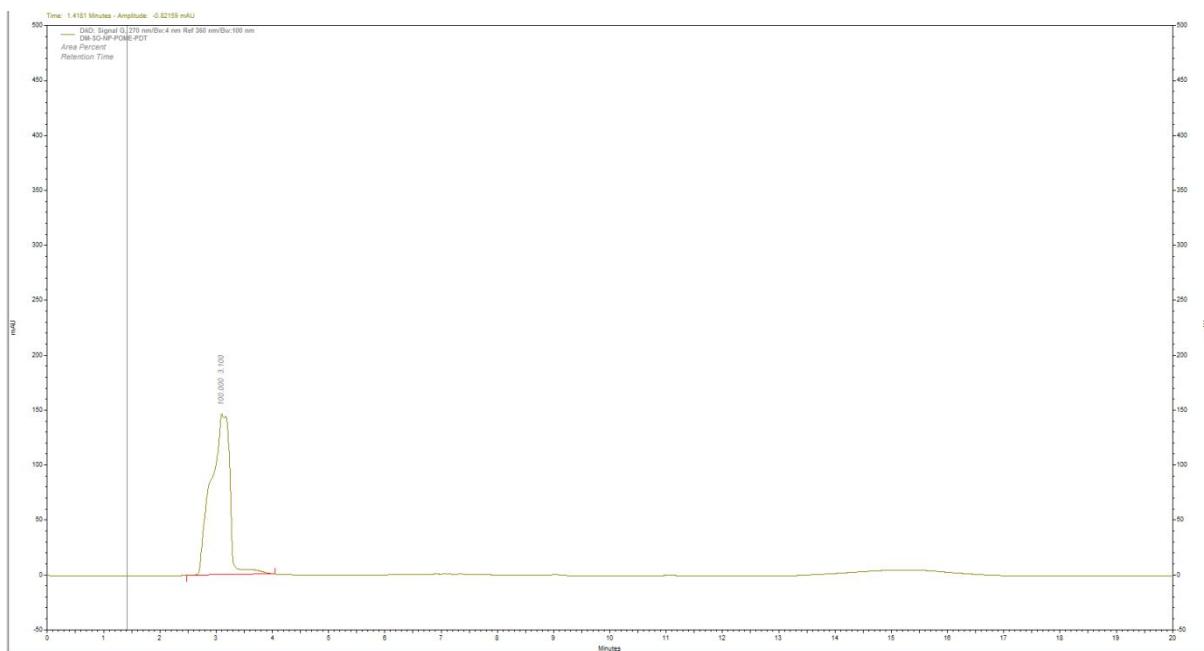
### HPLC of crude reaction mixture



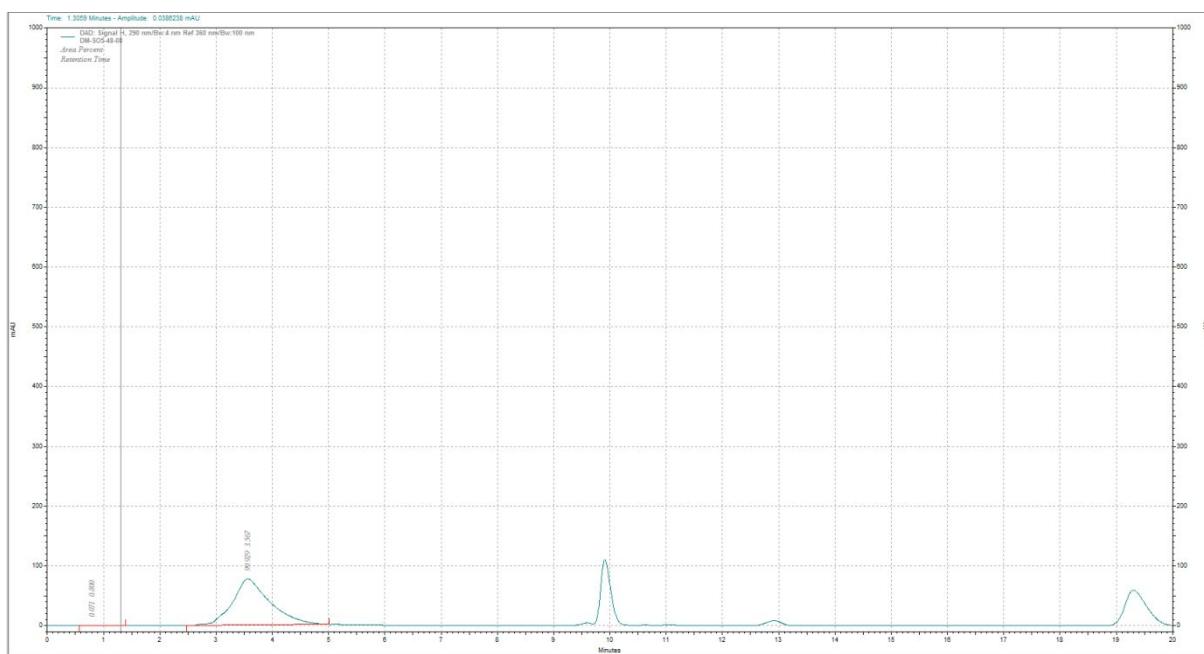
DAD: Signal A,  
250 nm/Bw:4 nm  
Ref 360  
nm/Bw:100 nm  
Results

Retention Time	Area	Area %	Height	Height %
1.600	79989	0.09	0	0.00
2.333	87102804	99.82	3614686	99.94
4.293	73853	0.08	2138	0.06
<b>Totals</b>	<b>87256646</b>	<b>100.00</b>	<b>3616824</b>	<b>100.00</b>

**(4-Methoxyphenyl)(naphthalen-2-yl)sulfane ( $\beta:\alpha > 20:1$ ) (2b): HPLC of isolated material**



**HPLC of crude reaction mixture**



DAD: Signal H,

290 nm/Bw:4 nm

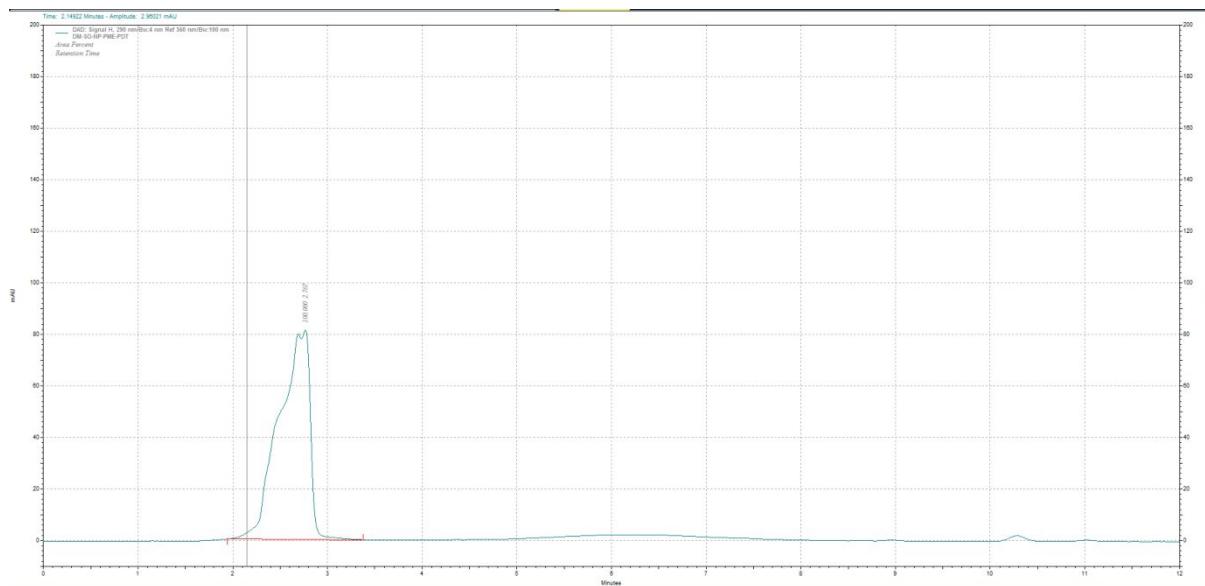
Ref 360

nm/Bw:100 nm

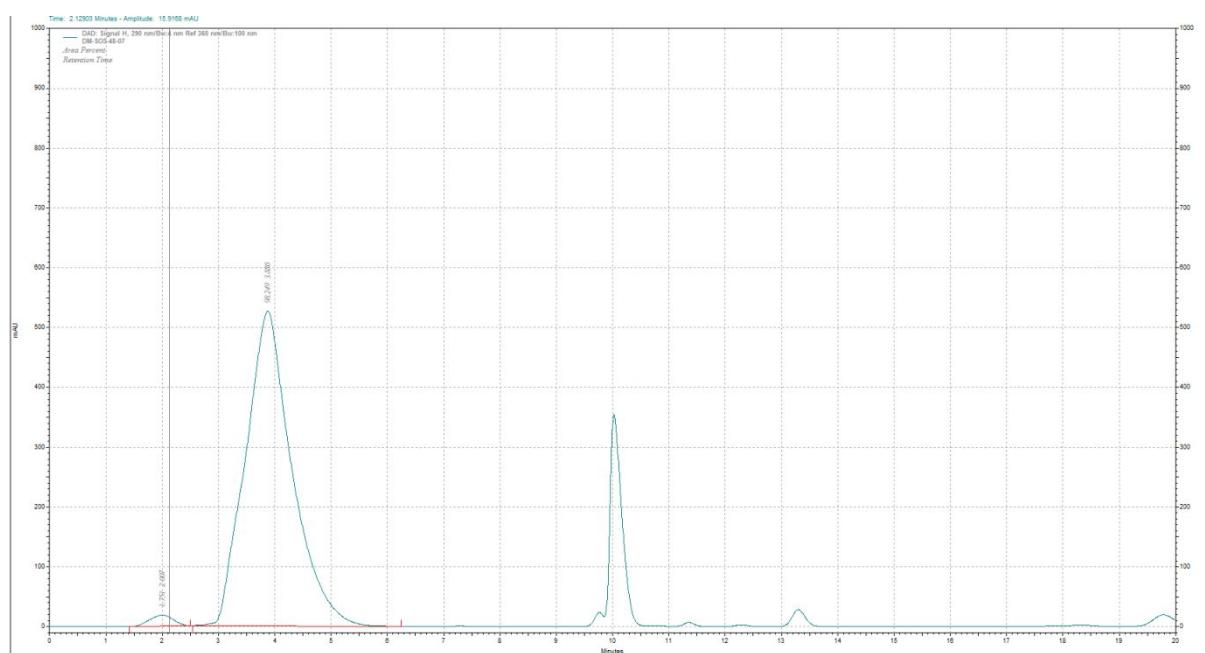
Results

Retention Time	Area	Area %	Height	Height %
0.800	5327	0.07	226	0.14
3.567	7479481	99.93	162240	99.86
Totals	7484808	100.00	162466	100.00

### Naphthalen-2-yl(p-tolyl)sulfane ( $\beta:\alpha > 20:1$ ) (2c): HPLC of isolated material



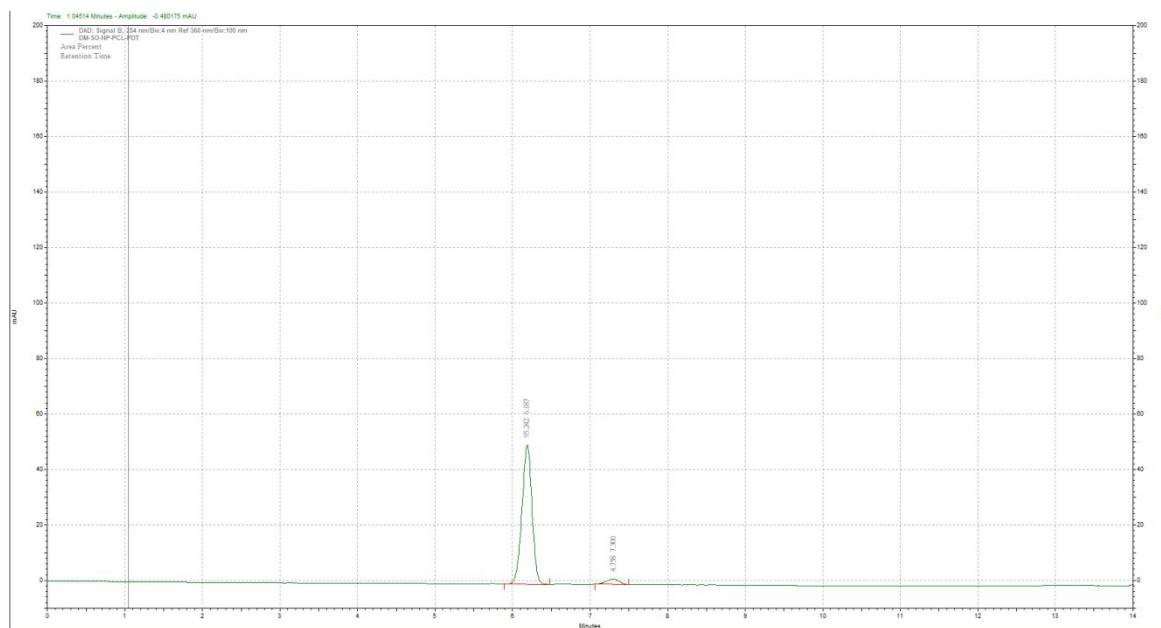
### HPLC of crude reaction mixture



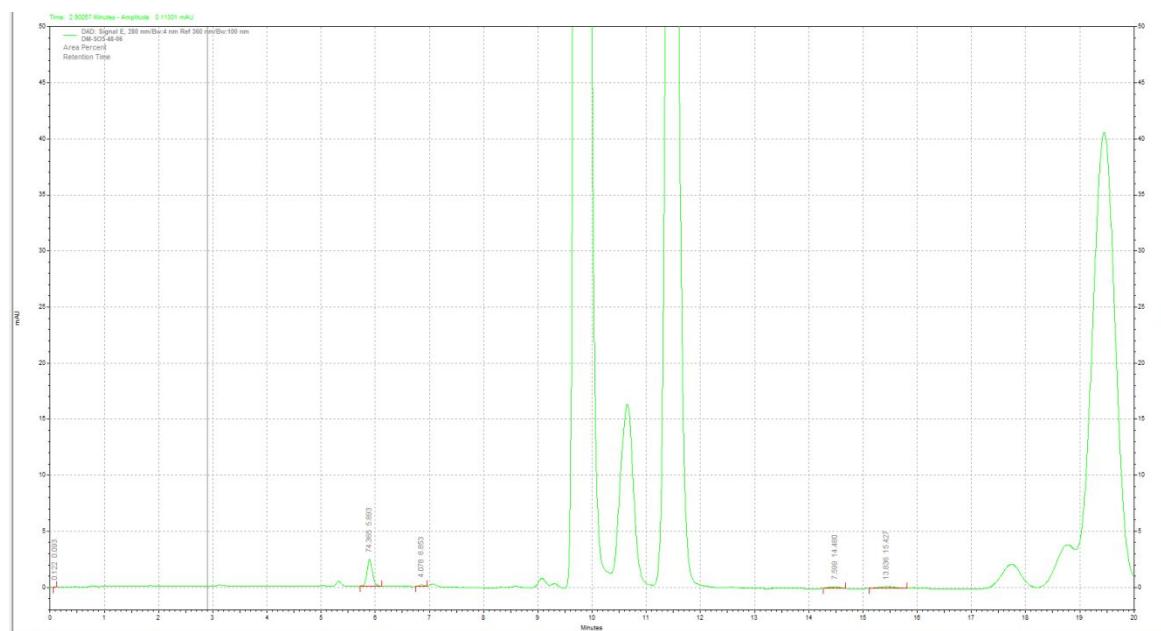
**DAD: Signal H,  
290 nm/Bw:4 nm  
Ref 360  
nm/Bw:100 nm  
Results**

Retention Time	Area	Area %	Height	Height %
2.007	1125109	1.75	38681	3.39
3.880	63144684	98.25	1103358	96.61
<b>Totals</b>	<b>64269793</b>	<b>100.00</b>	<b>1142039</b>	<b>100.00</b>

**(4-Chlorophenyl)(naphthalen-2-yl)sulfane ( $\beta:\alpha$  18:1) (2d): HPLC of isolated material**



**HPLC of crude reaction mixture**

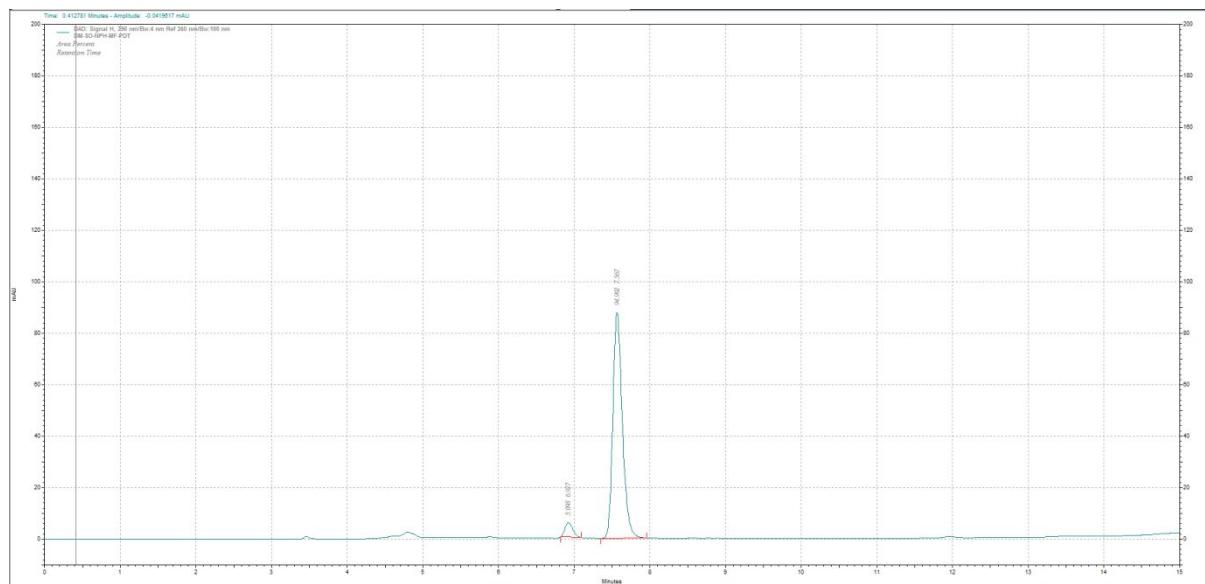


**DAD: Signal E,  
280 nm/Bw:4 nm  
Ref 360  
nm/Bw:100 nm  
Results**

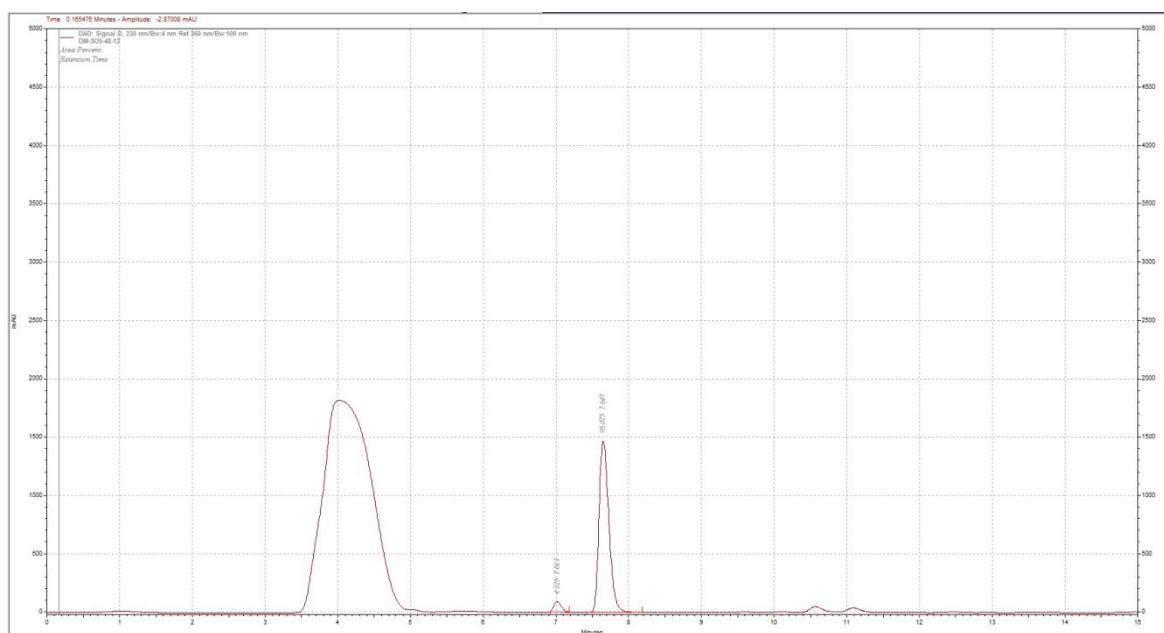
Retention Time	Area	Area %	Height	Height %
0.093	56	0.12	23	0.39
5.893	34156	74.37	4991	84.28
6.853	1873	4.08	323	5.45
14.480	3490	7.60	256	4.32
15.427	6355	13.84	329	5.56

Totals	45930	100.00	5922	100.00
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**(3-Fluorophenyl)(naphthalen-2-yl)sulfane ( $\beta:\alpha > 20:1$ ) (2e): HPLC of isolated material**



**HPLC of crude reaction mixture**



DAD: Signal D,

230 nm/Bw:4 nm

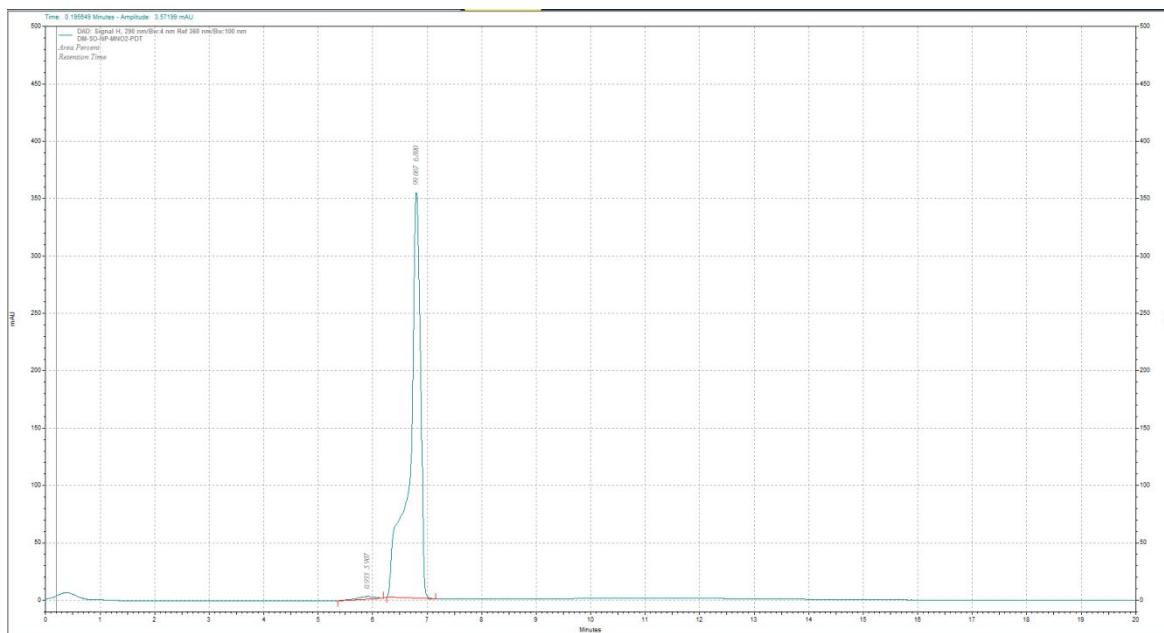
Ref 360

nm/Bw:100 nm

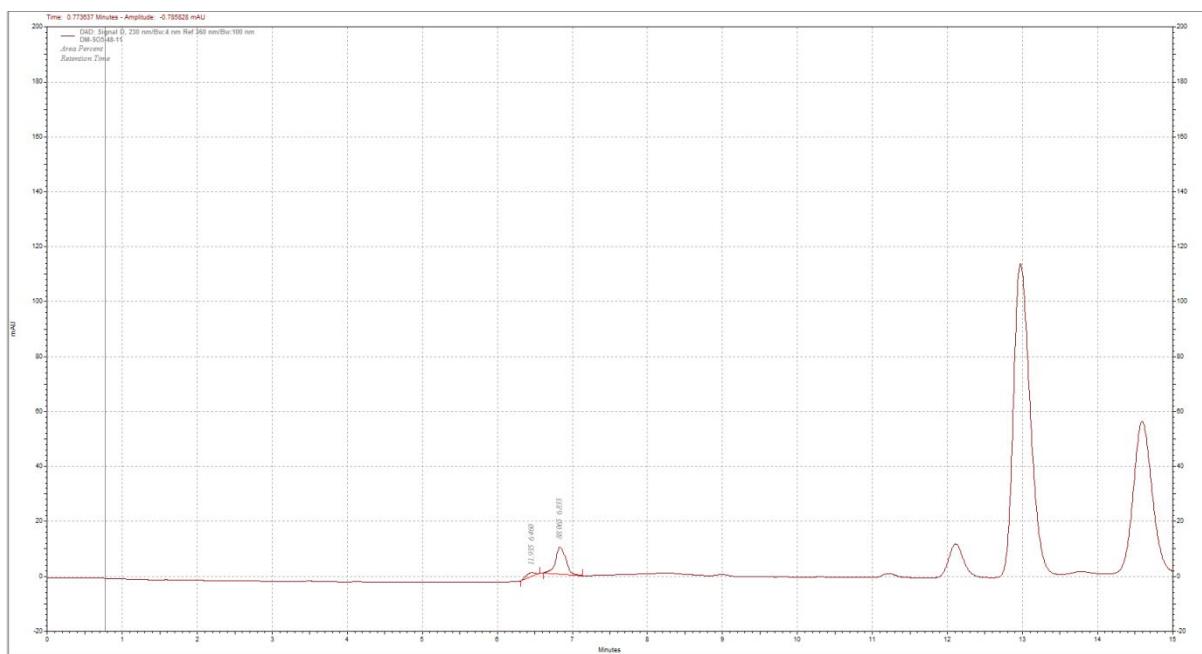
Results

Retention Time	Area	Area %	Height	Height %
7.013	1251097	4.13	178321	5.46
7.647	29077910	95.87	3085016	94.54
Totals	30329007	100.00	3263337	100.00

## Naphthalen-2-yl(3-nitrophenyl)sulfane ( $\beta:\alpha$ 8:1) (2f): HPLC of isolated material



## HPLC of crude reaction mixture



DAD: Signal D,

230 nm/Bw:4 nm

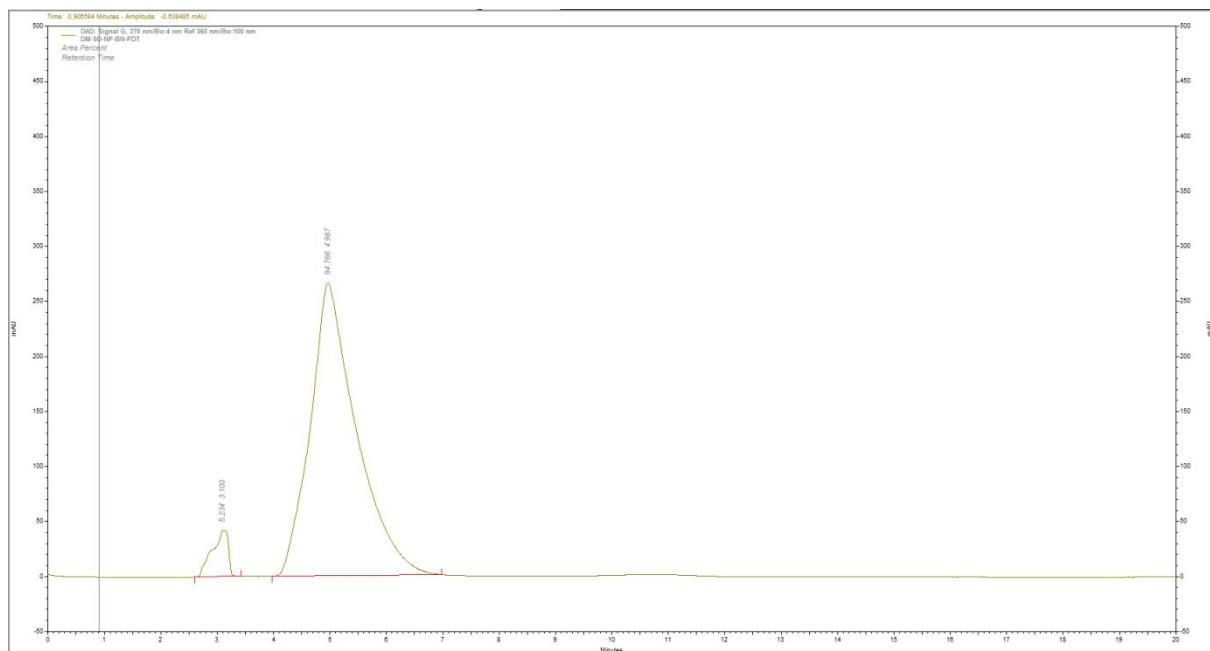
Ref 360

nm/Bw:100 nm

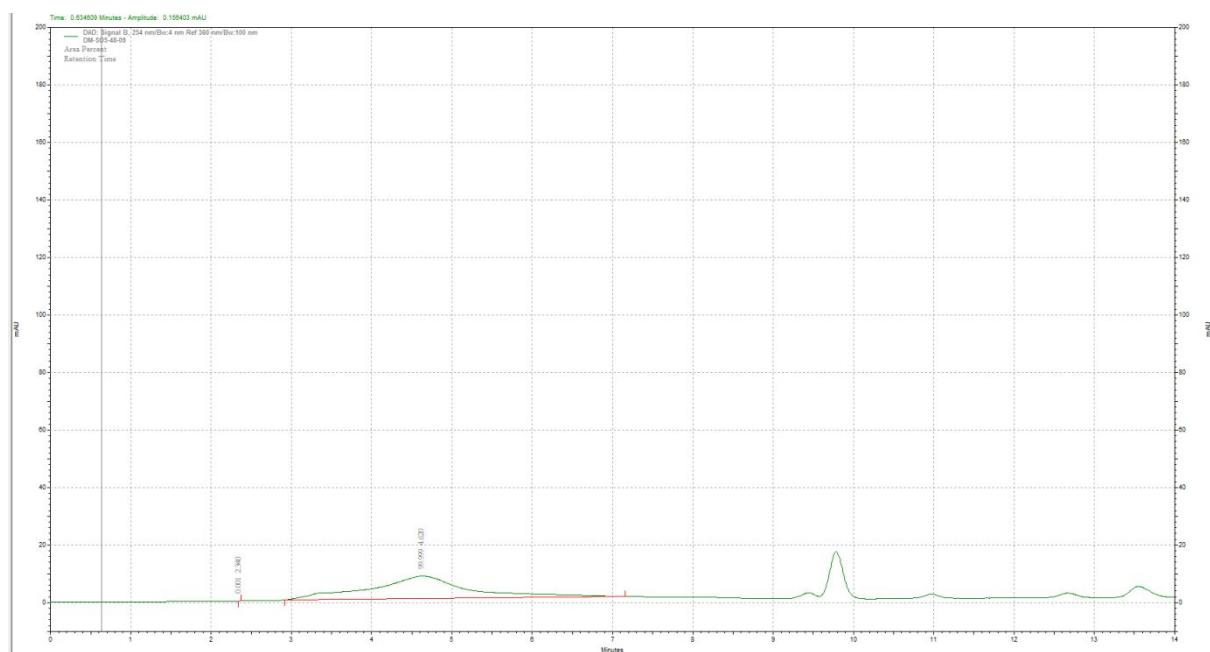
Results

Retention Time	Area	Area %	Height	Height %
6.460	26625	11.94	3021	12.73
6.833	196453	88.06	20710	87.27
Totals	223078	100.00	23731	100.00

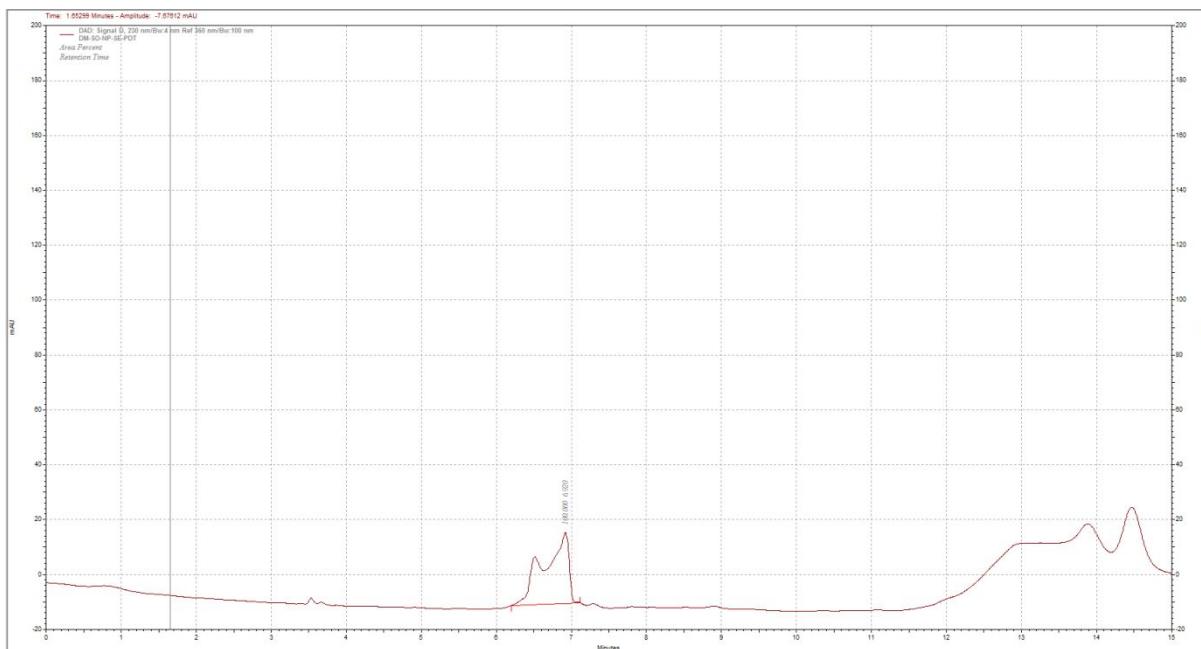
### Benzyl(naphthalen-2-yl)sulfane (2g): HPLC of isolated material



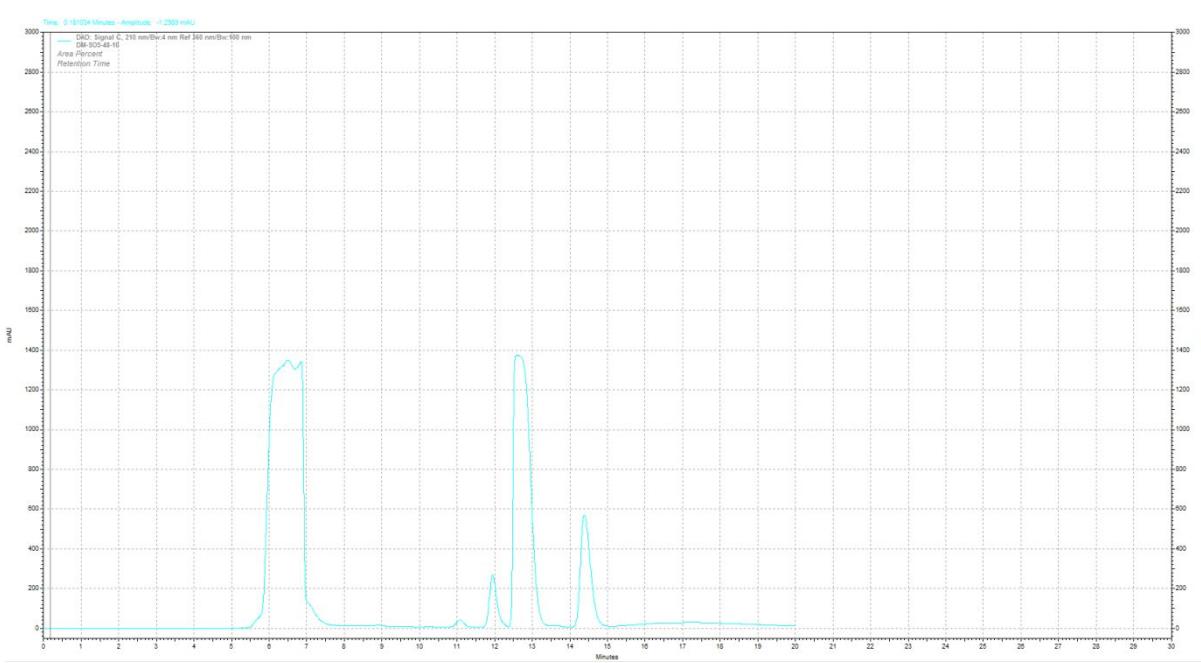
### HPLC of crude reaction mixture



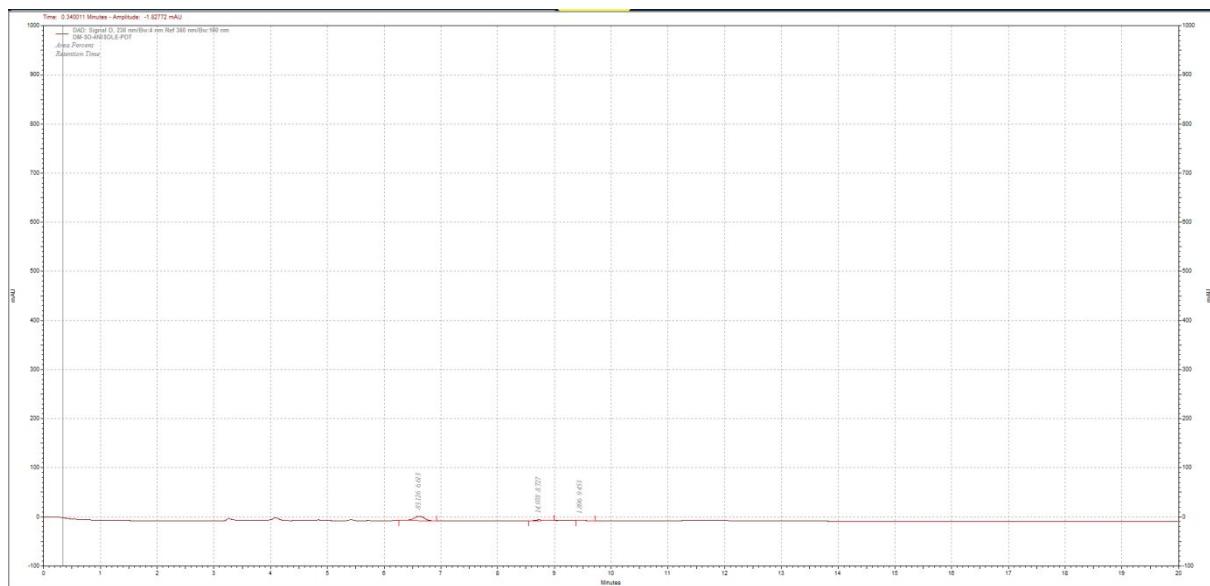
## Naphthalen-2-yl(phenyl)selane (2h): HPLC of isolated material



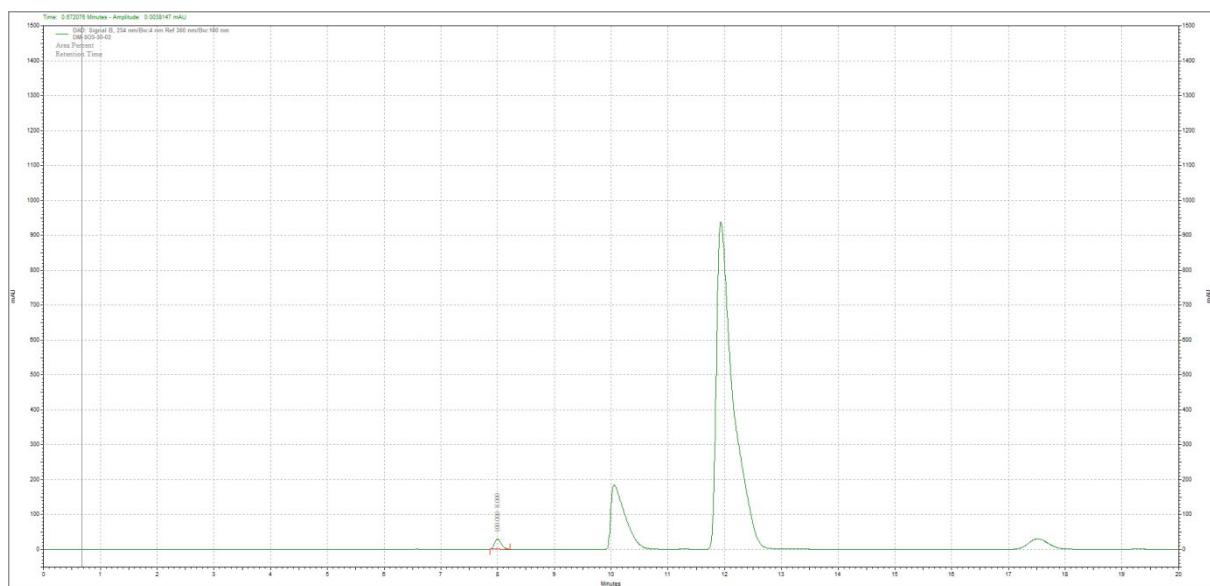
## HPLC of crude reaction mixture



**(2-Methoxyphenyl)(phenyl)sulfane (*ortho*:*others* >30:1) (2n): HPLC of isolated material**



**HPLC of crude reaction mixture**



**DAD: Signal B,**

**254 nm/Bw :4 nm**

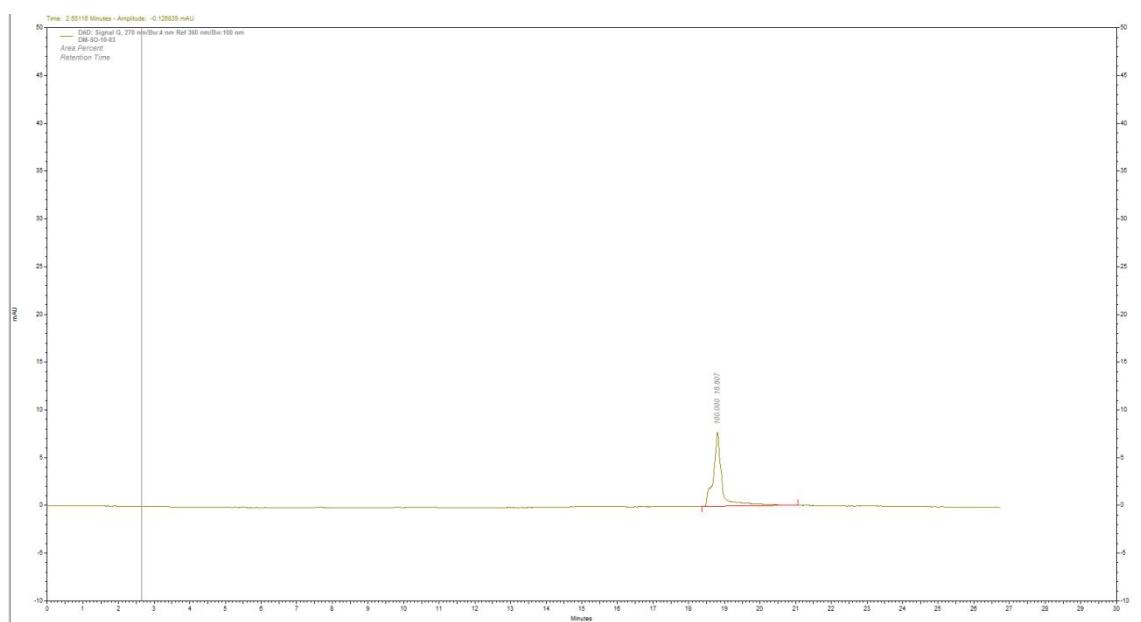
**Ref 360**

**nm/Bw :100 nm**

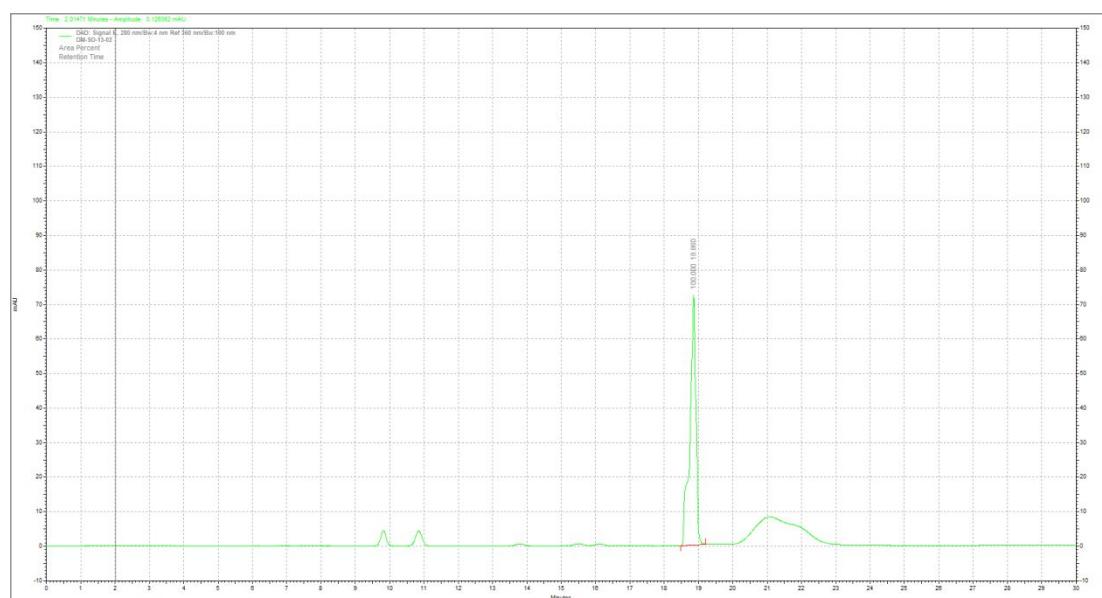
**Results**

Retention Time	Area	Area %	Height	Height %
8.000	507563	100.00	61561	100.00
Totals	507563	100.00	61561	100.00

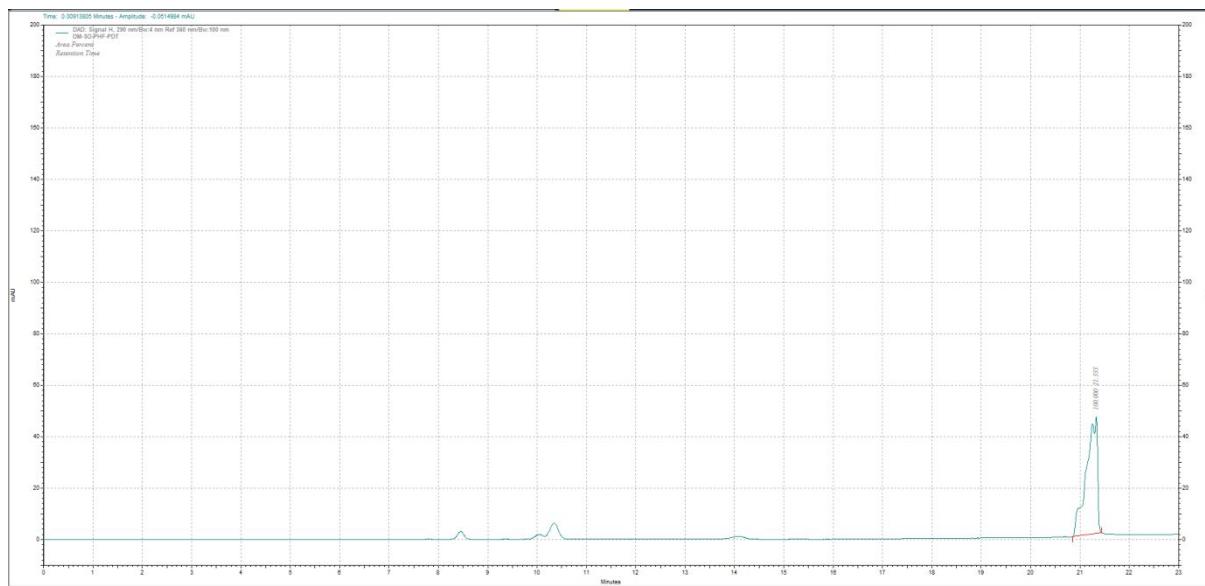
### (3,5-Dimethylphenyl)(4-methoxyphenyl)sulfane (2r): HPLC of isolated material



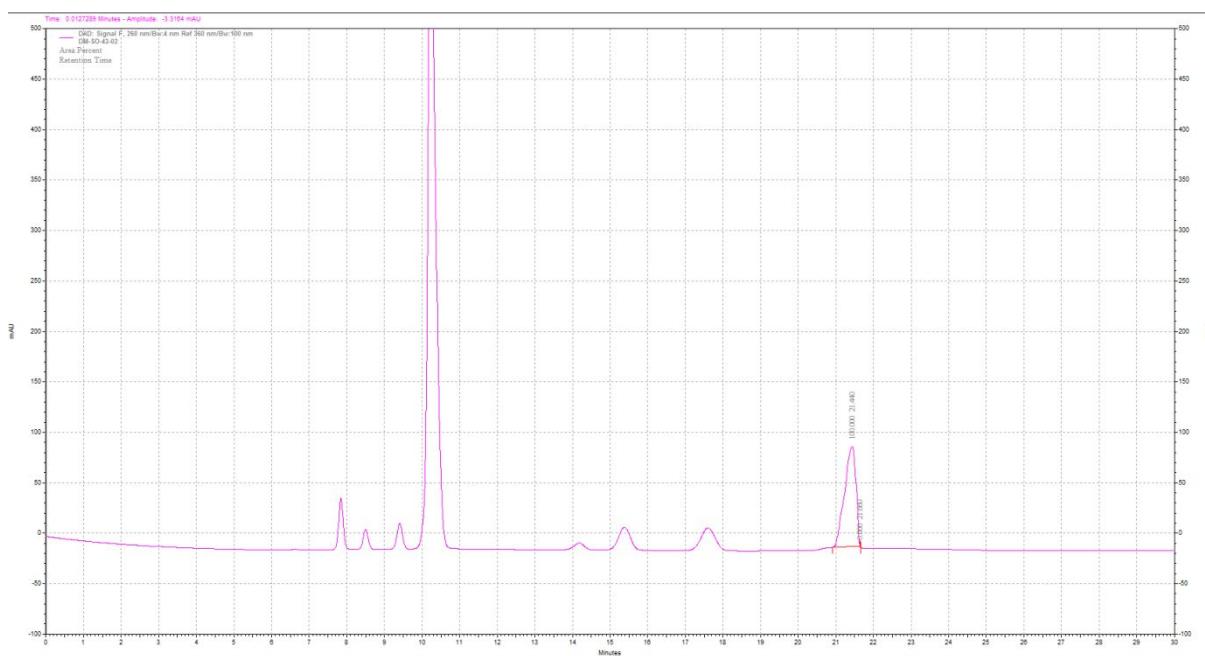
### HPLC of crude reaction mixture



**(2-Fluorophenyl)(phenyl)sulfane (*ortho*:*others* >30:1) (2t): HPLC of isolated material**



**HPLC of crude reaction mixture**



**DAD: Signal A,**

**250 nm/Bw:4 nm**

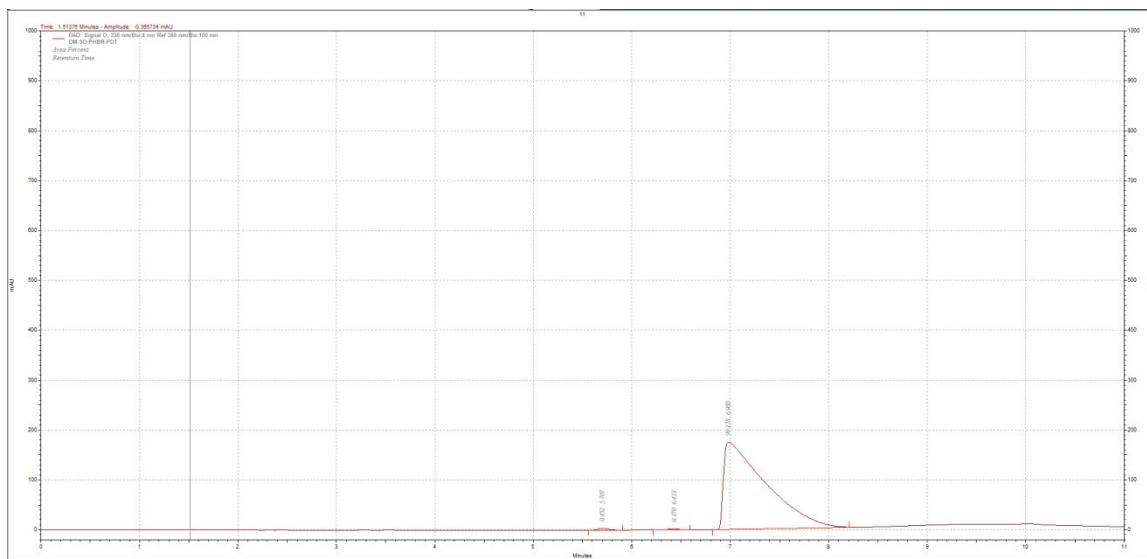
**Ref 360**

**nm/Bw:100 nm**

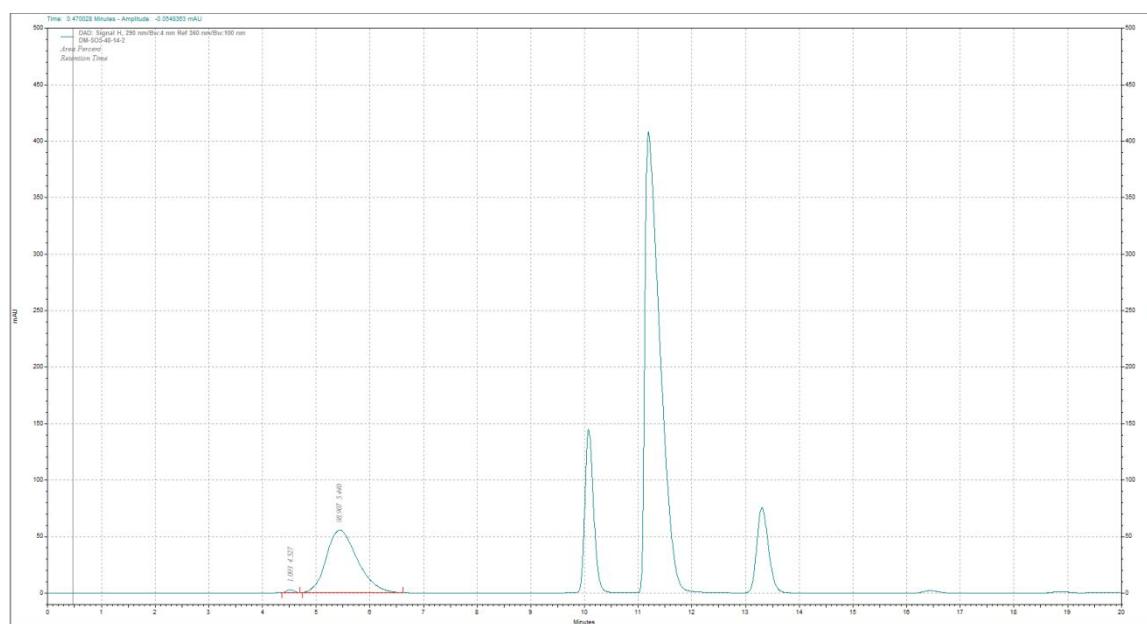
**Results**

Retention Time	Area	Area %	Height	Height %
21.433	6245179	100.00	296775	100.00
21.847	12	0.00	0	0.00
<b>Totals</b>	<b>6245191</b>	<b>100.00</b>	<b>296775</b>	<b>100.00</b>

**(2-Bromophenyl)(phenyl)sulfane (*ortho*:*others* >30:1) (2u): HPLC of isolated material**



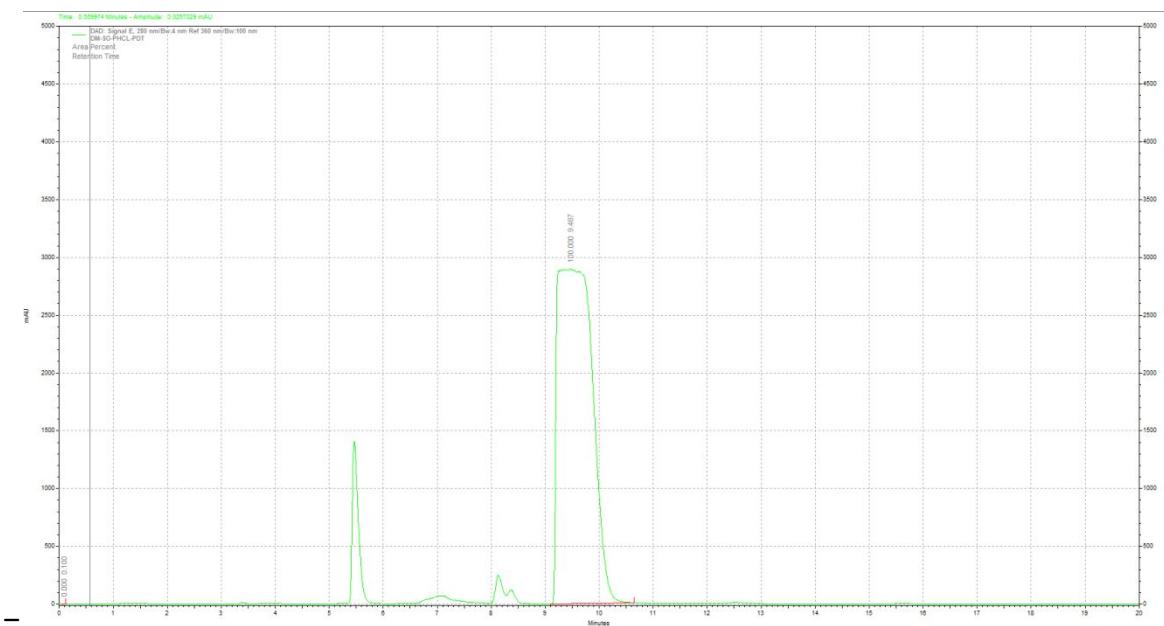
**HPLC of crude reaction mixture**



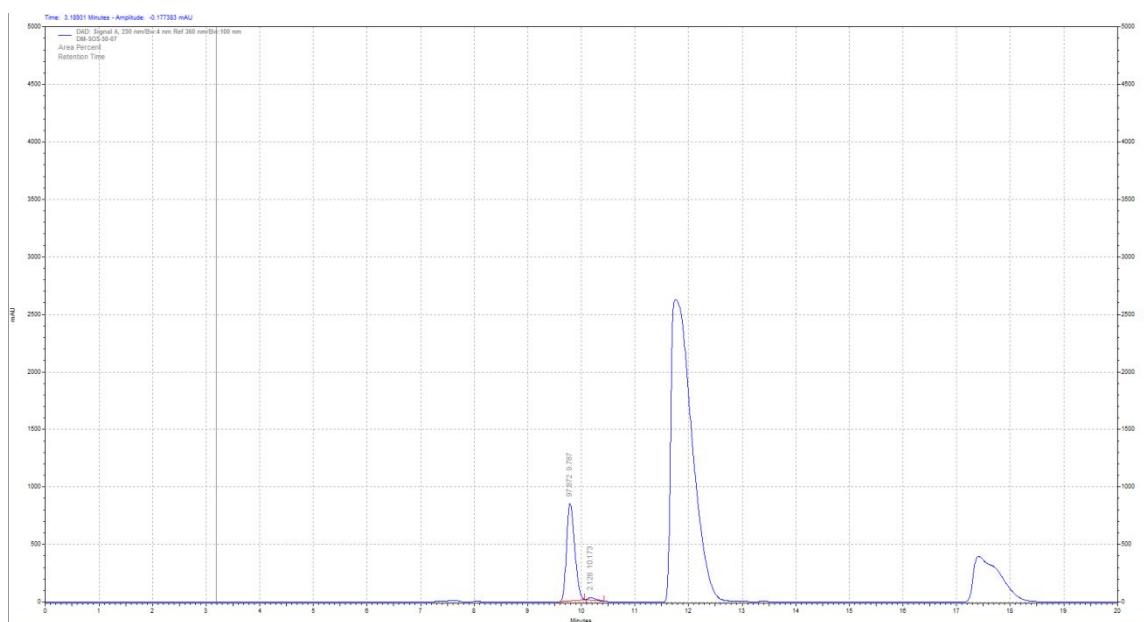
DAD: Signal H,  
290 nm/Bw:4 nm  
Ref 360  
nm/Bw:100 nm  
Results

Retention Time	Area	Area %	Height	Height %
<hr/>				
4.527	51357	1.09	5586	4.61
5.440	4646942	98.91	115640	95.39
<hr/>				
Totals	4698299	100.00	121226	100.00

**(3-Chlorophenyl)(phenyl)sulfane (*meta:others* >20:1) (2v): HPLC of isolated material**



**HPLC of crude reaction mixture**

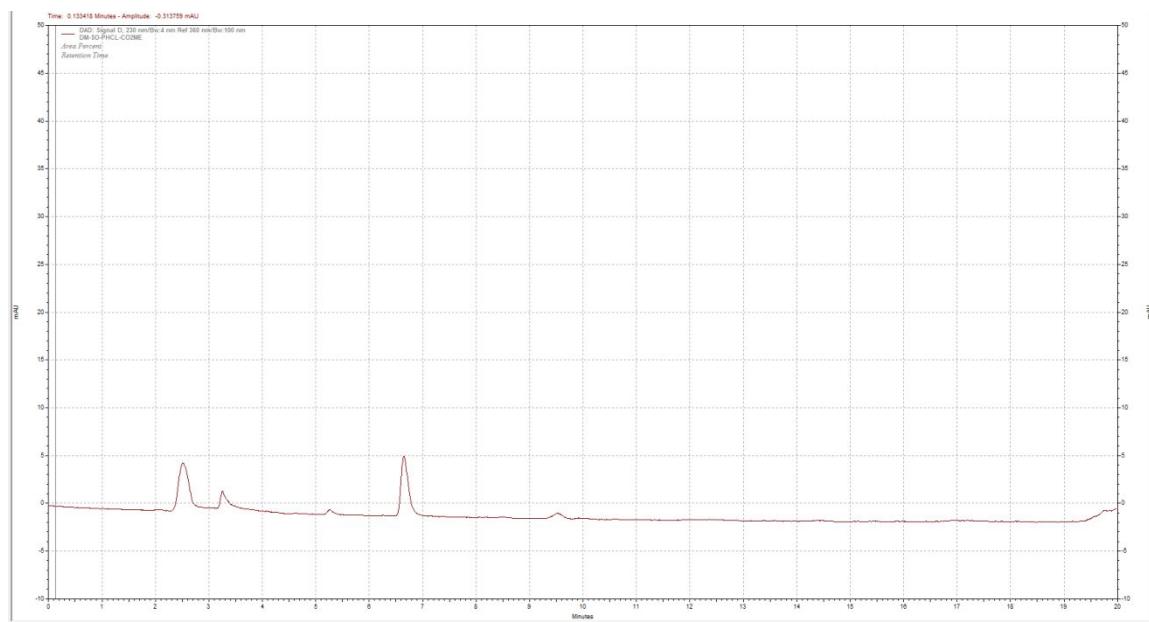


DAD: Signal A,  
250 nm/Bw:4 nm  
Ref 360  
nm/Bw:100 nm  
Results

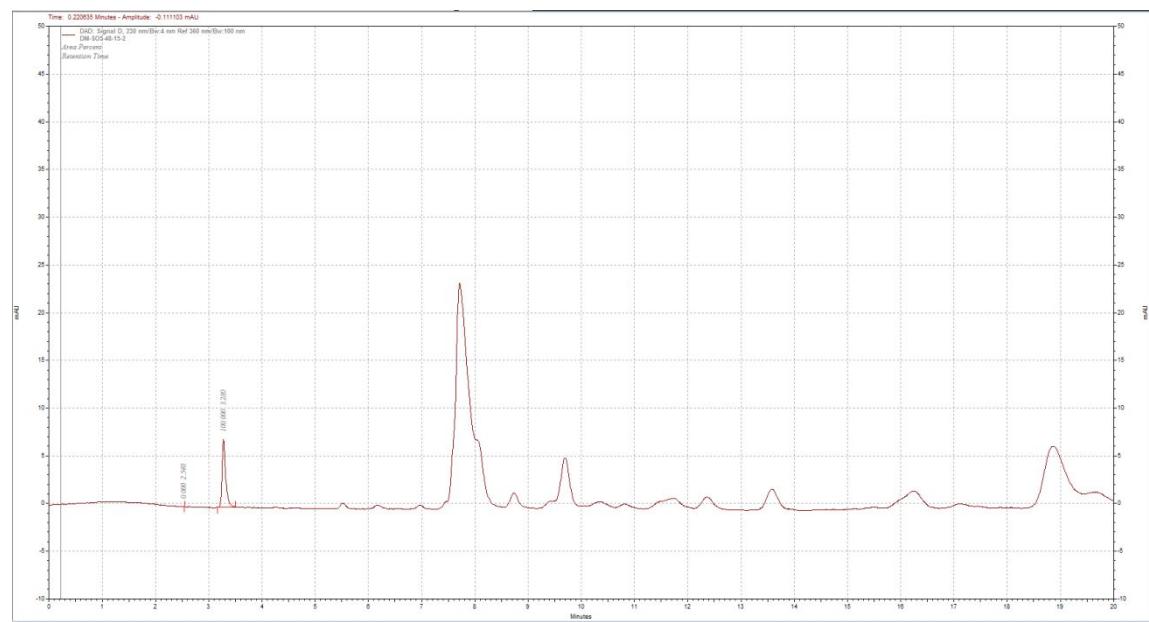
Retention Time	Area	Area %	Height	Height %
9.787	18786121	97.87	1771675	97.79
10.173	408508	2.13	40113	2.21

Totals	19194629	100.00	1811788	100.00
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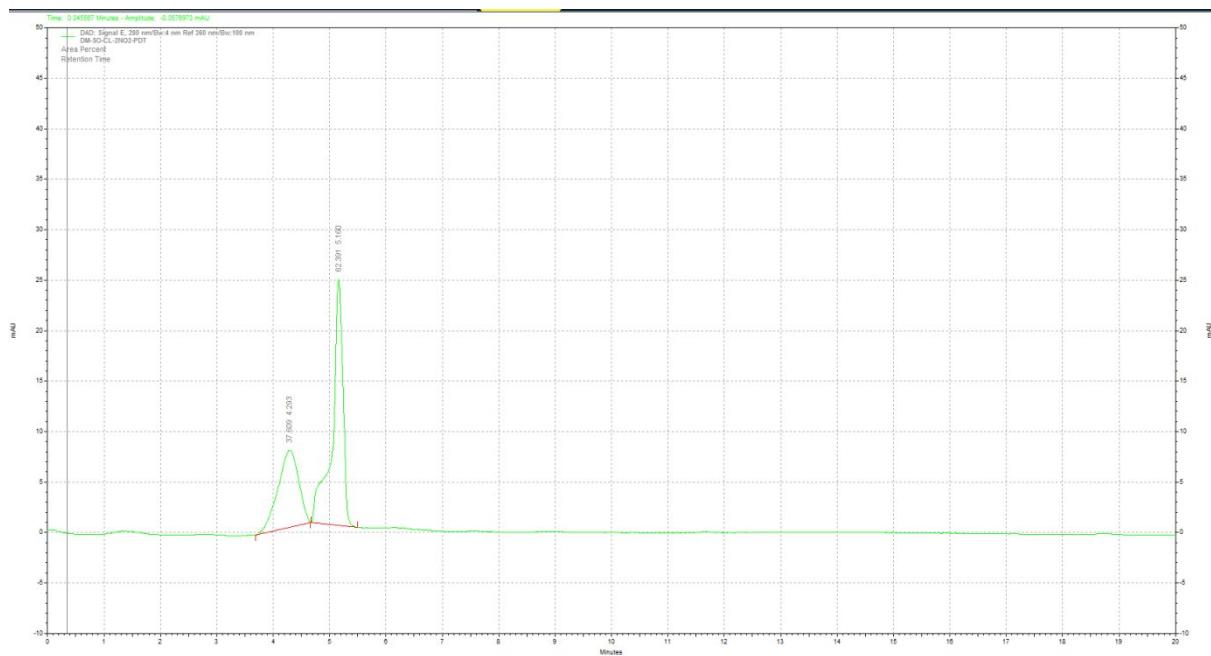
### Methyl 2-((2-chlorophenyl)thio)benzoate (2x): HPLC of isolated material



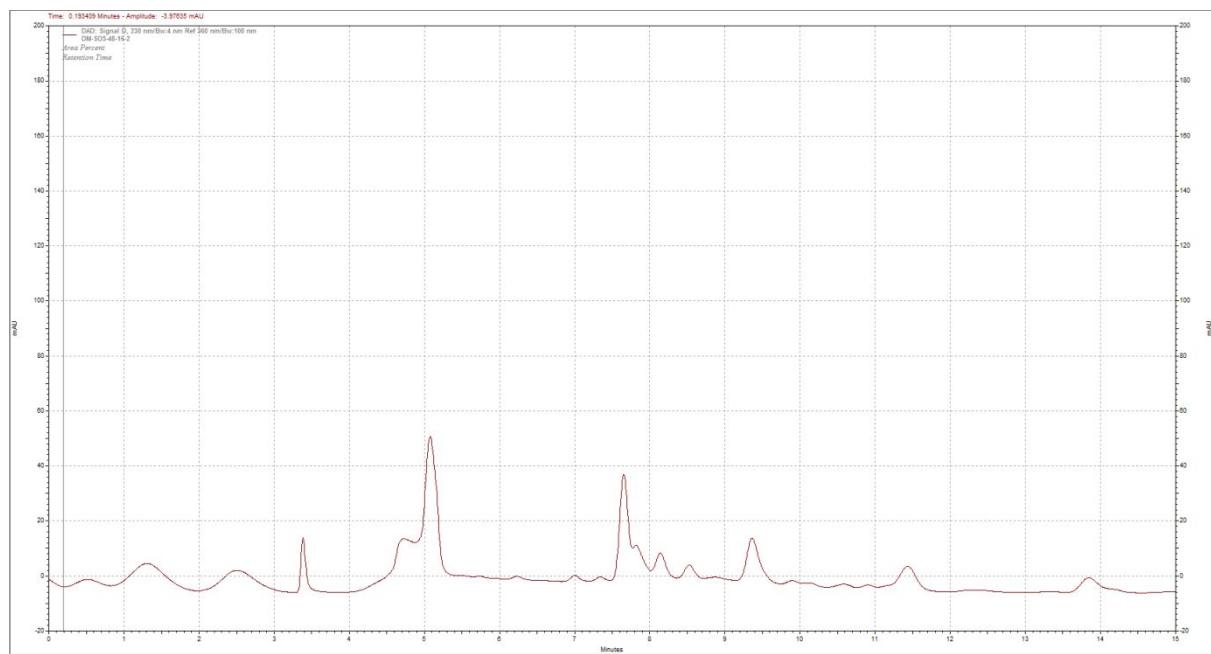
### HPLC of crude reaction mixture



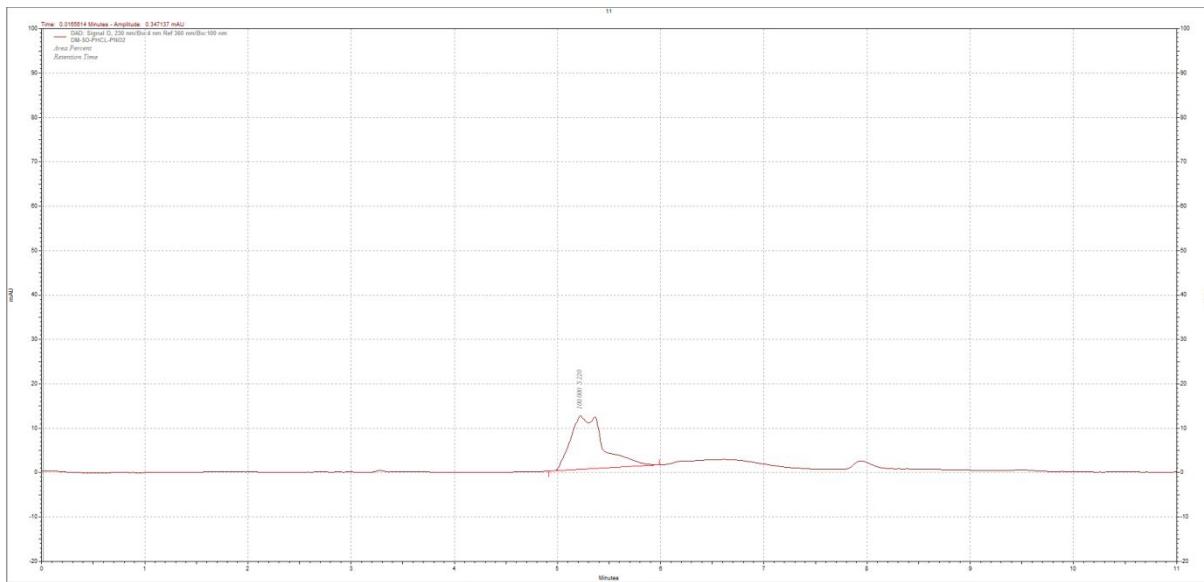
**(2-Chlorophenyl)(2-nitrophenyl)sulfane (2y): HPLC of isolated material**



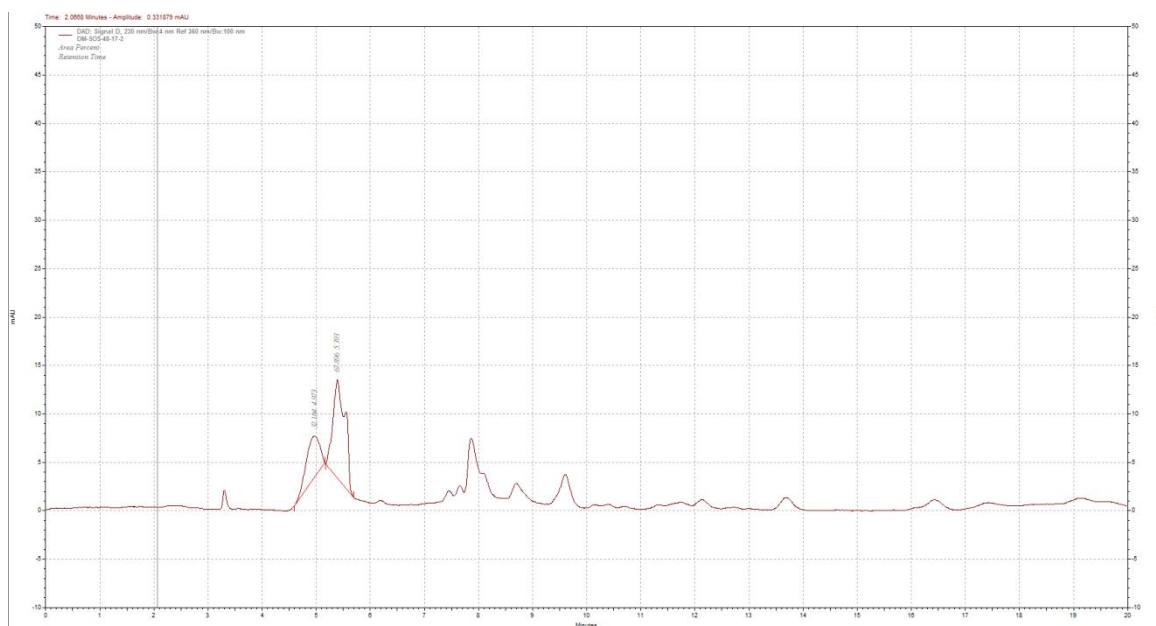
**HPLC of crude reaction mixture**



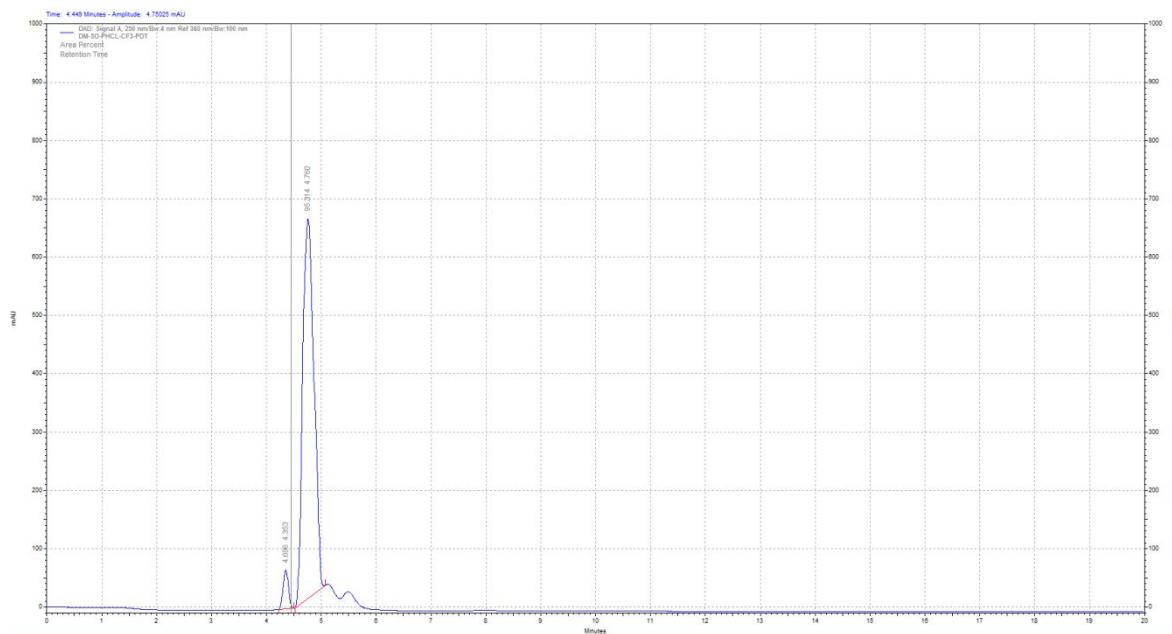
### (3-Chlorophenyl)(4-nitrophenyl)sulfane (2z): HPLC of isolated material



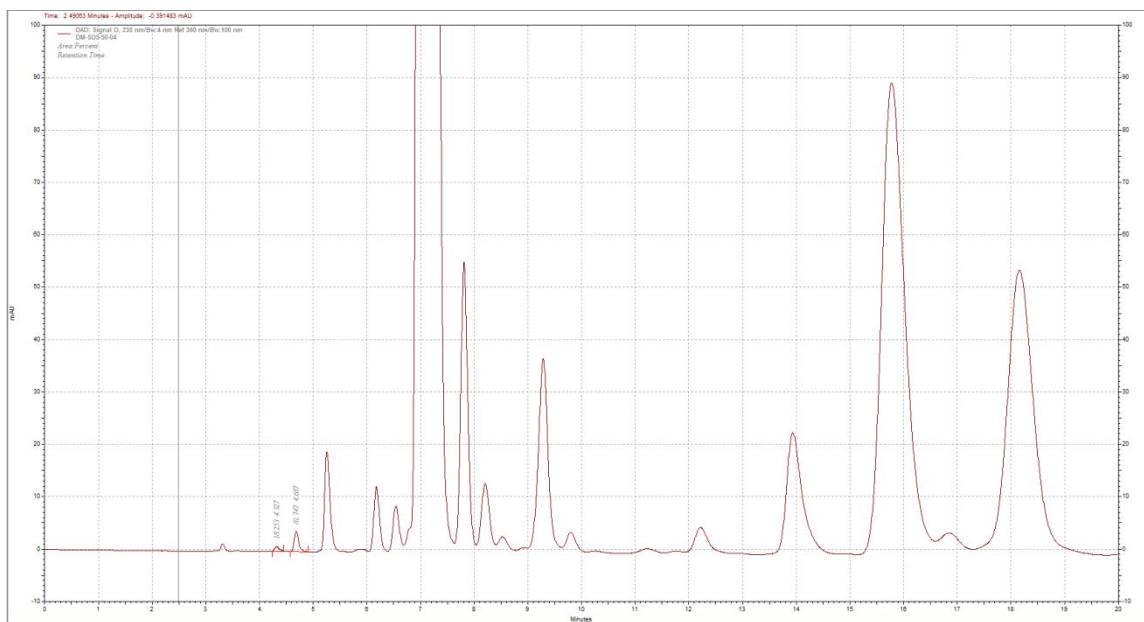
### HPLC of crude reaction mixture



**(3-Chlorophenyl)(4-(trifluoromethyl)phenyl)sulfane (*meta:others* 4.5:1) (2aa): HPLC of isolated material**



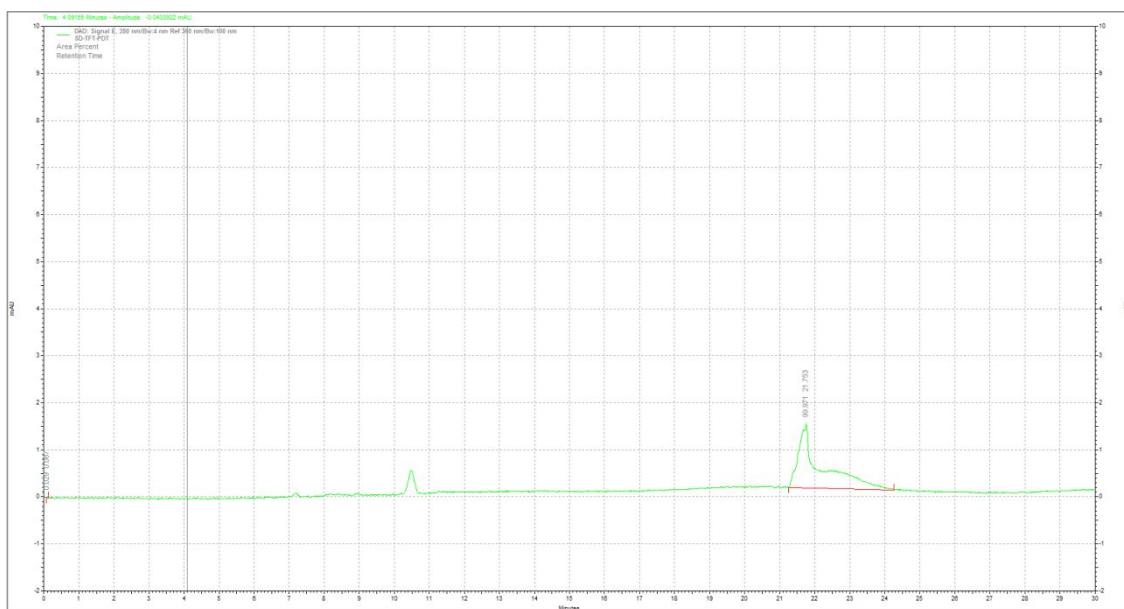
**HPLC of crude reaction mixture**



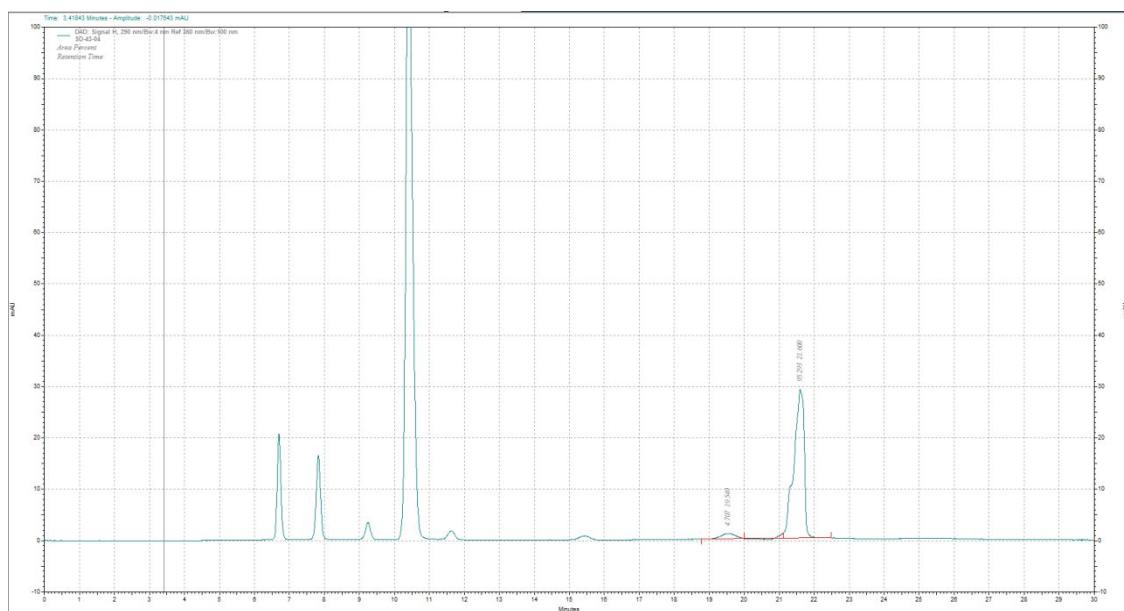
DAD: Signal D,  
230 nm/Bw:4 nm  
Ref 360  
nm/Bw:100 nm  
Results

Retention Time	Area	Area %	Height	Height %
4.327	10325	18.25	1770	18.10
4.687	46242	81.75	8011	81.90
Totals	56567	100.00	9781	100.00

**Phenyl(3-(trifluoromethyl)phenyl)sulfane (*meta*:*others* > 20:1) (2ab): HPLC of isolated material**



**HPLC of crude reaction mixture**



DAD: Signal H,

290 nm/Bw:4 nm

Ref 360

nm/Bw:100 nm

Results

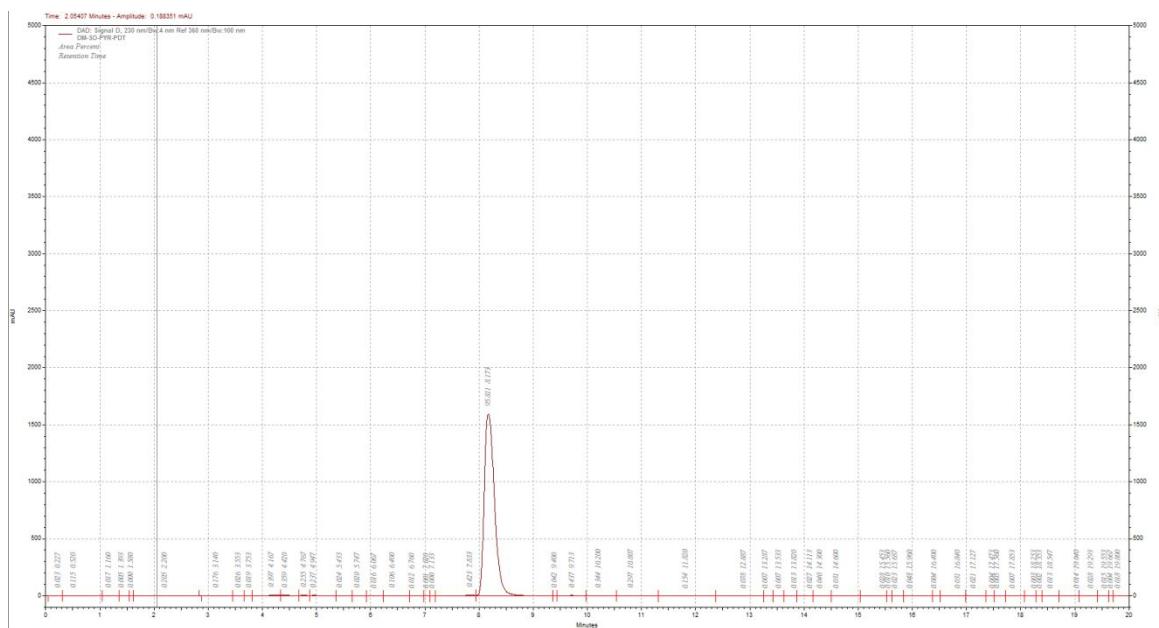
Retention Time	Area	Area %	Height	Height %
19.540	61510	4.71	2204	3.49
21.600	1245381	95.29	60872	96.51

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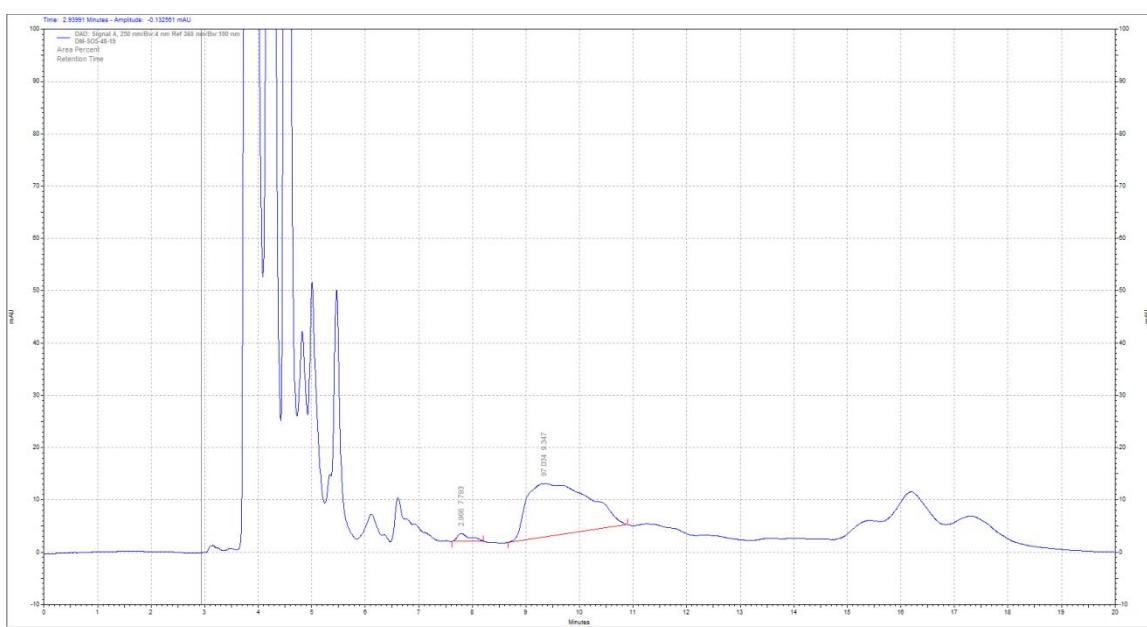
1

Totals	1306891	100.00	63076	100.00
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### 3-(*p*-Tolylthio)pyridine (*C3:others >30:1*) (3a): HPLC of isolated material



### HPLC of crude reaction mixture

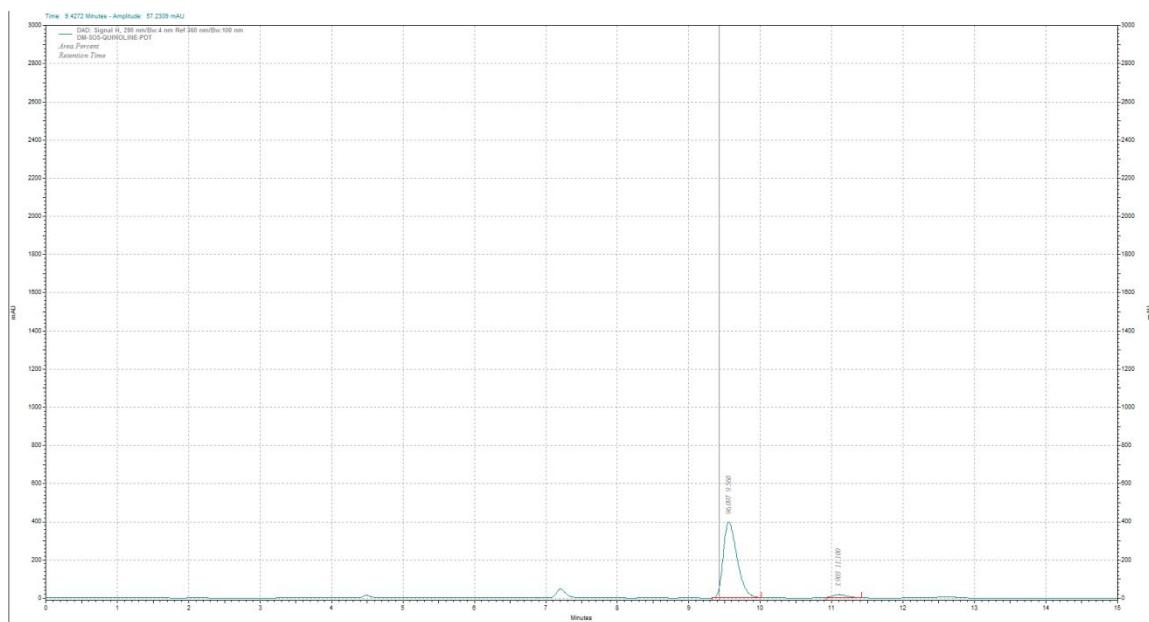


DAD: Signal A,  
250 nm/Bw:4 nm  
Ref 360  
nm/Bw:100 nm  
Results

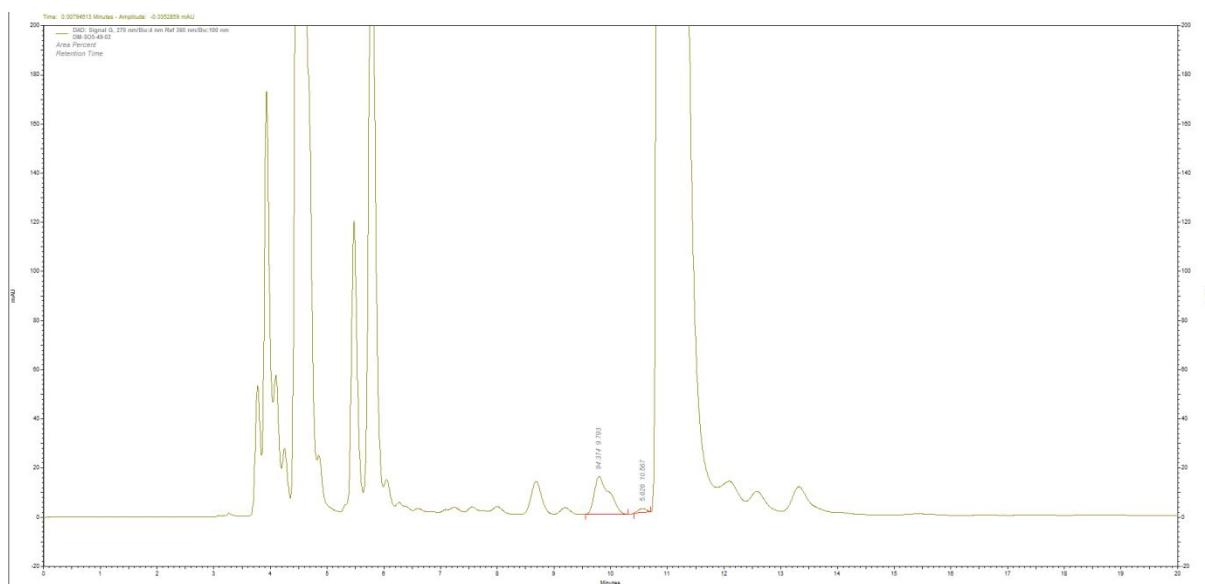
Retention Time	Area	Area %	Height	Height %
7.793	52013	2.97	3151	12.77
9.347	1701805	97.03	21531	87.23

Totals	1753818	100.00	24682	100.00
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**3-(Phenylthio)quinoline (*C*3:*others* = 17:1) (3c): HPLC of isolated material**



**HPLC of crude reaction mixture**



DAD: Signal G,  
270 nm/Bw:4 nm

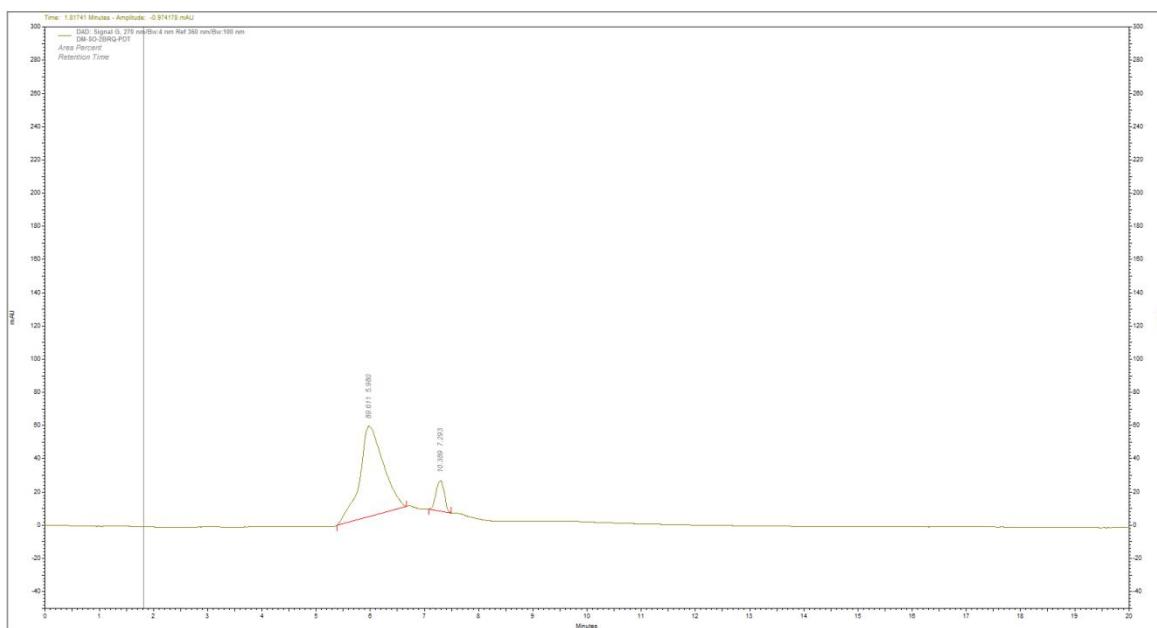
Ref 360  
nm/Bw:100 nm

Results

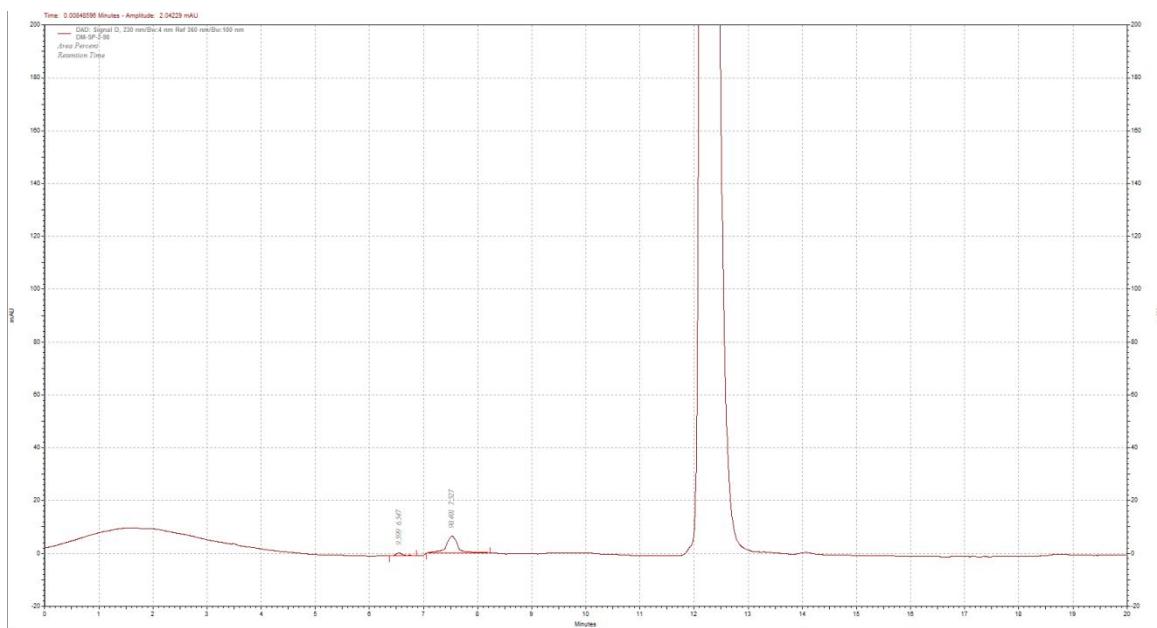
Retention Time	Area	Area %	Height	Height %
<hr/>				
9.793	589214	94.37	32463	90.58
10.567	35128	5.63	3376	9.42
Totals	624342	100.00	35839	100.00

P.

## 2-Bromo-3-(phenylthio)quinoline (3d): HPLC of isolated material



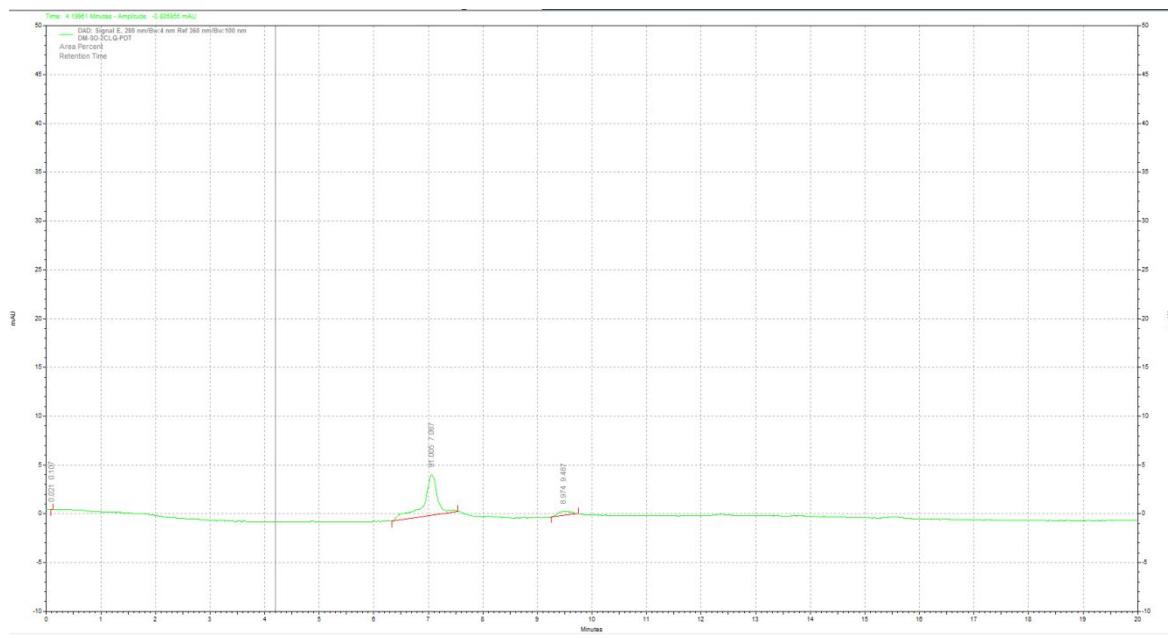
## HPLC of crude reaction mixture



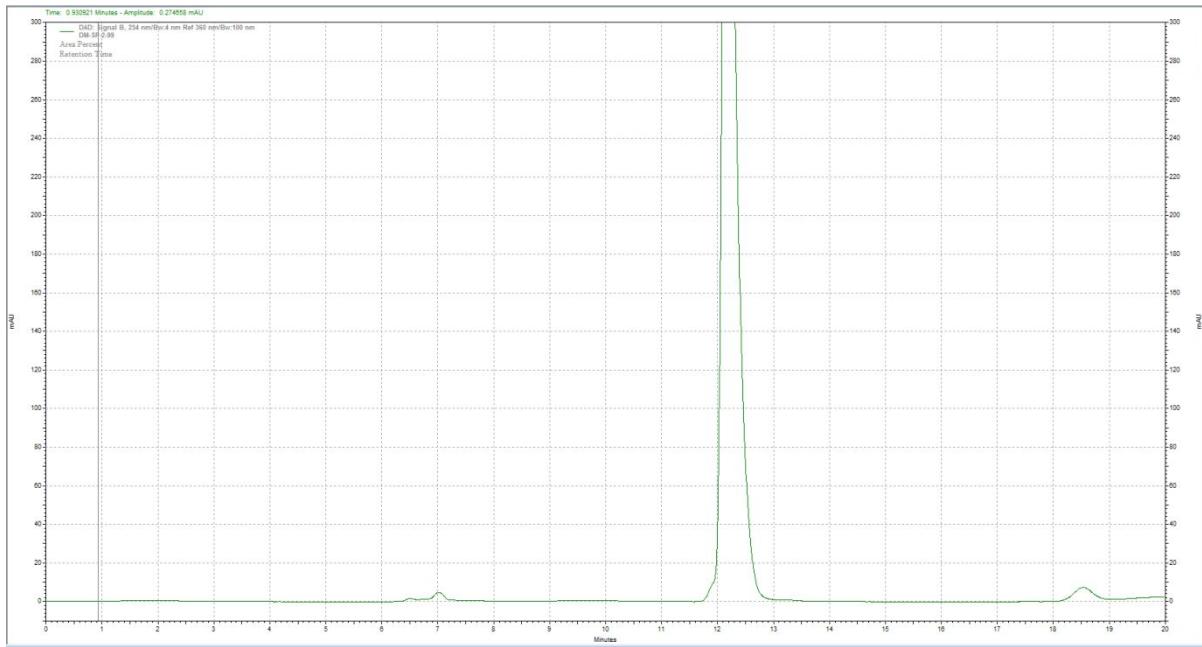
DAD: Signal D,  
 230 nm/Bw:4 nm  
 Ref 360  
 nm/Bw:100 nm  
 Results

Retention Time	Area	Area %	Height	Height %
6.547	22287	9.60	2223	14.10
7.527	209903	90.40	13544	85.90
Totals	232190	100.00	15767	100.00

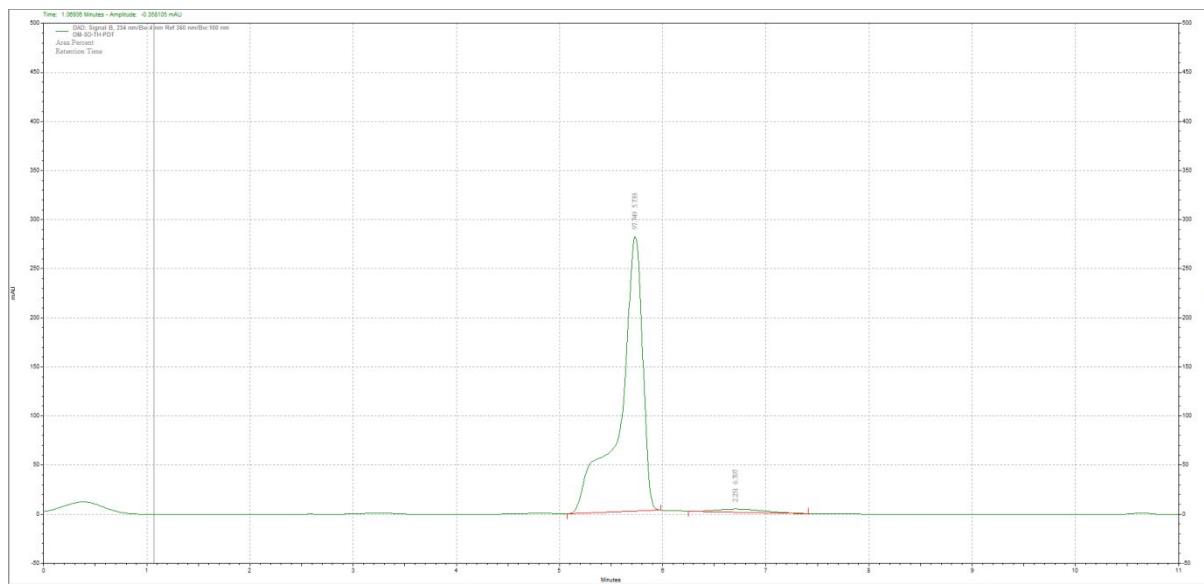
### 2-Chloro-3-(phenylthio)quinoline (3e): HPLC of isolated material



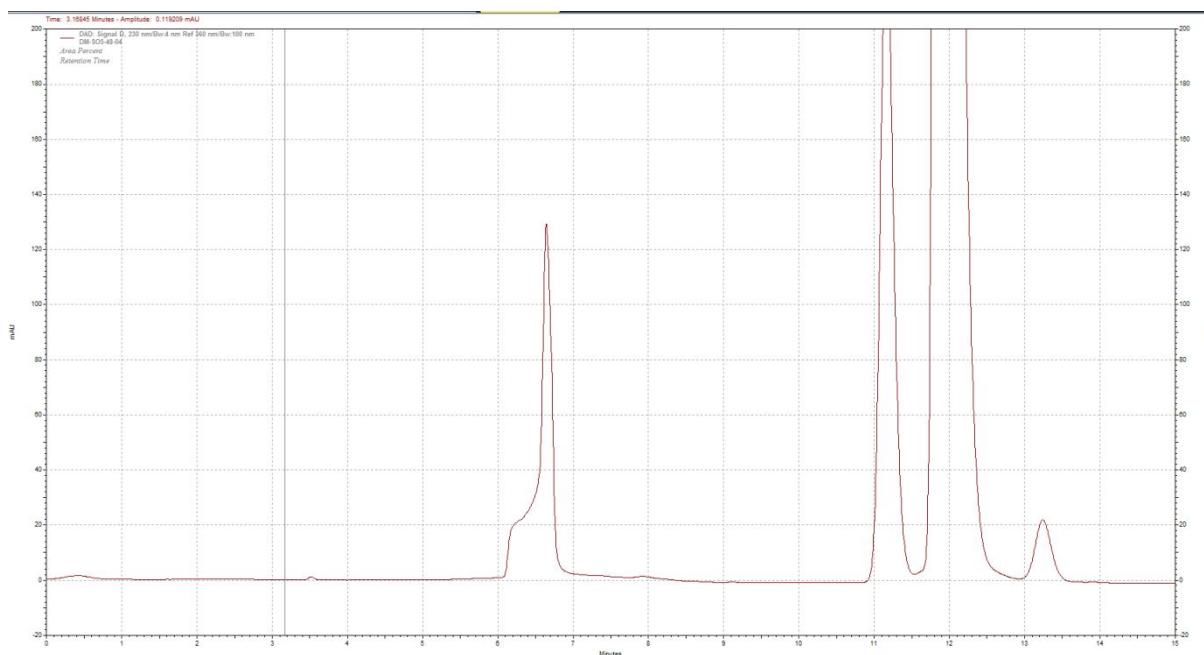
## HPLC of crude reaction mixture



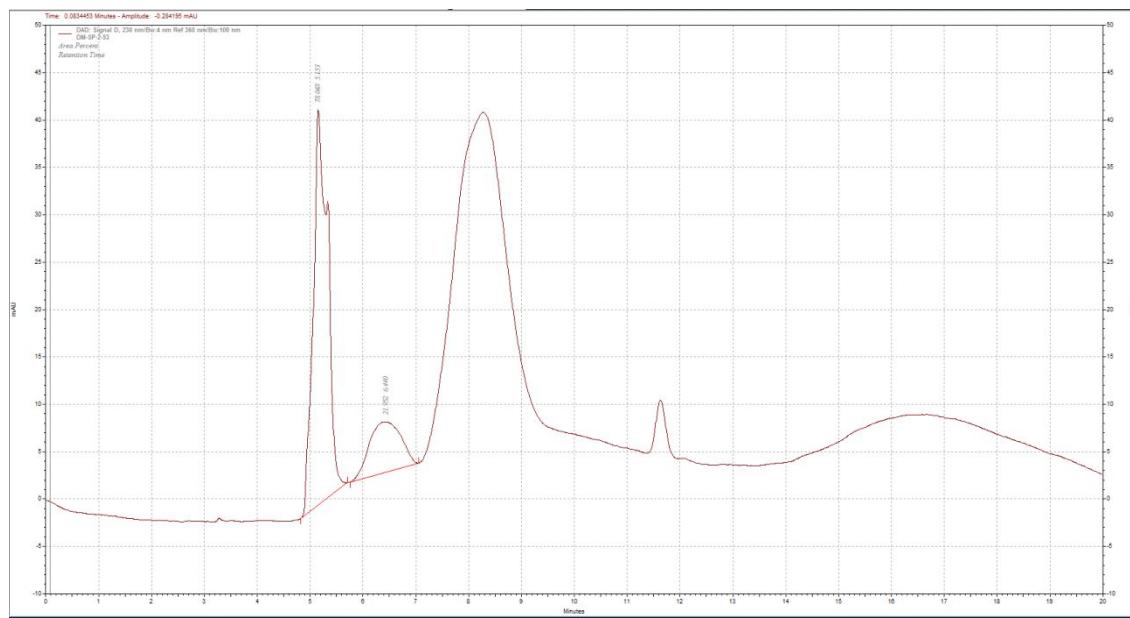
## 2-(Phenylthio)thiophene (3g): HPLC of isolated material



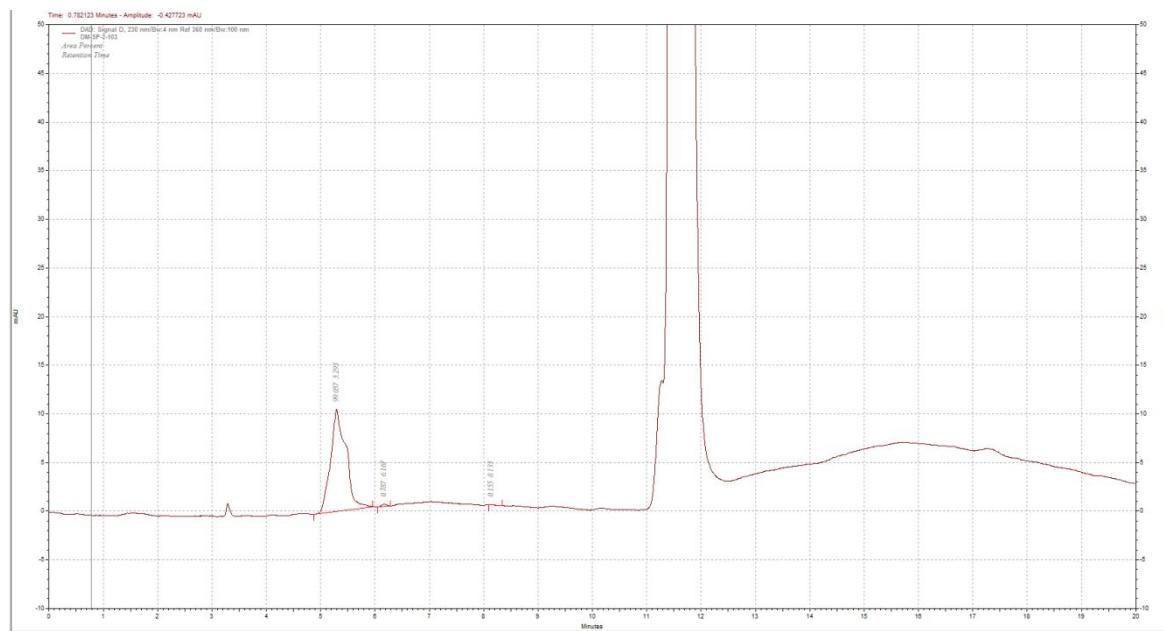
## HPLC of crude reaction mixture



**2-Phenyl-5-(phenylthio)thiophene (*C*5:*others* >30:1) (3j): HPLC of isolated material**



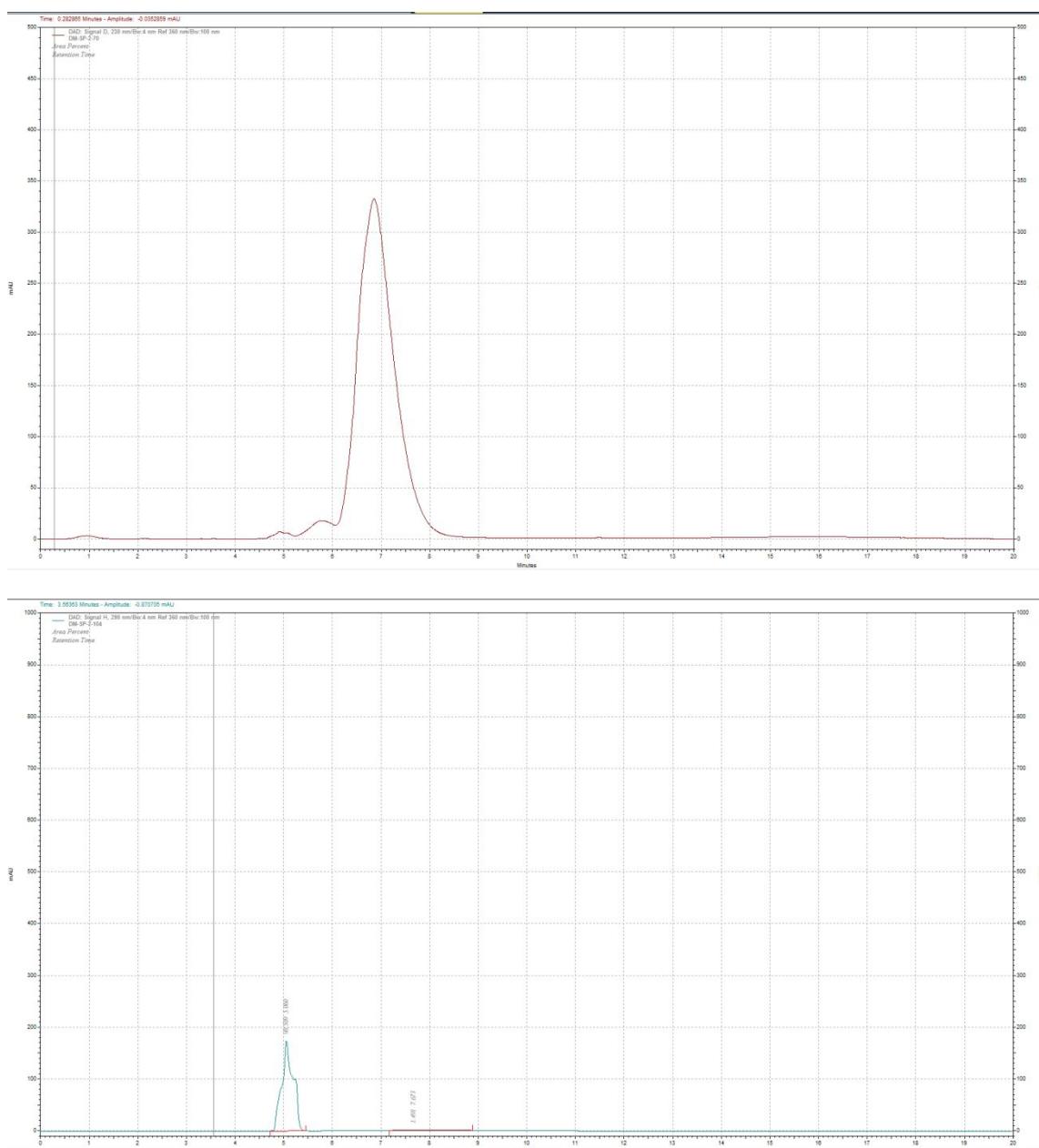
**HPLC of crude reaction mixture**



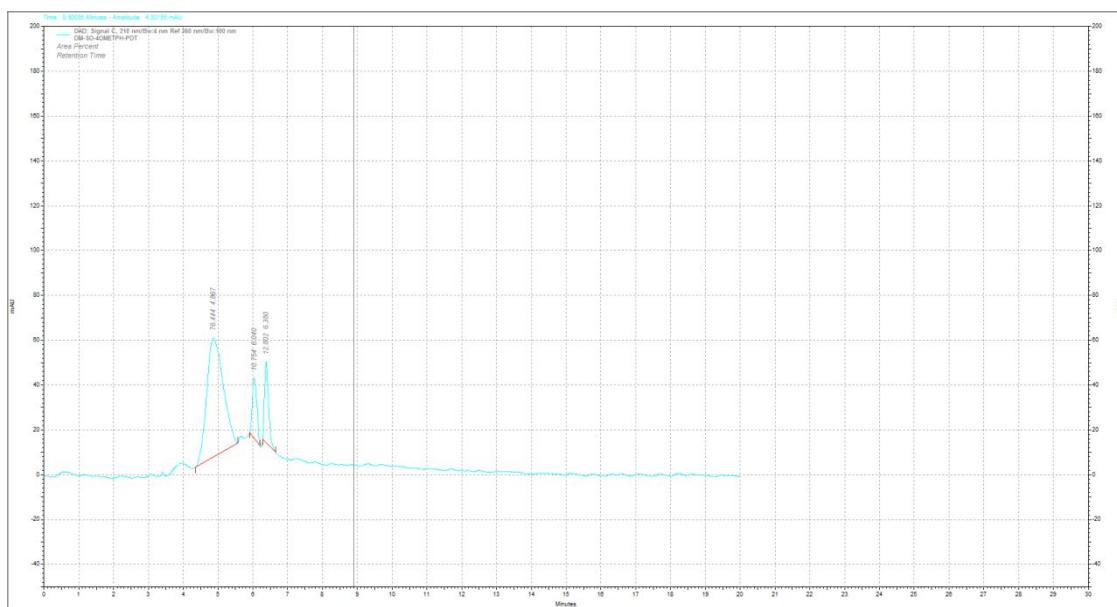
DAD: Signal D,  
230 nm/Bw:4 nm  
Ref 360  
nm/Bw:100 nm  
Results

Retention Time	Area	Area %	Height	Height %
5.293	429608	99.06	21988	97.27
6.167	3414	0.79	512	2.26
8.133	674	0.16	106	0.47
Totals	433696	100.00	22606	100.00

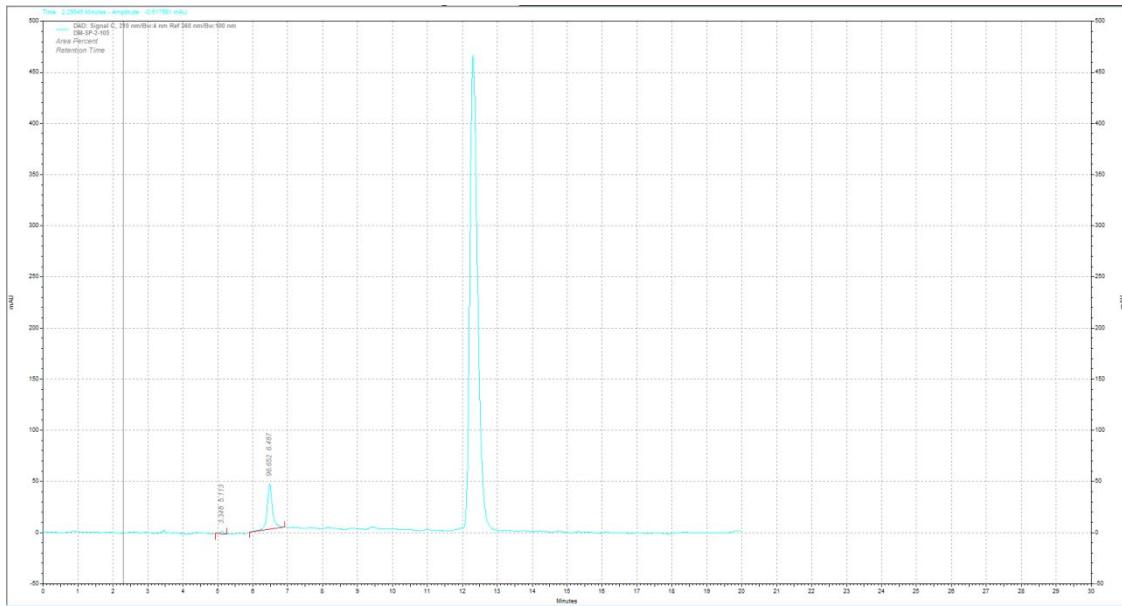
### 2-((4-Methoxyphenyl)thio)-5-phenylthiophene (*C5:others >30:1*) (3k):



**2-(4-Methoxyphenyl)-5-(phenylthio)thiophene (*C*5:*others* >20:1) (3l): HPLC of isolated material**



**HPLC of crude reaction mixture**



DAD: Signal C,

210 nm/Bw:4 nm

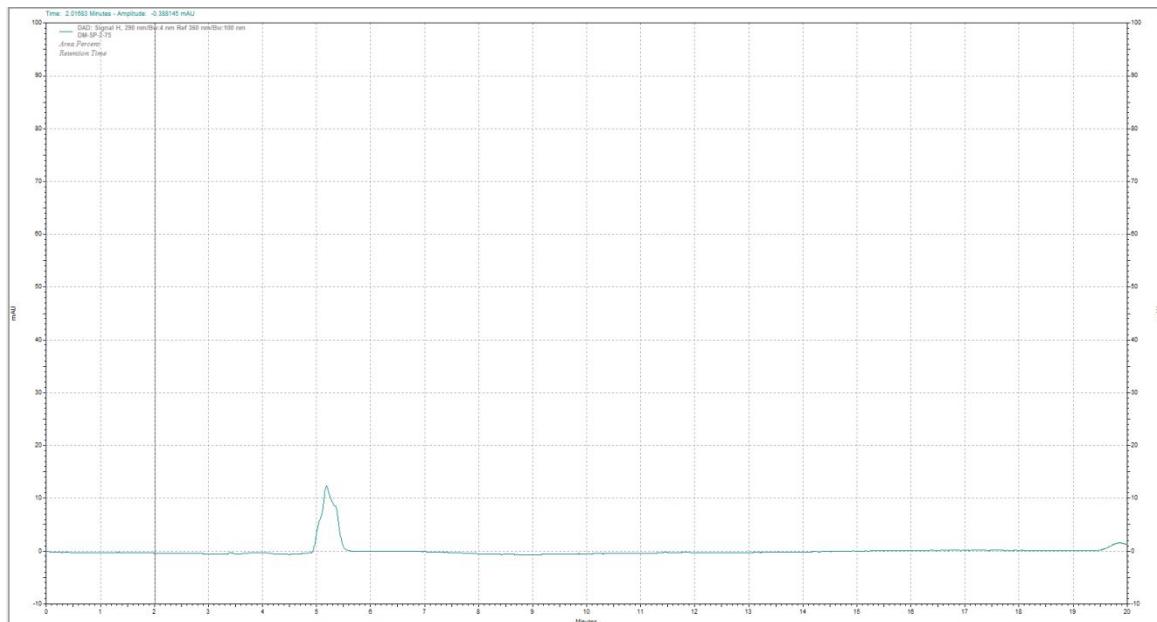
Ref 360

nm/Bw:100 nm

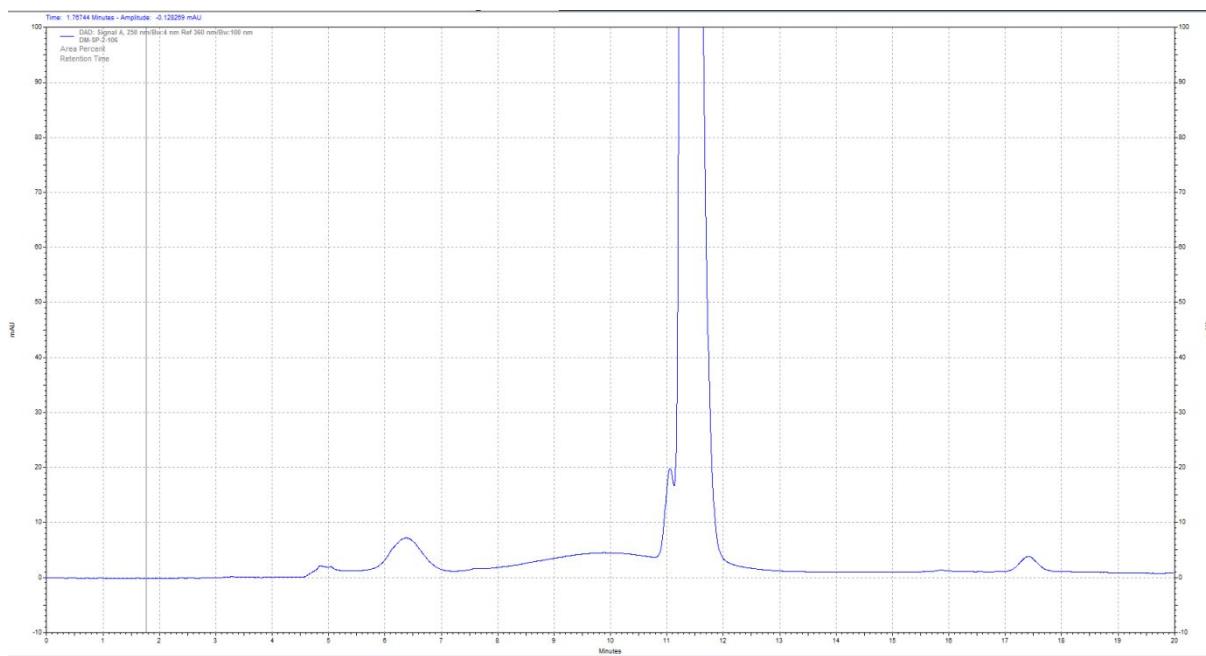
## Results

Retention Time	Area	Area %	Height	Height %
5.113	34396	3.35	4885	4.94
6.487	993087	96.65	94017	95.06
Totals	1027483	100.00	98902	100.00

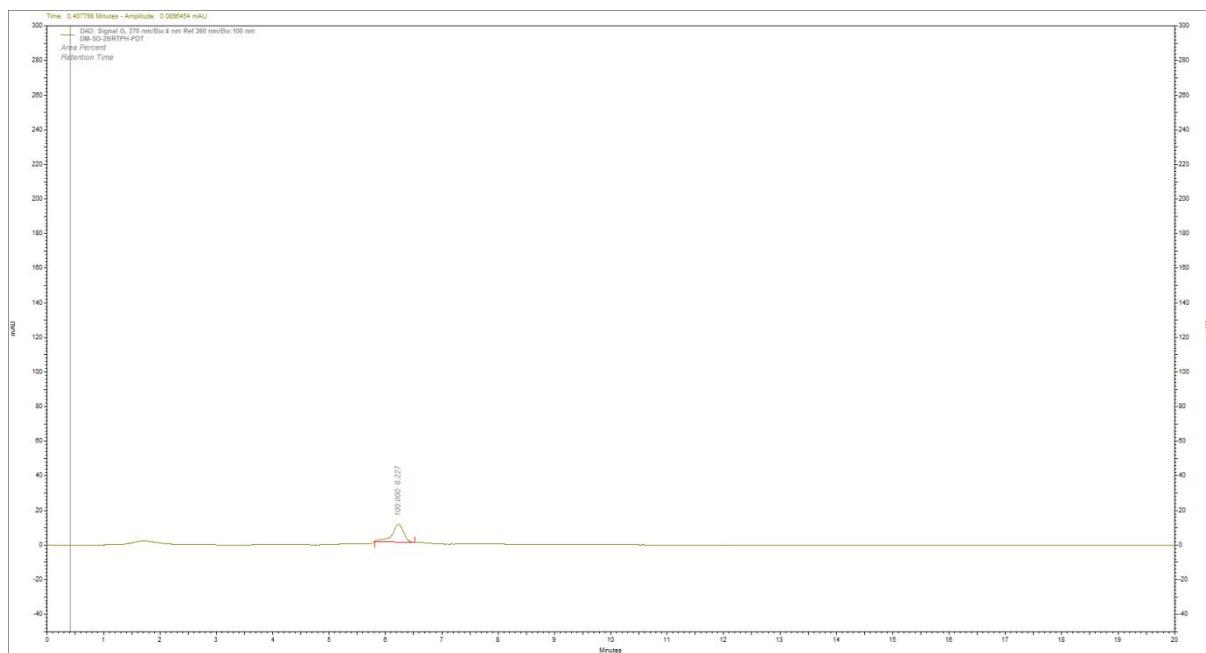
#### 2-(2-Nitrophenyl)-5-(phenylthio)thiophene (3m): HPLC of isolated material



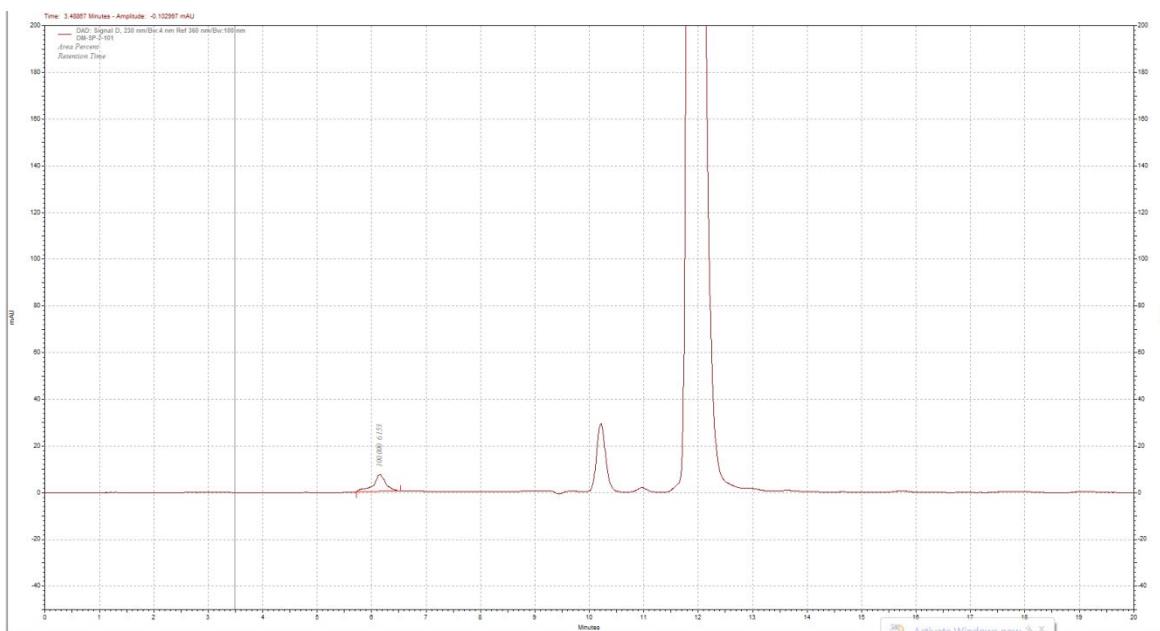
## HPLC of crude reaction mixture



#### 4-Phenyl-2-(phenylthio)thiophene (*C5:others >30:1*) (3n): HPLC of isolated material



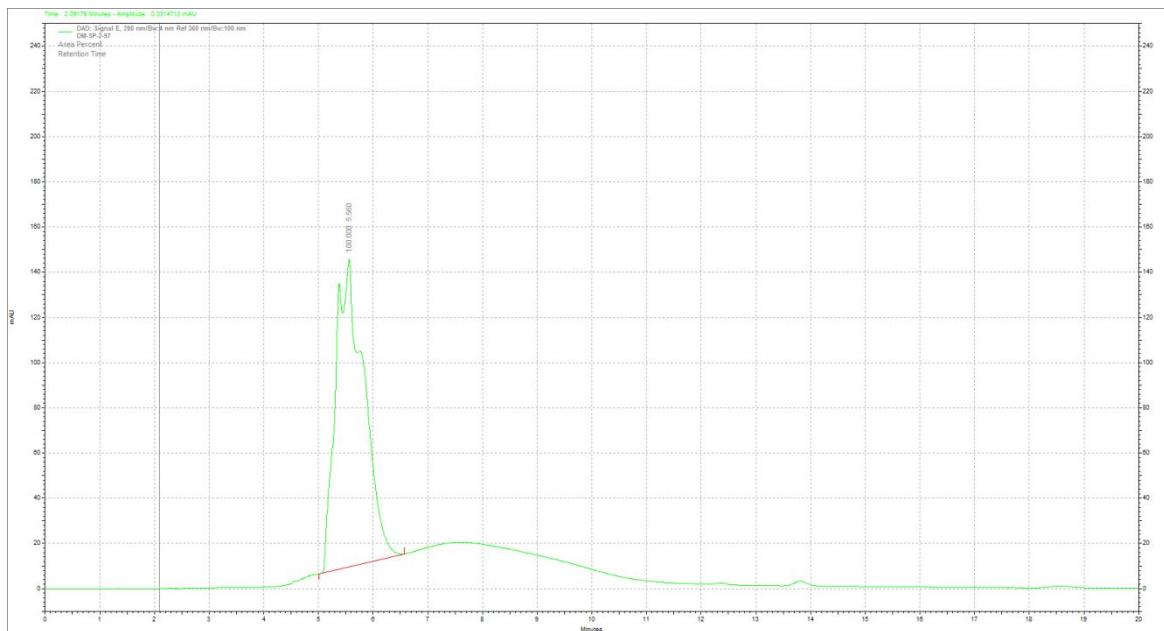
## HPLC of crude reaction mixture



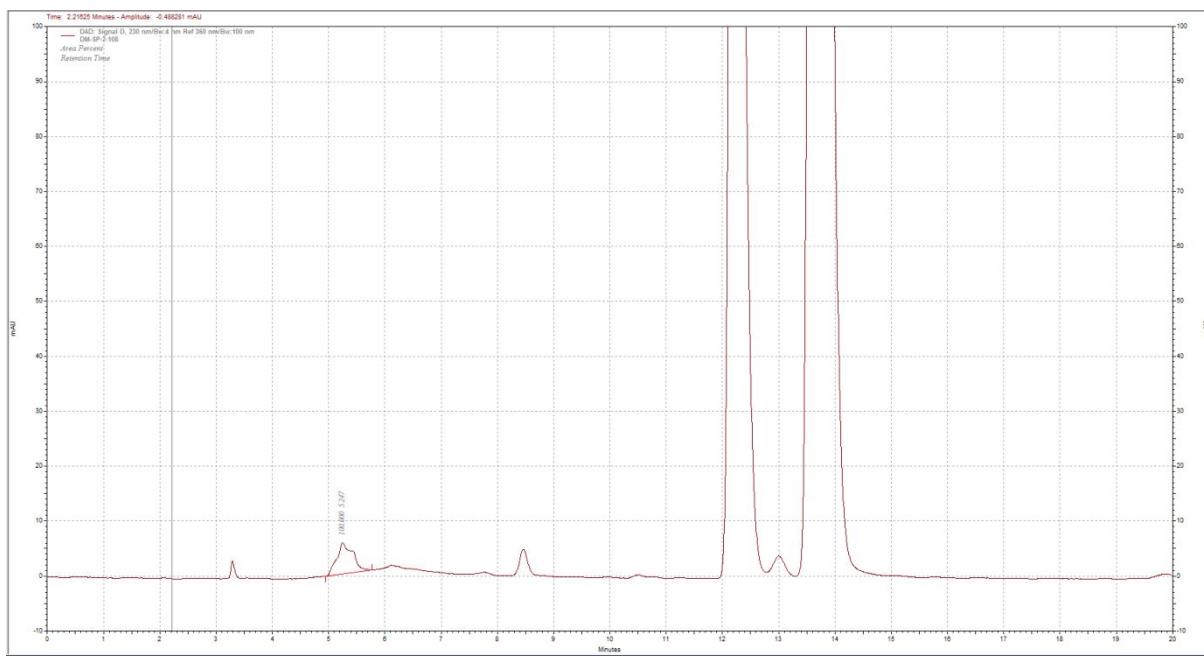
DAD: Signal D,  
230 nm/Bw:4 nm  
Ref 360  
nm/Bw:100 nm  
Results

Retention Time	Area	Area %	Height	Height %
6.153	235696	100.00	15132	100.00
Totals	235696	100.00	15132	100.00

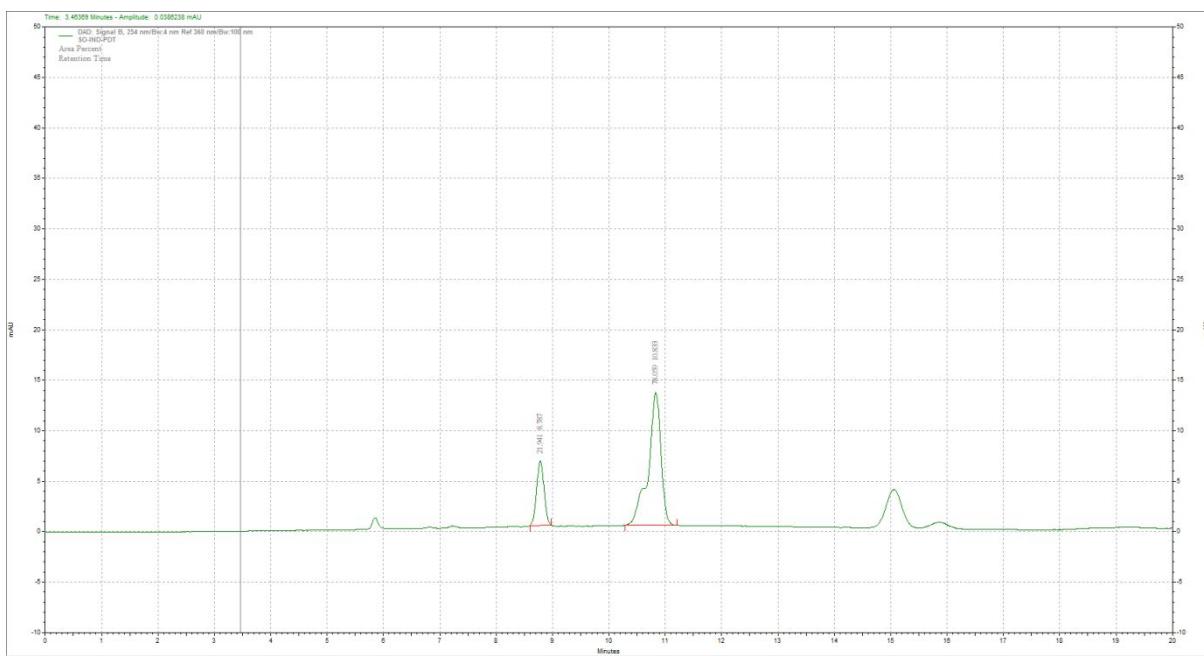
## 4-Phenyl-2-(phenylselanyl)thiophene (*C*5:*others* >30:1) (3o): HPLC of isolated material



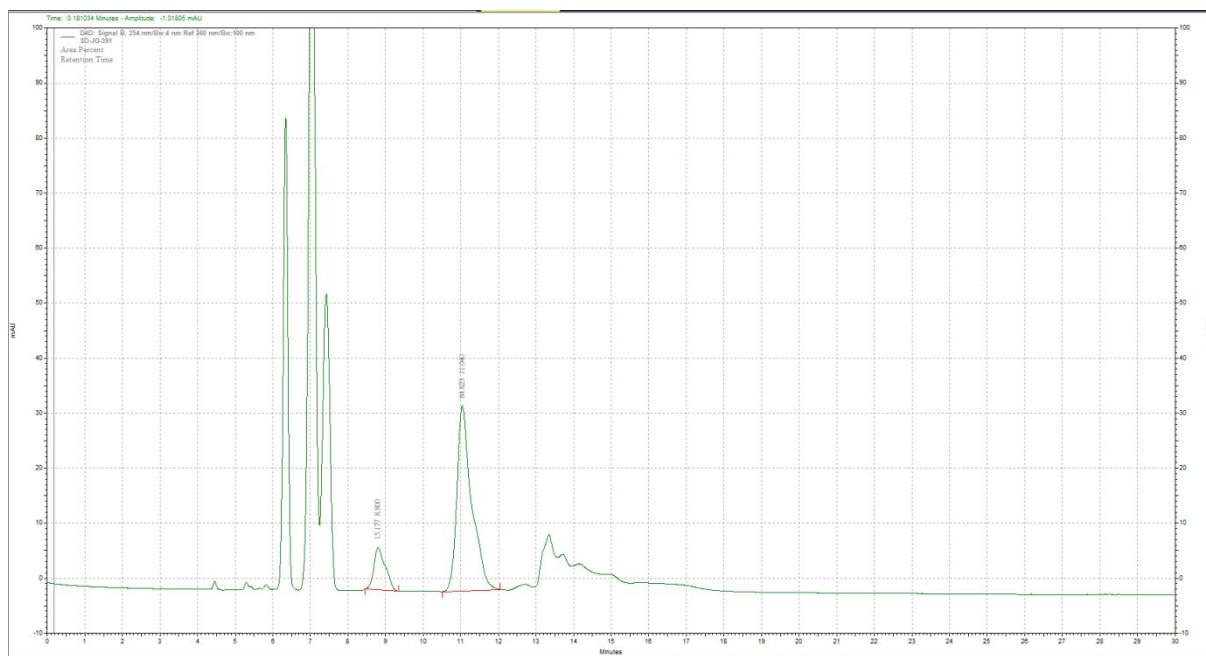
## HPLC of crude reaction mixture



### 1-Methyl-3-(phenylthio)-1H-indole (*C3:others 6:1*) (3q): HPLC of isolated material



### HPLC of crude reaction mixture

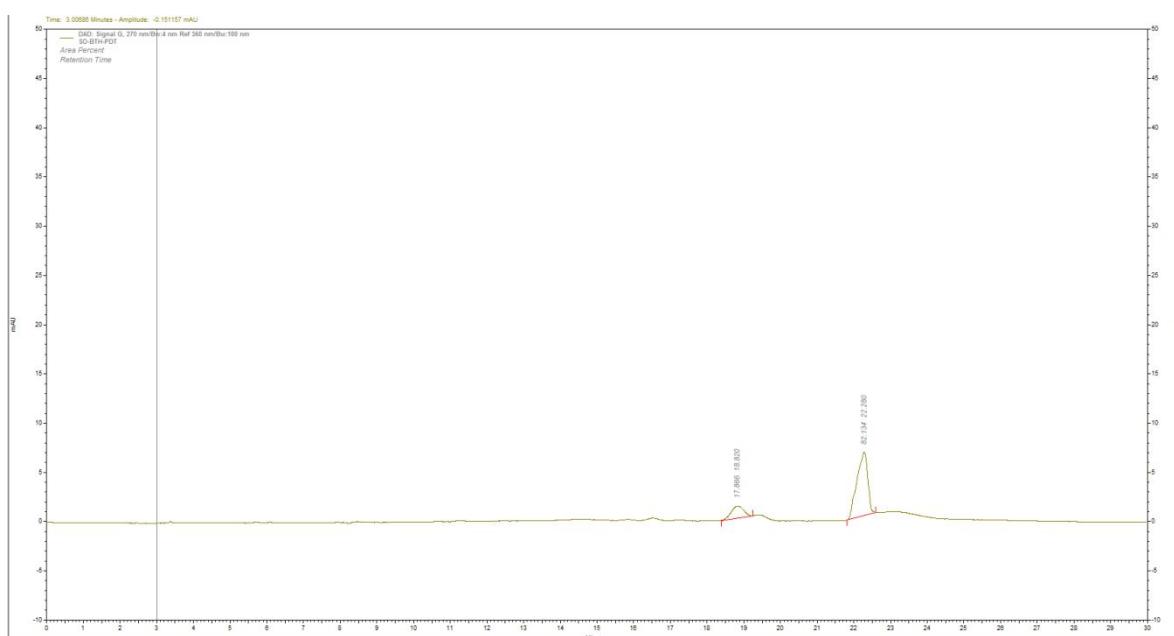


**DAD: Signal B,**  
**254 nm/Bw:4 nm**  
**Ref 360**  
**nm/Bw:100 nm**

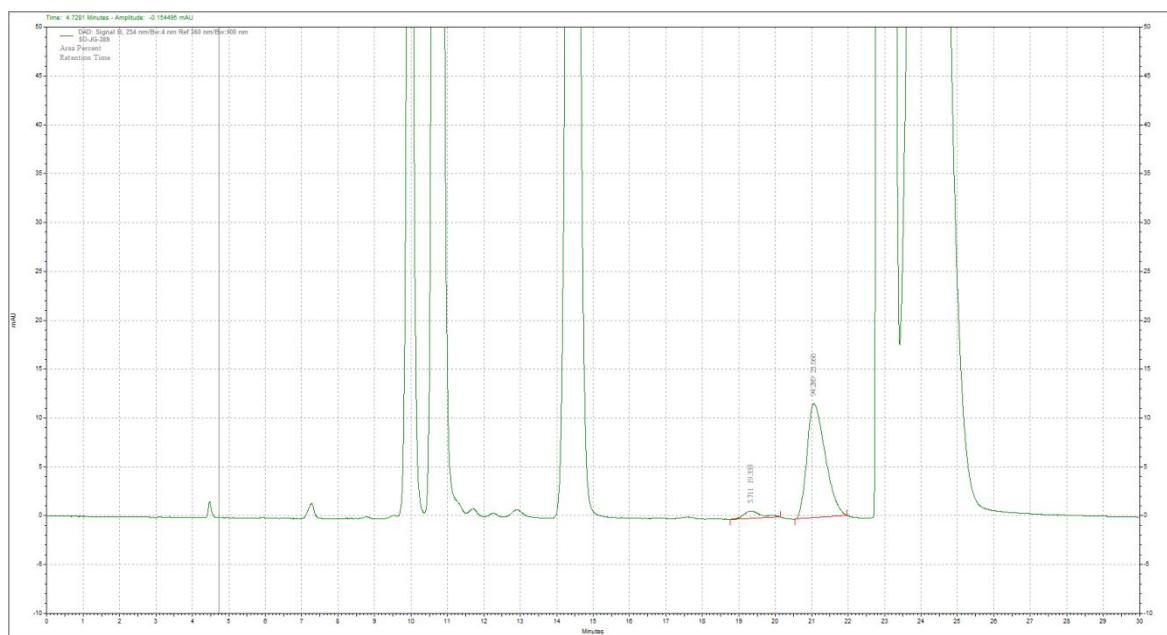
**Results**

Retention Time	Area	Area %	Height	Height %
8.800	343194	15.18	16225	18.70
11.040	1918064	84.82	70562	81.30
<b>Totals</b>	<b>2261258</b>	<b>100.00</b>	<b>86787</b>	<b>100.00</b>

### 3-((4-Methoxyphenyl)thio)benzo[b]thiophene (*C3:others 16:1*) (3r): HPLC of isolated material



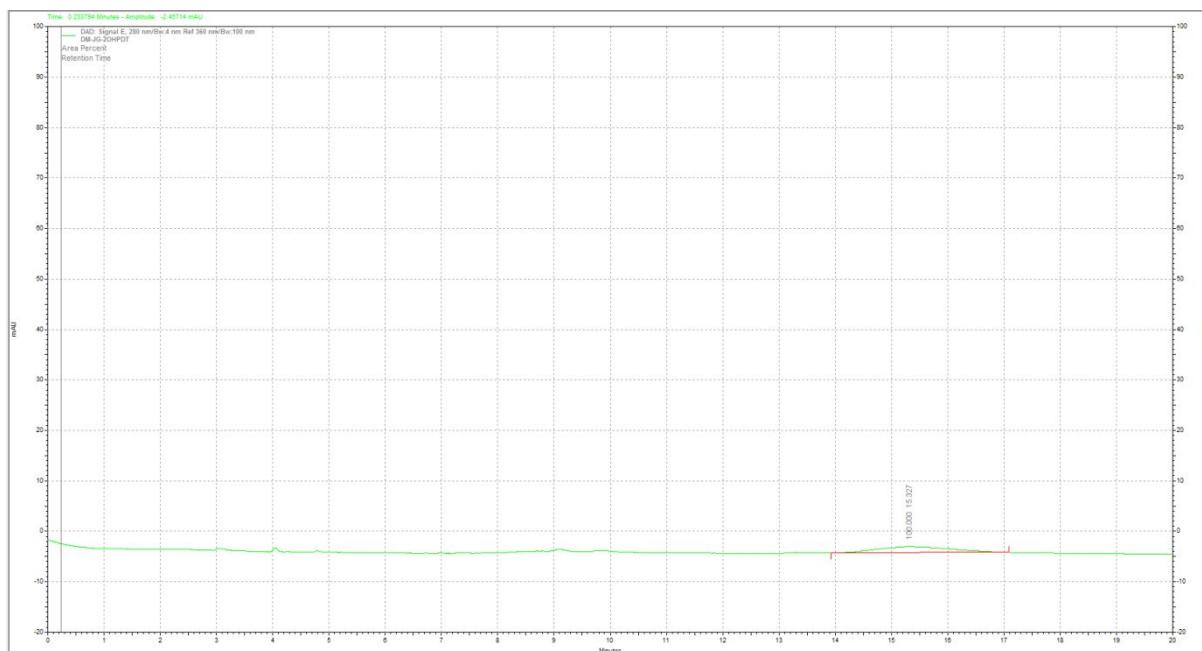
## HPLC of crude reaction mixture



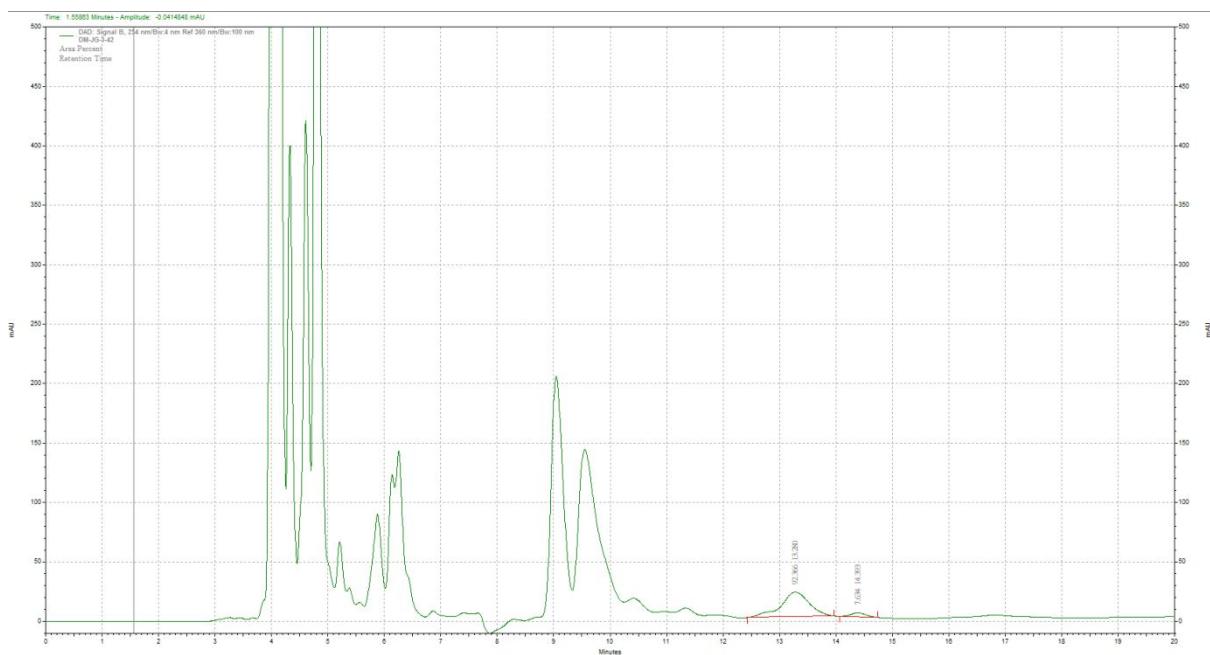
DAD: Signal B,  
 254 nm/Bw:4 nm  
 Ref 360  
 nm/Bw:100 nm  
 Results

Retention Time	Area	Area %	Height	Height %
19.333	51606	5.71	1555	5.97
21.060	852038	94.29	24494	94.03
<b>Totals</b>				
	903644	100.00	26049	100.00

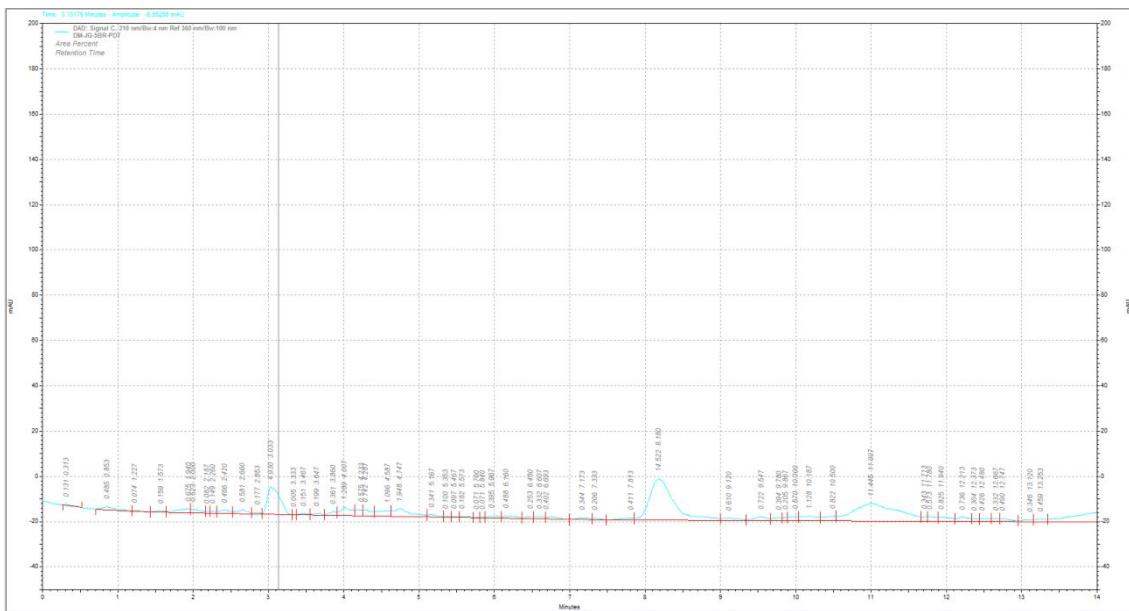
## 3-(Phenylthio)pyridin-2-ol (3w): HPLC of isolated material



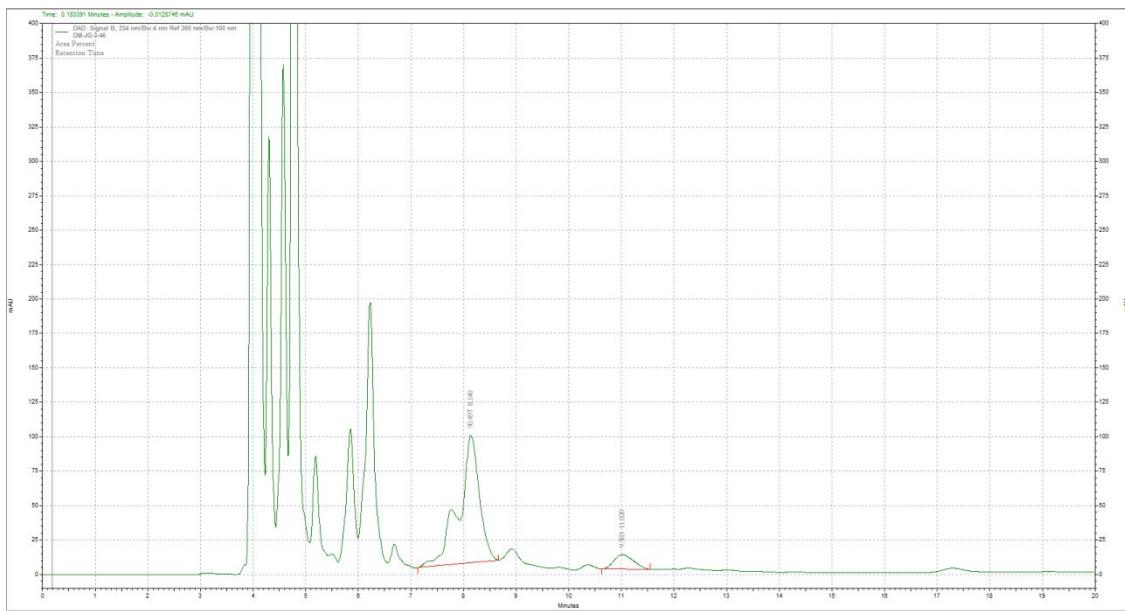
## HPLC of crude reaction mixture



## 5-Bromo-3-(phenylthio)pyridin-2-ol (3x) (C3:others = 10:1): HPLC of isolated material



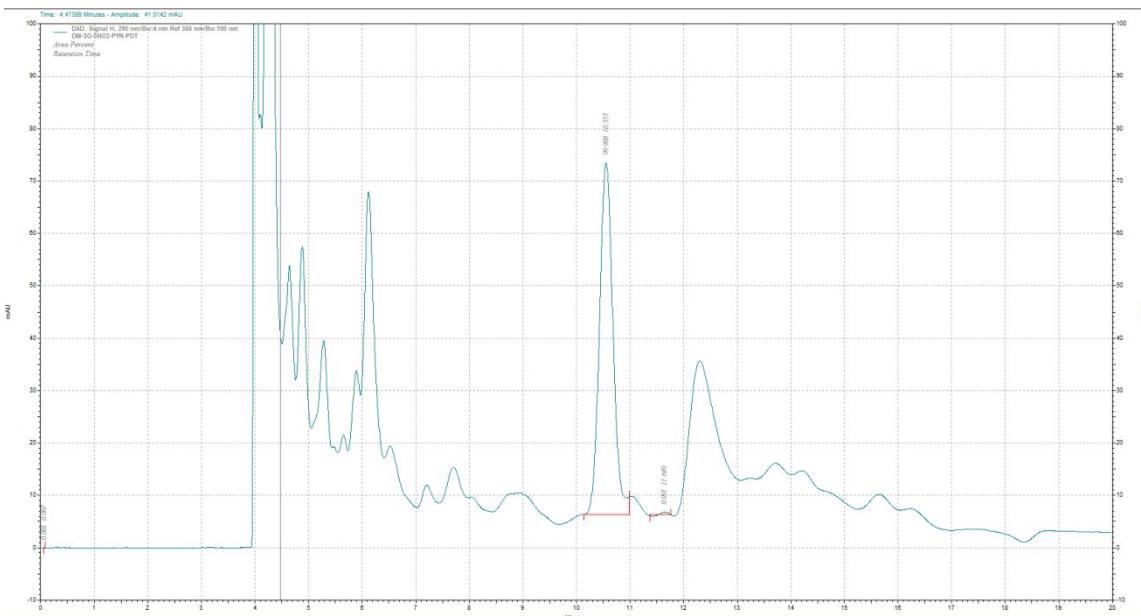
## HPLC of crude reaction mixture



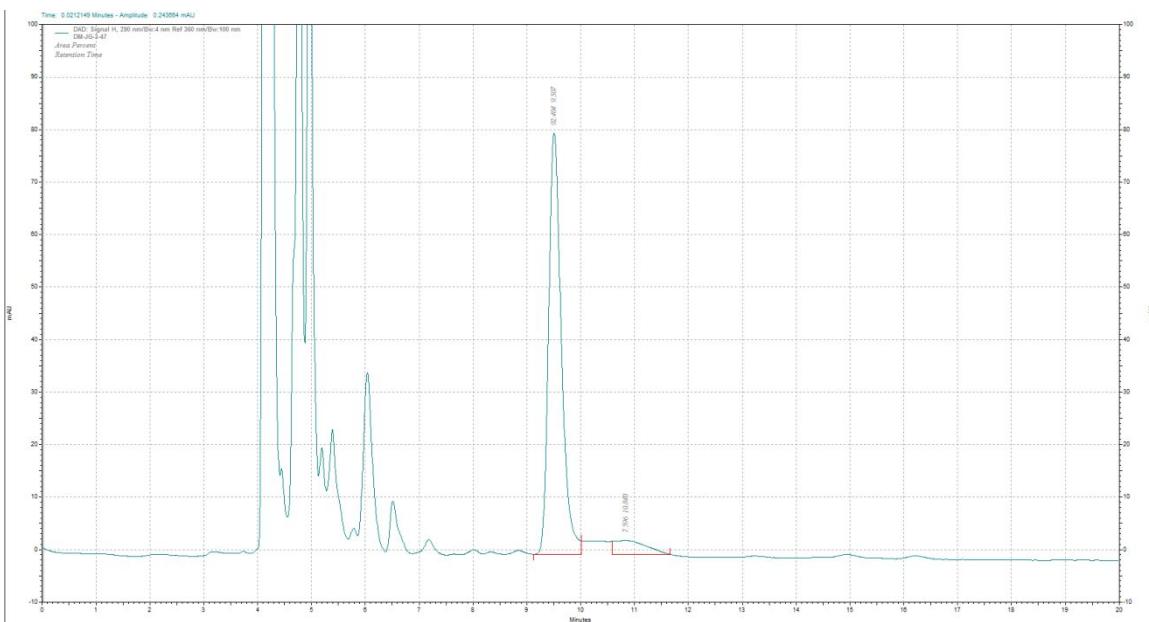
DAD: Signal B,  
254 nm/Bw :4 nm  
Ref 360  
nm/Bw :100 nm  
Results

Retention Time	Area	Area %	Height	Height %
8.140	5293002	90.50	193714	89.84
11.020	555841	9.50	21917	10.16
<b>Totals</b>	<b>5848843</b>	<b>100.00</b>	<b>215631</b>	<b>100.00</b>

### 5-Nitro-3-(phenylthio)pyridin-2-ol (C3:others 12:1) (3aa): HPLC of isolated material



HPLC of crude reaction mixture

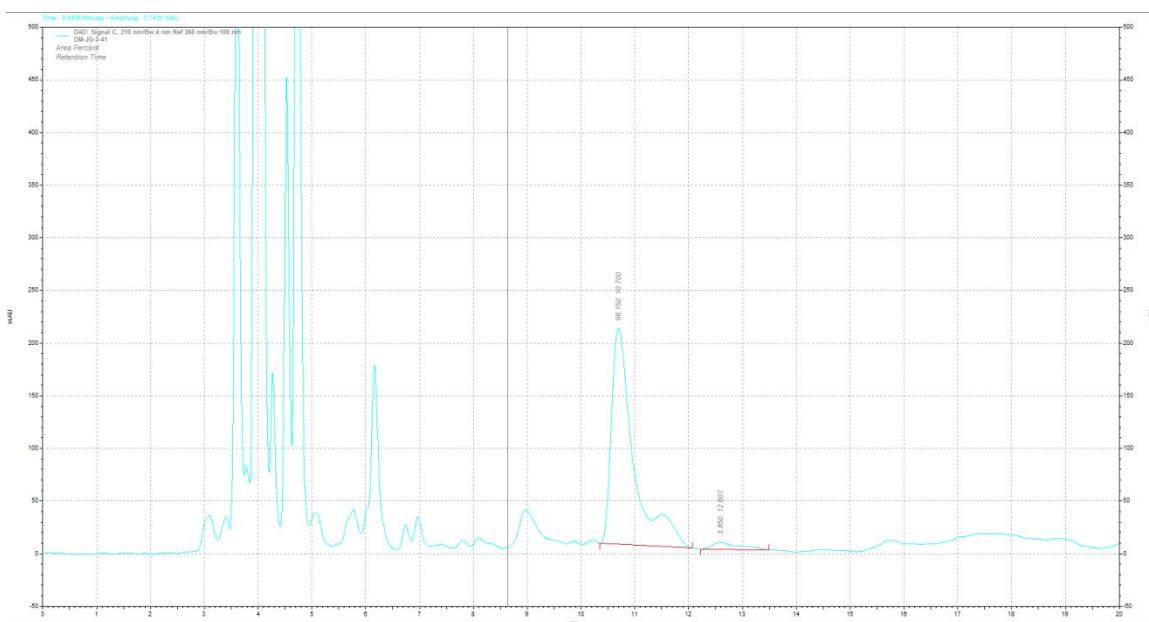


**DAD: Signal H,  
290 nm/Bw:4 nm  
Ref 360  
nm/Bw:100 nm  
Results**

Retention Time	Area	Area %	Height	Height %
9.507	2769791	92.40	168284	96.82
10.840	227680	7.60	5523	3.18

Totals	2997471	100.00	173807	100.00
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### 6-Methyl-3-(phenylthio)pyridin-2-ol (3ac): HPLC of crude reaction mixture



DAD: Signal C,

210 nm/Bw:4 nm

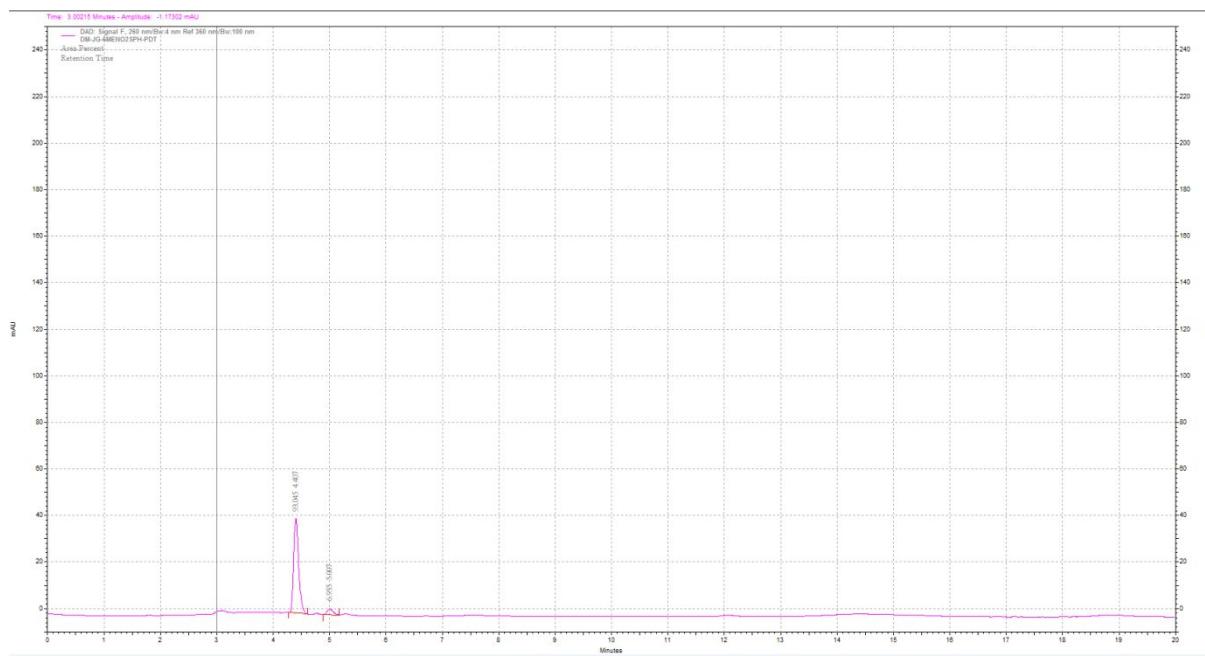
Ref 360

nm/Bw:100 nm

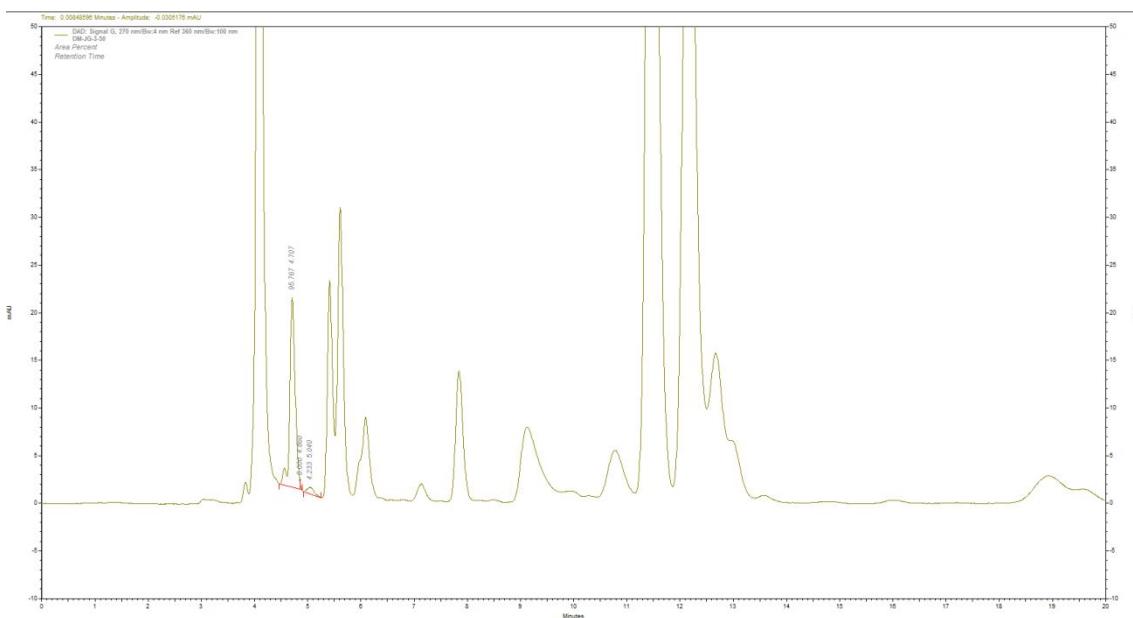
Results

Retention Time	Area	Area %	Height	Height %
10.700	12351166	96.15	430587	96.80
12.607	494516	3.85	14219	3.20
Totals	12845682	100.00	444806	100.00

**6-Methyl-3-((3-nitrophenyl)thio)pyridin-2-ol (*C3:others >20:1*) (3ad): HPLC of isolated material**



### HPLC of crude reaction mixture



DAD: Signal G,

270 nm/Bw:4 nm

Ref 360

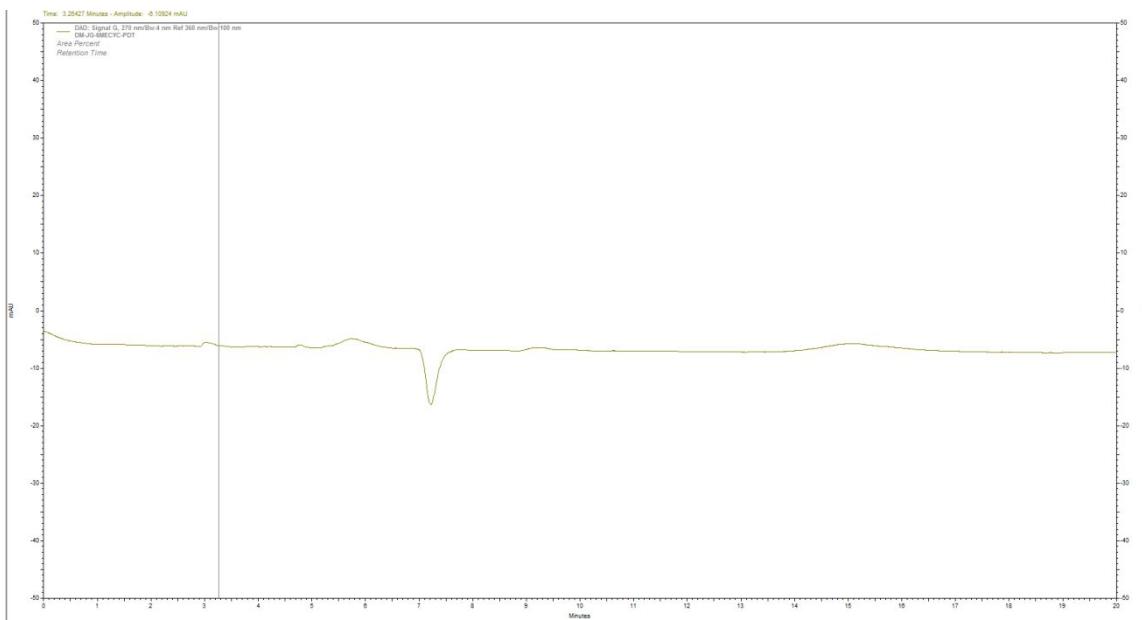
nm/Bw:100 nm

Results

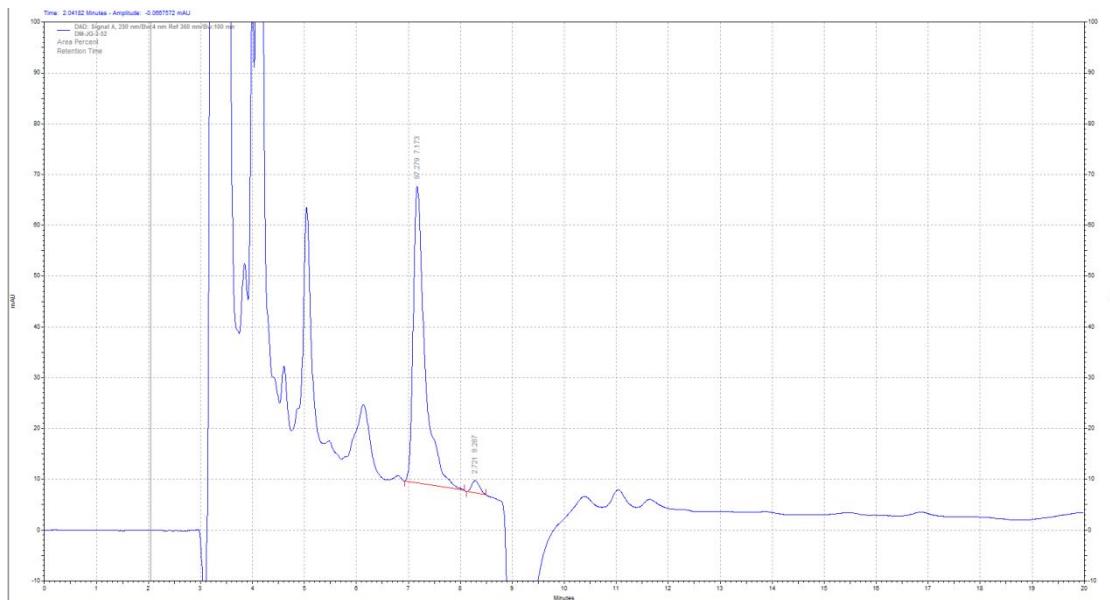
Retention Time	Area	Area %	Height	Height %
4.707	294437	95.77	41673	96.70
4.860	0	0.00	0	0.00
5.040	13015	4.23	1424	3.30

Totals	307452	100.00	43097	100.00
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### 3-(Cyclohexylthio)-6-methylpyridin-2-ol (C3:others >30:1) (3ae): HPLC of isolated material



**HPLC of crude reaction mixture**

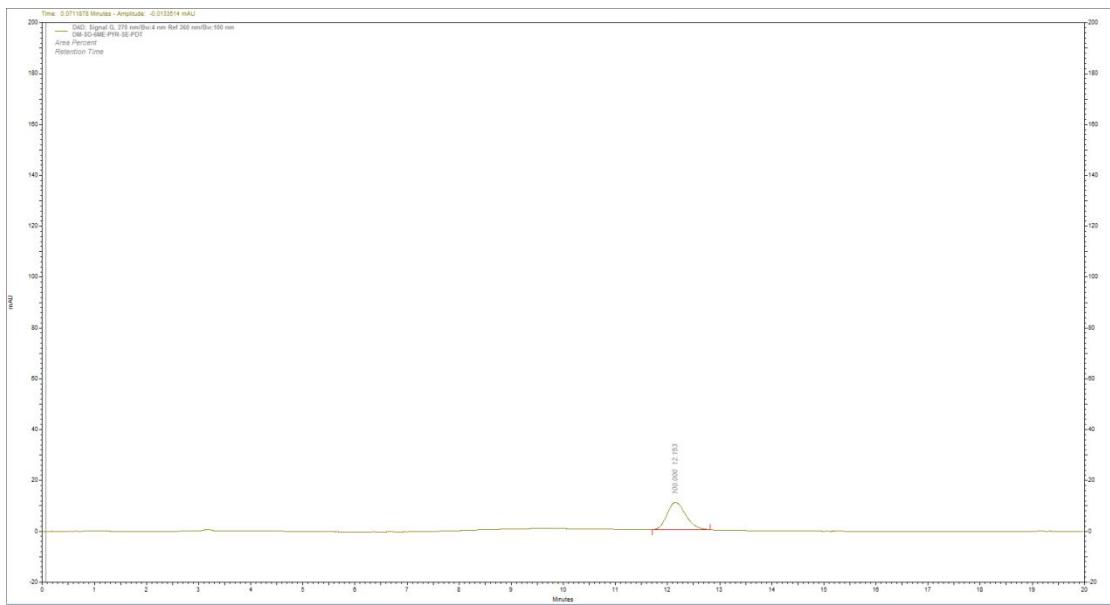


**DAD: Signal A,**  
**250 nm/Bw:4 nm**  
**Ref 360**  
**nm/Bw:100 nm**  
**Results**

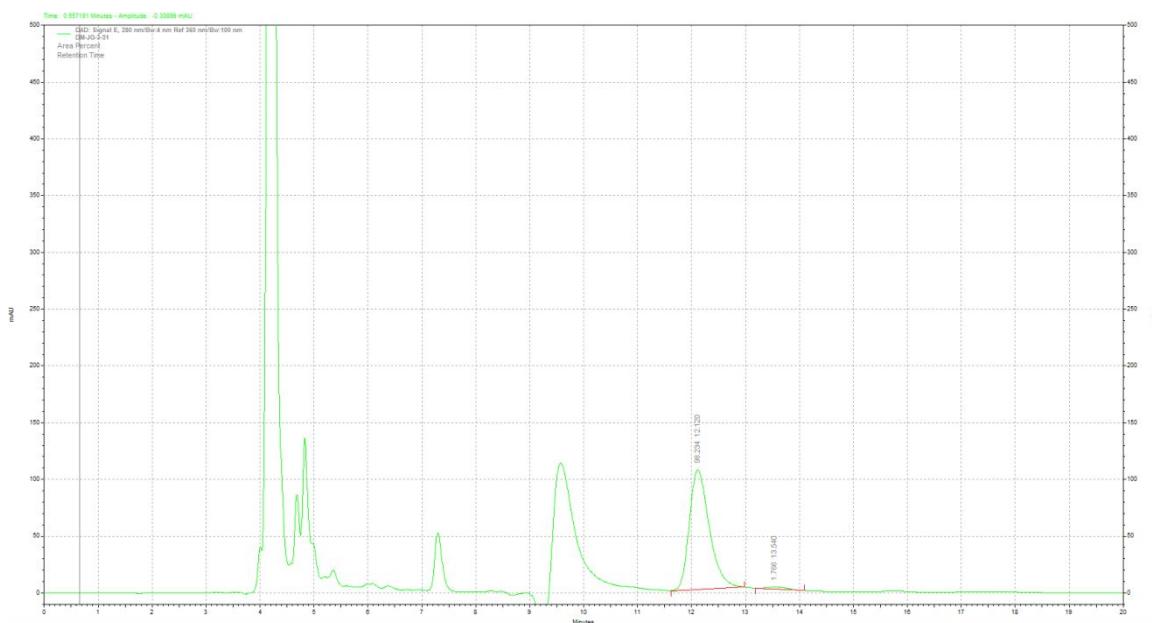
Retention Time	Area	Area %	Height	Height %
7.173	1906206	97.28	122684	96.00
8.287	53309	2.72	5107	4.00

Totals	1959515	100.00	127791	100.00
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### 6-Methyl-3-(phenylselanyl)pyridin-2-ol (C3:others >30:1) (3af): HPLC of isolated material



### HPLC of crude reaction mixture

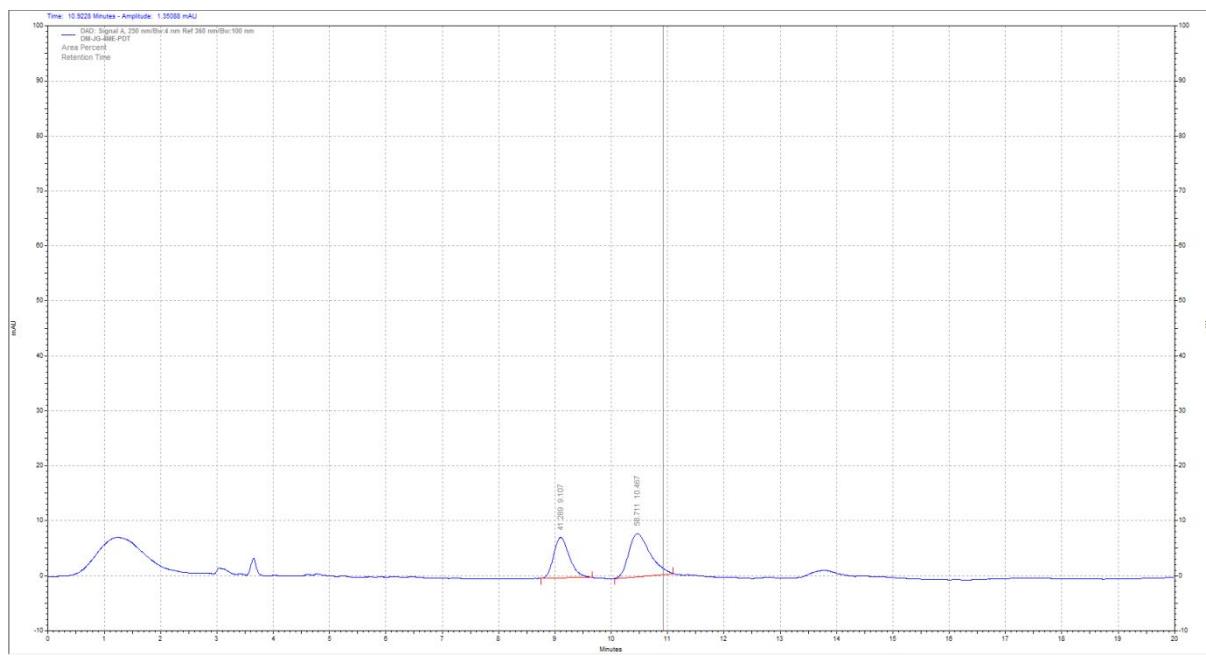


**DAD: Signal E,**  
**280 nm/Bw:4 nm**  
**Ref 360**  
**nm/Bw:100 nm**

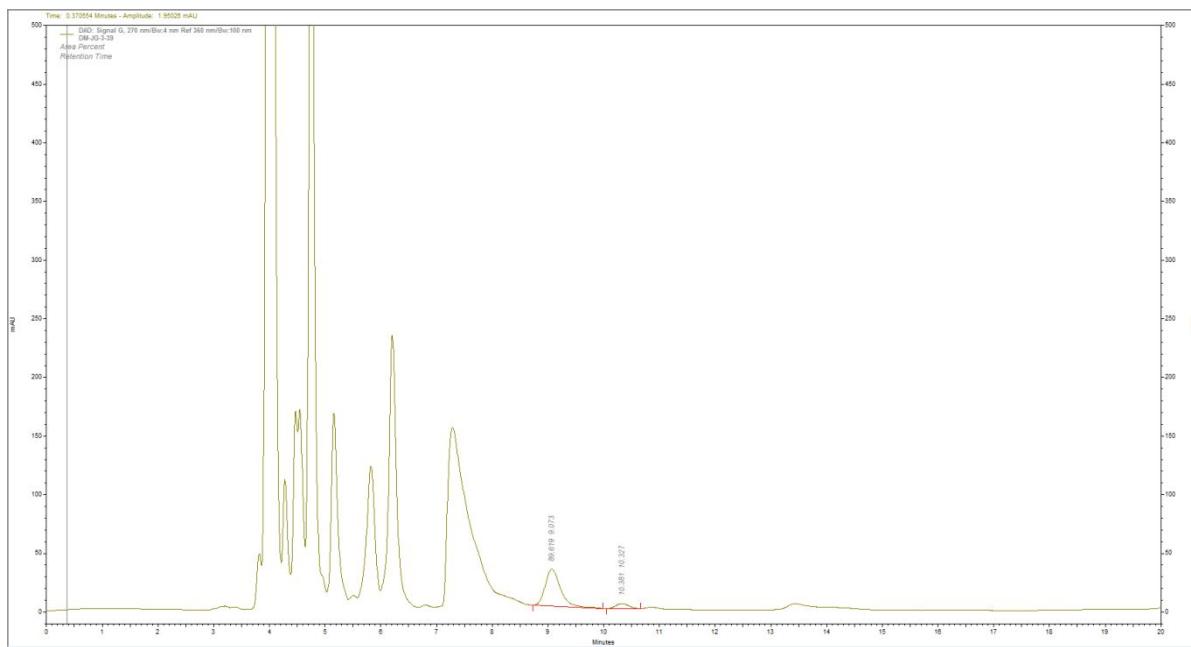
**Results**

Retention Time	Area	Area %	Height	Height %
12.120	5664803	98.23	220331	98.33
13.540	101811	1.77	3739	1.67
<b>Totals</b>	<b>5766614</b>	<b>100.00</b>	<b>224070</b>	<b>100.00</b>

**4-Methyl-3-(phenylthio)pyridin-2-ol (C3:others = 9:1) (3ag): HPLC of isolated material**



### HPLC of crude reaction mixture



DAD: Signal G,

270 nm/Bw:4 nm

Ref 360

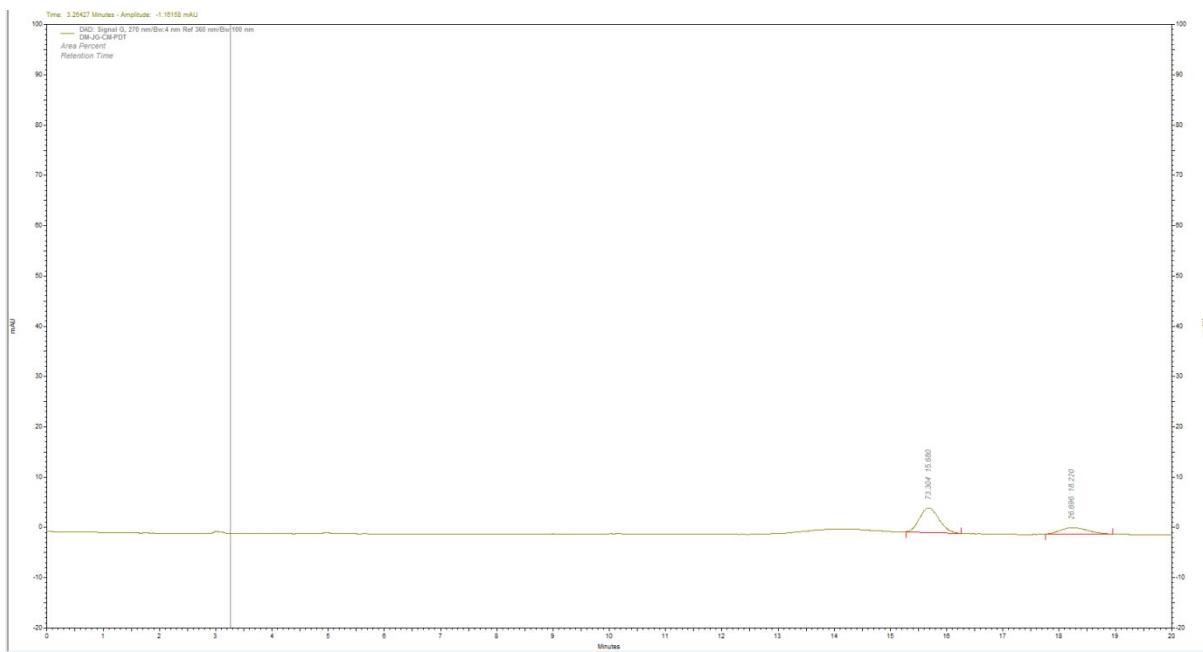
nm/Bw:100 nm

Results

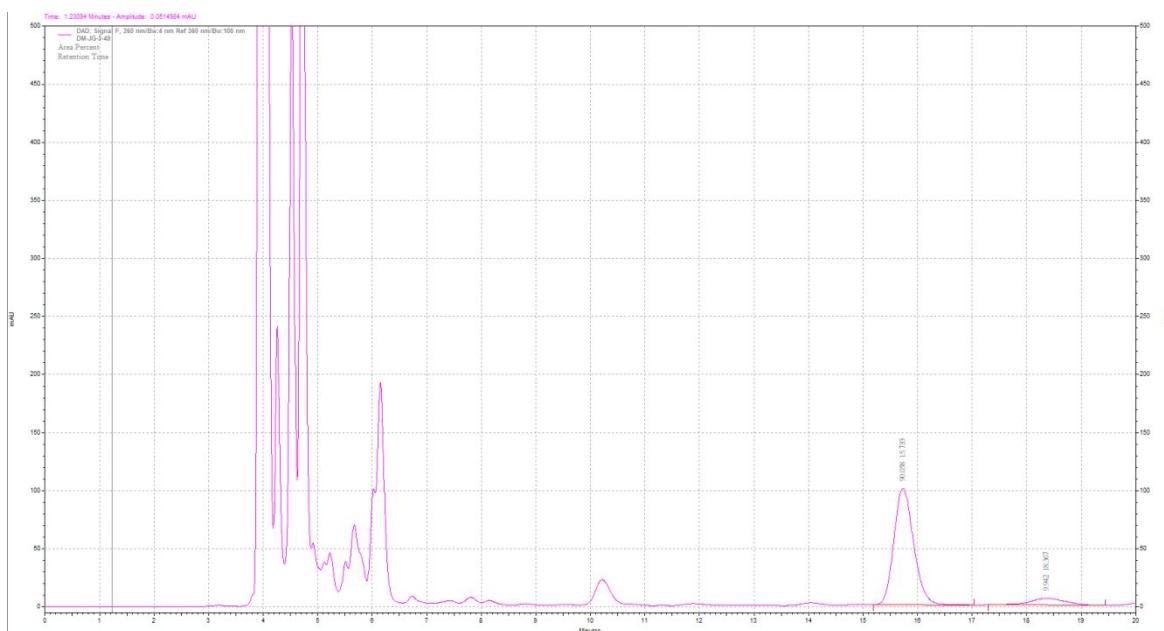
Retention Time	Area	Area %	Height	Height %
9.073	1256916	89.62	66158	87.97
10.327	145592	10.38	9049	12.03

Totals	1402508	100.00	75207	100.00
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### 4-(Phenylthio)phenanthridin-6(5H)-one (C3:C4 = 9:1)(3ah): HPLC of isolated material



### HPLC of crude reaction mixture

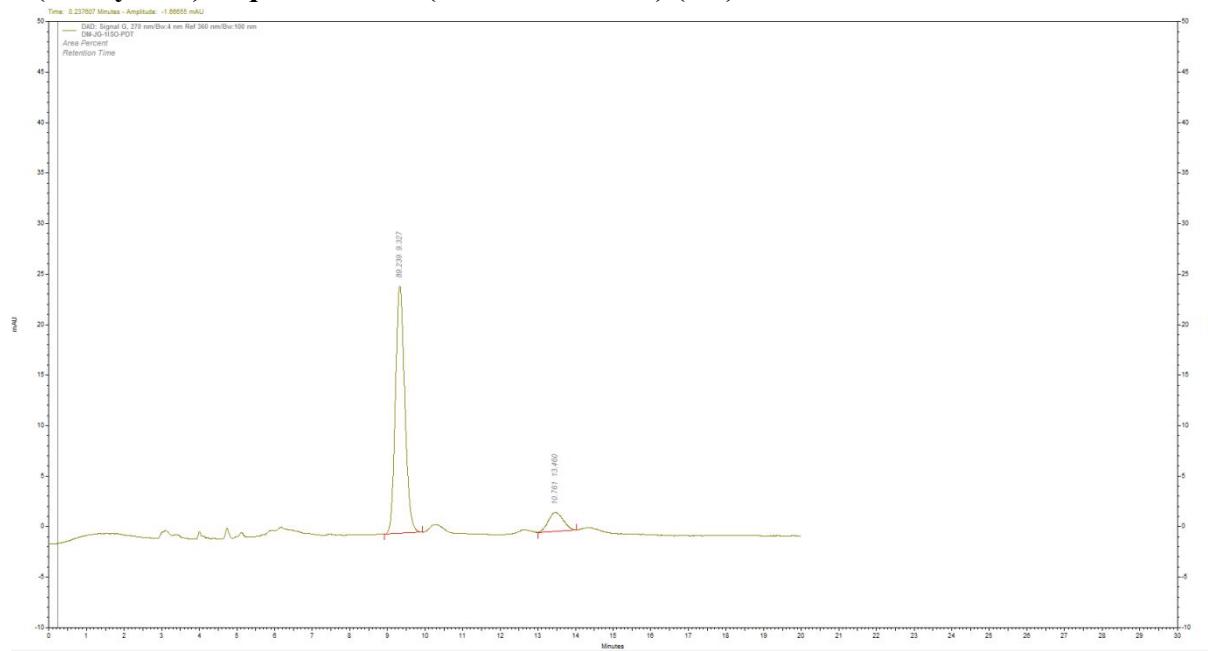


**DAD: Signal F,**  
**260 nm/Bw:4 nm**  
**Ref 360**  
**nm/Bw :100 nm**

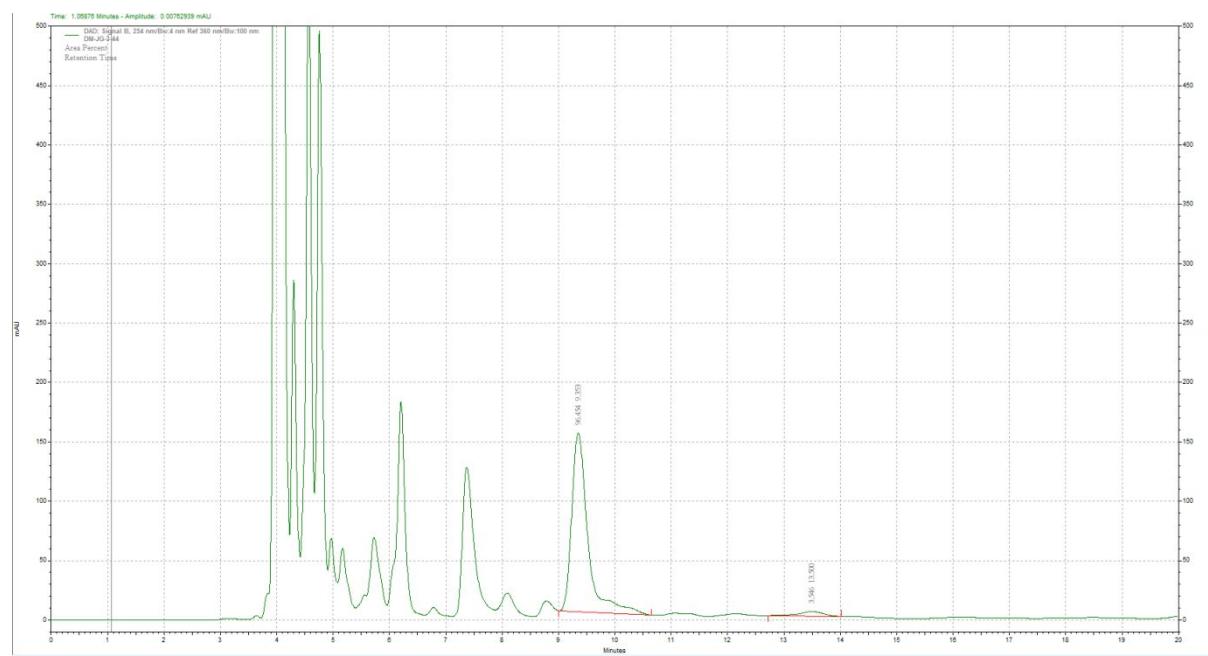
#### Results

Retention Time	Area	Area %	Height	Height %
15.733	5292676	90.06	210196	94.43
18.367	584257	9.94	12398	5.57
<b>Totals</b>	<b>5876933</b>	<b>100.00</b>	<b>222594</b>	<b>100.00</b>

### 4-(Phenylthio)isoquinolin-1-ol (C4:others >20:1) (3ai): HPLC of isolated material



### HPLC of crude reaction mixture



**DAD: Signal B,**

**254 nm/Bw:4 nm**

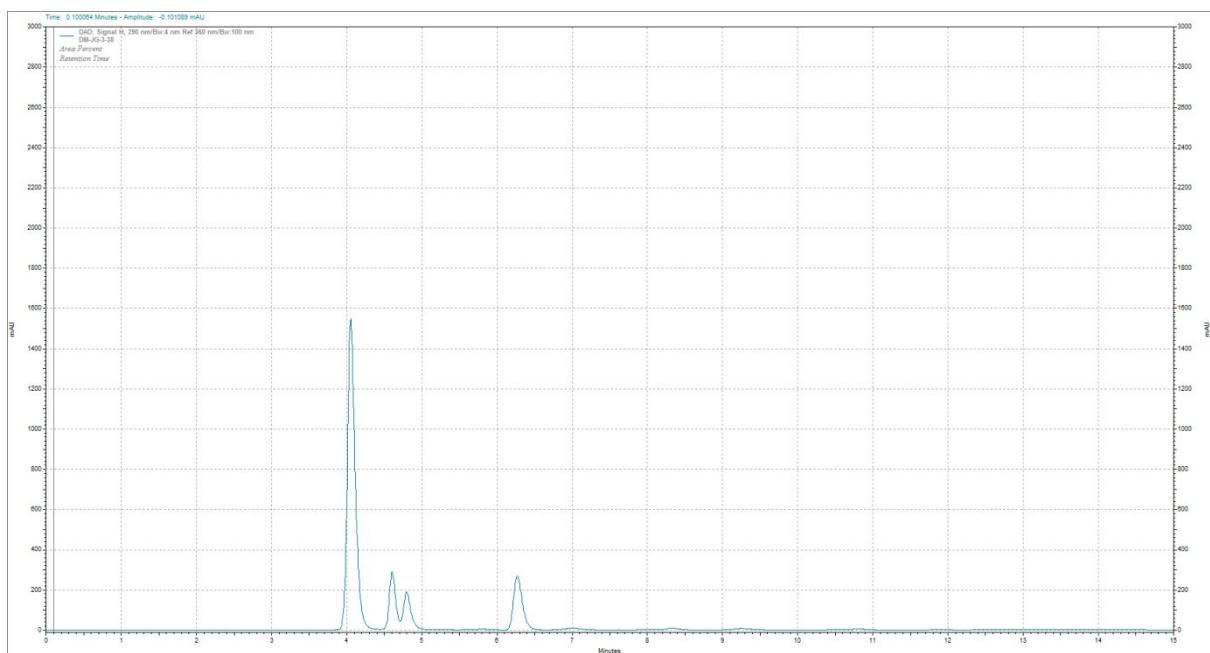
**Ref 360**

**nm/Bw:100 nm**

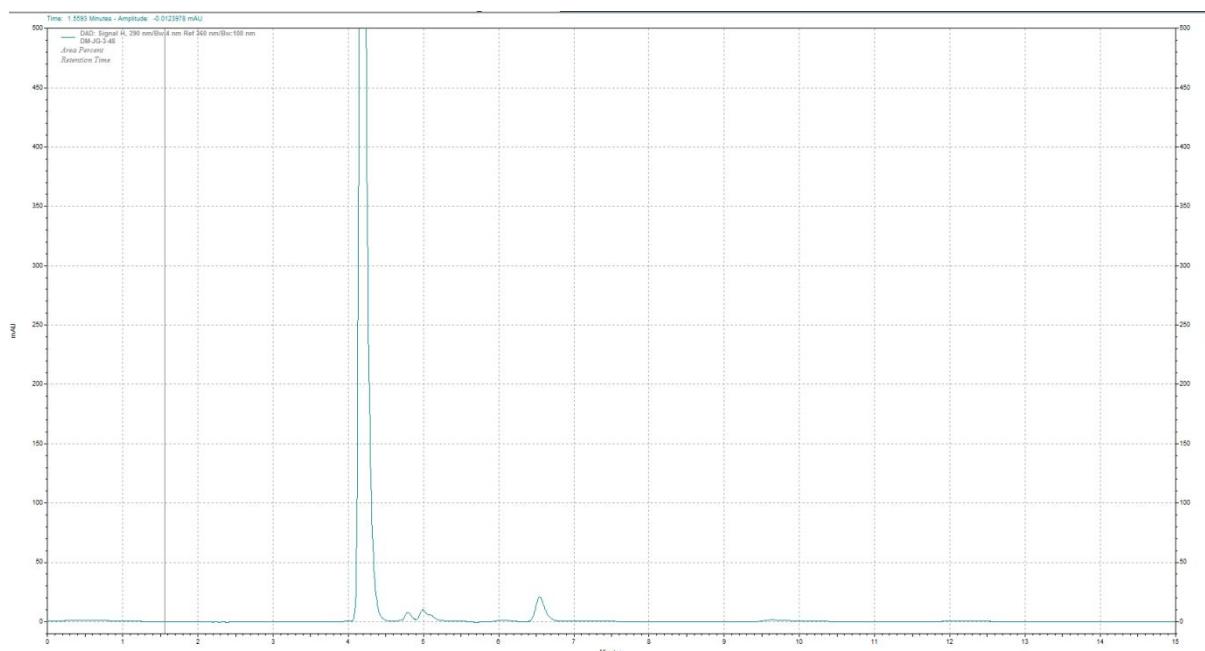
**Results**

Retention Time	Area	Area %	Height	Height %
9.353	6316349	96.45	315893	97.55
13.500	232192	3.55	7924	2.45
<b>Totals</b>	<b>6548541</b>	<b>100.00</b>	<b>323817</b>	<b>100.00</b>

### 3-(Phenylthio)quinolin-4-ol (3aj): HPLC of crude reaction mixture



### 3-(Phenylthio)quinoline-2,4-diol (3al): HPLC of crude reaction mixture



## 5. References

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- [14] Yields are of isolated materials. Selectivity mentioned in the manuscript is of crude reaction mixture.

## **Computational Section- Part II**

## 6. Computational Methods.

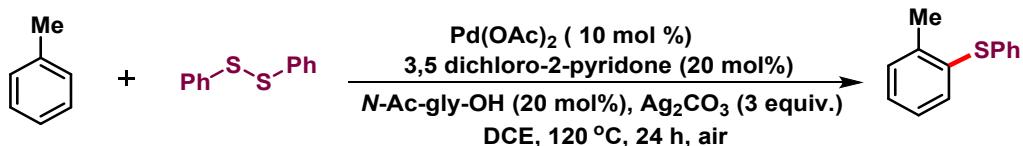
Density functional theory (DFT) calculations were performed with *Gaussian 16* rev. B.01.<sup>1</sup> Geometry optimizations were initially performed using the global-hybrid meta-NGA (nonseparable gradient approximation) MN15 functional<sup>2</sup> with the def2-SVP<sup>3,4</sup> Karlsruhe-family basis set and the optimized structures further refined with a mix of larger basis set consisting of triple- $\zeta$  valence def2-TZVPD (where ‘D’ indicates diffuse basis functions) for Pd<sup>5,6</sup> and Ag<sup>5,6</sup> atoms and def2-SVP<sup>3,4</sup> for all other atoms (BS1). MN15 functional was chosen as it performs much better than many other functionals (e.g.  $\omega$ B97X-D and TPSS) in predicting transition metal (TM) reaction barrier heights and giving better geometries for both TM complexes and organic molecules.<sup>2</sup> Minima and transition structures on the potential energy surface (PES) were confirmed using harmonic frequency analysis at the same level of theory, showing respectively zero and one imaginary frequency. Where appropriate for cases where visual inspection of TS imaginary frequency is not obvious, intrinsic reaction coordinate (IRC) analyses<sup>7,8</sup> were performed to confirm that the found TSs connect to the right reactants and products. Single point (SP) corrections were performed using MN15 functional and def2-QZVP<sup>3</sup> basis set for all atoms. The SMD implicit continuum solvation model<sup>9</sup> was used to account for the effect of dichloroethane (DCE) solvent on the computed Gibbs energy profile. Gibbs energies were evaluated at the reaction temperature of 393.15 K (120°C), using a quasi-RRHO treatment of vibrational entropies.<sup>10,11</sup> Vibrational entropies of frequencies below 100 cm<sup>-1</sup> were obtained according to a free rotor description, using a smooth damping function to interpolate between the two limiting descriptions. The free energies were further corrected using standard concentration of 1 mol/L, which were used in solvation calculations. Unless otherwise stated, the final SMD (dichloroethane)-MN15/def2-QZVP//MN15/BS1 Gibbs energies are used for discussion throughout. *All Gibbs energy values in the text and figures are quoted in kcal mol<sup>-1</sup>.*

Non-covalent interactions (NCIs) were analyzed using NCIPLLOT<sup>12</sup> calculations. The .wfn files for NCIPLLOT were generated at MN15/DGDZVP<sup>13,14</sup> level of theory. NCI indices calculated with NCIPLLOT were visualized at a gradient isosurface value of  $s = 0.5$  au. These are colored according to the sign of the second eigenvalue ( $\lambda_2$ ) of the Laplacian of the density ( $\nabla^2\rho$ ) over the range of -0.1 (blue = attractive) to +0.1 (red = repulsive). Molecular orbitals are visualized using an isosurface value of 0.05 au throughout. All molecular structures and molecular orbitals were visualized using PyMOL software.<sup>15</sup>

Geometries of all optimized structures (in .xyz format with their associated energy in Hartrees) are included in a separate folder named *structures\_xyz* with an associated README file. All these data have been deposited with this Supporting Information.

## 7. Model reaction

For computational modeling, we have chosen the following reaction (Scheme S1) for mechanistic studies.



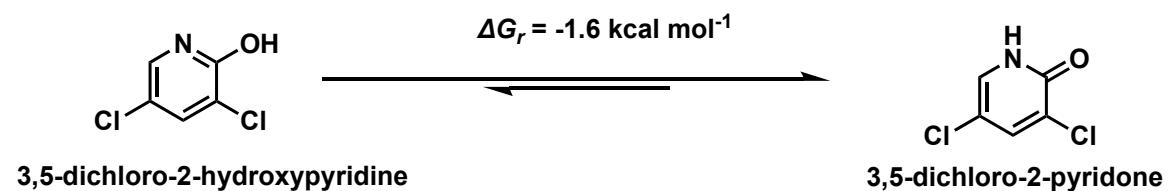
**Scheme S1.** Model reaction used for computational mechanistic studies.

### 7.1 Conformational considerations

Diphenylsulfane guess rotamers were generated by varying the C-S-S-C dihedral angles. The resultant rotamers were pre-optimized using the GFN2-xTB<sup>16</sup> extended semiempirical tight-binding method in the *xtb* program<sup>17,18</sup> from Grimme's group. The resultant distinct clusters were further optimized using DFT and the lowest energy structure is used throughout.

### 7.2 Ligand tautomerism

The equilibrium between the two tautomeric forms of the pyridone ligand is computed. It was found that 3,5-dichloro-2-pyridone is 1.6 kcal mol<sup>-1</sup> more stable than 3,5-dichloro-2-hydroxypyridine (Scheme S2). For structures involving either tautomer in the Gibbs energy profile calculation, the energy of the most stable form of the ligand (i.e., 3,5-dichloro-2-pyridone) is used.

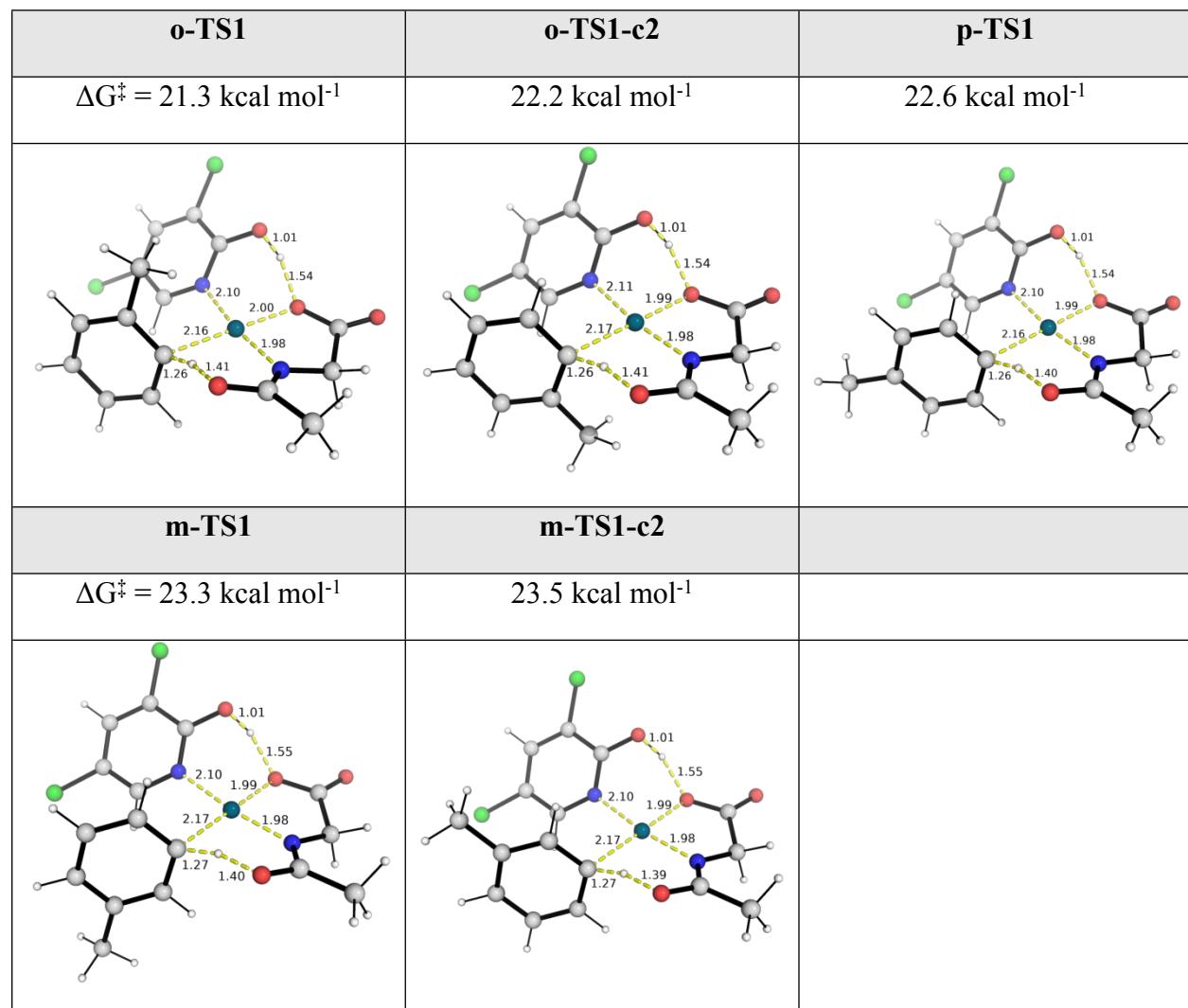


**Scheme S2.** Model reaction used for computational mechanistic studies.

## 8. C–H activation transition states (TSs)

### 8.1 C–H activation TSs using MPAA *N*-acetylglycine as internal base, with 3,5 dichloro-2-hydroxypyridine as co-ligand

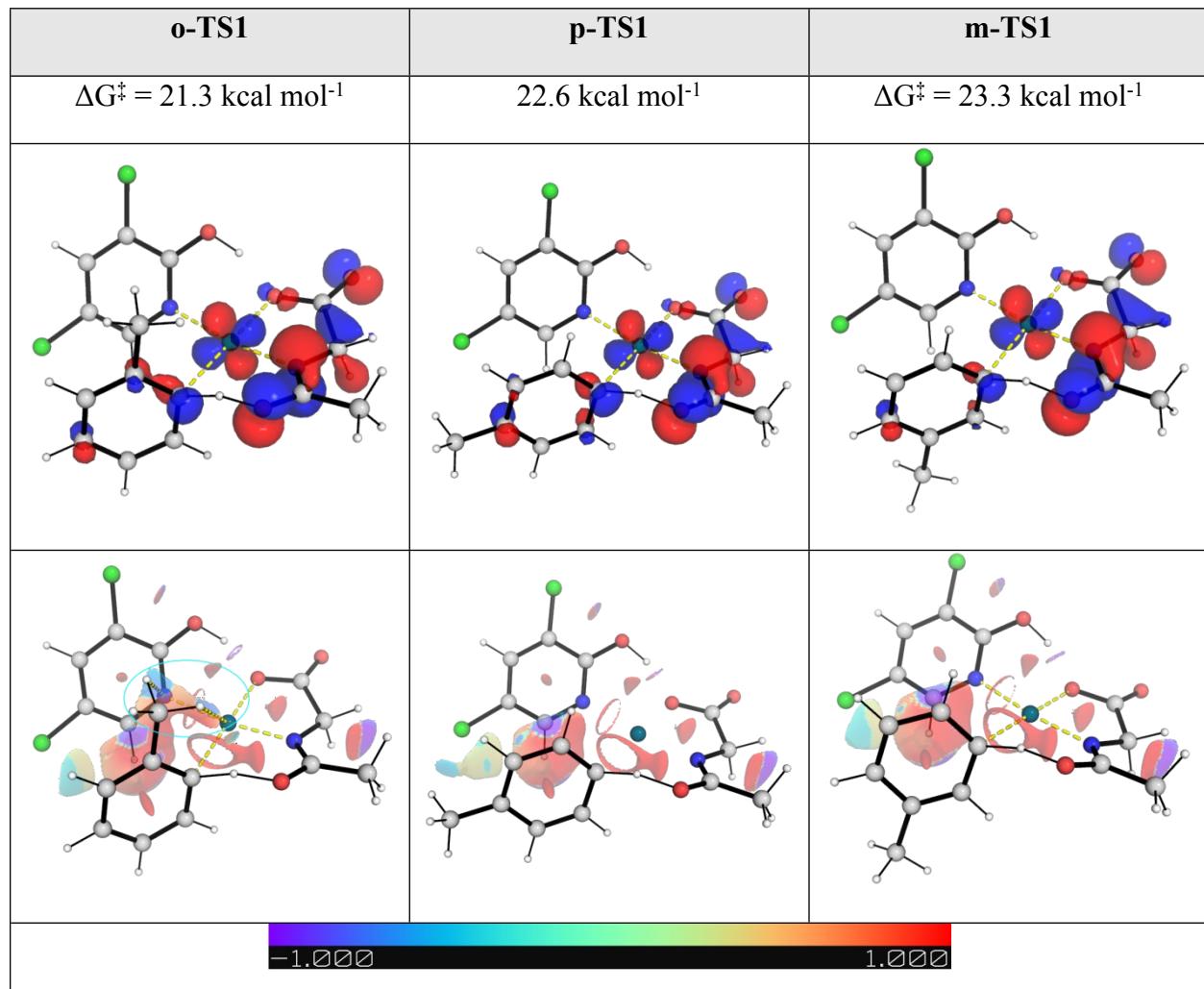
The transition states for the concerted metalation deprotonation (CMD) C–H activation step with MPAA as internal base involving 3,5-dichloro-2-hydroxypyridine co-ligand is shown in Figure S1. For *ortho*- and *meta*-C–H activation TSs, both conformers were considered. The TS for the activation of *ortho*-C–H bond (**o-TS1**) has the lowest activation barrier, at 21.3 kcal mol<sup>-1</sup>; the TS for the activation of *para*-C–H bond (**p-TS1**) is 1.3 kcal mol<sup>-1</sup> higher, at 22.6 kcal mol<sup>-1</sup> whereas the TS for the activation of *meta*-C–H bond (**m-TS1**) is 2.0 kcal mol<sup>-1</sup> higher, at 23.3 kcal mol<sup>-1</sup>.



**Figure S1.** DFT optimized transition state structures for the C–H activation of toluene with 3,5-dichloro-2-hydroxypyridine co-ligand. Activation barriers are taken relative to the sum of starting materials.

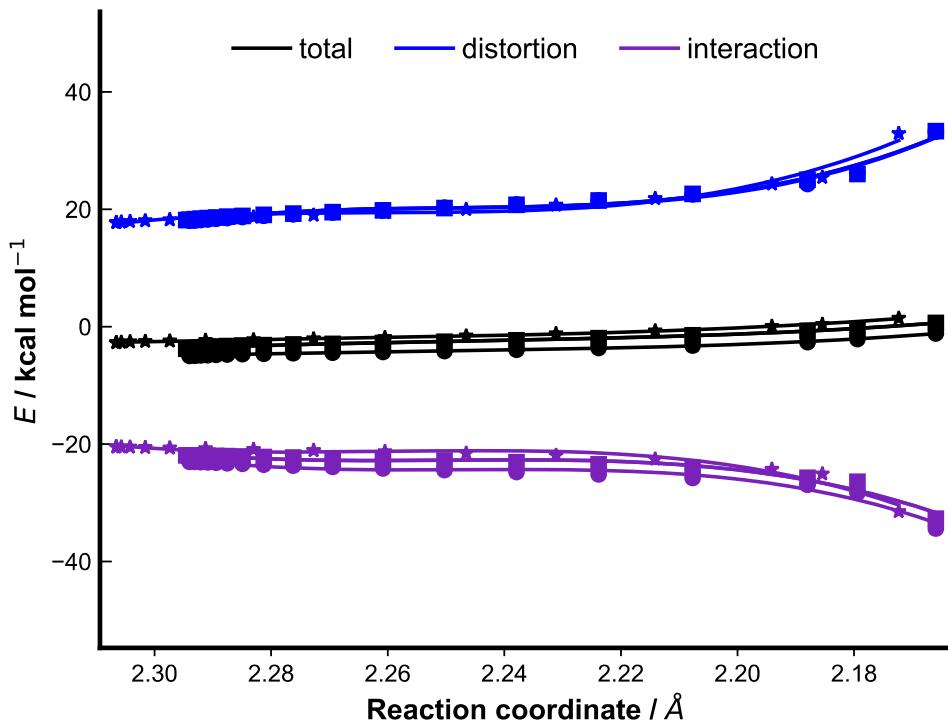
Figure S2 shows the HOMO structures and the non-covalent interaction (NCI) plots for the lowest barrier regioselective C–H activation TSs. The HOMO structures show similar electronic distribution, suggesting similar orbital interactions in these TSs. For the NCI plots, there seems to be more favourable interactions in the TS for the activation of *ortho*-C–H bond

(circled in cyan) compared to the other two positions, although a quantitative comparison is difficult given these plots.



**Figure S2.** HOMO and NCI plots for the C–H activation of toluene using MPAA as internal base, with 3,5 dichloro-2-hydroxypyridine co-ligand. HOMOs are plotted at an isosurface value of 0.05 au.

We further carried out the distortion-interaction<sup>19,20</sup>/activation strain<sup>20–24</sup> (DI–AS) analysis on the key TSs to discern the factors affecting regioselectivity in the C–H activation step. Geometries are taken from along the IRC reaction coordinate at every 3<sup>rd</sup> point interval and single point solvent-phase calculations were performed at SMD (dichloroethane)-MN15/def2-QZVP level of theory to obtain DI–AS profiles, shown in Figure S3 below. From the DI–AS plot, we see that the TS for the activation of the *ortho*-C–H bond is lowest due to more favourable interaction energies along the IRC, while the strain energies are similar for all three TSs.



**Figure S3.** The activation strain or distortion-interaction analyses applied to the IRC paths along the rate-determining C–H activations transition states. All energies are calculated at SMD (dichloroethane)-MN15/def2-QZVP and used without any further corrections. Circle markers are points along *ortho*-C–H activation TS; star markers are points along *meta*-C–H activation TS; square markers are points along *para*-C–H activation TS.

## 8.2 C–H activation TSs using MPAA *N*-acetylglycine as internal base, with 3,5 dichloro-2-pyridone as co-ligand

The transition states for the concerted metalation deprotonation (CMD) C–H activation step with MPAA as internal base involving 3,5-dichloro-2-pyridone co-ligand is shown in Figure S4. For *ortho*- and *meta*-C–H activation TSs, the corresponding lowest energy conformer from section 1.4.2 previously was used. The TS for the activation of *ortho*-C–H bond (**o-TS1'**) is at 24.2  $\text{kcal mol}^{-1}$  while that for *para*-C–H bond (**p-TS1'**) is at 25.5  $\text{kcal mol}^{-1}$  and that for *meta*-C–H bond (**m-TS1'**) is at 26.6  $\text{kcal mol}^{-1}$ . All these TSs have higher barriers than the corresponding TSs using 3,5-dichloro-2-hydroxypyridine as the coordinating ligand (Figure S1). This is potentially due to the better electron-donating ability of the lone pair on the N atom rather than from the O atom, allowing the TSs in Figure S1 (ligand in 3,5-dichloro-2-hydroxypyridine form) to be stabilised to a larger extent than those in Figure S4 (ligand in 3,5-dichloro-2-pyridone form).

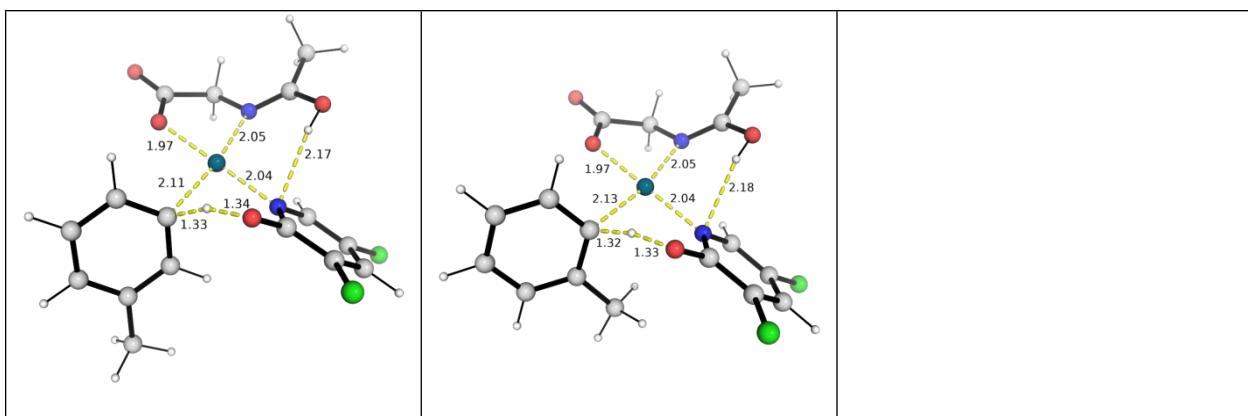
<b>o-TS1'</b>	<b>p-TS1'</b>	<b>m-TS1'</b>
24.2 kcal mol <sup>-1</sup>	$\Delta G^\ddagger = 25.5$ kcal mol <sup>-1</sup>	26.6 kcal mol <sup>-1</sup>

**Figure S4.** DFT optimized transition state structures for the C–H activation of toluene with 3,5 dichloro-2-pyridone co-ligand. Activation barriers are taken relative to the sum of starting materials.

### 8.3 C–H activation TSs using deprotonated pyridone ligand as internal base, with MPAA as co-ligand

The transition states for the concerted metalation deprotonation (CMD) C–H activation step with deprotonated pyridone ligand as internal base involving N-acetylglycine co-ligand is shown in Figure S5. The TS for the activation of *ortho*-C–H bond (**o-TS1''**) is at 26.6 kcal mol<sup>-1</sup> while that for *para*-C–H bond (**p-TS1''**) is at 26.8 kcal mol<sup>-1</sup> and that for *meta*-C–H bond (**m-TS1''**) is at 27.8 kcal mol<sup>-1</sup>. All these TSs have higher barriers than the corresponding TSs using MPAA N-acetylglycine as internal base and 3,5-dichloro-2-hydroxypyridine as the coordinating ligand (Figure S1).

<b>o-TS1''</b>	<b>p-TS1''</b>	<b>m-TS1''</b>
26.6 kcal mol <sup>-1</sup>	26.8 kcal mol <sup>-1</sup>	27.8 kcal mol <sup>-1</sup>
<b>m-TS1''-c2</b>	<b>o-TS1''-c2</b>	
$\Delta G^\ddagger = 27.8$ kcal mol <sup>-1</sup>	$\Delta G^\ddagger = 28.0$ kcal mol <sup>-1</sup>	

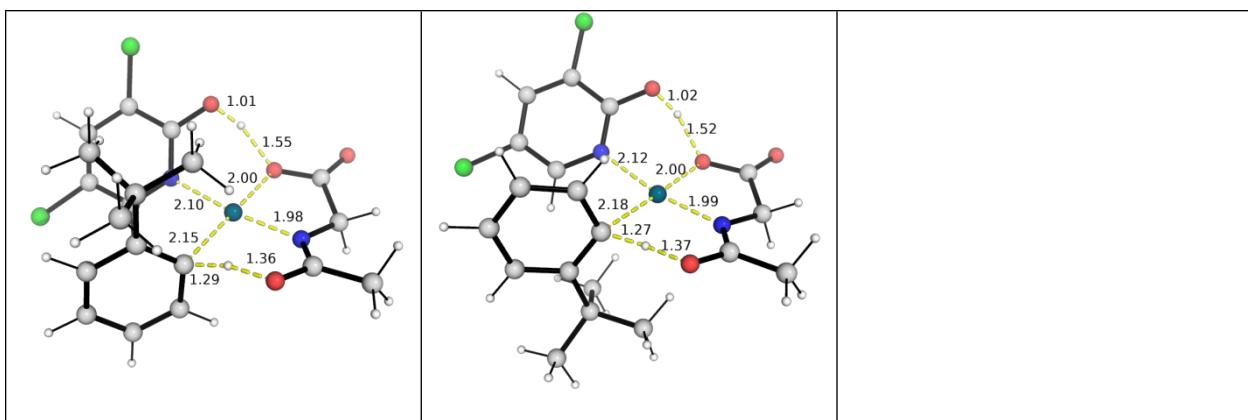


**Figure S5.** DFT optimized transition state structures for the C–H activation of toluene using pyridone as internal base and N-acetylglycine as co-ligand. Activation barriers are taken relative to the sum of starting materials.

#### 8.4 C–H activation TSs using tert-butylbenzene substrate

The DFT-optimized TSs for C–H activation step utilizing tert-butyl benzene substrate and the associated relative activation barriers are shown in Figure S6. For *ortho*- and *meta*-C–H activation TSs, both conformers were considered. The TS for the activation of *meta*-C–H bond (**m-TS1-tbz**) has the lowest activation barrier; the TS for the activation of *para*-C–H bond (**p-TS1-tbz**) is 0.5 kcal mol<sup>−1</sup> higher whereas the TS for the activation of *ortho*-C–H bond (**m-TS1**) is 1.2 kcal mol<sup>−1</sup> higher. These findings are consistent with the computed relative barriers for the C–H activation of tert-butyl benzene substrate as reported by van Gemmeren and co-workers.<sup>25</sup>

<b>m-TS1-tbz</b>	<b>m-TS1-tbz-c2</b>	<b>p-TS1-tbz</b>
$\Delta\Delta G^\ddagger = 0.0 \text{ kcal mol}^{-1}$	0.3 kcal mol <sup>−1</sup>	0.5 kcal mol <sup>−1</sup>
<b>o-TS-tbz</b>	<b>m-TS1-tbz-c2</b>	
$\Delta\Delta G^\ddagger = 1.2 \text{ kcal mol}^{-1}$	2.6 kcal mol <sup>−1</sup>	



**Figure S6.** DFT optimized transition state structures for the C–H activation of tert-butyl benzene substrate with 3,5 dichloro-2-hydroxypyridine co-ligand. Activation barriers are taken relative to the lowest energy TS.

## 9. Oxidative addition/insertion transition states (TSs)

We considered all the possibilities for the oxidative addition (OA) of diphenyl disulfide substrate into Pd-centre. The mechanistic possibilities for the OA step involving neutral, cationic and anionic Pd-species are shown in Figures S7, S8 and S9 respectively. The OA step into  $\text{Pd}(\text{OAc})_2$  species before C–H activation step was also considered (Figure S10). All these possibilities (OA with different combinations/arrangements of ligands) suggest that the oxidative addition mechanism has very high barriers. In addition, these barriers are all higher than the C–H activation step, inconsistent with the experimental observation that the C–H activation step is the turnover-frequency-determining transition state (TDTS).

### 9.1 Mechanistic possibilities for the OA step involving neutral Pd-species

Starting from the *ortho*-C–H activated complex, we first consider the insertion where the MPAA ligand loses one coordination side on Pd-centre, giving a vacant site for diphenyl disulfide coordination and subsequent insertion. We found that these TSs have a barrier of 39.5 kcal mol<sup>-1</sup> (**OA-1**) and 40.6 kcal mol<sup>-1</sup> (**OA-2**).

We next consider the OA of diphenyl disulfide substrate into the *ortho*-C–H activated complex where the pyridone ligand is lost from the coordination, with only MPAA present in the OA TSs (**OA-3** and **OA-4**). These TSs also have high barriers with **OA-3** at 37.8 kcal mol<sup>-1</sup> while **OA-4** is at 35.8 kcal mol<sup>-1</sup>.

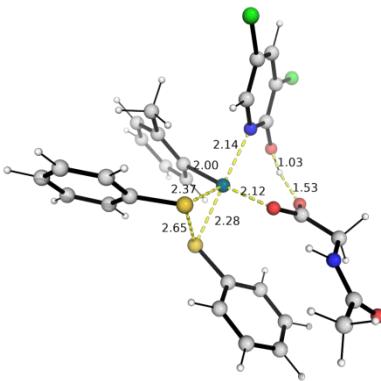
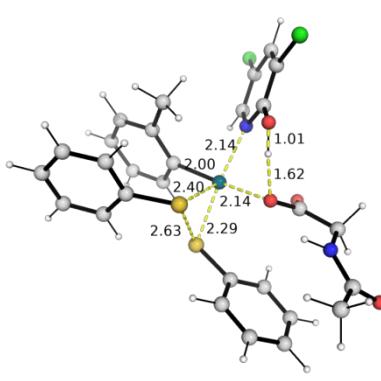
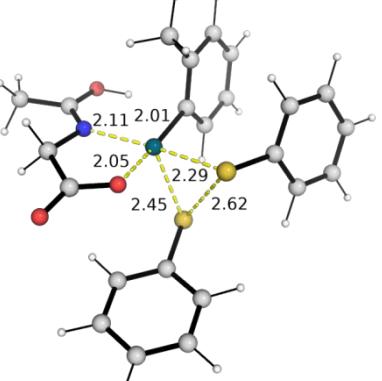
Next, we consider the OA TSs where the MPAA ligand is lost from coordination while the pyridone ligand remains. These TSs also have rather high barrier, with **OA-5** at 34.2 kcal mol<sup>-1</sup> and **OA-6** at 36.3 kcal mol<sup>-1</sup>.

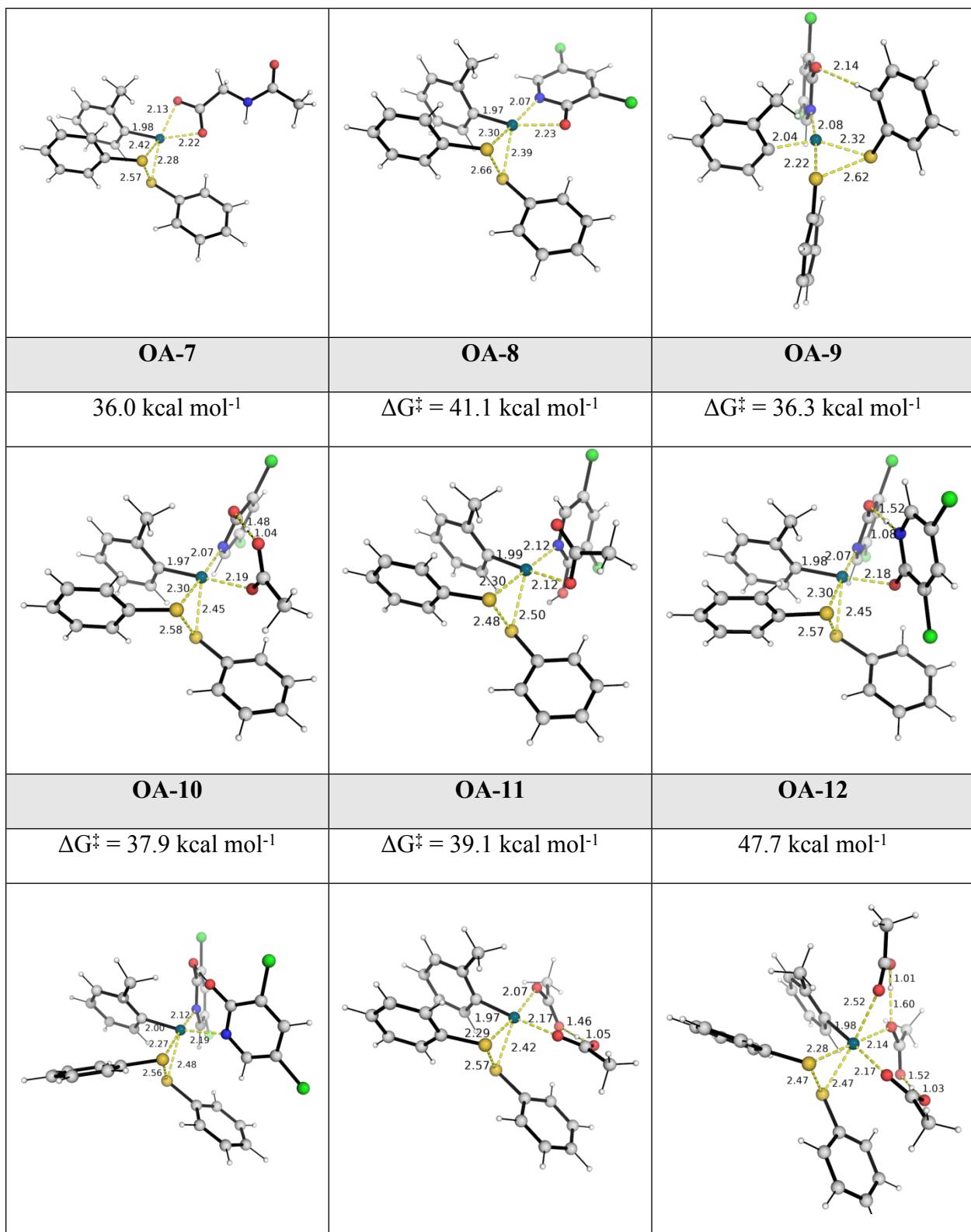
Next, from the *ortho*-C–H activated complex, we consider the OA TSs where an acetate ligand replaces the MPAA ligand. These TSs again have high barriers, with **OA-7** at 36.0 kcal mol<sup>-1</sup> and **OA-8** at 41.1 kcal mol<sup>-1</sup>.

We also consider the OA TSs in which another pyridone ligand replaces the MPAA ligand (**OA-9** and **OA-10**). These also have high barriers, with **OA-9** at 36.3 kcal mol<sup>-1</sup> and **OA-10** at 37.9 kcal mol<sup>-1</sup>.

Next, we consider the OA TSs in which the acetate molecules replace both the pyridone ligand and the MPAA ligand. For Pd-species undergoing OA with two acetates (**OA-11**), the barrier is at 39.1 kcal mol<sup>-1</sup>; the TS with three acetates (**OA-12**) has the barrier is at 47.7 kcal mol<sup>-1</sup>.

All these computed barriers suggest that the oxidative insertion of diphenyl disulfide into the C–H activated Pd-species is difficult and unlikely to be the actual mechanism.

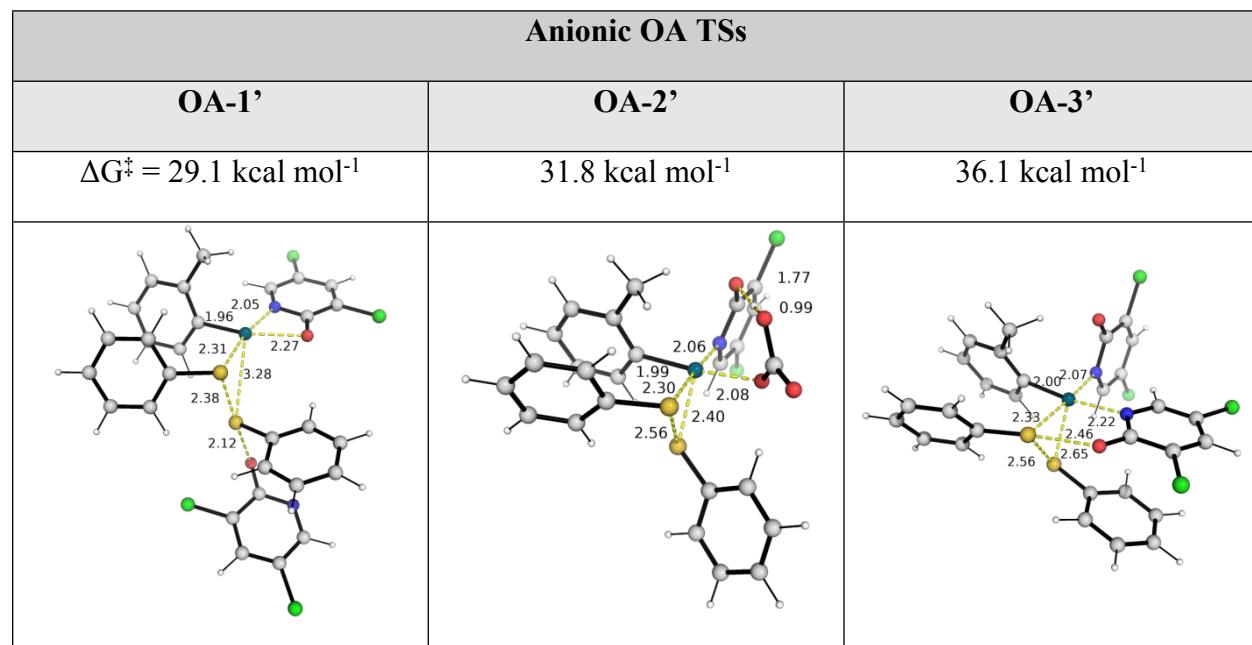
Neutral OA TSs		
OA-1	OA-2	OA-3
39.5 kcal mol <sup>-1</sup>	40.6 kcal mol <sup>-1</sup>	37.8 kcal mol <sup>-1</sup>
		
OA-4	OA-5	OA-6
35.8 kcal mol <sup>-1</sup>	$\Delta G^\ddagger = 34.2 \text{ kcal mol}^{-1}$	36.3 kcal mol <sup>-1</sup>



**Figure S7.** DFT optimized transition state structures for the oxidative addition of diphenyl disulfide into neutral Pd-species. Activation barriers are taken relative to the sum of starting materials.

## 9.2 Mechanistic possibilities for the OA step involving anionic Pd-species

The OA step involving anionic Pd-species was also considered. The results are shown in Figure S8. These TSs have barriers that are also quite high. **OA-1'** starting guess structure has the anionic pyridone N-atom coordinating to Pd, however, it proves to be unfavorable for it to stay coordinated – geometry optimization moves the anionic pyridone molecule away from the Pd-center. Comparing **OA-1'** and **OA-3'**, it looks like having the pyridone anion coordinated to Pd is less favorable than having it away from the Pd center. Nevertheless, these barriers are all higher than the TDTS C–H activation step and are less likely to be the mechanism.



**Figure S8.** DFT optimized transition state structures for the oxidative addition of diphenyl disulfide into anionic Pd-species. Activation barriers are taken relative to the sum of starting materials.

### 9.3 Mechanistic possibilities for the OA step involving cationic Pd-species

The OA step involving cationic Pd-species was also considered. The result is shown in Figure S9. The cationic OA insertion TS has a very high barrier of 67.5 kcal mol<sup>-1</sup>.

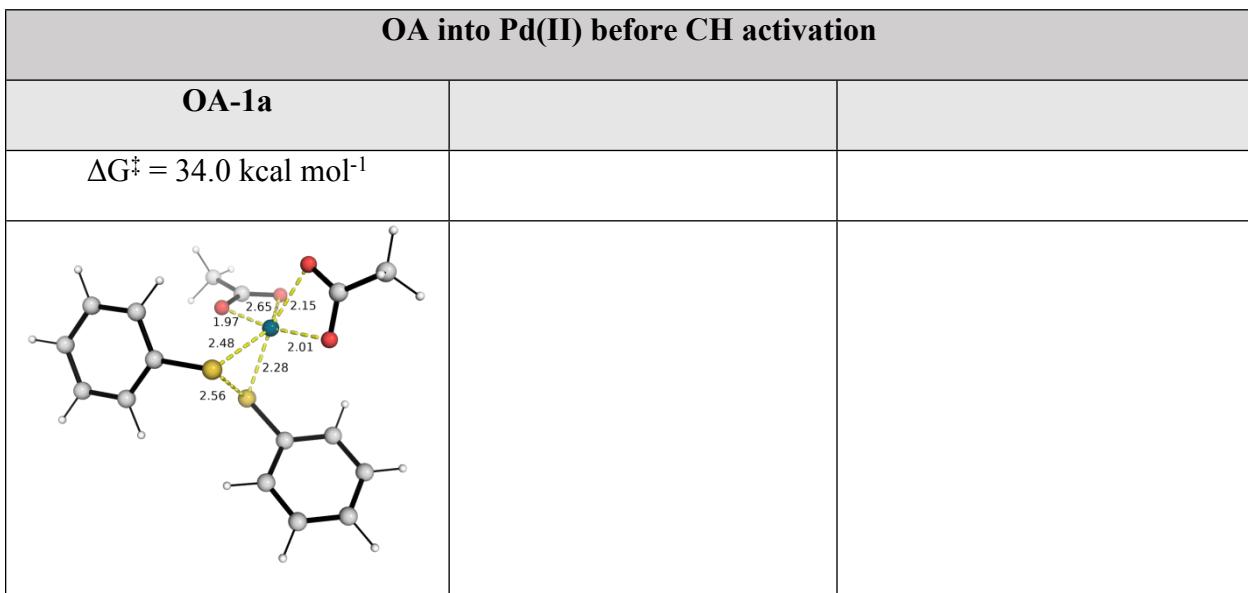
Cationic OA TSs		
<b>OA-1''</b>		
$\Delta G^\ddagger = 67.5 \text{ kcal mol}^{-1}$		



**Figure S9.** DFT optimized transition state structures for the oxidative addition of diphenyl disulfide into cationic Pd-species. Activation barriers are taken relative to the sum of starting materials.

#### 9.4 Mechanistic possibilities for the OA step into $\text{Pd}(\text{OAc})_2$ species before C–H activation step

The OA step into  $\text{Pd}(\text{OAc})_2$  species before C–H activation step was also considered. This TS (**OA-1a**, Figure S10) has a high barrier of  $34.0 \text{ kcal mol}^{-1}$ . Oxidative insertion into Pd(II) catalyst before CH activation step is less likely as this barrier is higher than firstly CH activation step as shown in Figure S1.



**Figure S10.** DFT optimized transition state structures for the oxidative addition of diphenyl disulfide into  $\text{Pd}(\text{OAc})_2$  species before C–H activation step. Activation barriers are taken relative to the sum of starting materials.

#### 10. Migratory insertion transition states (TSs)

The alternative migratory insertion (MI) of diphenyl disulfide substrate into C–H activated Pd-species was also considered. These TSs (Figure S11) have very high barriers and the MI step is unlikely the mechanism for the present reaction.

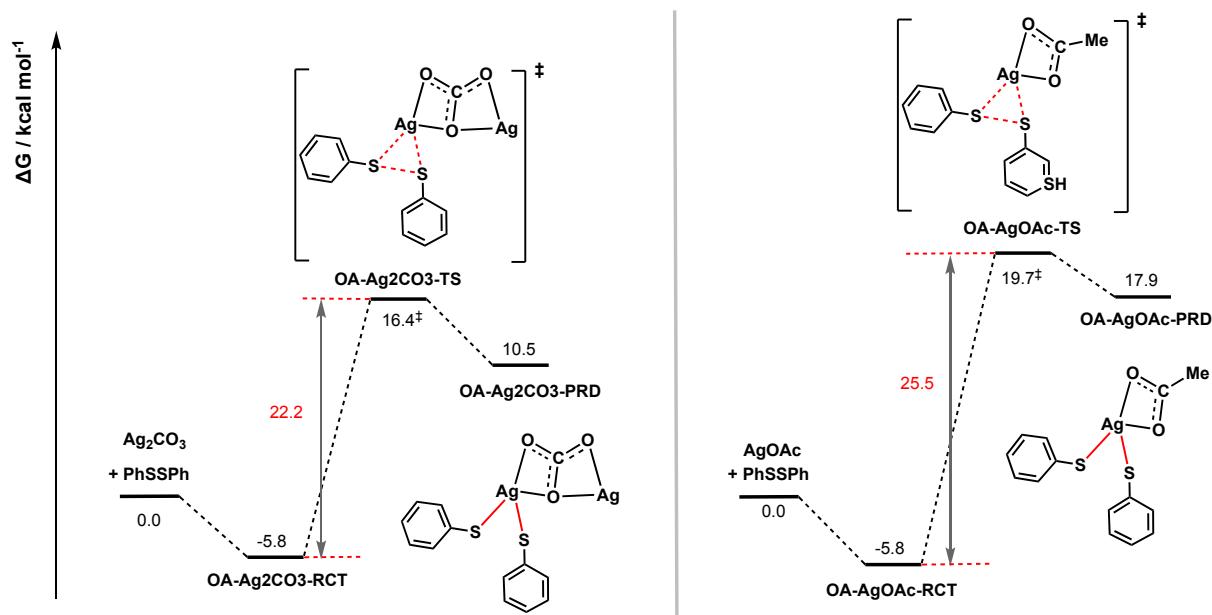
Migratory insertion TSs		
MI-1	MI-2	
$\Delta G^\ddagger = 57.2 \text{ kcal mol}^{-1}$	$55.7 \text{ kcal mol}^{-1}$	

**Figure S11.** DFT optimized transition state structures for the migratory insertion of diphenyl disulfide into C–H activated species. Activation barriers are taken relative to the sum of starting materials.

## 11. Transmetalation pathways

### 11.1 Oxidative insertion into Ag catalyst species

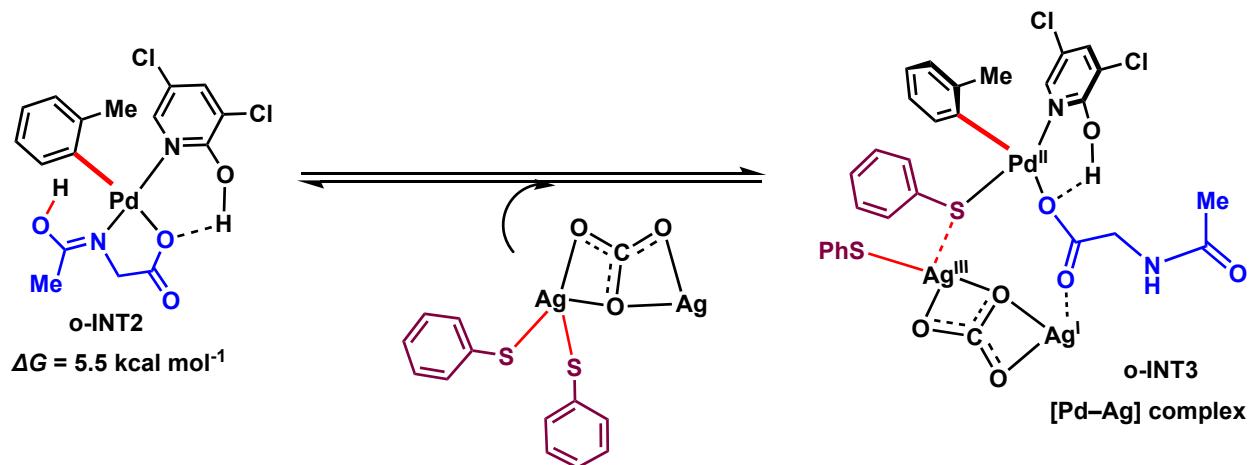
The oxidative insertion of diphenyl disulfide into Ag catalyst was considered. The energy profiles for the insertion into  $\text{Ag}_2\text{CO}_3$  and  $\text{AgOAc}$  are shown in Figure S12. The insertion of diphenyl disulfide into  $\text{Ag}_2\text{CO}_3$  has lower activation barrier of  $22.2 \text{ kcal mol}^{-1}$  compared to the insertion into  $\text{AgOAc}$ , which has a barrier of  $25.5 \text{ kcal mol}^{-1}$ .



**Figure S12.** Gibbs energy profile for the insertion of diphenyl disulfide into Ag catalyst species.

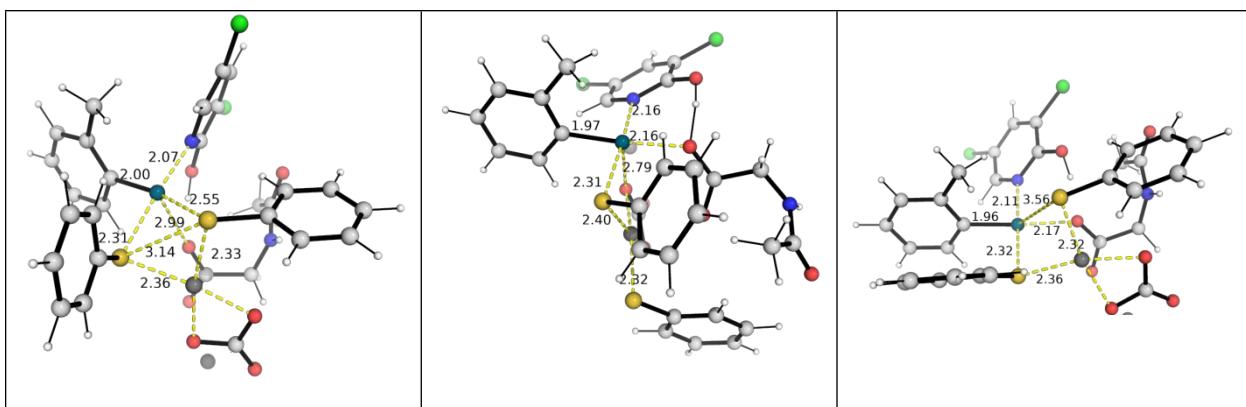
## 11.2 Transmetalated Pd-Ag species

The diphenyl disulfide inserted silver complex can undergo a transmetallation-like process in which a PhS-group is transferred from the Ag-centre to the Pd-centre (Scheme S3). The resulting complex is optimized, taking into account of various isomers that can be formed (Figure S13). This [Pd–Ag] complex formation is exergonic and may be possible to occur.



**Scheme S3.** Formation of [Pd–Ag] complex with the formation of Pd–SPh bond.

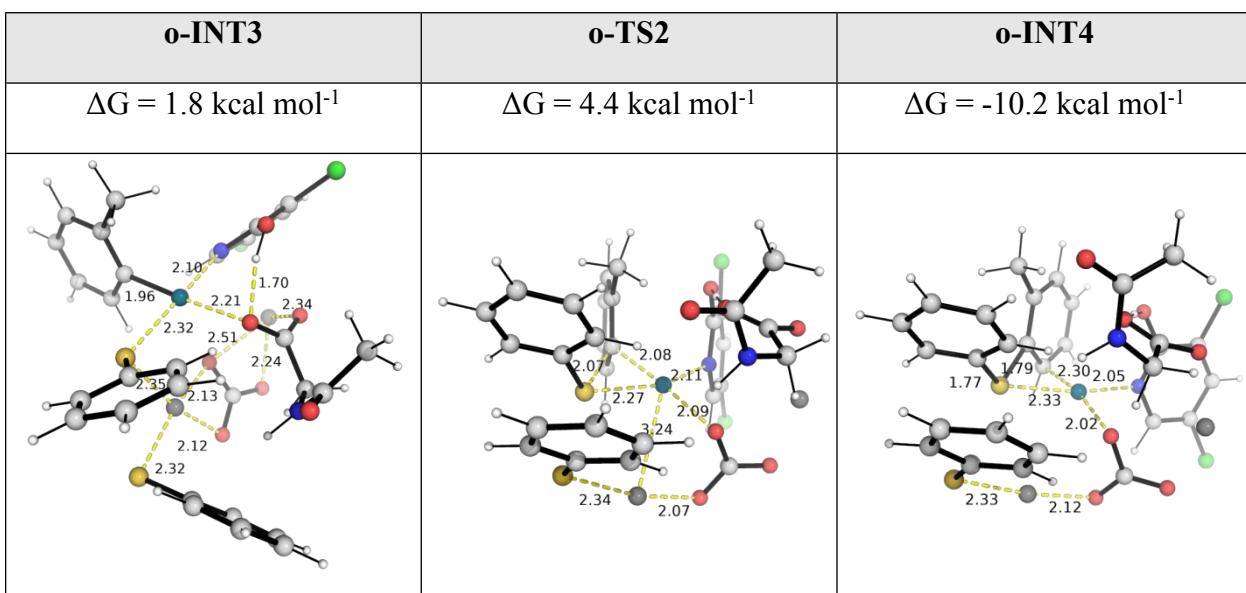
<b>o-INT3</b>	<b>o-INT3-c2</b>	<b>o-INT3-c3</b>
$\Delta G = 1.8 \text{ kcal mol}^{-1}$	$\Delta G = 4.7 \text{ kcal mol}^{-1}$	$\Delta G = 4.9 \text{ kcal mol}^{-1}$
<b>o-INT3-c4</b>	<b>o-INT3-c5</b>	<b>o-INT3-c6</b>
$\Delta G = 5.8 \text{ kcal mol}^{-1}$	$\Delta G = 6.3 \text{ kcal mol}^{-1}$	$\Delta G = 8.0 \text{ kcal mol}^{-1}$



**Figure S13.** DFT optimized structures for possible isomers of [Pd–Ag] complex. Gibbs energies are taken relative to the sum of starting materials.

## 12. Reductive elimination step

The DFT optimized structures for the reductive elimination step forming the sulfane product is shown in Figure S14. This step has a very low barrier of 2.6 kcal mol<sup>-1</sup> from the transmetalated Pd–Ag complex **o-INT3**. In addition, this step is highly exergonic, forming **o-INT4** at -10.2 kcal mol<sup>-1</sup> and is irreversible.



**Figure S14.** DFT optimized structures for the reductive elimination step, forming the sulfane product. Activation barriers are taken relative to the sum of starting materials.

## 13. Release of product

The possible reactions for the release of sulfane product show in Table S11 were computed. From the Gibbs energy of reaction, we can see that reaction **R1**, in which a dichlorohydroxypyridine

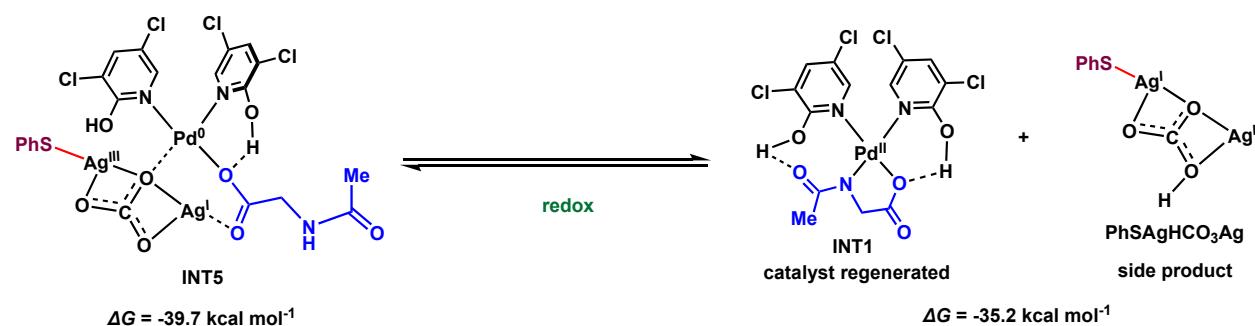
S/N	Reaction	$\Delta G_r /$ kcal mol <sup>-1</sup>
R1	<p>o-INT4 <math>\Delta G = -10.2 \text{ kcal mol}^{-1}</math></p> <p>INT5 <math>\Delta G = -39.7 \text{ kcal mol}^{-1}</math></p>	-29.5
R2	<p>o-INT4 <math>\Delta G = -10.2 \text{ kcal mol}^{-1}</math></p> <p>INT5a <math>\Delta G = -26.8 \text{ kcal mol}^{-1}</math></p>	-16.6
R3	<p>Pd(0)(dichloropyridone)<sub>2</sub></p> <p>Pd(0)(dichlorohydroxypyridine)<sub>2</sub></p>	-15.3
R4	<p>o-INT4 <math>\Delta G = -10.2 \text{ kcal mol}^{-1}</math></p> <p>Pd(0)(dichlorohydroxypyridine)<sub>2</sub> <math>\Delta G = 28.3 \text{ kcal mol}^{-1}</math></p>	38.5
R5	<p>o-INT4 <math>\Delta G = -10.2 \text{ kcal mol}^{-1}</math></p> <p>PhS + PhSAgCO<sub>3</sub>AgMPAA</p> <p>Pd(0)(dichlorohydroxypyridine)<sub>2</sub> <math>\Delta G = 27.9 \text{ kcal mol}^{-1}</math></p>	38.1

**Table S11.** Computed Gibbs energy of reaction for the release of sulfane product.

ligand displaces the sulfane product, is most exergonic and favourable. All other possibilities were less favoured thermodynamically.

#### 14. Regeneration of catalyst *via* redox

Scheme S4 shows the regeneration of active catalyst **INT1**, with the release of the side product, from **INT5**. This completes the reaction cycle as **INT1** subsequently carries out the second cycle of C–H activation of toluene substrate. This reaction has is thermodynamically uphill by 4.5 kcal mol<sup>-1</sup>.



**Scheme S4.** Redox chemistry to regenerate the activate Pd(II)-catalyst complex **INT1**.

#### 15. Optimized structures and absolute energies, zero-point energies

Geometries of all optimized structures (in .xyz format with their associated energy in Hartrees) are included in a separate folder named *final\_xyz* with an associated *readme.txt* file. All these data have been deposited and uploaded to zenodo.org (DOI: 10.5281/zenodo.6473595).

Absolute values (in Hartrees) for SCF energy, zero-point vibrational energy (ZPE), enthalpy and quasi-harmonic Gibbs free energy (at 120°C/393.15 K) for optimized structures are given below. Single point corrections in SMD dichloroethane using MN15/def2-QZVP level of theory are also included.

Structure	E/au	ZPE/au	H/au	T.S/au	qh-G/au	SP	MN15/def2-QZVP
<b>dichloropyridon</b>							
e	-1241.531241	0.075518	-1241.4422	0.056518	-1241.498495	-1242.658717	
<b>dichlorohydroxypyridine</b>							
	-1241.534533	0.075253	-1241.4458	0.056284	-1241.501935	-1242.656084	

<b>HOAc</b>	-228.644533	0.062197	-228.57411	0.041723	-228.61541	-229.06955300
<b>Nacetylglycine</b>	-436.253431	0.118206	-436.12004	0.061666	-436.17856	-437.0589
<b>diphenylsulfane</b>						
<b>-c1</b>	-1258.182435	0.185397	-1257.9754	0.077159	-1258.048302	-1259.5116
<b>diphenylsulfane</b>						
<b>-c2</b>	-1258.182434	0.185402	-1257.9754	0.077087	-1258.048268	-1259.5116
<b>toluene</b>	-270.978507	0.128304	-270.83852	0.052789	-270.889069	-271.483625
<b>sulfane_product</b>	-899.481193	0.211292	-899.24815	0.075438	-899.320402	-900.642338
<b>acetate</b>	-228.059294	0.048219	-228.00312	0.04228	-228.044179	-228.581974
<b>PdOAc2_monomer</b>						
<b>-</b>	-583.809931	0.104326	-583.68809	0.068364	-583.753096	-584.645295
<b>carbonate</b>	-263.114881	0.014696	-263.09435	0.03674	-263.131093	-263.990498
<b>hydrogen_carbonate</b>						
<b>-</b>	-263.954044	0.027165	-263.92041	0.037775	-263.95818	-264.53534
<b>dichloropyridone_anion</b>						
<b>-</b>	-1240.978252	0.06161	-1240.9034	0.056248	-1240.959333	-1242.175766
<b>silver_acetate</b>	-374.748694	0.050631	-374.68765	0.052688	-374.738246	-375.185492
<b>silver_carbonate</b>						
<b>-</b>	-556.727692	0.017256	-556.6994	0.055206	-556.753788	-557.23599
<b>INT1-c2</b>	-3045.897064	0.249714	-3045.6038	0.129126	-3045.723633	-3048.914896
<b>INT1</b>	-3045.904173	0.248385	-3045.6124	0.129179	-3045.732411	-3048.919312
<b>o-INT1</b>	-2075.30424	0.301978	-2074.9602	0.124203	-2075.076122	-2077.710254
<b>o-TS1</b>	-2075.300574	0.297941	-2074.9614	0.120697	-2075.075154	-2077.703191
<b>o-INT2</b>	-2075.328504	0.303104	-2074.9835	0.124438	-2075.099178	-2077.73239
<b>o-TS1-c2</b>	-2075.29935	0.298015	-2074.9602	0.120293	-2075.073781	-2077.701938
<b>p-TS1</b>	-2075.297389	0.29771	-2074.9583	0.122341	-2075.072793	-2077.700357
<b>m-TS1</b>	-2075.295151	0.297641	-2074.956	0.123081	-2075.070707	-2077.699099
<b>m-TS1-c2</b>	-2075.296956	0.29781	-2074.9578	0.12099	-2075.071828	-2077.69953
<b>o-TS1'</b>	-2075.293472	0.297261	-2074.9545	0.124959	-2075.070573	-2077.696068
<b>p-TS1'</b>	-2075.290643	0.297012	-2074.9518	0.125693	-2075.068196	-2077.693603
<b>m-TS1'</b>	-2075.289724	0.297103	-2074.9508	0.124652	-2075.066822	-2077.692308
<b>o-TS1''</b>	-2075.280299	0.297519	-2074.9409	0.123248	-2075.05625	-2077.693388

<b>p-TS1''</b>	-2075.277323	0.297299	-2074.9379	0.126039	-2075.054419	-2077.692051
<b>m-TS1''</b>	-2075.276427	0.297352	-2074.937	0.12516	-2075.052979	-2077.690925
<b>m-TS1''-c2</b>	-2075.276104	0.297381	-2074.9367	0.125002	-2075.052607	-2077.690955
<b>o-TS1''-c2</b>	-2075.277067	0.297654	-2074.9377	0.122569	-2075.052475	-2077.691705
<b>OA-1</b>	-3333.504386	0.488399	-3332.9516	0.175313	-3333.11168	-3337.218941
<b>OA-2</b>	-3333.503976	0.489254	-3332.9505	0.172959	-3333.109426	-3337.219069
<b>OA-3</b>	-2091.924403	0.412273	-2091.4623	0.140157	-2091.592099	-2094.535308
<b>OA-4</b>	-2091.922895	0.41162	-2091.4604	0.146858	-2091.593983	-2094.535106
<b>OA-5</b>	-2897.209491	0.368631	-2896.7915	0.142346	-2896.922038	-2900.138164
<b>OA-6</b>	-2897.197782	0.367806	-2896.7801	0.1442	-2896.911985	-2900.133172
<b>OA-7</b>	-3125.896901	0.432044	-3125.4071	0.159664	-3125.553874	-3129.231227
<b>OA-8</b>	-3125.884104	0.43232	-3125.3935	0.162192	-3125.541639	-3129.222581
<b>OA-9</b>	-4138.790092	0.444906	-4138.2818	0.172609	-4138.43976	-4142.823632
<b>OA-10</b>	-4138.785231	0.44467	-4138.277	0.174234	-4138.435911	-4142.820018
<b>OA-11</b>	-2112.997973	0.419159	-2112.5268	0.146005	-2112.661819	-2115.633871
<b>OA-12</b>	-2341.670266	0.483562	-2341.1259	0.165995	-2341.278728	-2344.716051
<b>OA-1'</b>	-4138.257842	0.431185	-4137.7628	0.178003	-4137.923502	-4142.350059
<b>OA-2'</b>	-3161.255141	0.39812	-3160.8011	0.155308	-3160.944312	-3164.704798
<b>OA-3'</b>	-4138.25794	0.432072	-4137.7624	0.171764	-4137.920354	-4142.342129
<b>OA-1''</b>	-2897.591438	0.380336	-2897.1609	0.141483	-2897.291948	-2900.570625
<b>MI-1</b>	-2091.880643	0.411057	-2091.4194	0.139241	-2091.549654	-2094.503175
<b>MI-2</b>	-2112.964759	0.418241	-2112.4942	0.147036	-2112.630045	-2115.605964
<b>OA1a</b>	-1841.976653	0.289364	-1841.647	0.12417	-1841.759839	-1844.128462
<b>o-INT3</b>	-3890.355386	0.50805	-3889.77	0.205109	-3889.956475	-3894.530563
<b>o-INT3-c2</b>	-3890.355068	0.508072	-3889.7696	0.206122	-3889.956468	-3894.525731
<b>o-INT3-c3</b>	-3890.342641	0.509531	-3889.7564	0.204446	-3889.941795	-3894.527631
<b>o-INT3-c4</b>	-3890.339004	0.508355	-3889.7535	0.20688	-3889.940286	-3894.524034
<b>o-INT3-c5</b>	-3890.338264	0.507479	-3889.7535	0.206272	-3889.940389	-3894.52243
<b>o-INT3-c6</b>	-3890.339742	0.509043	-3889.7538	0.204522	-3889.939668	-3894.521978
<b>o-TS2</b>	-3890.350562	0.507478	-3889.7673	0.200896	-3889.950444	-3894.527686

<b>o-INT4</b>	-3890.365369	0.507798	-3889.7813	0.201848	-3889.965129	-3894.551044
<b>INT5</b>	-4232.469899	0.372719	-4232.0286	0.190955	-4232.200511	-4236.611729
<b>OA-Ag2CO3-RCT</b>	-1814.970465	0.203932	-1814.7325	0.110839	-1814.834526	-1816.784788
<b>OA-Ag2CO3-TS</b>	-1814.934978	0.203142	-1814.6984	0.112338	-1814.800248	-1816.748089
<b>OA-Ag2CO3-PRD</b>	-1814.940576	0.203824	-1814.7026	0.113395	-1814.805546	-1816.757834
<b>OA-AgOAc-RCT</b>	-1632.990324	0.237555	-1632.7196	0.105885	-1632.817855	-1634.734261
<b>OA-AgOAc-TS</b>	-1632.952354	0.236684	-1632.683	0.108998	-1632.781578	-1634.691826
<b>OA-AgOAc-PRD</b>	-1632.95382	0.237312	-1632.6832	0.108569	-1632.782245	-1634.695562
<b>Pd(0)(dichlorohydroxypyridine)2</b>	-2610.810229	0.152113	-2610.6275	0.101947	-2610.723115	-2613.043666
<b>Pd(0)(dichloropyridone)2</b>	-2610.775437	0.151945	-2610.5927	0.104184	-2610.689344	-2613.018295
<b>INT5a-c2</b>	-2990.867198	0.298235	-2990.5153	0.15655	-2990.657959	-2993.904456
<b>INT5a</b>	-2990.870863	0.297922	-2990.5194	0.155132	-2990.661044	-2993.905653
<b>INT5b</b>	-2521.031204	0.432438	-2520.5394	0.164159	-2520.689641	-2524.100421
<b>INT5b-c2</b>	-2521.016813	0.432271	-2520.5247	0.167188	-2520.676649	-2524.101074
<b>PhSAGCO3Ag MPAA</b>	-1621.505028	0.220161	-1621.2486	0.11317	-1621.354118	-1623.428967
<b>PhSAGCO3Ag MPAA-c2</b>	-1621.47822	0.218096	-1621.2223	0.123236	-1621.333841	-1623.415531
<b>PhSAGCO3Ag MPAA-c3</b>	-1621.477246	0.217408	-1621.2217	0.12529	-1621.334744	-1623.414986
<b>HCO3Ag</b>	-410.630056	0.028918	-410.59219	0.046966	-410.639012	-411.129522
<b>PhSAG</b>	-775.802216	0.092273	-775.69656	0.059677	-775.753935	-776.486407
<b>PhSAGHCO3Ag</b>	-1186.473506	0.122067	-1186.3276	0.091273	-1186.410754	-1187.650318

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