

## **SUPPORTING INFORMATION**

### **Fluorescent small molecules are BIG enough to sense biomacromolecule: Synthesis of aromatic thioesters and understanding their interactions with ctDNA**

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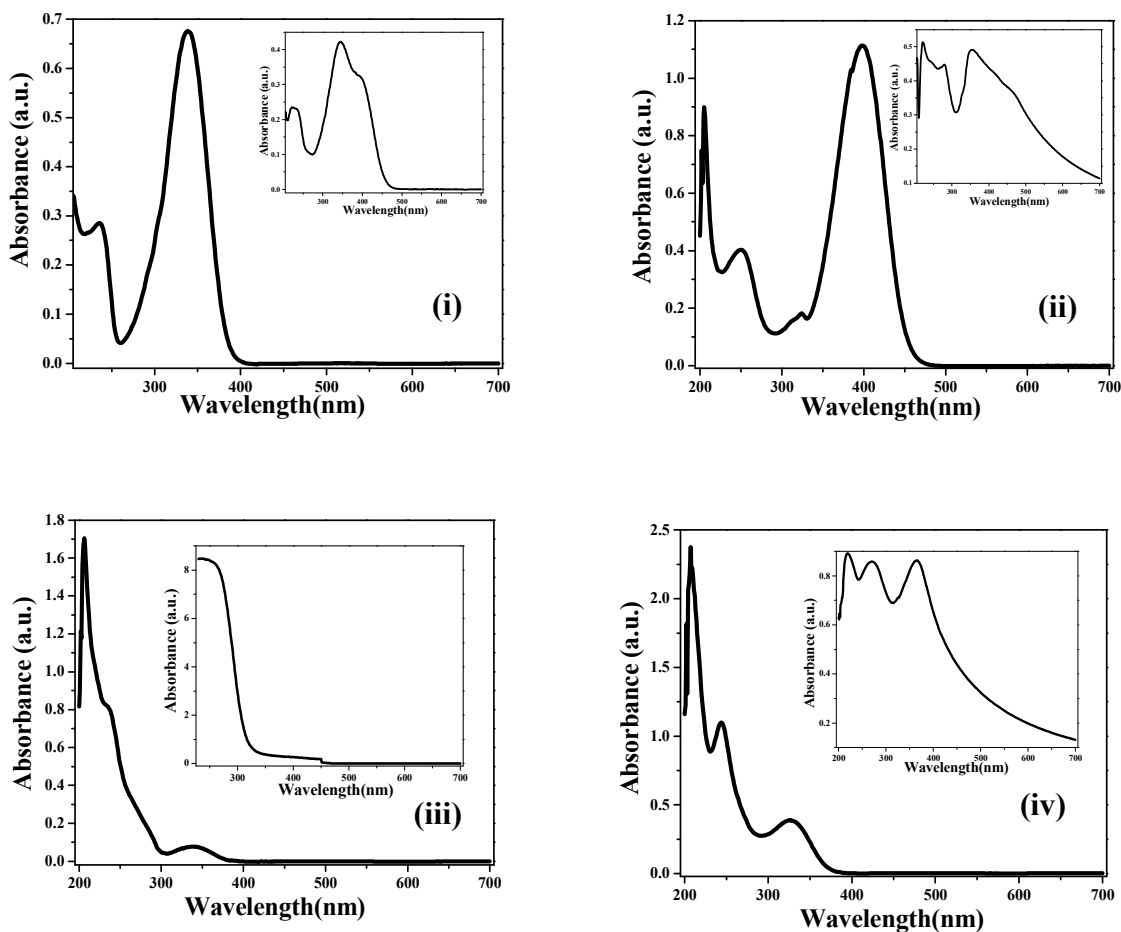
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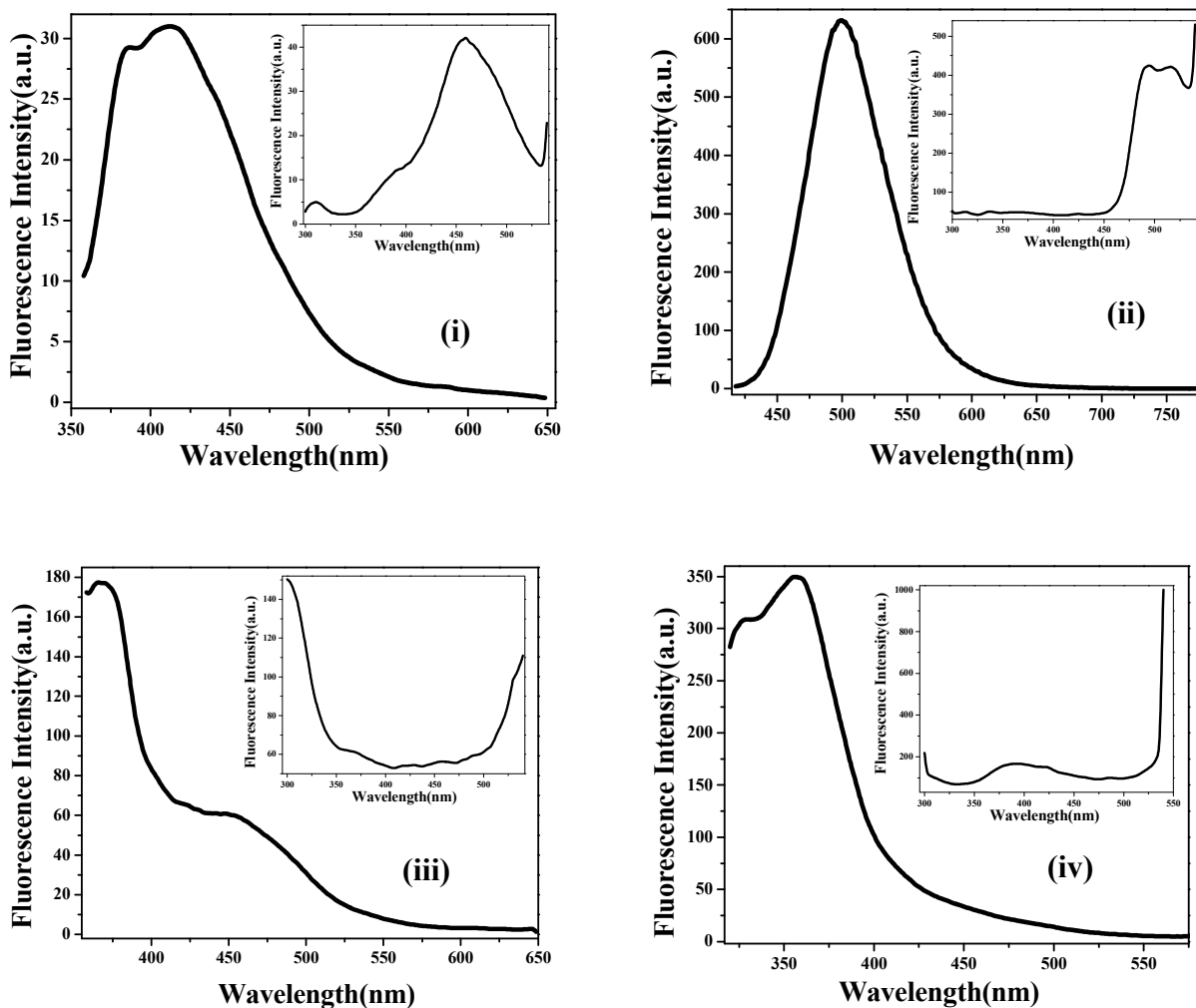
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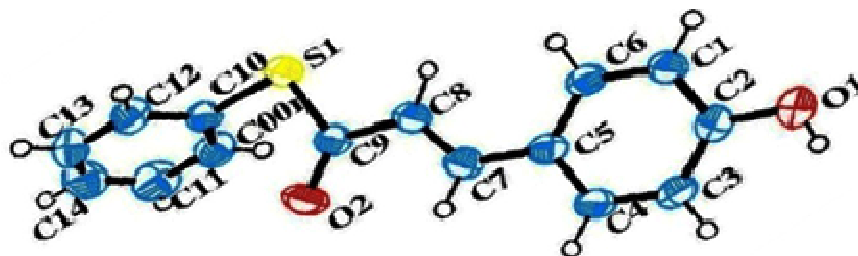
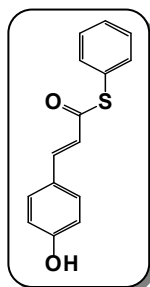
**Figure S1 (a).** UV-Vis spectra of **(i)** *p*-hydroxycinnamic-thiophenyl ester **(1)**, **(ii)** *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester **(2)**, **(iii)** *S*-phenyl-3-(4-chlorophenyl)-3-(phenylthio)propane thioate **(3)** **(iv)** *N*<sup>1</sup>,*N*<sup>1</sup>,*N*<sup>2</sup>,*N*<sup>2</sup>-tetramethyl-1,2-bis(phenylthio)ethene-1,2-diamine **(4)** in EtOH medium. UV-Vis spectra of these compounds in Tris-HCl buffer (10 mM, pH 7.4) are shown in the insets.



**Figure S1 (b).** Fluorescence spectra of **(i)** *p*-hydroxycinnamic-thiophenyl ester (**1**), **(ii)** *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (**2**), **(iii)** *S*-phenyl-3-(4-chlorophenyl)-3-(phenylthio)propane thioate (**3**) **(iv)** *N*<sup>1</sup>,*N*<sup>1</sup>,*N*<sup>2</sup>,*N*<sup>2</sup>-tetramethyl-1,2-bis(phenylthio)ethene-1,2-diamine (**4**) in EtOH medium. Fluorescence spectra of these compounds in Tris-HCl buffer (10 mM, pH 7.4) are shown in the insets.

## Single Crystal XRD data of synthesized compound (1, 2 and 4):

### 1. *p*-Hydroxycinnamic-thiophenyl ester (1)



Single crystal XRD structure of *p*-hydroxycinnamic-thiophenyl ester (1). It is obtained as light yellow crystals. Crystallization was done using dichloromethane. The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication with a CCDC reference number CCDC 1523138.

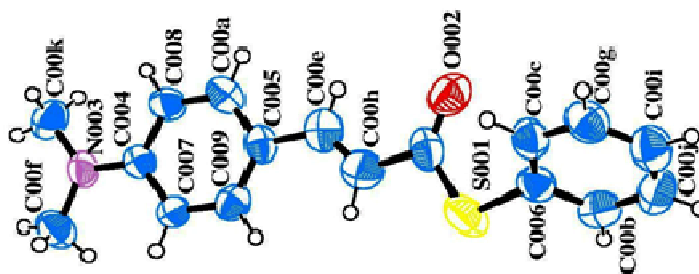
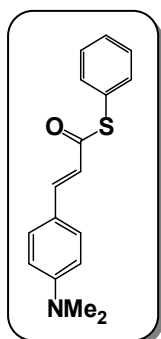
**Table S1. Single crystal X-ray diffraction data and experimental details for *p*-hydroxycinnamic-thiophenyl ester (1).**

CCDC number	1523138
Chemical formula	C <sub>15</sub> H <sub>12</sub> O <sub>2</sub> S
Formula weight	256.31
Crystal system	Monoclinic
Space group	P 21/n
Unit cell dimensions	a=16.6461(6), b=7.6854(3), c=20.8254(8)Å, α=90°, β=98.583(2)°, γ=90°
V/Å <sup>3</sup>	2634.40(17)
Z	8
T/K	296
μ (MoKα)/mm <sup>-1</sup>	0.236
R1 for observed data/wR2 for all data	0.0663( 5065) and 0.2219( 6619)
Number independent reflections	6649
Wavelength(λ/ Å)	0.71073
R-factor (%)	6.6
θ min/° and θ max/°	1.695° and 28.452°

Measurement	Bruker AXS Model (SMART APEX II CCD Detector based Single Crystal XRD System)
Software for refinement	SHELXL-2014/6 (Sheldrick, 2014)
Refinement method	Full matrix least squares on $F^2$
Software for molecular plotting	ORTEP
Software for geometrical calculation	SHELXTL

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## 2. *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (**2**)



Single crystal XRD structure of *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (**2**). It is obtained as yellow crystals. Crystallization was done using dichloromethane. The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication with a CCDC reference number CCDC 1523157.

**Table S2. Single crystal X-ray diffraction data and experimental details for *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (**2**)**

CCDC number	1523157
Chemical formula	C <sub>17</sub> H <sub>17</sub> NOS
Formula weight	283.37
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a=6.2317(5), b=7.5812(6), c=15.8318(13)Å, α=90°, β=97.343(3)°, γ = 90°
V/Å <sup>3</sup>	741.82(10)
Z	2
T/K	296
μ (MoKα)/mm <sup>-1</sup>	0.213
R1 for observed data/wR2 for all data	0.0672( 2160) and 0.1995( 3290)
Number independent reflections	3442
Wavelength(λ/ Å)	0.71073
R-factor (%)	6.7
θ min/° and θ max/°	1.297° and 27.605°
Measurement	Bruker AXS Model (SMART APEX II CCD Detector based Single Crystal XRD System)
Software for refinement	SHELXL-2014/6 (Sheldrick, 2014)

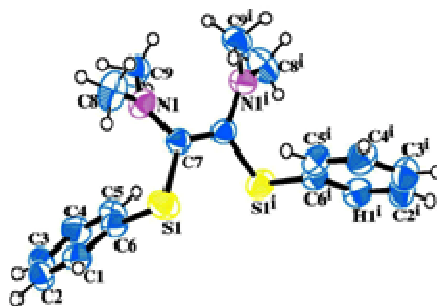
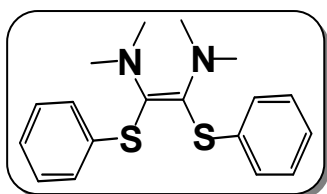
Refinement method Full matrix least squares on  $F^2$

Software for molecular plotting ORTEP

Software for geometrical calculation SHELXTL

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### 3. $N^1, N^1, N^2, N^2$ -tetramethyl-1,2-bis(phenylthio) ethene-1,2-diamine (**4**)



Single crystal XRD structure of  $N^1, N^1, N^2, N^2$ -tetramethyl-1, 2-bis (phenylthio) ethene-1, 2-diamine (**4**). It is obtained as white crystals. Crystallization was done using petroleum ether (60-80°C). The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication with a CCDC reference number CCDC 1004693.

**Table S3. Single crystal X-ray diffraction data and experimental details for  $N^1, N^1, N^2, N^2$ -tetramethyl-1,2-bis(phenylthio) ethene-1,2-diamine (**4**)**

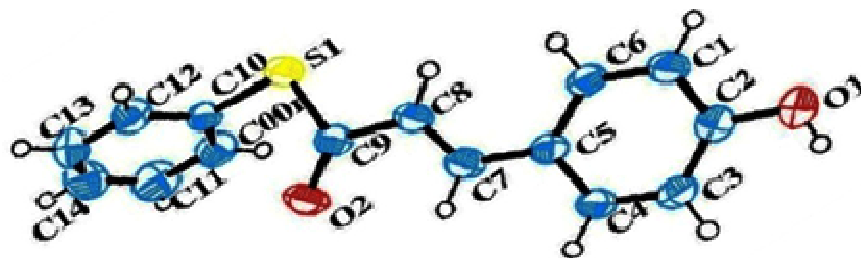
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CCDC number	1004693
Chemical formula	C <sub>18</sub> H <sub>22</sub> N <sub>2</sub> S <sub>2</sub>
Formula weight	330.47
Crystal system	Monoclinic
Space group	P 2/c
Unit cell dimensions	a=16.6147(13), b=11.1160(13), c=11.1363(11)Å, $\alpha=90^\circ$ , $\beta=121.806(7)^\circ$ , $\gamma=90^\circ$
V/Å <sup>3</sup>	1747.9(3)
Z	4
T/K	296
$\mu$ (MoK $\alpha$ )/mm <sup>-1</sup>	0.303
R1 for observed data/wR2 for all data	0.0454( 1757)and 0.1452( 2160)

Number independent reflections	14546
Wavelength( $\lambda$ / Å)	0.71073
R-factor (%)	4.5
$\theta$ min/ $^\circ$ and $\theta$ max/ $^\circ$	0.997 $^\circ$ and 28.27 $^\circ$
Measurement	Bruker AXS Model (SMART APEX II CCD Detector based Single Crystal XRD System)
Software for refinement	SHELXL-2014/6 (Sheldrick, 2014)
Refinement method	Full matrix least squares on F <sup>2</sup>
Software for molecular plotting	ORTEP
Software for geometrical calculation	SHELXTL

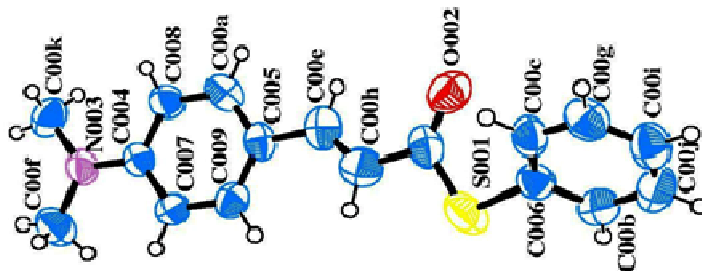
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Table S4. Selected bond lengths and bond angles for *p*-hydroxycinnamic-thiophenyl ester (1)



Bond lengths (Å)					
S1-C10	1.761(2)	C18-C17	1.395(3)	C17-C16	1.378(3)
S1-C9	1.767(2)	C18-C21	1.455(3)	C23-C22	1.465(3)
S2-C24	1.761(3)	C10-C00R	1.383(3)	C21-C22	1.326(4)
S2-C23	1.774(3)	C10-C12	1.384(3)	C12-C13	1.371(3)
O4-C23	1.214(3)	C7-C8	1.329(3)	C00R-C11	1.371(4)
O1-C2	1.359(3)	C2-C3	1.378(3)	C24-C29	1.377(4)
O2-C9	1.213(3)	C2-C1	1.391(3)	C24-C25	1.383(4)
O3-C15	1.363(3)	C6-C1	1.364(3)	C20-C19	1.371(3)
C5-C4	1.395(3)	C15-C16	1.380(3)	C29-C28	1.380(4)
C5-C6	1.400(3)	C15-C19	1.389(3)	C13-C14	1.379(4)
C5-C7	1.448(3)	C3-C4	1.371(3)	C11-C14	1.361(4)
C18-C20	1.395(3)	C9-C8	1.454(3)	C25-C26	1.381(5)
C28-C27	1.357(5)	C27-C26	1.370(5)		
Bond angles (degree)					
C10-S1-C9	100.94(10)	C24-S2-C23	104.08(11)	C2-O1-H34	109.5
C4-C5-C6	117.1(2)	C4-C5-C7	120.1(2)	C6-C5-C7	122.8(2)
C20-C18-C17	117.7(2)	C20-C18-C21	118.5(2)	C17-C18-C21	123.7(2)
C00R-C10-C12	119.7(2)	C00R-C10-S1	120.12(18)	C12-C10-S1	120.14(17)
C8-C7-C5	127.6(2)	O1-C2-C3	123.1(2)	O1-C2-C1	117.4(2)
C3-C2-C1	119.5(2)	C1-C6-C5	121.5(2)	O3-C15-C16	122.9(2)
O3-C15-C19	117.4(2)	C16-C15-C19	119.7(2)	C4-C3-C2	120.1(2)
O2-C9-C8	124.8(2)	O2-C9-S1	122.20(18)	C8-C9-S1	112.99(16)
C6-C1-C2	120.1(2)	C7-C8-C9	121.0(2)	C16-C17-C18	121.2(2)
C17-C16-C15	120.0(2)	C3-C4-C5	121.6(2)	O4-C23-C22	125.2(2)
O4-C23-S2	123.94(19)	C22-C23-S2	110.89(17)	C22-C21-C18	128.5(2)
C13-C12-C10	119.8(2)	C21-C22-C23	120.9(2)	C29-C24-C25	119.4(3)
C29-C24-S2	122.5(2)	C25-C24-S2	118.0(2)	C19-C20-C18	121.3(2)
C11-C00R-C10	120.1(2)	C20-C19-C15	120.1(2)	C12-C13-C14	119.7(3)
C24-C29-C28	119.6(3)	C14-C11-C00R	119.8(3)	C26-C25-C24	120.3(3)
C11-C14-C13	120.9(3)	C27-C28-C29	120.7(3)	C28-C27-C26	120.5(3)
C27-C26-C25	119.5(3)				

**Table S5. Selected bond lengths and bond angles for *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (2)**



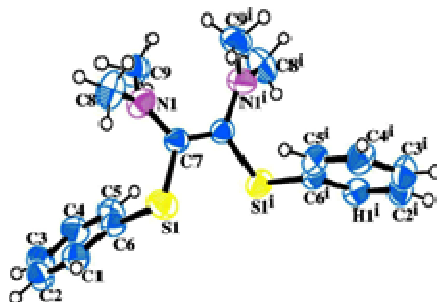
**Bond lengths(Å)**

S001-C00D	1.735(8)	S001-C006	1.759(5)	O002-C00D	1.224(8)
N003-C004	1.361(6)	N003-C00F	1.443(8)	N003-C00K	1.446(8)
C004-C007	1.400(8)	C004-C008	1.405(8)	C005-C00A	1.386(9)
C005-C009	1.398(8)	C005-C00E	1.465(8)	C006-C00C	1.379(8)
C006-C00B	1.385(8)	C007-C009	1.386(7)	C008-C00A	1.356(8)
C00B-C00J	1.390(8)	C00C-C00G	1.368(9)	C00G-C00I	1.362(10)
C00I-C00J	1.352(10)	C00D-C00H	1.500(9)	C00E-C00H	1.272(9)

**Bond angles(degree)**

C00D-S001-C006	105.1(3)	C004-N003-C00F	120.9(5)	C004-N003-C00K	121.6(5)
C00F-N003-C00K	117.4(5)	N003-C004-C007	121.6(5)	N003-C004-C008	121.9(5)
C007-C004-C008	116.5(5)	C00A-C005-C009	116.2(5)	C00A-C005-C00E	118.9(6)
C009-C005-C00E	124.8(6)	C00C-C006-C00B	118.9(5)	C00C-C006-S001	122.4(5)
C00B-C006-S001	118.2(5)	C009-C007-C004	120.5(5)	C00A-C008-C004	122.2(6)
C007-C009-C005	122.3(5)	C008-C00A-C005	122.2(6)	C006-C00B-C00J	119.3(6)
C00G-C00C-C006	120.5(6)	O002-C00D-C00H	127.3(7)	O002-C00D-S001	123.9(5)
C00H-C00D-S001	108.9(5)	C00H-C00E-C005	127.1(7)	C005-C00E-H00E	116.4
C00I-C00G-C00C	120.5(6)	C00E-C00H-C00D	121.4(7)	C00J-C00I-C00G	119.9(6)
C00I-C00J-C00B	120.8(6)				

Table S6. Selected bond lengths and bond angles for  $N^1,N^1,N^2,N^2$ -tetramethyl-1,2-bis(phenylthio) ethene-1,2-diamine (4)

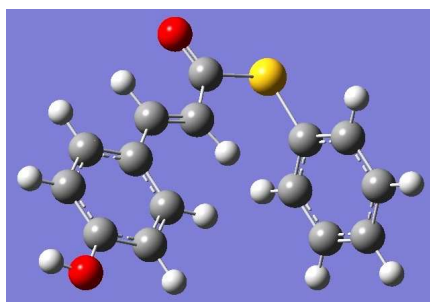


Bond lengths (Å)					
S1-C6	1.7739(16)	C7-C7	1.358(3)	C1-C2	1.381(2)
S1-C7	1.7817(15)	C7-N1	1.385(2)	C4-C5	1.379(2)
C6-C5	1.391(2)	N1-C9	1.443(2)	C4-C3	1.381(3)
C6-C1	1.395(2)	N1-C8	1.447(2)	C2-C3	1.377(3)
Bond angles (degree)					
C6-S1-C7	102.35(7)	C7-C7-S1	120.80(6)	C2-C1-C6	119.94(15)
C5-C6-C1	119.19(15)	N1-C7-S1	115.88(11)	C5-C4-C3	120.54(16)
C5-C6-S1	122.63(12)	C7-N1-C9	119.90(15)	C3-C2-C1	120.57(15)
C1-C6-S1	118.04(12)	C7-N1-C8	121.27(15)	C2-C3-C4	119.66(16)
C7-C7-N1	123.27(9)	C9-N1-C8	118.35(16)	C4-C5-C6	120.09(15)

### Computational details:

Theoretical calculations were done with the help of Gaussian 09 package [1]. DFT calculations were performed to optimize geometry using B3LYP exchange-correlation functional [2] together with standard 6-311<sup>+</sup>G(d,p) basis set [3]. The structure was optimized in gas phase since the solvent effect has a secondary role on the geometrical parameters.

### *p*-Hydroxycinnamic-thiophenyl ester (1)



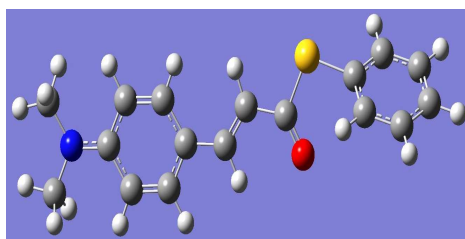
**E = -1127.6735826 Ha; No Imaginary frequency**

### Cartesian Coordinates

C	-4.6497337939	0.4971557424	-0.0000598659
C	-4.5574919158	-0.8954425973	-0.0000616062
C	-3.300213227	-1.5118435116	-0.0000409164
C	-2.1534098063	-0.7386747572	-0.0000186693
C	-2.2170142551	0.6692632179	-0.000015966
C	-3.4900343637	1.2624558505	-0.0000371491
H	-5.6223239088	0.9799340859	-0.0000763731
H	-3.2484052272	-2.5937588509	-0.0000426655
H	-1.1910116324	-1.2363572	-0.0000029879
H	-3.569400682	2.3441894674	-0.0000360386
C	-1.0416449974	1.5283890794	0.000007296
H	-1.2377467405	2.5981643166	0.0000048181
C	0.2541872523	1.1566517239	0.0000319432
H	0.5577431488	0.1195642197	0.0000367873
C	1.3039929515	2.1863063788	0.0000535546
C	3.0581441293	-0.138865996	0.0000344782
C	3.0939361316	-0.8409226544	1.2097499412

C	3.0939616857	-0.8408888361	-1.2096999044
C	3.1448751971	-2.2337051812	1.2068173404
H	3.0830934551	-0.2945310726	2.1452599374
C	3.1449005296	-2.2336714705	-1.2068051255
H	3.0831390165	-0.2944711322	-2.1451948856
C	3.1675524483	-2.9319256677	-0.0000034127
H	3.1711084777	-2.7719221669	2.1476841456
H	3.1711538132	-2.7718621861	-2.147686414
H	3.2099226454	-4.0152165973	-0.0000181161
O	-5.6505081441	-1.7095302288	-0.0000836953
H	-6.4565140169	-1.1818577363	-0.0000898206
O	1.116922661	3.3815375007	0.00003036
S	3.0600611678	1.6584942601	0.0000600103

***p*-N,N-dimethylaminocinnamic-thiophenyl ester (2)**



**E = -1186.4346975 Ha; No Imaginary frequency**

**Cartesian Coordinates**

C	2.780439459	-2.7232416035	-0.643121543
C	1.7909179576	-1.8291964962	-0.2832779956
C	1.9250765857	-0.4442247578	-0.4987006191
C	3.1221565614	-0.0110953657	-1.0958589204
C	4.1259177501	-0.8907314343	-1.4636765175
C	3.9816060714	-2.282226375	-1.2554599364
H	2.6237270194	-3.7749570385	-0.4484491457
H	0.8918895857	-2.2185094205	0.1806658845
H	3.2668375634	1.0499629146	-1.2722140345
H	5.0255904714	-0.4942233796	-1.9128016742
C	0.916276722	0.5327015075	-0.1371266315
H	1.1622678639	1.5691046167	-0.3575012225
C	-0.2874738504	0.3174116805	0.4361418776
H	-0.6378761718	-0.6749232416	0.6967682977
C	-1.1853072237	1.440177857	0.7283379352
C	-3.6647752048	2.3655205001	1.7001921196
C	-3.2684194649	3.3232498335	2.6370548376
C	-4.8164620607	2.5705795618	0.9365306485
C	-4.019180721	4.4845965121	2.7998436219
H	-2.3768115647	3.1607346242	3.2293460946
C	-5.5707204259	3.7292755546	1.1134332159
H	-5.1155811969	1.8278321528	0.2067171348
C	-5.1721643946	4.6884428477	2.0423339688
H	-3.7042802734	5.2290807875	3.5224704507
H	-6.4647690313	3.8835648904	0.5197018608
H	-5.7568998114	5.5916671738	2.1757379356
O	-0.9704059285	2.6090495379	0.5146565583
S	-2.7442022324	0.8440521845	1.5002071379
N	4.9612834144	-3.1731858635	-1.6338901867
C	6.229916121	-2.6826784635	-2.1507225225
H	6.8522424225	-3.5309936661	-2.4303800949

H	6.0821901359	-2.0695243136	-3.0451445321
H	6.7778943517	-2.0840622787	-1.4107788115
C	4.8428169536	-4.5817656529	-1.2875778546
H	5.693067549	-5.1216755682	-1.7006855096
H	4.8286369104	-4.7442056549	-0.2016067043
H	3.9338600968	-5.0198911329	-1.7114671333

**Table S7 (a): Comparison of the change of selected bond lengths and bond angles when *p*-hydroxycinnamic-thiophenyl ester (1) interacts with B form of ctDNA**

Selected bond lengths(Å)			Selected bond angles(degree)			Selected dihedral angles(degree)		
Selected bond lengths	Before binding with ctDNA (in optimized structure)	After binding with ctDNA (in docked structure)	Selected bond angles	Before binding with ctDNA (in optimized structure)	After binding with ctDNA (in docked structure)	Selected dihedral angles	Before binding with ctDNA (in optimized structure)	After binding with ctDNA (in docked structure)
S1-C10	1.798	1.798	<C10-S1-C9	106.650	106.642	*<H34-O1-C2-C3	180.001	129.028
S1-C9	1.834	1.834	<S1-C9-O2	115.625	115.674	<O1-C2-C1-C6	179.984	179.972
O1-C2	1.363	1.363	<O2-C9-C8	125.543	125.533	*<C6-C5-C7-C8	179.992	176.058
O2-C9	1.209	1.209	<C2-O1-H34	110.087	110.085	<C5-C7-C8-C9	180.001	179.975
C7-C8	1.348	1.348	*<O1-C2-C3	117.197	122.846	*<C7-C8-C9-S1	179.986	174.451
#C9-C8	1.471	1.472	<S1-C10-C12	120.098	120.119	*<O2-C9-S1-C10	179.994	39.263
#O1-H34	0.964	0.963	<S1-C9-C8	118.831	118.794	<C9-S1-C10-C12	88.237	89.729
C5-C7	1.456	1.456	*<O1-C2-C1	122.887	117.234	*<C9-S1-C10-C001	91.763	93.224
			<C7-C8-C9	119.573	119.550			
			<S1-C10-C001	120.098	120.087			

# and \* indicate the prominent changes of bond lengths and bond angles or dihedral angles respectively.

**Table S7 (b): Change of structural parameters (selected bond lengths) of *p*-hydroxycinnamic-thiophenyl ester (**1**) after its binding with B form of ctDNA**

Selected bonds lengths (Å)	Selected bonds lengths (Å) in docked structure of	
	(1)-B chain of ctDNA complex	(1)-A chain of ctDNA complex
#(Guanine)H <sub>21</sub> -O <sub>2</sub> of ( <b>1</b> )	4.693	#2.537
#(Guanine)H <sub>22</sub> -O <sub>2</sub> of ( <b>1</b> )	3.470	#2.906
#(Guanine)H <sub>3</sub> -O <sub>2</sub> of ( <b>1</b> )	#2.568	4.741
(Guanine)N <sub>2</sub> -H <sub>34</sub> of ( <b>1</b> )	7.567	9.317
(Guanine)H <sub>1</sub> -O <sub>2</sub> of ( <b>1</b> )	5.394	5.095
(Guanine)H <sub>1</sub> -O <sub>2</sub> of ( <b>1</b> )	5.201	8.524

#Possibility of hydrogen bonding.

**Table S8 (a): Comparison of the change of selected bond lengths and bond angles when *p*-*N*, *N*-dimethylaminocinnamic-thiophenyl ester (**2**) interacts with B form of ctDNA**

Selected bond lengths(Å)			Selected bond angles(degree)			Selected dihedral angles(degree)		
Selected bond lengths	Before binding with ctDNA (in optimized structure)	After binding with ctDNA (in docked structure)	Selected bond angles	Before binding with ctDNA (in optimized structure)	After binding with ctDNA (in docked structure)	Selected dihedral angles	Before binding with ctDNA (in optimized structure)	After binding with ctDNA (in docked structure)
S001-C00d	1.839	1.839	* <C006-S001-C00d	101.955	101.959	*<C00f-N003-C004-C008	173.902	31.746
#S001-C006	1.789	1.788	*<S001-C00d-O002	122.645	122.631	*<C00k-N003-C004-C007	174.605	19.698
#N003-C004	1.377	1.376	*<O002-C00d-C00h	126.597	126.620	<N003-C004-C007-C009	1.005	0.984
N003-C00f	1.455	1.455	*<C004-N003-C00k	119.958	120.242	*<C00a-C005-C00e-C00h	179.862	23.423
O002-C00d	1.207	1.207	<C004-N003-C00f	120.198	119.966	*<C009-C005-C00e-C00h	179.504	23.044
#N003-C00k	1.455	1.454	*<C00f-N003-C00k	118.807	118.760	<C005-C00e-C00h-C00d	0.125	0.162
C005-C00e	1.449	1.449	*<S001-C00d-C00h	110.757	110.748	*<C00e-C00h-C00d-S001	179.820	8.756
#C00d-C00h	1.467	1.466	*<N003-C004-C008	121.587	121.602	*<C00e-C00h-C00d-O002	179.556	8.457
#C00h-C00e	1.351	1.350	*<S001-C006-C00b	119.176	119.180	*<C00h-C00d-S001-C006	1.807	127.576
			*<C00e-C00h-C00d	120.560	120.571	*<O002-C00d-S001-C006	2.058	127.86
			*<C005-C00e-C00h	128.215	128.236	*<C00d-S001-C006-C00b	112.101	130.815
						*<C00d-S001-C006-C00c	109.977	128.797

# and \* indicate the prominent changes of bond lengths and bond angles or dihedral angles respectively.

**Table S8 (b): Change of structural parameters (selected bond lengths) of *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (2) after its binding with B form of ctDNA**

Selected bonds lengths (Å)	Selected bonds lengths (Å) in docked structure of	
	(2)-B chain of ctDNA complex	(2)-A chain of ctDNA complex
(Guanine)H22-N003 of (2)	3.692	3.870
(Guanine)H1- N003 of (2)	6.281	5.861
(Guanine)H22-O002of (2)	6.801	4.138
(Guanine)H21- N003 of (2)	3.870	3.829
(Guanine)H21-N003 of (2)	4.132	3.829
(Guanine)H1-N003of (2)	6.281	5.861
(Guanine)H3-N003 of (2)	5.734	5.915
(Guanine)H1-N003 of (2)	3.410	7.562

## **Cytotoxicity assays of *p*-hydroxycinnamic-thiophenyl ester (1), *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (2)**

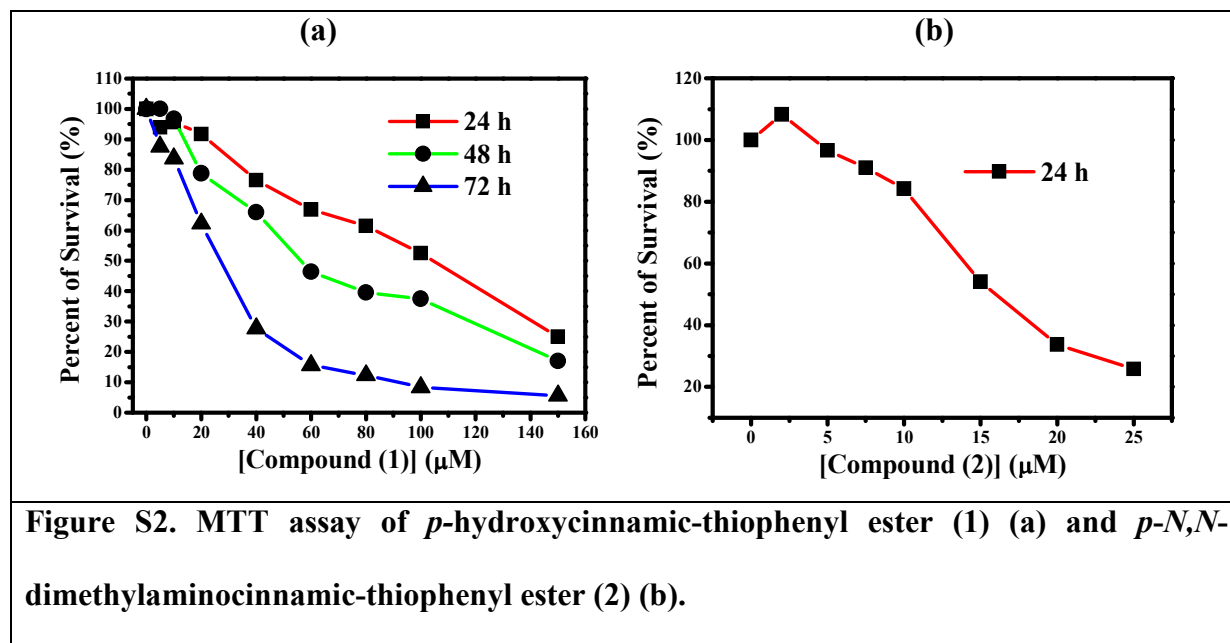
### ***MTT assay of (1) and (2):***

Assay for cytotoxicity of (1) and (2) were performed in 96-well format using the MTT assay on HEK293 cells [4]. Cells maintained in DMEM media with 10 % FBS were plated at a density of  $5 \times 10^3$  cells per well for 24 hrs. Cells were then treated with different concentrations of the compound (1) for 24, 48 and 72 hrs and 24 hrs for compound (2) at 37°C in a 5% CO<sub>2</sub> incubator. Post-treatment, 10 µl of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) (5 mg ml<sup>-1</sup>) was added to each well and incubated for 4 hrs at 37°C. Media was then removed and formazon crystals were dissolved in 100 µl DMSO. After 45 mins. plates were read at 572 nm in a microplate reader (BioTek ELISA Reader, USA). Controls of DMSO, complete medium, compounds with MTT reagent without cells were also checked.

The cell cytotoxicity assay performed on the normal human cell line, HEK293 using the MTT assay method showed a concentration- and time-dependent effect. The compound showed toxicity towards the cells which increased with increasing concentration of the compound as also the period of exposure (24-, 48- and 72-hrs). At 30 µM, more than 82% of the cells survived after 24 hrs. This value was approximately 70% and 45% at 48- and 72-hrs, respectively. Corresponding results are shown in Figure S2.

### ***In-vivo* viability assay of (1) and (2):**

The *in-vivo* cytotoxicity of these compounds were measured in *Saccharomyces cerevisiae* 699 (MATa ade2-1 ura3-1 trp1-1 leu2-3, 112 his3-11, 15 ceul-100) cells. Cultures at a concentration of  $6 \times 10^4$  cells per ml (at approximately 16 hrs growth) were grown in the presence of the test



samples at 40 μM concentration for varying period of time and the viability of the cells were checked at intervals. The cells were assayed for viability using trypan blue (0.4% in saline).

The effect of these compounds on *S. cerevisiae* cells were evaluated at 40 μM up to 10 days. No toxicity of the compound was observed after checking for viability of the cells at 0-, 2- and 10-days.

## References

- [1] Frisch, M.J.; Trucks, G.W.; Schlegel, H.B.; Scuseria, G.E.; Robb, M.A.; Cheeseman, J.R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G.A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H.P.; Izmaylov, A.F.; Bloino, J.; Zheng, G.; Sonnenberg, J.L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery Jr, J.A.; Peralta, J.E.; Ogliaro, F.; Bearpark, M.; Heyd, J.J.; Brothers, E.; Kudin, K.N.; Staroverov, V.N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J.C.; Iyengar, S.S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N.J.; Klene, M.; Knox, J.E.; Cross, J.B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R.E.; Yazyev, O.; Austin, A.J.; Cammi, R.; Pomelli, C.; Ochterski, J.W.; Martin, R.L.; Morokuma, K.; Zakrzewski, V.G.; Voth, G.A.; Salvador, P.; Dannenberg, J.J.; Dapprich, S.; Daniels, A.D.; Farkas, O.; Foresman, J.B.; Ortiz, J.V.; Cioslowski, J.; Fox, D.J. Gaussian 09, Revision B.01 Gaussian, Inc.: Wallingford, C.T. 2009.
- [2] Hehre, W.J.; Radom, L.; Schleyer, P.V.R. Pople, J.A. Ab initio Molecular Orbital Theory. Wiley: New York. 1986.
- [3] Tao, J.; Li, S. Theoretical study on the mechanism of the petasis-type boronic mannich reaction of organoboronic acids, amines, and  $\alpha$ -hydroxy aldehydes. *Chin. J. Chem.* **2010**, *28*, 41.
- [4] Mosmann, T. Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. *Journal of Immunological Methods*, **1983**, *65*, 55.

$^1\text{H}$  and  $^{13}\text{C}$  NMR, LCMS and IR spectra for the synthesized products

Figure S3 (a)  $^1\text{H}$  NMR of *p*-Hydroxycinnamic-thiophenyl ester (1)

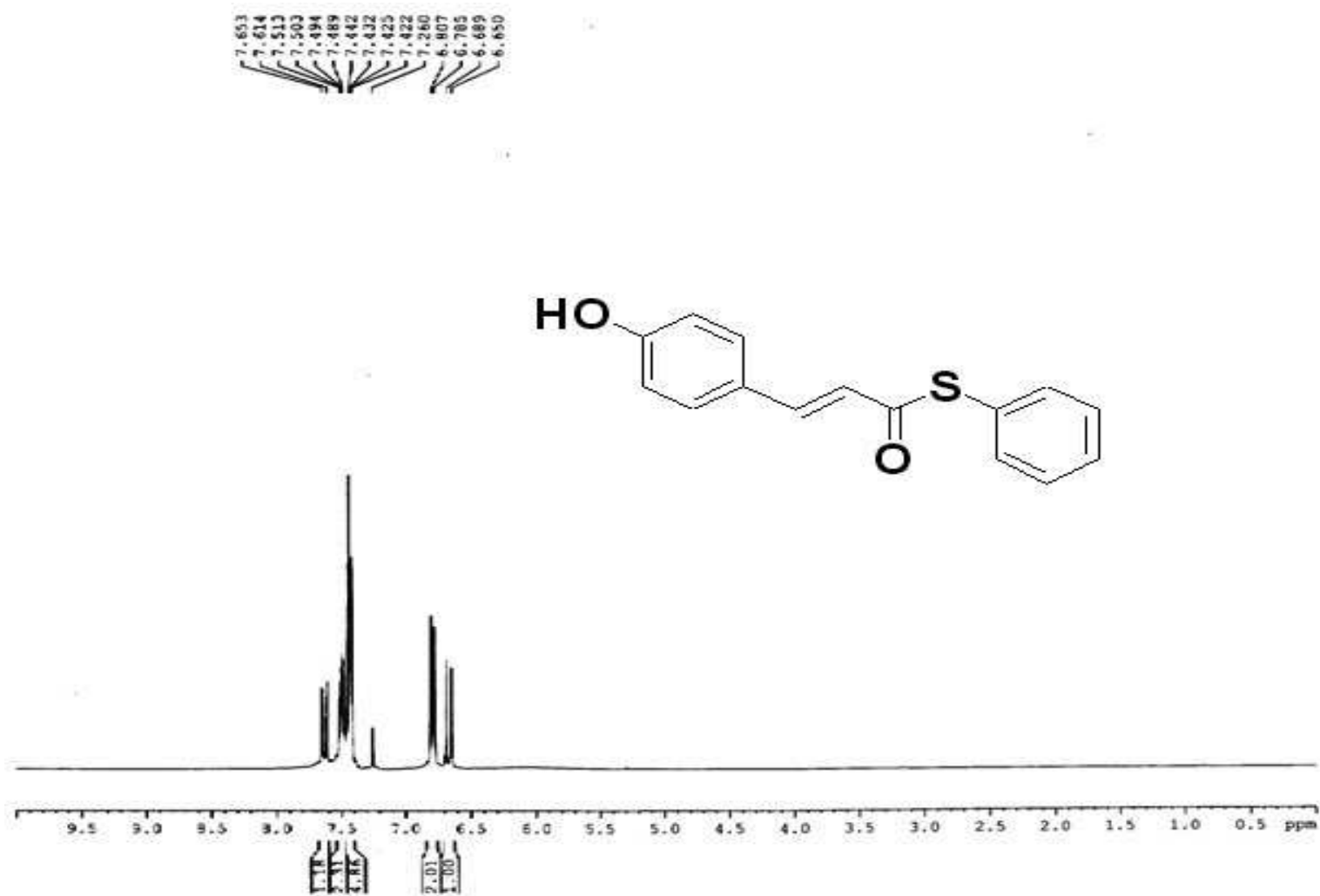


Figure S3 (b)  $^{13}\text{C}$  NMR of *p*-Hydroxycinnamic-thiophenyl ester (1)

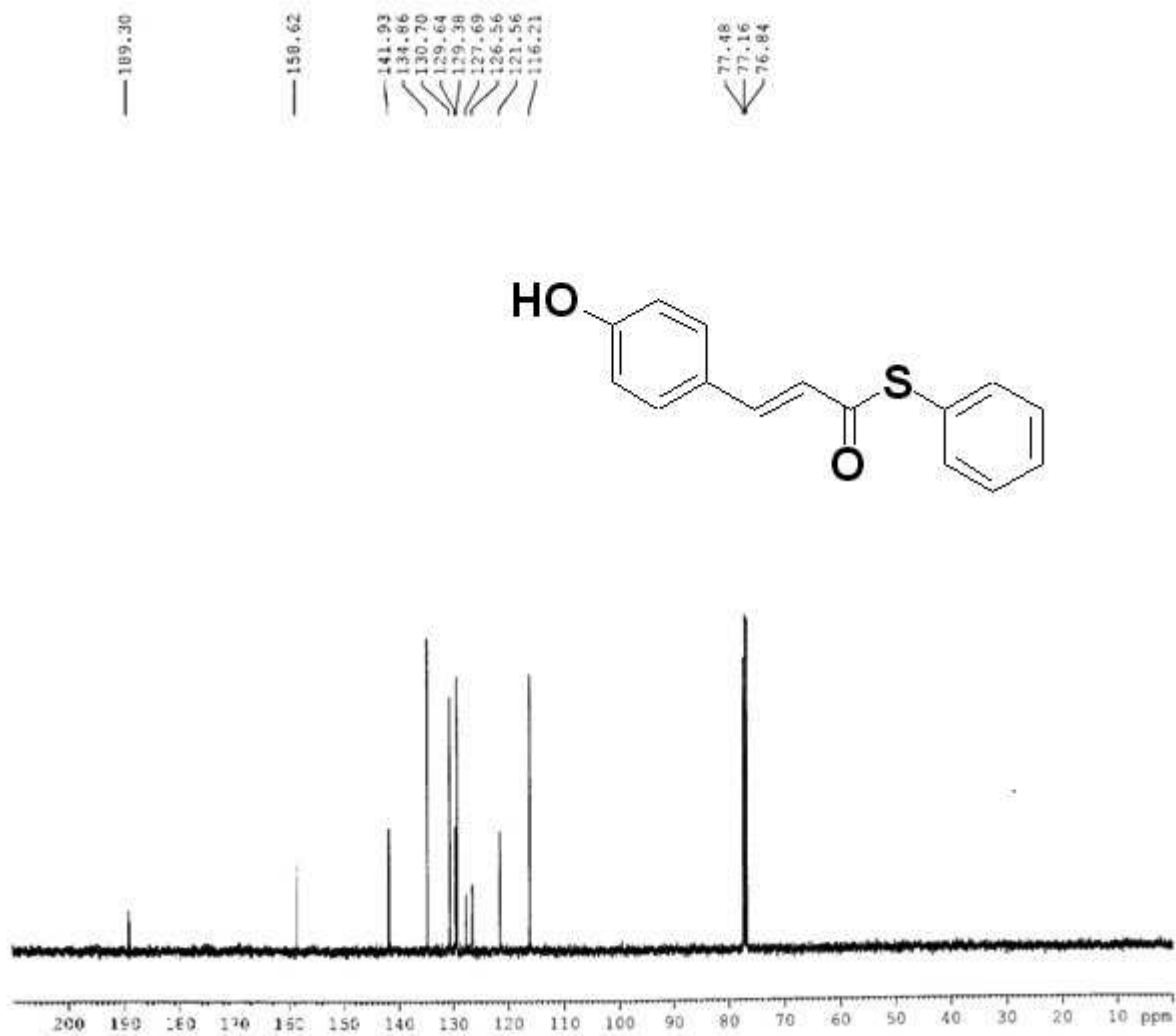


Figure S3 (c) LCMS of *p*-Hydroxycinnamic-thiophenyl ester (1)

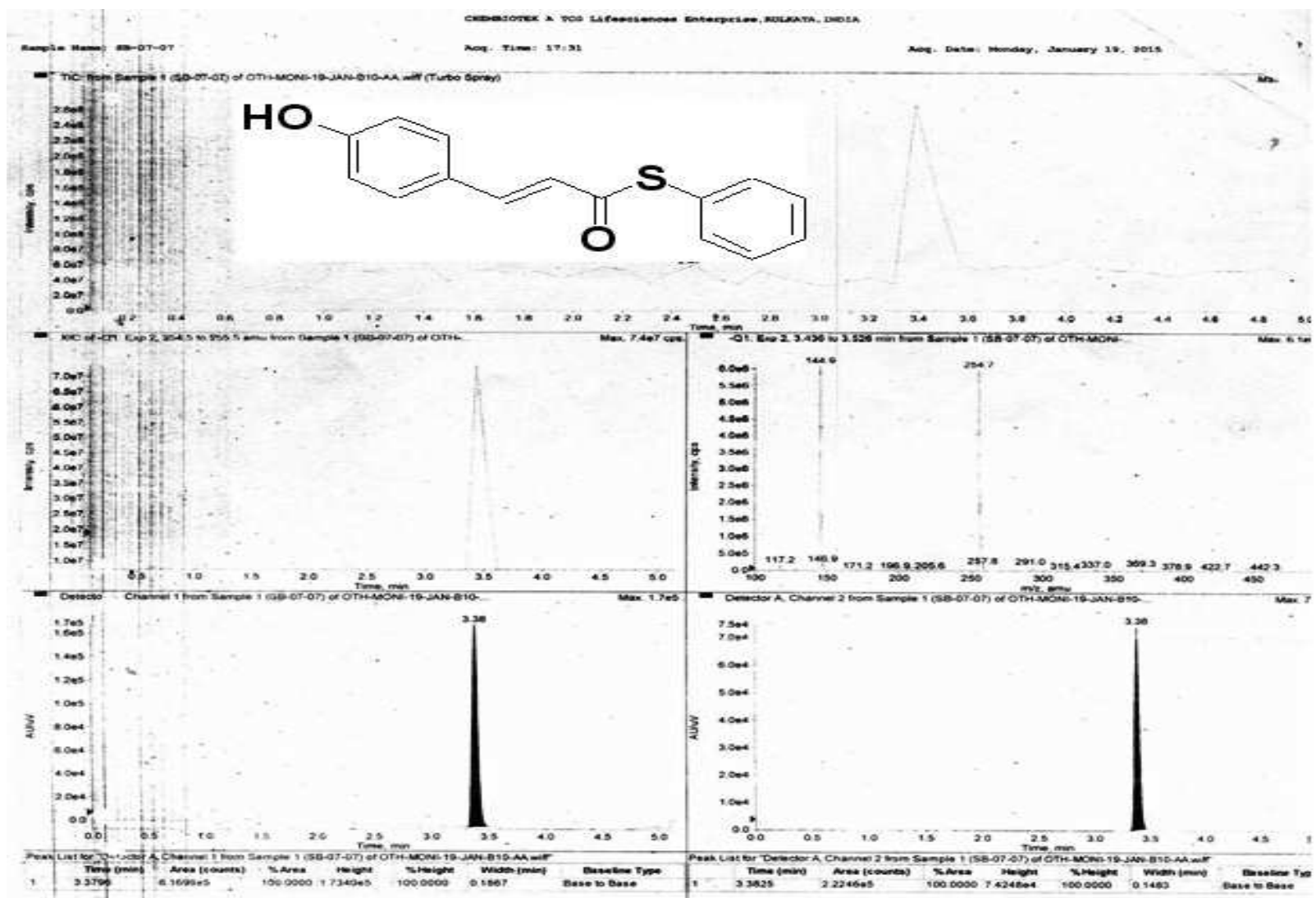


Figure 3S (d) IR Spectra of *p*-Hydroxycinnamic-thiophenyl ester (1)

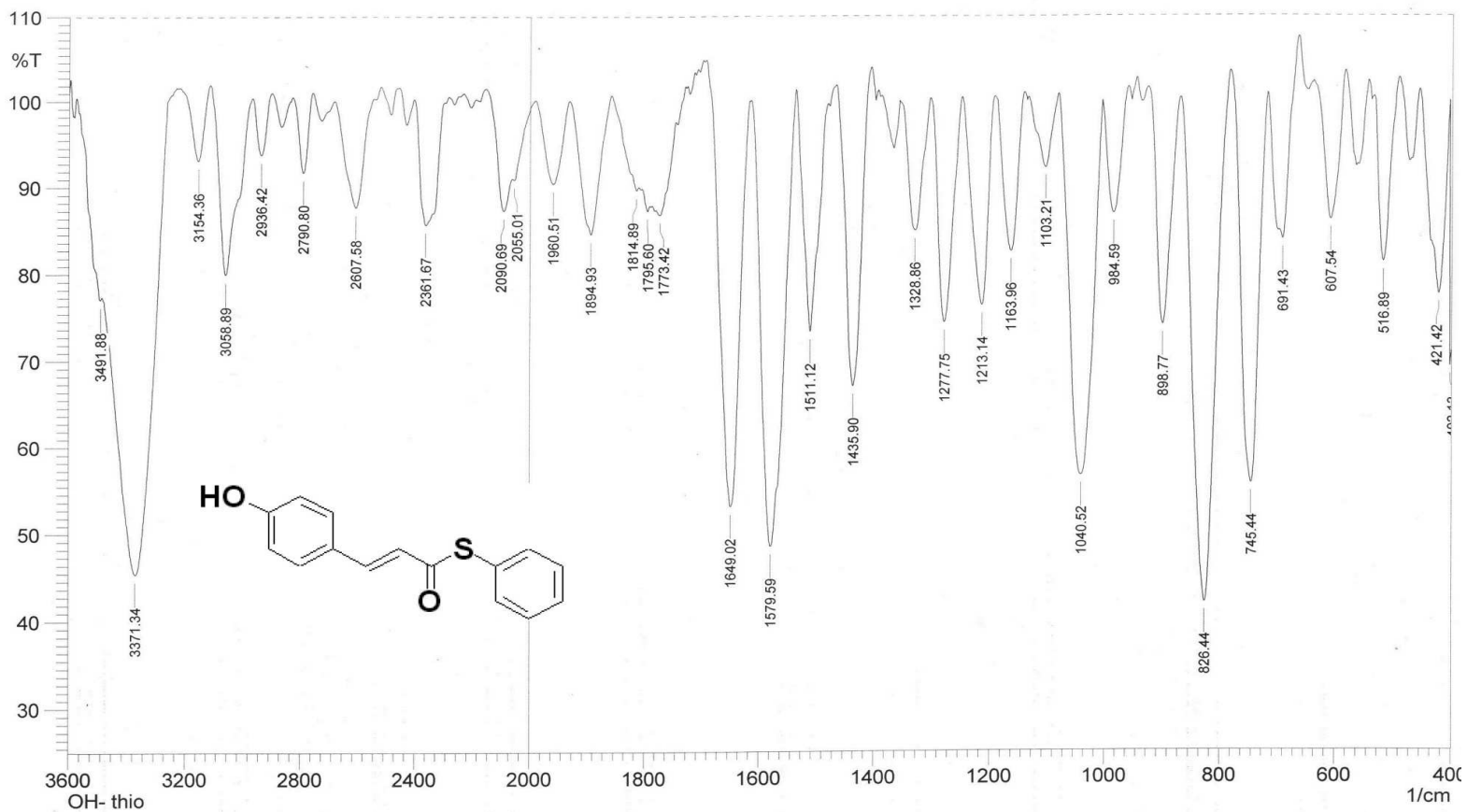


Figure S4 (a)  $^1\text{H}$  NMR of *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (2)

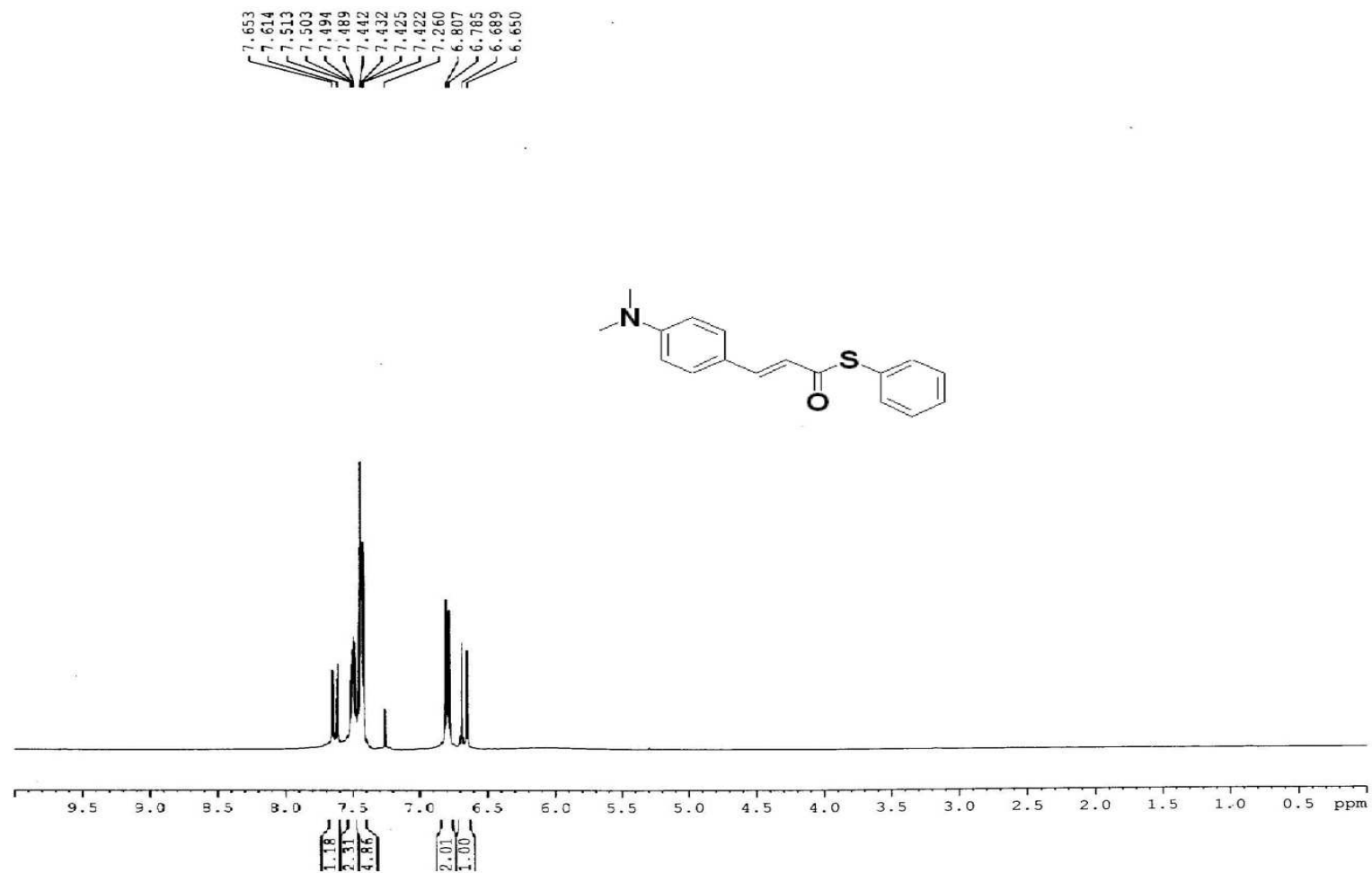


Figure S4 (b)  $^{13}\text{C}$  NMR of *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (2)

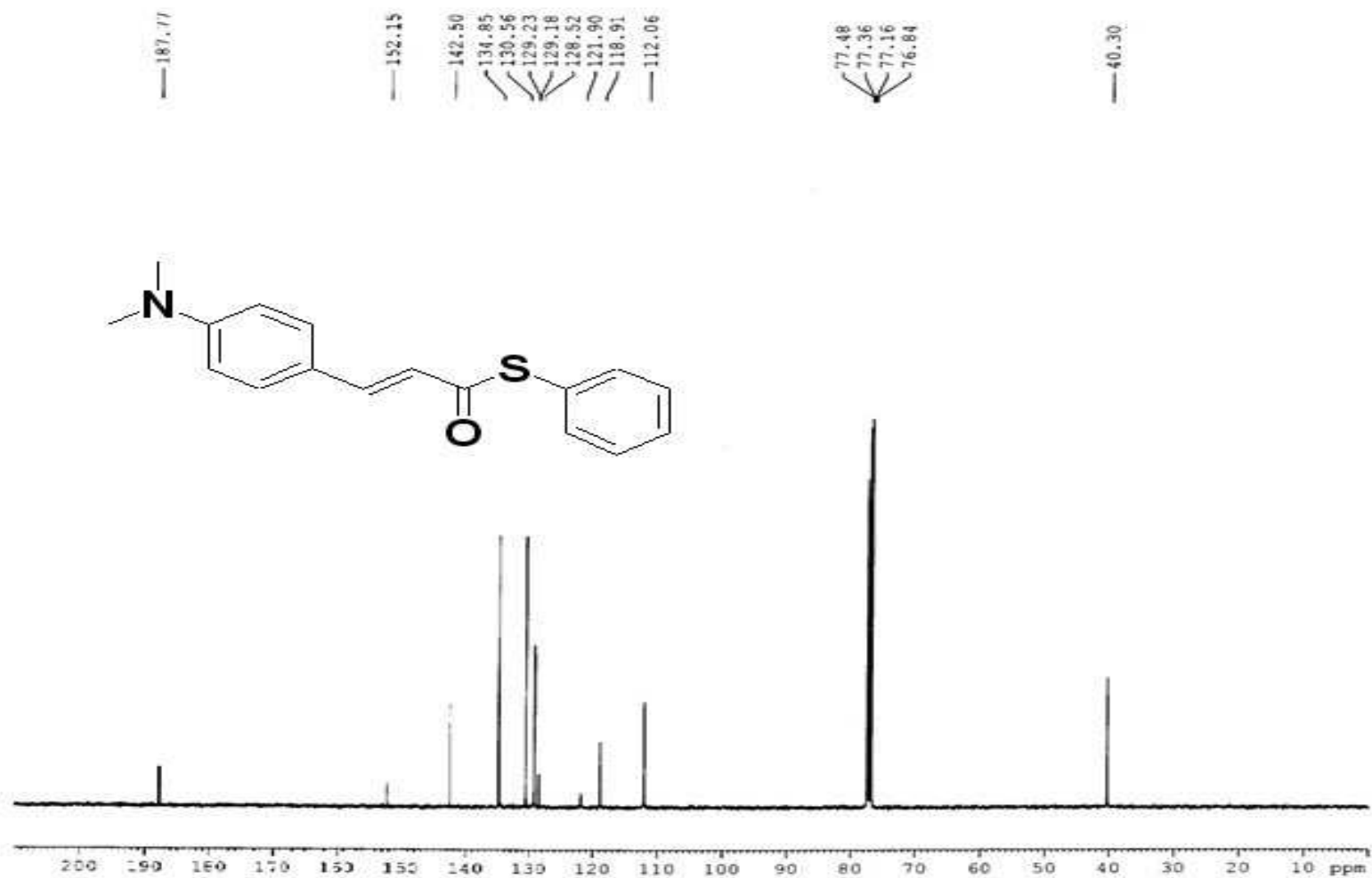
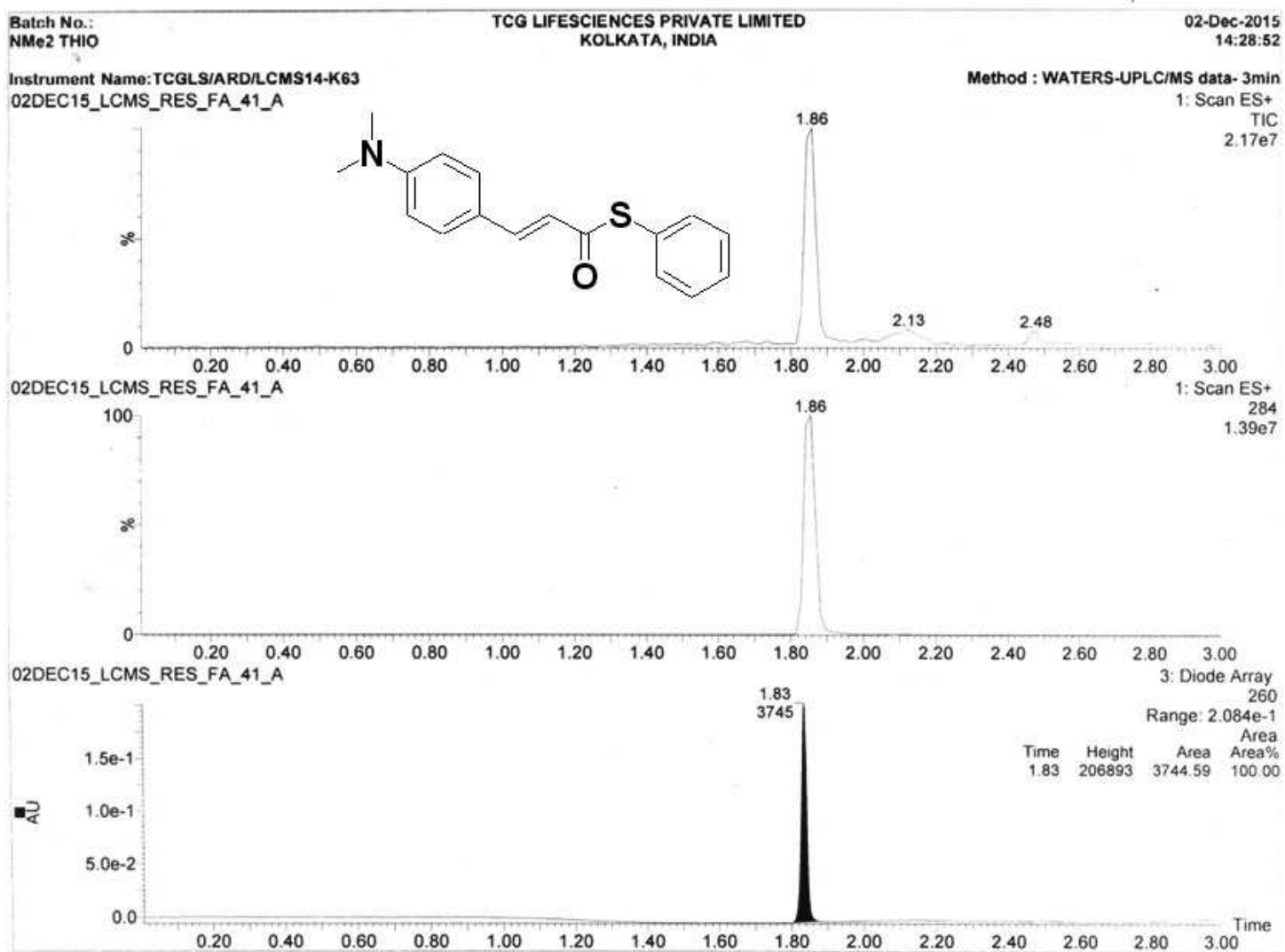


Figure S4 (c) LCMS of *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (2)



Batch No.:  
NMe2 THIO

TCG LIFE SCIENCES PRIVATE LIMITED  
KOLKATA, INDIA

02-Dec-2015  
14:28:52  
Checked By  
1. Scan ES+  
1.36e7

02DEC15\_LCMS\_RES\_FA\_41\_A 138 (1.855) Cm (137:138)

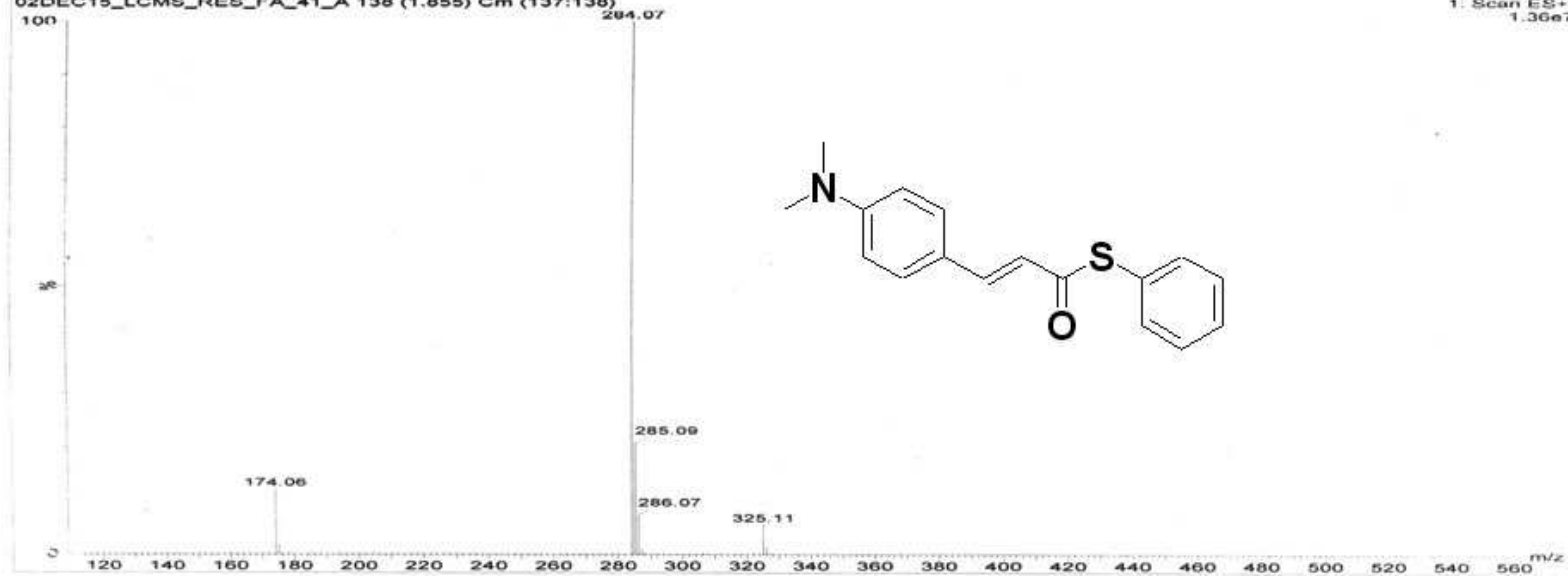


Figure S4 (d) IR Spectra of *p*-*N,N*-dimethylaminocinnamic-thiophenyl ester (2)

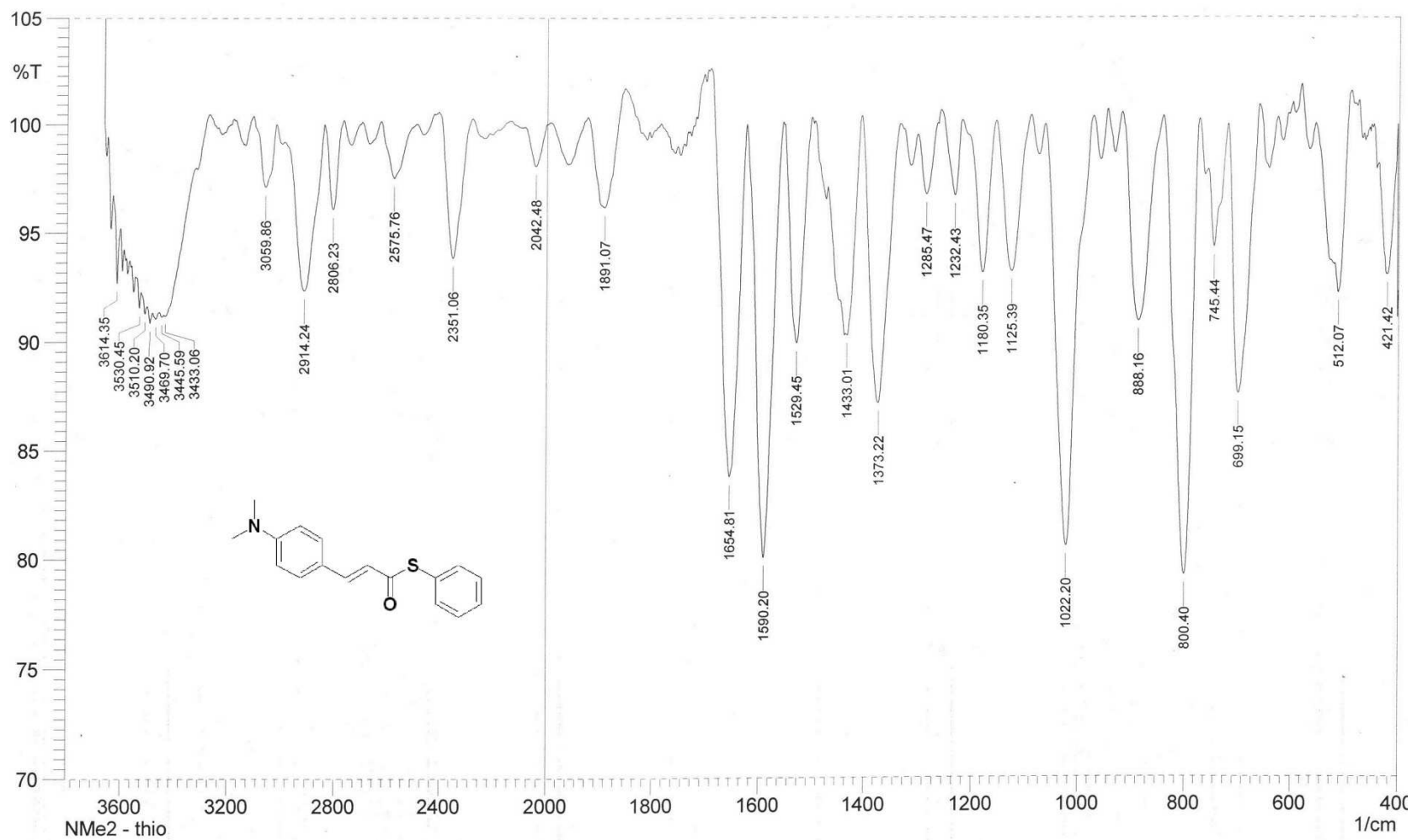


Figure S5 (a)  $^1\text{H}$  NMR of *S*-phenyl-3-(4-chlorophenyl)-3-(phenylthio) propane thioate (3)

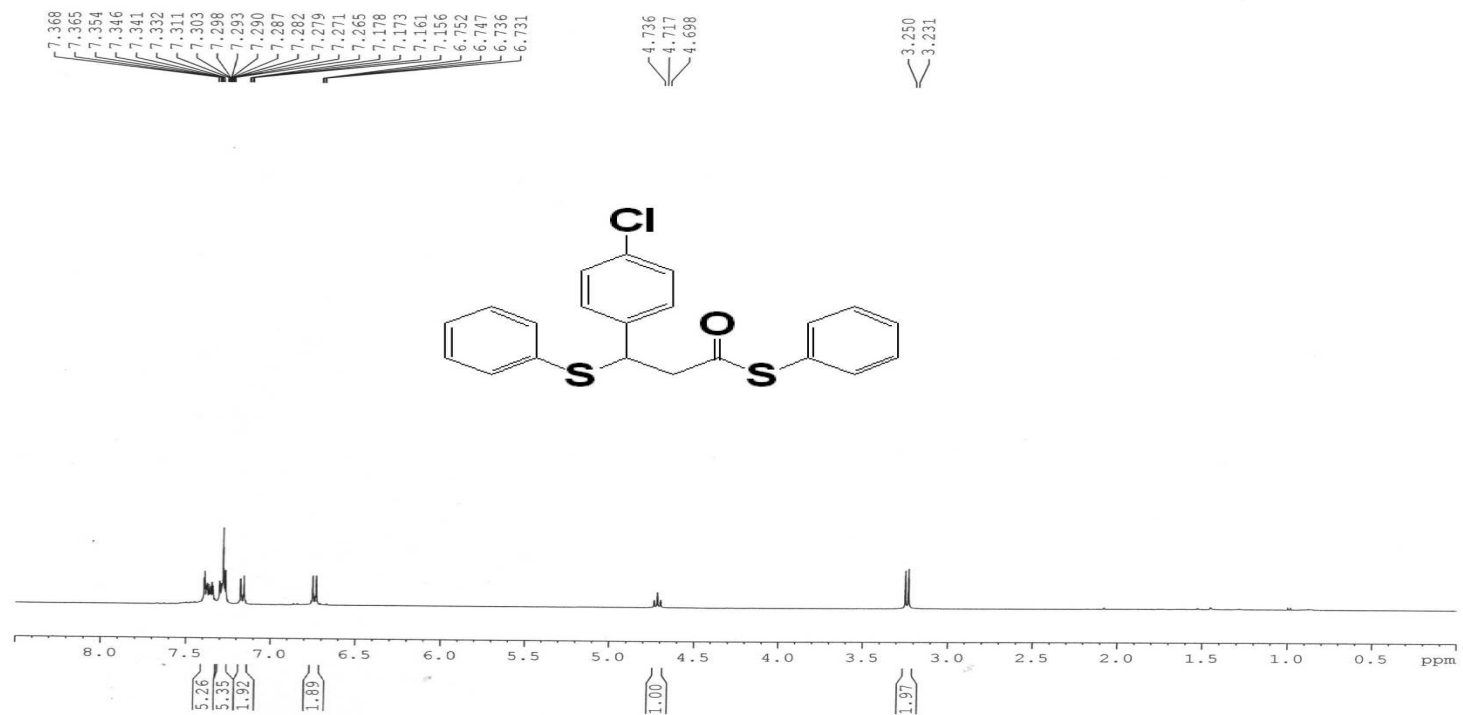


Figure S5 (b)  $^{13}\text{C}$  NMR of *S*-phenyl-3-(4-chlorophenyl)-3-(phenylthio) propane thioate (3)

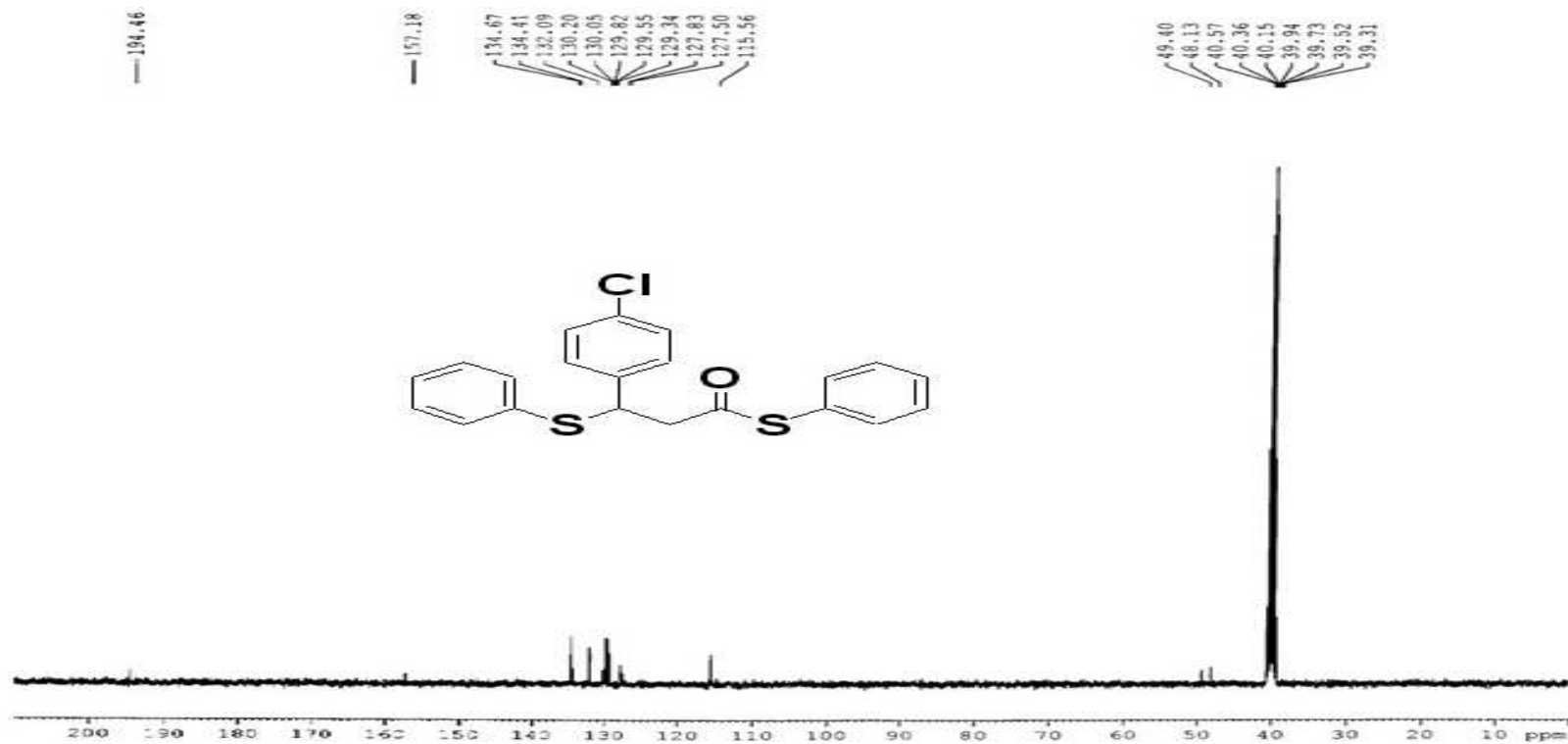
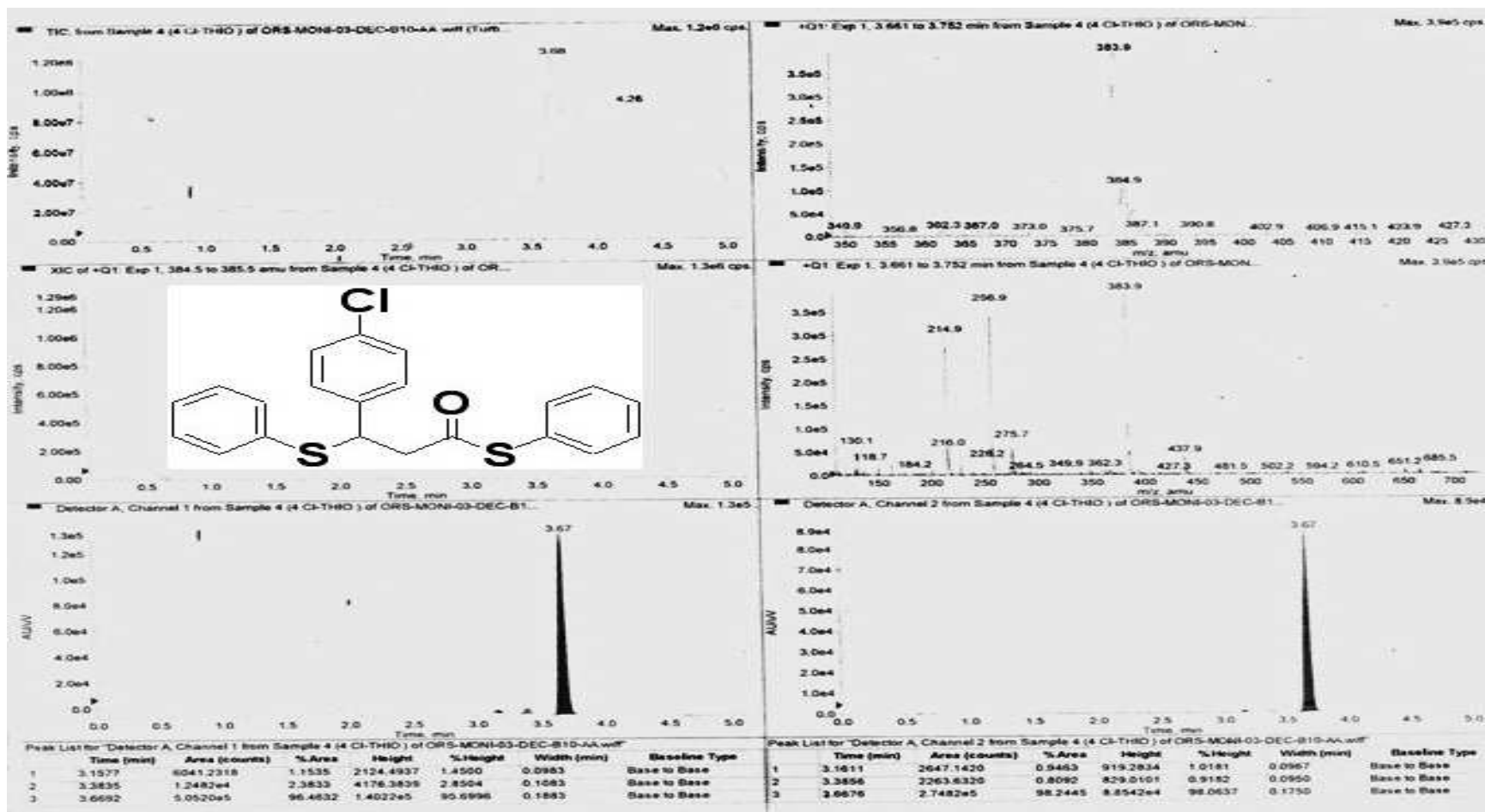
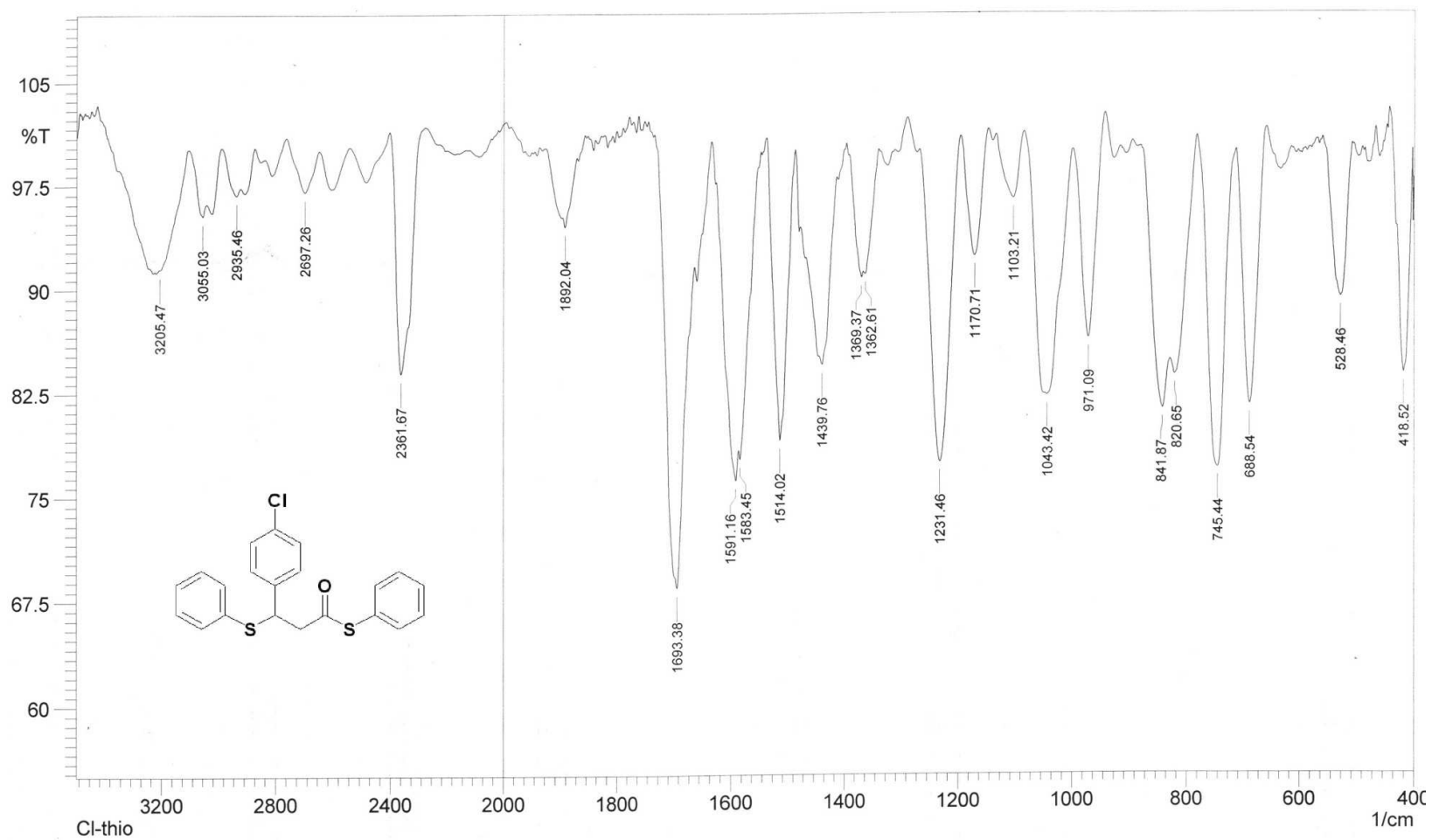


Figure S5 (c) LCMS of *S*-phenyl-3-(4-chlorophenyl)-3-(phenylthio) propane thioate (3)





**Figure S5 (d) IR of *S*-phenyl-3-(4-chlorophenyl)-3-(phenylthio) propane thioate (3)**

Figure S6 (a)  $^1\text{H}$  NMR of  $N^1, N^1, N^2, N^2$ -tetramethyl-1,2-bis(phenylthio)ethene-1,2-diamine (4)

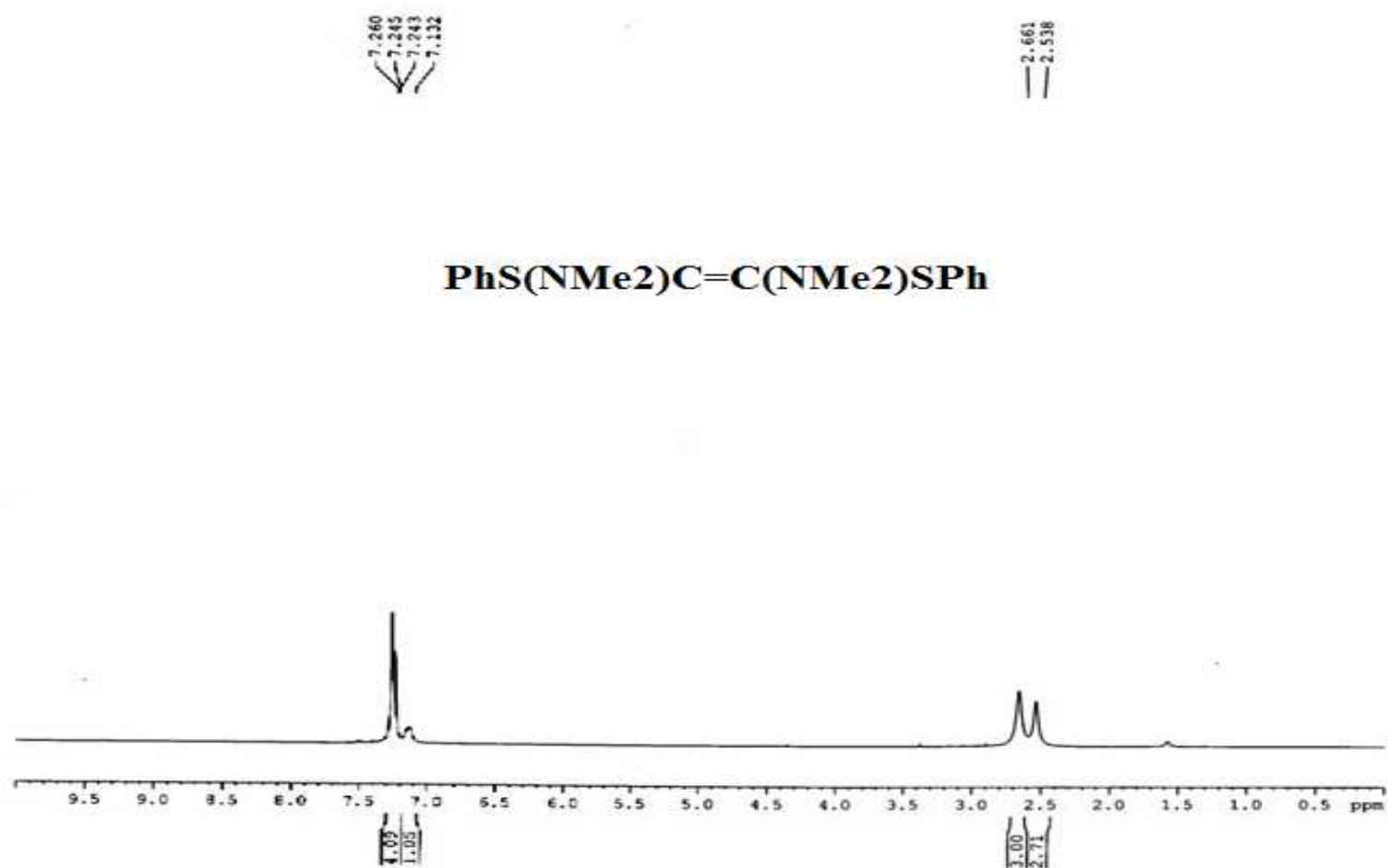


Figure S6 (b)  $^{13}\text{C}$  NMR of  $N^1,N^1,N^2,N^2$ -tetramethyl-1,2-bis(phenylthio)ethene-1,2-diamine (4)

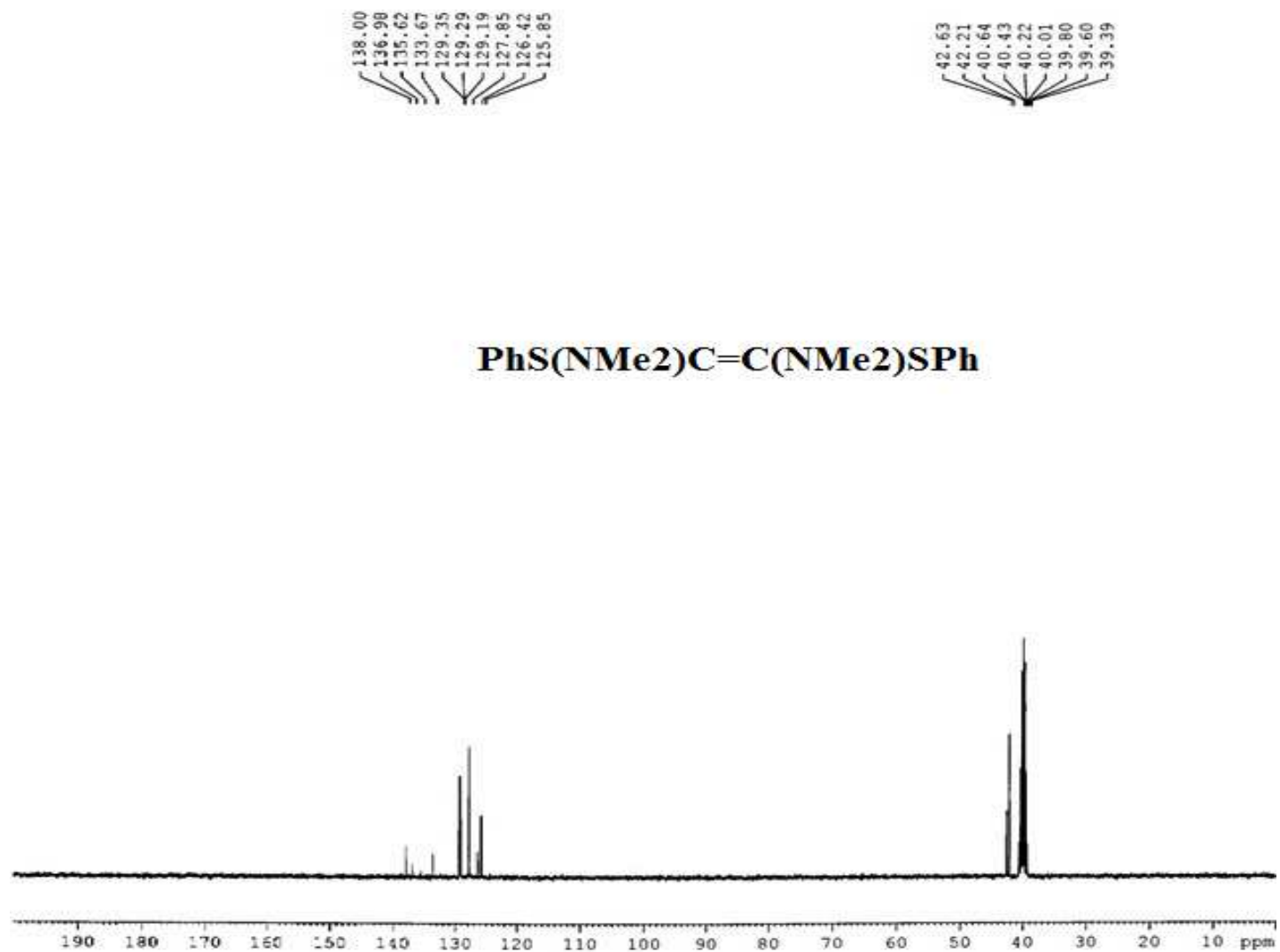


Figure S6 (c) LCMS of  $N^1, N^1, N^2, N^2$ -tetramethyl-1,2-bis(phenylthio)ethene-1,2-diamine (4)

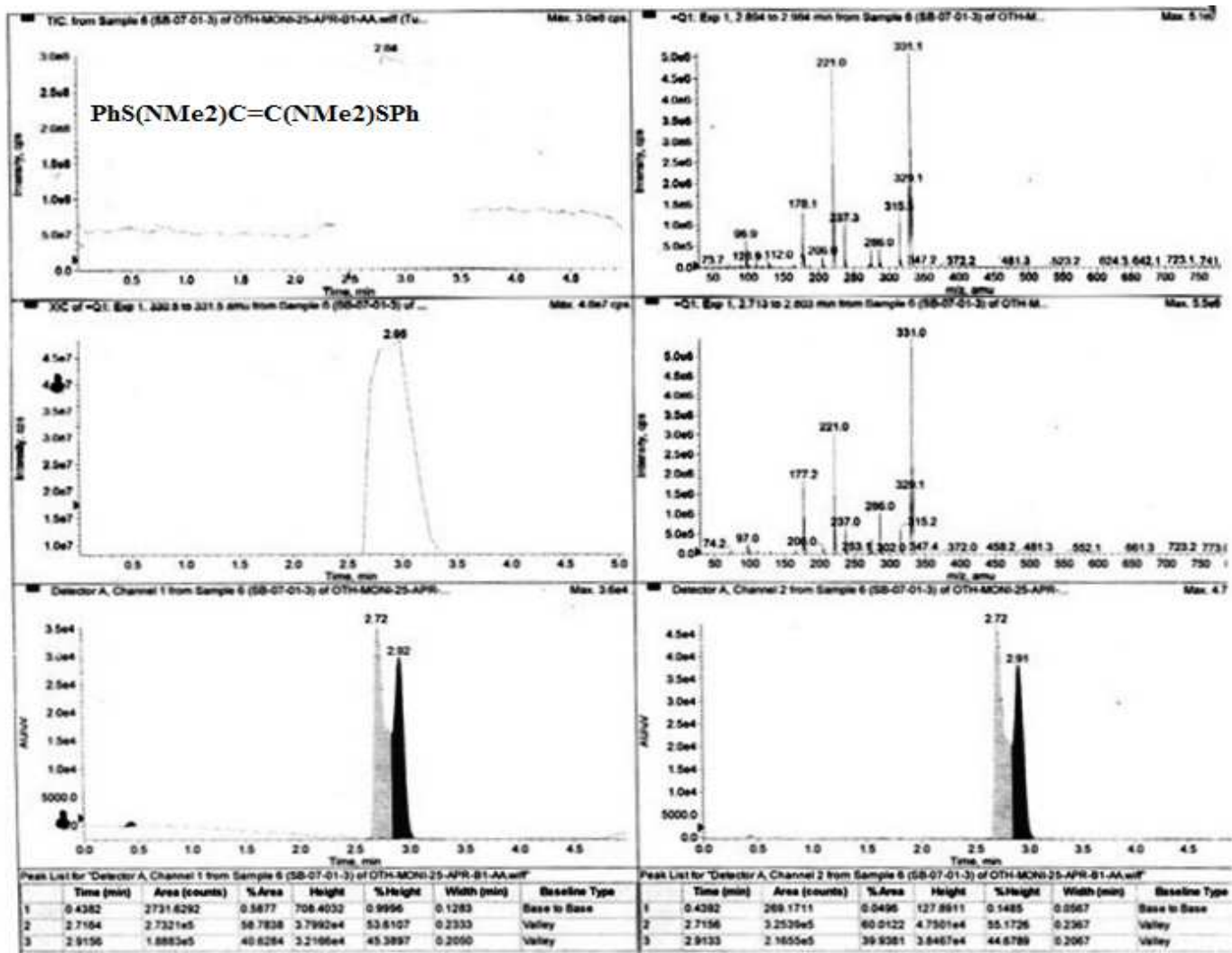


Figure S6 (d) IR Spectra of  $N^1, N^1, N^2, N^2$ -tetramethyl-1,2-bis(phenylthio)ethene-1,2-diamine

