New Benzimidazoles Targeting Breast Cancer: Synthesis, Pin1 Inhibition, 2D NMR Binding, and Computational Studies

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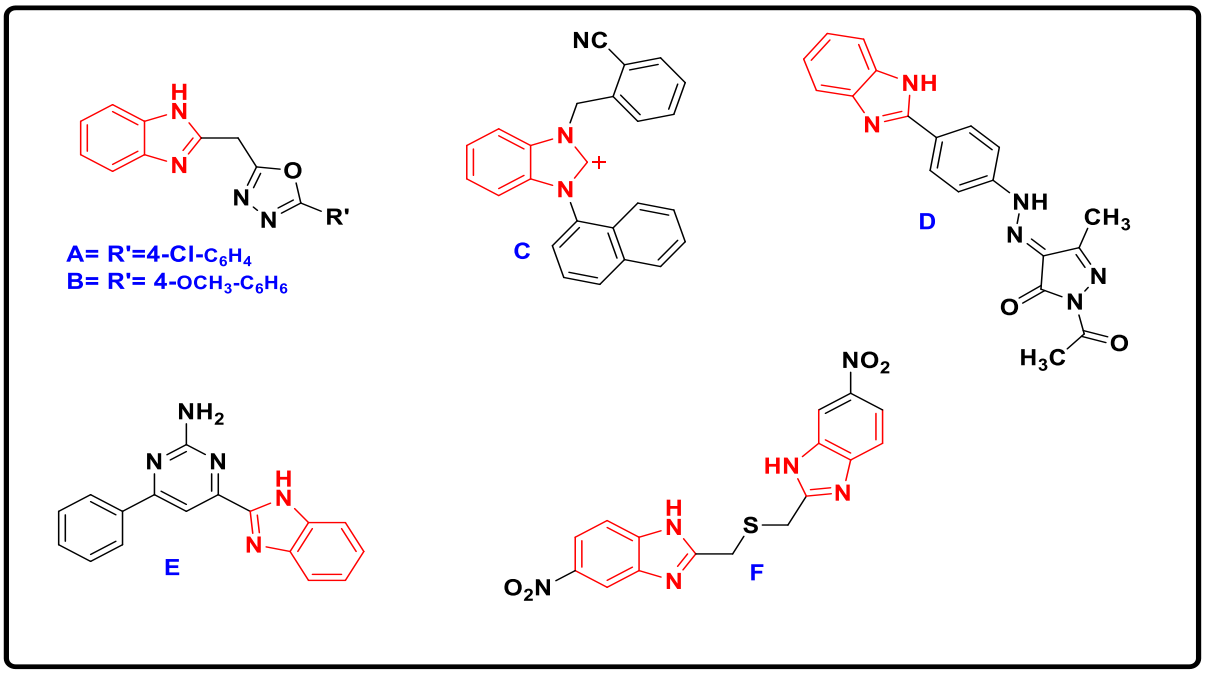


Chart S1. Structures of some known benzimidazoles derivatives with antiproliferative activity against breast cancer cell lines with IC_{50} against MCF7 is >100μM.

List of spectroscopic spectra of the compounds

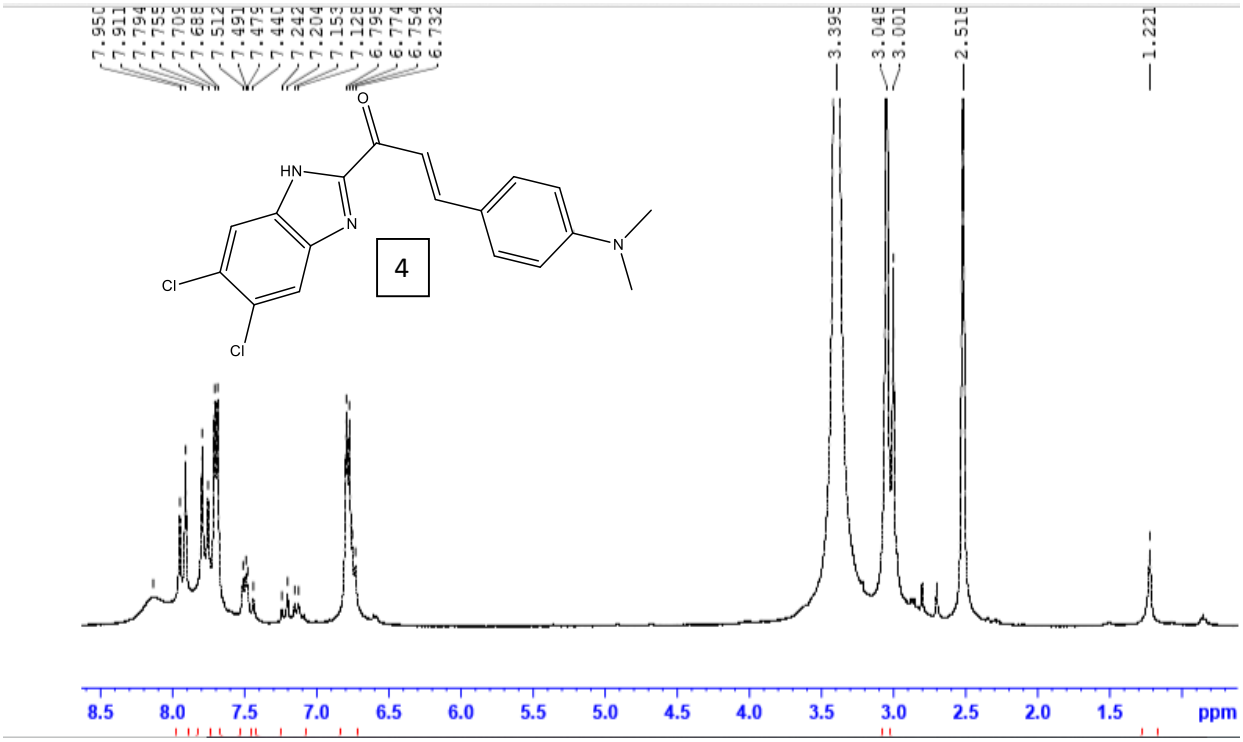
compound	^{1}H NMR	^{13}C NMR	IR
4	δ: 3.05 (s, 6H, $N(CH_3)_2$), 6.78 (d, *J*=8.3 Hz, 2H, Ar-H), 7.7 (d, *J* = 8.3 Hz, 2H, Ar-H), 7.77 (d, *J*=12.6 Hz, 1H), 7.93 (d, *J*=12.6 Hz ,1H), 8.13 (s, 2H, Benz-H), 13.66 (s, 1H, NH).		1349 (C-N), 1555 (C=N), 1641 (C=O), 3422 (N-H).
5	δ: 2.88 (s, 6H, $N(CH_3)_2$), 2.9 (s, 2H, pyrazole-H), 4.9 (s, 1H, NH), 6.72 (d, *J*=8.2 Hz, 2H, Ar-H), 7.2 (d, *J*=8.2 Hz, 2H, Ar-H), 7.6 (s, 1H, Benz-H), 7.88 (s, 1H, Benz-H)		
6	δ: 3.06 (s, 6H, $N(CH_3)_2$), 6.76 (s, 2H, NH_2), 6.87 (d, *J*=8 Hz, 2H, Ar-H), 7.61 (s, 1H, pyridine-H), 7.85 (d, *J*=8 Hz, 2H, Ar-H), 8.06 (s, 2H, Benz-H).		1610 (C=N), 2214 (C≡N), 3225 and 3356 (NH_2).
7	δ:2.9 (d, 1H, pyrane-H), 3.11 (s, 6H, $N(CH_3)_2$), 4.5 (s, 2H, NH_2), 6.86 (d, *J*=8.6 Hz, 2H, Ar-H), 7.2 (d, *J*=8 Hz, 1H, pyrane-H), 7.84 (d, *J*=8.6 Hz, 2H, Ar-H), 8.06 (s, 2H, Benz-H).	δ: 44.59 (CH_3), 68.87 (CH), 112.20 (CH), 116.88 (CH_2), 119.04 (CH), 133.78 (CH_2), 133.78 (CH_2), 154.82 (CH_2), 159.32 (CH).	1611 (C=N), 2208 (C≡N), 3225 and 3424 (NH_2).
8	δ: 2.81 (s, 6H, $N(CH_3)_2$), 3.0 (d, *J*=6.5 Hz, 2H, isoxazoline-H), 5.75 (t, 1H, isoxazoline-H), 7.11 (d, *J*=8.2 Hz, 2H, Ar-H), 7.27 (d, *J*=8.2 Hz, 2H, Ar-H), 7.72 (s, 1H, Benz-H), 8.03 (s, 1H, Benz-H).		

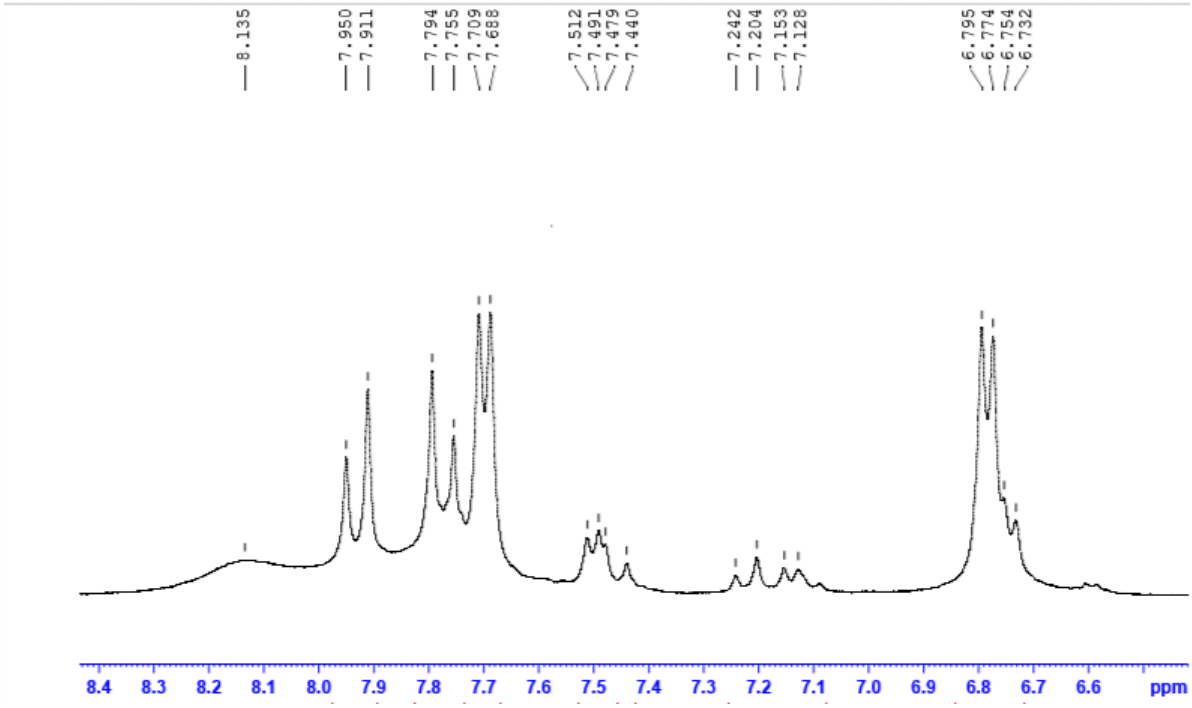
9	δ: 2.68 (s, 3H, $COCH_3$), 6.19 (s, 2H, $COCH_2$), 7.63 (d, *J*=8.2 Hz, 2H, Ar-H), 7.86 (s, 1H, Benz-H), 8.0 (s, 1H, Benz-H), 8.27 (d, *J*=8.2 Hz, 2H, Ar-H).		1654, 1689 (C=O).
10	δ:2.02 (s, 3H, CH_3), 7.09 (d, *J*=8 Hz, 2H, Ar-H), 7.2 (d, *J*=8 Hz, 2H, Ar-H), 7.4 (d, *J*=8 Hz, 2H, Ar-H), 7.46 (d, *J*=8 Hz, 2H, Ar-H), 8.95 (s, 2H, methelene-H), 8.69 (s, 1H, Benz-H), 8.86 (s, 1H, Benz-H), 9.7 (s, 1H, pyrazanobenzimidazole-H).	δ:20.9, 102.2, 112.4, 117.1, 119.5, 124.2, 128.9, 129.9, 130.5, 131.1, 131.5, 132.1, 134.2, 138.5, 145.1, 167.3.	
11	δ: 2.06 (s, 3H, CH_3), 7.18 – 7.41 (m, 4H, Ar-H), 7.58 (d, *J*= 7.4 Hz, 2H, Ar-H), 7.68 (d, *J*=7.6 Hz, 2H, Ar-H), 8.13 (s, 1H, Benz-H), 8.25 (s, 1H, Benz-H), 8.85 (s, 2H, methelene-H), 8.91 (s, 1H, pyrazanobenzimidazole-H).		
12	δ:4.64 (s, 2H, CH_2-Ph), 7.26-7.48 (m, 5H, Ar-H), 7.67 (d, *J*=7.2 Hz, 2H, Ar-H), 7.8 (d, *J*=7.2 Hz ,2H, Ar-H), 8.07 (s, 2H , Benz-H), 8.52 (s, 2H, methelene-H), 8.77 (s, 1H, byrazanobenzimidazole-H)	δ: 64.73 (CH_2), 101.23 (CH), 112.02 (CH), 115.08 (CH), 120.65 (CH), 123.35 (CH_2), 124.97 (CH_2), 127.31 (CH), 128.93 (CH), 131.08 (CH), 132.34 (CH), 136.66 (CH_2), 139.54 (CH_2), 140.25 (CH), 142.96 (CH_2), 144.21 (CH_2), 162.19 (CH).	

13	δ: 1.25 (s, 3H, CH_3), 7.77 (d, *J*=7.7 Hz, 2H, Ar-H), 8.1 (d, *J*=7.7 Hz, 2H, Ar-H), 8.33 (s, 1H, Benz-H), 8.93(s, 1H, Benz-H), 9.68 (s, 1H, pyrazanobenzimidazole-H).		
14	δ: 7.19 (d, *J*=7.7 Hz, 2H, Ar-H), 7.3 (d, *J*=7.7 Hz, 2H, Ar-H), 7.74 (s, 2H, Benz-H), 8.11 (s, 1H, pyridinonobenzimidazole-H), 8.85 (s, 1H, pyridinobenzimidazole-H), 9.07 (s, 1H, OH).		1219-1296 (C-O),1557-1642 (C=C,C=N), 3448 (OH).

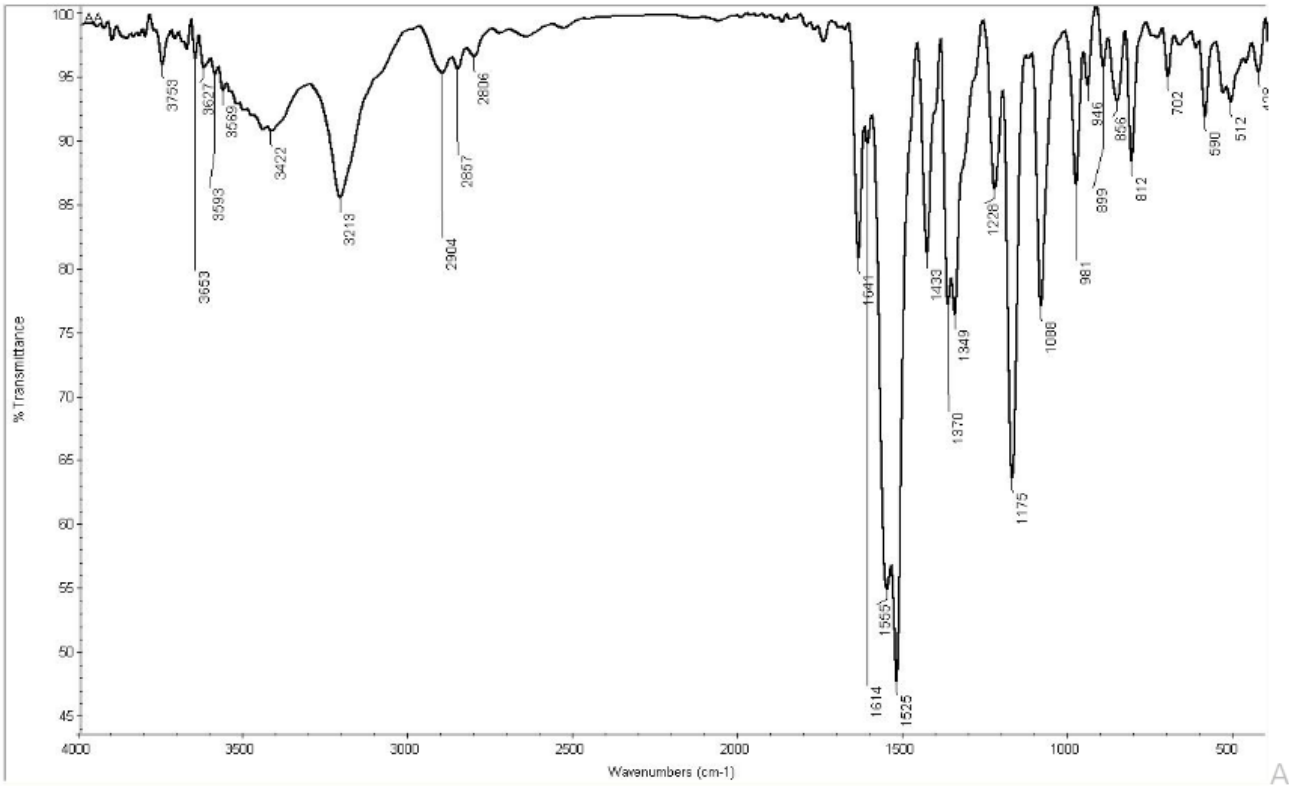
^{1}H NMR of compound 4

1H NMR

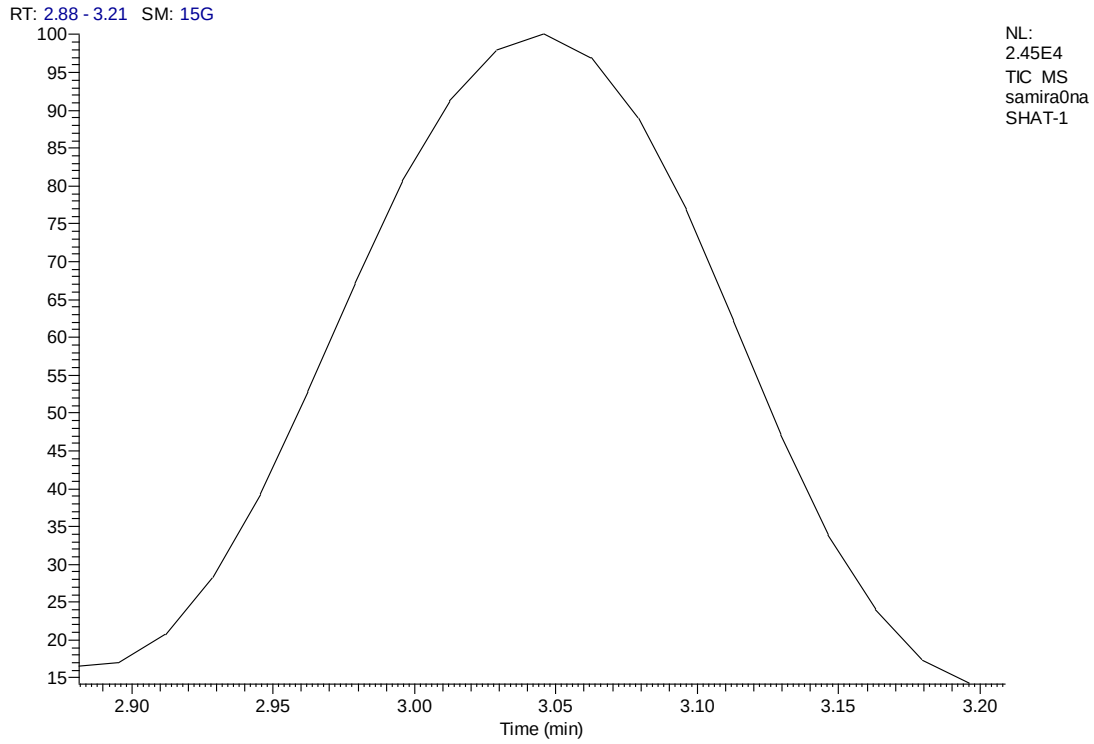


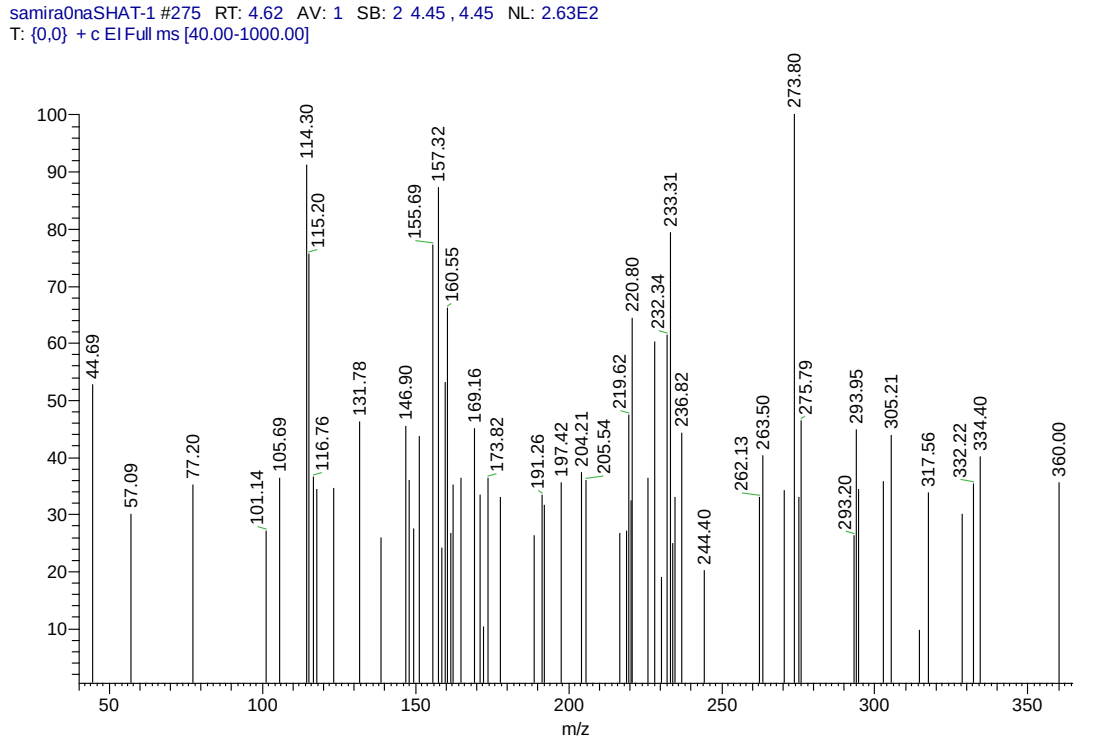


IR of compound 4

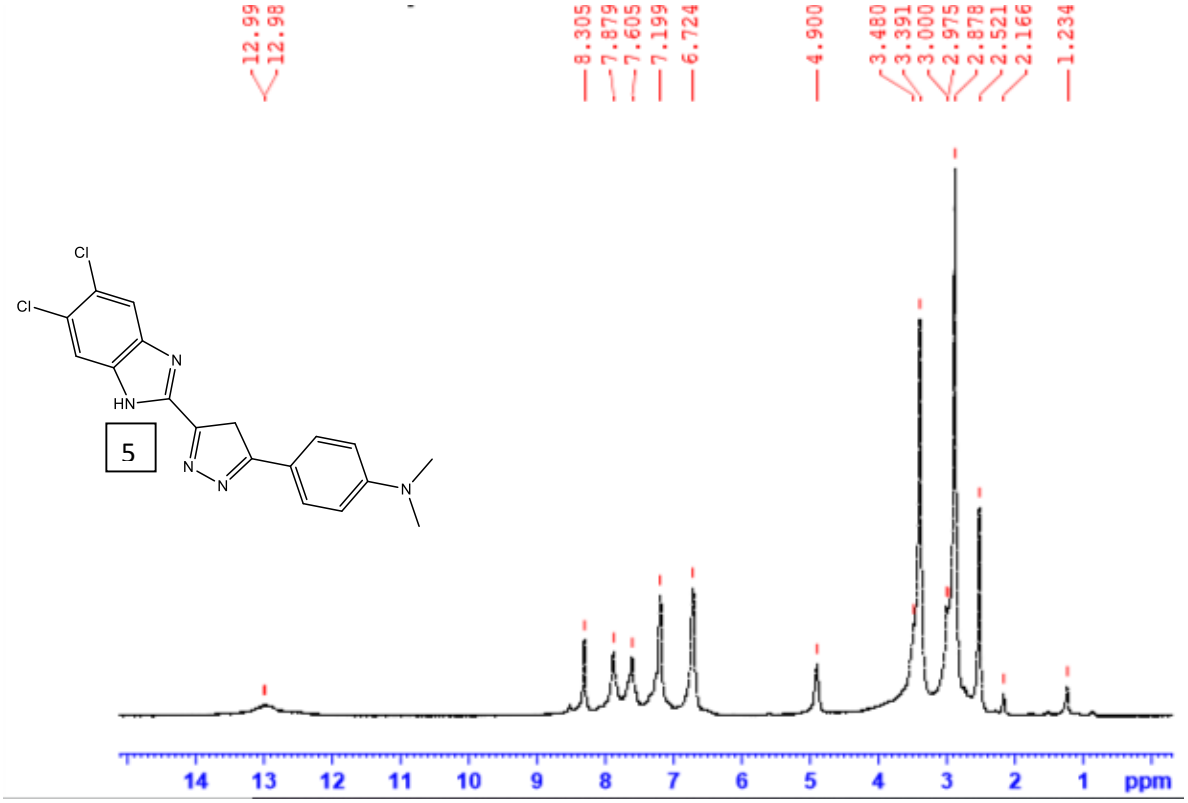


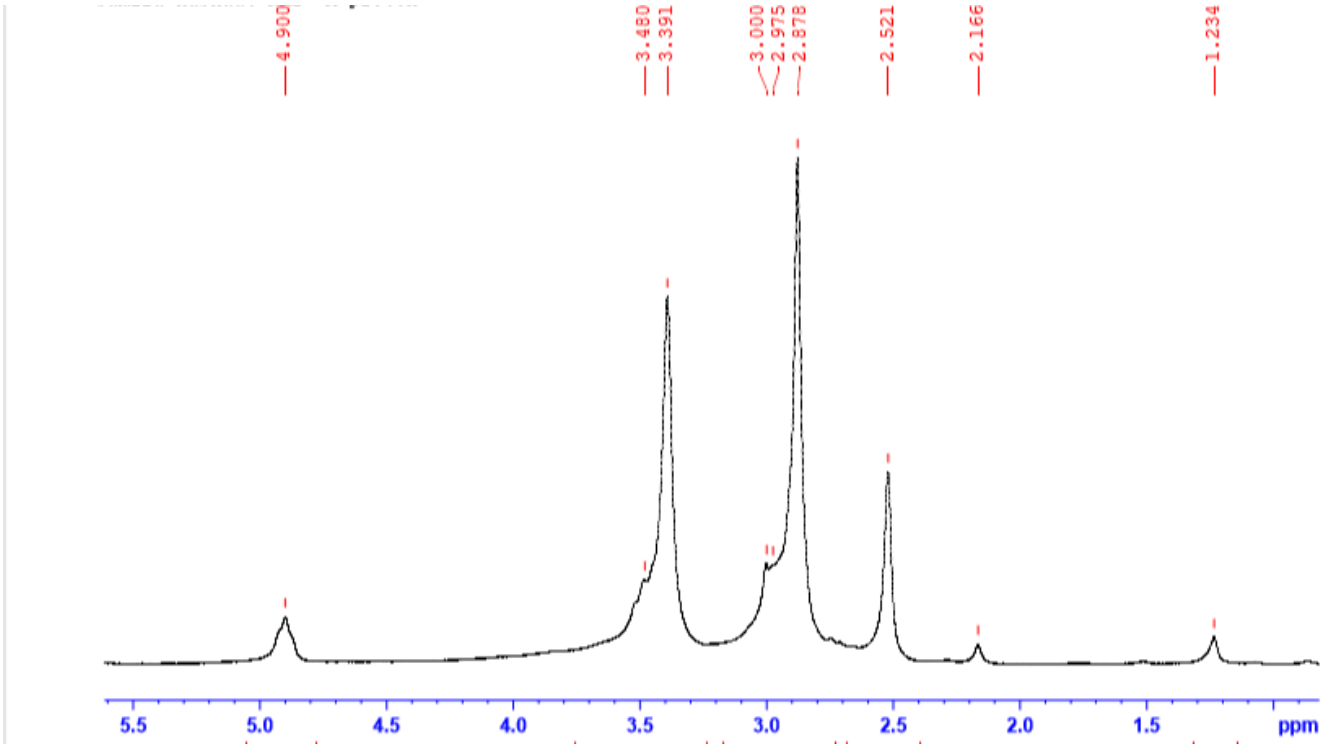
Mass of compound 4

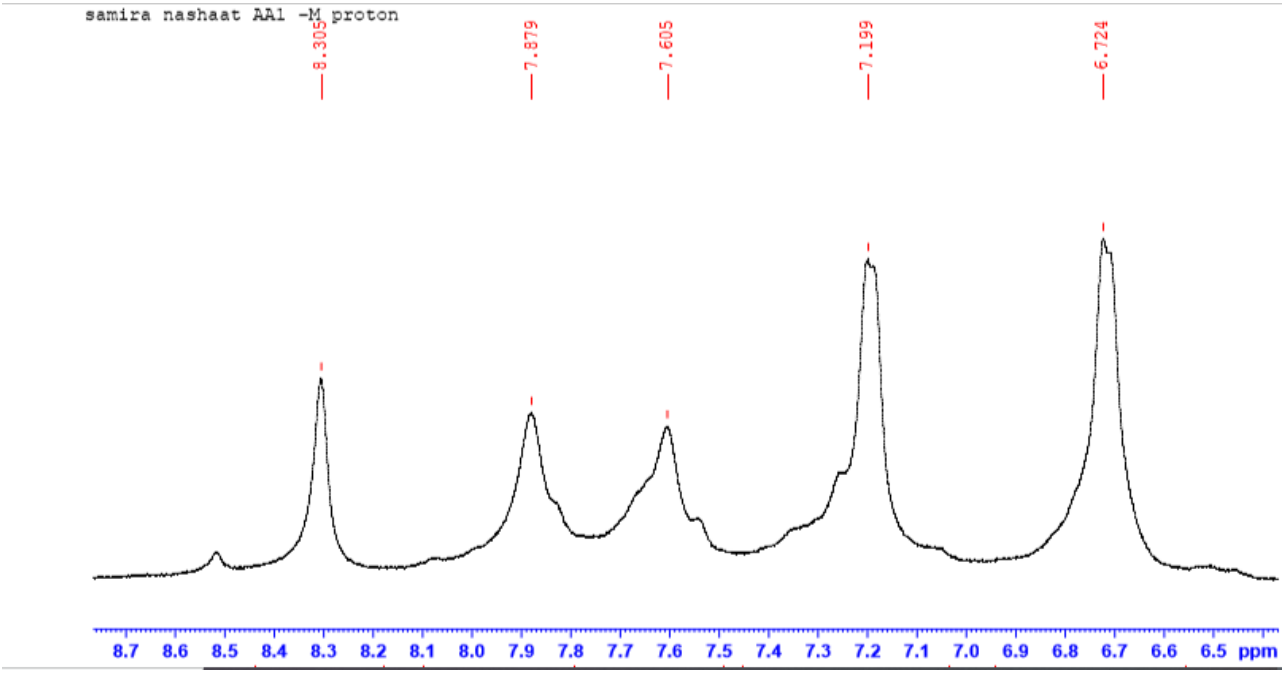




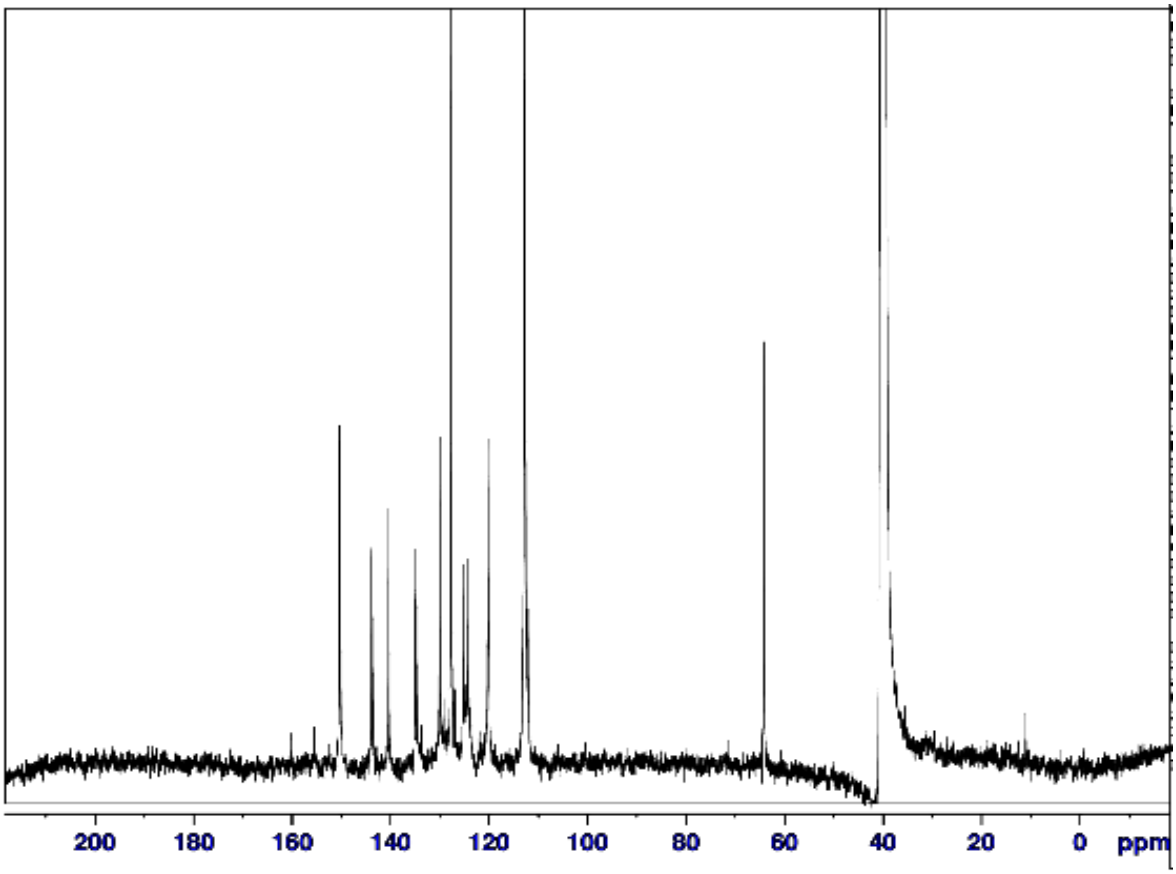
^{1}H NMR of compound 5



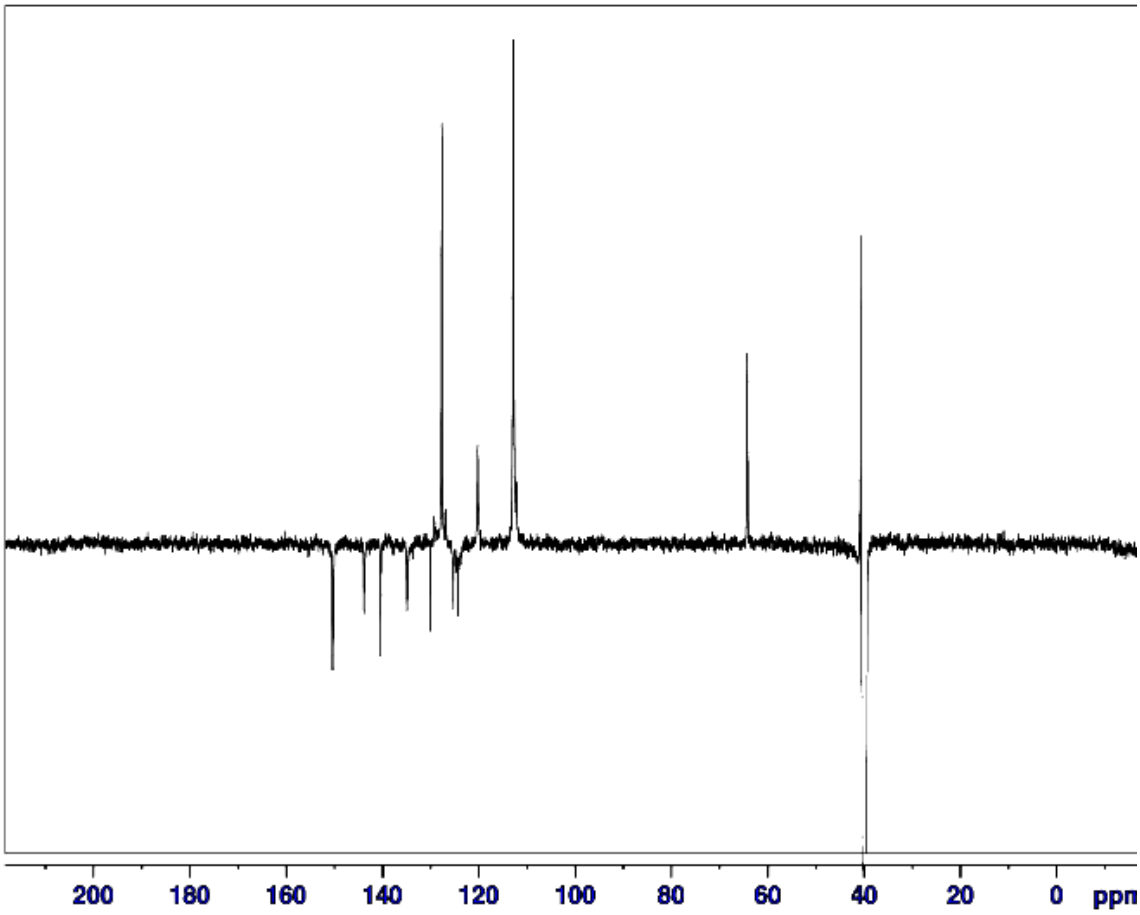




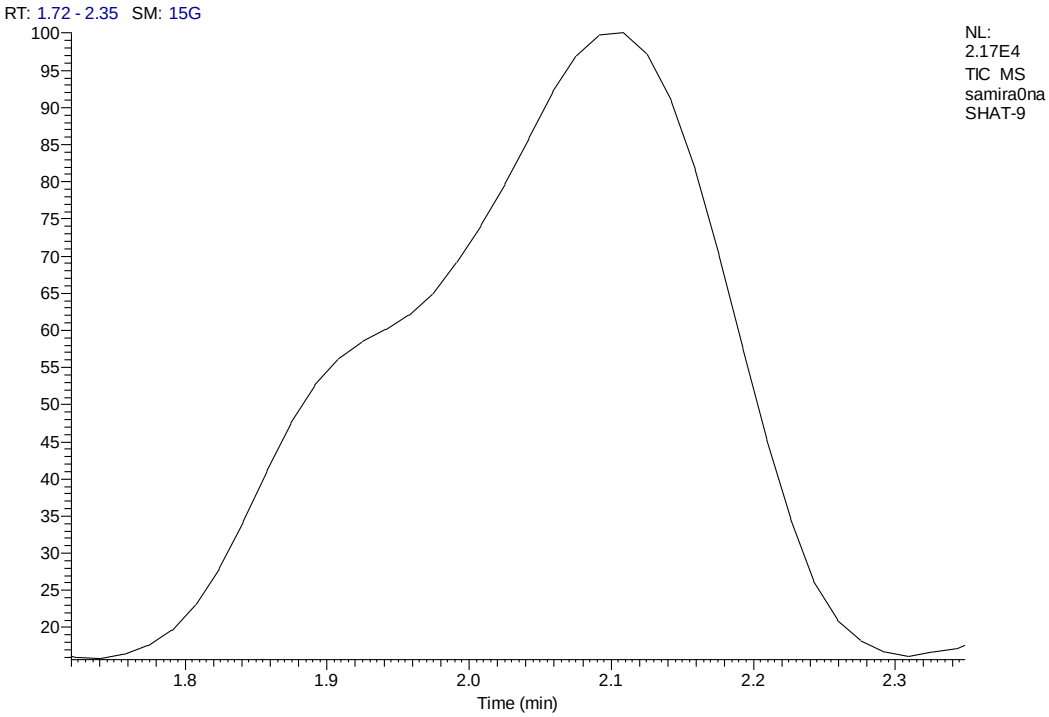
^{13}C NMR of compound 5

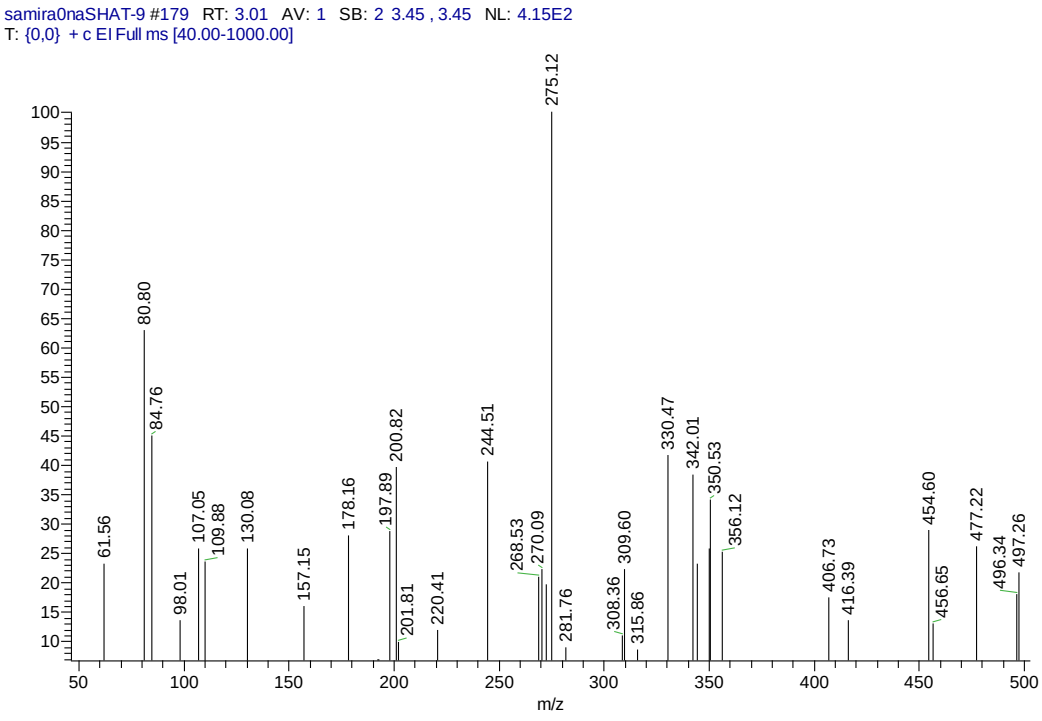


APT of compound 5

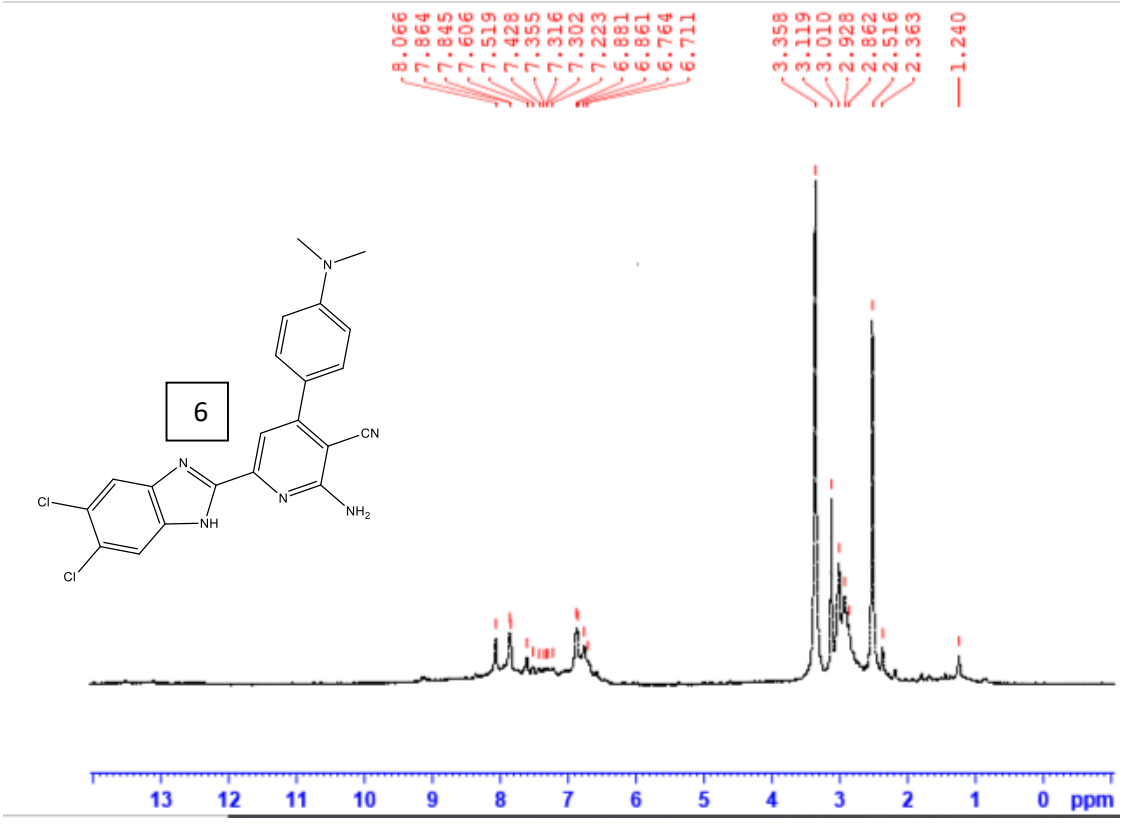


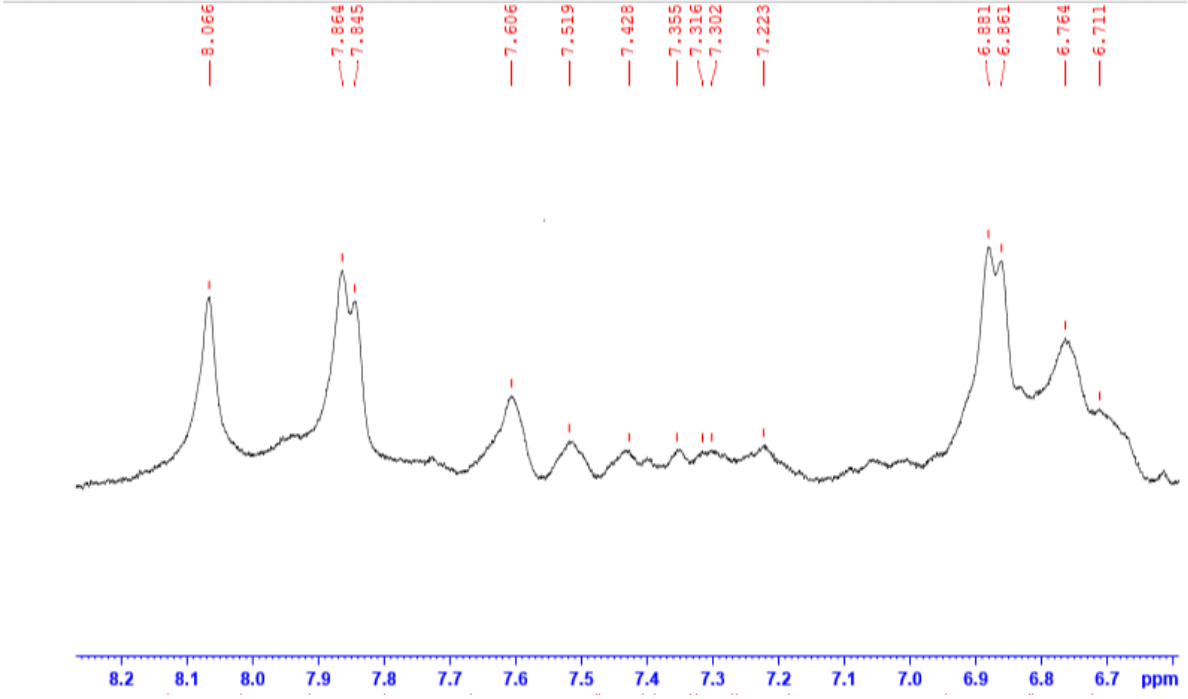
Mass of compound 5



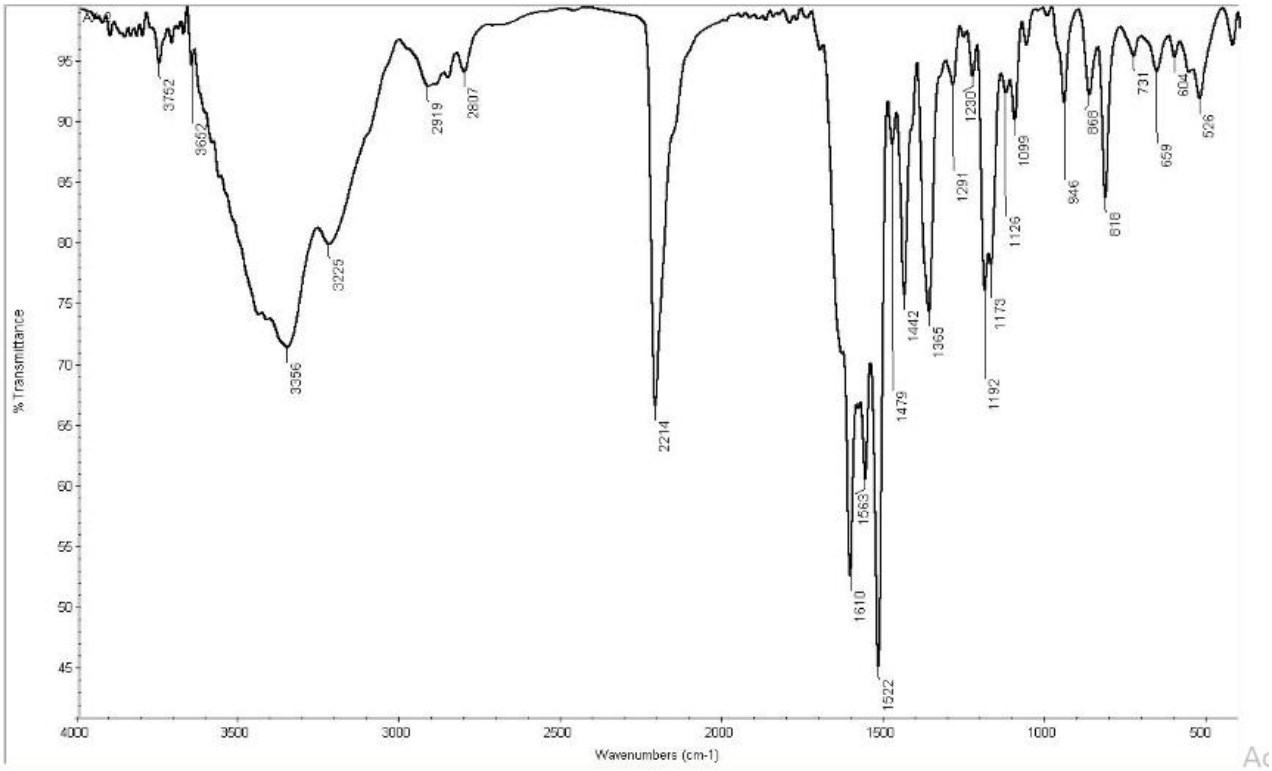


^{1}H NMR of compound 6

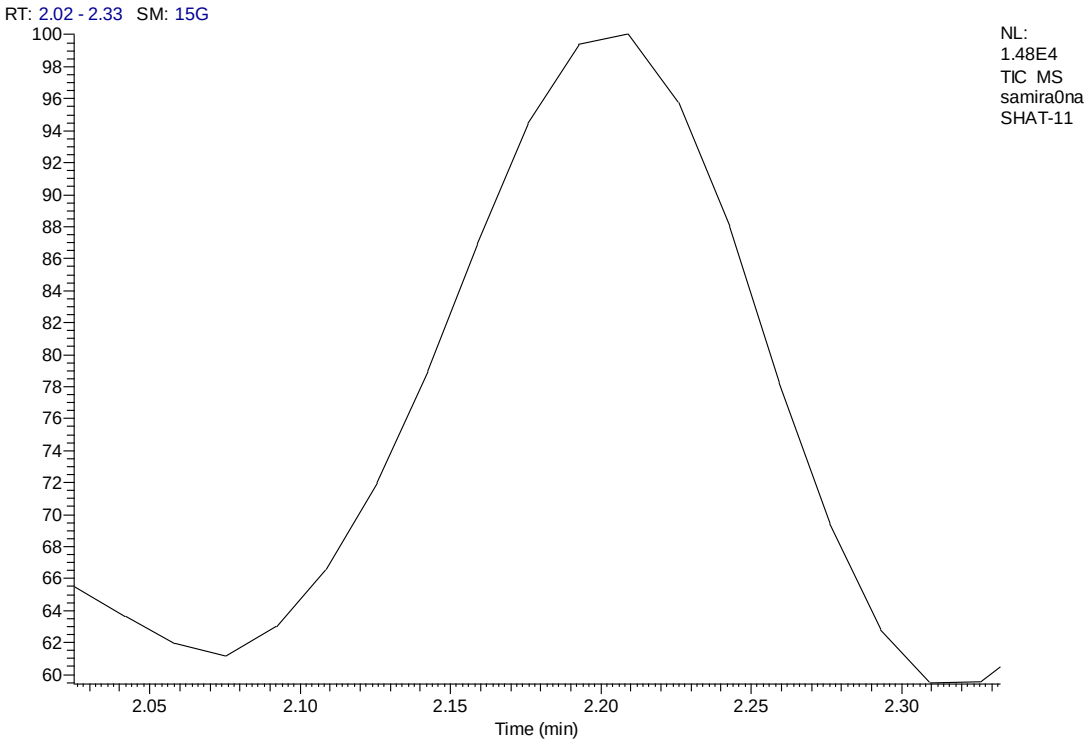


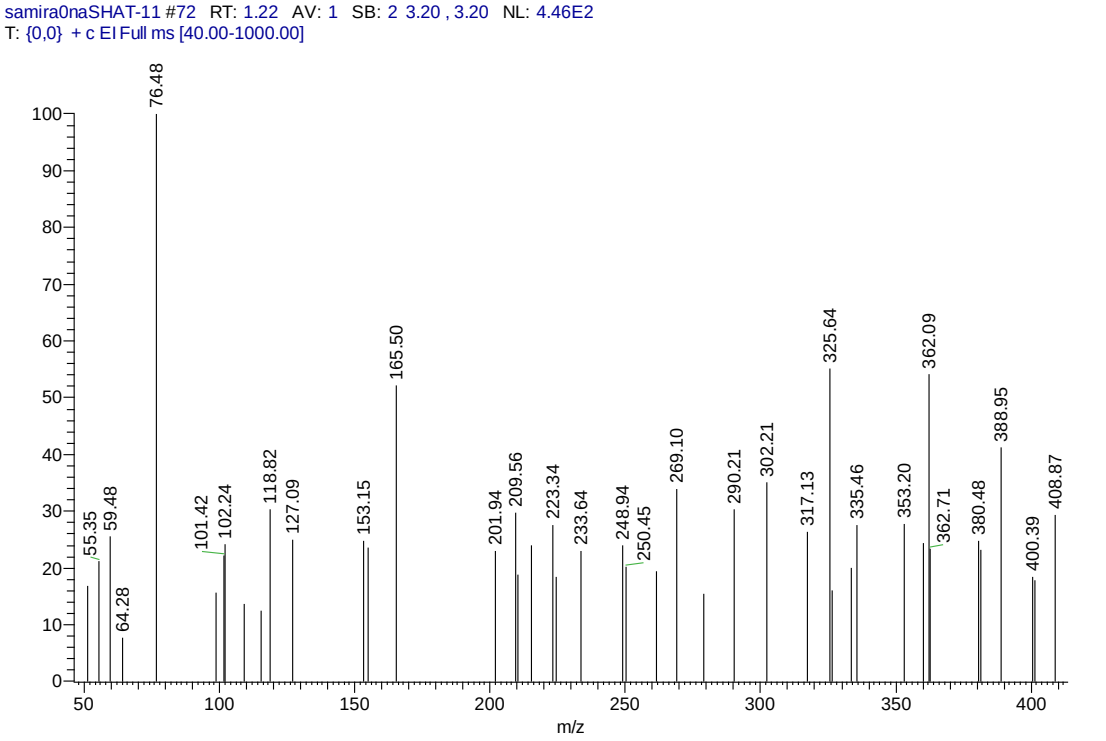


IR of compound 6

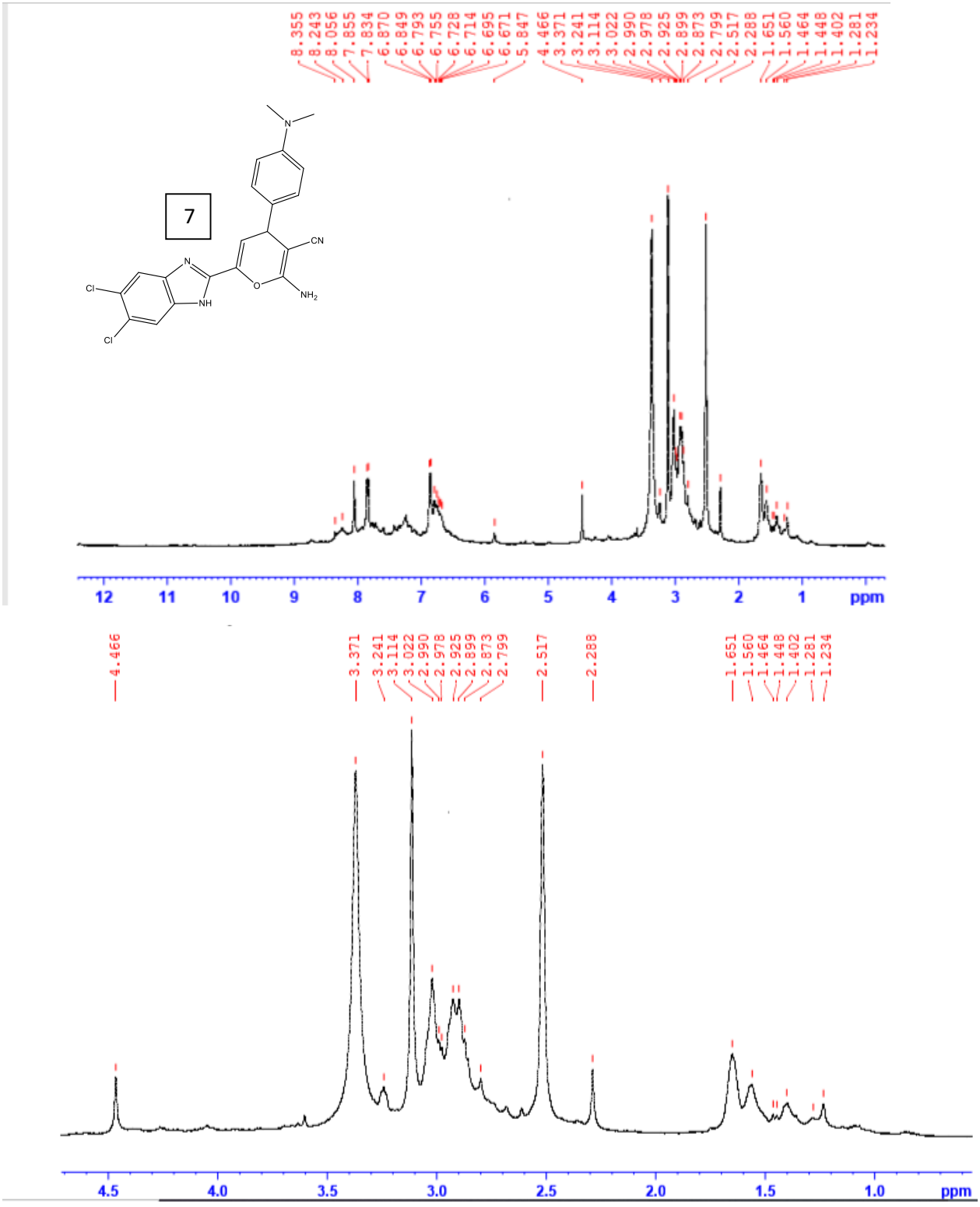


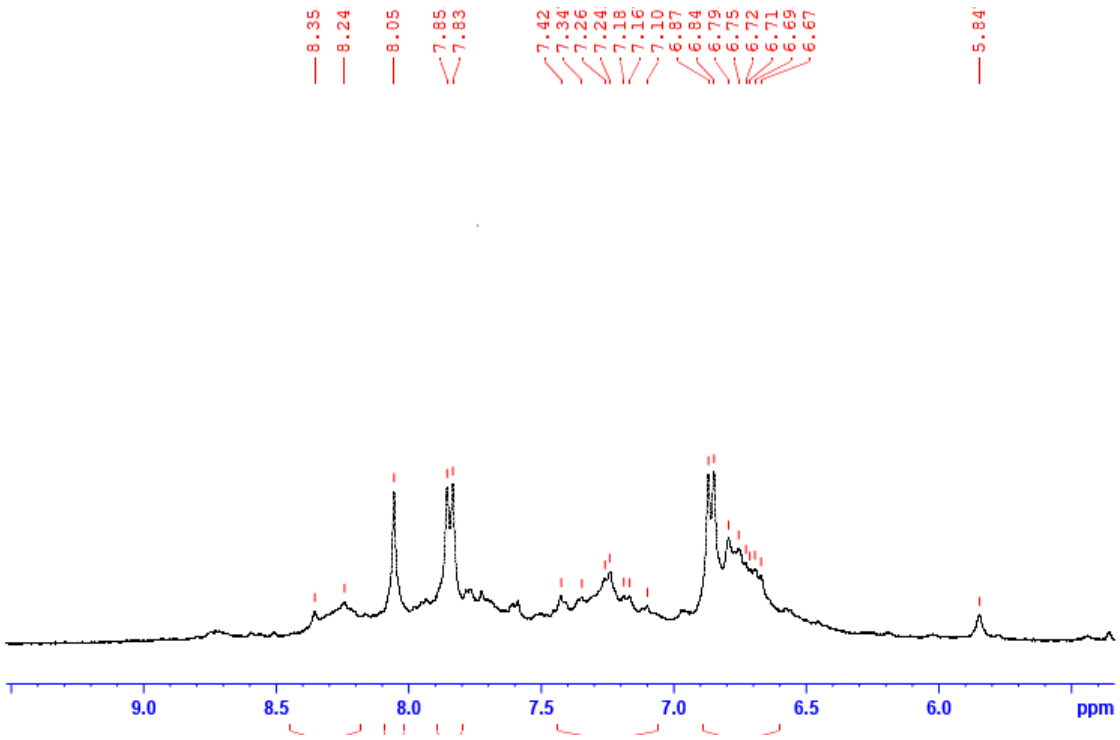
Mass of compound 6



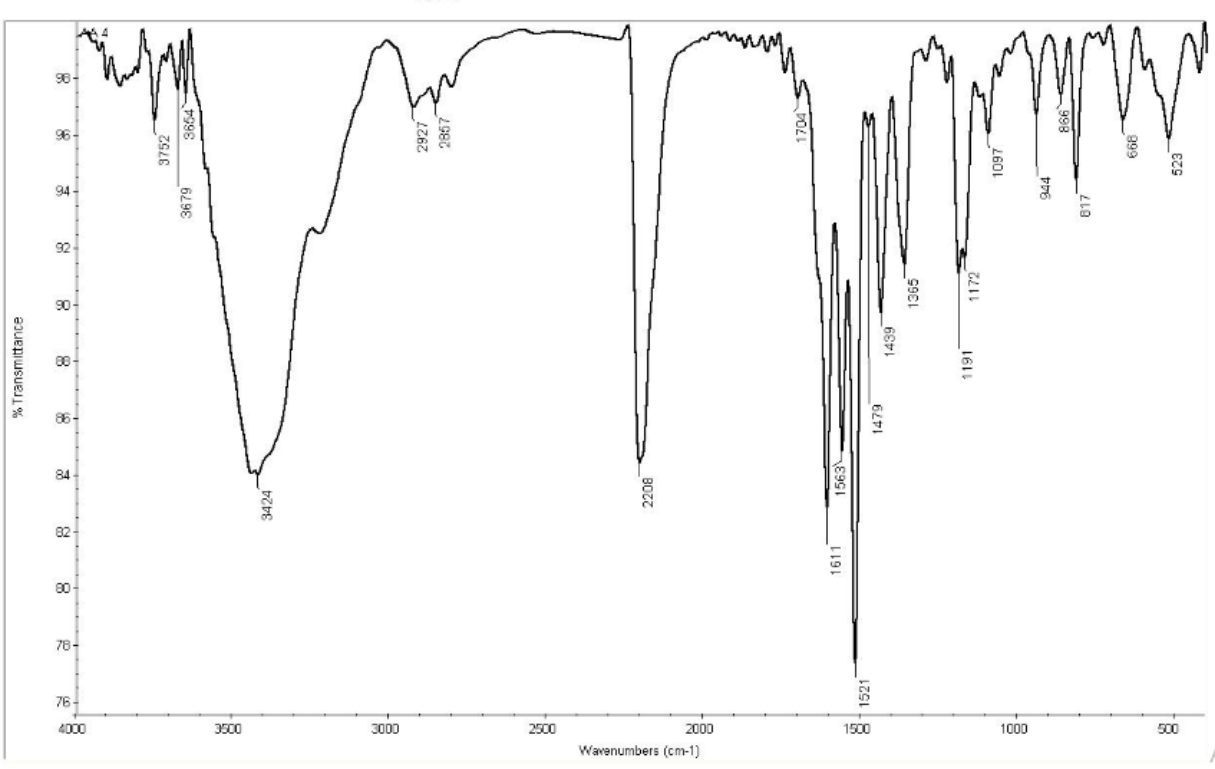


^{1}H NMR of compound 7

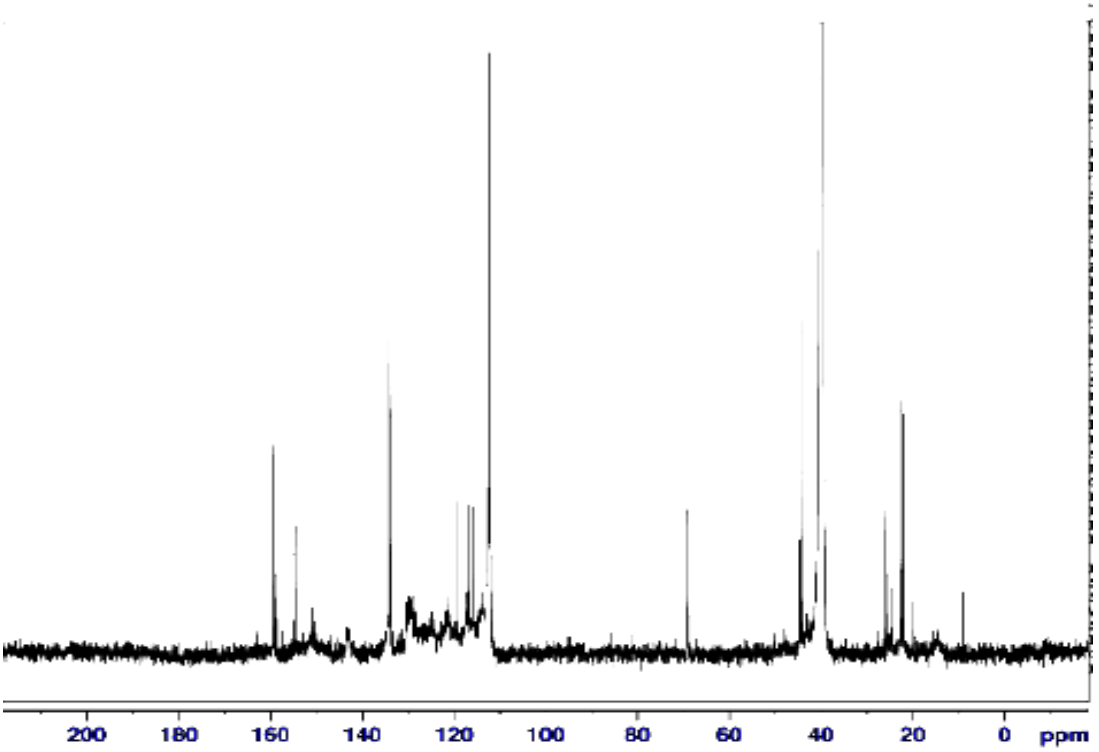




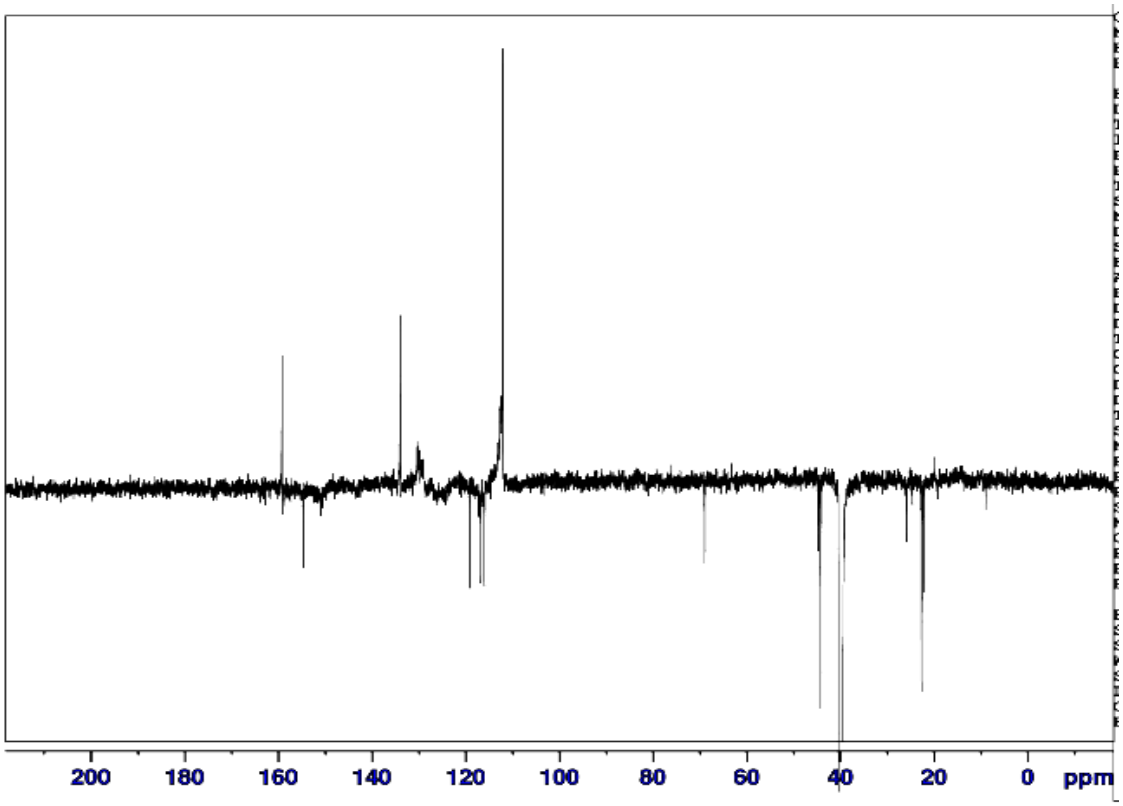
IR of compound 7



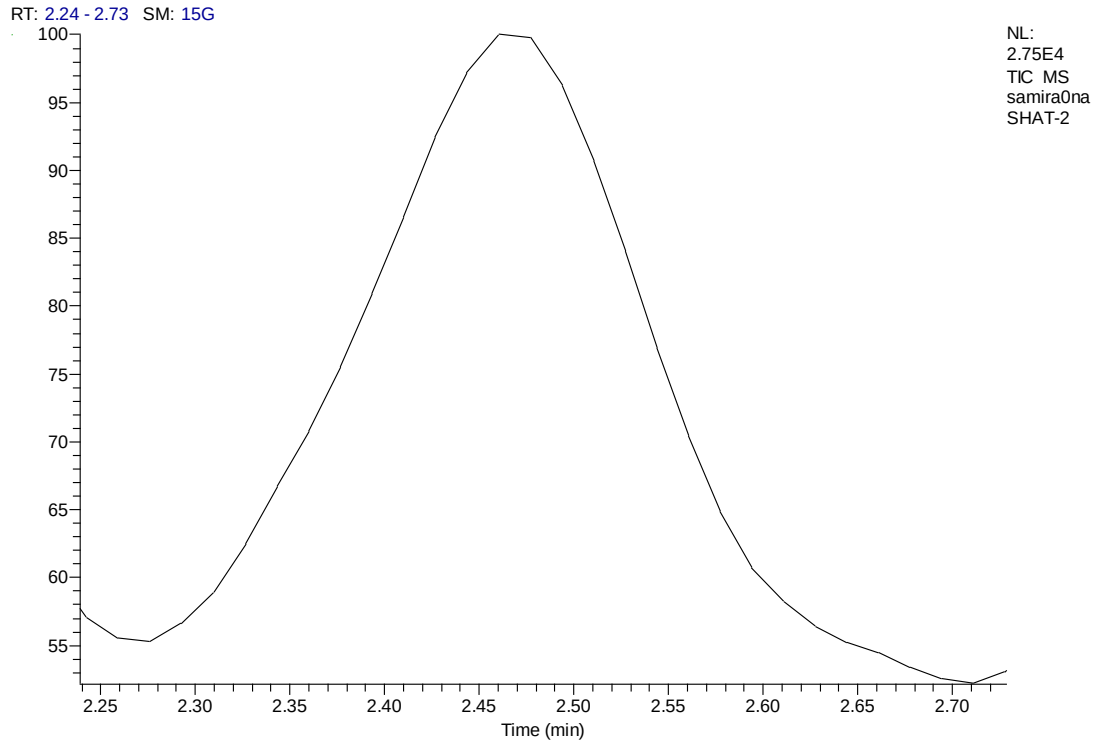
^{13}C NMR of compound 7

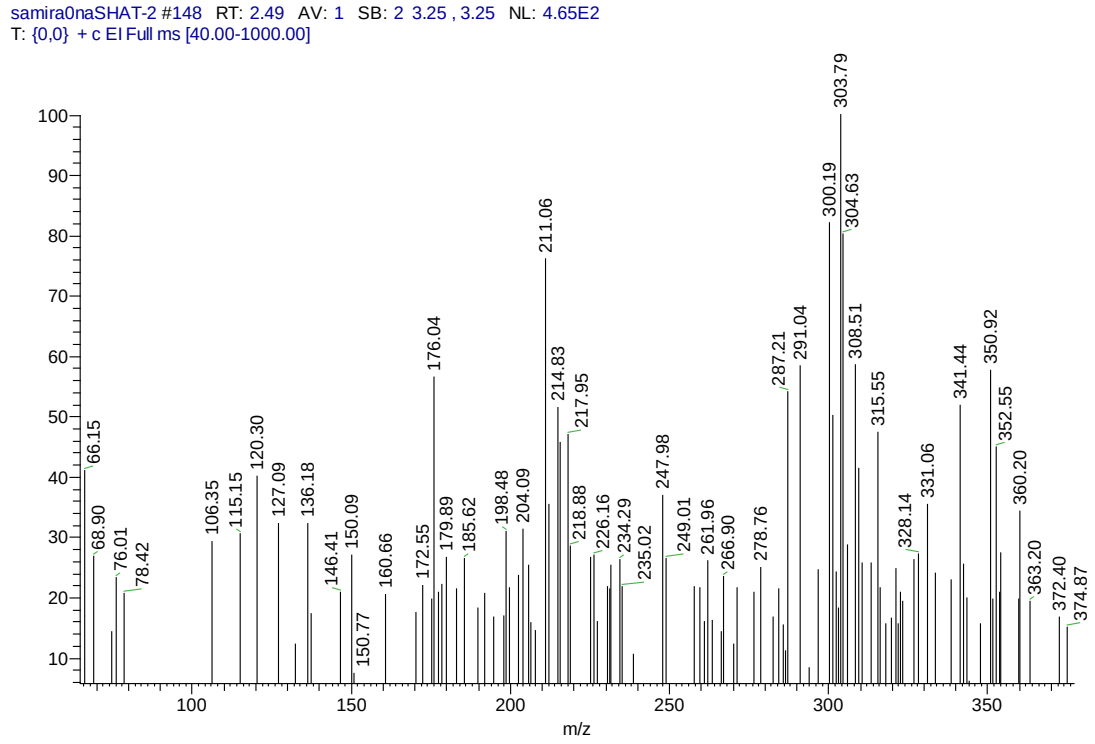


APT of compond 7

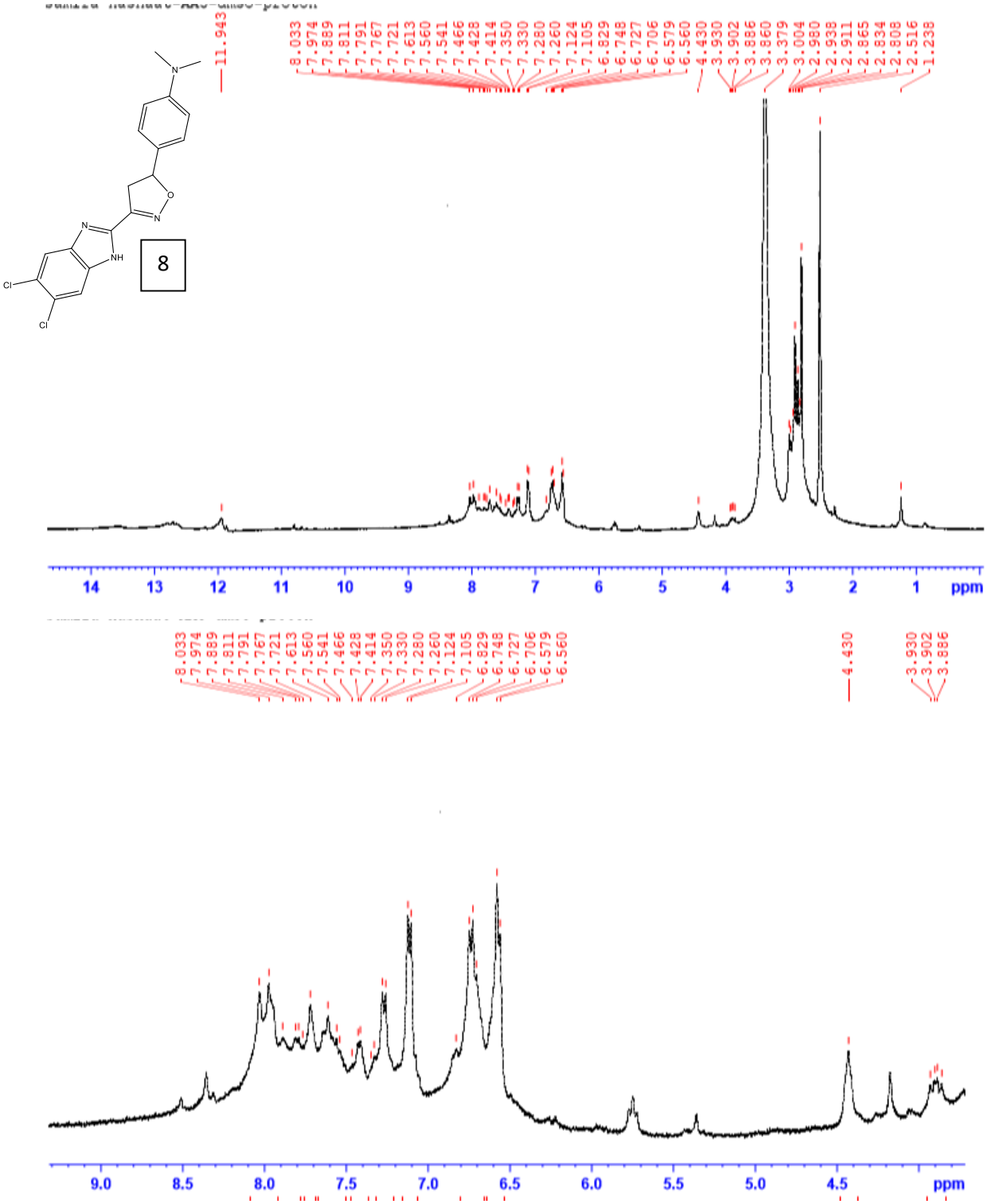


Mass of compound 7





^{1}H NMR of compound 8



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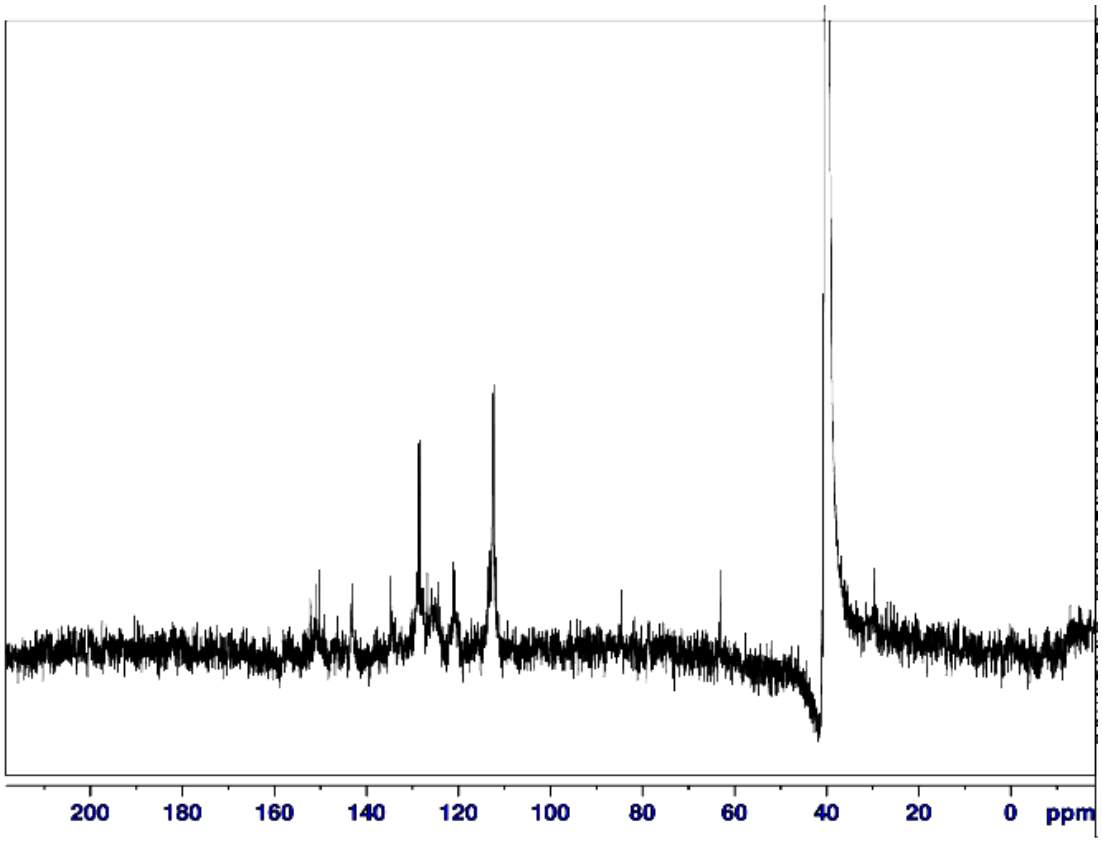

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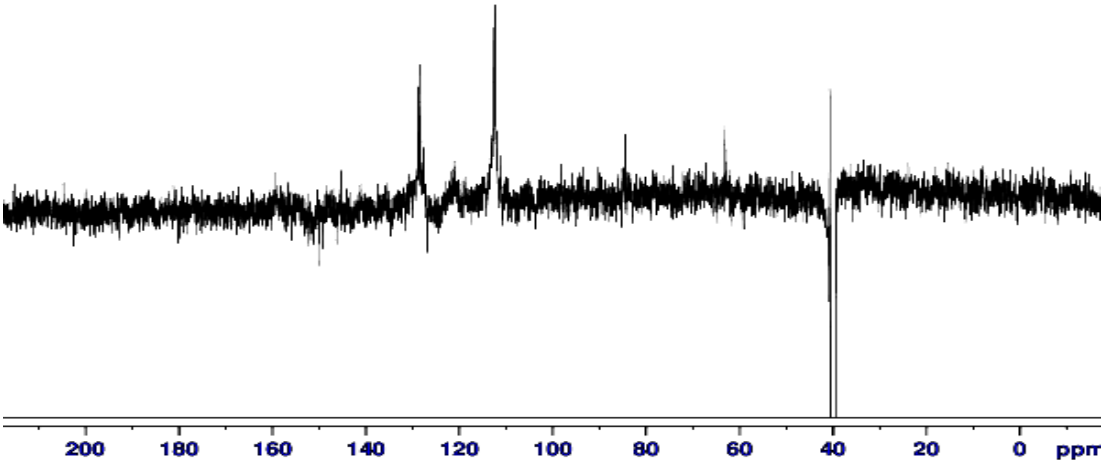
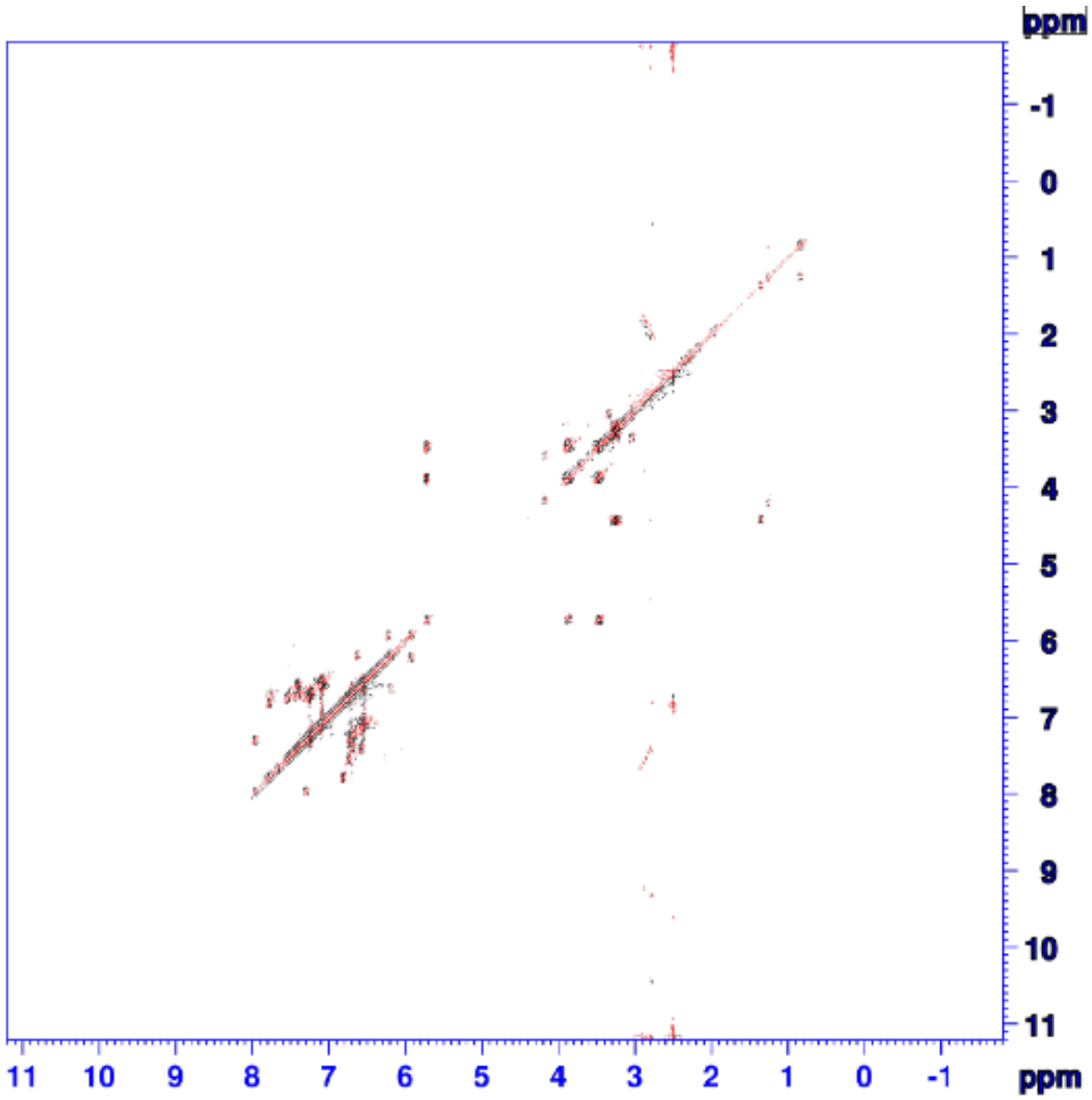


Cosy of compound 8



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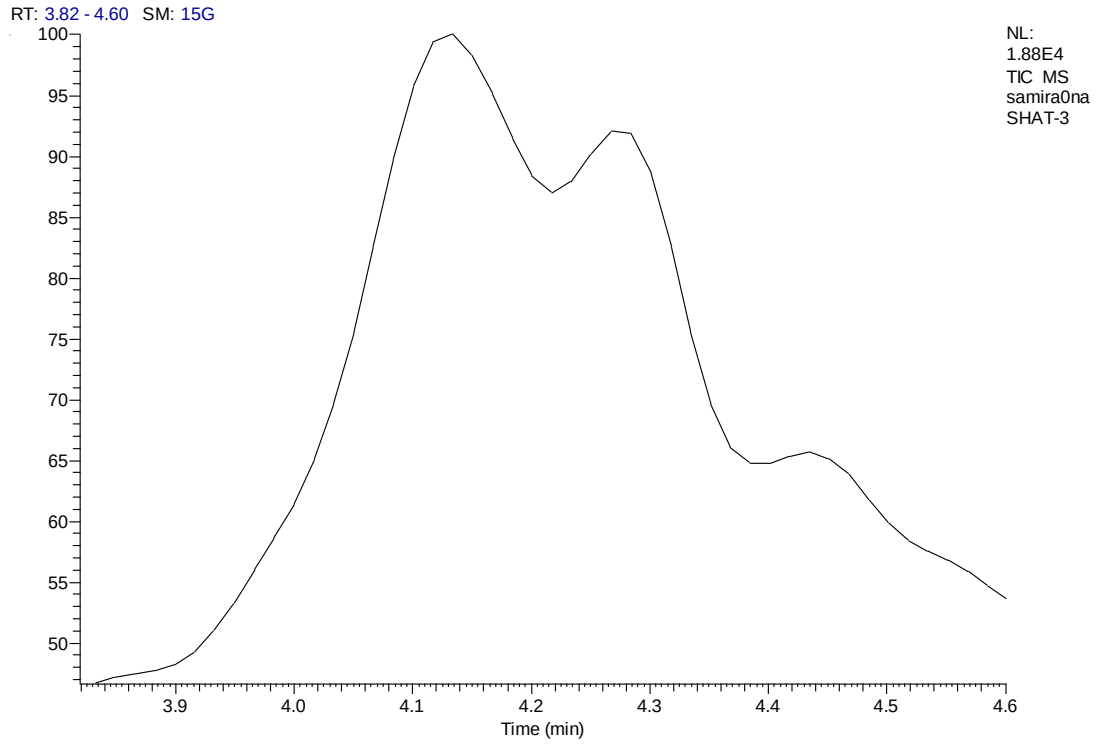
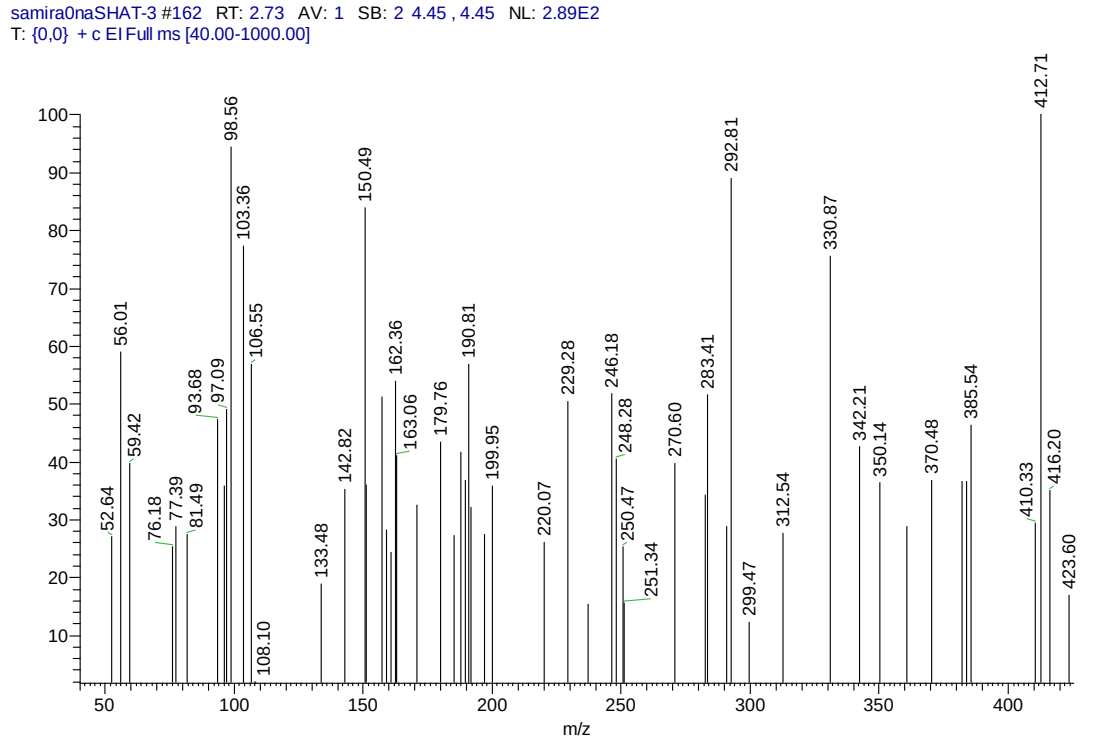
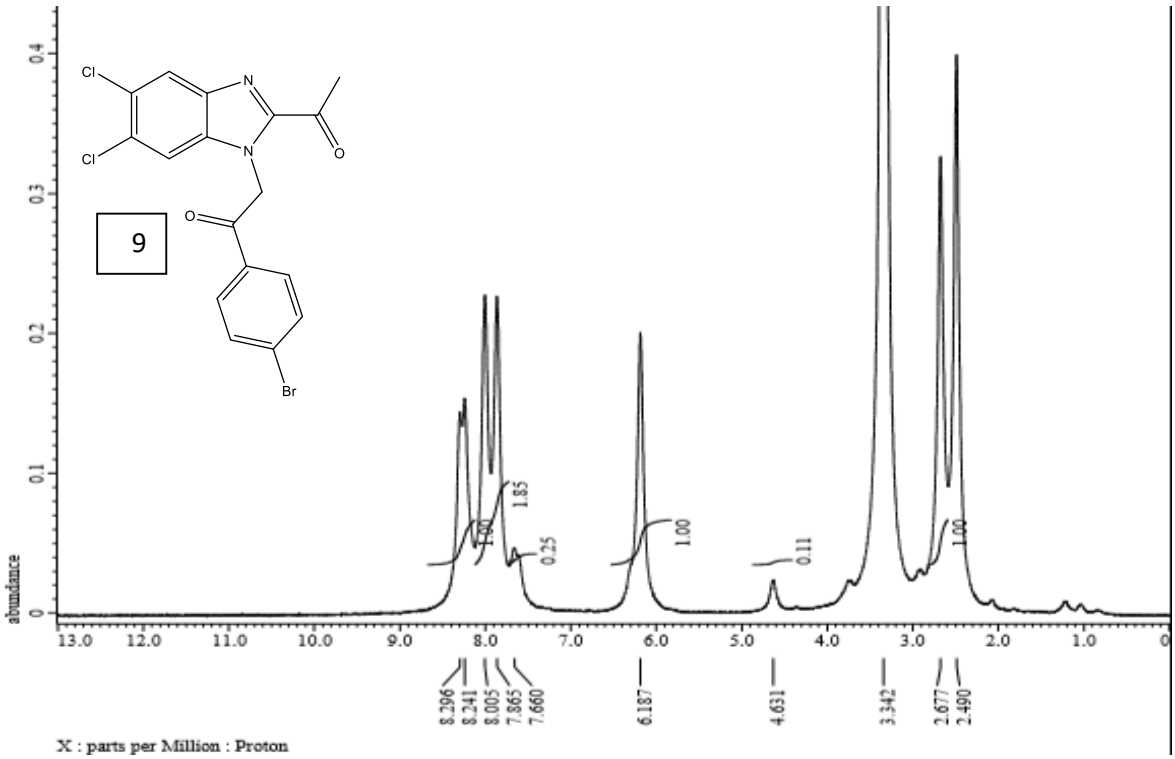
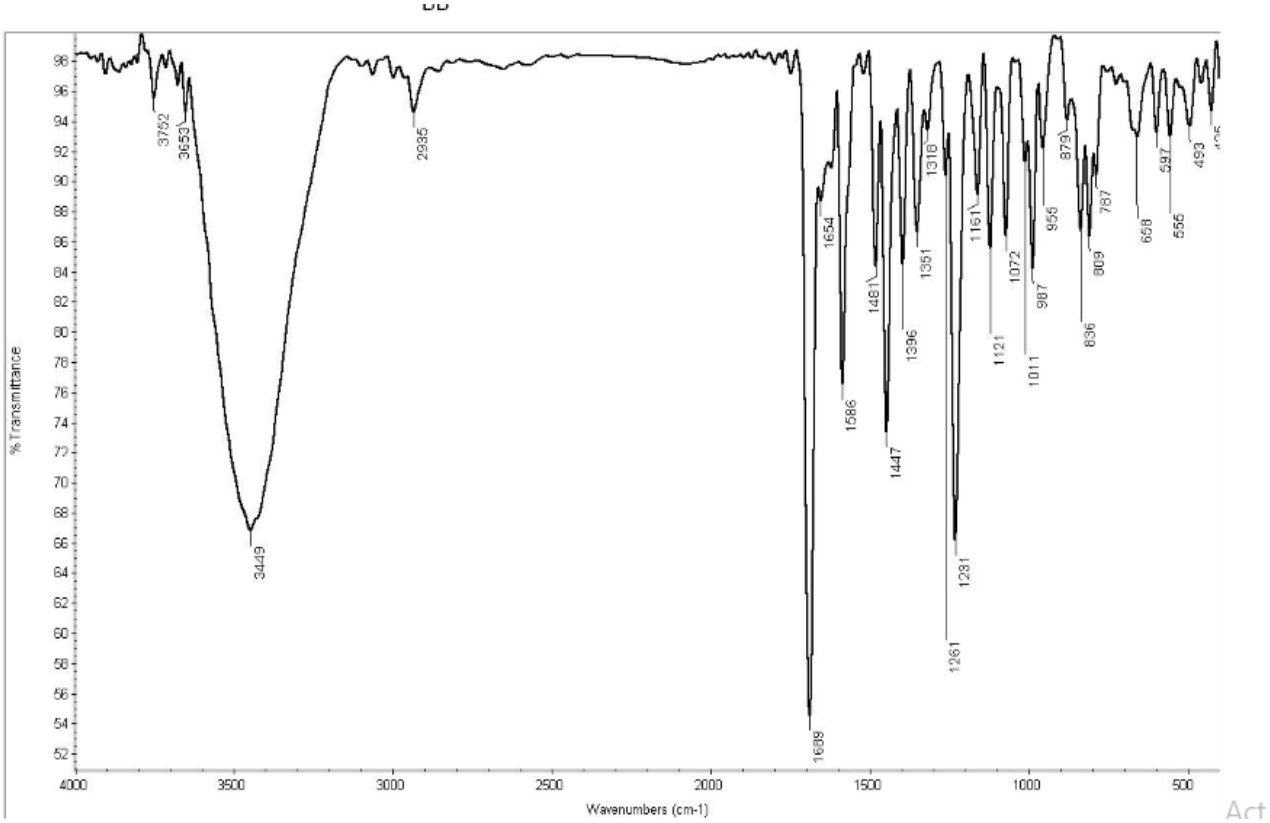




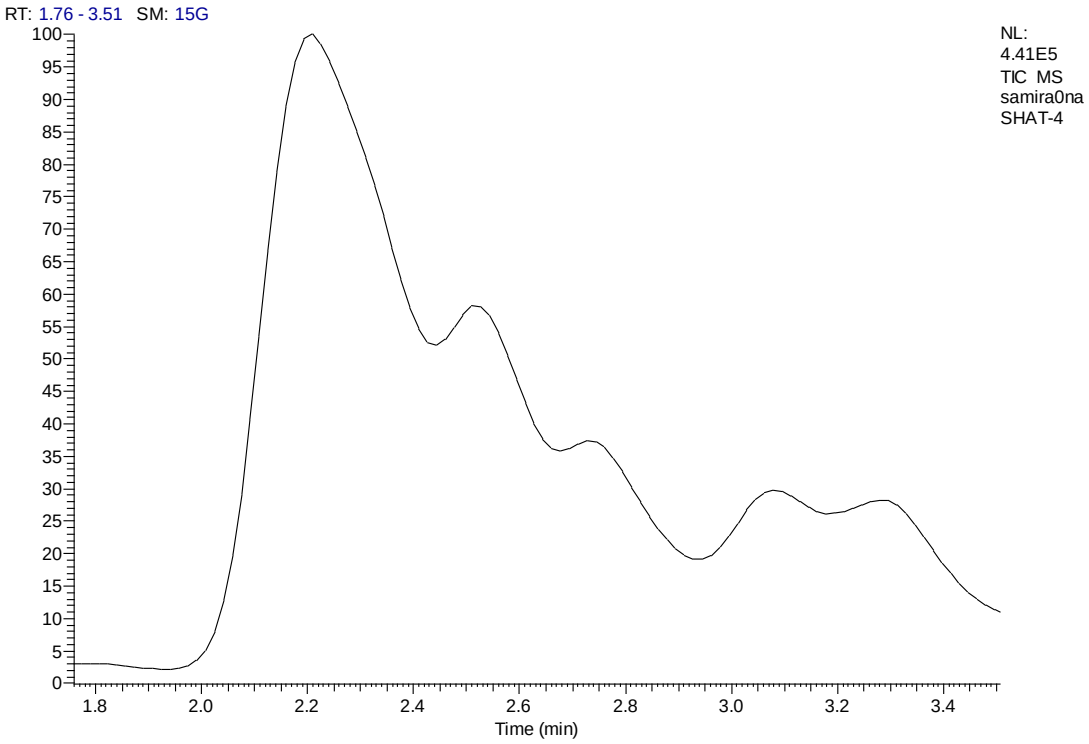
^{1}H NMR of compound 9

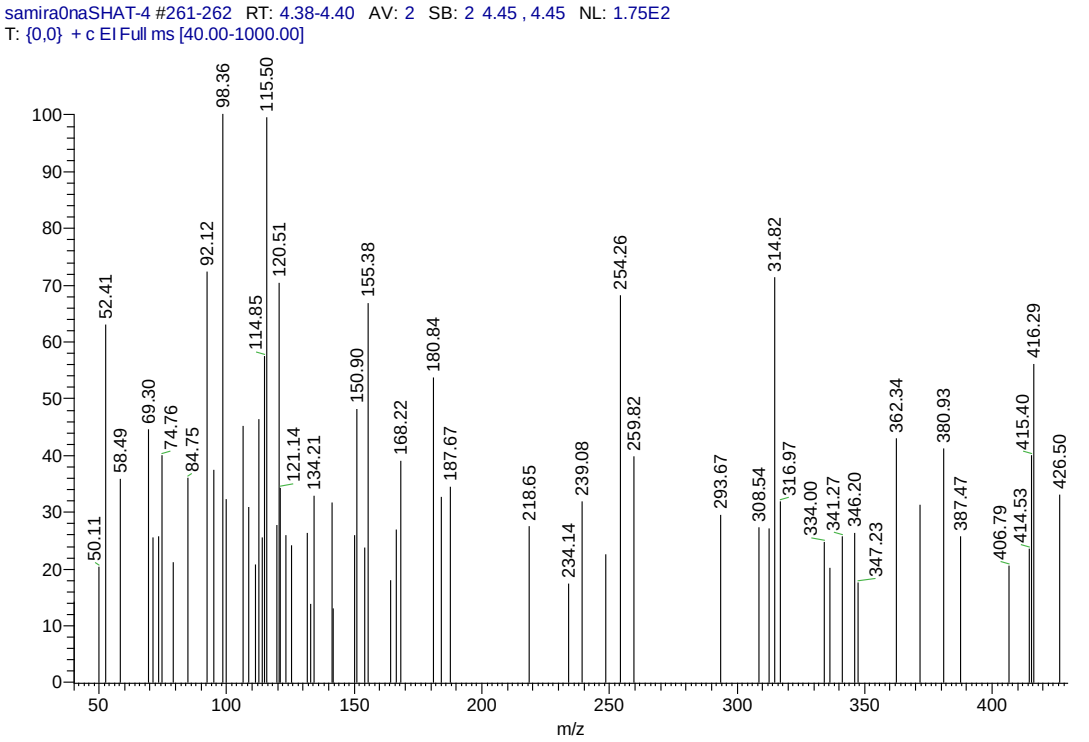

Cl
Cl
N
N
O
O
Br
9
abundance
0.4
0.3
0.2
0.1
0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
1.00
1.85
0.25
1.00
0.11
1.00
8.296
8.241
8.005
7.865
7.660
6.187
4.631
3.342
2.677
2.490
X : parts per Million : Proton

IR of compound 9

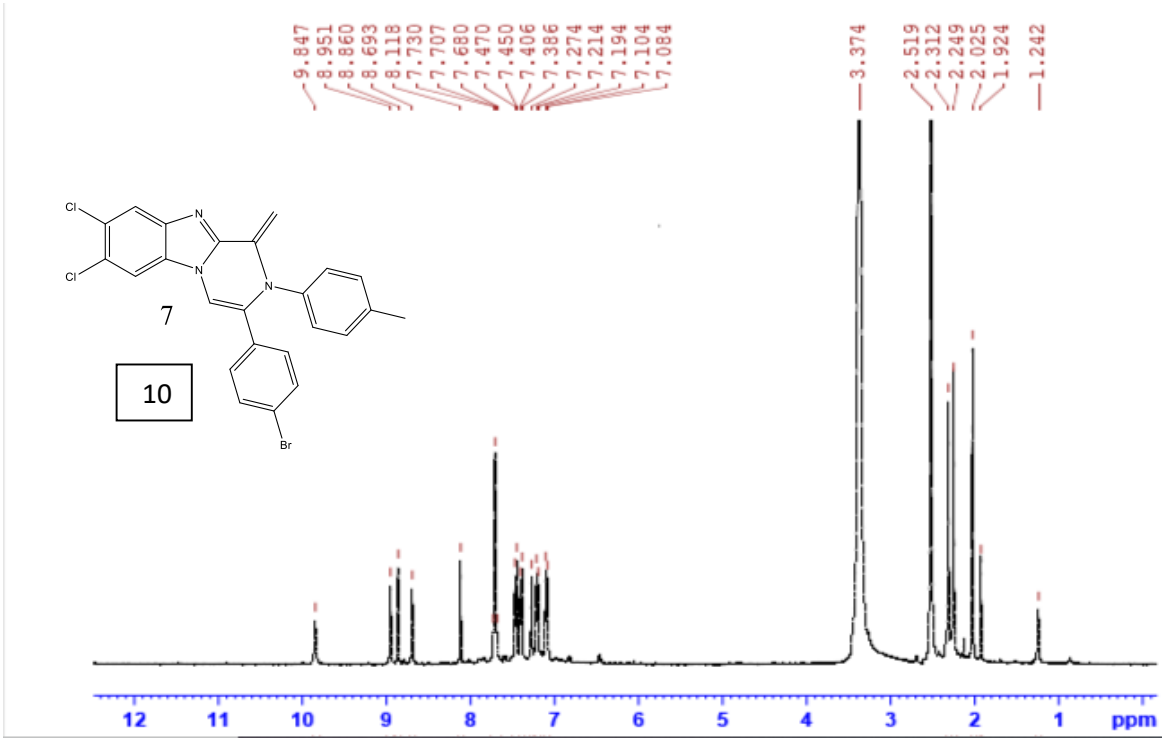


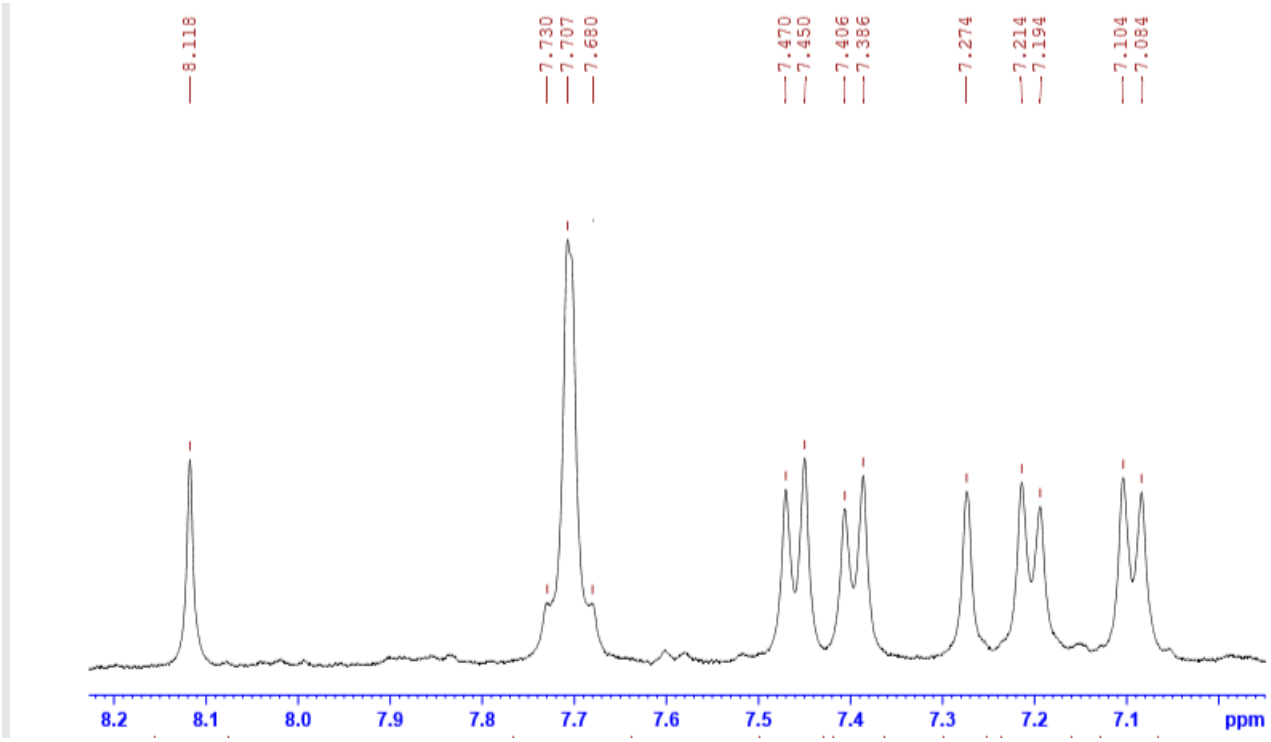
Mass of compound 9

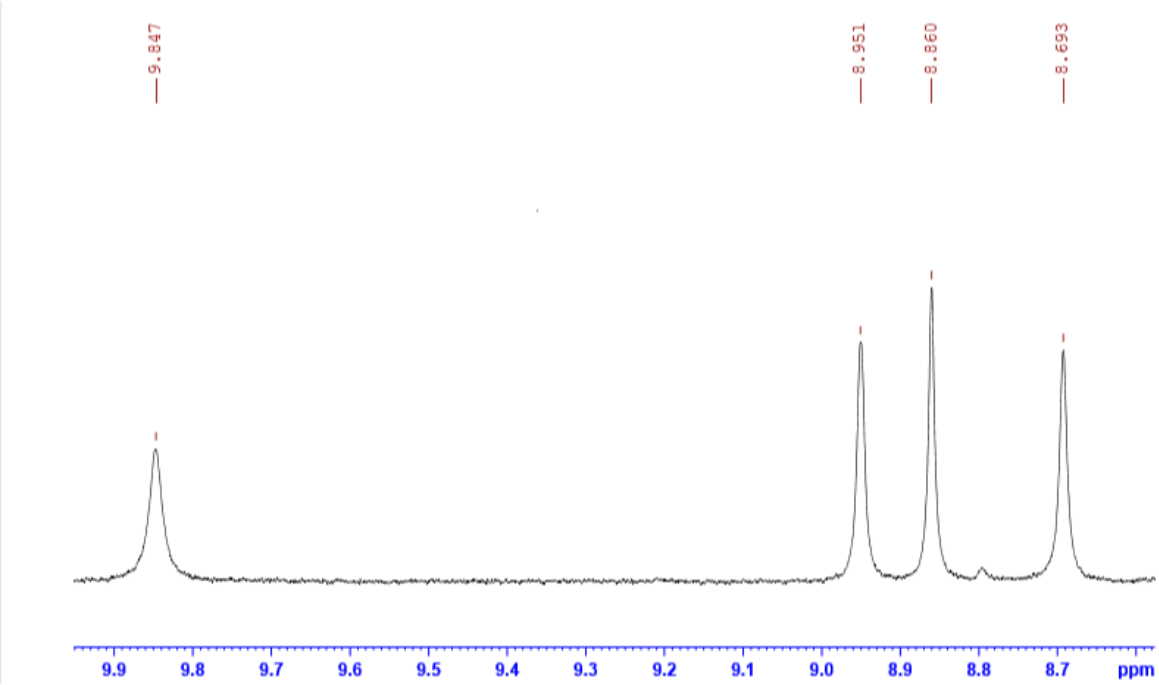




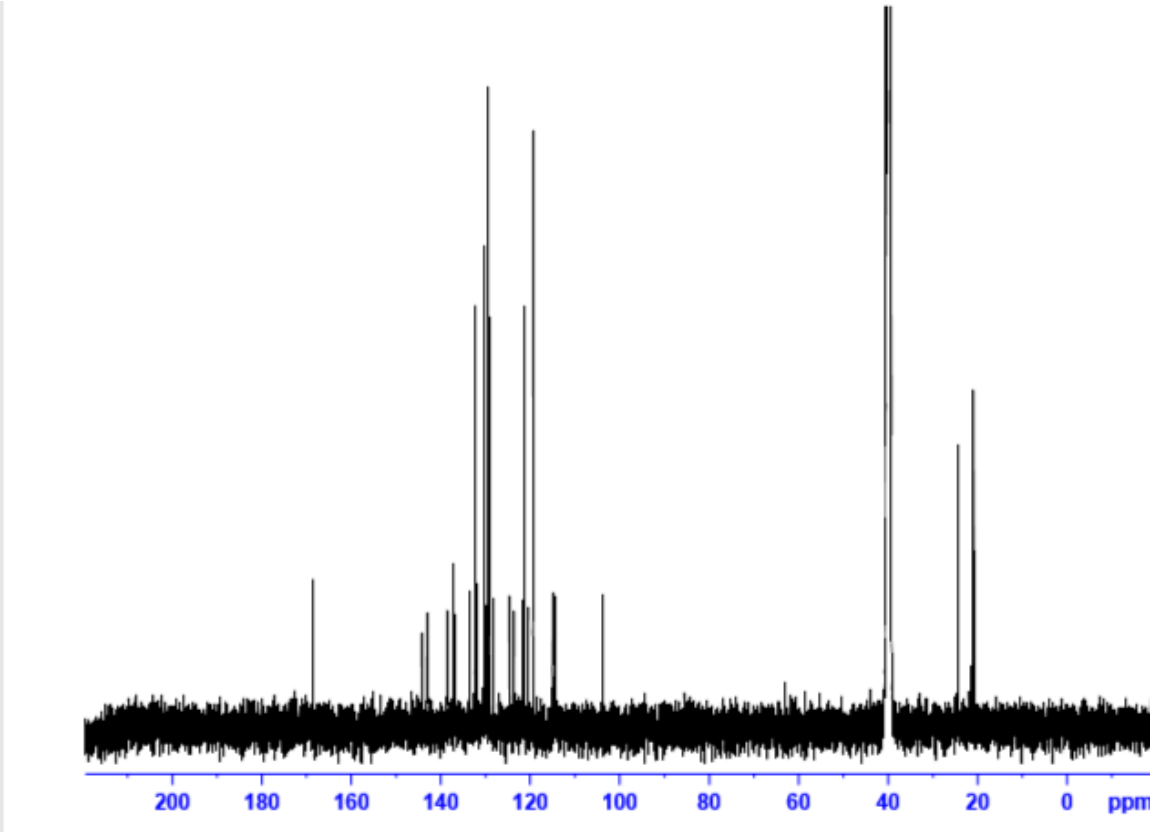
^{1}H NMR of compound 10



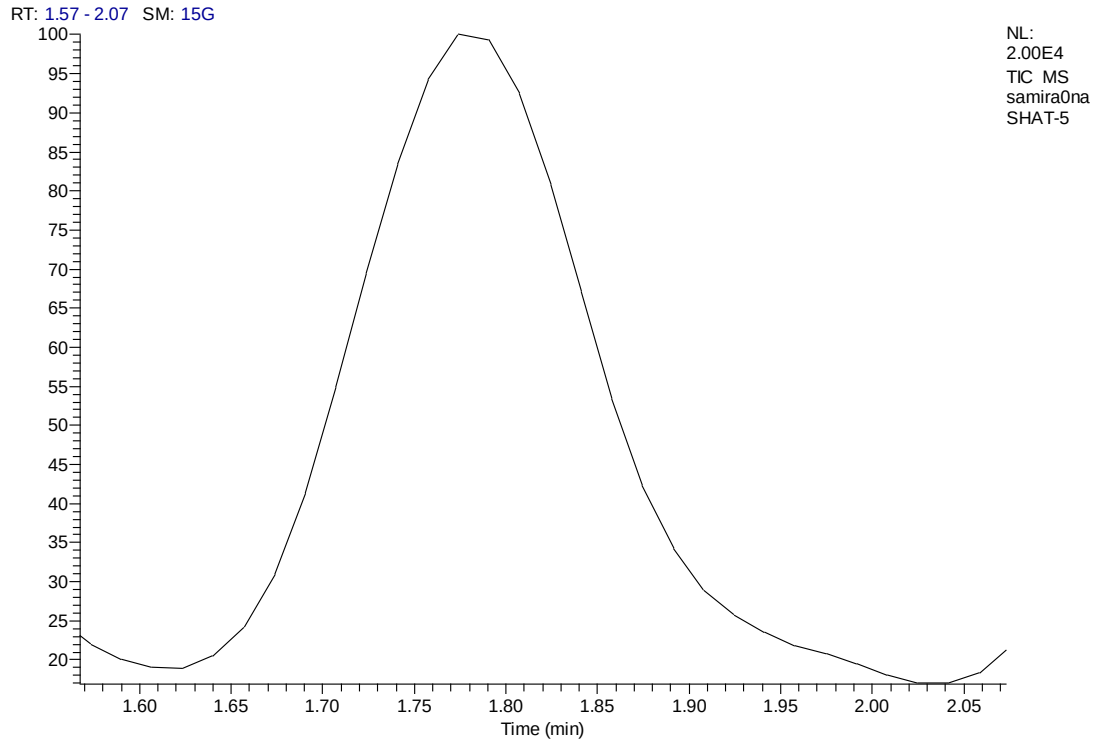


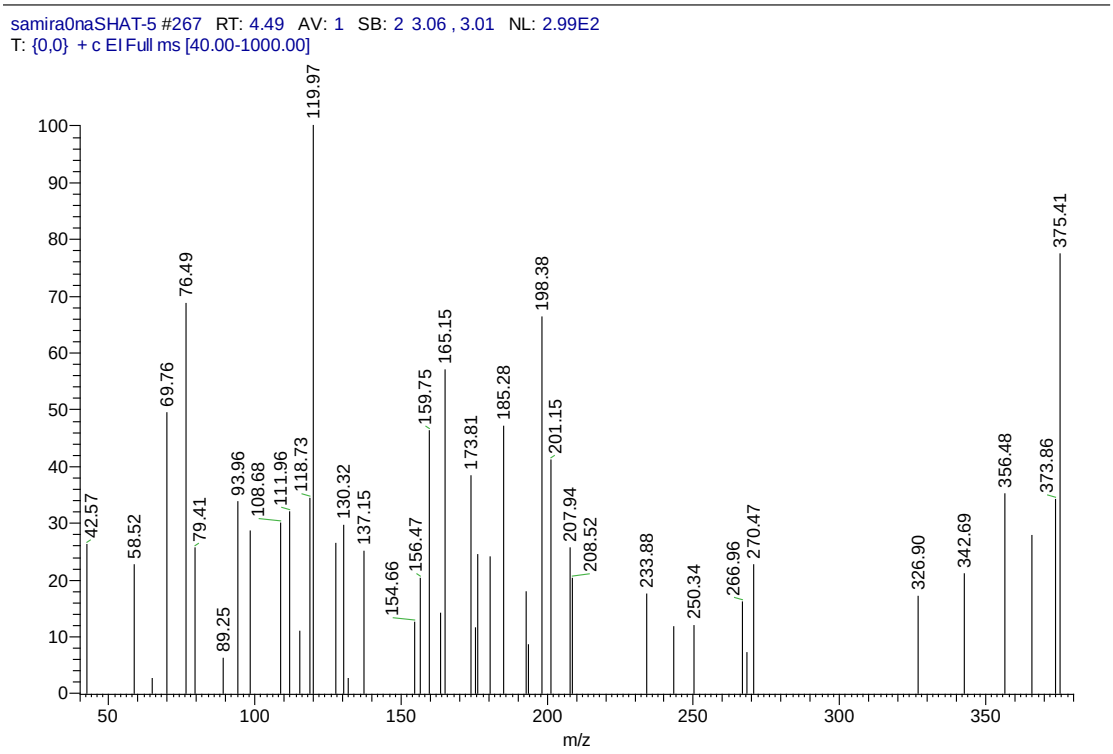


^{13}C NMR of compound 10

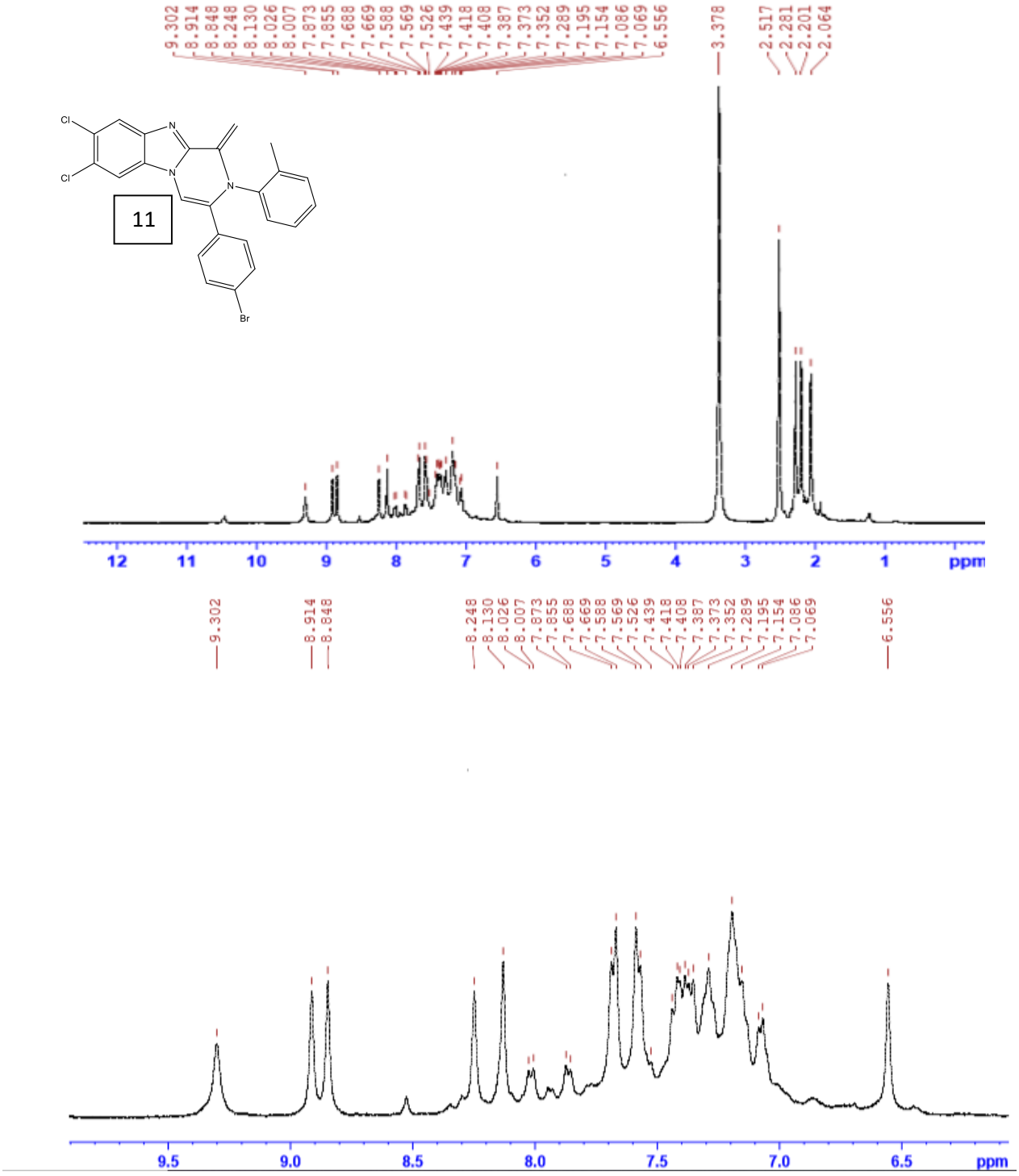


Mass of compound 10

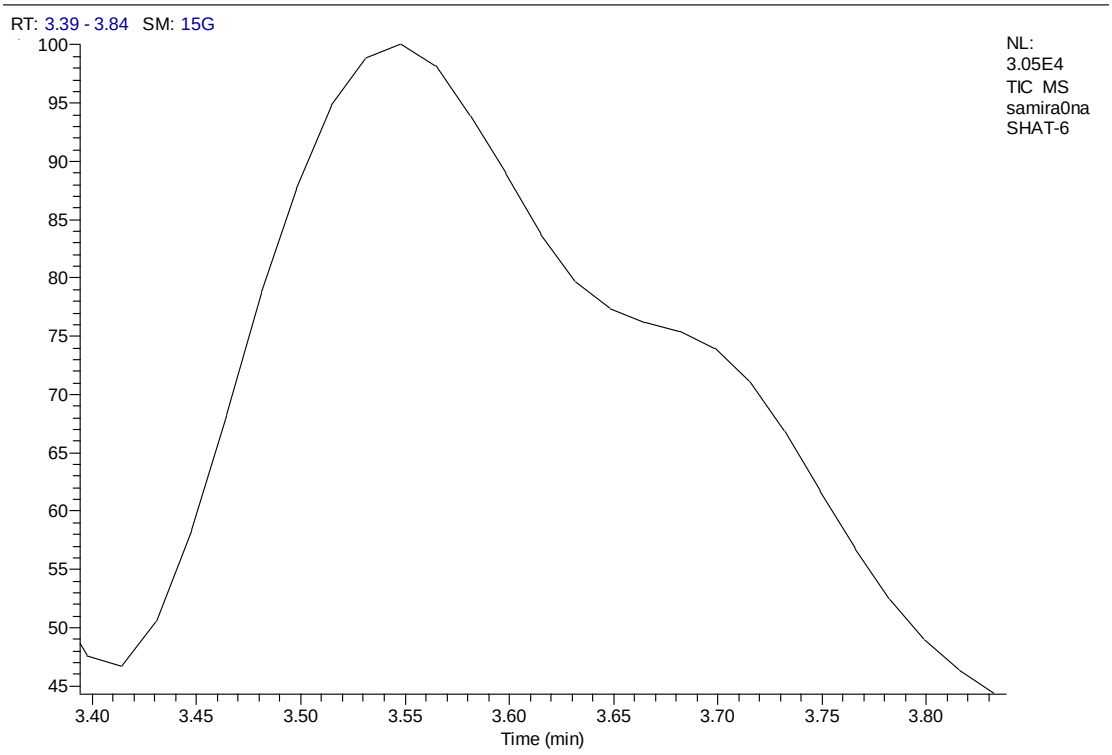


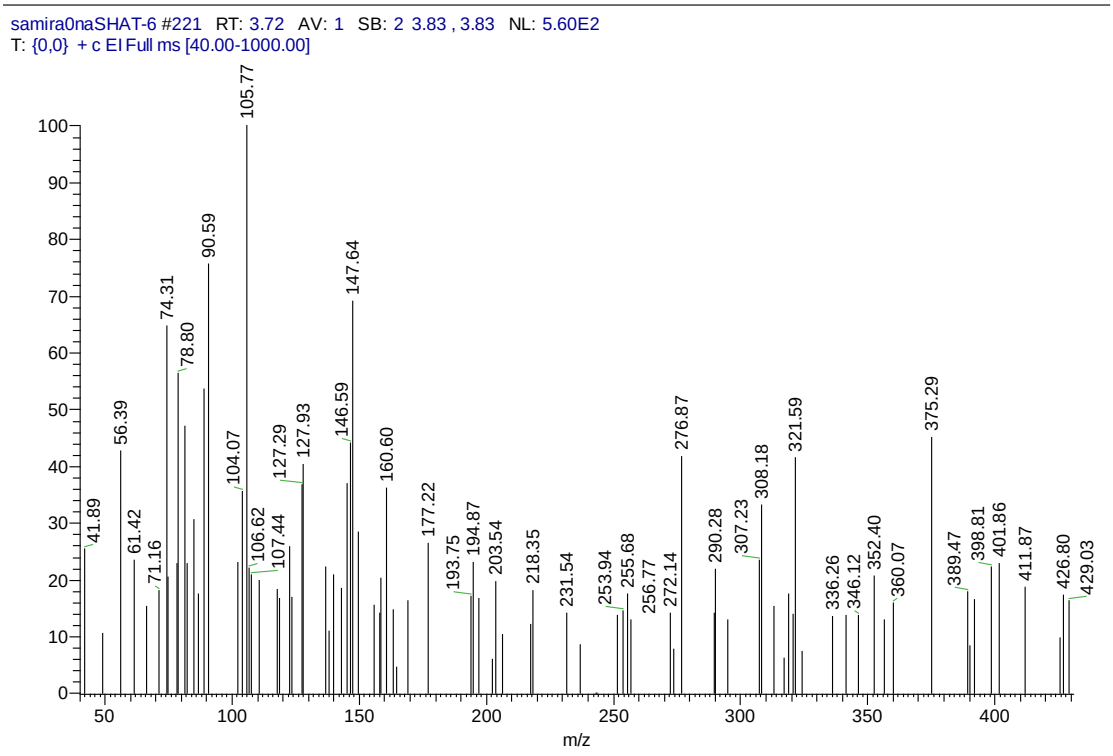


^{1}H NMR of compound 11

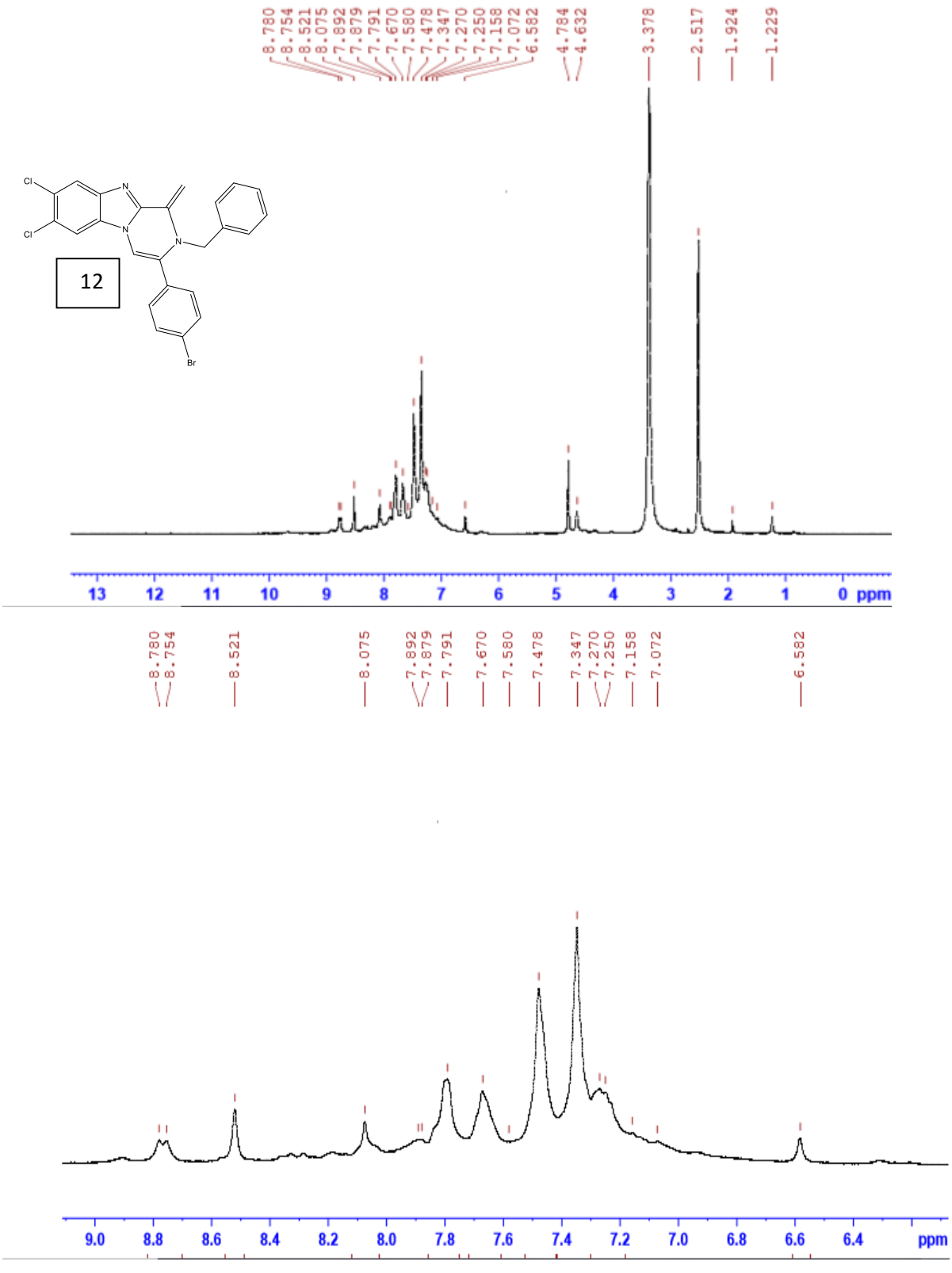


Mass of compound 11

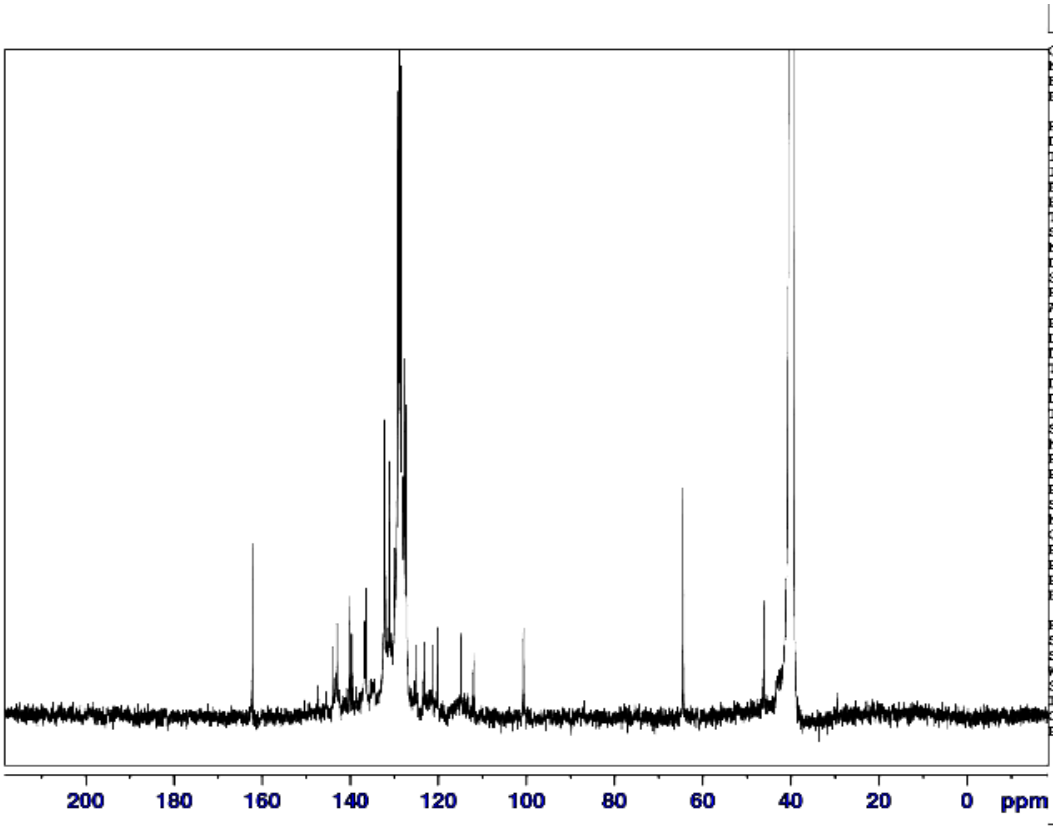




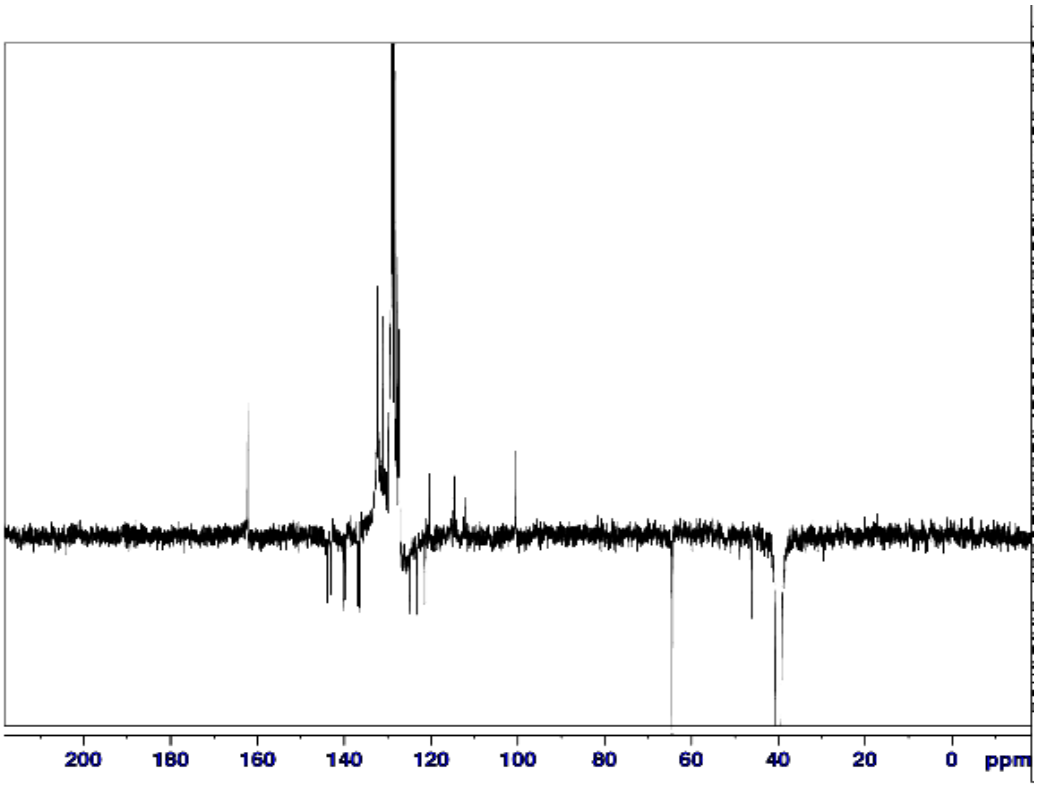
^{1}H NMR of compound 12


8.780
8.754
8.521
8.075
7.892
7.879
7.791
7.670
7.580
7.478
7.347
7.270
7.250
7.158
7.072
6.582
4.784
4.632
3.378
2.517
1.924
1.229
Cl
Cl
N
N
N
Br
12
13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 ppm

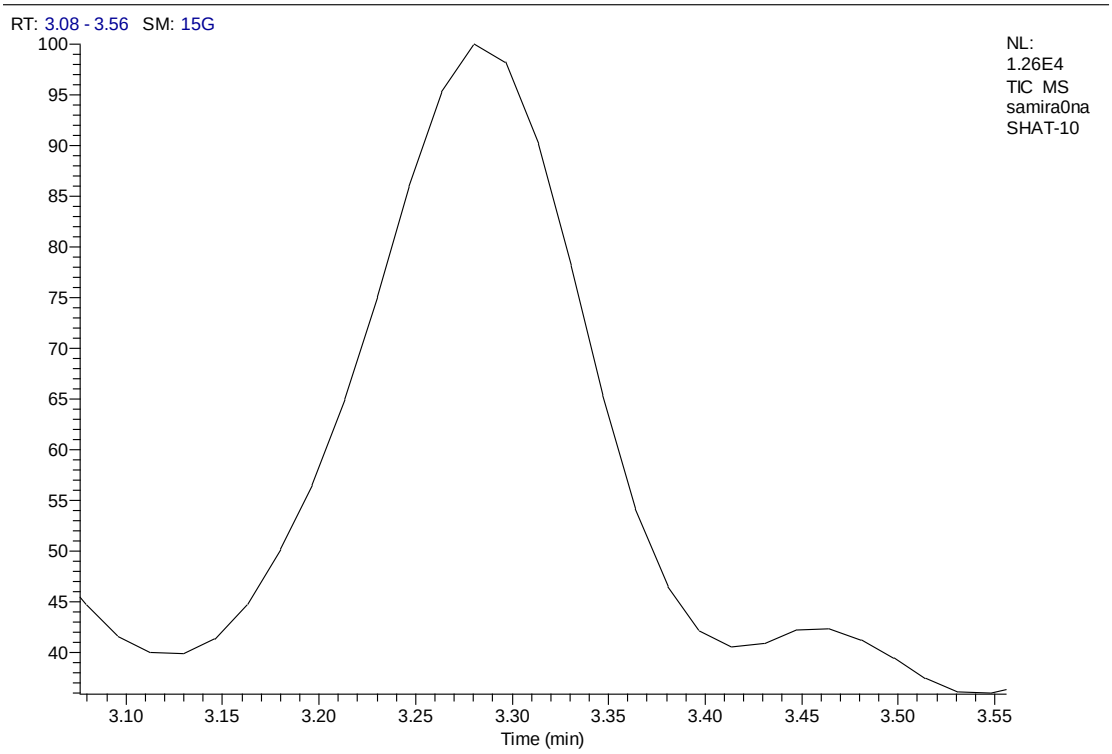
^{13}C NMR of compound 12

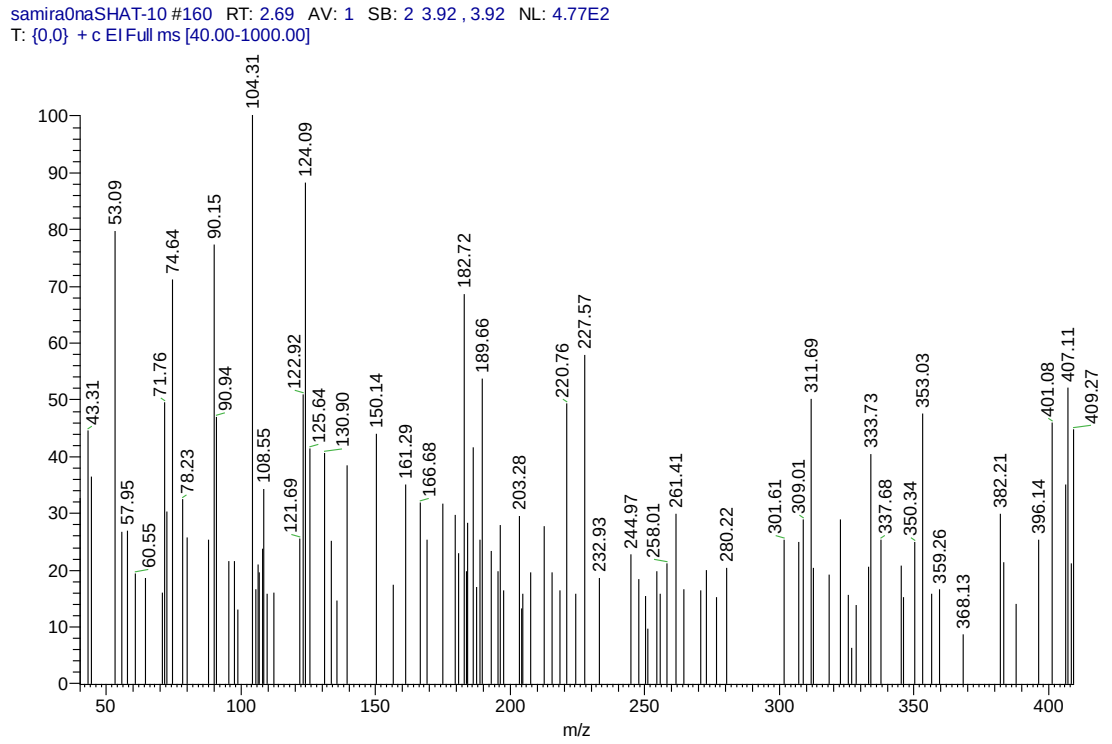


APT of compound 12

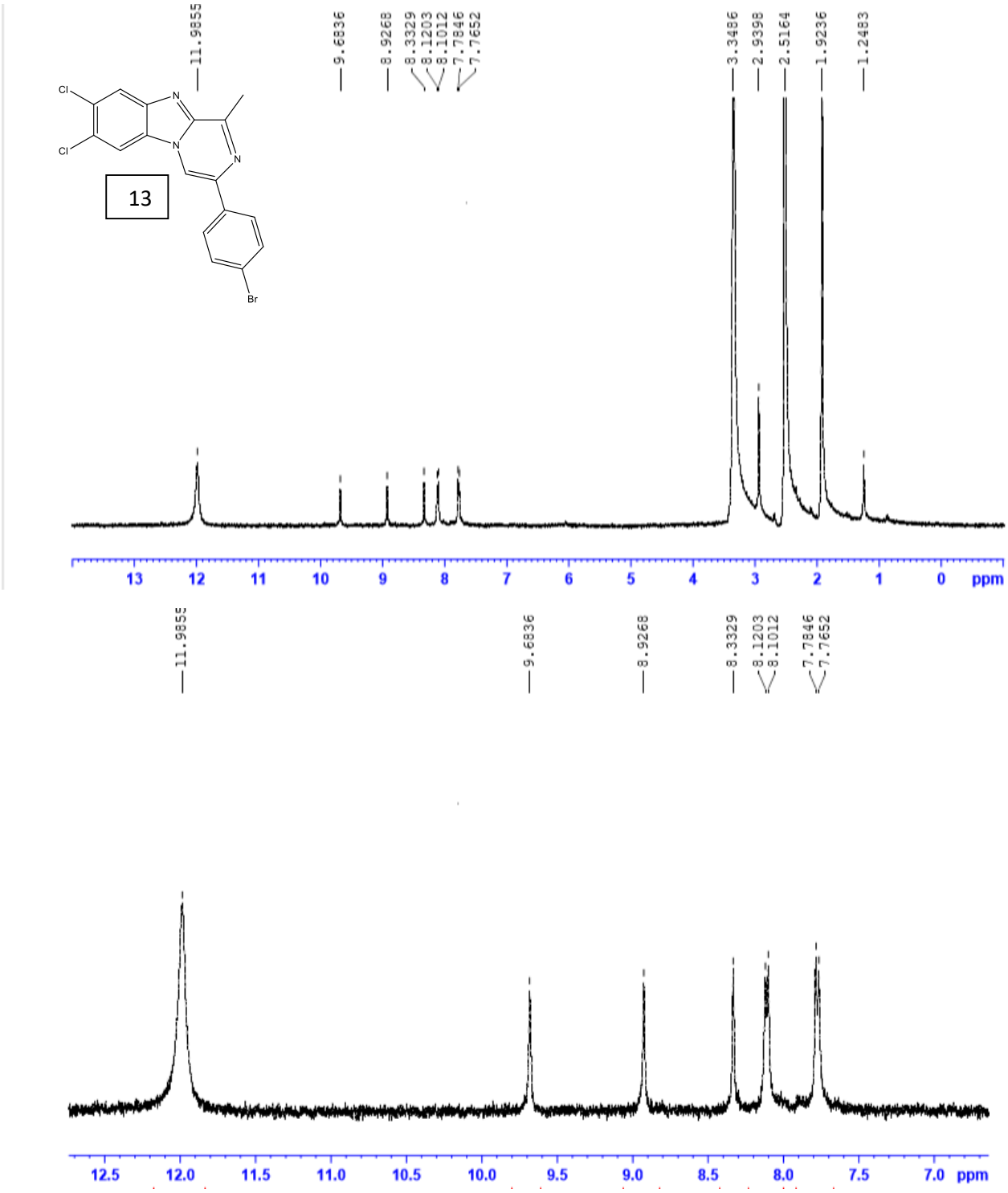


Mass of compound 12

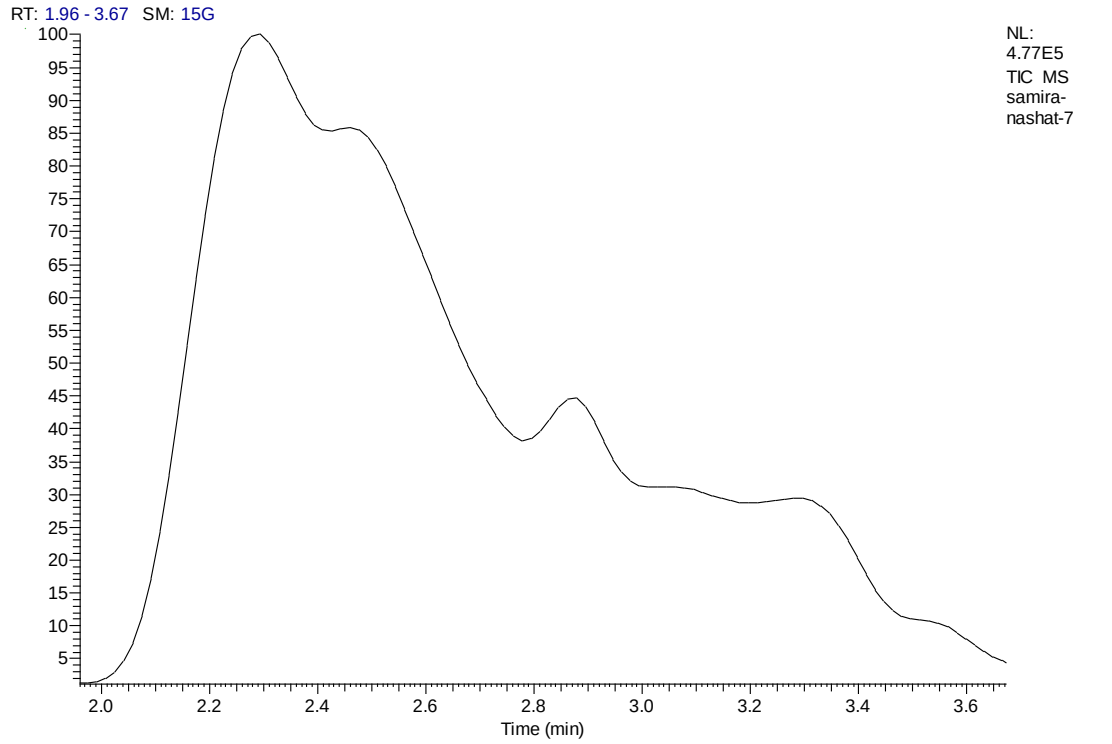


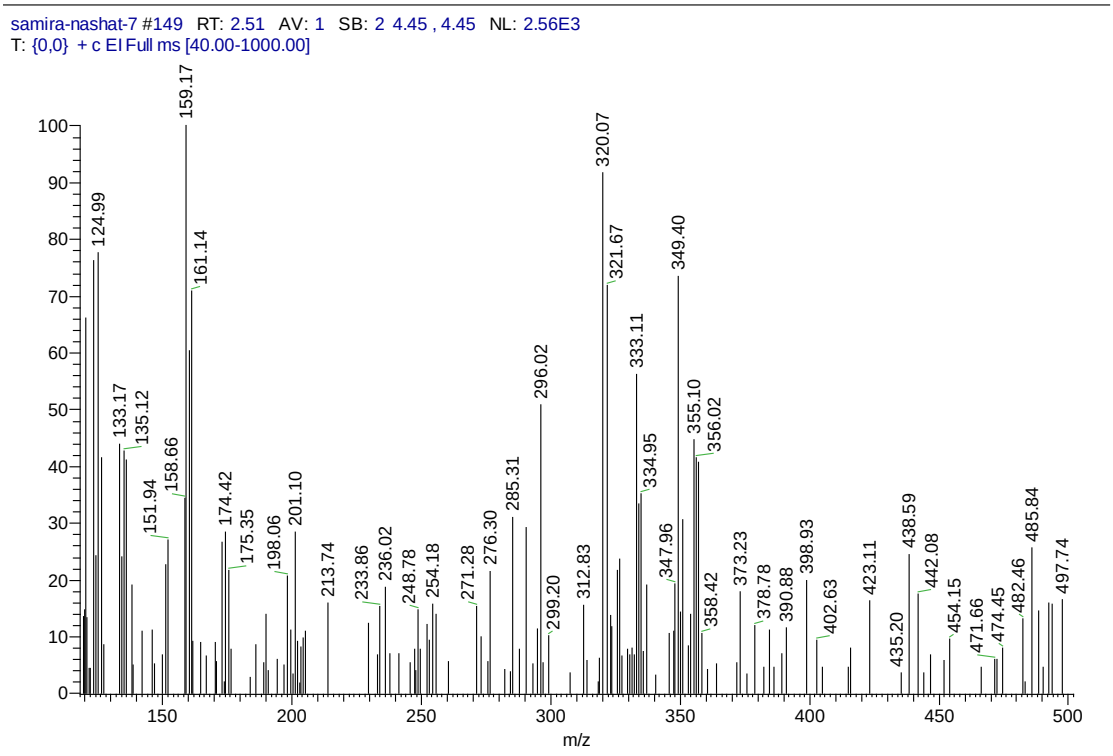


^{1}H NMR of compound 13

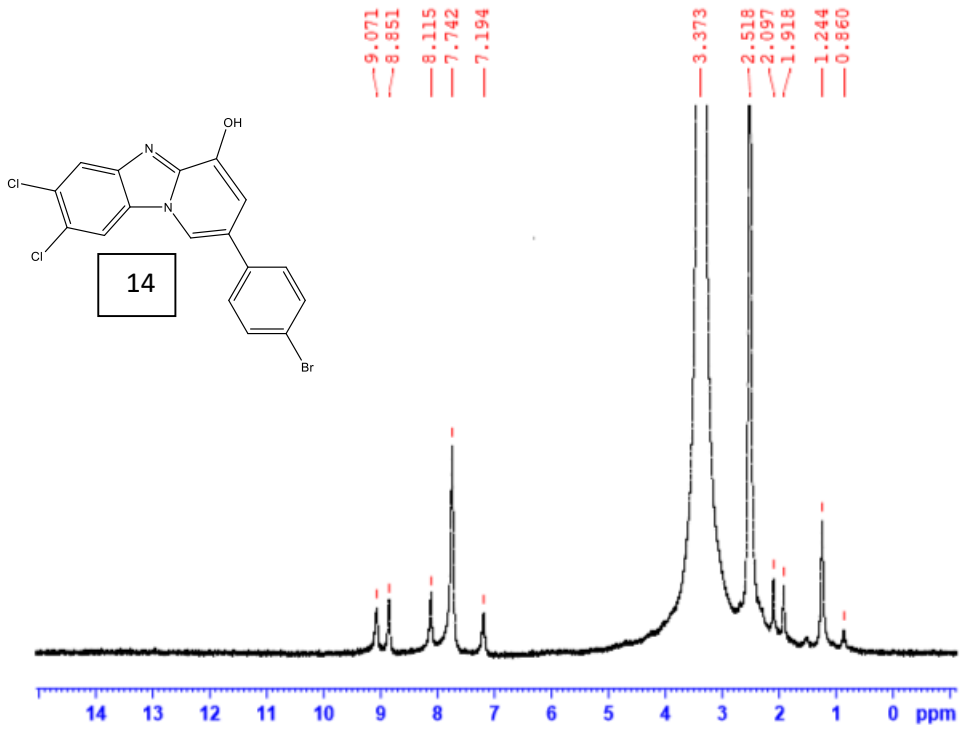


Mass of compound 13

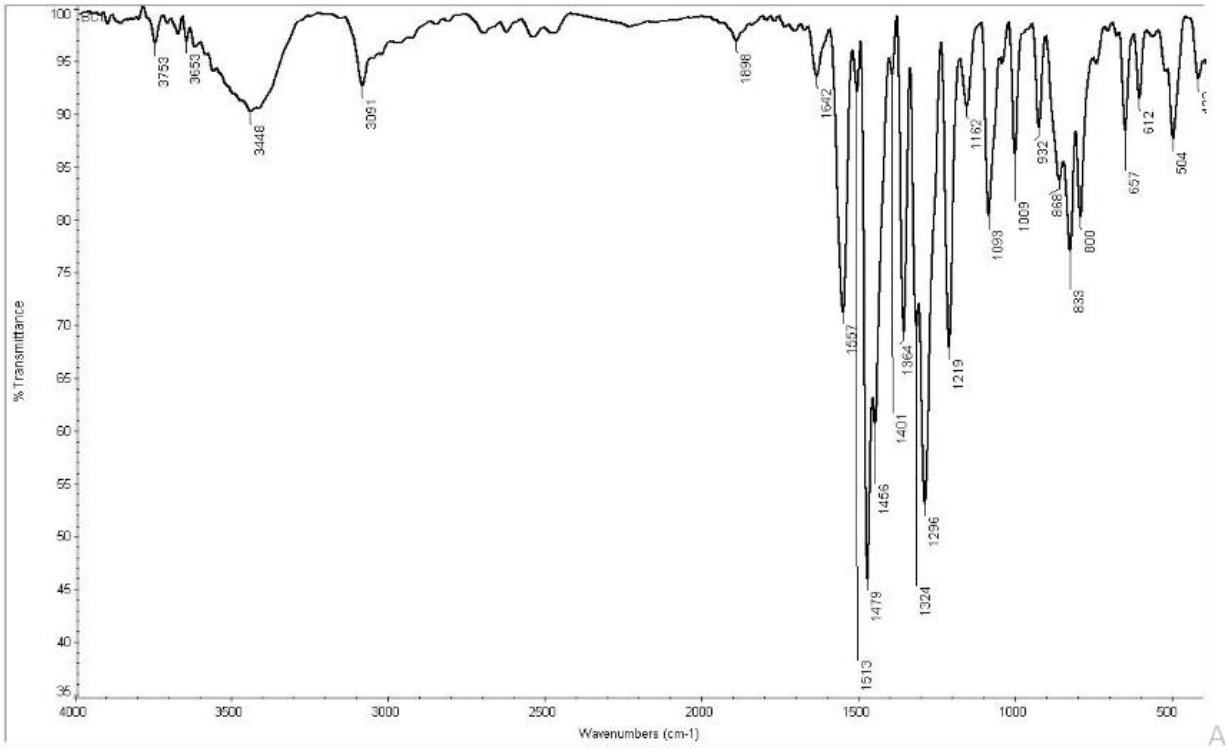




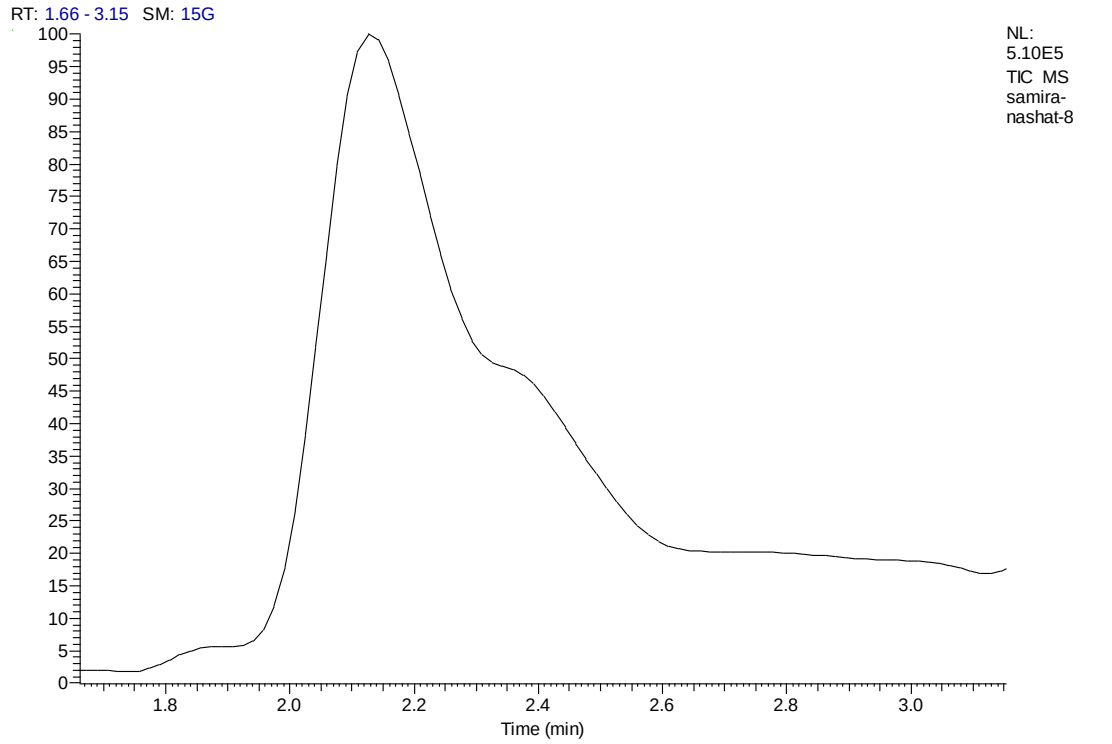
^{1}H NMR of compound 14

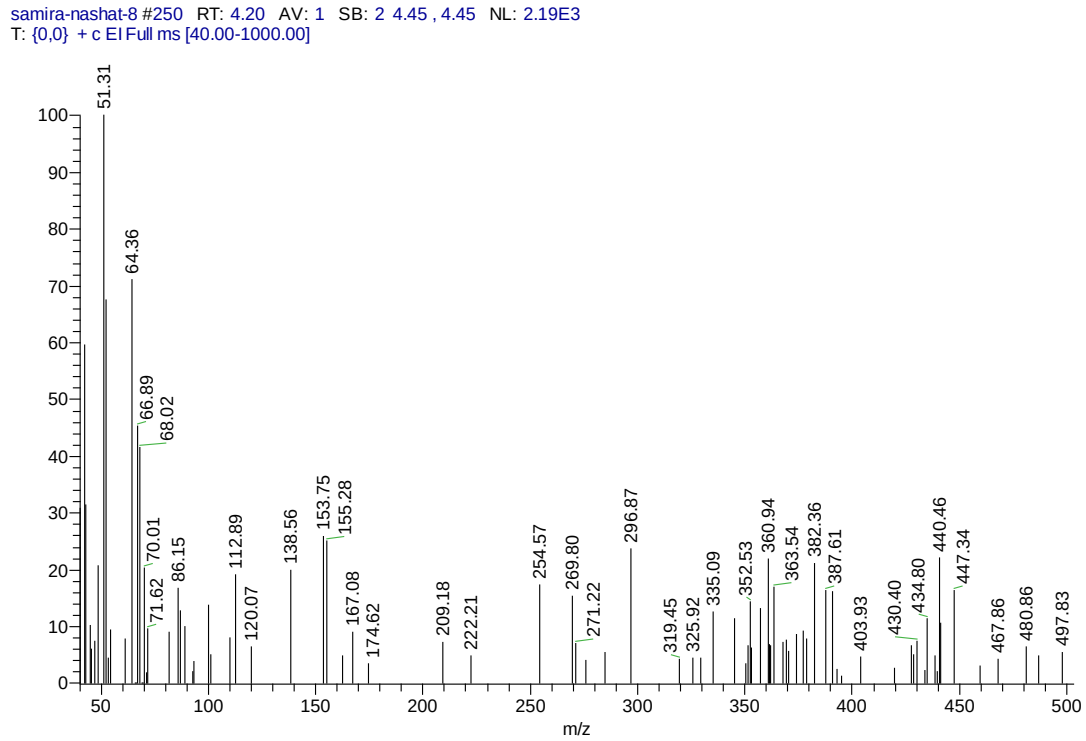


IR of compound 14



Mass of compound 14

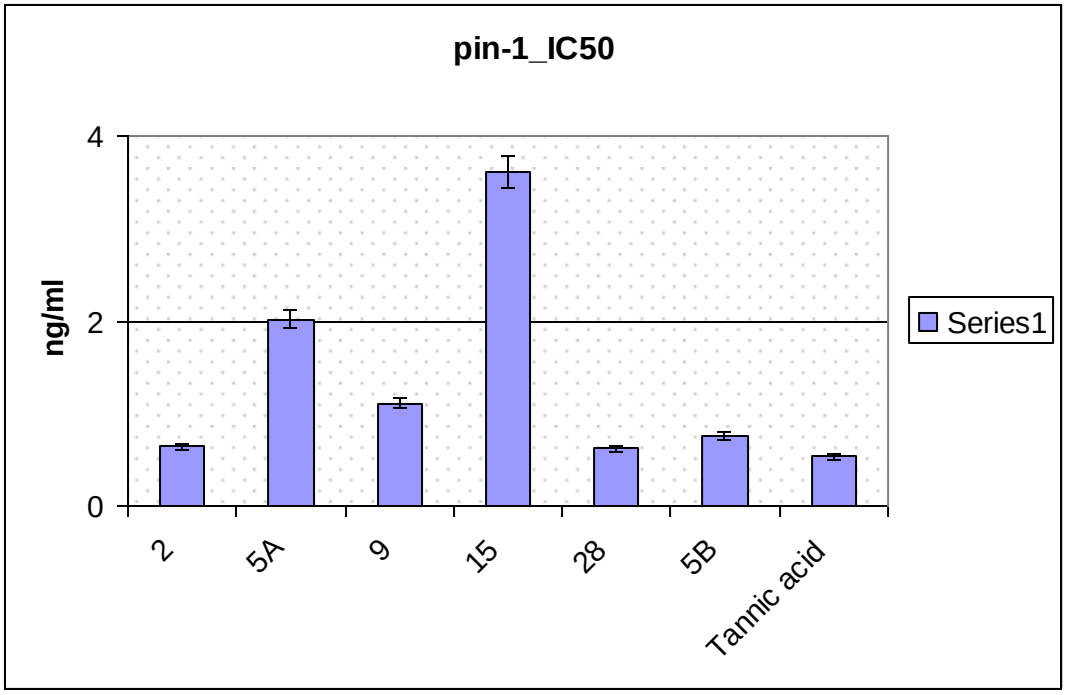




: Dr.Samira Nashaat	email: Samiranashaat2@gmail.com	**mob.** 01011509651	Researcher
		: EGFR enzyme assay	Assay
		: 05 compounds.	Samples
		: ---	Cell line
		: ---	Reference
		: 28/06/2020	Date

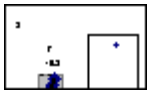
Lab Report

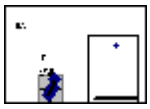
ser	Compound		Results
	code	MW g/mol	pin-1 IC50 nM
1	2	372.25	0.646±0.03
2	5A	362.29	2.019±0.1
3	9	497.22	1.106±0.06
4	15	440.62	3.609±0.16
5	28	324.87	0.617±0.03
6	5B	375.25	0.76±0.04
***	Tannic acid	1701	0.535±0.02


pin-1_IC50
ng/ml
4
2
0
2
5A
9
15
28
5B
Tannic acid
Series1

Detailed results

pin-1

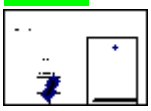
code	IC50	conc	log	%inh	T2	T1	ΔT	RFU2	RFU1	ΔRFU	slope	K.Activity	EC
2		100	2	85.21	30	0	30	288	0	288	64.9	17.7504	120
		10	1	66.97	30	0	30	643	0	643	64.9	39.6302	120
		1	0	51.1	30	0	30	952	0	952	64.9	58.6749	120
		0.1	-1	39.19	30	0	30	1184	0	1184	64.9	72.9738	120
EC				0	30	0	30	1947	0	1947	64.9	120	120

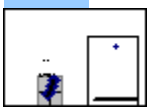
code	IC50	conc.ng/ml	log conc	%inh	T2	T1	ΔT	RFU2	RFU1	ΔRFU	slope	K.Activity	EC
5A		100	2	84.8	30	0	30	296	0	296	64.9	18.2435	120
		10	1	55.21	30	0	30	872	0	872	64.9	53.7442	120
		1	0	43.76	30	0	30	1095	0	1095	64.9	67.4884	120
		0.1	-1	29.94	30	0	30	1364	0	1364	64.9	84.0678	120
EC				0	30	0	30	1947	0	1947	64.9	120	120

code	IC50	conc.ng/ml	log conc	%inh	T2	T1	ΔT	RFU2	RFU1	ΔRFU	slope	K.Activity	EC
9		100	2	87.52	30	0	30	243	0	243	64.9	14.9769	120
		10	1	69.49	30	0	30	594	0	594	64.9	36.6102	120
		1	0	42.17	30	0	30	1126	0	1126	64.9	69.3991	120
		0.1	-1	34.72	30	0	30	1271	0	1271	64.9	78.3359	120
EC				0	30	0	30	1947	0	1947	64.9	120	120

code	IC50	conc.ng/ml	log conc	%inh	T2	T1	ΔT	RFU2	RFU1	ΔRFU	slope	K.Activity	EC
15		100	2	82.49	30	0	30	341	0	341	64.9	21.0169	120
		10	1	54.9	30	0	30	878	0	878	64.9	54.114	120
		1	0	34.36	30	0	30	1278	0	1278	64.9	78.7673	120
		0.1	-1	23.73	30	0	30	1485	0	1485	64.9	91.5254	120
EC				0	30	0	30	1947	0	1947	64.9	120	120

code	IC50	conc.ng/ml	log conc	%inh	T2	T1	ΔT	RFU2	RFU1	ΔRFU	slope	K.Activity	EC
28		100	2	86.7	30	0	30	259	0	259	64.9	15.963	120
		10	1	66.97	30	0	30	643	0	643	64.9	39.6302	120
		1	0	50.33	30	0	30	967	0	967	64.9	59.5994	120
		0.1	-1	40.27	30	0	30	1163	0	1163	64.9	71.6795	120
EC				0	30	0	30	1947	0	1947	64.9	120	120

code	IC50	conc.ng/ml	log conc	%inh	T2	T1	ΔT	RFU2	RFU1	ΔRFU	slope	K.Activity	EC
Tannic acid		100	2	86.03	30	0	30	272	0	272	64.9	16.7643	120
		10	1	70.01	30	0	30	584	0	584	64.9	35.9938	120
		1	0	52.18	30	0	30	931	0	931	64.9	57.3806	120
		0.1	-1	39.96	30	0	30	1169	0	1169	64.9	72.0493	120
EC				0	30	0	30	1947	0	1947	64.9	120	120

code	IC50	conc.ng/ml	log conc	%inh	T2	T1	ΔT	RFU2	RFU1	ΔRFU	slope	K.Activity	EC
5B		100	2	84.8	30	0	30	296	0	296	64.9	18.2435	120
		10	1	67.39	30	0	30	635	0	635	64.9	39.1371	120
		1	0	49.1	30	0	30	991	0	991	64.9	61.0786	120
		0.1	-1	38.01	30	0	30	1207	0	1207	64.9	74.3914	120
EC				0	30	0	30	1947	0	1947	64.9	120	120

2	y = 15.393x + 52.922
5A	y = 17.601x + 44.628
9	y = 18.572x + 49.188
15	y = 19.682x + 39.029
28	y = 15.593x + 53.272
Tannic acid	y = 15.603x + 54.242