Supporting Information's

Synthesis, Biological Activities and Computational Studies of *Bis*-Schiff Bases of 4-Hydroxyacetophenone: Insights from *In Vitro*, Molecular Docking and Dynamic Simulation Approach

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Table-S1: Molecular docking results of the compounds against AChE and BuChE

No.	*ΔG*	RMSD	H. B	EInt.	*ΔG*	RMSD	H. B	EInt.
	AChE (PDB:4EY6)				BuChE (4BDS)			
(2a)	-6.787	1.941	-8.071	-24.898	-8.689	1.893	-7.461	-17.278
(2b)	-6.860	1.836	-9.034	-15.497	-6.247	1.245	-12.045	-29.683
(2e)	-6.702	1.295	-9.528	-21.735	-7.464	1.762	-10.104	-28.660
(2f)	-7.071	1.693	-9.205	-19.083	-8.205	1.741	-11.914	-30.134
(2g)	-7.047	2.605	-10.350	-26.815	-8.211	1.472	-11.529	-25.651
(2j)	-6.585	1.553	-11.602	-29.201	-8.060	1.471	-12.714	-29.050
Standard	-7.585	1.049	-32.408	-12.285	-5.314	1.635	-23.164	-9.130
Tacrine	-5.368	1.457	-18.243	-8.399	-4.502	1.199	-17.444	-7.249

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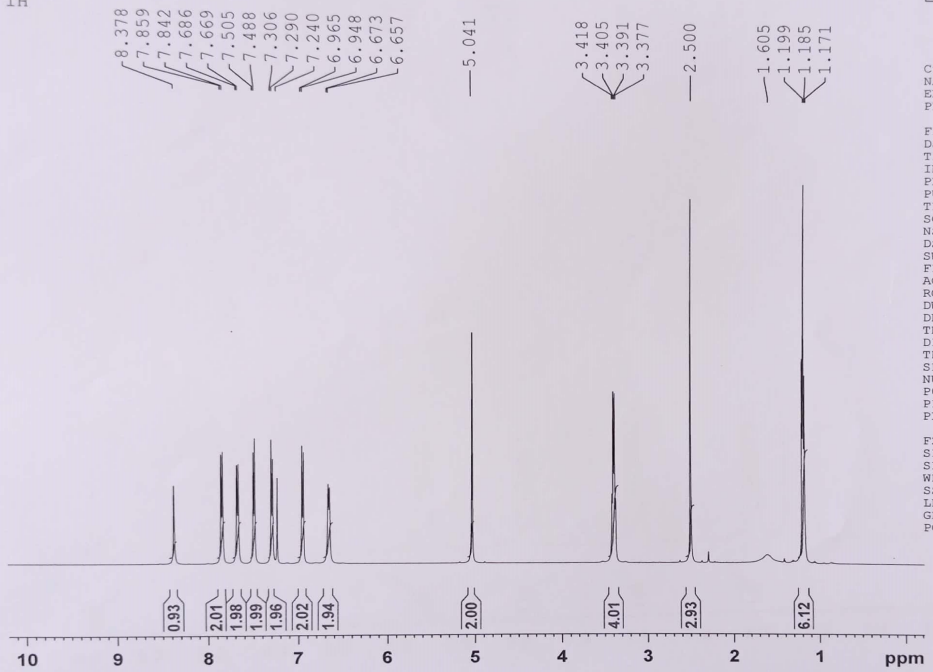

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LAB # 109-B

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TD                      65536
SOLVENT                 CDCl3
NS                         32
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FIDRES                0.305176 Hz
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RG                        101
DW                     50.000 usec
DE                     11.31 usec
TE                     298.0 K
D1                  2.00000000 sec
TD0                         1
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P0                     2.33 usec
P1                     7.00 usec
PLW1               17.96400070 W

F2 - Processing parameters
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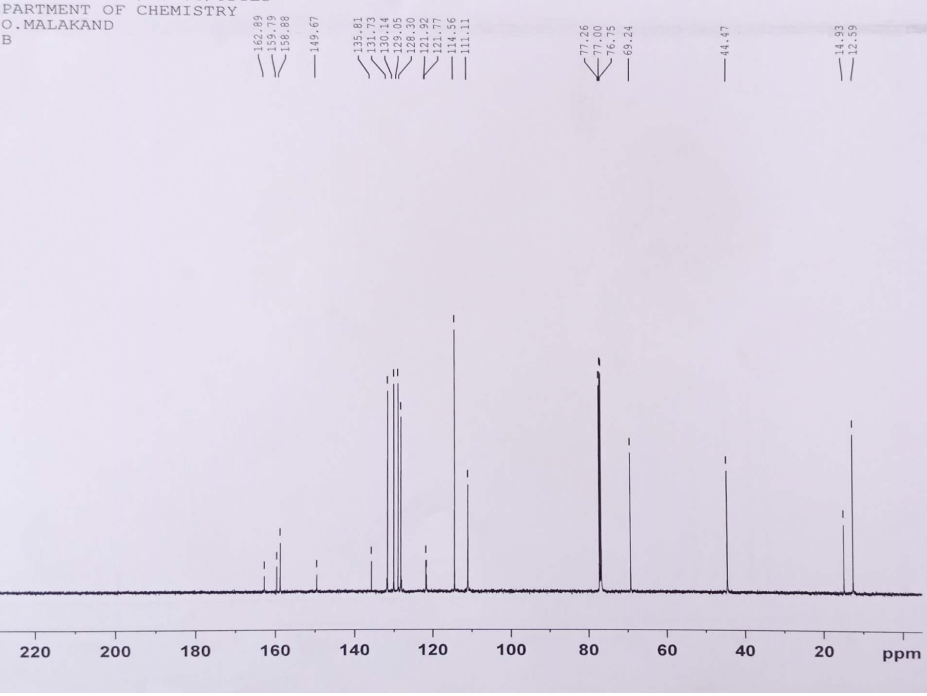

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LAB # 109-B

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TD 32768
SOLVENT CDCl3
NS 8192
DS 4
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FIDRES 1.838408 Hz
AQ 0.5439488 sec
RG 101
DW 16.600 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 8
SFO1 125.7722507 MHz
NUC1 13C
P1 15.00 usec
PLW1 119.40000153 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 80.00 usec
PLW2 17.96400070 W
PLW12 0.13754000 W
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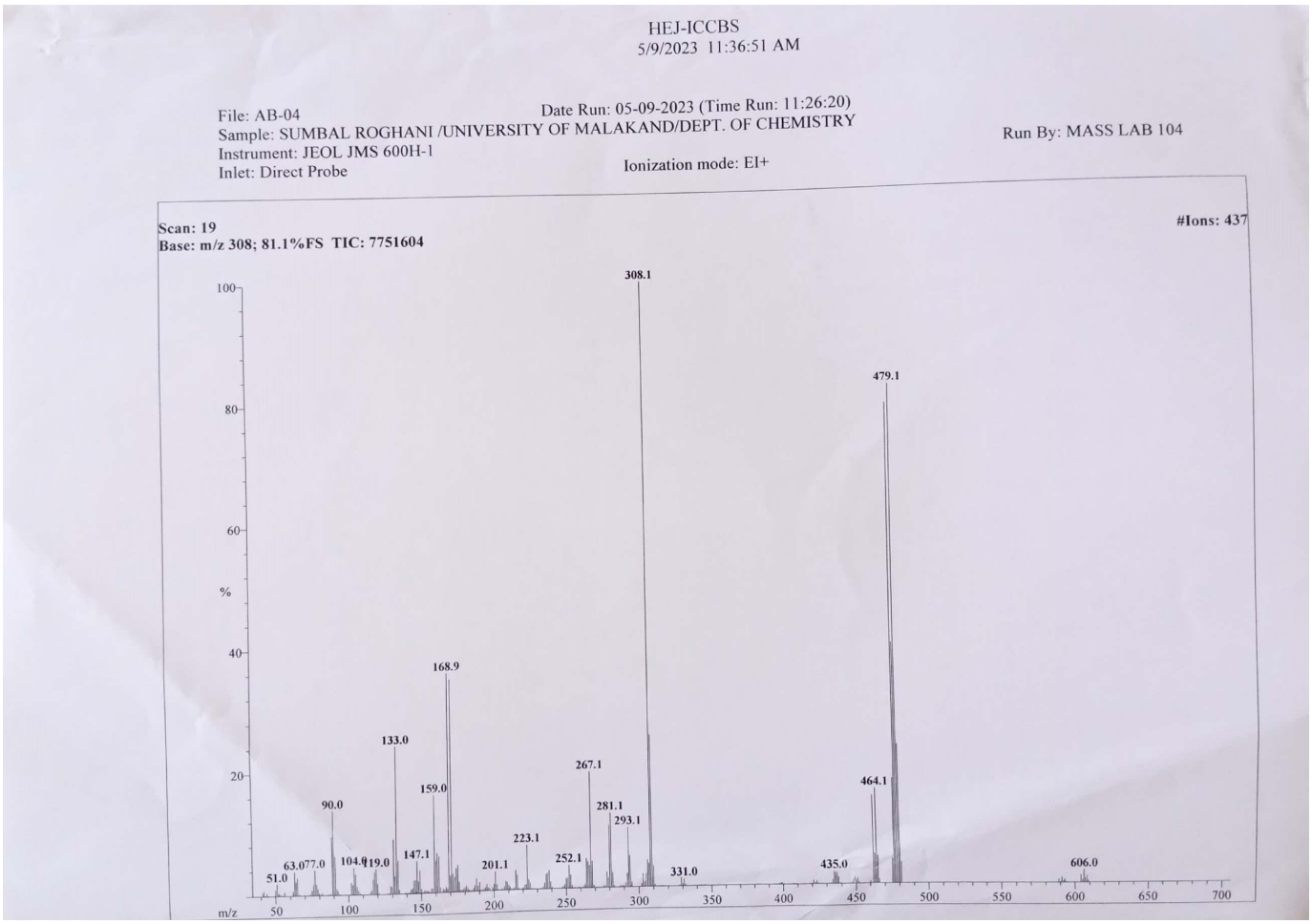

Figure-S1: ^{1}H-, ^{13}C-NMR and EI-MS spectra of compound **2a**

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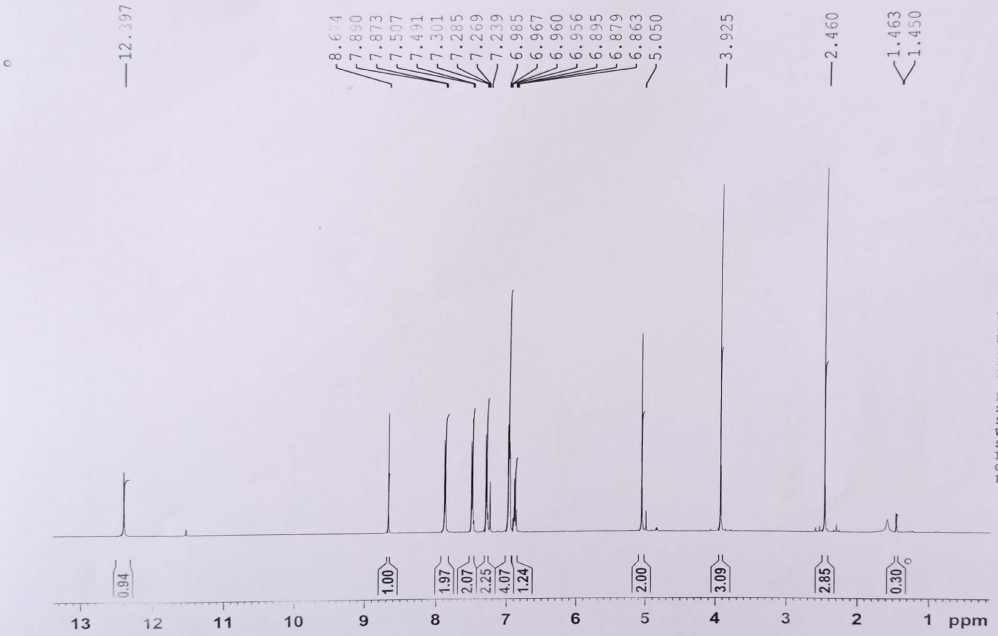

AVANCE 500 MHZ
LAB # 108

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PROCNO                       1

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TD                      32768
SOLVENT                 CDCl3
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RG                         101
DW                     55.000 usec
DE                      6.50 usec
TE                     298.0 K
D1                  2.00000000 sec
TD0                          1
SFO1             500.3340026 MHz
NUC1                        1H
P0                      3.25 usec
P1                      9.75 usec
PLW1            10.00000000 W

F2 - Processing parameters
SI                       32768
SF               500.3300221 MHz
WDW                         EM
SSB          0
LB                      1.00 Hz
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AVANCE 500 MHZ
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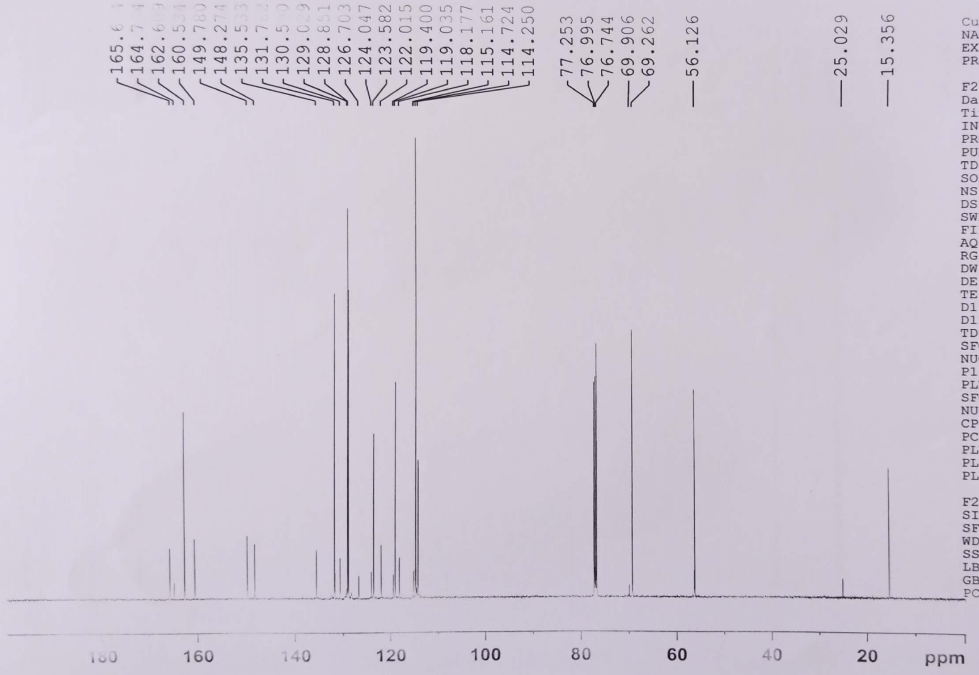

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EXPNO	2
PROCNO	1

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PULPROG	zgpg
TD	32768
SOLVENT	CDCl3
NS	8571
DS	8
SWH	30120.482 Hz
FIDRES	1.838408 Hz
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RG	101
DW	16.600 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	12
SFO1	125.8225465 MHz
NUC1	13C
P1	16.00 usec
PLW1	145.00000000 W
SFO2	500.3320013 MHz
NUC2	1H
CPDPRG[2	waltz65
PCPD2	80.00 usec
PLW2	10.00000000 W
PLW12	0.14854001 W
PLW13	0.07471200 W

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WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.00	

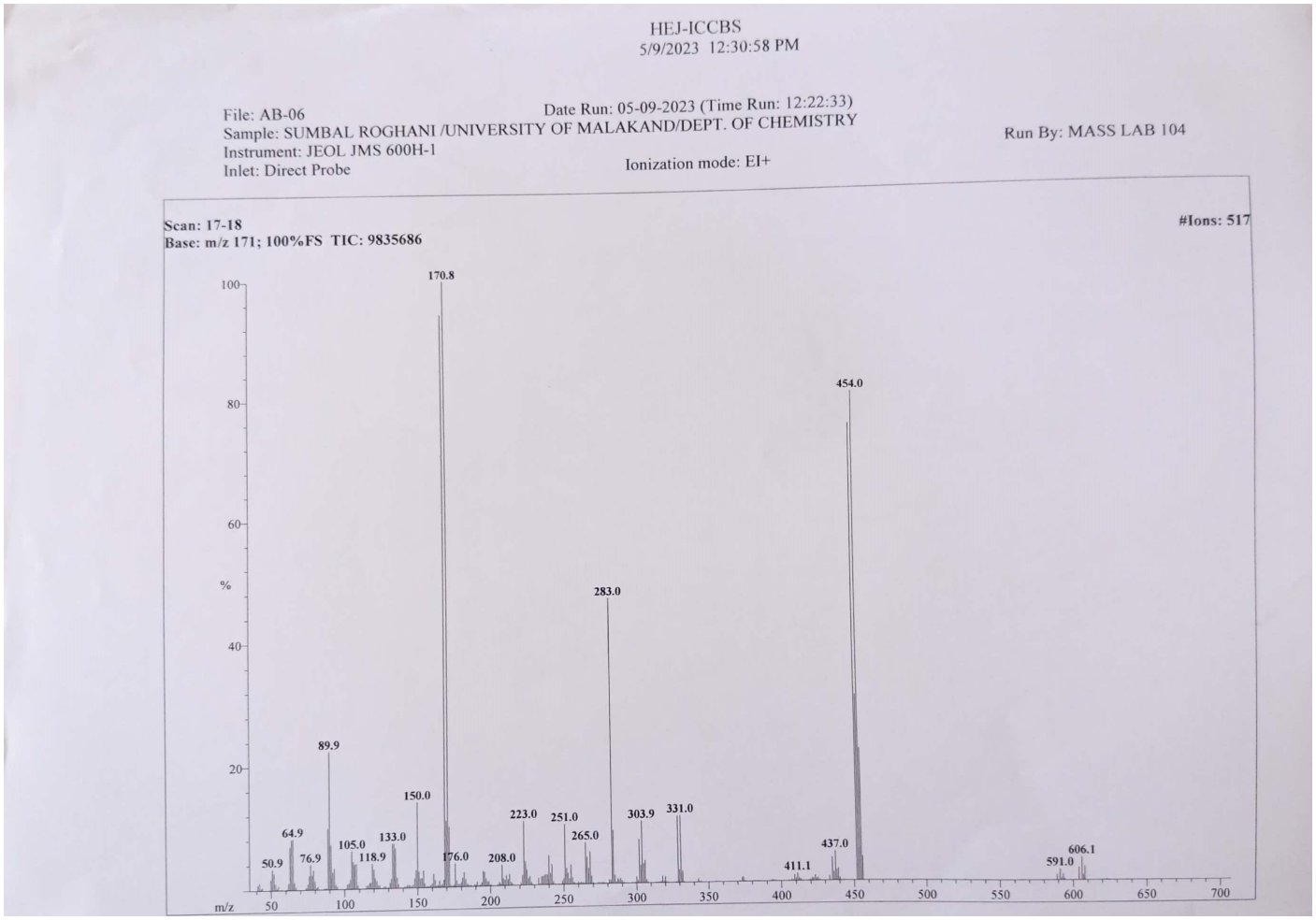

Figure-S2: ^{1}H-, ^{13}C-NMR and EI-MS spectra of compound **2b**

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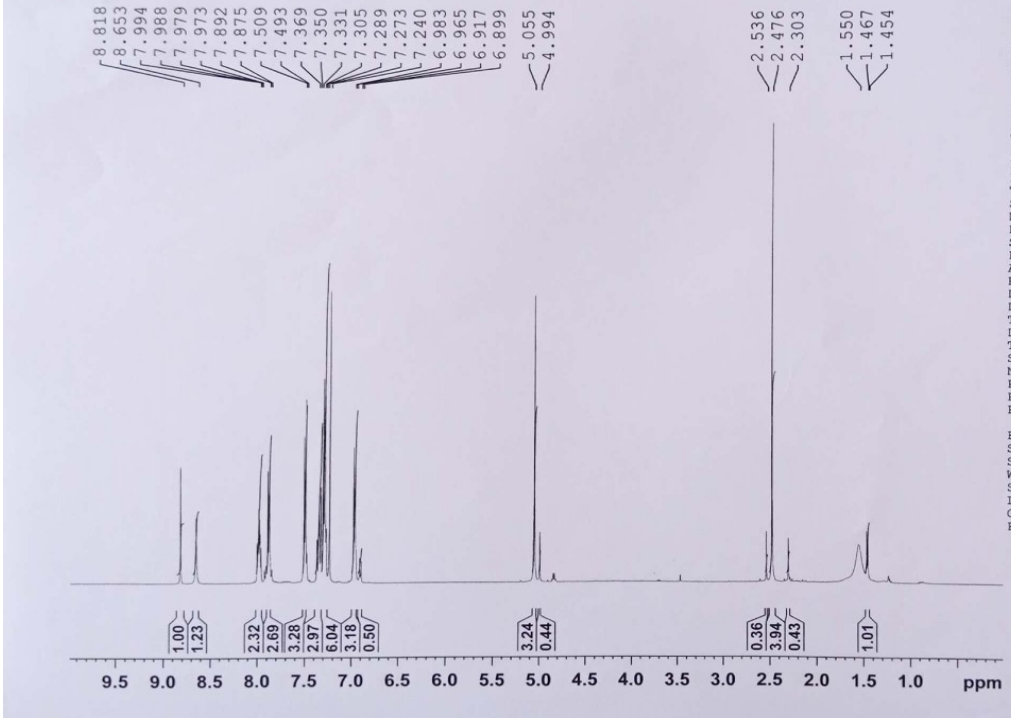

AVANCE 500 MHZ
LAB # 108

Current Data Parameters

NAME	May07-23
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20230507
Time	12.25 h
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PROBHD	Z8107_0198 (PH
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	32
DS	0
SWH	9090.909 Hz
FIDRES	0.554865 Hz
AQ	1.8022400 sec
RG	101
DW	55.000 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
TD0	1
SFO1	500.3340026 MHz
NUC1	1H
P0	3.25 usec
P1	9.75 usec
PLW1	10.00000000 W

F2 - Processing parameters

SI	32768
SF	500.3300221 MHz
WDW	EM
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LB	1.00 Hz
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PC	1.00

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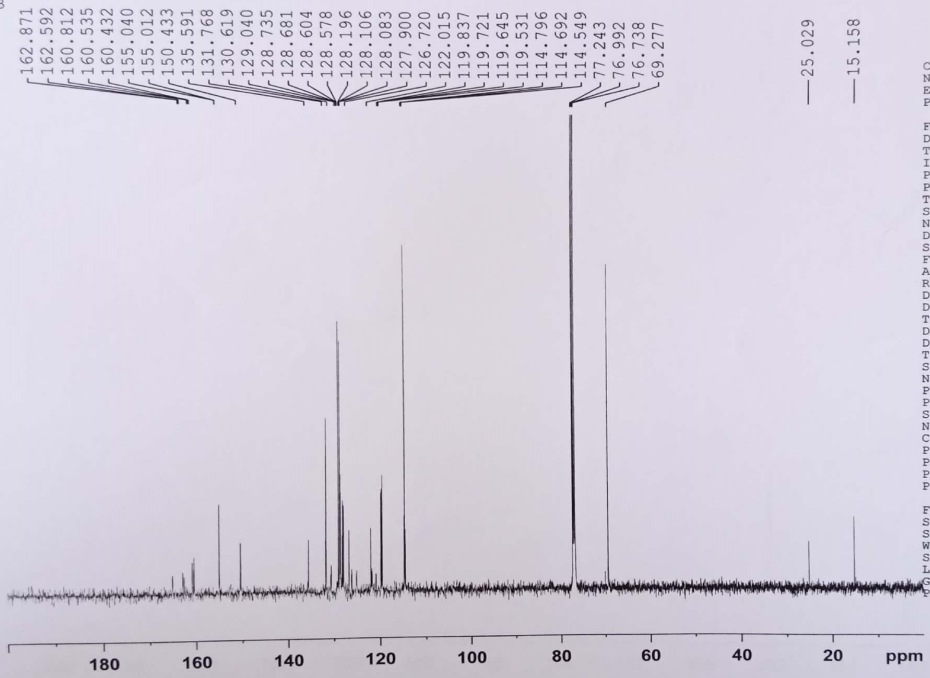

AVANCE 500 MHZ
LAB # 108

Current Data Parameters

NAME	May07-23
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

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Time	21.19 h
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PULPROG	zgpg
TD	32768
SOLVENT	CDCl3
NS	12288
DS	8
SWH	30120.482 Hz
FIDRES	1.838408 Hz
AQ	0.5439488 sec
RG	101
DW	16.600 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	12
SFO1	125.8225465 MHz
NUC1	13C
P1	16.00 usec
PLW1	145.00000000 W
SFO2	500.3320013 MHz
NUC2	1H
CPDPRG[2	waltz65
PCPD2	80.00 usec
PLW2	10.00000000 W
PLW12	0.14854001 W
PLW13	0.07471200 W

F2 - Processing parameters

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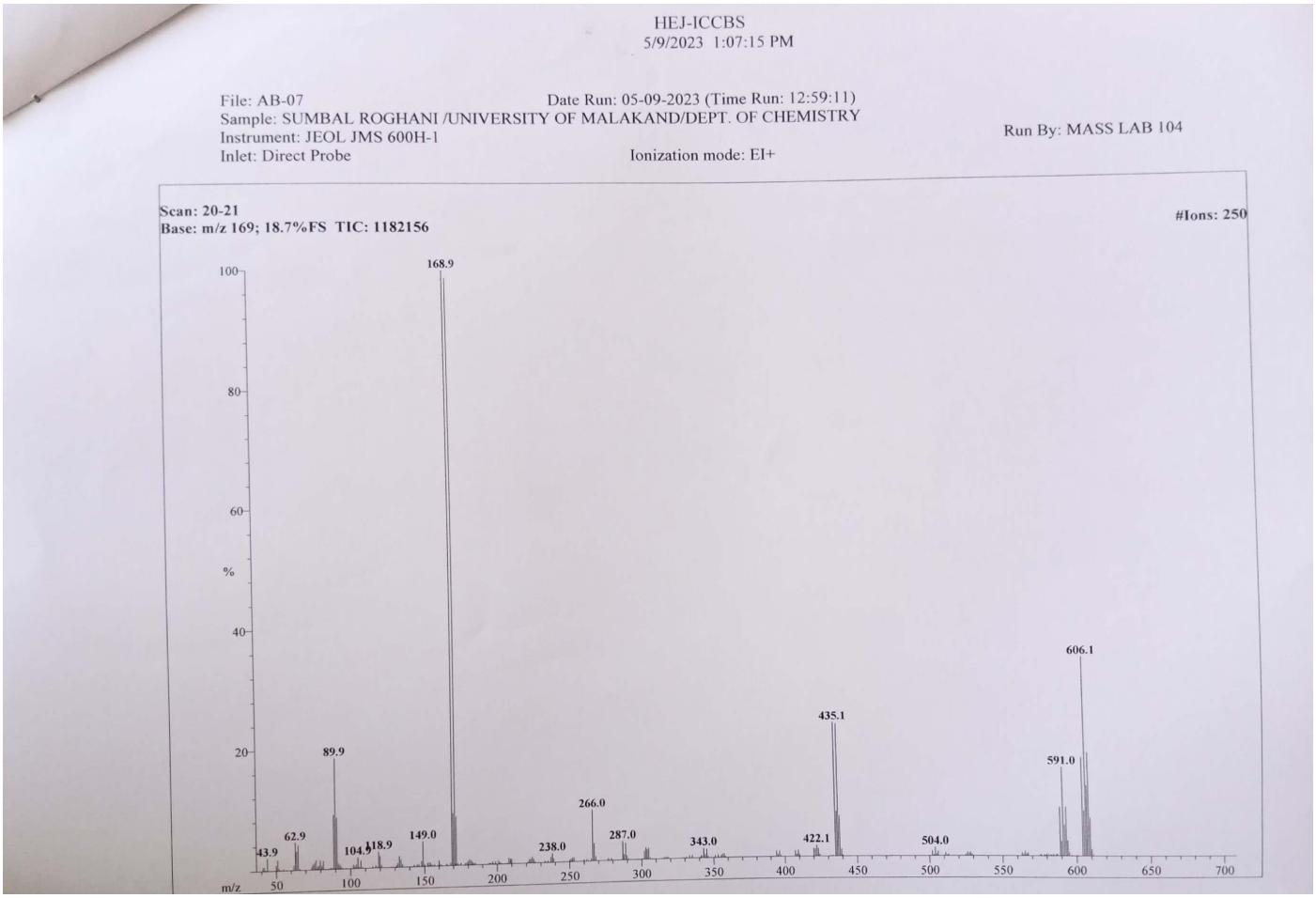

Figure-S3: ^{1}H-, ^{13}C-NMR and EI-MS spectra of compound **2c**

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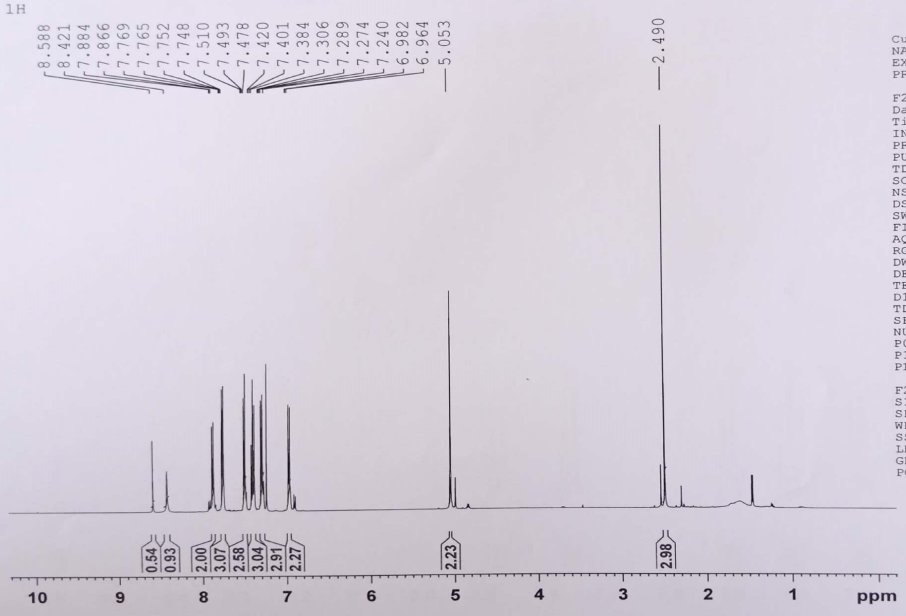

AVANCE NEO
500 MHz
LAB # 109-B

Current Data Parameters
NAME May07-23
EXPNO 1
PROCNO 1

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PROBHD Z859201_0007 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 101
DW 50.000 usec
DE 11.31 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
SFO1 500.1340010 MHz
NUC1 1H
P0 2.33 usec
P1 7.00 usec
PLW1 17.96400070 W

F2 - Processing parameters
SI 65536
SF 500.1300220 MHz
WDW EM
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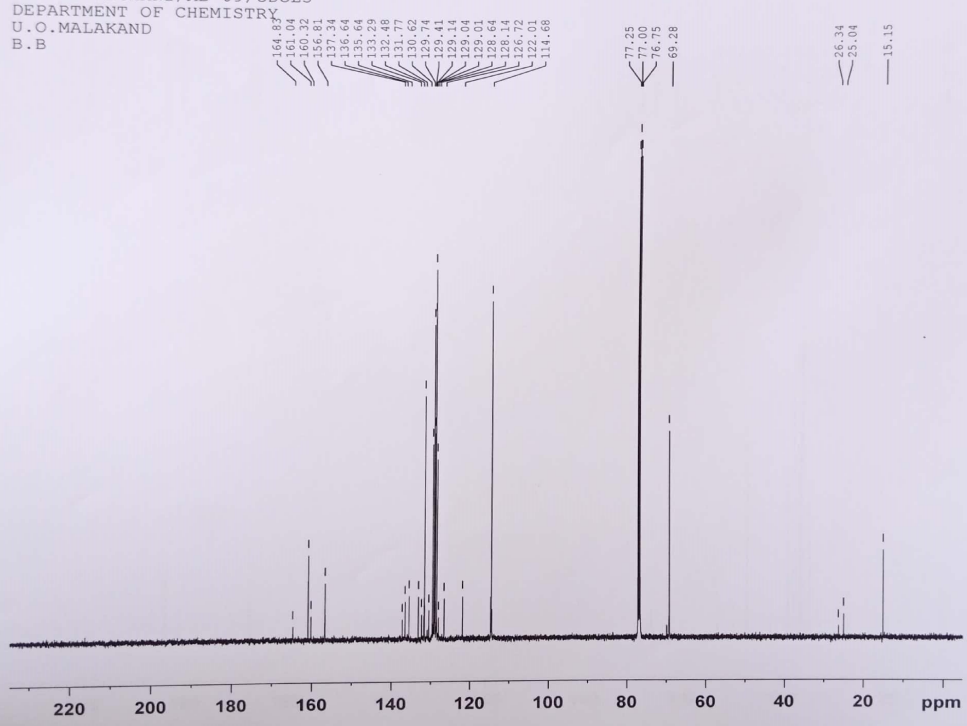

AVANCE NEO
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LAB # 109-B

Current Data Parameters
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EXPNO 2
PROCNO 1

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PROBHD Z859201_0007 (
PULPROG zgpg
TD 32768
SOLVENT CDCl3
NS 8192
DS 4
SWH 30120.482 Hz
FIDRES 1.838408 Hz
AQ 0.5439488 sec
RG 101
DW 16.600 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 8
SFO1 125.7722507 MHz
NUC1 13C
P1 15.00 usec
PLW1 119.40000153 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 80.00 usec
PLW2 17.96400070 W
PLW12 0.13754000 W
PLW13 0.06918100 W

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PC 1.40

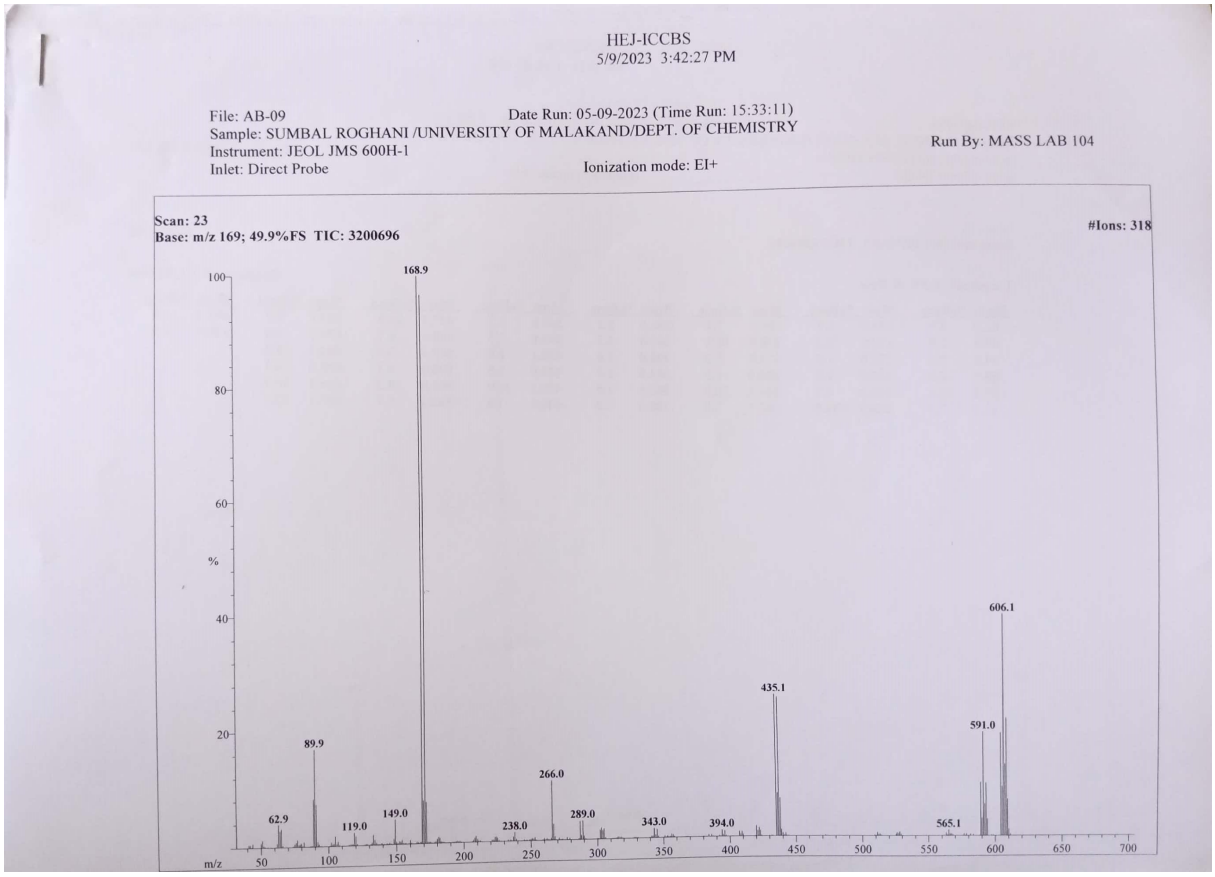

Figure-S4: ^{1}H-, ^{13}C-NMR and EI-MS spectra of compound **2d**

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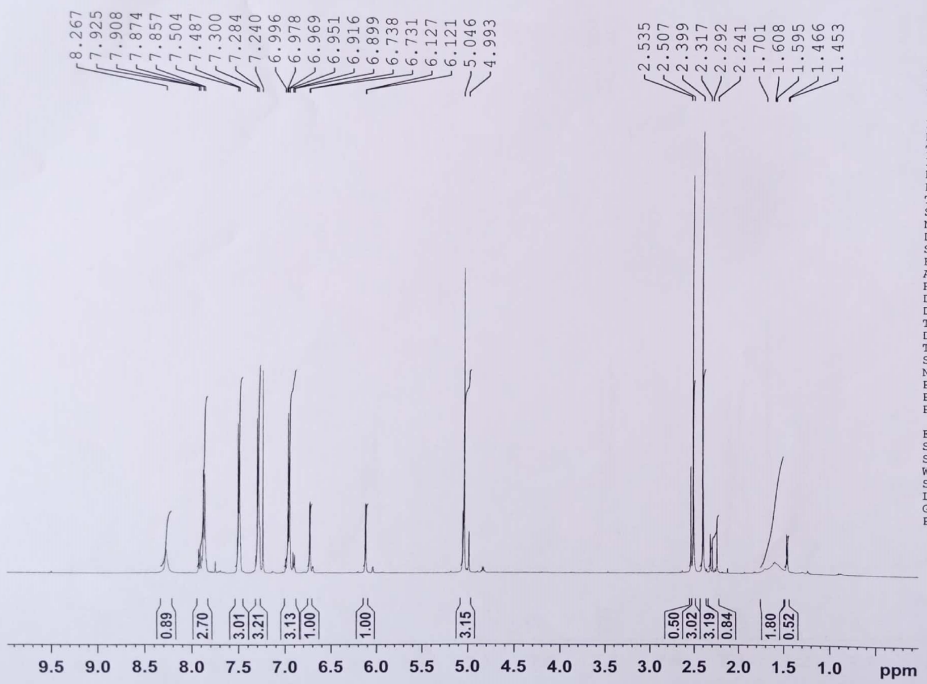

AVANCE 500 MHZ
LAB # 108

Current Data Parameters

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PROCNO	1

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TD	32768
SOLVENT	CDC13
NS	32
DS	0
SWH	9090.909 Hz
FIDRES	0.554865 Hz
AQ	1.8022400 sec
RG	101
DW	55.000 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
TD0	1
SFO1	500.3340026 MHz
NUC1	1H
P0	3.25 usec
P1	9.75 usec
PLW1	10.00000000 W

F2 - Processing parameters

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SF	500.3300221 MHz
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GB	0
PC	1.00

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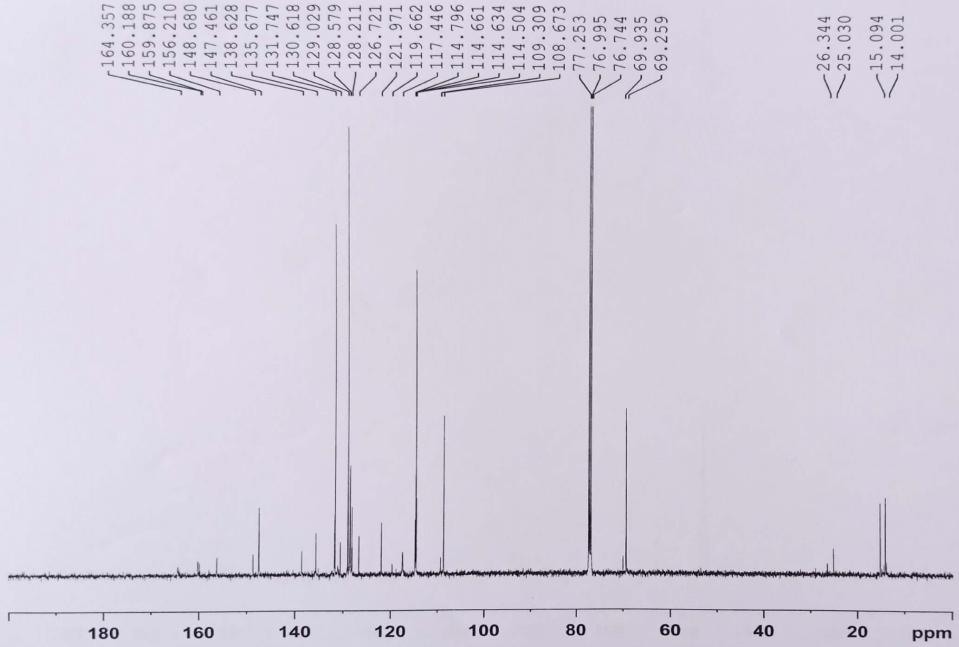

AVANCE 500 MHZ
LAB # 108

Current Data Parameters

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PROCNO	1

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TD	32768
SOLVENT	CDCl3
NS	12288
DS	8
SWH	30120.482 Hz
FIDRES	1.838408 Hz
AQ	0.5439488 sec
RG	101
DW	16.600 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	12
SFO1	125.8225465 MHz
NUC1	13C
P1	16.00 usec
PLW1	145.00000000 W
SFO2	500.3320013 MHz
NUC2	1H
CPDPRG[2	waltz65
PCPD2	80.00 usec
PLW2	10.00000000 W
PLW12	0.14854001 W
PLW13	0.07471200 W

F2 - Processing parameters

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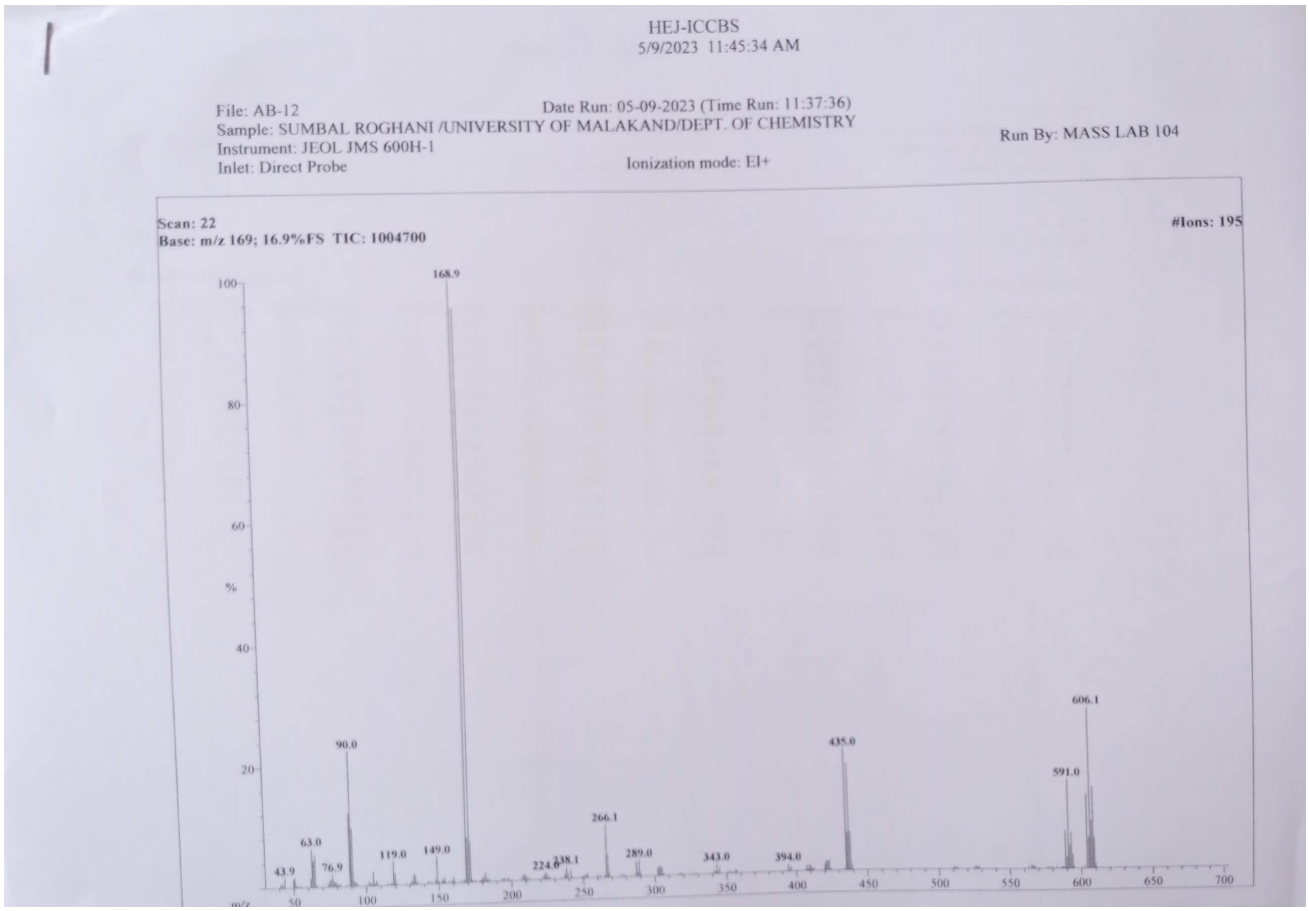
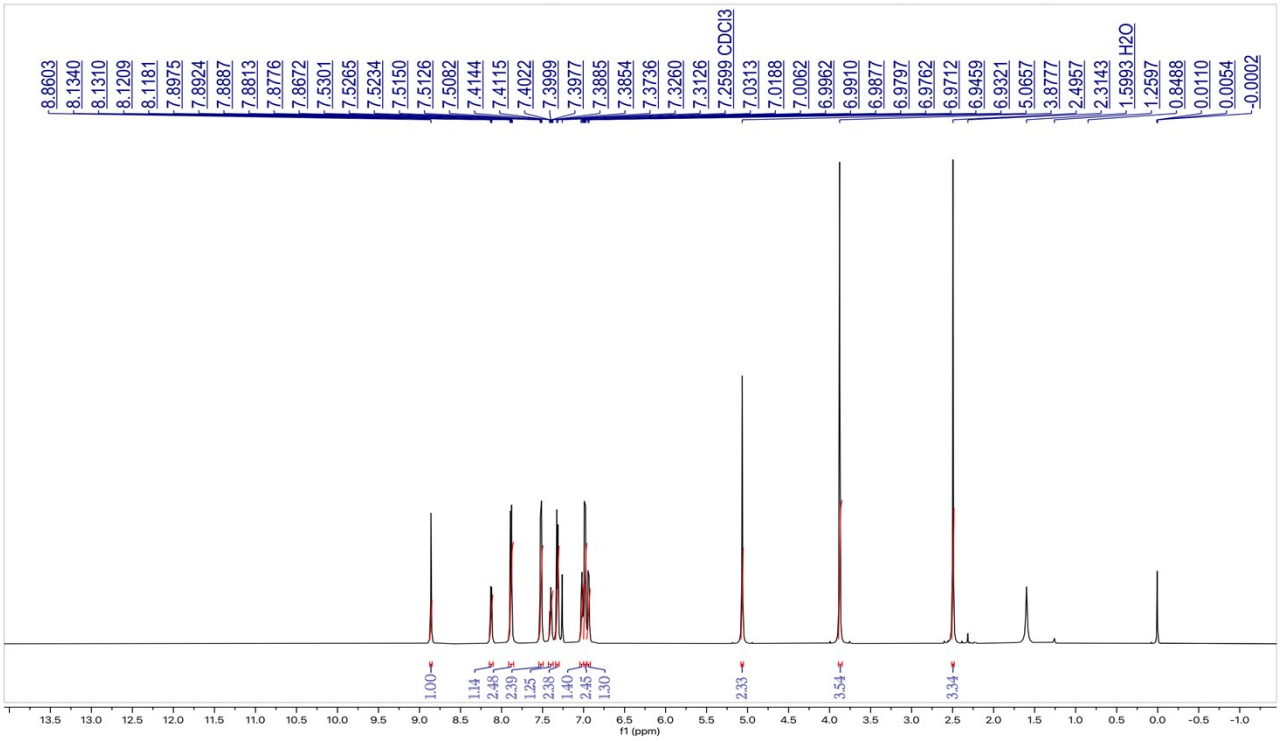


Figure-S5: ^{1}H-, ^{13}C-NMR and EI-MS spectra of compound **2e**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7.5301
7.5265
7.5234
7.5150
7.5126
7.5082
7.4144
7.4115
7.4022
7.3999
7.3977
7.3885
7.3854
7.3736
7.3260
7.3126
7.2599 CDCl3
7.0313
7.0188
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6.9877
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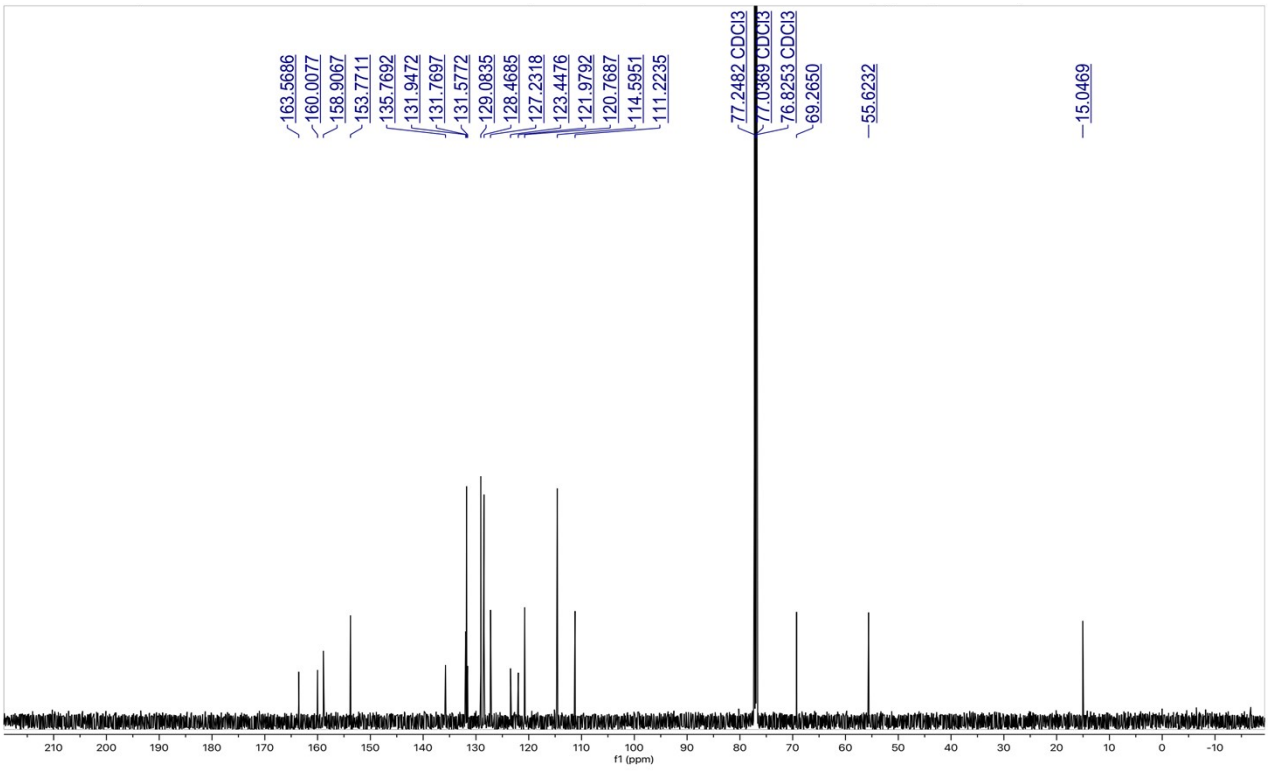
6.9762
6.9712
6.9459
6.9321
5.0657
3.8777
2.4957
2.3143
1.5993 H2O
1.2597
0.8488
0.0110
0.0054
-0.0002
1.00
1.14
2.48
2.39
1.25
2.38
1.40
2.45
1.30
2.33
3.54
3.34
f1 (ppm)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123.4476
121.9792
120.7687
114.5951
111.2235
77.2482 CDCl3
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69.2650
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15.0469
f1 (ppm)

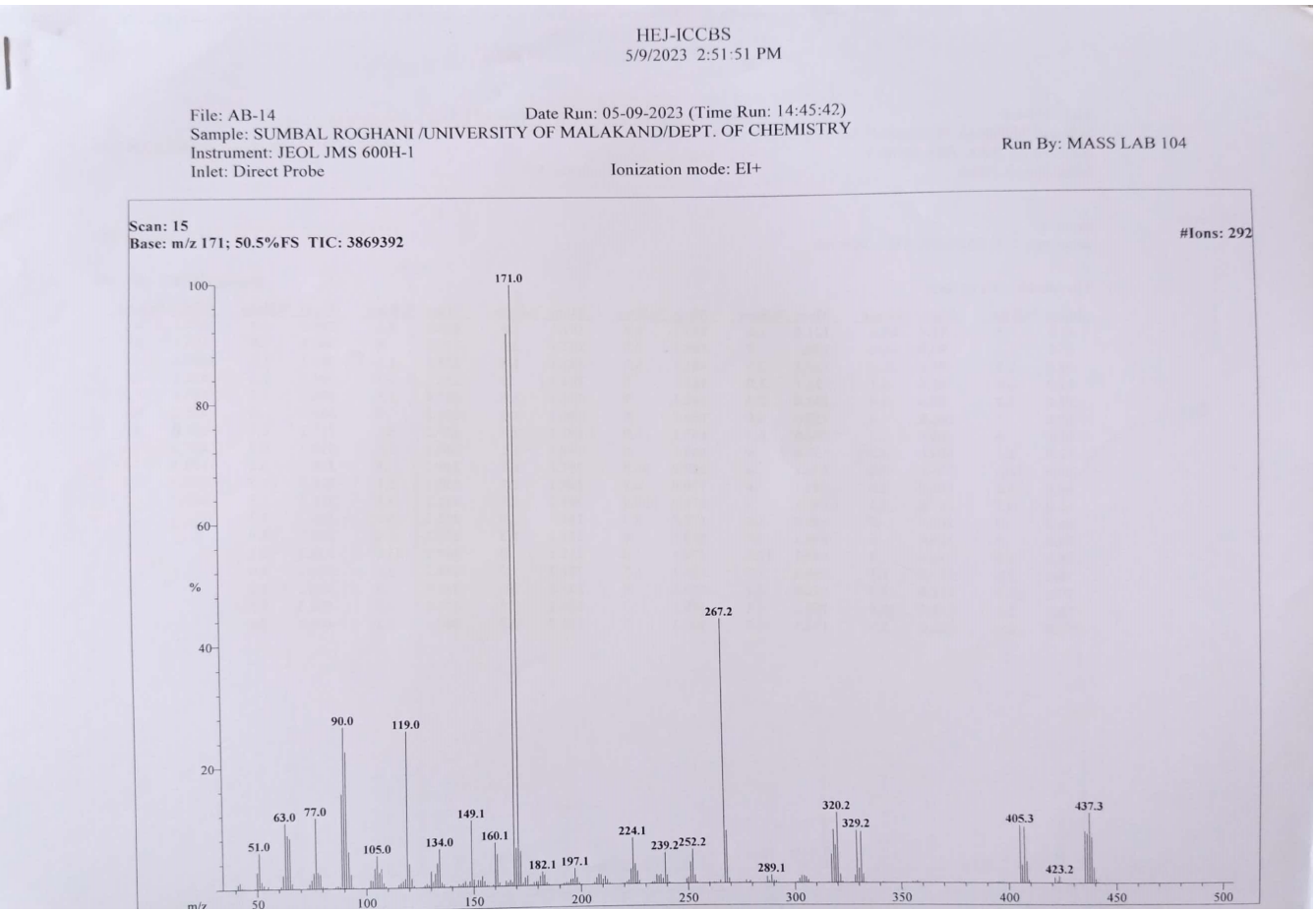
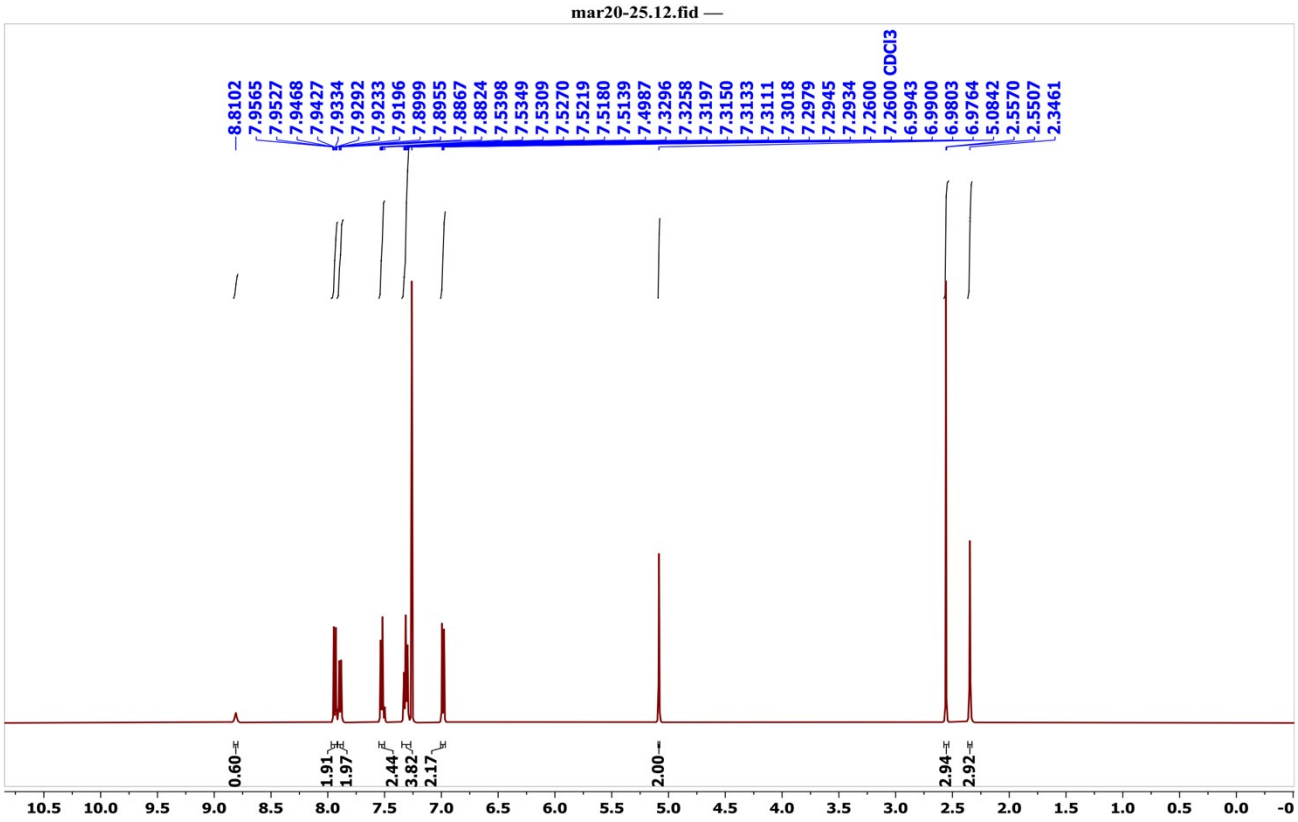


Figure-S6: ^{1}H-, ^{13}C-NMR and EI-MS spectra of compound **2f**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7.8824
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7.5139
7.4987
7.3296
7.3258
7.3197
7.3150
7.3133
7.3111
7.3018
7.2979
7.2945
7.2934
7.2600 CDCl3
6.9943
6.9900
6.9803
6.9764
5.0842
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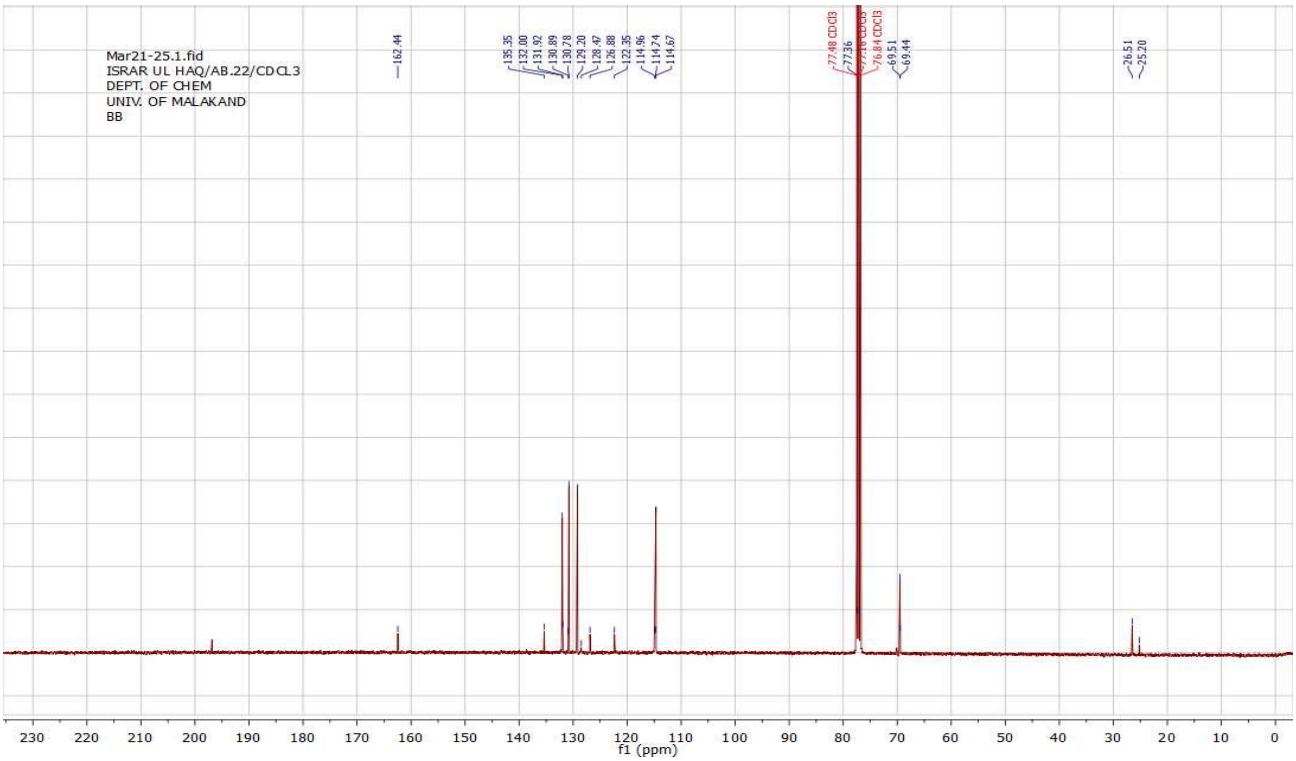
2.92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ISRAR UL HAQ/AB.22/CDCL3
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UNIV. OF MALAKAND
BB
162.44
135.35
132.00
131.92
130.89
130.78
129.20
128.47
126.88
122.35
114.96
114.74
114.67
77.48 CDCl3
77.36
77.16 CDCl3
76.84 CDCl3
69.51
69.44
26.51
25.20
f1 (ppm)

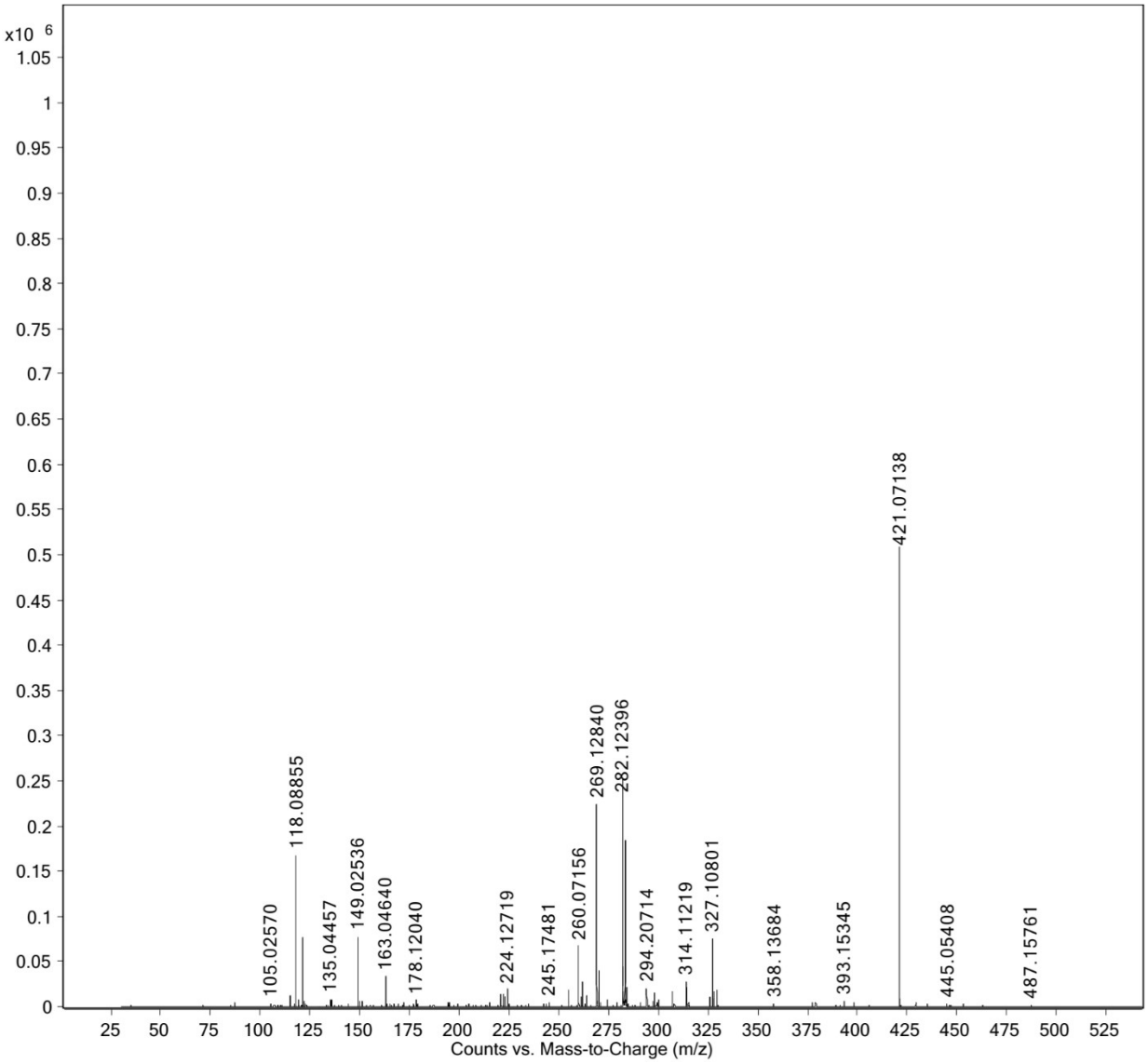
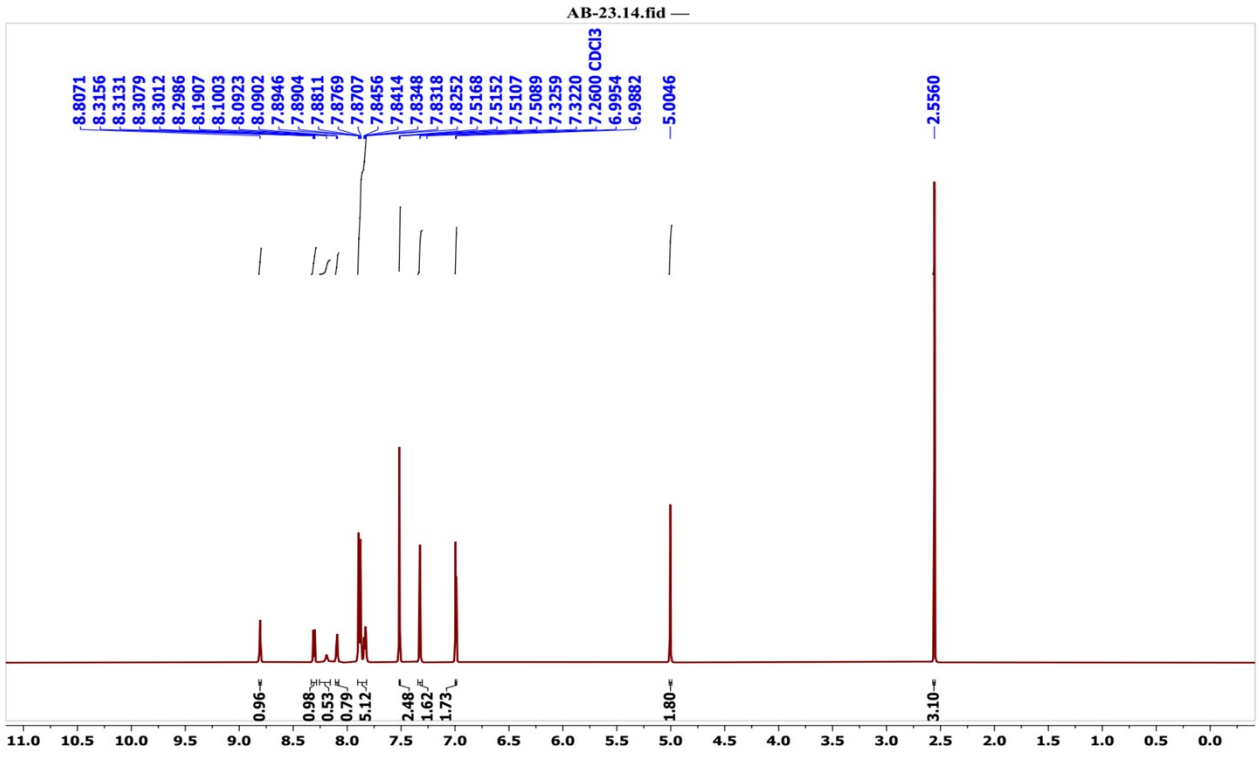
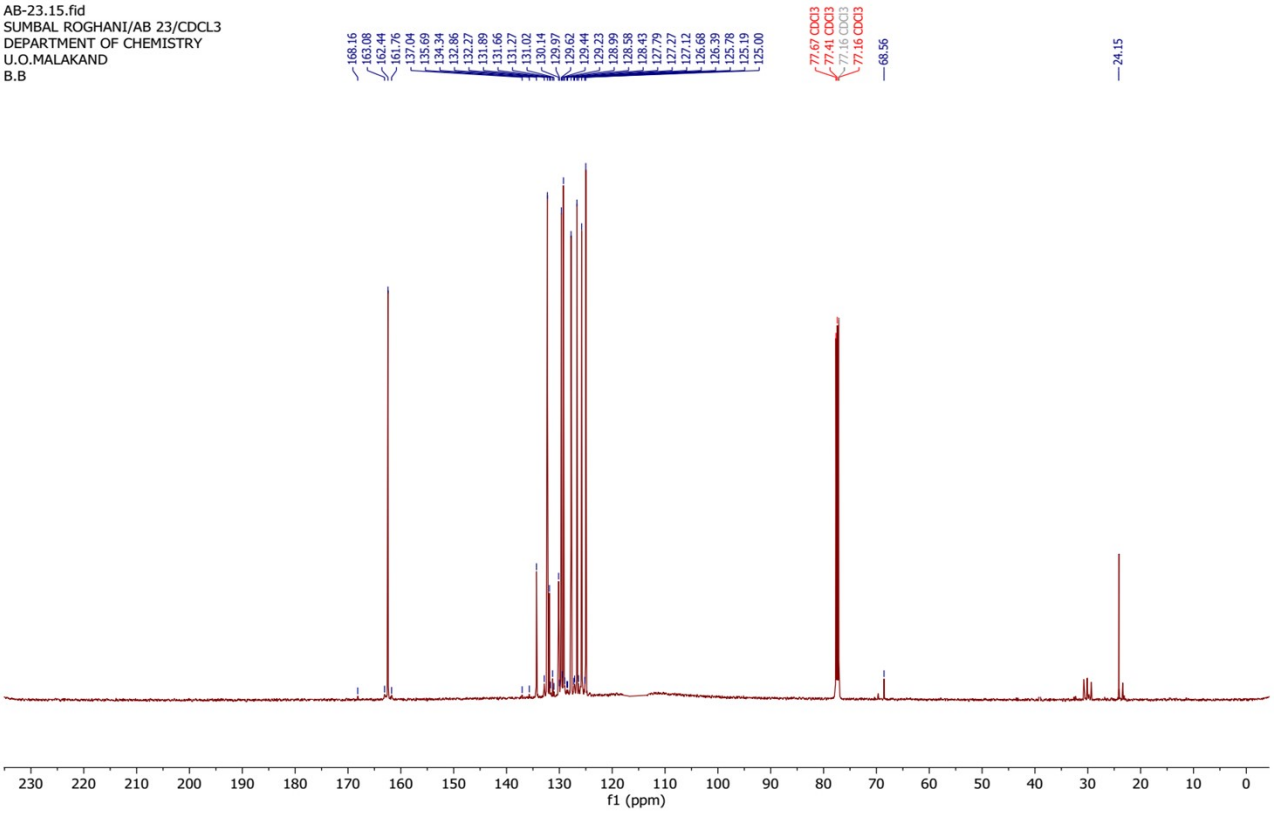


Figure-S7: ^{1}H-, ^{13}C-NMR and EI-MS spectra of compound **2g**


AB-23.14.fid
8.8071
8.3156
8.3131
8.3079
8.3012
8.2986
8.1907
8.1003
8.0923
8.0902
7.8946
7.8904
7.8811
7.8769
7.8707
7.8456
7.8414
7.8348
7.8318
7.8252
7.5168
7.5152
7.5107
7.5089
7.3259
7.3220
7.2600 CDCl3
6.9954
6.9882
5.0046
2.5560
0.96
0.98
0.53
0.79
5.12
2.48
1.62
1.73
1.80
3.10


AB-23.15.fid
SUMBAL ROGHANI/AB 23/CDCL3
DEPARTMENT OF CHEMISTRY
U.O.MALAKAND
B.B
168.16
163.08
162.44
161.76
137.04
135.69
134.34
132.86
132.27
131.89
131.66
131.27
131.02
130.14
129.97
129.62
129.44
129.23
128.99
128.58
128.43
127.79
127.27
127.12
126.68
126.39
125.78
125.19
125.00
77.67 CDCl3
77.41 CDCl3
77.16 CDCl3
77.16 CDCl3
68.56
24.15
f1 (ppm)

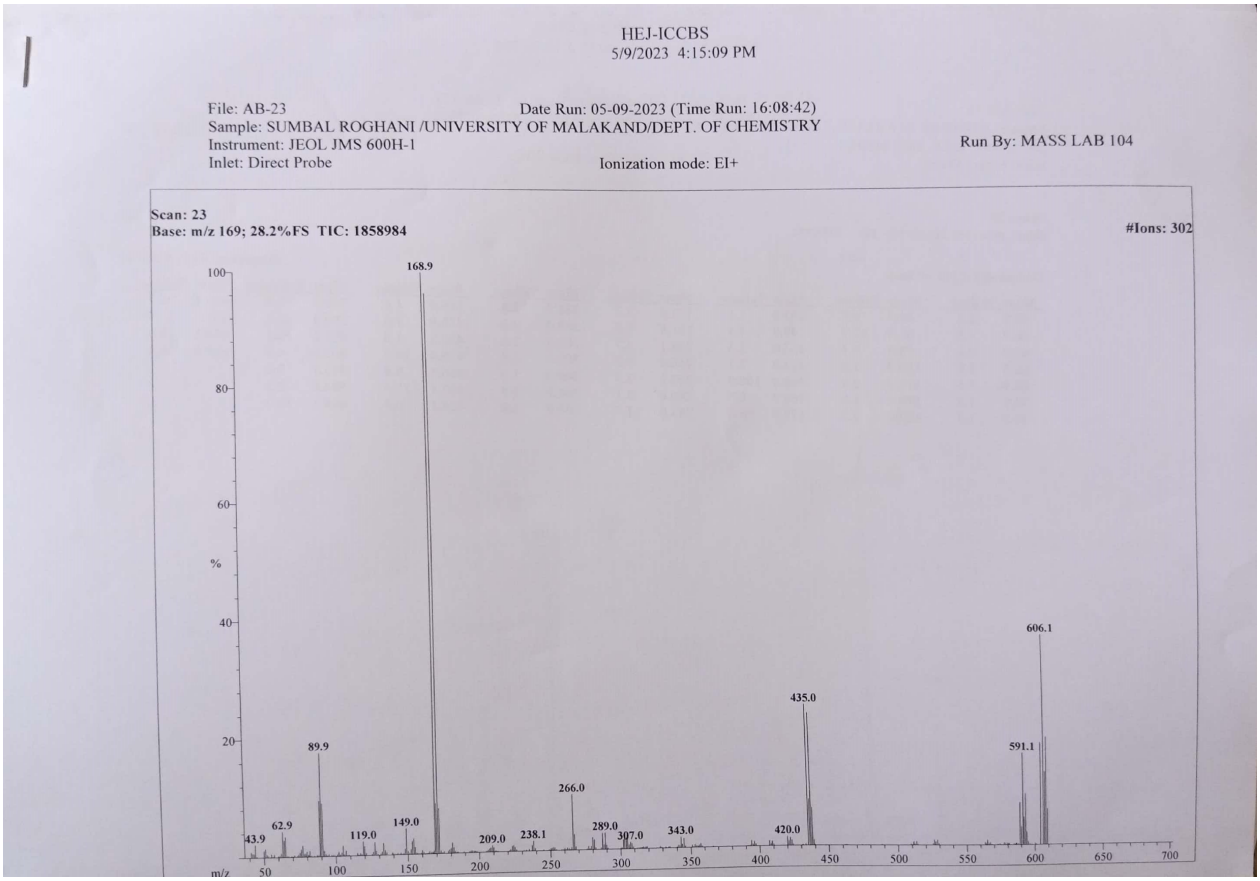
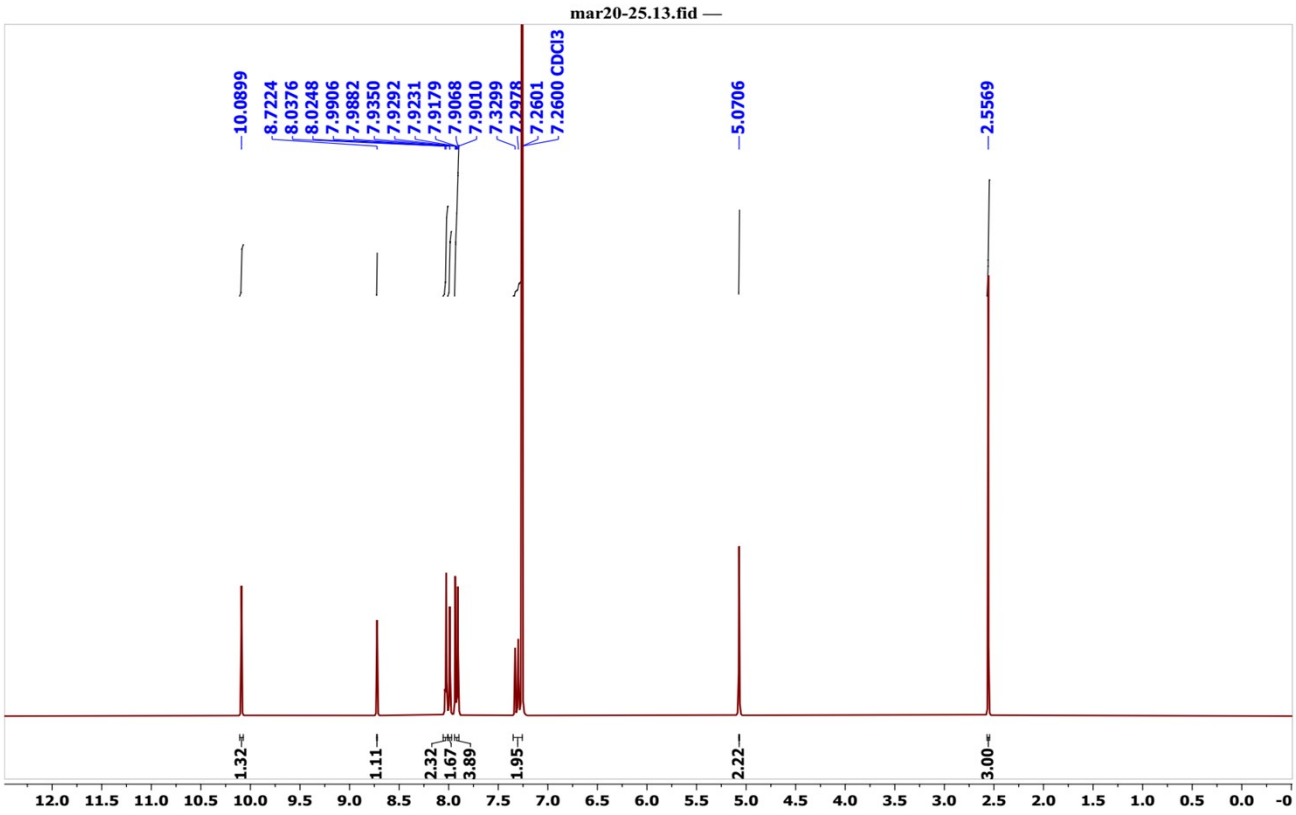
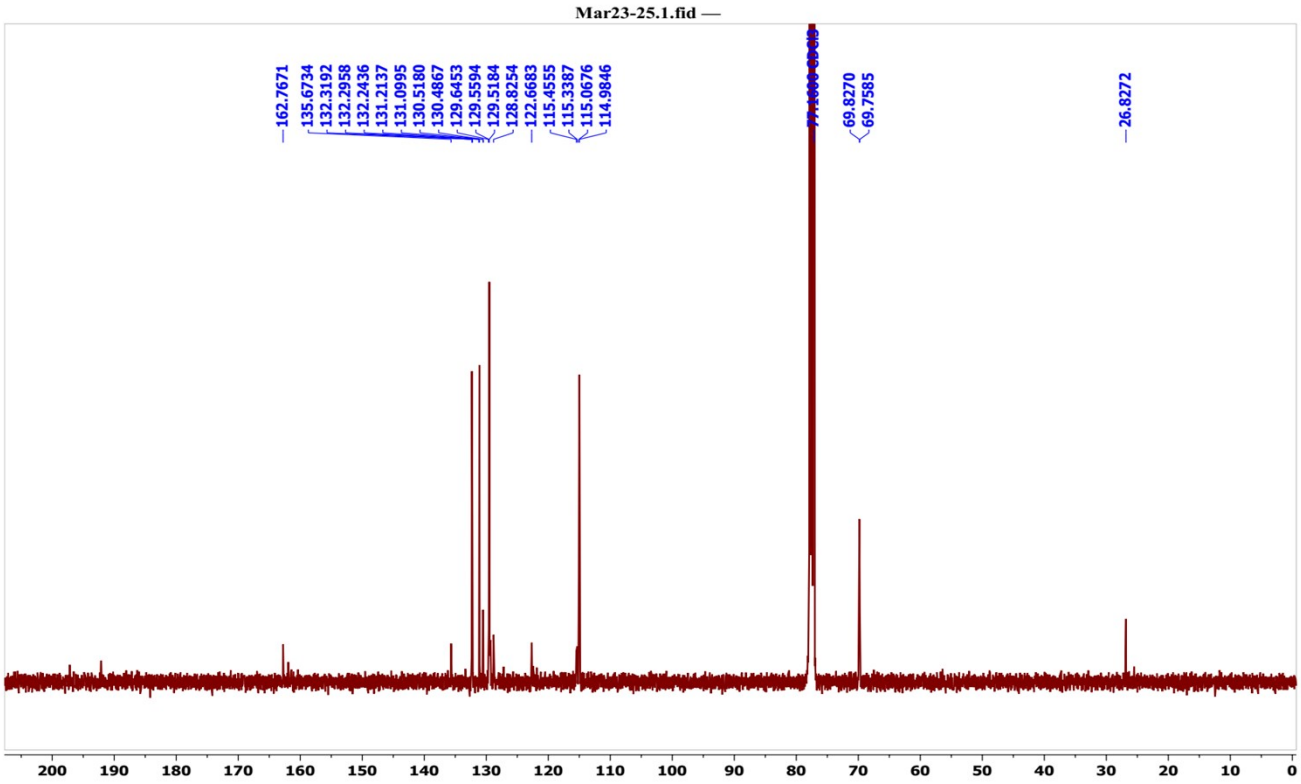


Figure-S8: ^{1}H-, ^{13}C-NMR and EI-MS spectra of compound **2h**


mar20-25.13.fid —
10.0899
8.7224
8.0376
8.0248
7.9906
7.9882
7.9350
7.9292
7.9231
7.9179
7.9068
7.9010
7.3299
7.2978
7.2601
7.2600 CDCl3
5.0706
2.5569
1.32
1.11
2.32
1.67
3.89
1.95
2.22
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0


Mar23-25.1.fid —
162.7671
135.6734
132.3192
132.2958
132.2436
131.2137
131.0995
130.5180
130.4867
129.6453
129.5594
129.5184
128.8254
122.6683
115.4555
115.3387
115.0676
114.9846
77.1600 77.0368
69.8270
69.7585
26.8272
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

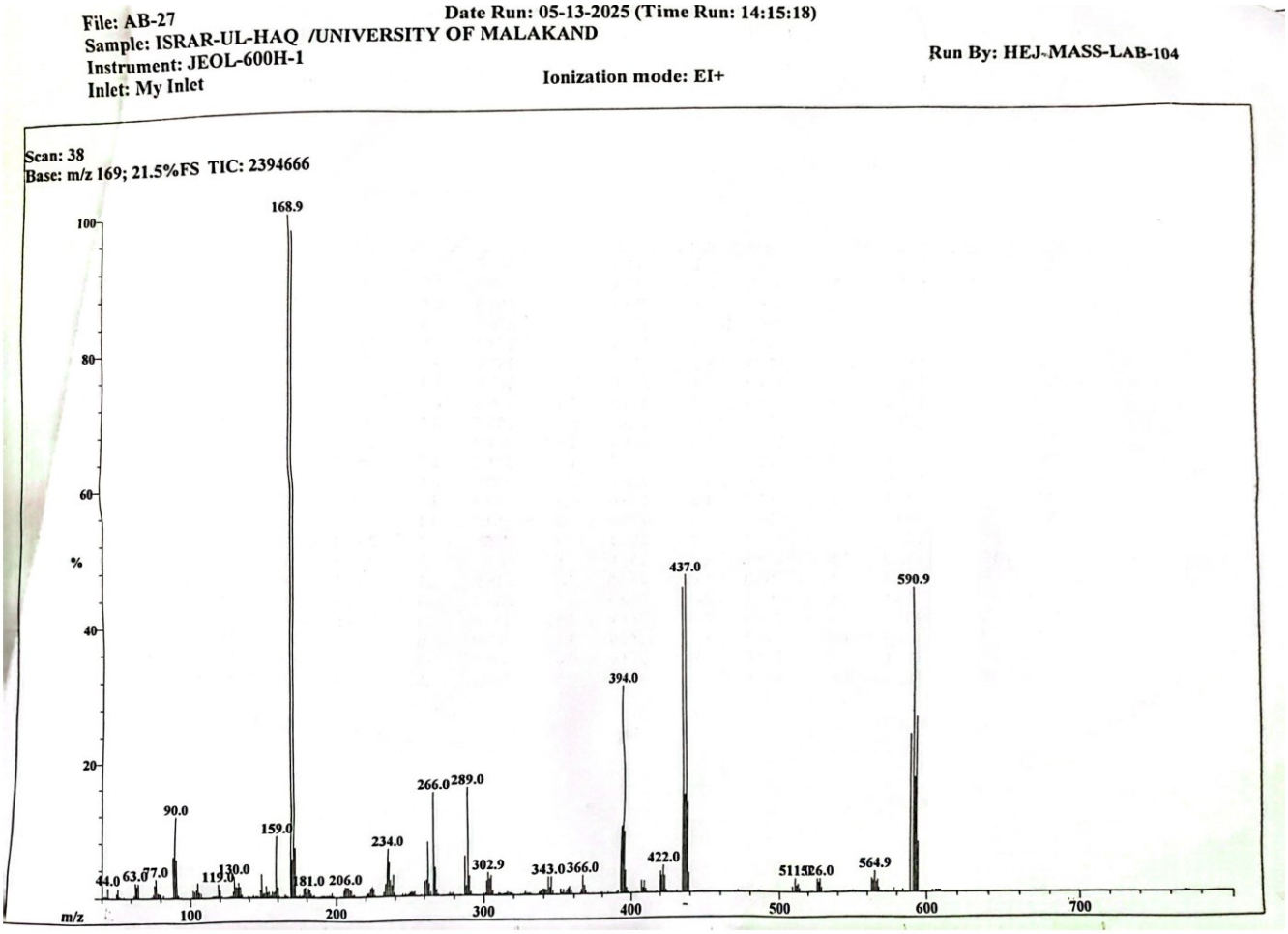
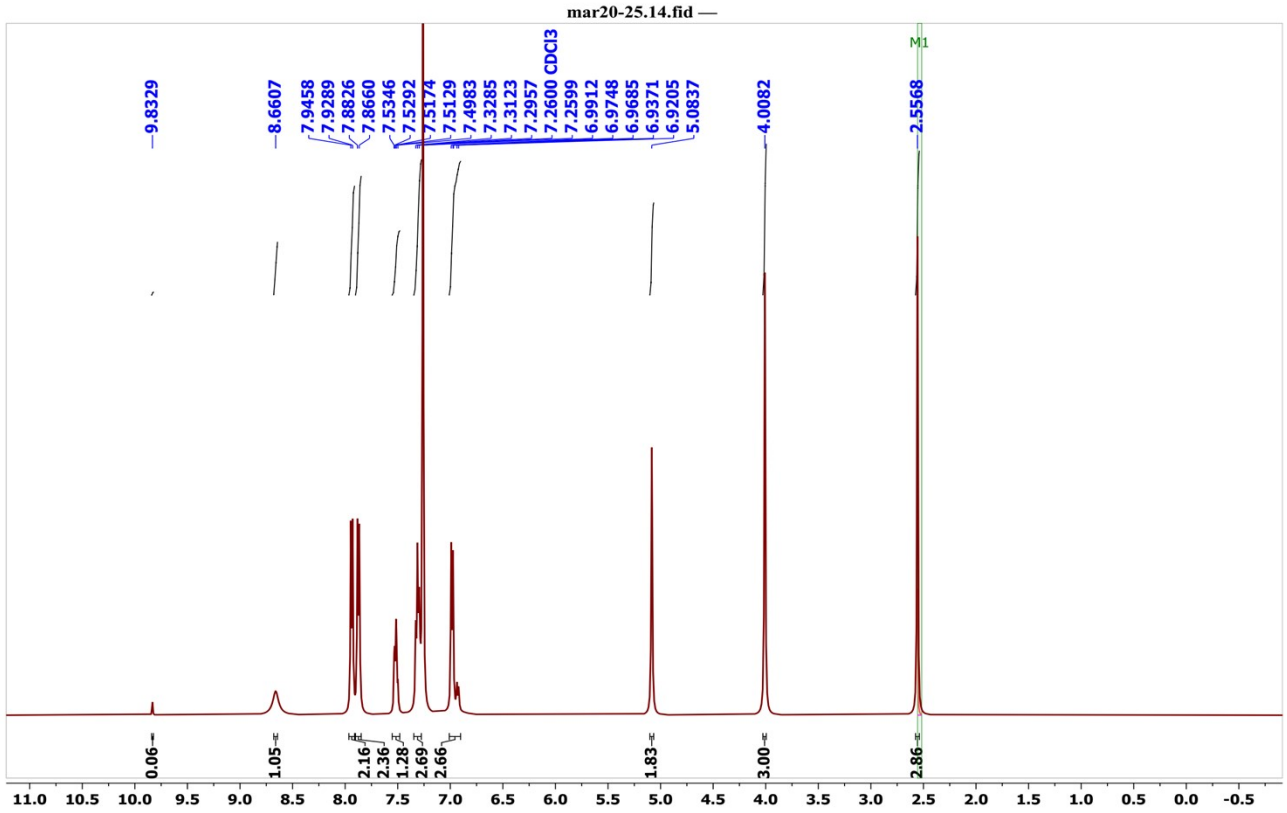
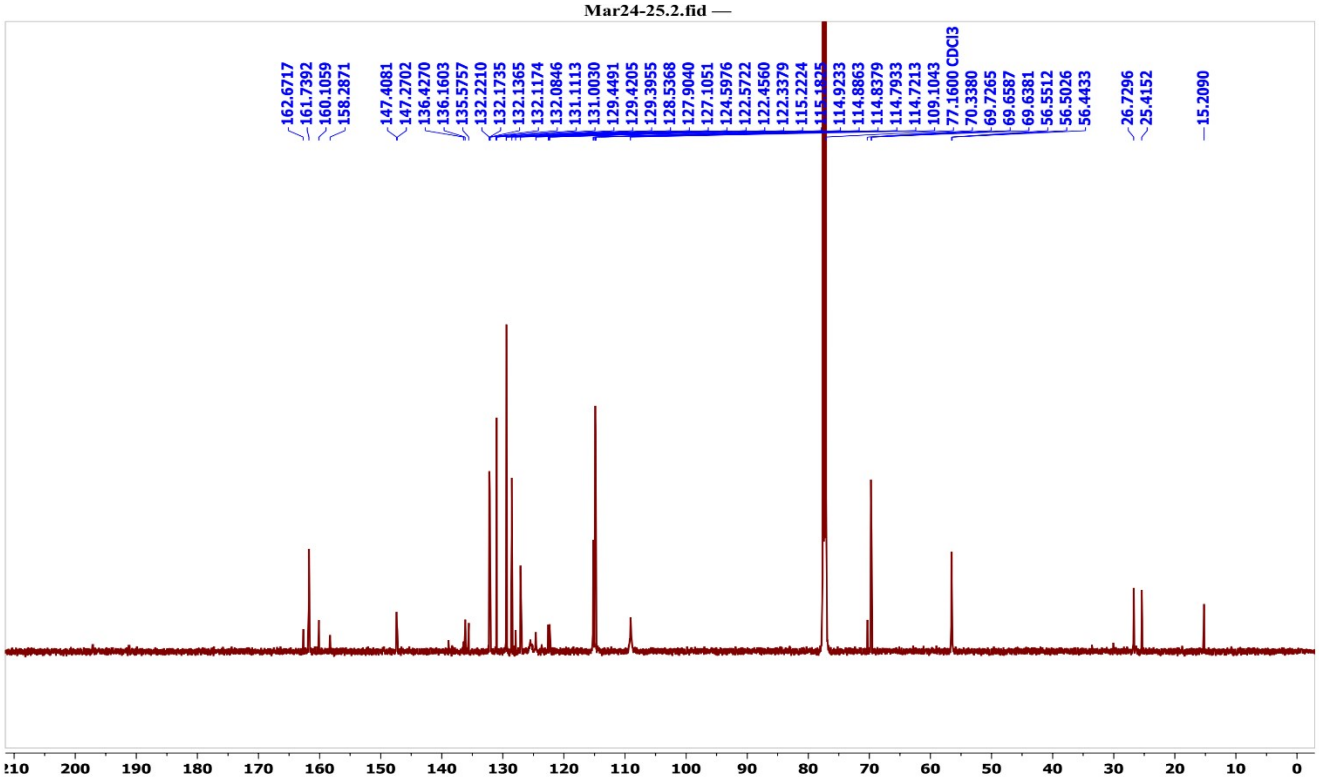


Figure-S9: ^{1}H-, ^{13}C-NMR and EI-MS spectra of compound **2i**


mar20-25.14.fid
M1
9.8329
8.6607
7.9458
7.9289
7.8826
7.8660
7.5346
7.5292
7.5174
7.5129
7.4983
7.3285
7.3123
7.2957
7.2600 CDCl3
7.2599
6.9912
6.9748
6.9685
6.9371
6.9205
5.0837
4.0082
2.5568
0.06
1.05
2.16
2.36
1.28
2.69
2.66
1.83
3.00
2.86


Mar24-25.2.fid
162.6717
161.7392
160.1059
158.2871
147.4081
147.2702
136.4270
136.1603
135.5757
132.2210
132.1735
132.1365
132.1174
132.0846
131.1113
131.0030
129.4491
129.4205
129.3955
128.5368
127.9040
127.1051
124.5976
122.5722
122.4560
122.3379
115.2224
115.1825
114.9233
114.8863
114.8379
114.7933
114.7213
109.1043
77.1600 CDCl3
70.3380
69.7265
69.6587
69.6381
56.5512
56.5026
56.4433
26.7296
25.4152
15.2090

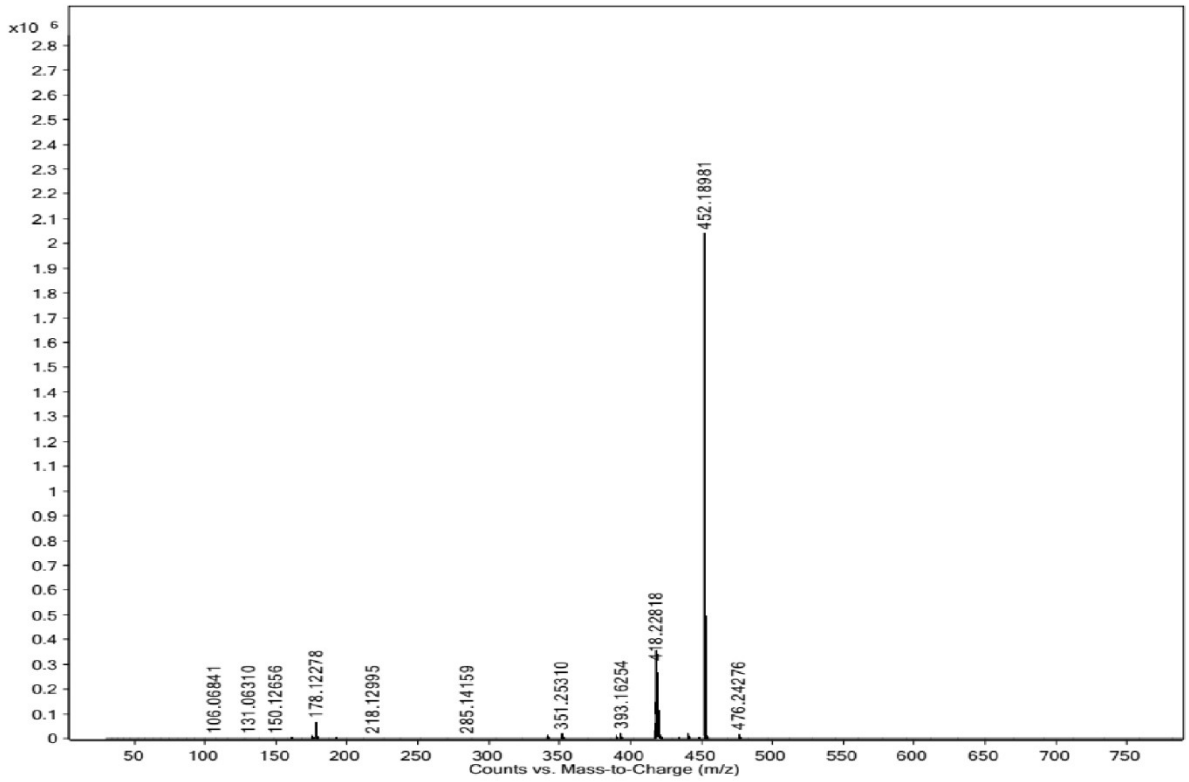


Figure-S10: ^{1}H-, ^{13}C-NMR and HRESI-MS spectra of compound **2j**