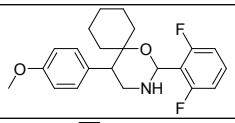
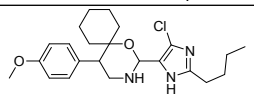
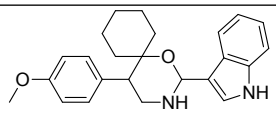
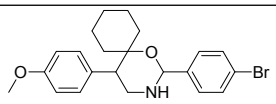
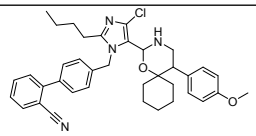
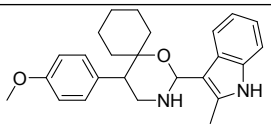
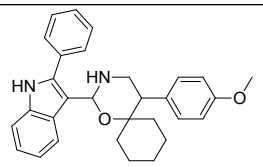
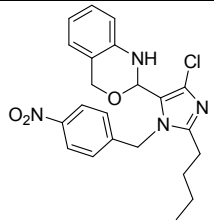
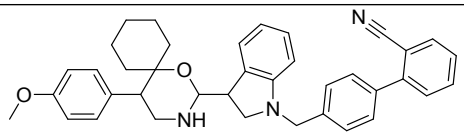
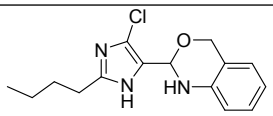
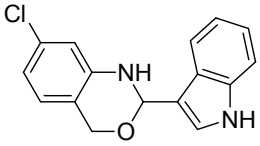
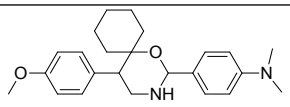
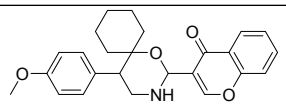
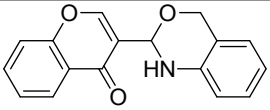
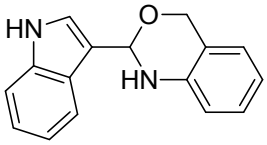
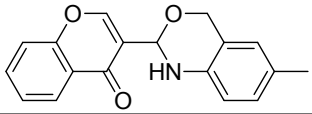
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

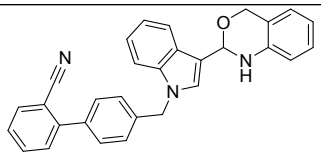
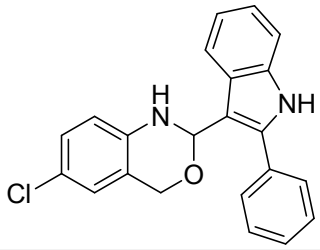
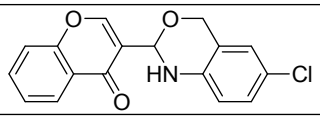
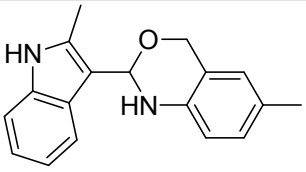
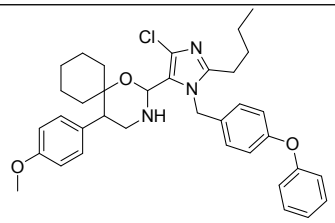
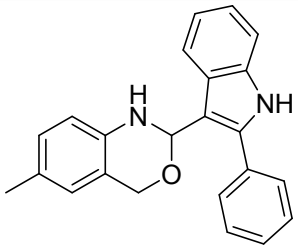
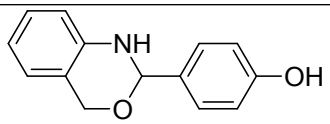
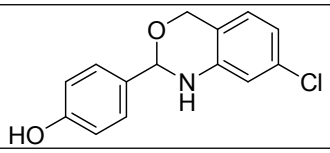
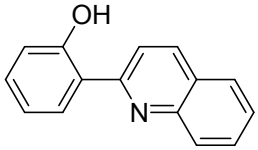
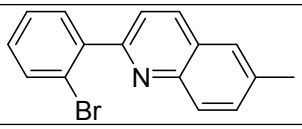
Screening of Quinoline, 1,2-benzoxazine, and 1,3-oxazine- based small molecules against targeting isolated methionyl-tRNAsynthetase and A549 and HCT116 cancer cells including an in silico binding mode analysis

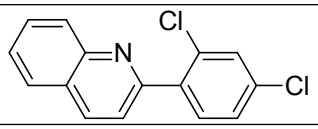
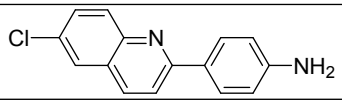
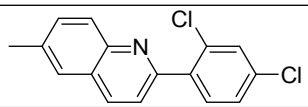
Hanumantharayappa Bharathkumar, Chakrabhavi Dhananjaya Mohan, Shobith Rangappa, Taehee Kang, Keerthy H K, Julian E. Fuchs, Nam Hoon Kwon, Andreas Bender, Sunghoon Kim, Basappa, Kanchugarakoppal S Rangappa

Supplementary Table 1: List compounds structures used for MRS screening:

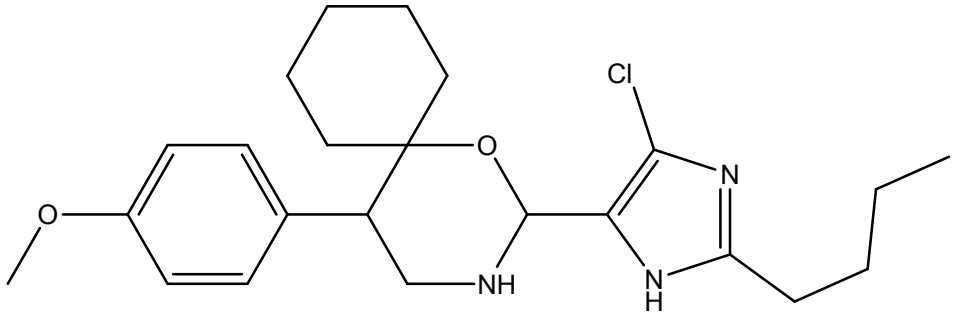
Compound Number	Structure
Compound-1	
Compound-2	
Compound-3	
Compound-4	
Compound-5	
Compound-6	

Compound-7	
Compound-8	
Compound-9	
Compound-10	
Compound-11	
Compound-12	
Compound-13	
Compound-14	
Compound-15	
Compound 16	

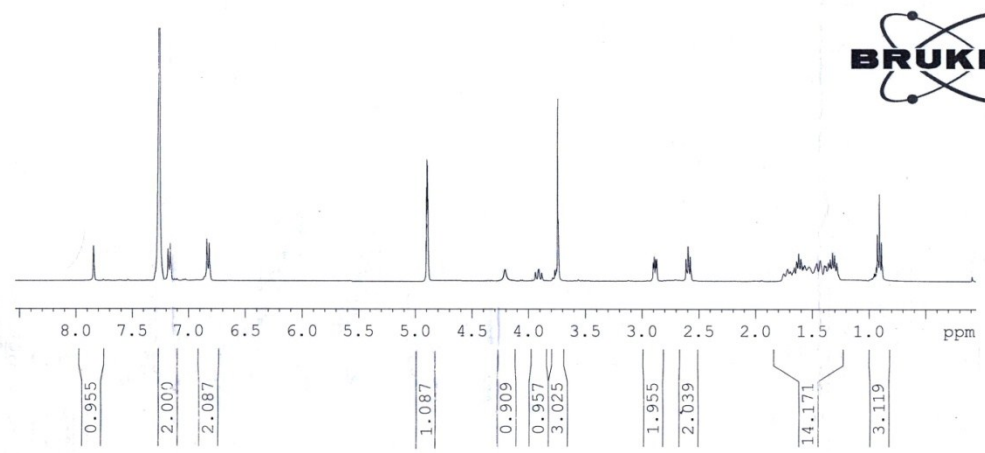
Compound 17	
Compound-18	
Compound 19	
Compound 20	
Compound 21	
Compound 22	
Compound 23	
Compound 24	
Compound 25	
Compound 26	

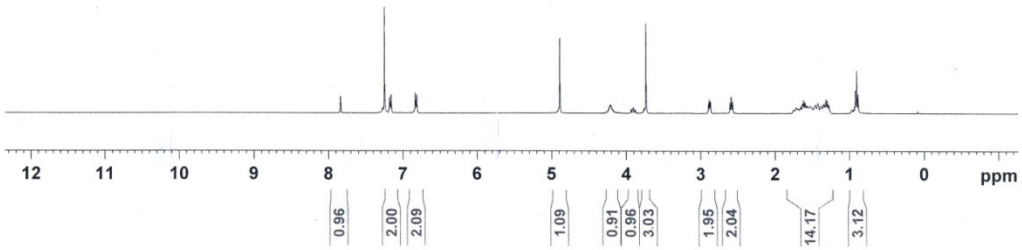
Compound 27	
Compound 28	
Compound 29	

Compound 2: 2-(2-butyl-4-chloro-1H-imidazol-5-yl)-5-(4-methoxyphenyl)-1-oxa-3-azaspiro[5.5]undecane.

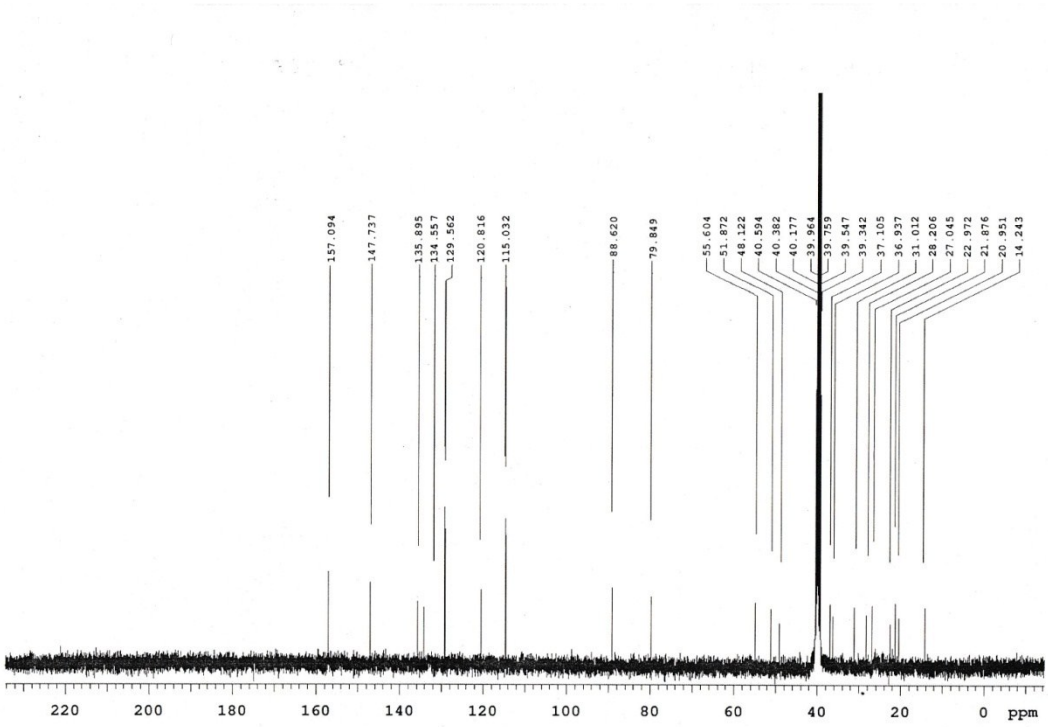


^{1}H NMR:


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 ppm
0.955
2.000
2.087
1.087
0.909
0.957
3.025
1.955
2.039
14.171
3.119

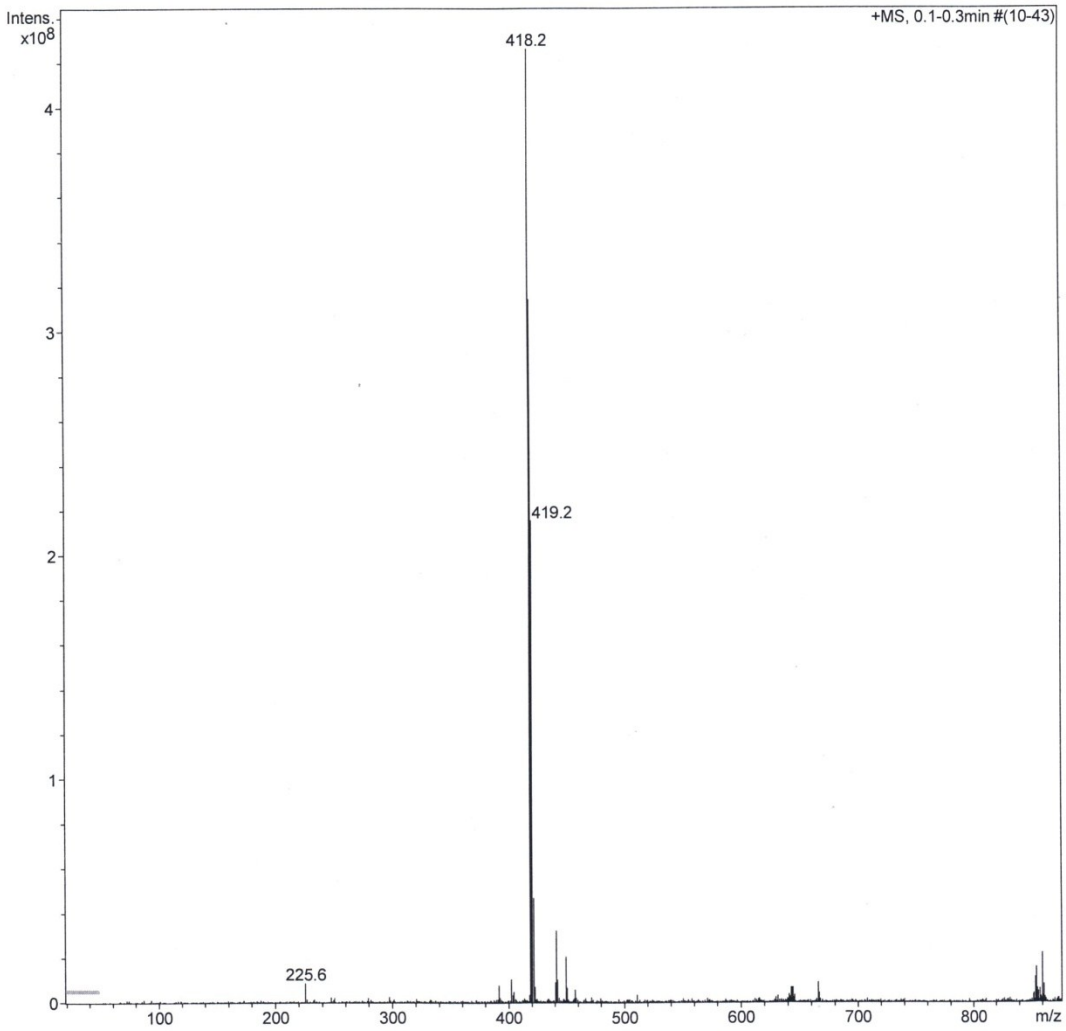

12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.96
2.00
2.09
1.09
0.91
0.96
3.03
1.95
2.04
14.17
3.12

^{13}C NMR:

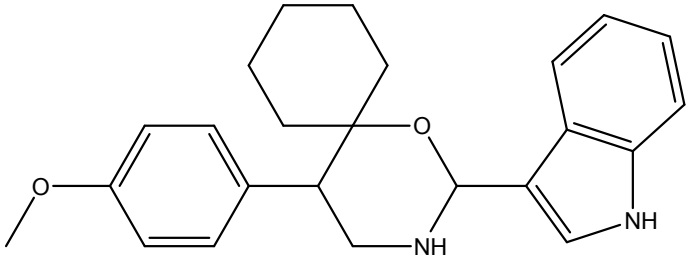

157.094
147.737
135.895
134.557
129.562
120.816
115.032
88.620
79.849
55.604
51.872
48.122
40.594
40.382
40.177
39.964
39.759
39.547
39.342
37.105
36.937
31.012
28.206
27.045
22.972
21.876
20.951
14.243
220
200
180
160
140
120
100
80
60
40
20
0
ppm

Mass:

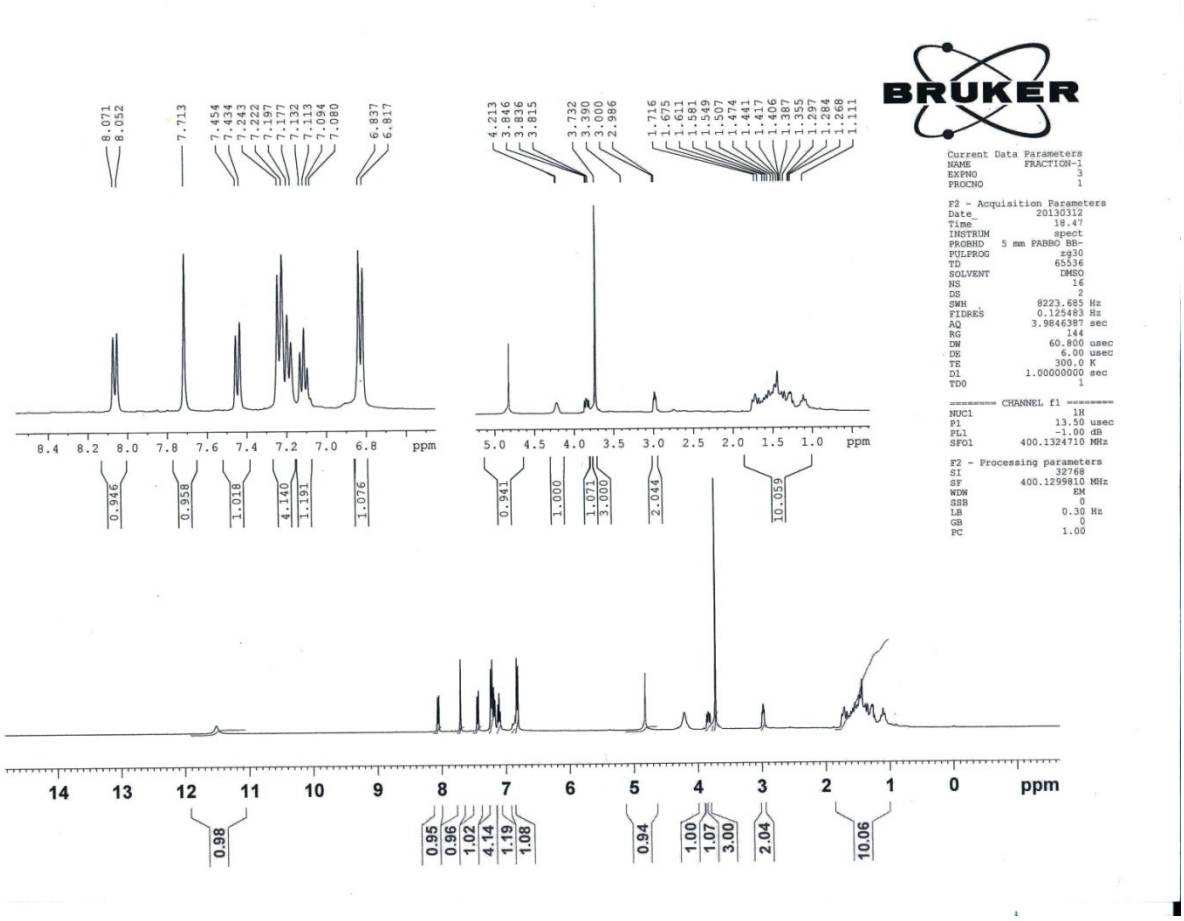
Method	DEF_MS.M			Operator	MBU
Sample Name				Instrument	HCTultra ETD II
Acquisition Parameter					
Ion Source Type	ESI	Ion Polarity	Positive	Alternating Ion Polarity	off
Mass Range Mode	319 µs	Scan Begin	50 m/z	Scan End	1300 m/z
Capillary Exit	109.0 Volt	Skimmer	40.0 Volt	Trap Drive	49.6
Accumulation Time	Ultra Scan	Averages	5 Spectra	Auto MS/MS	off



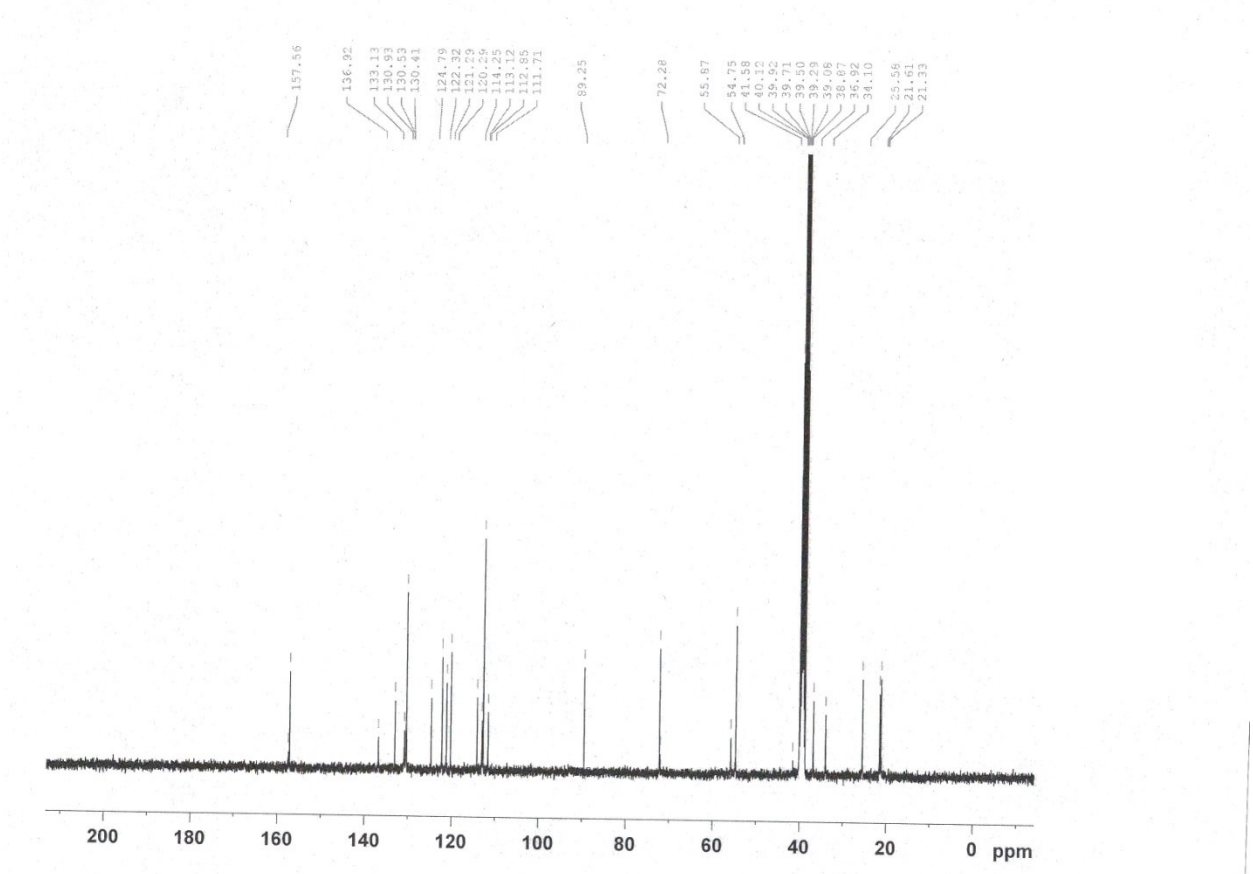
Compound 3: 2-(1H-indol-3-yl)-5-(4-methoxyphenyl)-1-oxa-3-azaspiro[5.5]undecane



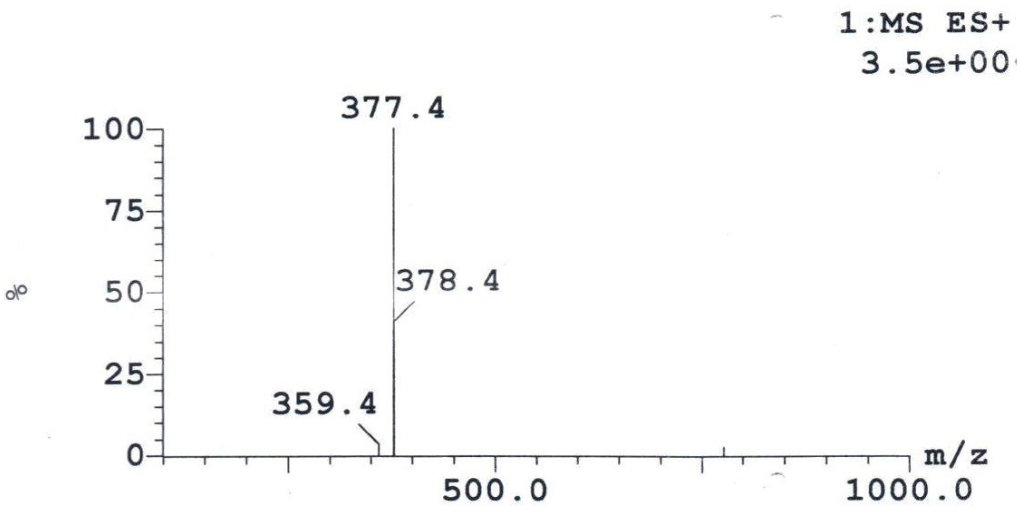
^{1}H NMR



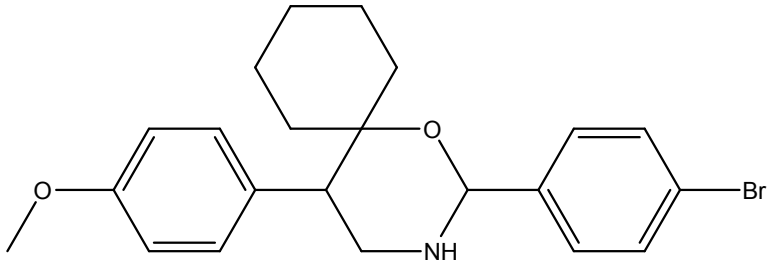
^{13}C NMR:


157.56
136.92
133.13
130.93
130.53
130.41
124.79
122.32
121.29
120.25
114.25
113.12
112.85
111.71
69.25
72.28
55.87
54.75
41.58
40.12
39.92
39.71
39.50
39.29
39.06
38.87
36.92
34.10
25.56
21.61
21.33
200
180
160
140
120
100
80
60
40
20
0 ppm

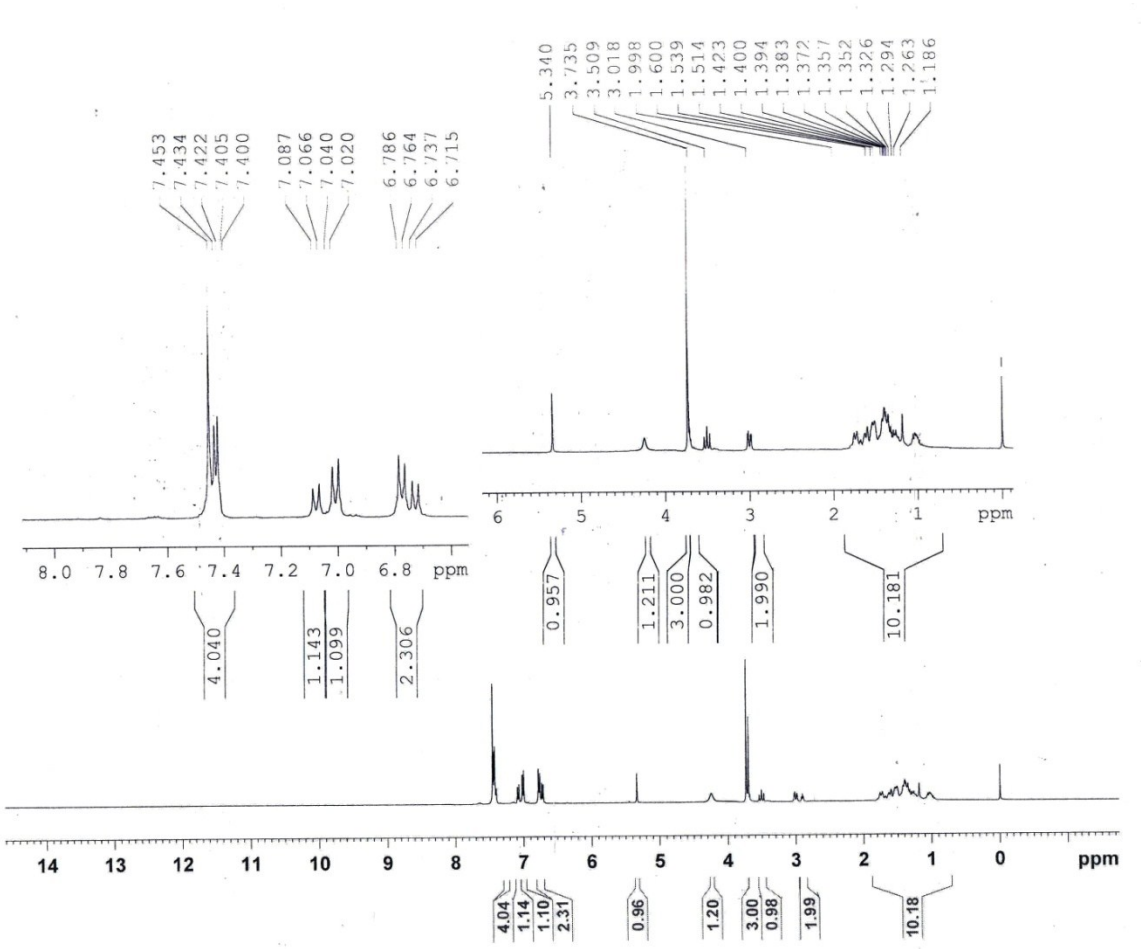
Mass:


1:MS ES+
3.5e+00
377.4
378.4
359.4
100
75
50
25
0
%
m/z
500.0
1000.0

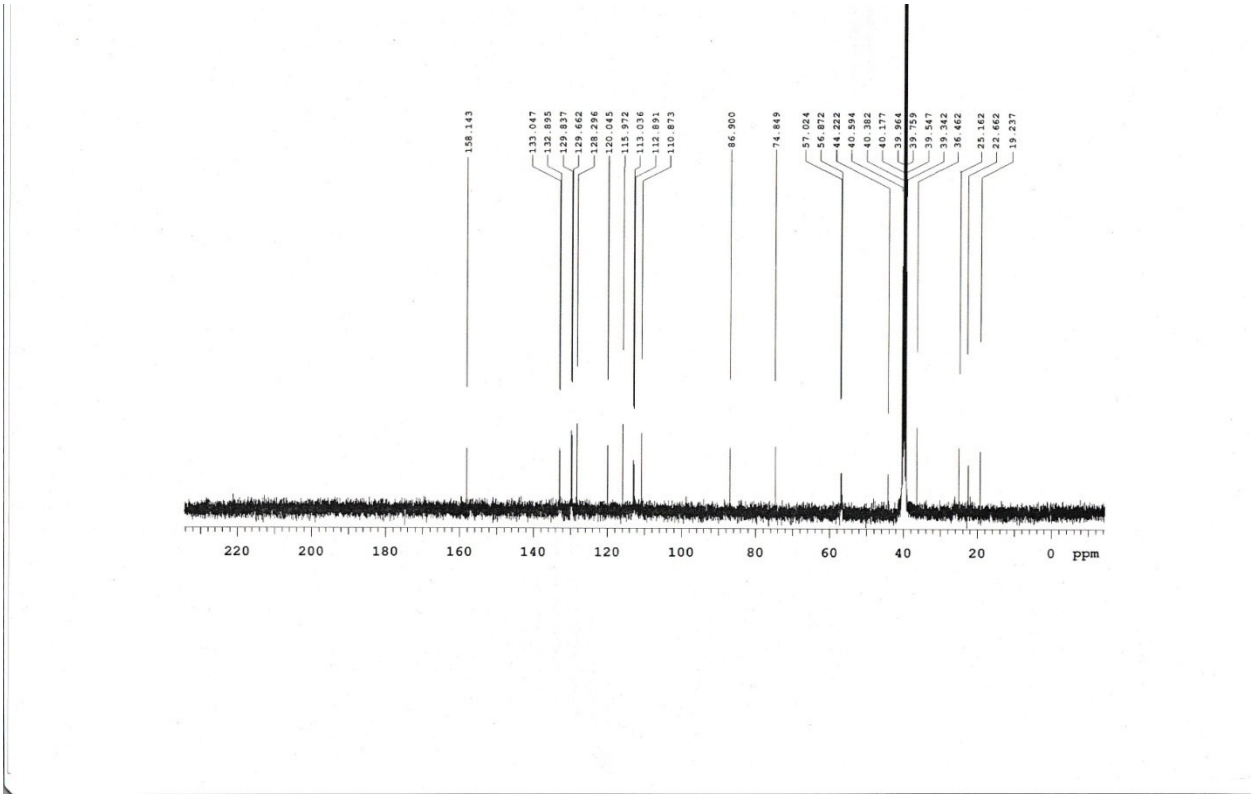
Compound 4: 2-(4-bromophenyl)-5-(4-methoxyphenyl)-1-oxa-3-azaspiro[5.5]undecane



1H-NMR:

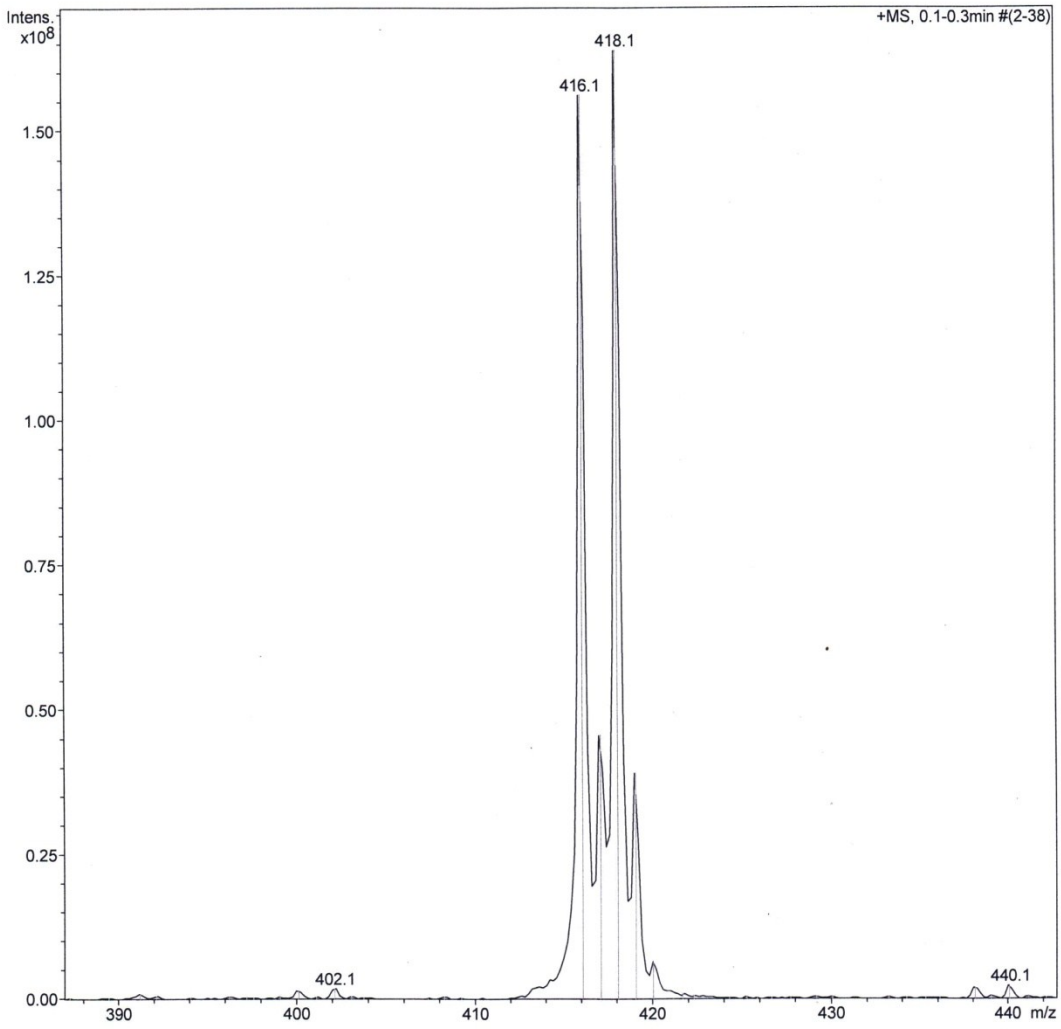


^{13}C NMR:

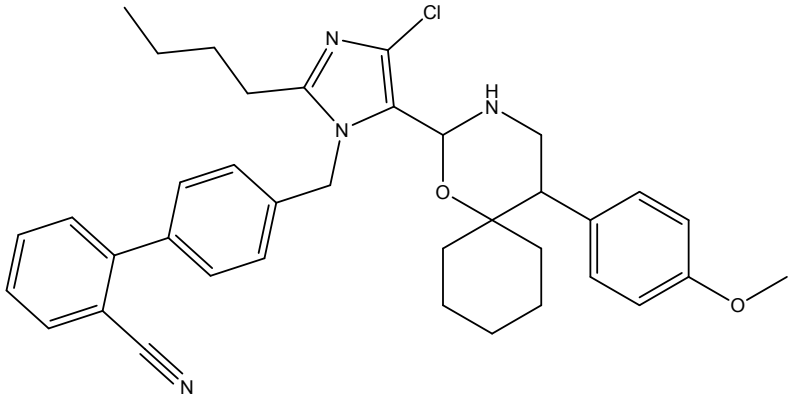

158.143
133.047
132.895
129.837
129.662
128.296
120.045
115.972
113.036
112.891
110.873
86.900
74.849
57.024
56.872
44.222
40.594
40.382
40.177
39.964
39.759
39.547
39.342
36.462
25.162
22.662
19.237
220
200
180
160
140
120
100
80
60
40
20
0
ppm

Mass:

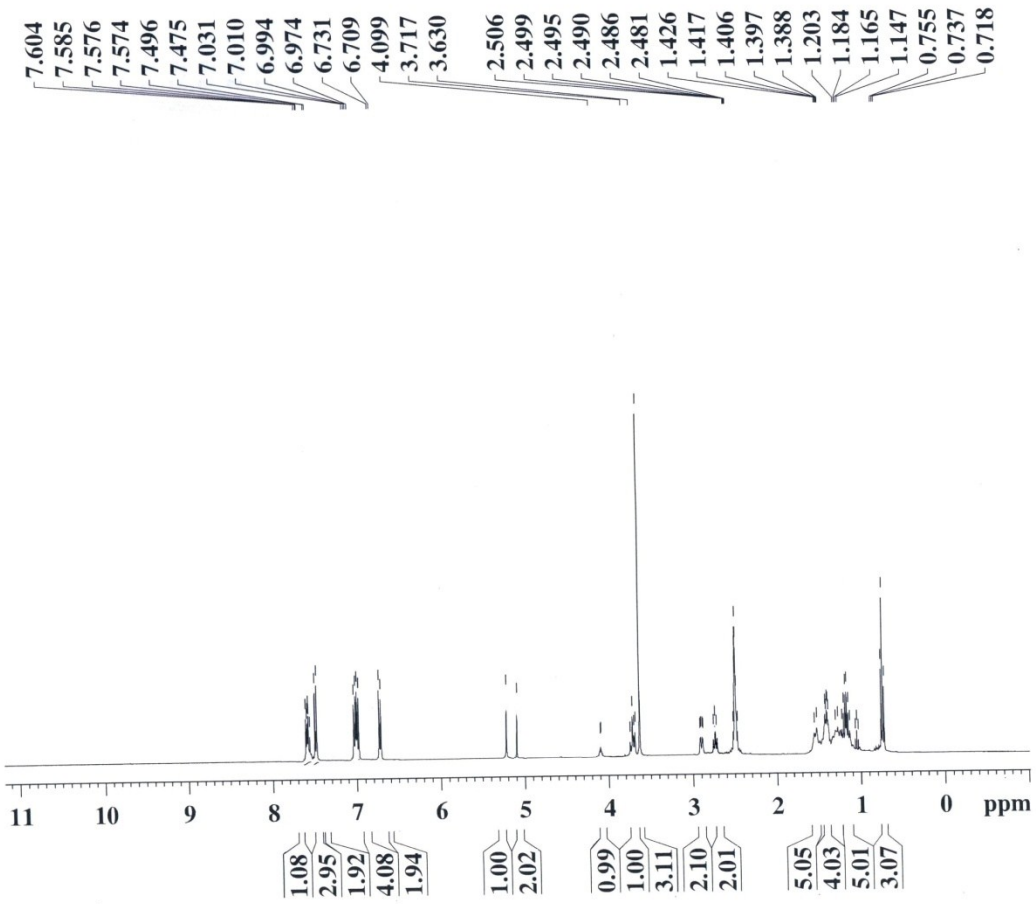
Method	DEF_MS.M			Operator	MBU
Sample Name				Instrument	HCTultra ETD II
Acquisition Parameter					
Ion Source Type	ESI	Ion Polarity	Positive	Alternating Ion Polarity	off
Mass Range Mode	200000 µs	Scan Begin	50 m/z	Scan End	900 m/z
Capillary Exit	109.0 Volt	Skimmer	40.0 Volt	Trap Drive	49.6
Accumulation Time	Ultra Scan	Averages	5 Spectra	Auto MS/MS	off



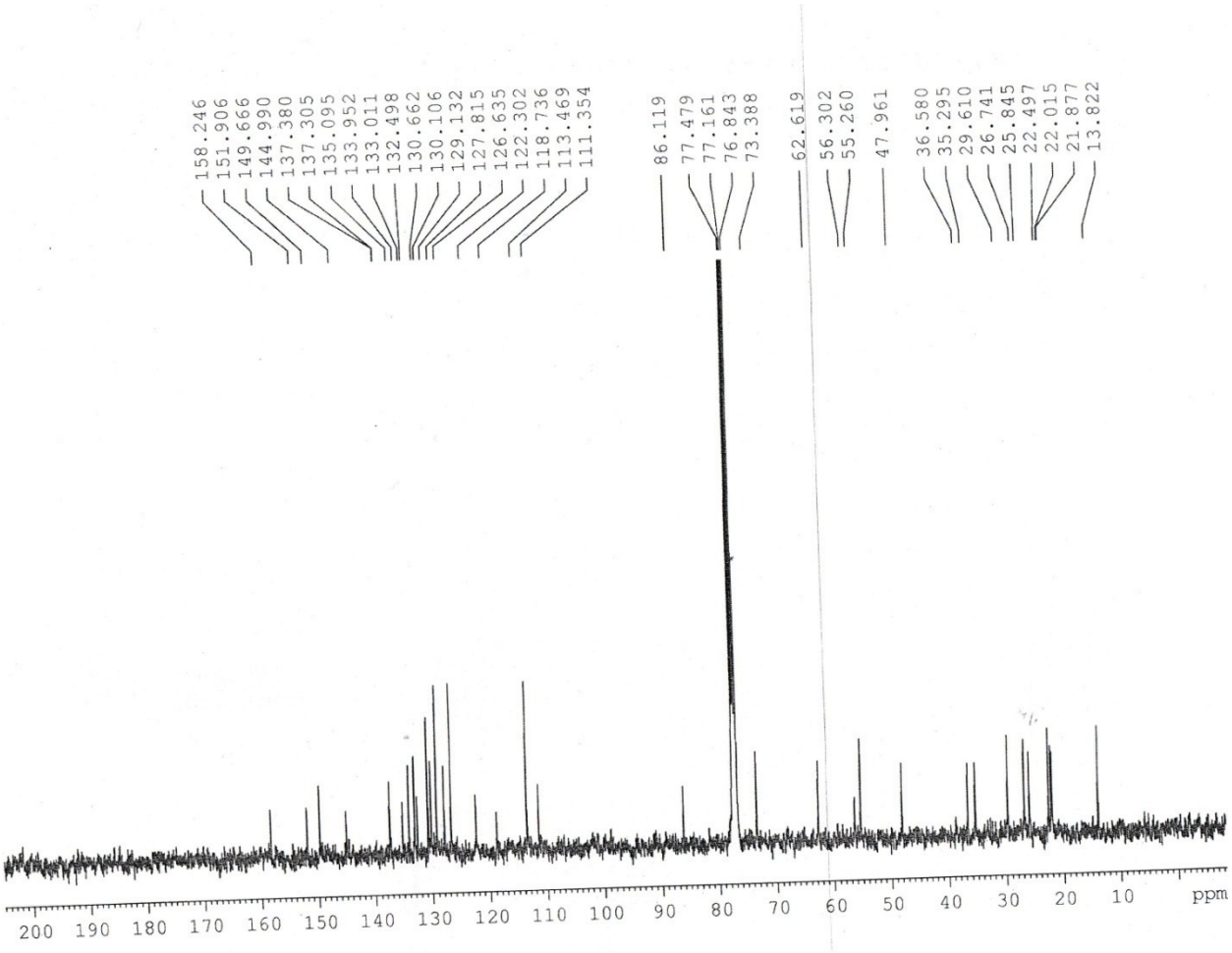
Compound 5: **4'-((2-butyl-4-chloro-5-(5-(4-methoxyphenyl)-1-oxa-3-azaspiro[5.5]undecan-2-yl)-1H-imidazol-1-yl)methyl)-[1,1'-biphenyl]-2-carbonitrile**



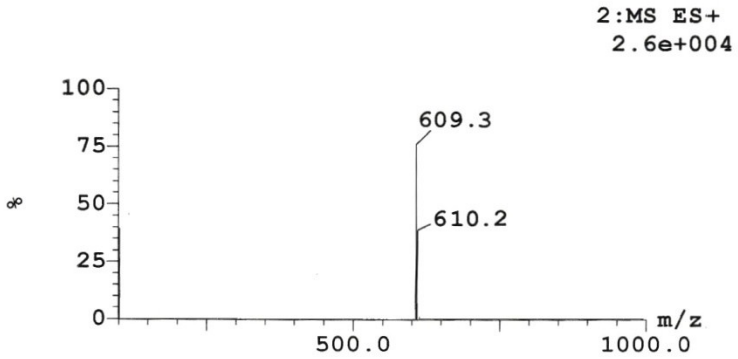
^{1}H-NMR:


7.604
7.585
7.576
7.574
7.496
7.475
7.031
7.010
6.994
6.974
6.731
6.709
4.099
3.717
3.630
2.506
2.499
2.495
2.490
2.486
2.481
1.426
1.417
1.406
1.397
1.388
1.203
1.184
1.165
1.147
0.755
0.737
0.718
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.08
2.95
1.92
4.08
1.94
1.00
2.02
0.99
1.00
3.11
2.10
2.01
5.05
4.03
5.01
3.07

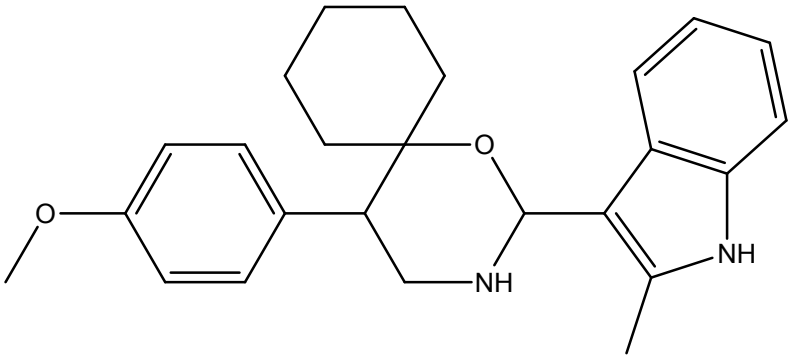
^{13}C-NMR:


158.246
151.906
149.666
144.990
137.380
137.305
135.095
133.952
133.011
132.498
130.662
130.106
129.132
127.815
126.635
122.302
118.736
113.469
111.354
86.119
77.479
77.161
76.843
73.388
62.619
56.302
55.260
47.961
36.580
35.295
29.610
26.741
25.845
22.497
22.015
21.877
13.822
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

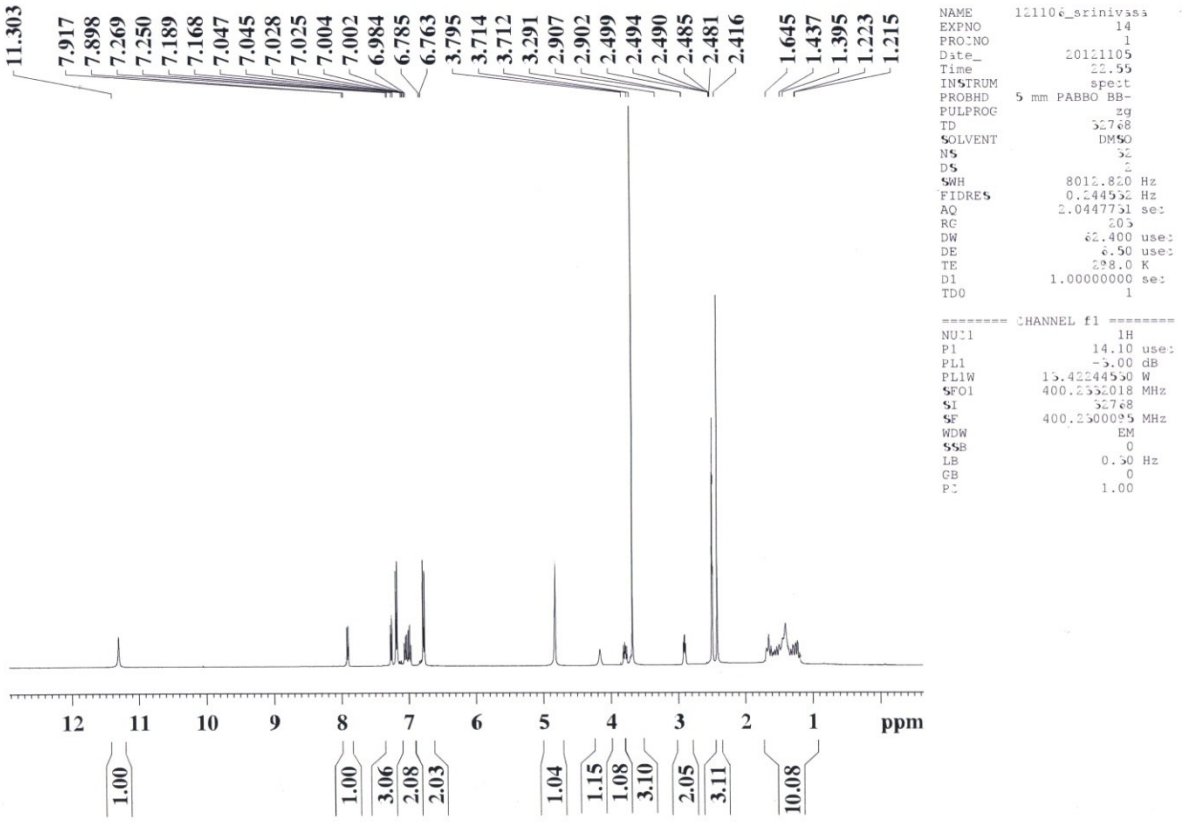
Mass:



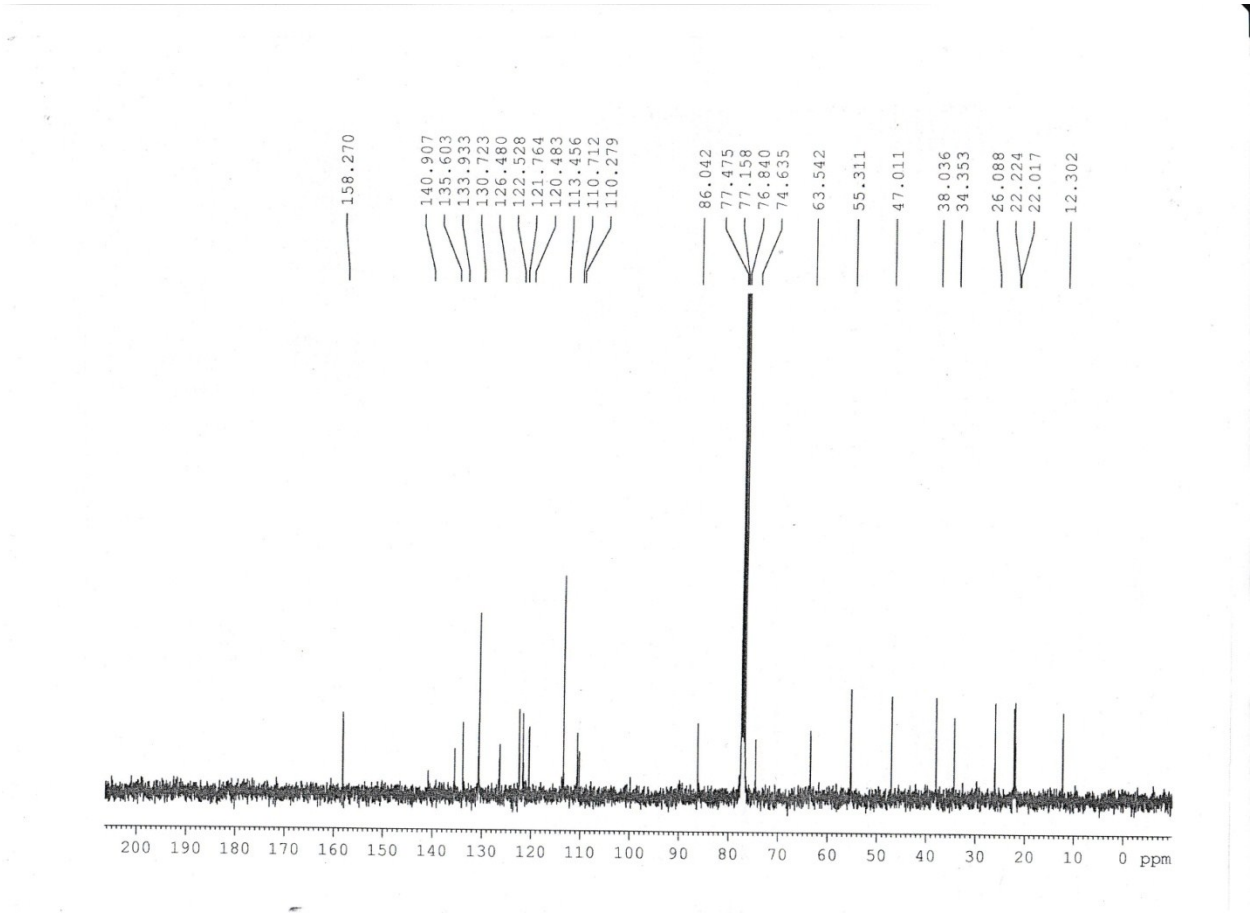
Compound 6: 5-(4-methoxyphenyl)-2-(2-methyl-1H-indol-3-yl)-1-oxa-3-azaspiro[5.5]undecane



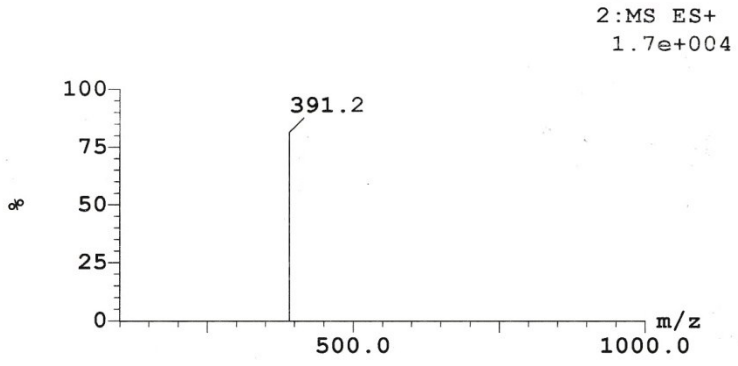
[1]H-NMR:



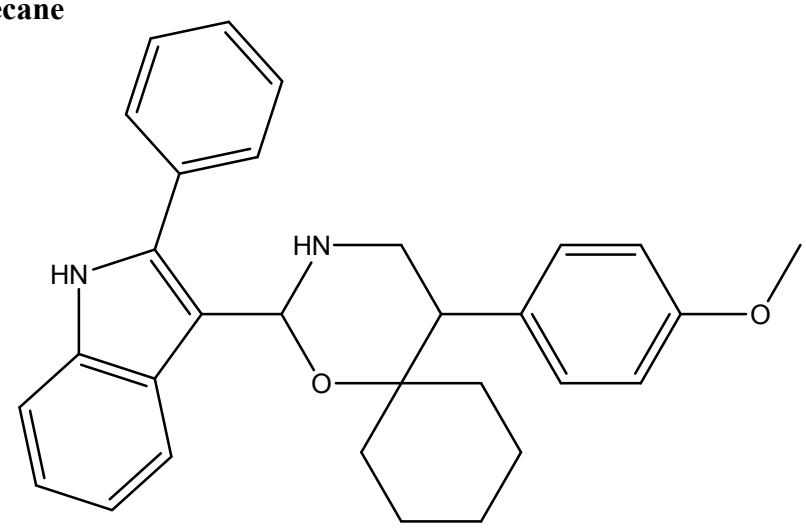
[13]C-NMR:


158.270
140.907
135.603
133.933
130.723
126.480
122.528
121.764
120.483
113.456
110.712
110.279
86.042
77.475
77.158
76.840
74.635
63.542
55.311
47.011
38.036
34.353
26.088
22.224
22.017
12.302
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

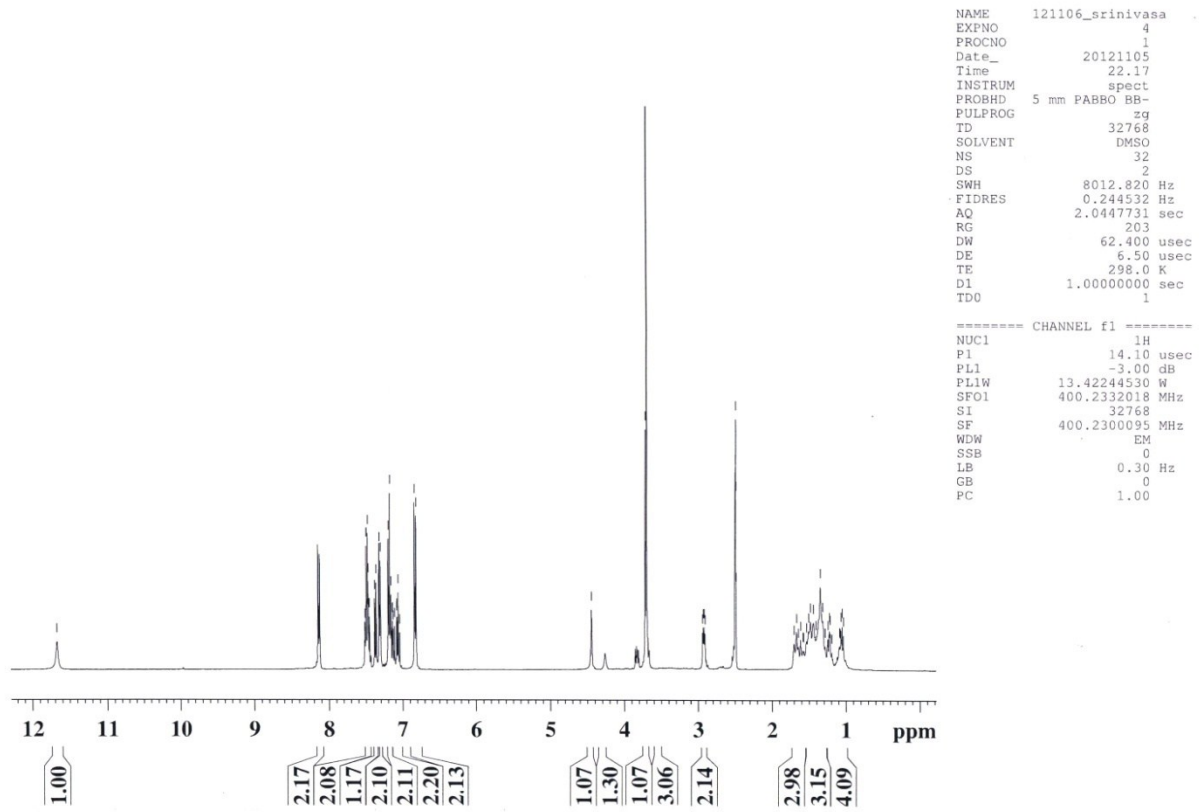
Mass:


2:MS ES+
1.7e+004
391.2
100
75
50
25
0
%
500.0
1000.0
m/z

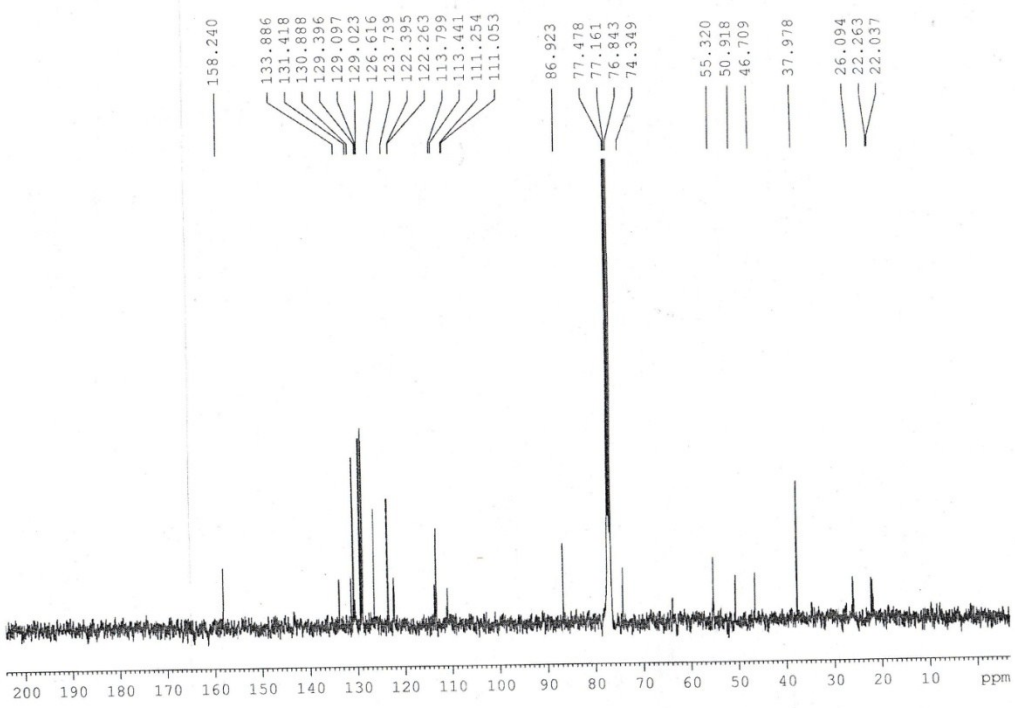
Compound 7: 5-(4-methoxyphenyl)-2-(2-phenyl-1H-indol-3-yl)-1-oxa-3-azaspiro[5.5]undecane



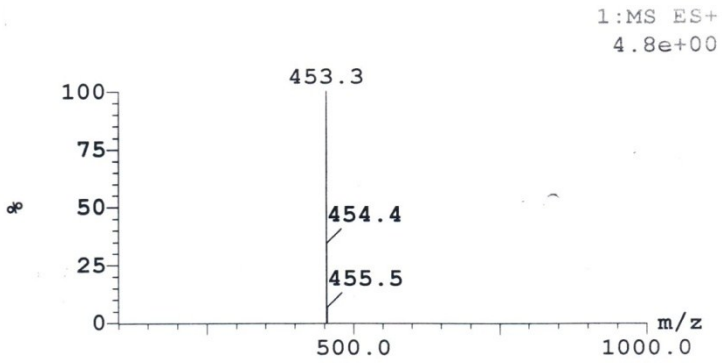
^{1}H-NMR:



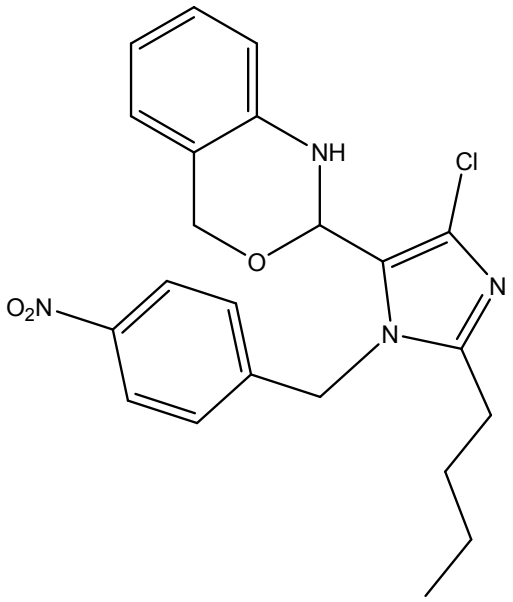
^{13}C-NMR:


158.240
133.886
131.418
130.888
129.396
129.097
129.023
126.616
123.739
122.395
122.263
113.799
113.441
111.254
111.053
86.923
77.478
77.161
76.843
74.349
55.320
50.918
46.709
37.978
26.094
22.263
22.037
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

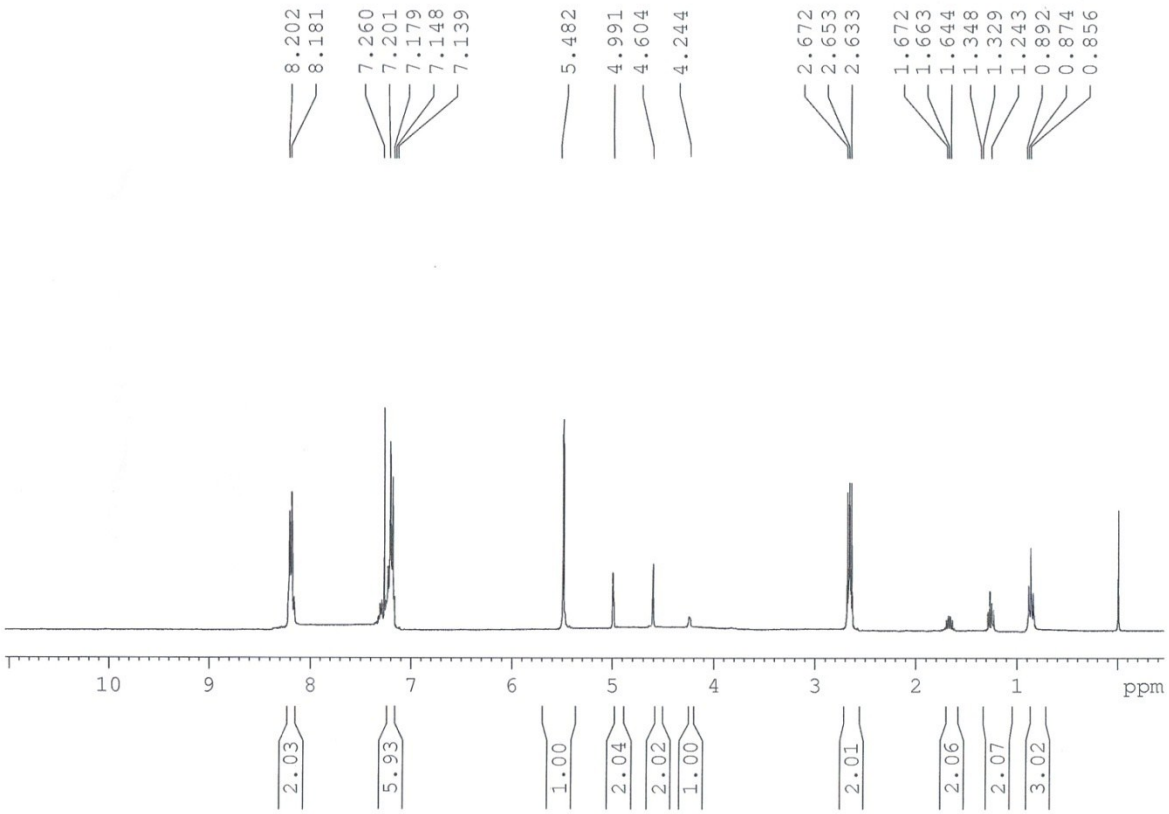
Mass:


1:MS ES+
4.8e+00
453.3
454.4
455.5
100
75
50
25
0
%
500.0
1000.0
m/z

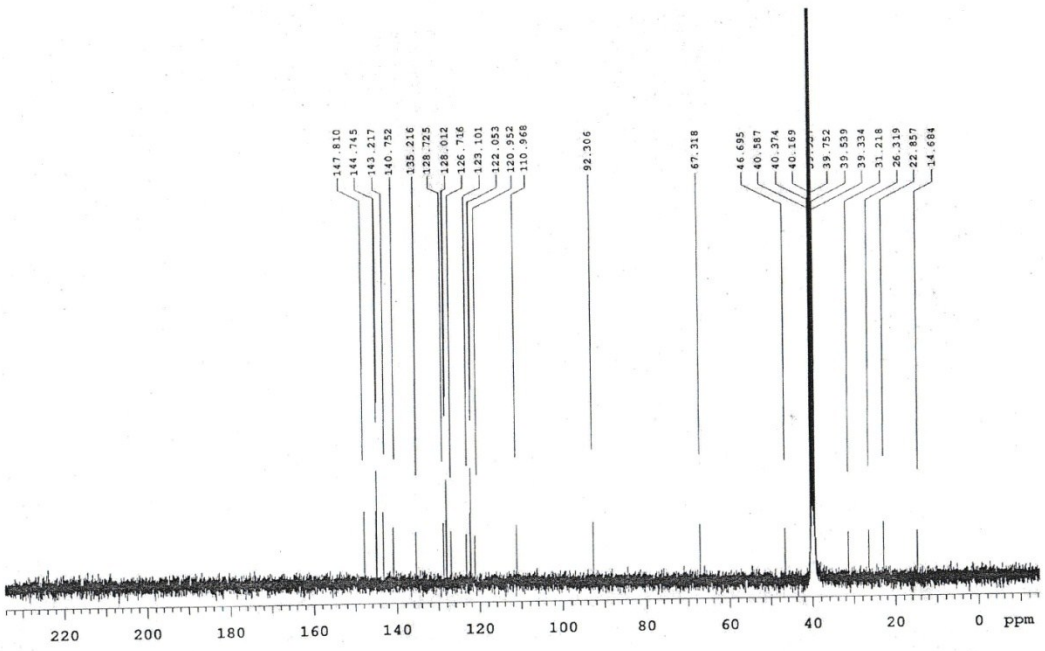
Compound 8: 2-(2-butyl-4-chloro-1-(4-nitrobenzyl)-1H-imidazol-5-yl)-2,4-dihydro-1H-benzo[d][1,3]oxazine



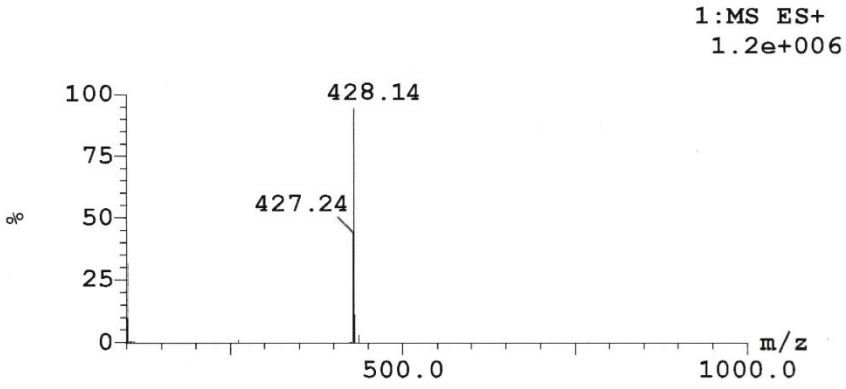
^{1}H-NMR:


8.202
8.181
7.260
7.201
7.179
7.148
7.139
5.482
4.991
4.604
4.244
2.672
2.653
2.633
1.672
1.663
1.644
1.348
1.329
1.243
0.892
0.874
0.856
10
9
8
7
6
5
4
3
2
1
ppm
2.03
5.93
1.00
2.04
2.02
1.00
2.01
2.06
2.07
3.02

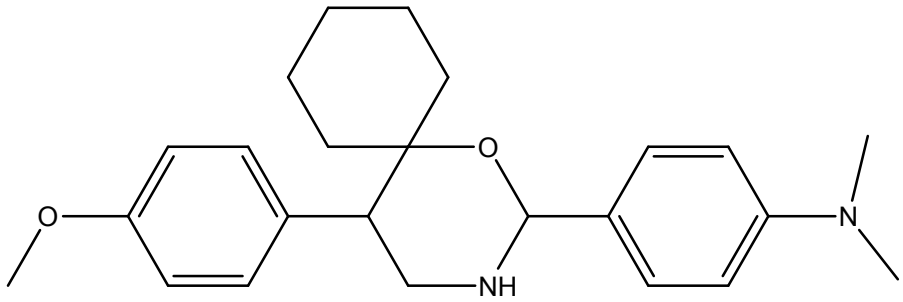
^{13}C-NMR:


147.810
144.745
143.217
140.752
135.216
128.725
128.012
126.716
123.101
122.053
120.952
110.968
92.306
67.318
46.695
40.587
40.374
40.169
39.752
39.539
39.334
31.218
26.319
22.857
14.684
220
200
180
160
140
120
100
80
60
40
20
0
ppm

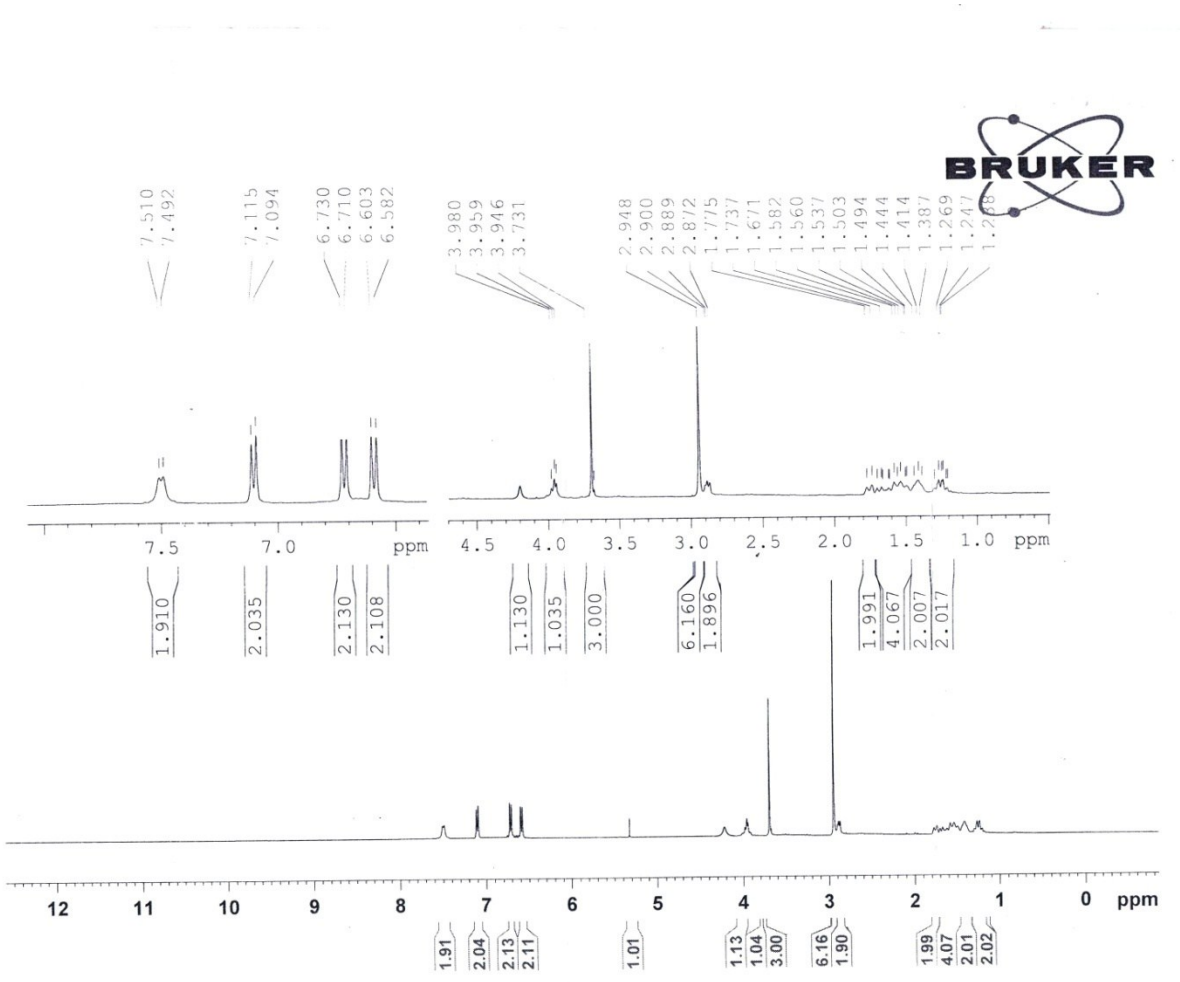
Mass:


1:MS ES+
1.2e+006
100
75
50
25
0
%
428.14
427.24
500.0
1000.0
m/z

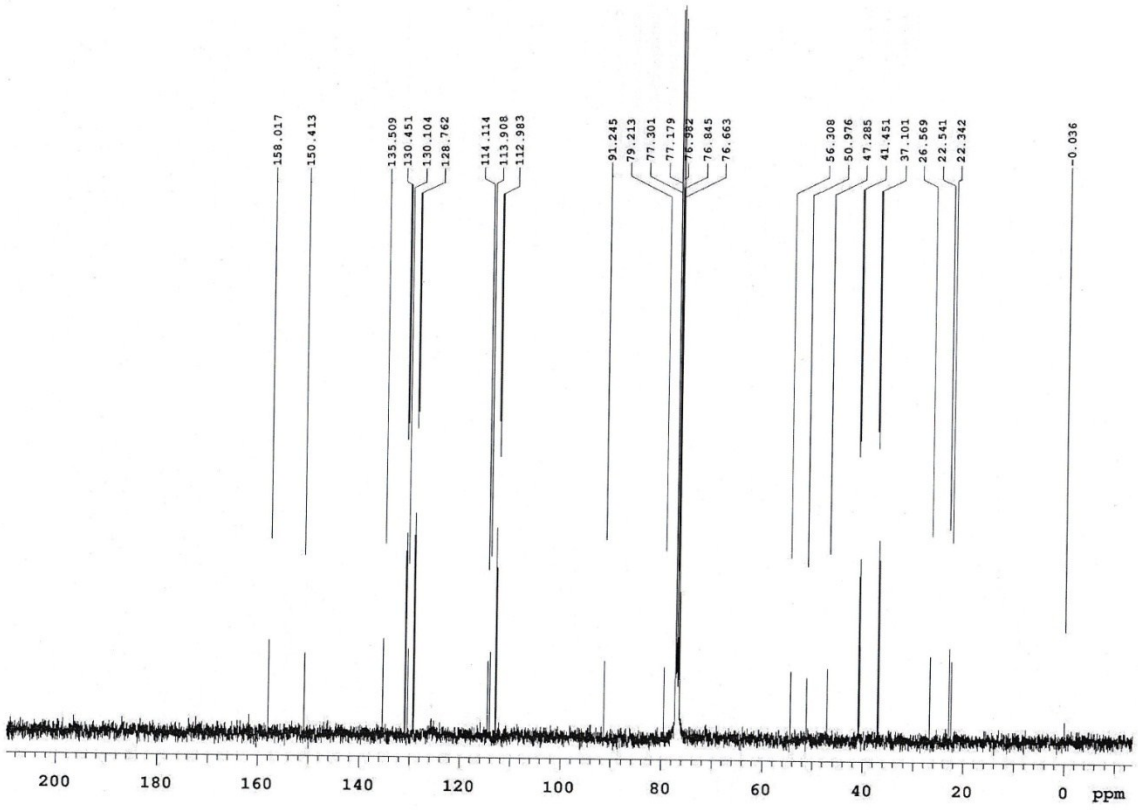
Compound 12: 4-(5-(4-methoxyphenyl)-1-oxa-3-azaspiro[5.5]undecan-2-yl)-N,N-dimethylaniline



1H-NMR:



^{13}C-NMR:

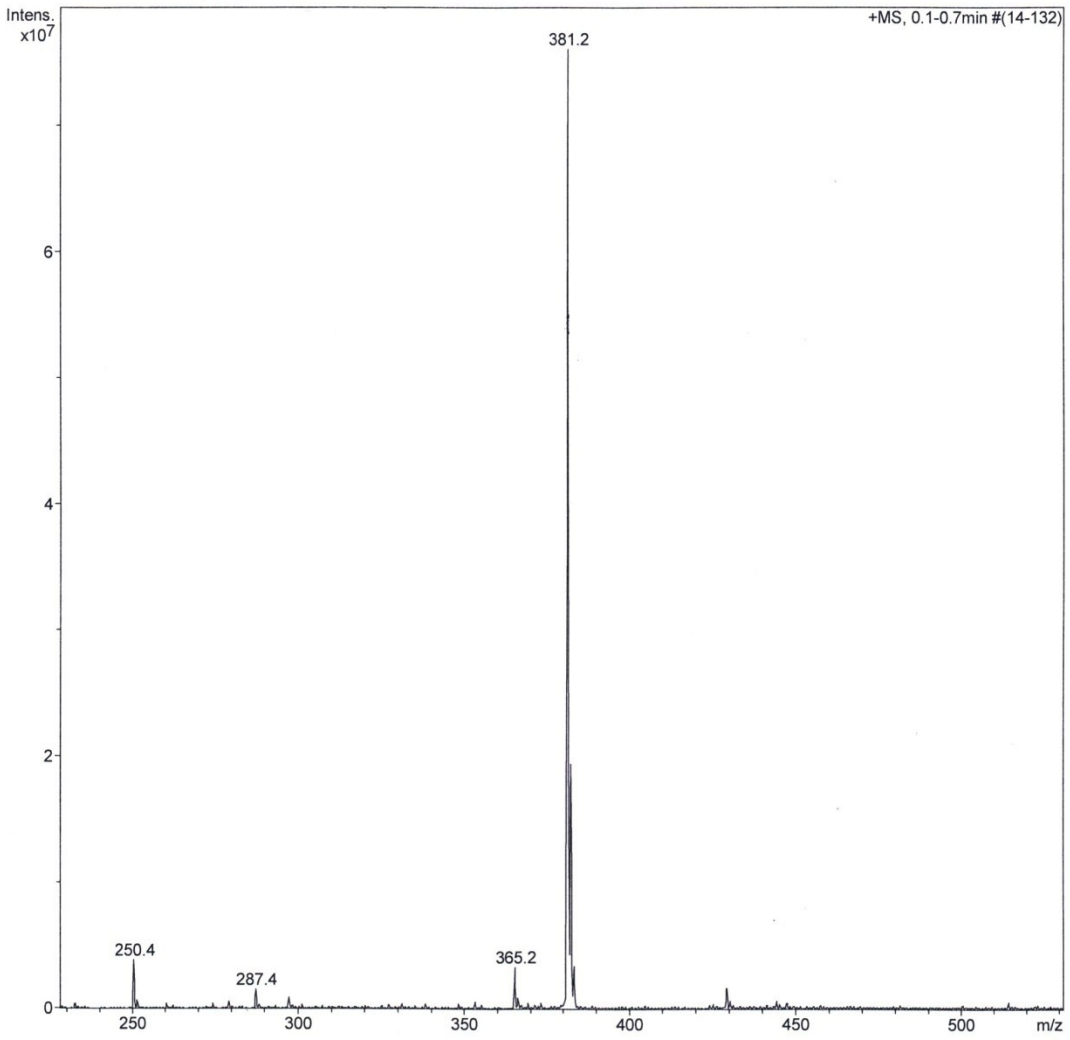

158.017
150.413
135.509
130.451
130.104
128.762
114.114
113.908
112.983
91.245
79.213
77.301
77.179
76.982
76.845
76.663
56.308
50.976
47.285
41.451
37.101
26.569
22.541
22.342
-0.036
200
180
160
140
120
100
80
60
40
20
0
ppm

Mass:

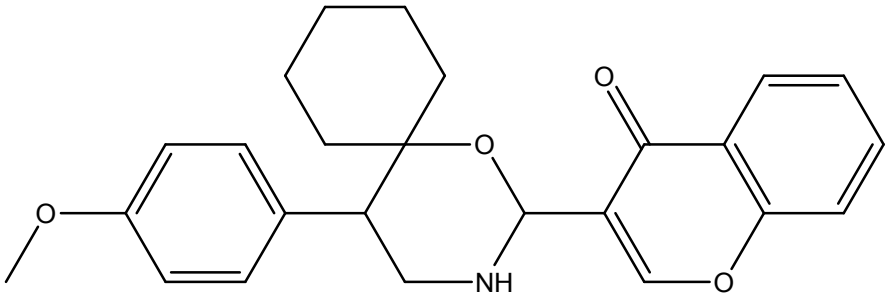
Method	DEF_MS.M	Operator	MBU
Sample Name		Instrument	HCTultra ETD II

Acquisition Parameter

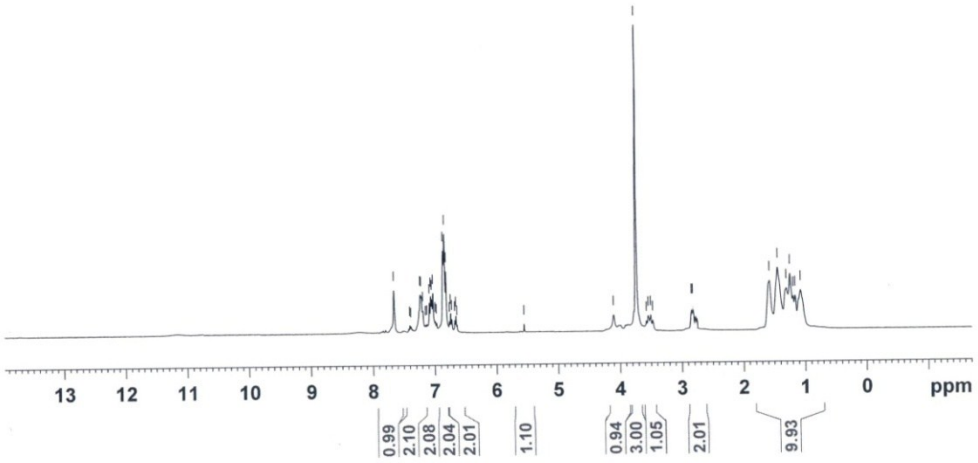
Ion Source Type	ESI	Ion Polarity	Positive	Alternating Ion Polarity	off
Mass Range Mode	200000 µs	Scan Begin	50 m/z	Scan End	800 m/z
Capillary Exit	109.0 Volt	Skimmer	40.0 Volt	Trap Drive	49.6
Accumulation Time	Ultra Scan	Averages	5 Spectra	Auto MS/MS	off



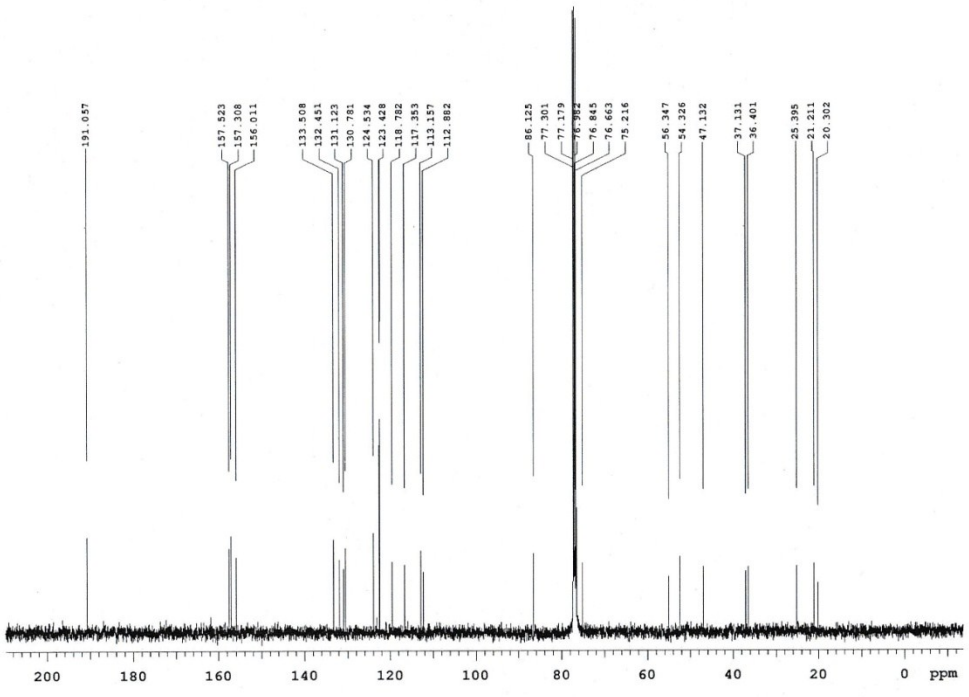
Compound 13: 3-(5-(4-methoxyphenyl)-1-oxa-3-azaspiro[5.5]undecan-2-yl)-4H-chromen-4-one



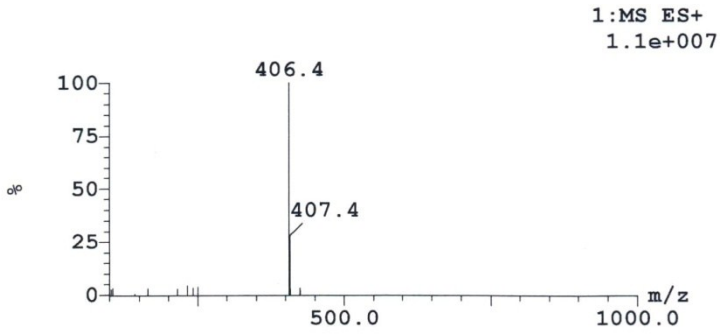
^{1}H-NMR:



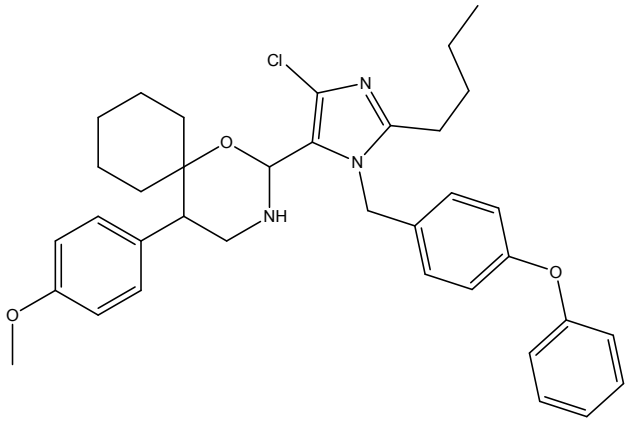
^{13}C-NMR:


191.057
157.523
157.308
156.011
133.508
132.451
131.123
130.781
124.534
123.428
118.782
117.353
113.157
112.882
86.125
77.301
77.179
76.982
76.845
76.663
75.216
56.347
54.326
47.132
37.131
36.401
25.395
21.211
20.302
200
180
160
140
120
100
80
60
40
20
0
ppm

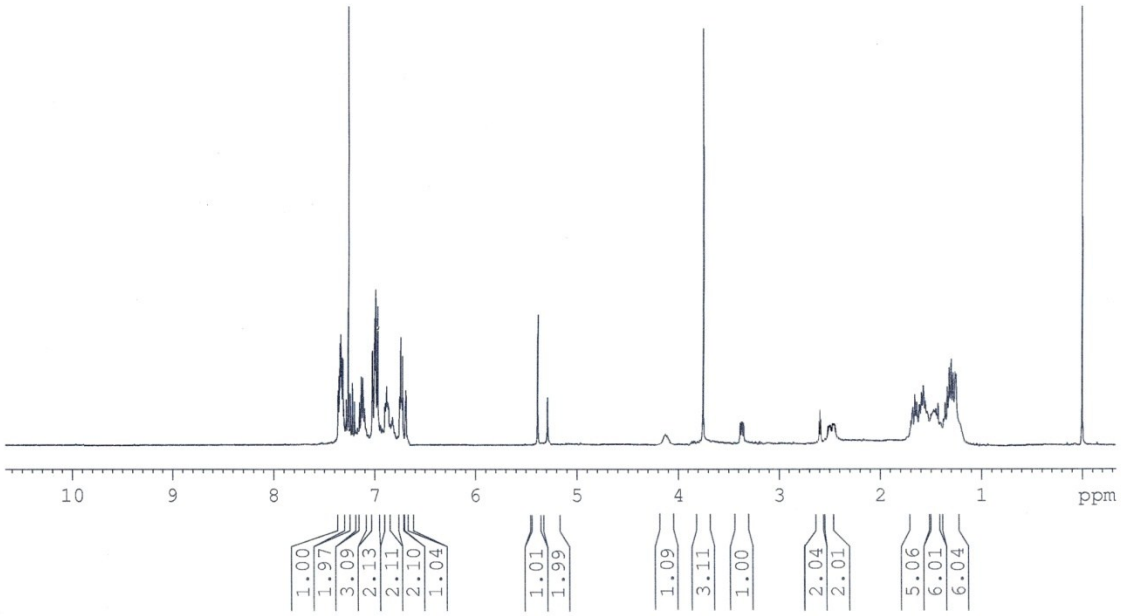
Mass:



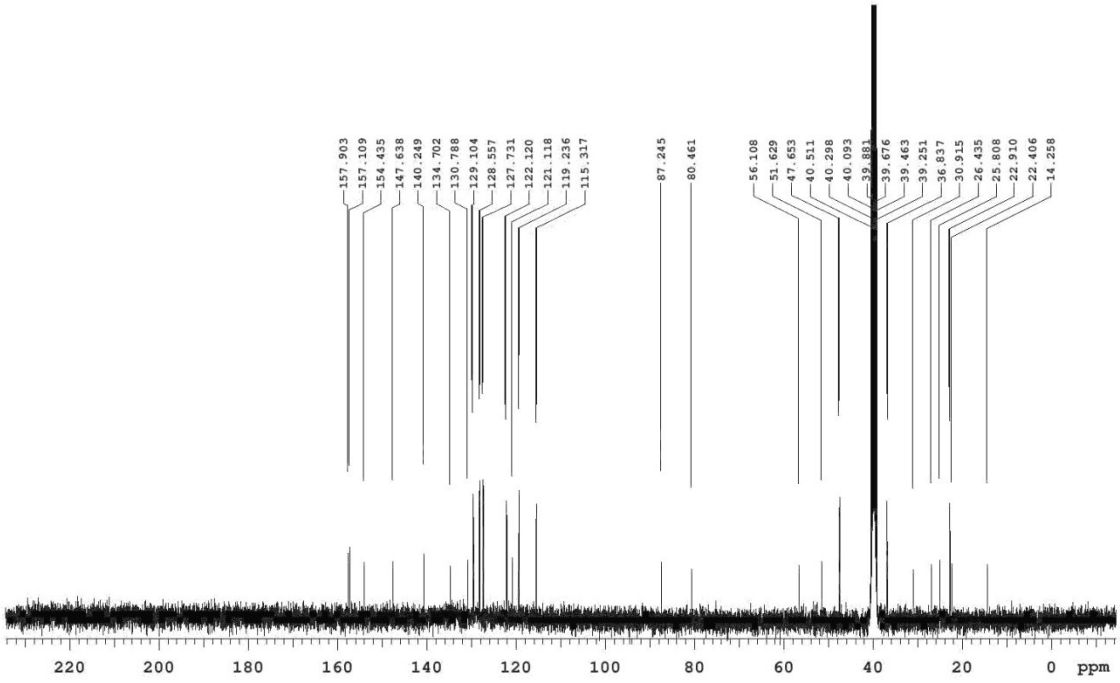
Compound 21: 2-(2-butyl-4-chloro-1-(4-phenoxybenzyl)-1H-imidazol-5-yl)-5-(4-methoxyphenyl)-1-oxa-3-azaspiro[5.5]undecane



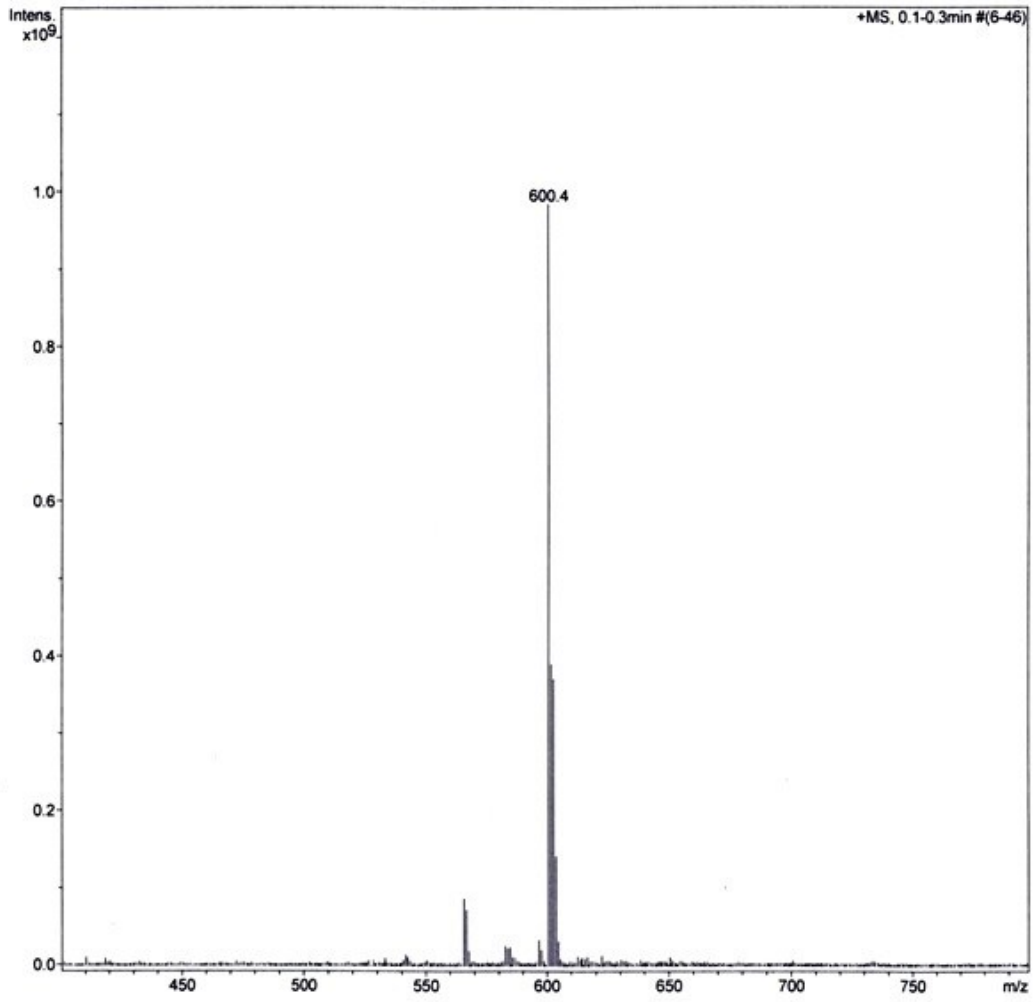
1H-NMR:


10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.97
3.09
2.13
2.11
2.10
1.04
1.01
1.99
1.09
3.11
1.00
2.04
2.01
5.06
6.01
6.04

^{13}C-NMR:


157.903
157.109
154.435
147.638
140.249
134.702
130.788
129.104
128.557
127.731
122.120
121.118
119.236
115.317
87.245
80.461
56.108
51.629
47.653
40.511
40.298
40.093
39.881
39.676
39.463
39.251
36.837
30.915
26.435
25.808
22.910
22.406
14.258
220
200
180
160
140
120
100
80
60
40
20
0
ppm

Mass:


Intens.
x10^9
+MS, 0.1-0.3min #(6-46)
600.4
1.0
0.8
0.6
0.4
0.2
0.0
450
500
550
600
650
700
750
m/z