Supplementary file

Vanillin-tethered quinazolin-2,4-dione analogues through five- and/or six- membered nitrogen-containing heterocycles as antibacterial agents: synthesis, biological evaluation and molecular docking study

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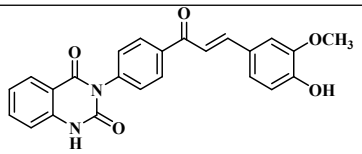
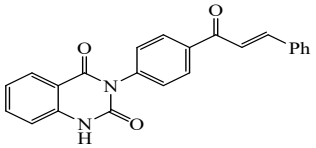
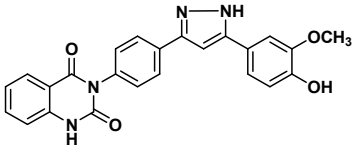
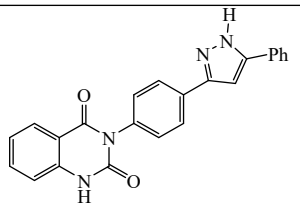
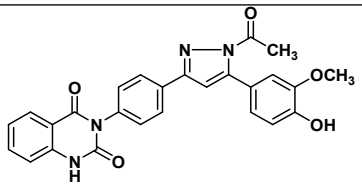
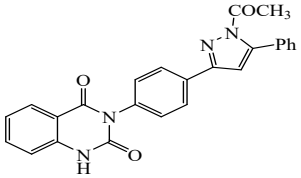
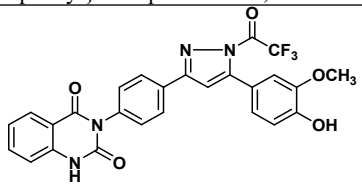
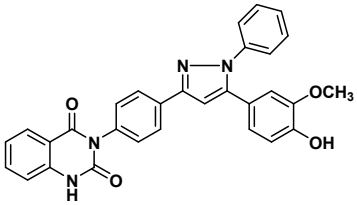
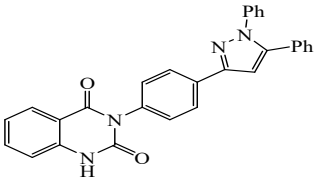
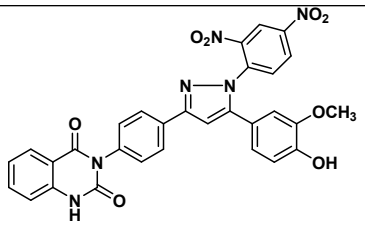
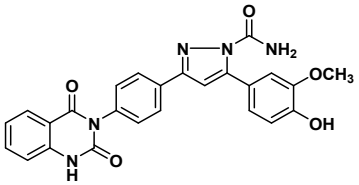
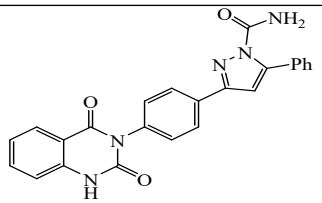
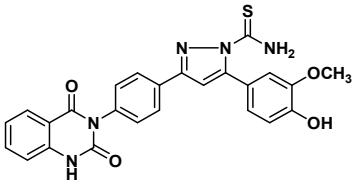
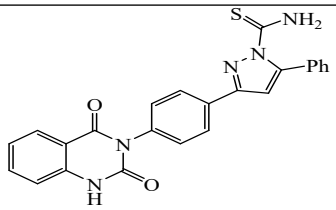
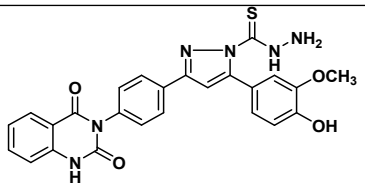
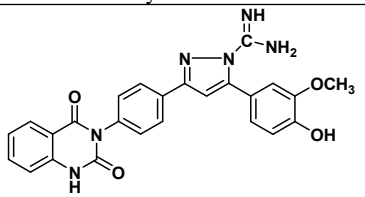
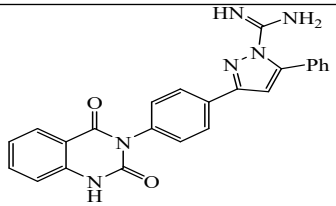
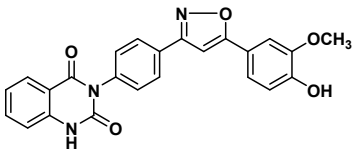
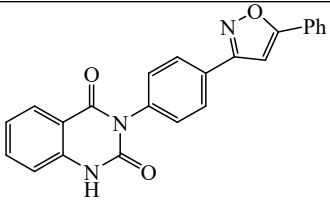
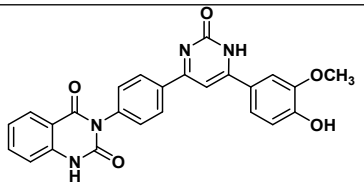
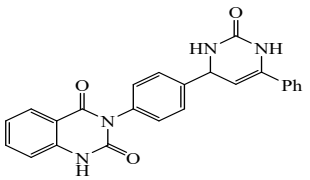
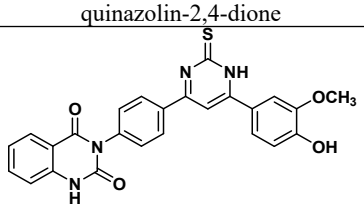
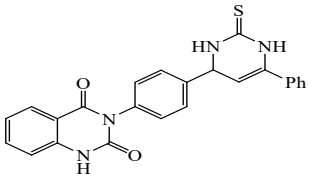
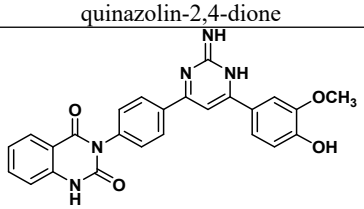
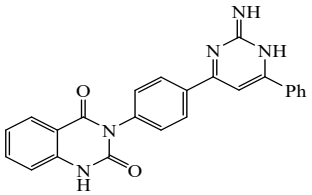
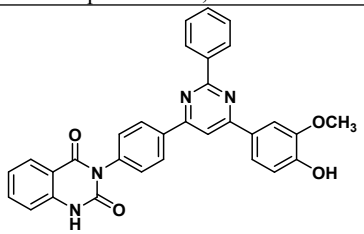
Table S1. A table of comparison with the previously published reports[1,2]

	2D Structure/Name	Temperature Color Yield % M.P. °C Crystallization	2D Structure/Name (reported work)	Temperature Color Yield % M.P. °C Crystallization
1	 3-{4-[3-(4-Hydroxy-3-methoxy-phenyl)-acryloyl]-phenyl}-1H-quinazolin-2,4-dione	stirring 24 hrs (0 to -10 °C) yellow 79 220-222 ethanol	 3-[4-(3-Phenyl-acryloyl)-phenyl]-1H-quinazolin-2,4-dione	stirring 24 hrs (0 to -10 °C) pale yellow 76 162-164 ethanol
2	 3-{4-[5-(4-Hydroxy-3-methoxy-phenyl)-1H-pyrazol-3-yl]-phenyl}-1H-quinazolin-2,4-dione	reflux 18 hrs white 80 275-277 benzene/ethanol	 3-[4-(5-Phenyl-1H-pyrazol-3-yl)-phenyl]-1H-quinazolin-2,4-dione	reflux 10 hrs white 88 274-276 benzene/ethanol
3	 3-{4-[1-Acetyl-5-(4-hydroxy-3-methoxy-phenyl)-1H-pyrazol-3-yl]-phenyl}-1H-quinazolin-2,4-dione	reflux 18 hrs white 78 280-282 benzene/ethanol	 3-[4-(1-Acetyl-5-phenyl-1H-pyrazol-3-yl)-phenyl]-1H-quinazolin-2,4-dione	reflux 12 hrs white 85 256-258 ethanol
4	 3-{4-[5-(4-Hydroxy-3-methoxy-phenyl)-1-(2,2,2-trifluoro-acetyl)-1H-pyrazol-3-yl]-phenyl}-1H-quinazolin-2,4-dione	reflux 24 hrs gray 75 292-294 benzene/ethanol	-	-
5	 3-{4-[5-(4-Hydroxy-3-methoxy-phenyl)-1-phenyl-1H-pyrazol-3-yl]-phenyl}-1H-quinazolin-2,4-dione	reflux 24 hrs white 81 250-252 benzene/ethanol	 3-[4-(1,5-Diphenyl-1H-pyrazol-3-yl)-phenyl]-1H-quinazolin-2,4-dione	reflux 10 hrs yellowish white 84 144-146 benzene/ethanol

6	 3-{4-[1-(2,4-Dinitro-phenyl)-5-(4-hydroxy-3-methoxy-phenyl)-1H-pyrazol-3-yl]-phenyl}-1H-quinazolin-2,4-dione	reflux 36 hrs orange 70 200-202 benzene/ethanol	-	-
7	 3-[4-(2,4-Dioxo-1,4-dihydro-2H-quinazolin-3-yl)-phenyl]-5-(4-hydroxy-3-methoxy-phenyl)-pyrazole-1-carboxylic acid amide	reflux 20 hrs white 80 320-322 benzene/ethanol	 3-[4-(2,4-Dioxo-1,4-dihydro-2H-quinazolin-3-yl)-phenyl]-5-phenyl-pyrazole-1-carboxylic acid amide	reflux 10 hrs yellowish white 83 180-182 benzene/ethanol
8	 3-[4-(2,4-Dioxo-1,4-dihydro-2H-quinazolin-3-yl)-phenyl]-5-(4-hydroxy-3-methoxy-phenyl)-pyrazole-1-carbothioic acid amide	reflux 20 hrs white 70 230-232 benzene/ethanol	 3-[4-(2,4-Dioxo-1,4-dihydro-2H-quinazolin-3-yl)-phenyl]-5-phenyl-pyrazole-1-carbothioic acid amide	reflux 10 hrs white 84 192-194 benzene/ethanol
9	 3-[4-(2,4-Dioxo-1,4-dihydro-2H-quinazolin-3-yl)-phenyl]-5-(4-hydroxy-3-methoxy-phenyl)-pyrazole-1-carbothioic acid hydrazide	reflux 24 hrs white 75 292-294 benzene/ethanol	-	-
10	 3-[4-(2,4-Dioxo-1,4-dihydro-2H-quinazolin-3-yl)-phenyl]-5-(4-hydroxy-3-methoxy-phenyl)-pyrazole-1-carboxamidine	reflux 20 hrs pale yellow 82 280-282 benzene/ethanol	 3-[4-(2,4-Dioxo-1,4-dihydro-2H-quinazolin-3-yl)-phenyl]-5-phenyl-pyrazole-1-carbox amidine	reflux 8 hrs yellowish white 78 144-146 benzene/ethanol

11	 3-{4-[5-(4-Hydroxy-3-methoxy-phenyl)-isoxazol-3-yl]-phenyl}-1H-quinazolin-2,4-dione	reflux 24 hrs pale yellow 72 298-300 benzene/ethanol	 3-[4-(5-Phenyl-isoxazol-3-yl)-phenyl]-1H-quinazolin-2,4-dione	reflux 8 hrs white 84 210-212 benzene/ethanol
12	 3-{4-[6-(4-Hydroxy-3-methoxy-phenyl)-2-oxo-1,2-dihydro-pyrimidin-4-yl]-phenyl}-1H-quinazolin-2,4-dione	reflux 20 hrs yellow 72 288-290 benzene/ethanol	 3-[4-(2-Hydroxy-6-phenyl-1,6-dihydro-pyrimidin-4-yl)-phenyl]-1H-quinazolin-2,4-dione	reflux 8 hrs white 85 150-152 benzene/ethanol
13	 3-{4-[6-(4-Hydroxy-3-methoxy-phenyl)-2-thioxo-1,2-dihydro-pyrimidin-4-yl]-phenyl}-1H-quinazolin-2,4-dione	reflux 24 hrs yellow 77 278-280 benzene/ethanol	 3-[4-(2-Mercapto-6-phenyl-1,6-dihydro-pyrimidin-4-yl)-phenyl]-1H-quinazolin-2,4-dione	reflux 10 hrs white 82 144-146 benzene/ethanol
14	 3-{4-[6-(4-Hydroxy-3-methoxy-phenyl)-2-imino-1,2-dihydro-pyrimidin-4-yl]-phenyl}-1H-quinazolin-2,4-dione	reflux 18 hrs yellow 77 260-262 benzene/ethanol	 3-[4-(2-Amino-6-phenyl-pyrimidin-4-yl)-phenyl]-1H-quinazolin-2,4-dione	reflux 10 hrs yellowish white 84 152-154 benzene/ethanol
15	 3-{4-[6-(4-Hydroxy-3-methoxy-phenyl)-2-phenyl-pyrimidin-4-yl]-phenyl}-1H-quinazolin-2,4-dione	reflux 20 hrs yellow 82 198-200 benzene/ethanol	-	-

(1) Abdelmonsef, A. H.; Mosallam, A. M. Synthesis, in Vitro Biological Evaluation and in Silico Docking Studies of New Quinazolin-2,4-dione Analogues as Possible Anticarcinoma Agents. *J. Heterocycl. Chem.* 2020, *57* (4), 1637–1654. https://doi.org/10.1002/jhet.3889.

(2) El-Naggar, M.; Rashdan, H. R. M.; Abdelmonsef, A. H. Cyclization of Chalcone Derivatives: Design, Synthesis, In Silico Docking Study, and Biological Evaluation of New Quinazolin-2,4-Diones Incorporating Five-, Six-, and Seven-Membered Ring Moieties as Potent Antibacterial

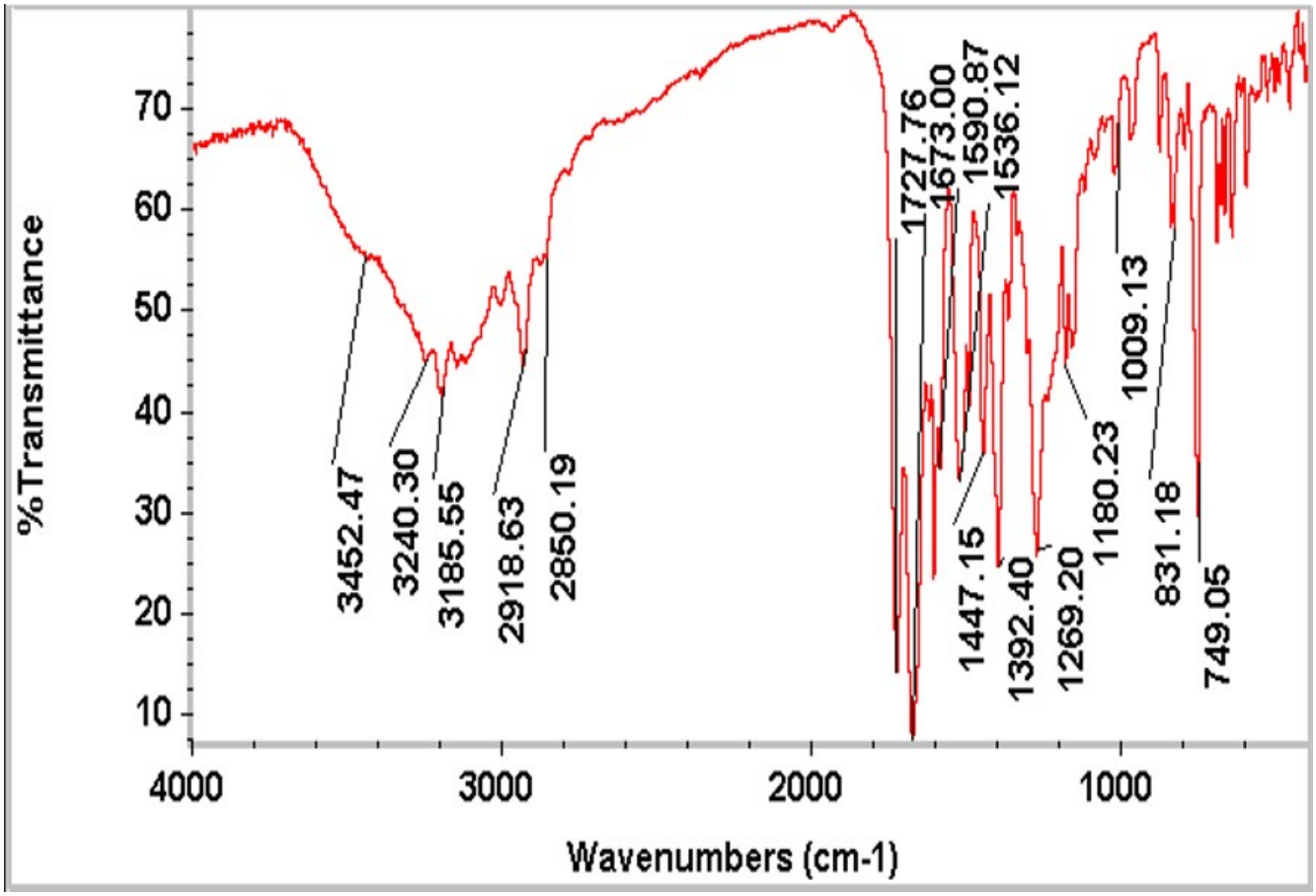


Figure S1. FT-IR spectrum of compound 1

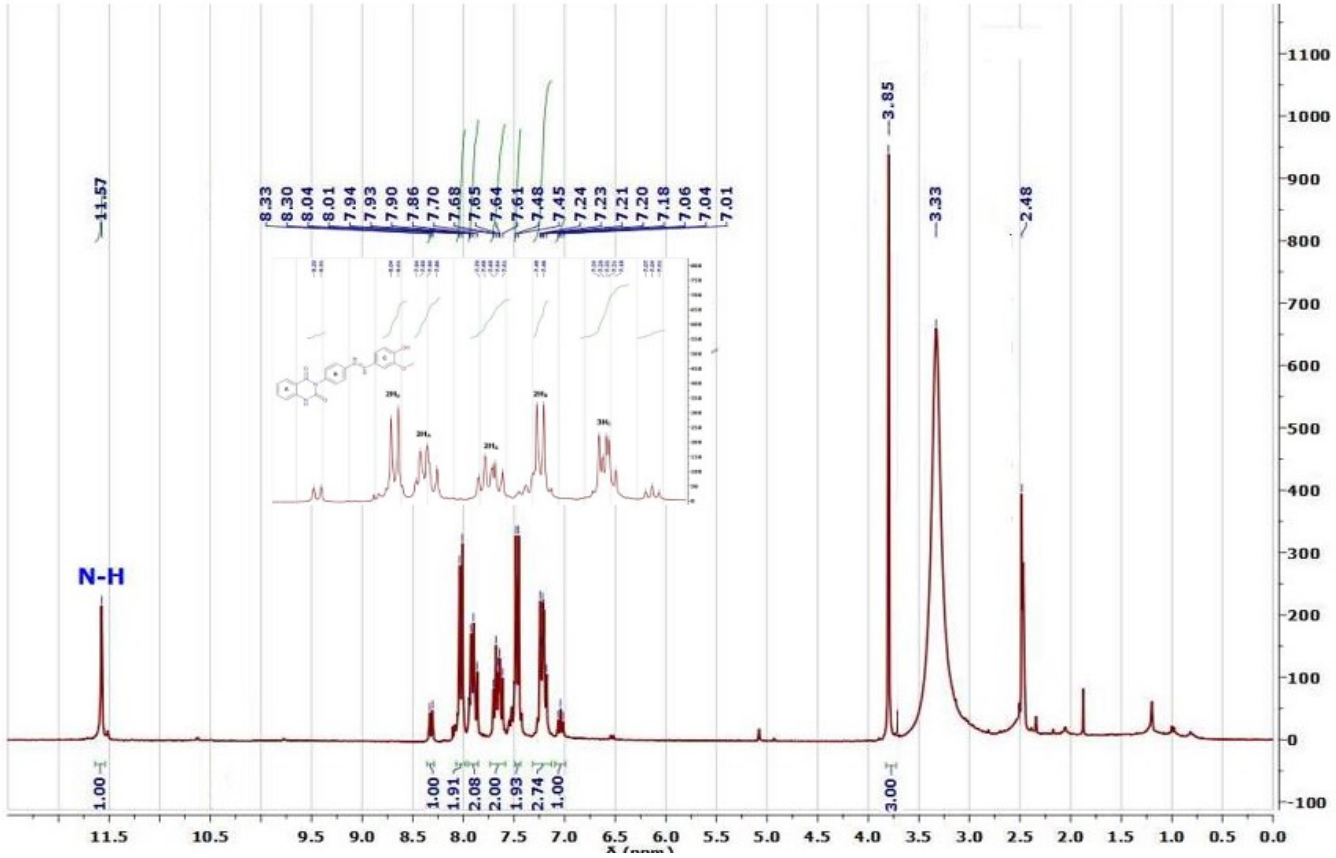


Figure S2. [1]HNMR spectrum of compound 1

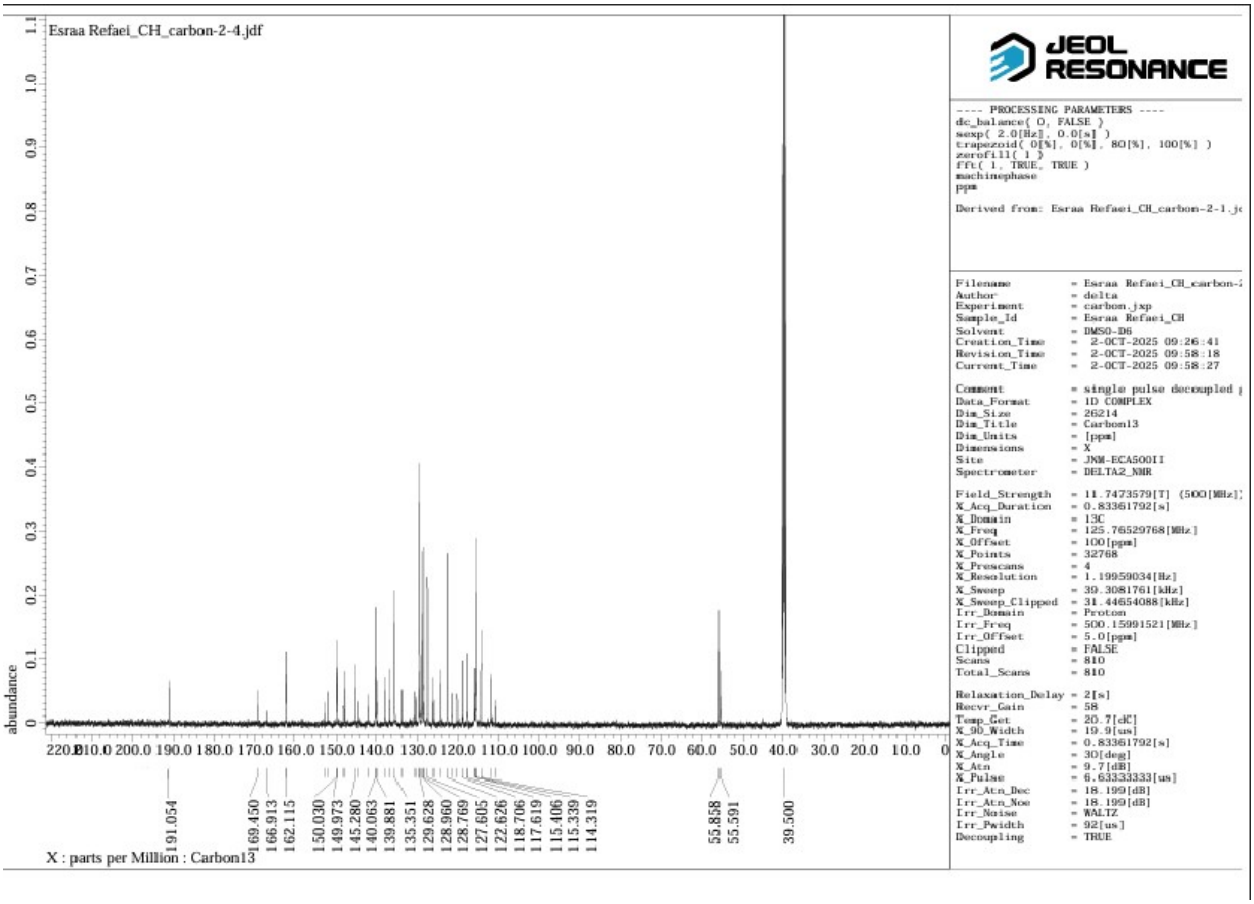


Figure S3. ^{13}CNMR spectrum of compound 1

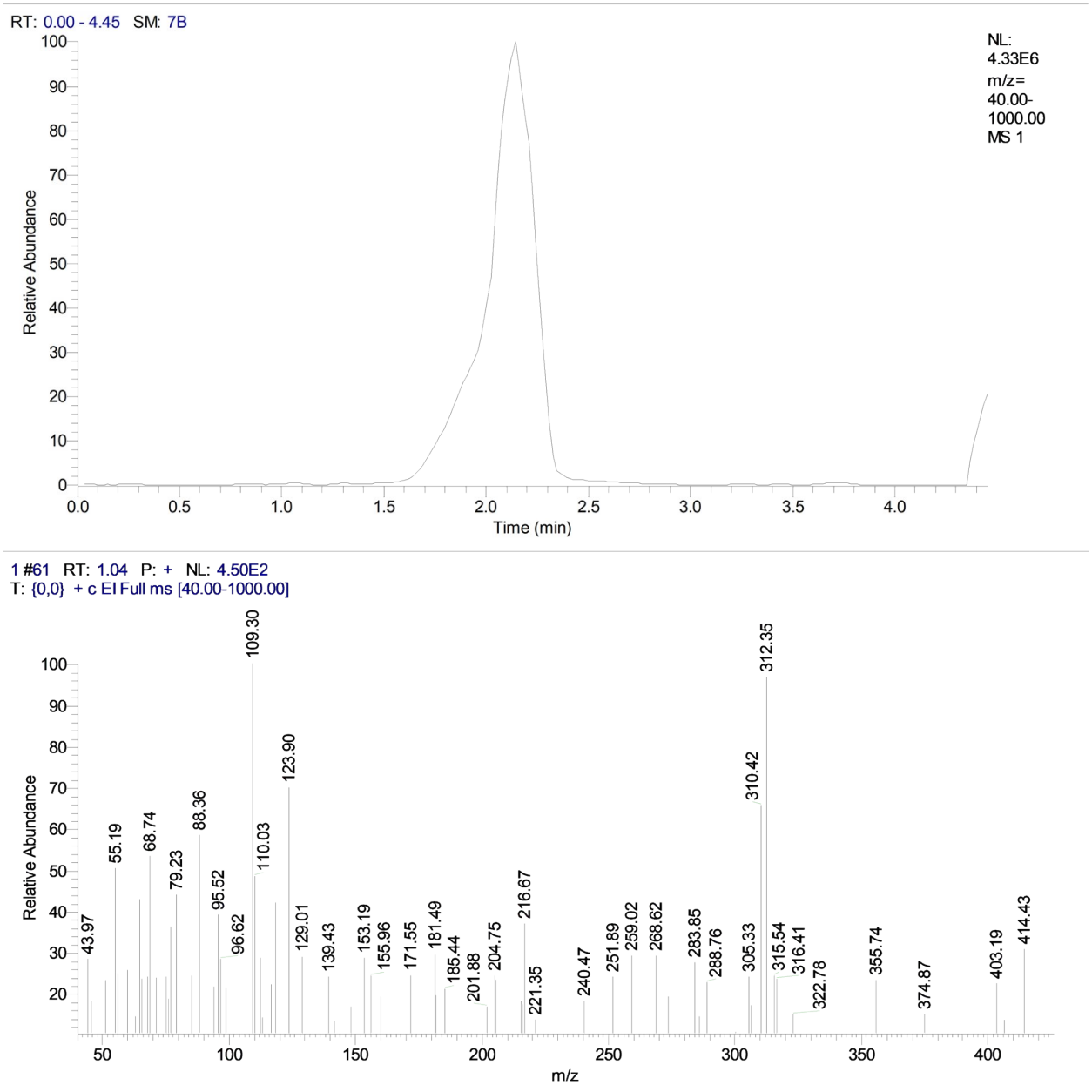


Figure S4. Mass spectrum of compound 1

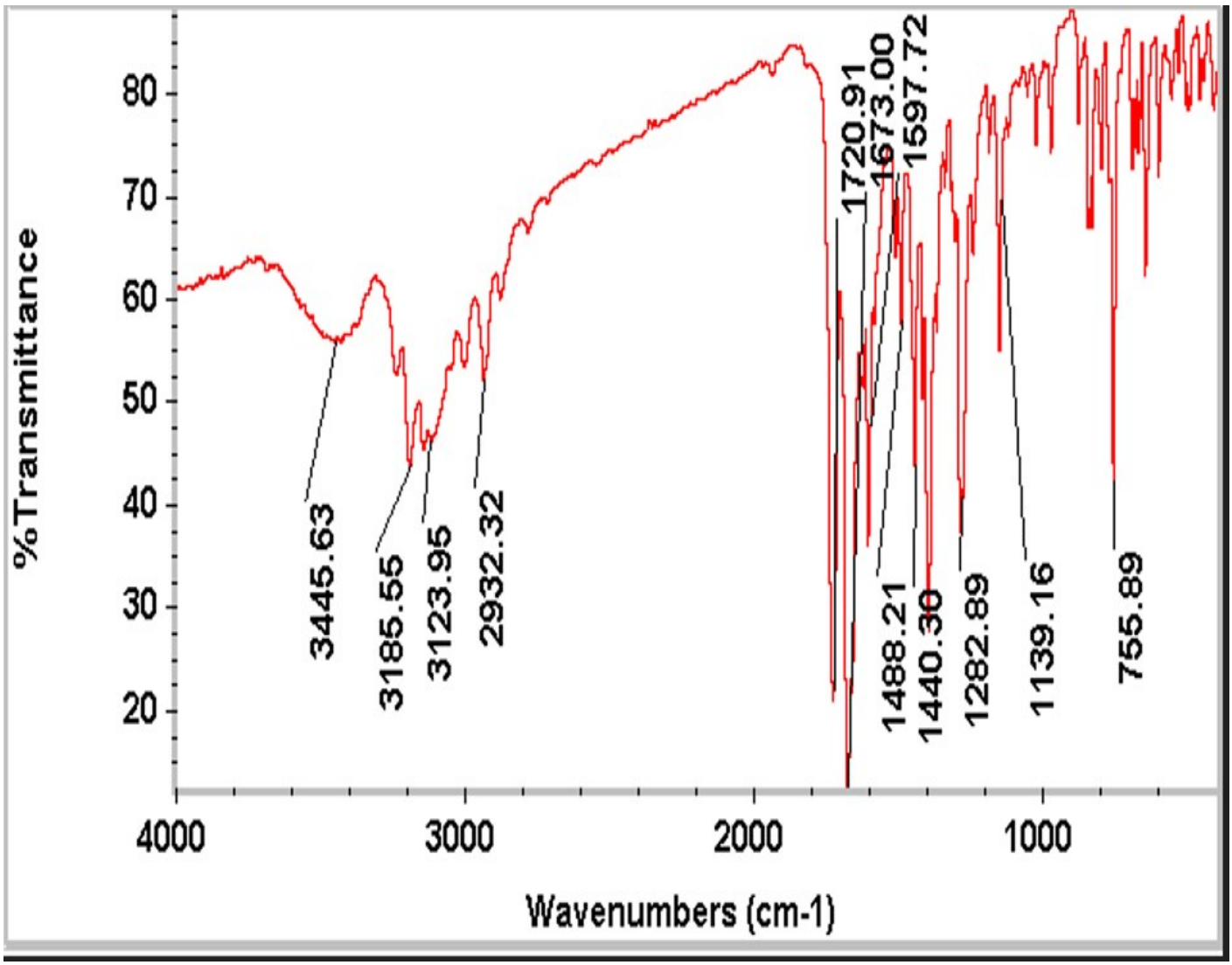


Figure S5. FT-IR spectrum of compound 2

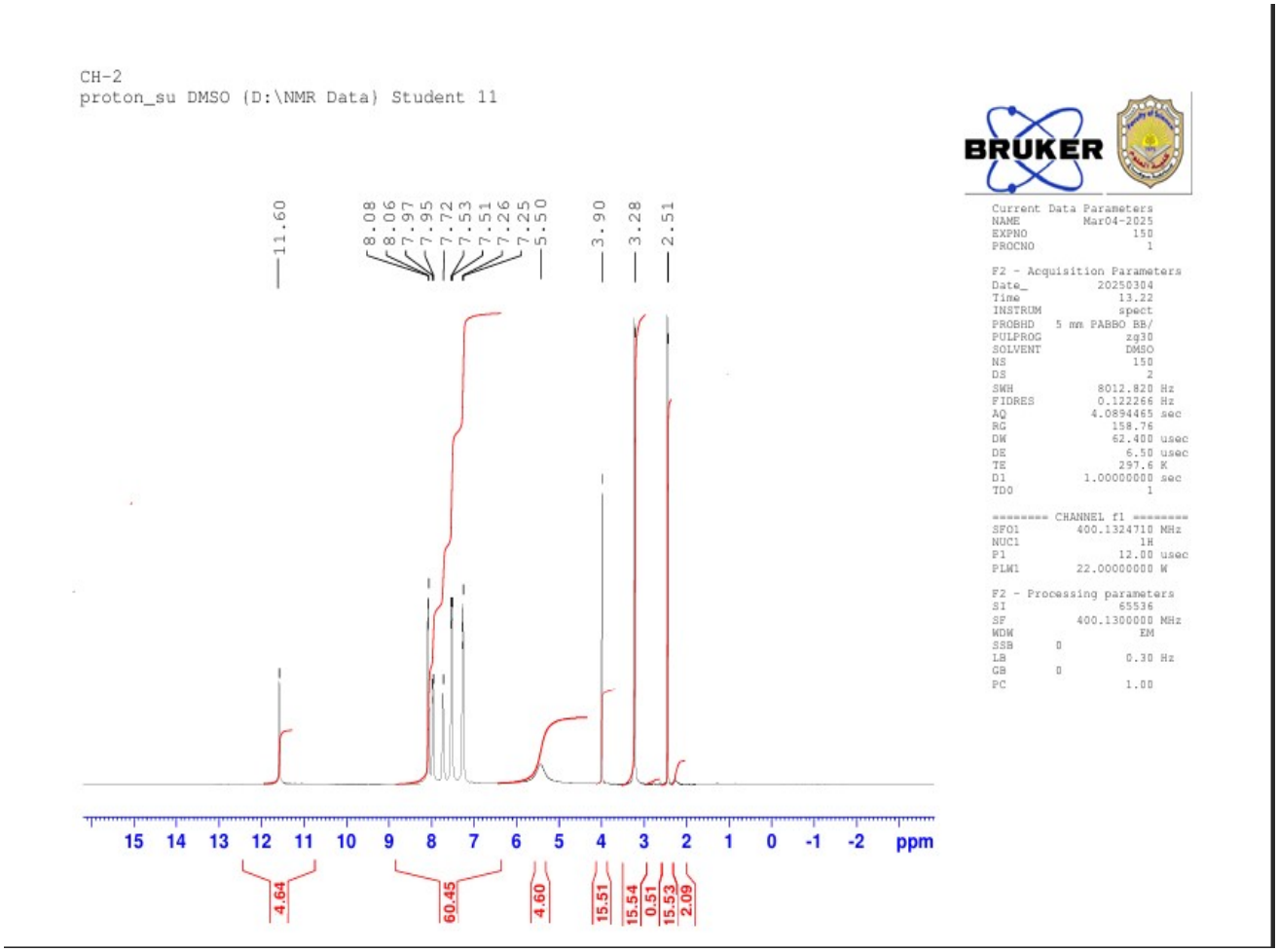


Figure S6. ^{1}HNMR spectrum of compound 2

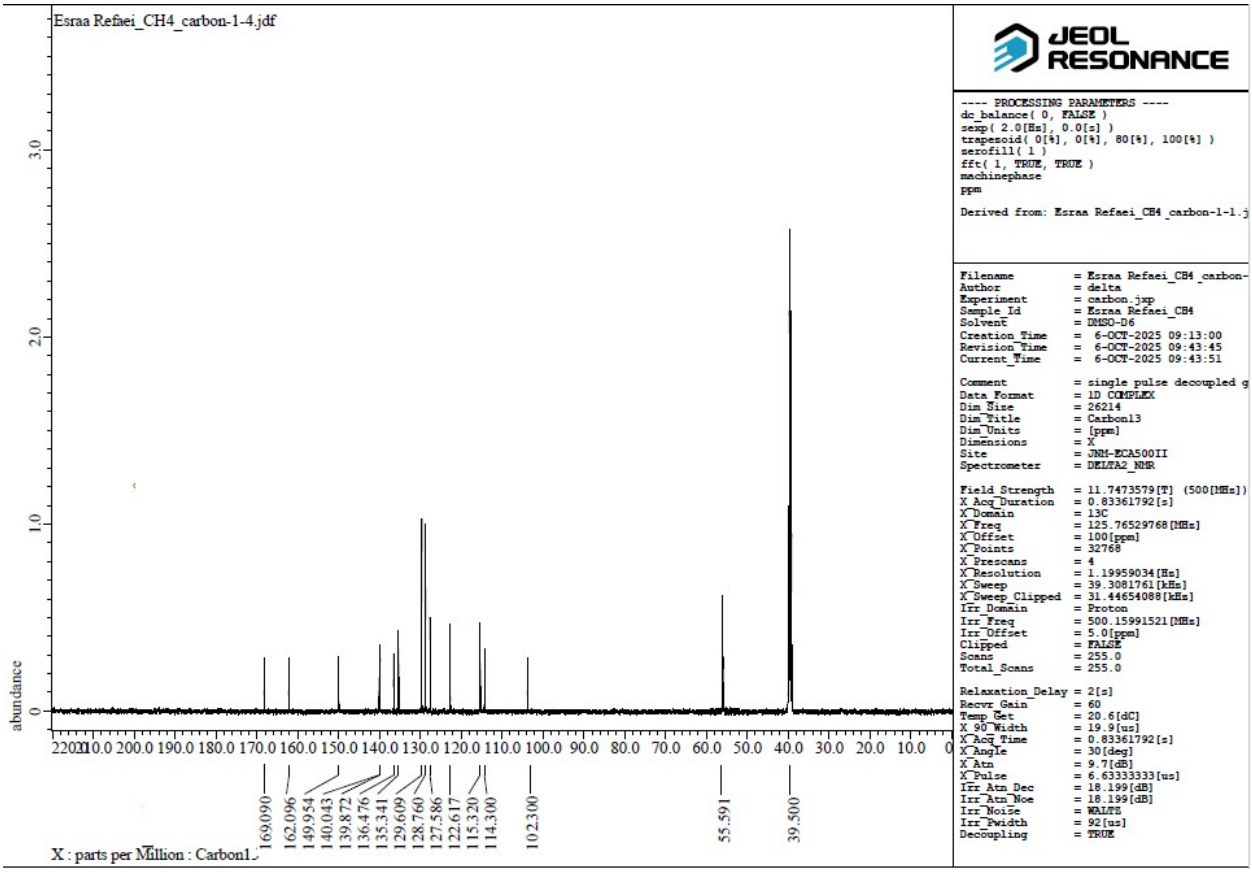
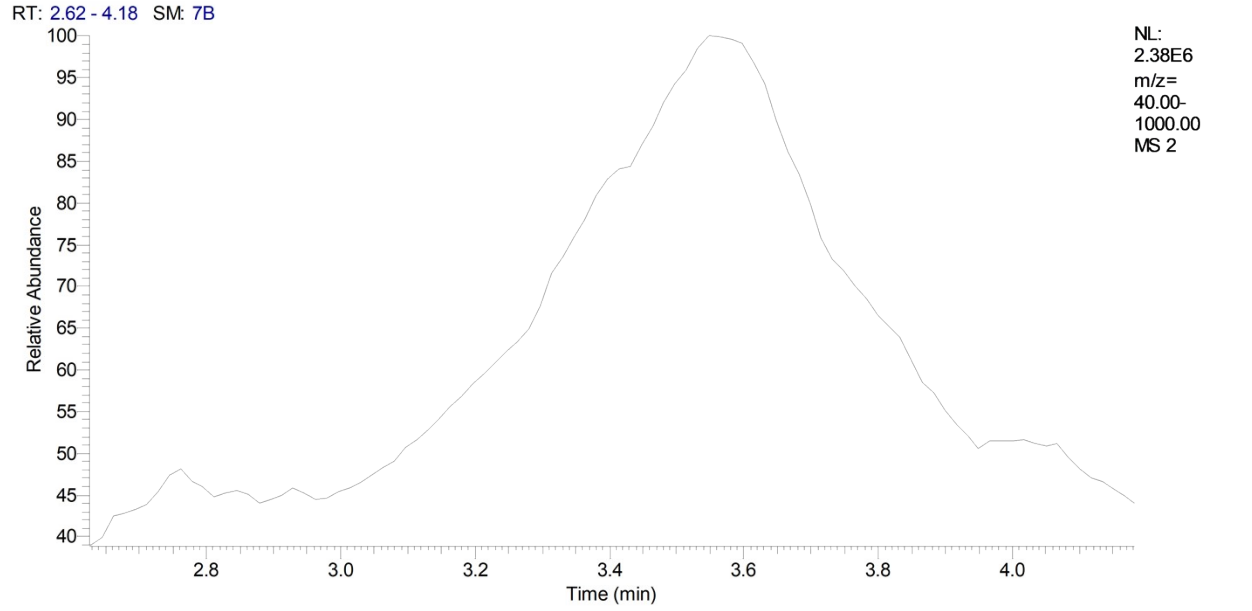


Figure S7. ^{13}CNMR spectrum of compound 2


RT: 2.62 - 4.18 SM: 7B
NL:
2.38E6
m/z=
40.00-
1000.00
MS 2
Relative Abundance
Time (min)

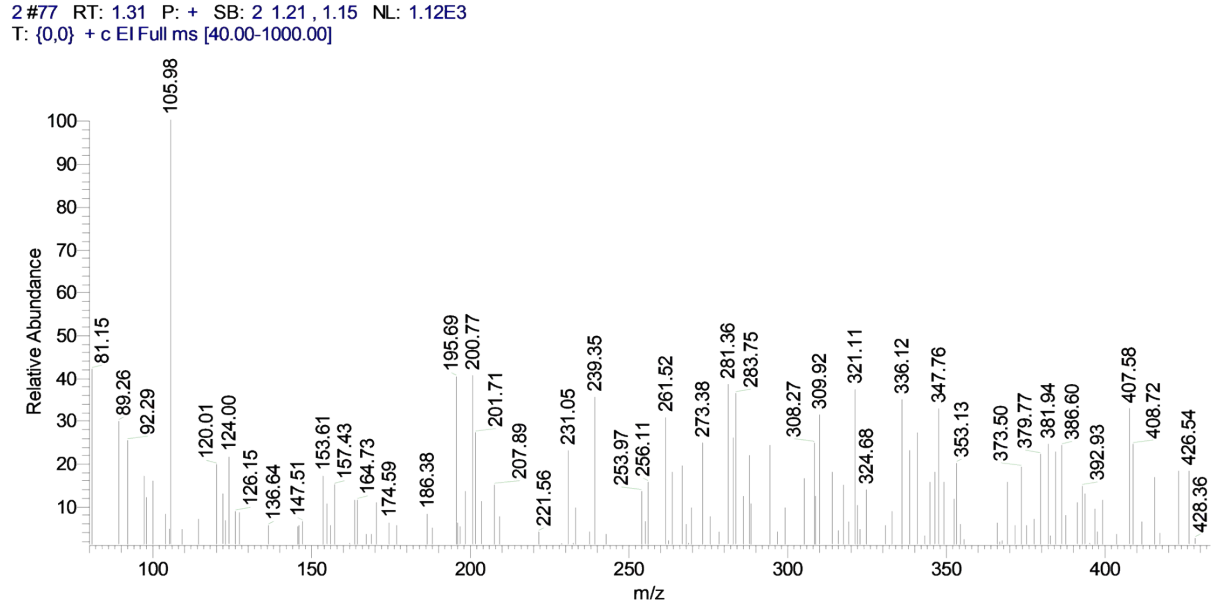

2 #77 RT: 1.31 P: + SB: 2 1.21 , 1.15 NL: 1.12E3
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
105.98
81.15
89.26
92.29
120.01
124.00
126.15
136.64
147.51
153.61
157.43
164.73
174.59
186.38
195.69
200.77
201.71
207.89
221.56
231.05
239.35
253.97
256.11
261.52
273.38
281.36
283.75
308.27
309.92
321.11
324.68
336.12
347.76
353.13
373.50
379.77
381.94
386.60
392.93
407.58
408.72
426.54
428.36

Figure S8. Mass spectrum of compound 2

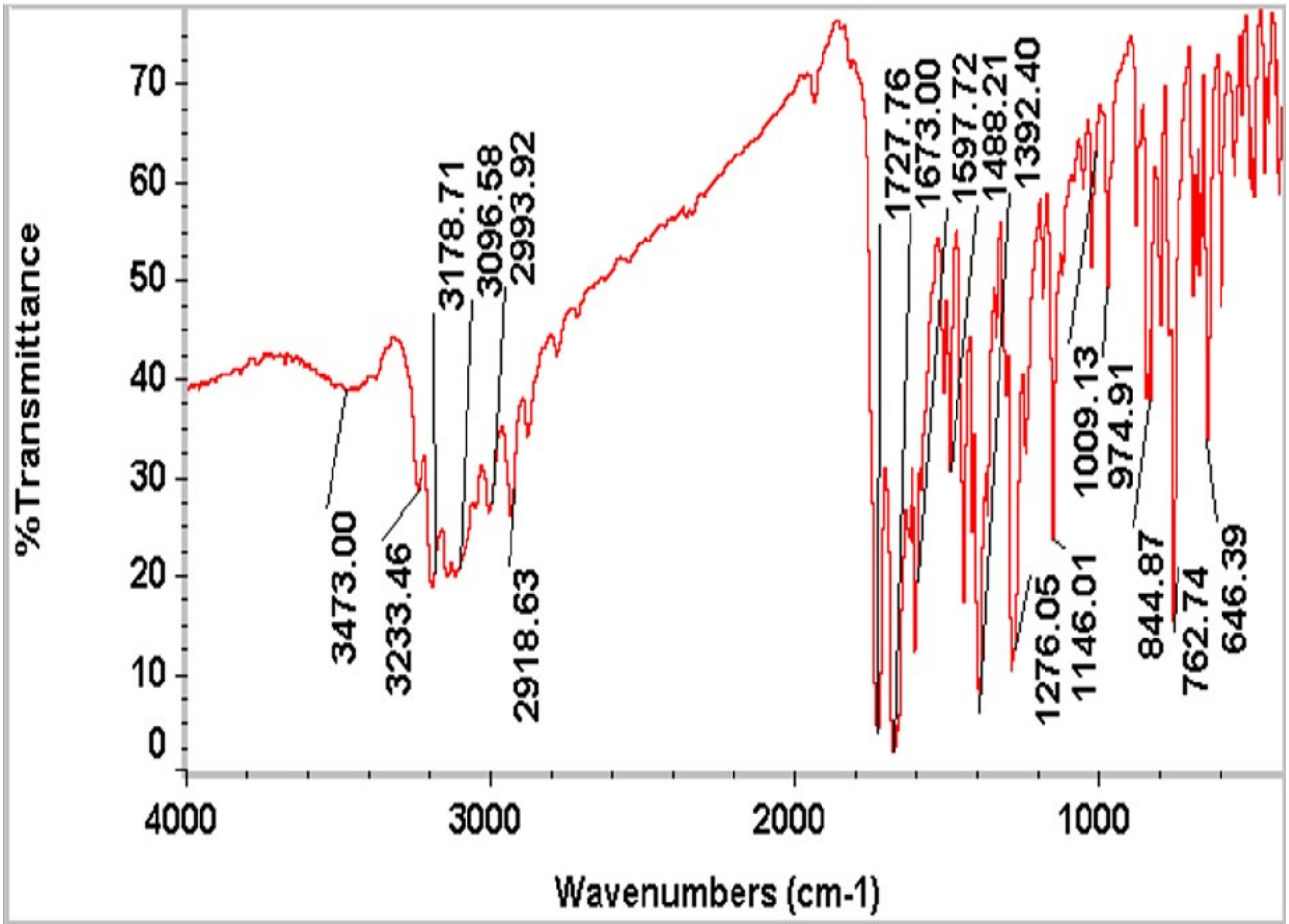


Figure S9. FT-IR spectrum of compound 3

Figure S10. [1]HNMR spectrum of compound 3

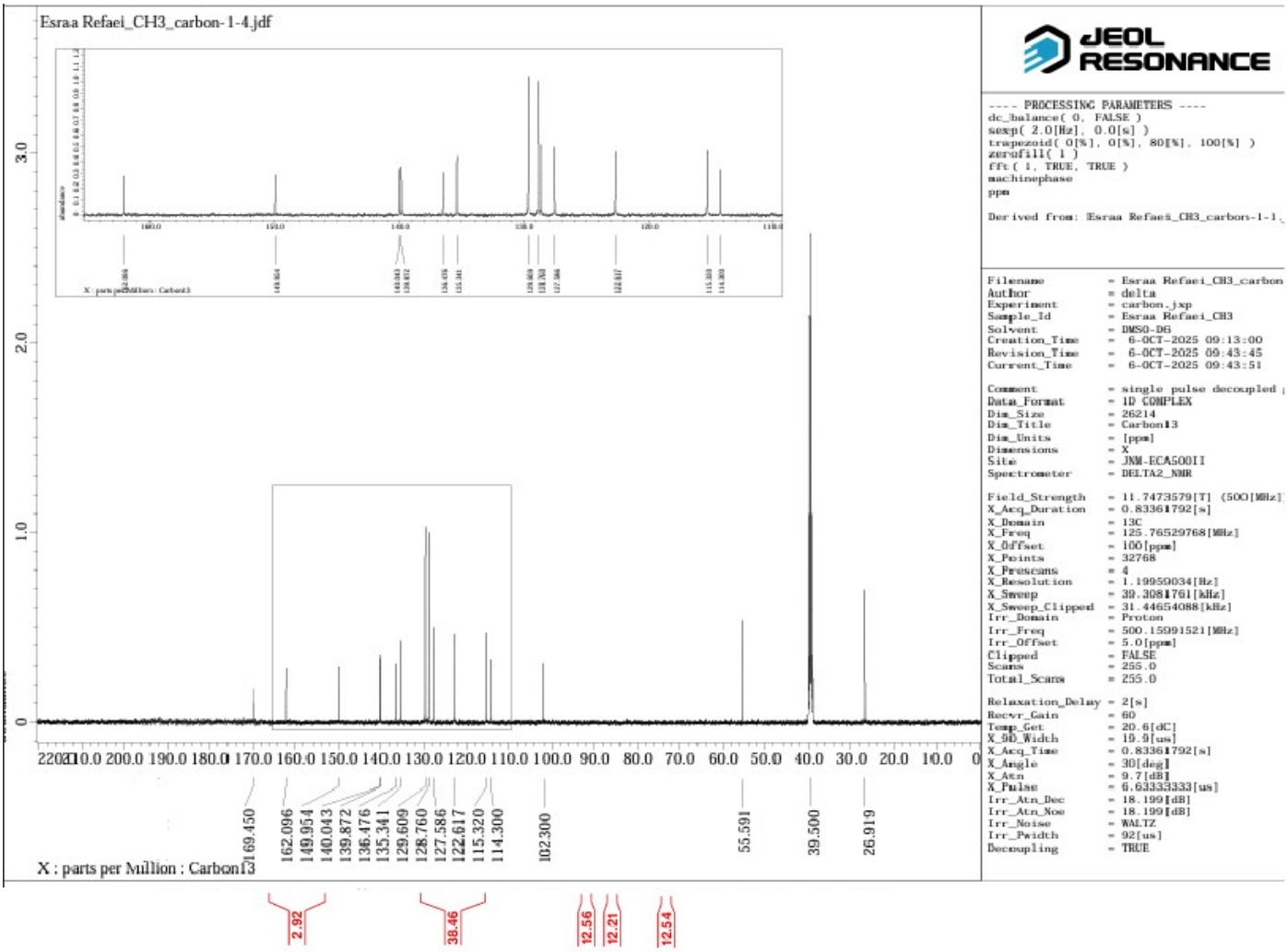
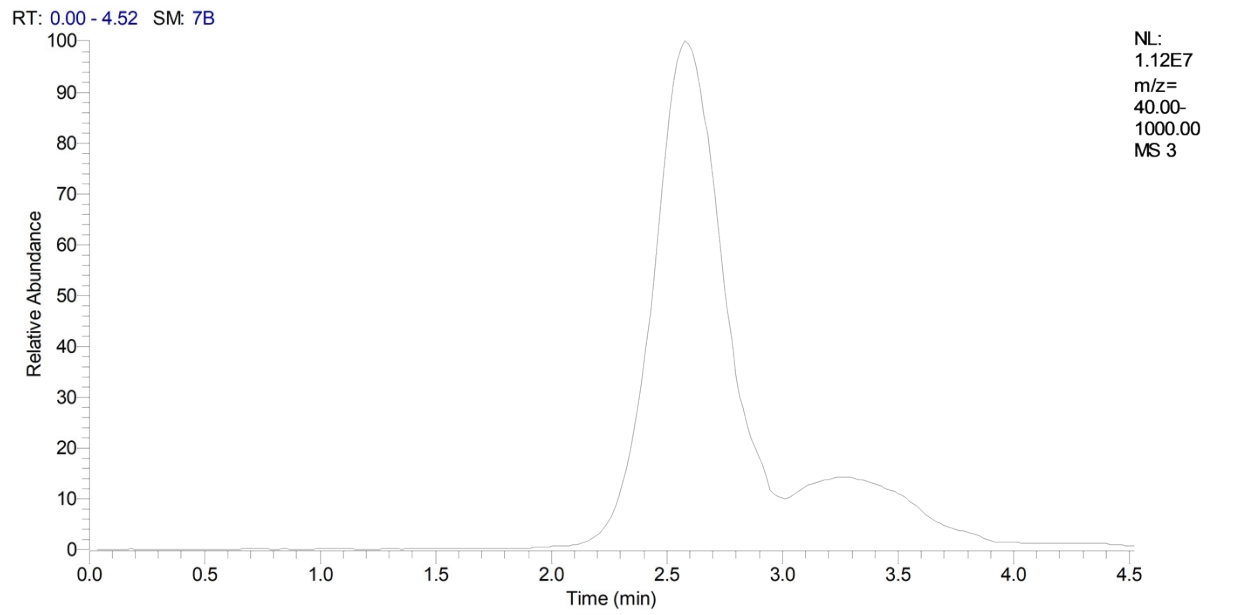


Figure S11. ^{13}CNMR spectrum of compound 3


RT: 0.00 - 4.52 SM: 7B
NL:
1.12E7
m/z=
40.00-
1000.00
MS 3
Relative Abundance
Time (min)

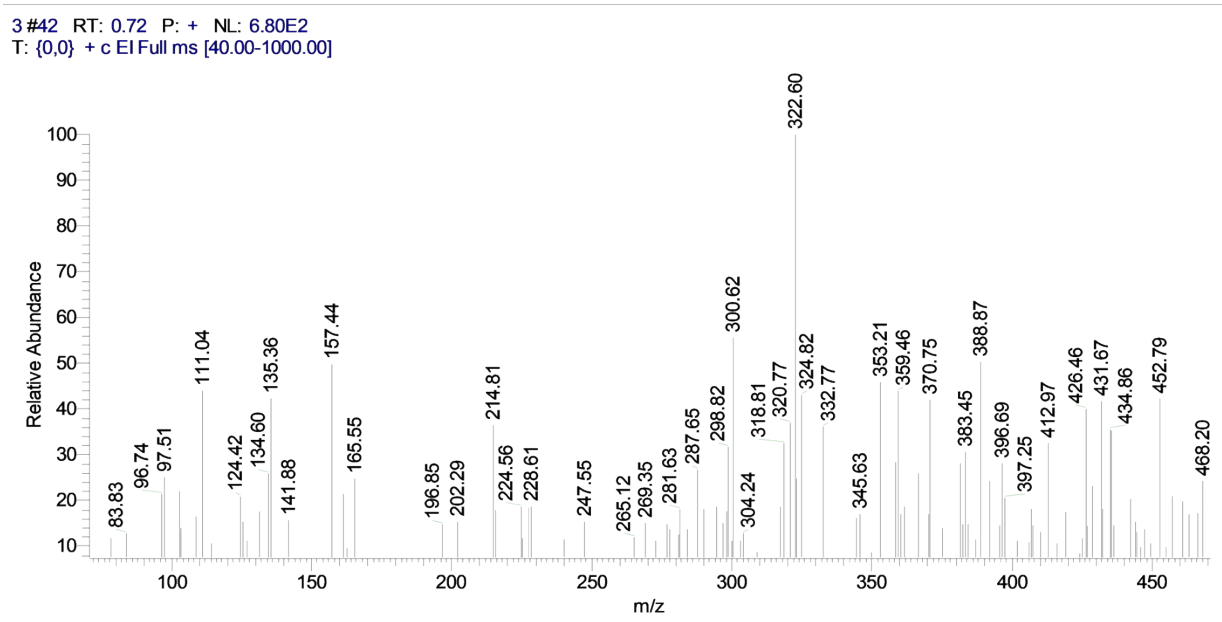

3 #42 RT: 0.72 P: + NL: 6.80E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
322.60
300.62
157.44
111.04
214.81
135.36
324.82
320.77
353.21
359.46
370.75
388.87
298.82
287.65
318.81
332.77
383.45
396.69
412.97
426.46
431.67
434.86
452.79
468.20
345.63
397.25
304.24
247.55
224.56
228.61
196.85
202.29
165.55
141.88
124.42
134.60
96.74
97.51
83.83

Figure S12. Mass spectrum of compound 3

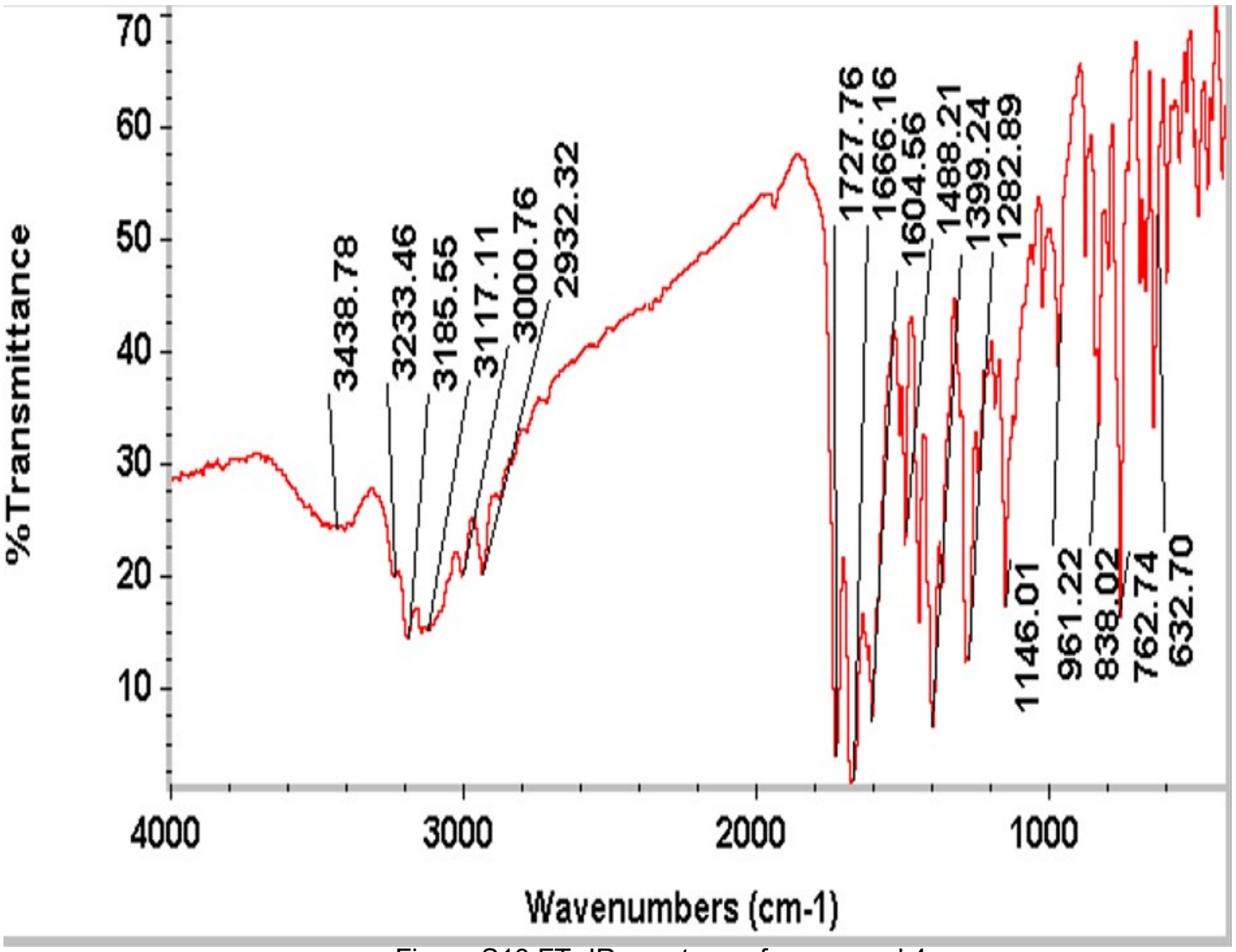


Figure S13.FT- IR spectrum of compound 4

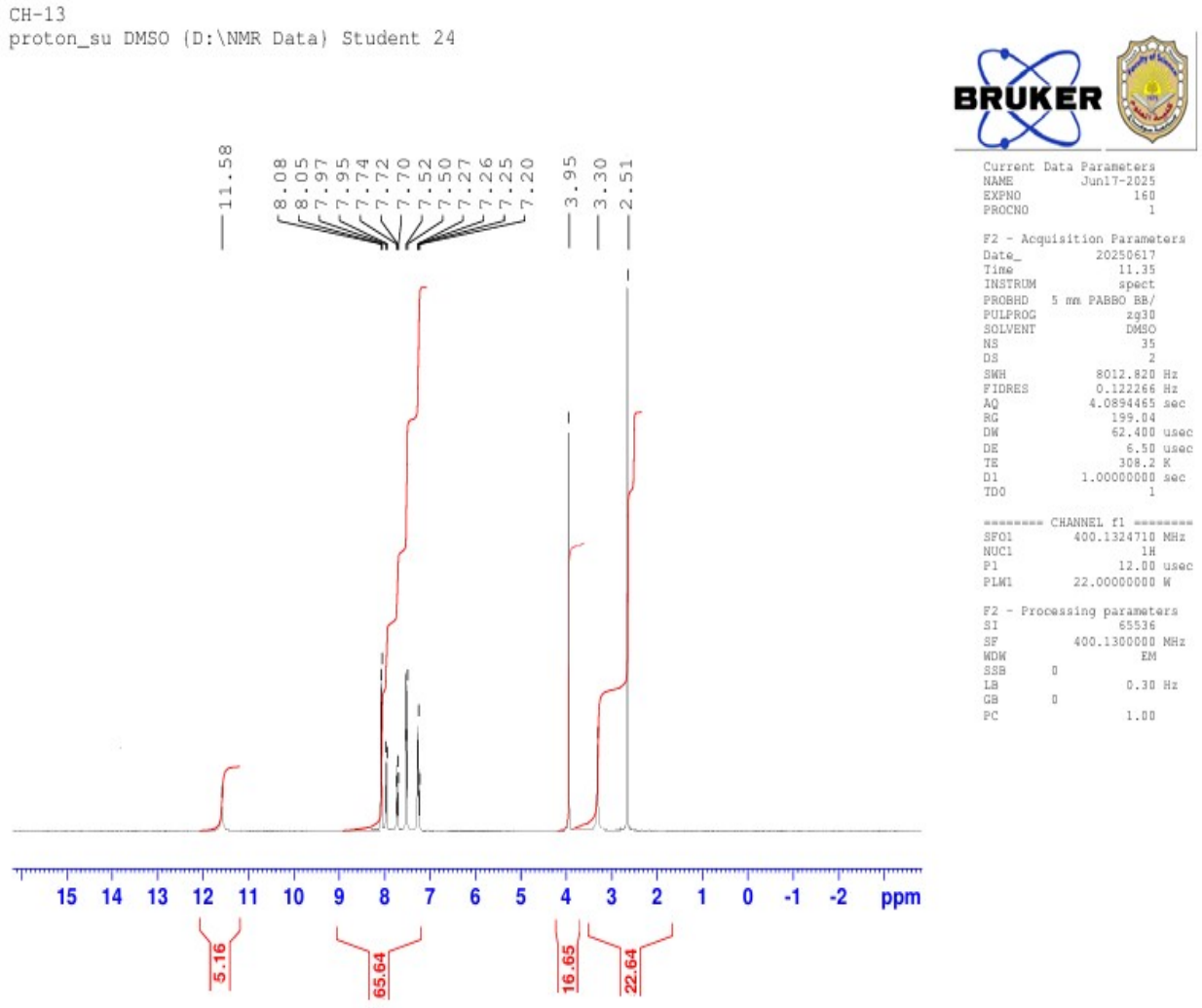


Figure S14. ^{1}HNMR spectrum of compound 4

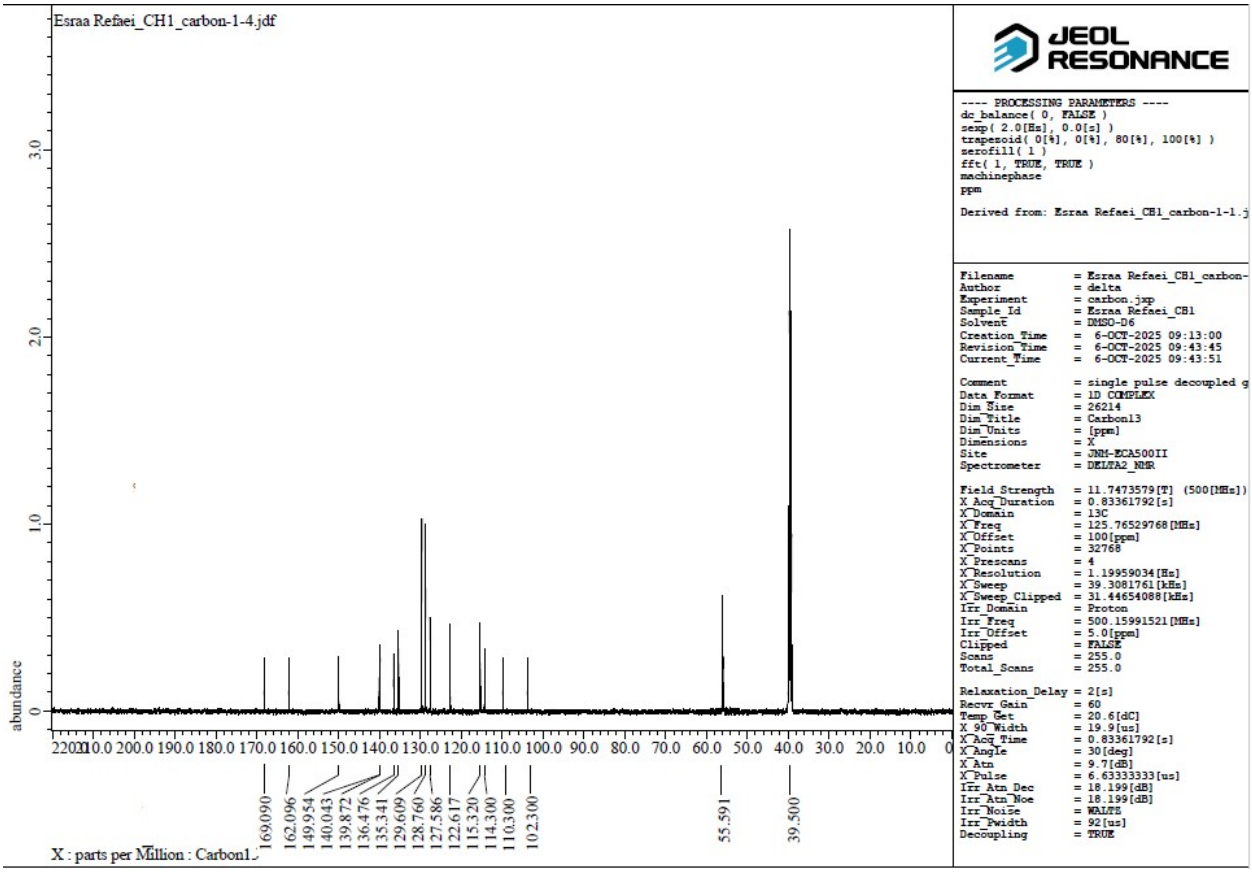
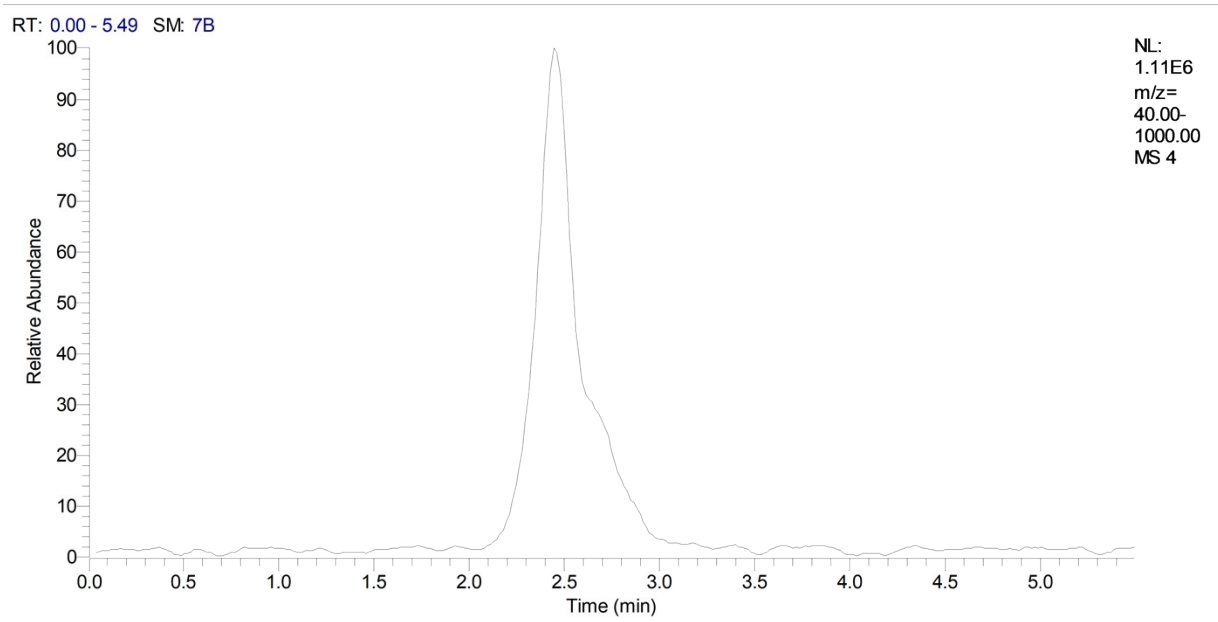


Figure S15. ^{13}CNMR spectrum of compound 4


RT: 0.00 - 5.49 SM: 7B
NL:
1.11E6
m/z=
40.00-
1000.00
MS 4
Relative Abundance
Time (min)

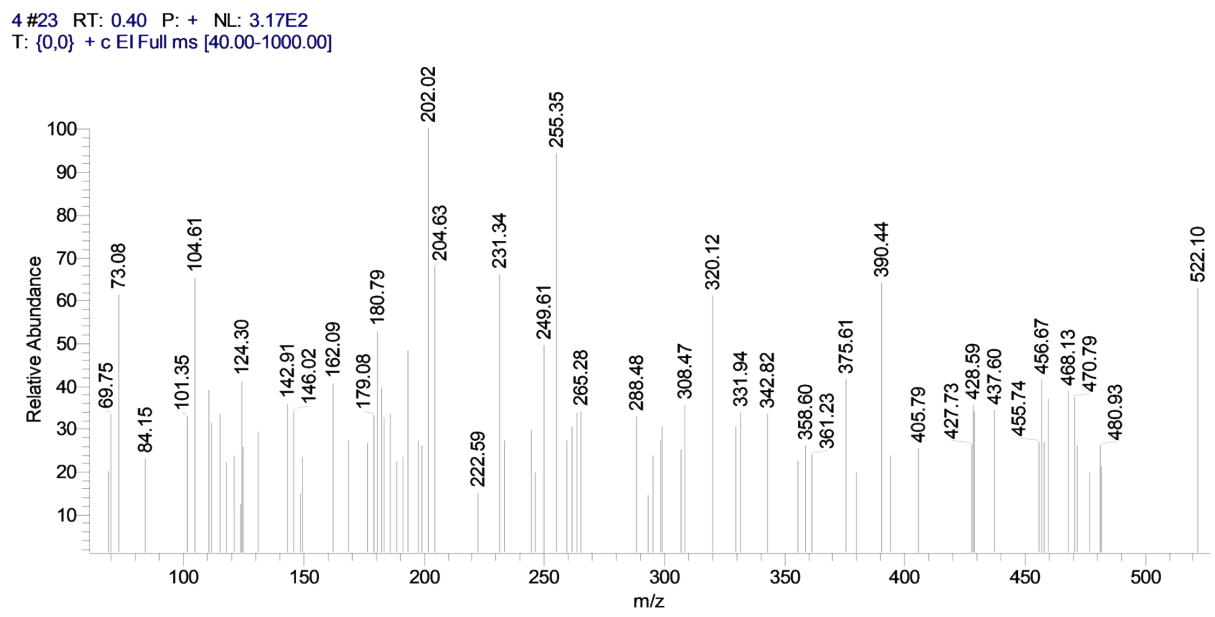
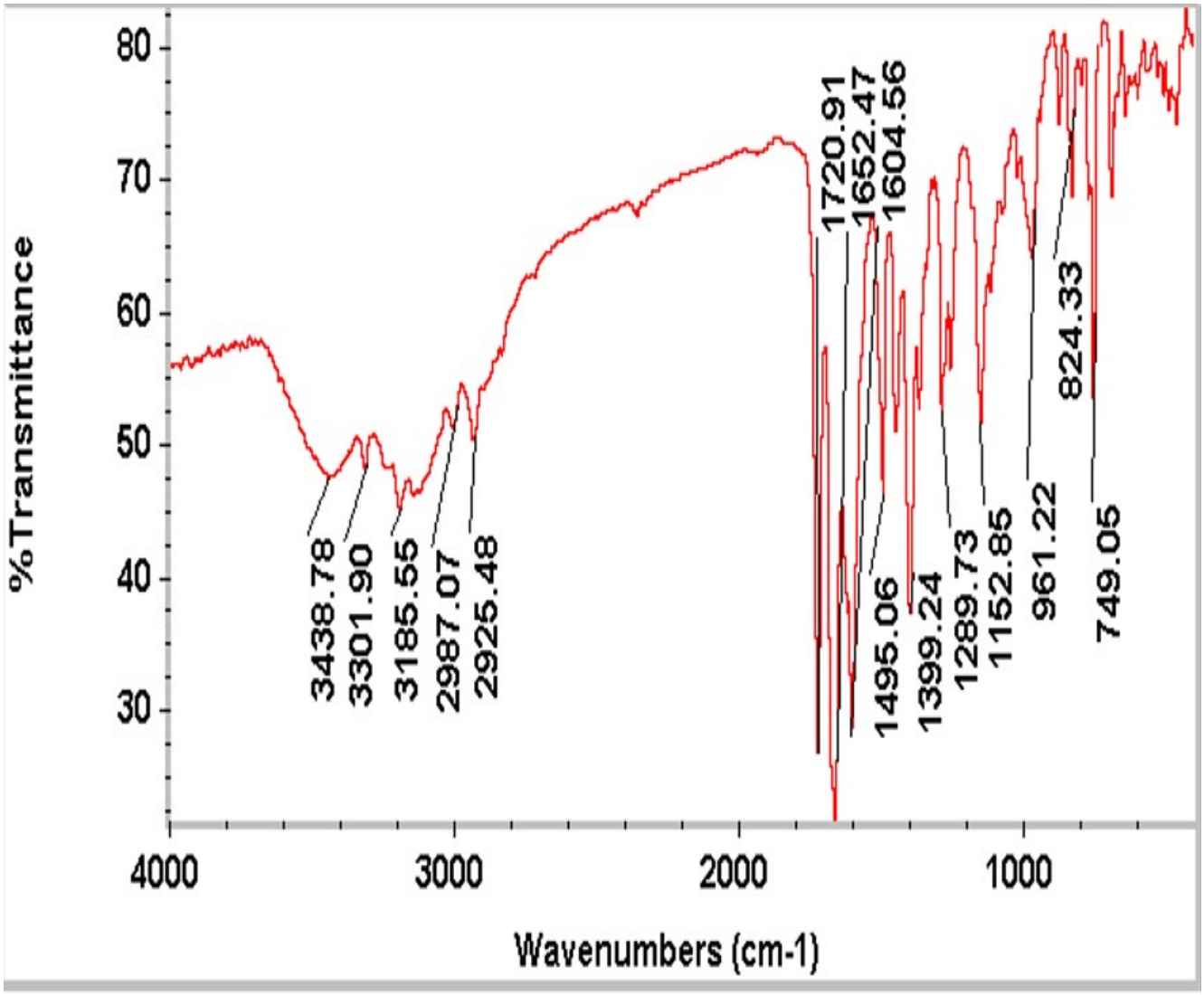

4 #23 RT: 0.40 P: + NL: 3.17E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
69.75
73.08
84.15
101.35
104.61
124.30
142.91
146.02
162.09
179.08
180.79
202.02
204.63
222.59
231.34
249.61
255.35
265.28
288.48
308.47
320.12
331.94
342.82
358.60
361.23
375.61
390.44
405.79
427.73
428.59
437.60
455.74
456.67
468.13
470.79
480.93
522.10

Figure S16. Mass spectrum of compound 4

Figure S17.FT- IR spectrum of compound 5



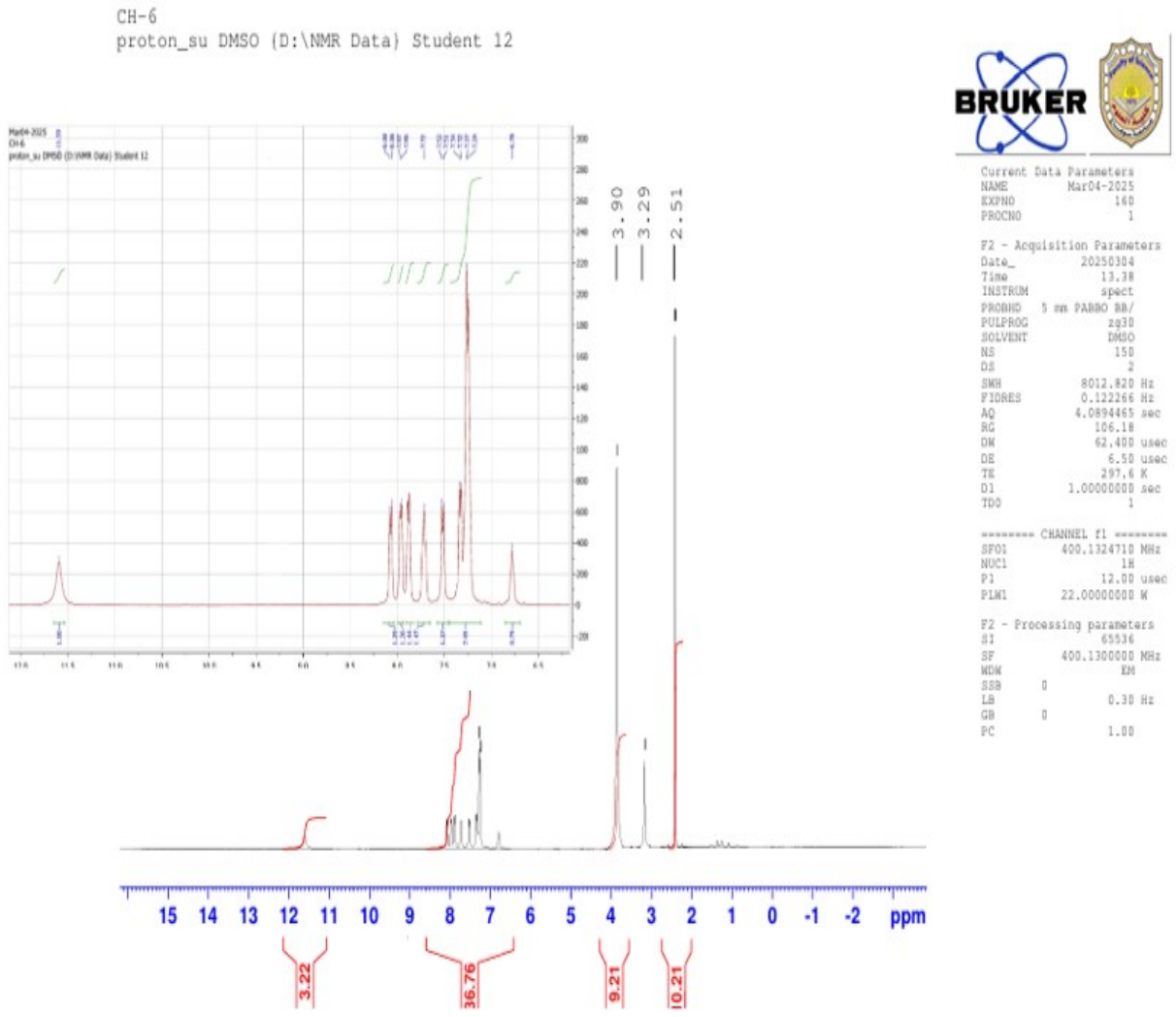


Figure S18. ^{1}HNMR spectrum of compound 5

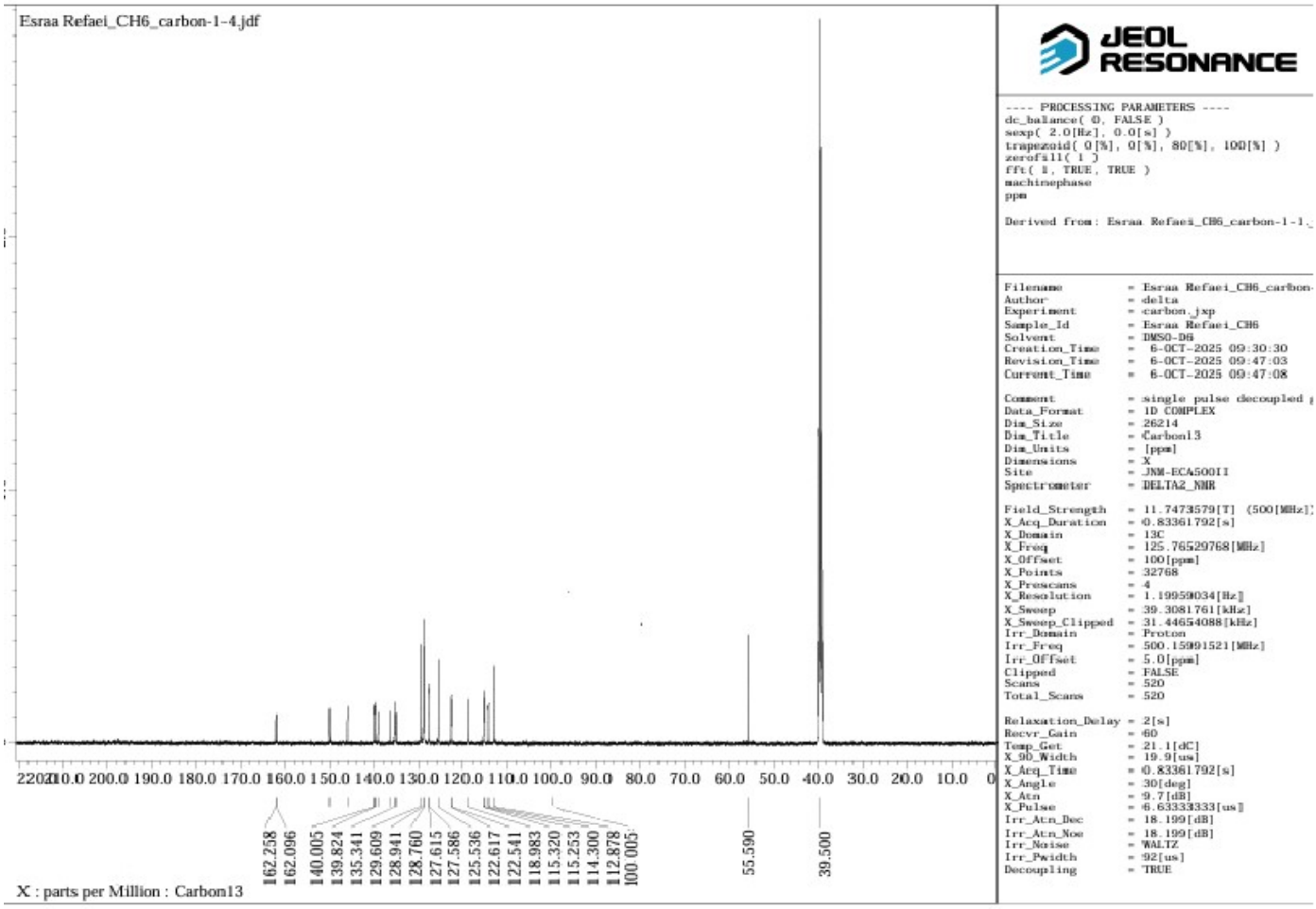


Figure S19. ^{13}CNMR spectrum of compound 5

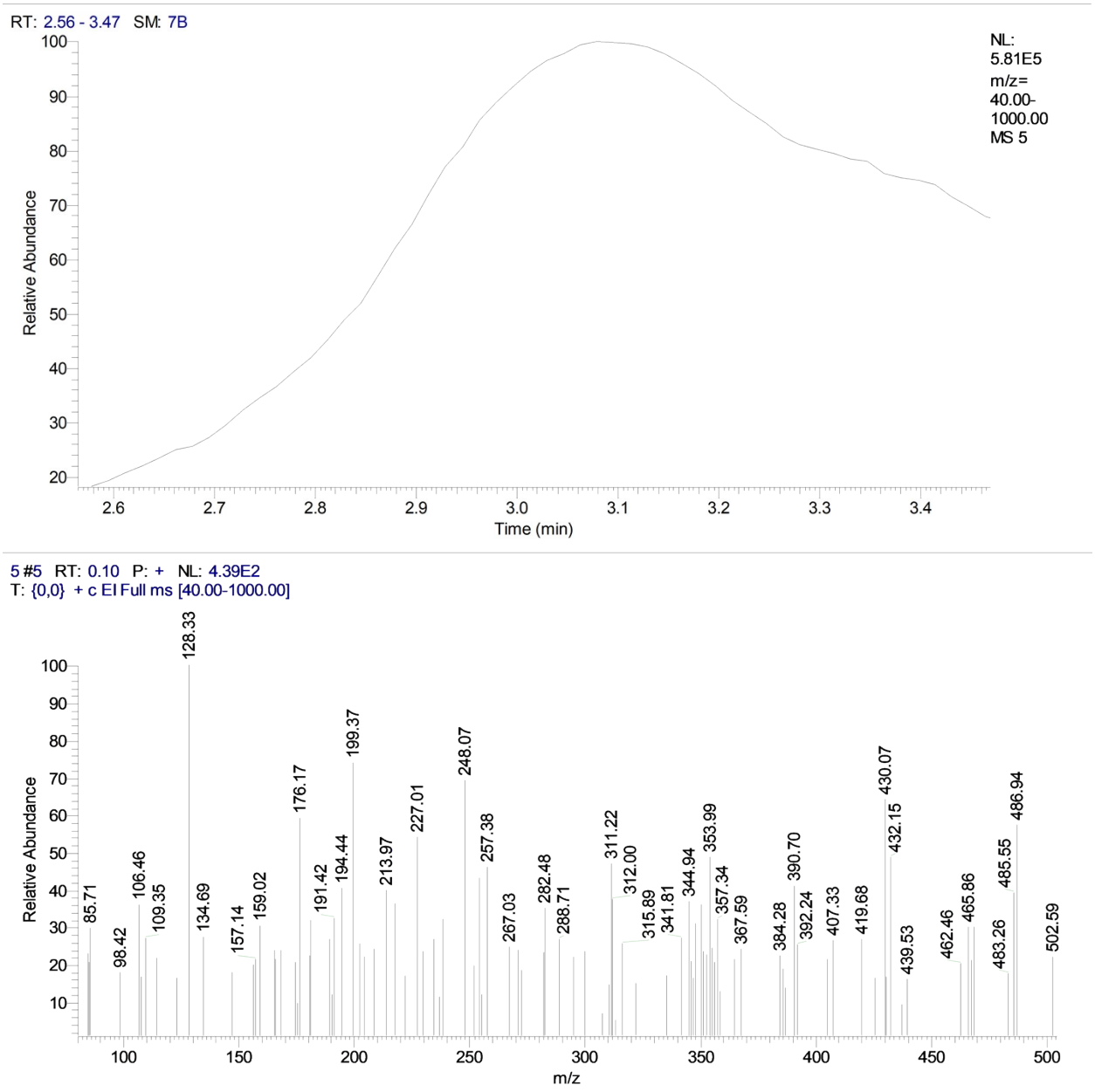


Figure S20. Mass spectrum of compound 5

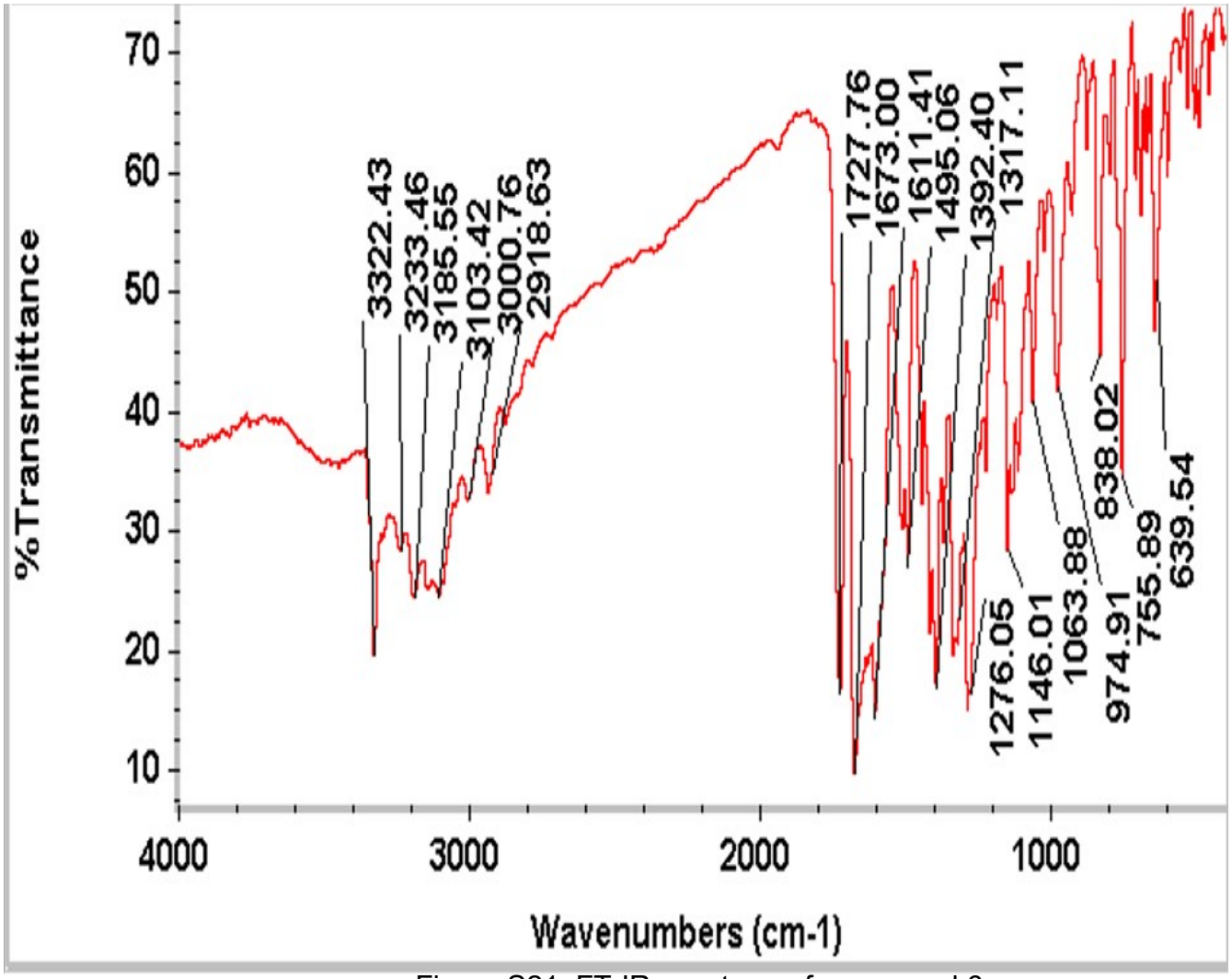


Figure S21. FT-IR spectrum of compound 6

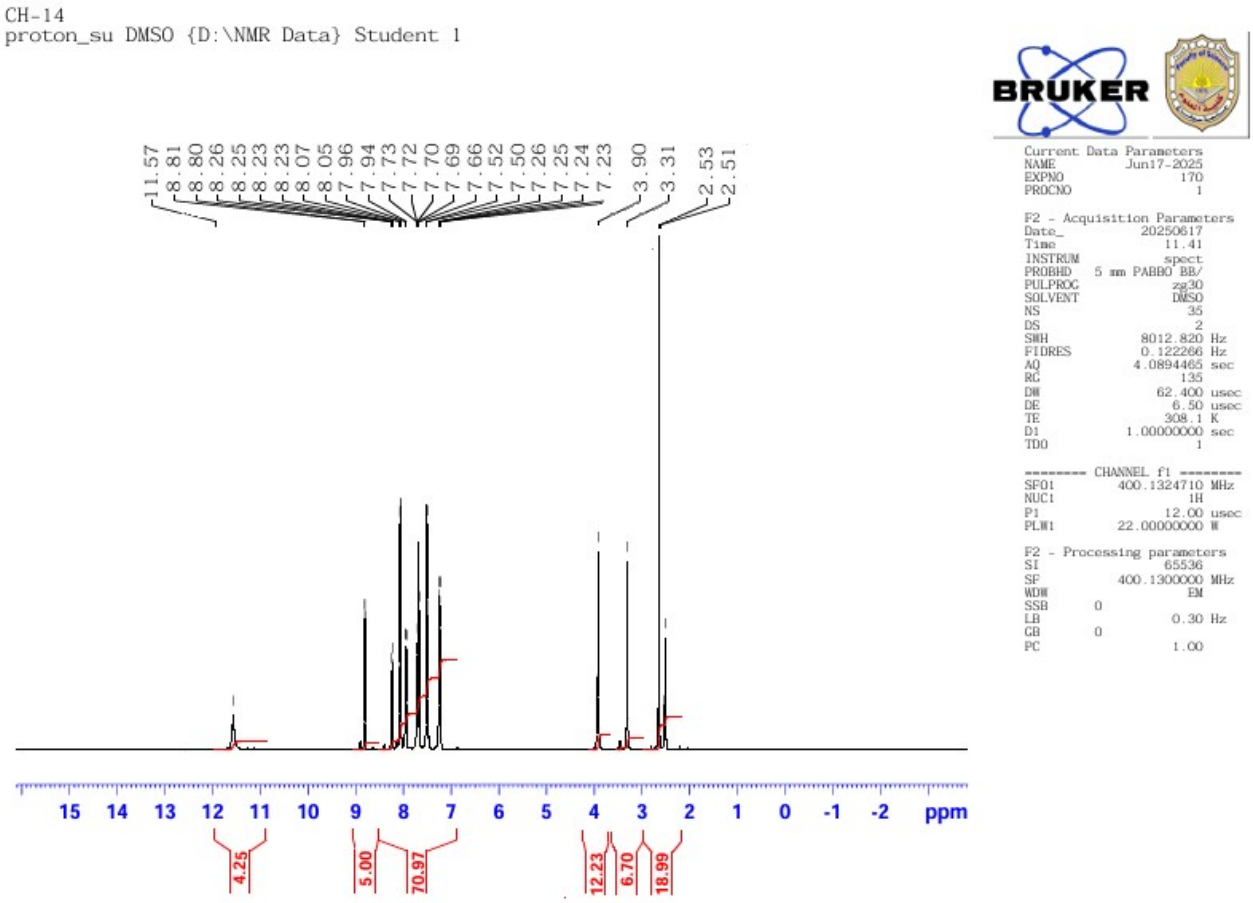


Figure S22. ^{1}HNMR spectrum of compound 6

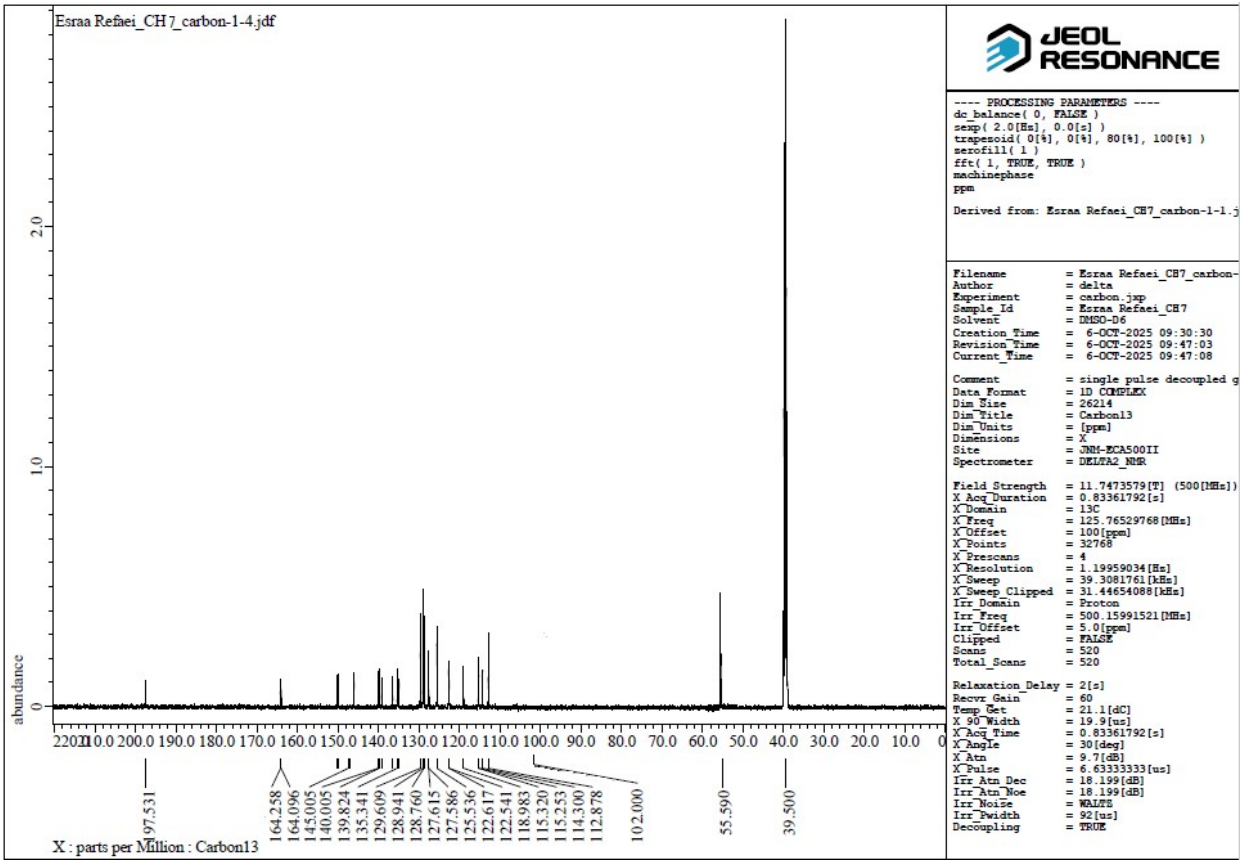


Figure S23. ^{13}CNMR spectrum of compound 6

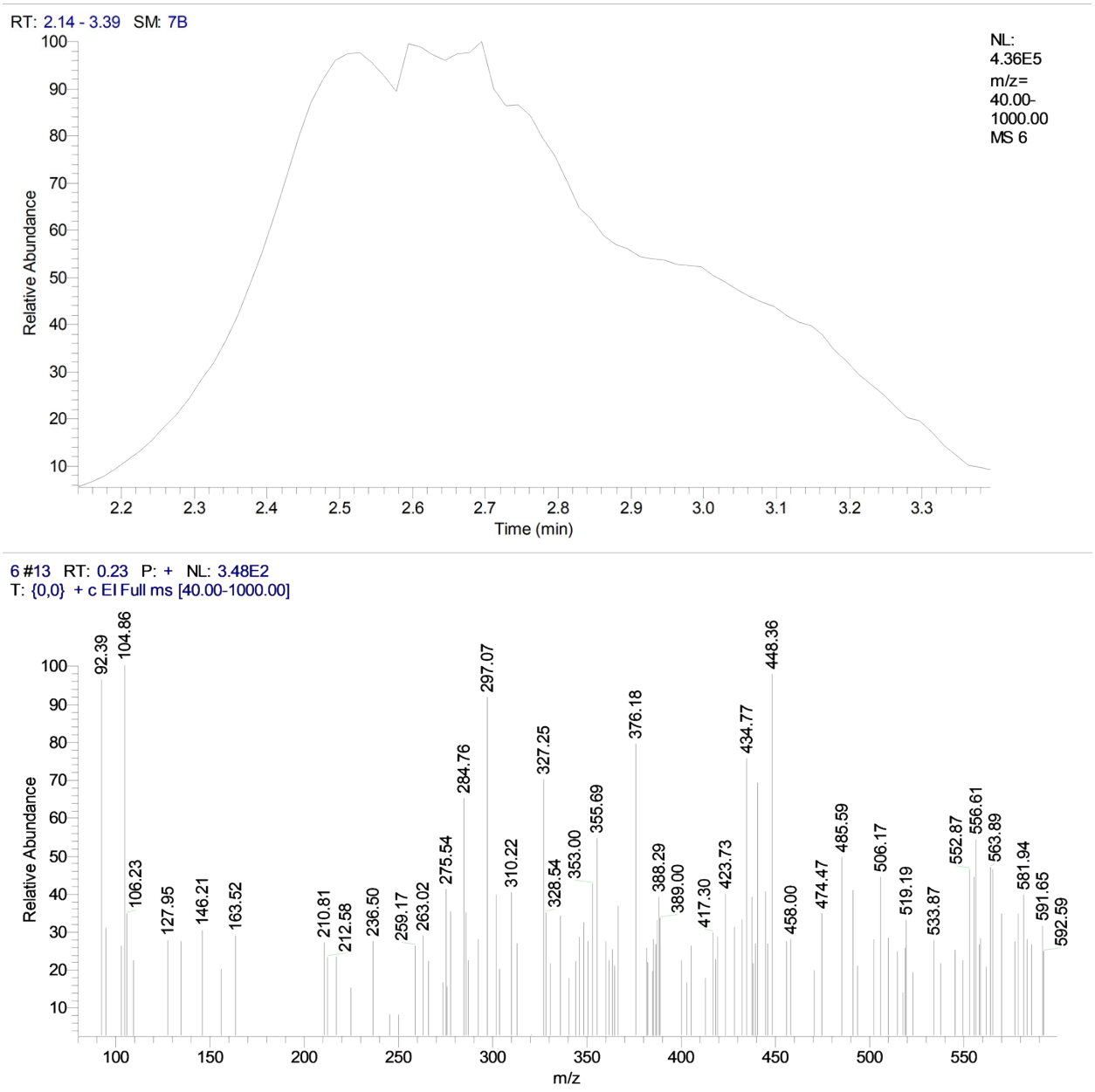


Figure S24. Mass spectrum of compound 6

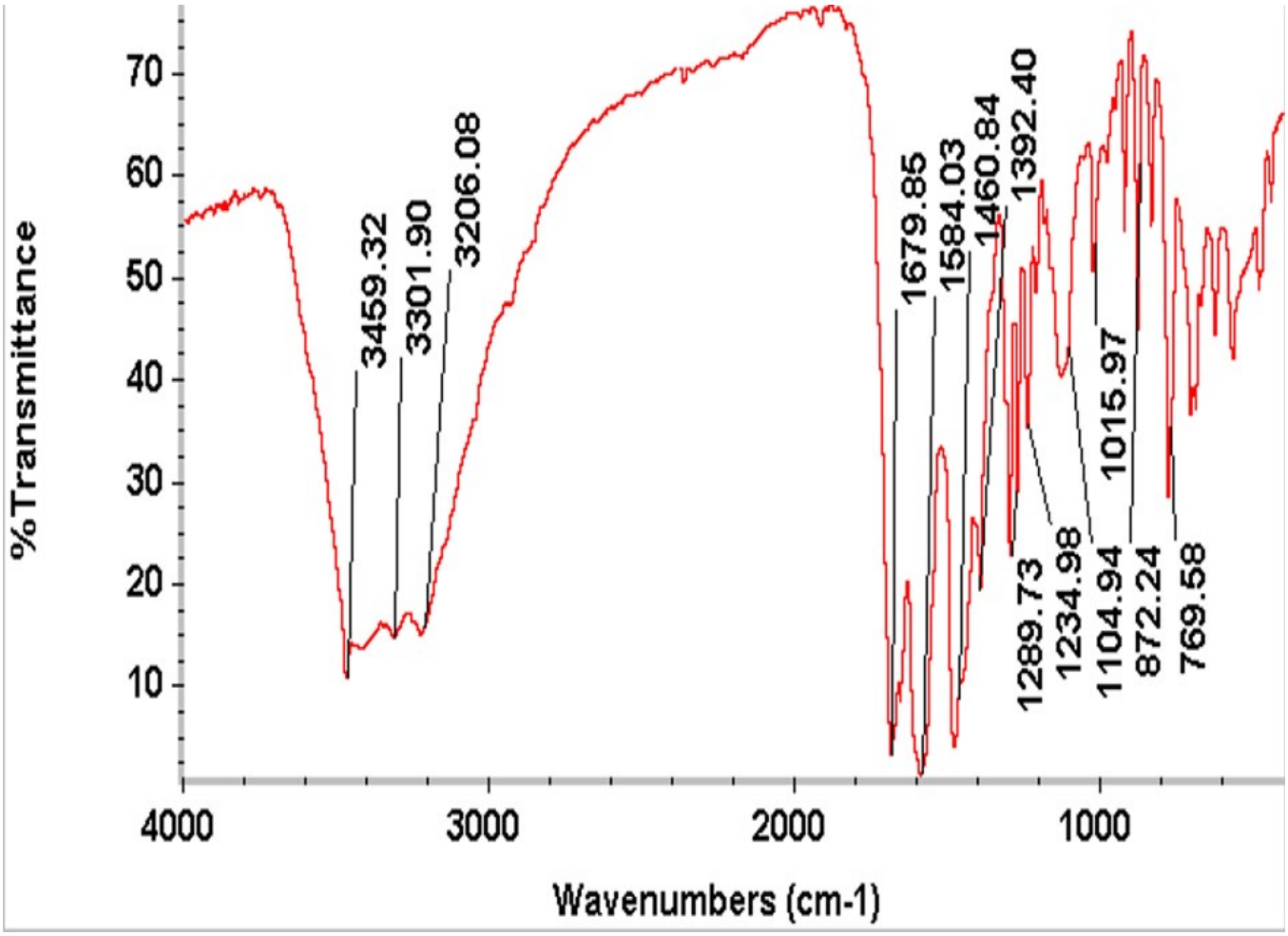


Figure S25.FT- IR spectrum of compound 7

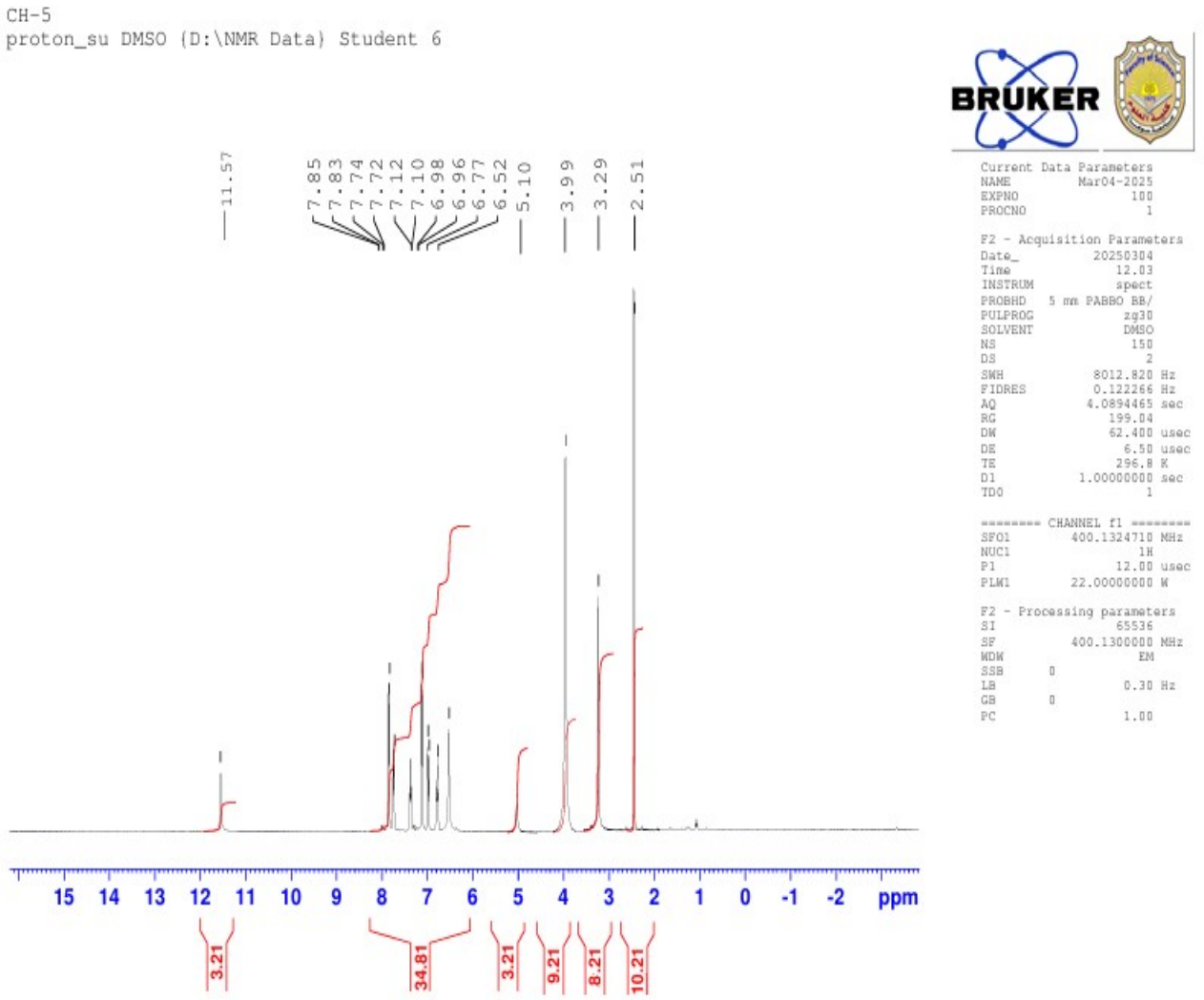


Figure S26. [1]HNMR spectrum of compound 7

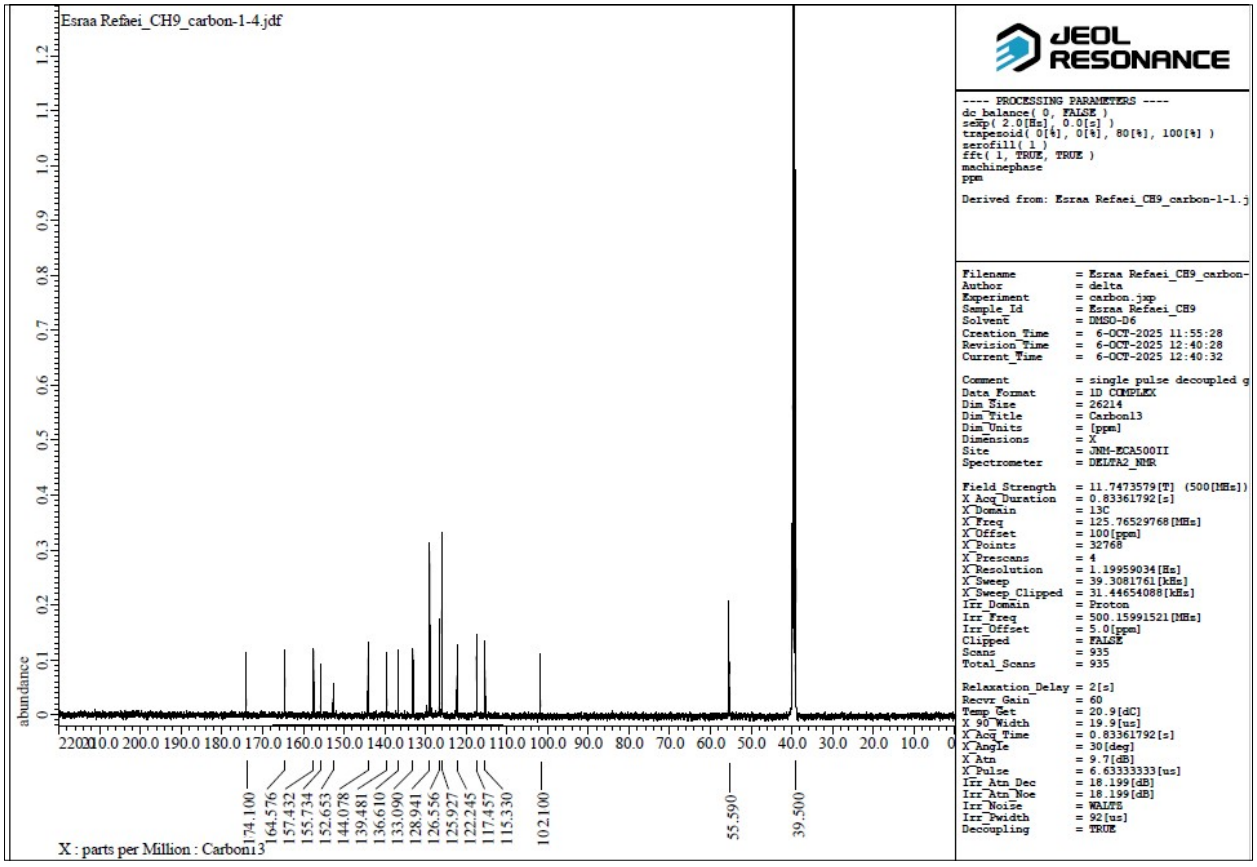
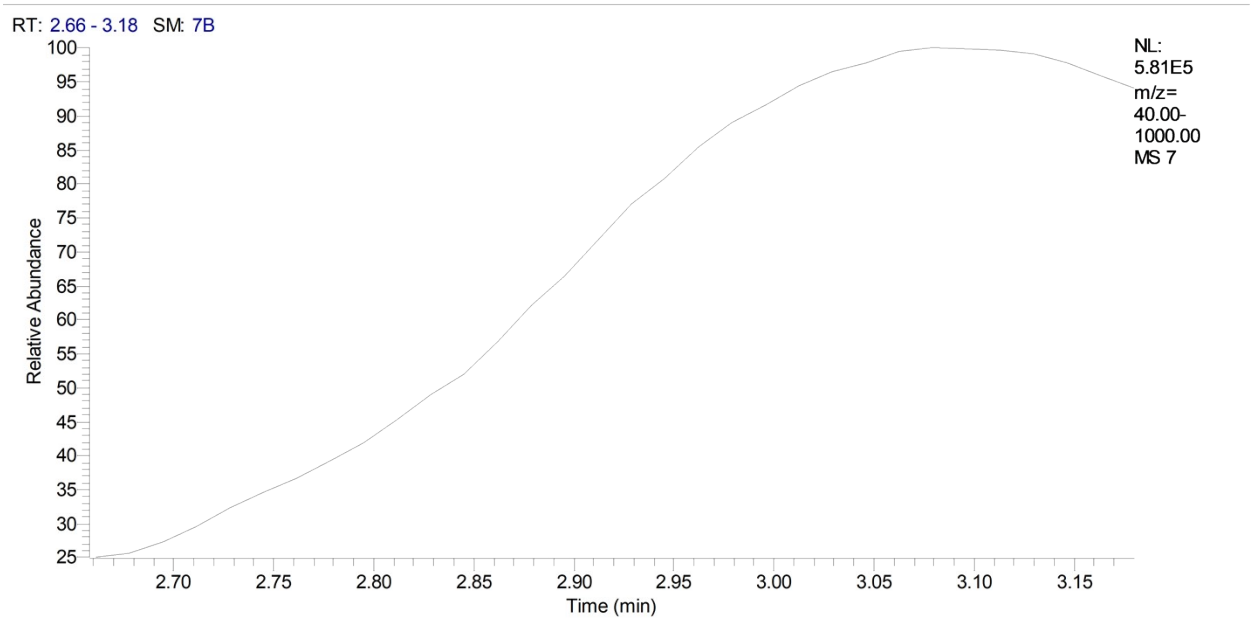


Figure S27. ^{13}CNMR spectrum of compound 7



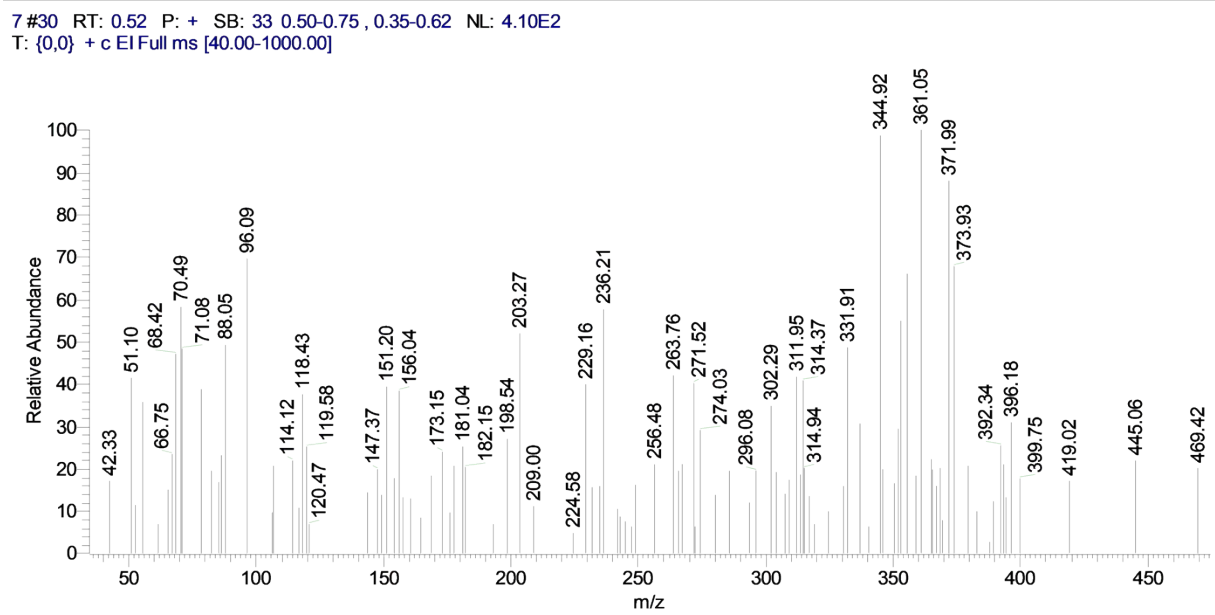


Figure S28. Mass spectrum of compound 7

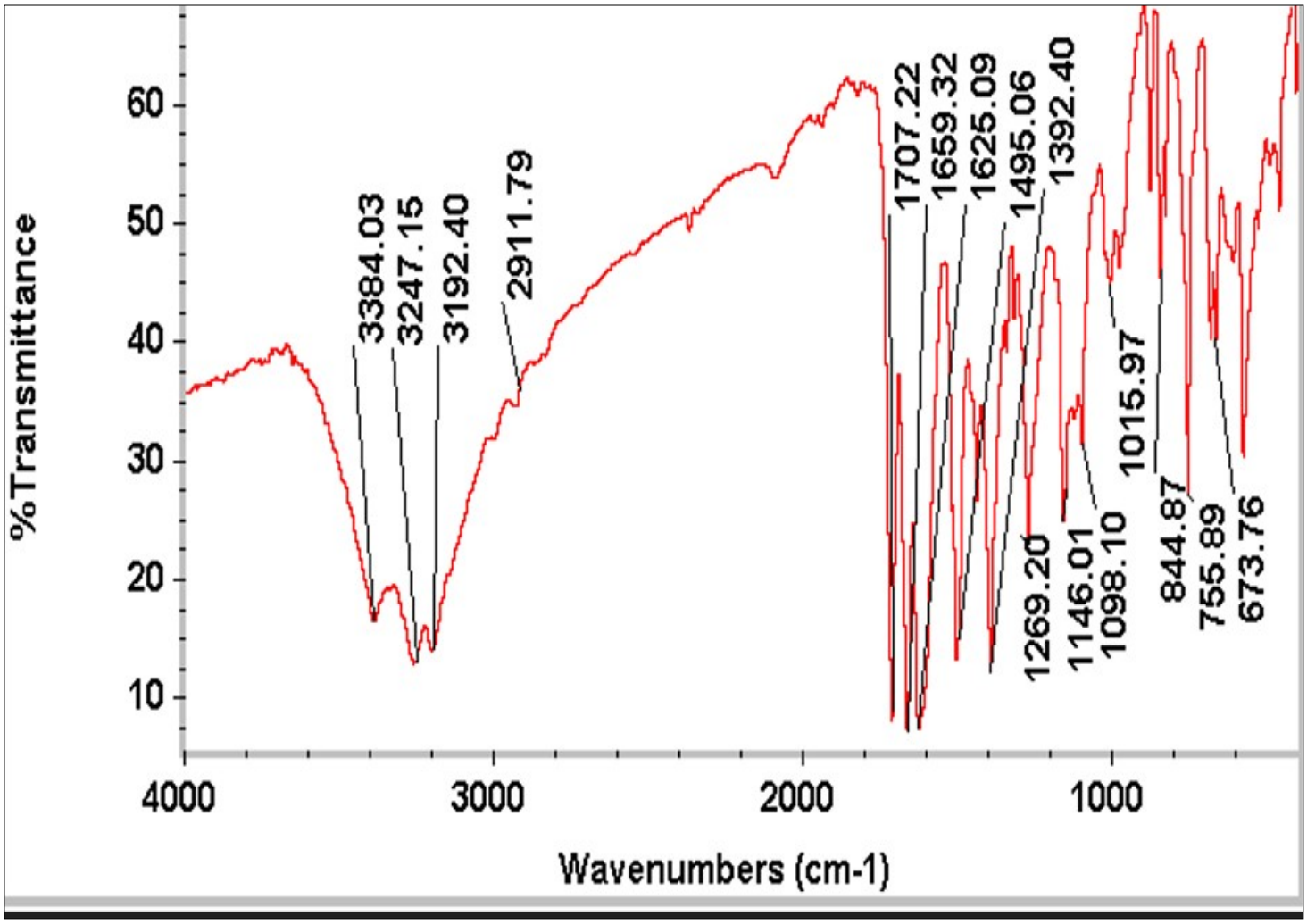


Figure S29.FT- IR spectrum of compound 8

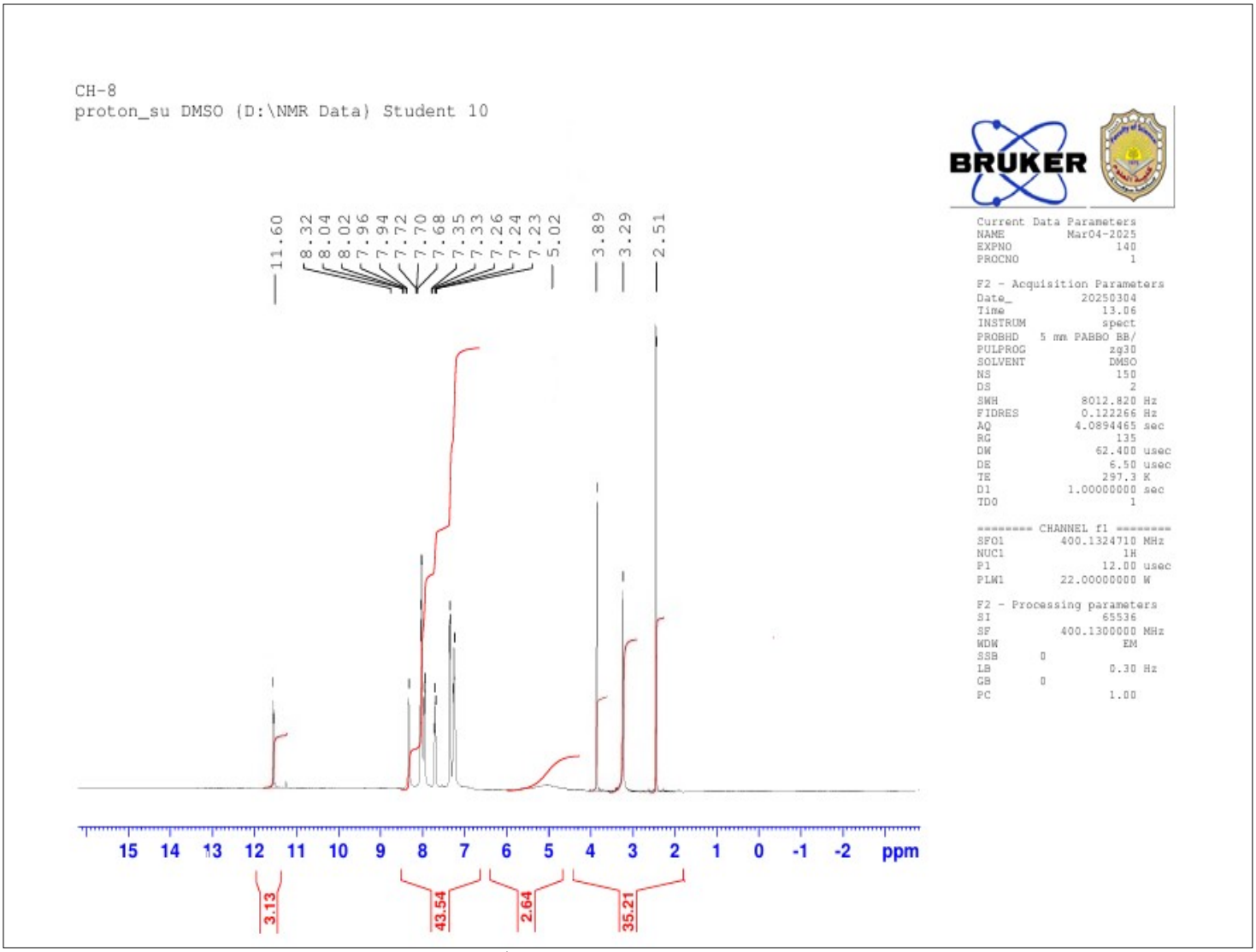


Figure S30. ^{1}HNMR spectrum of compound 8

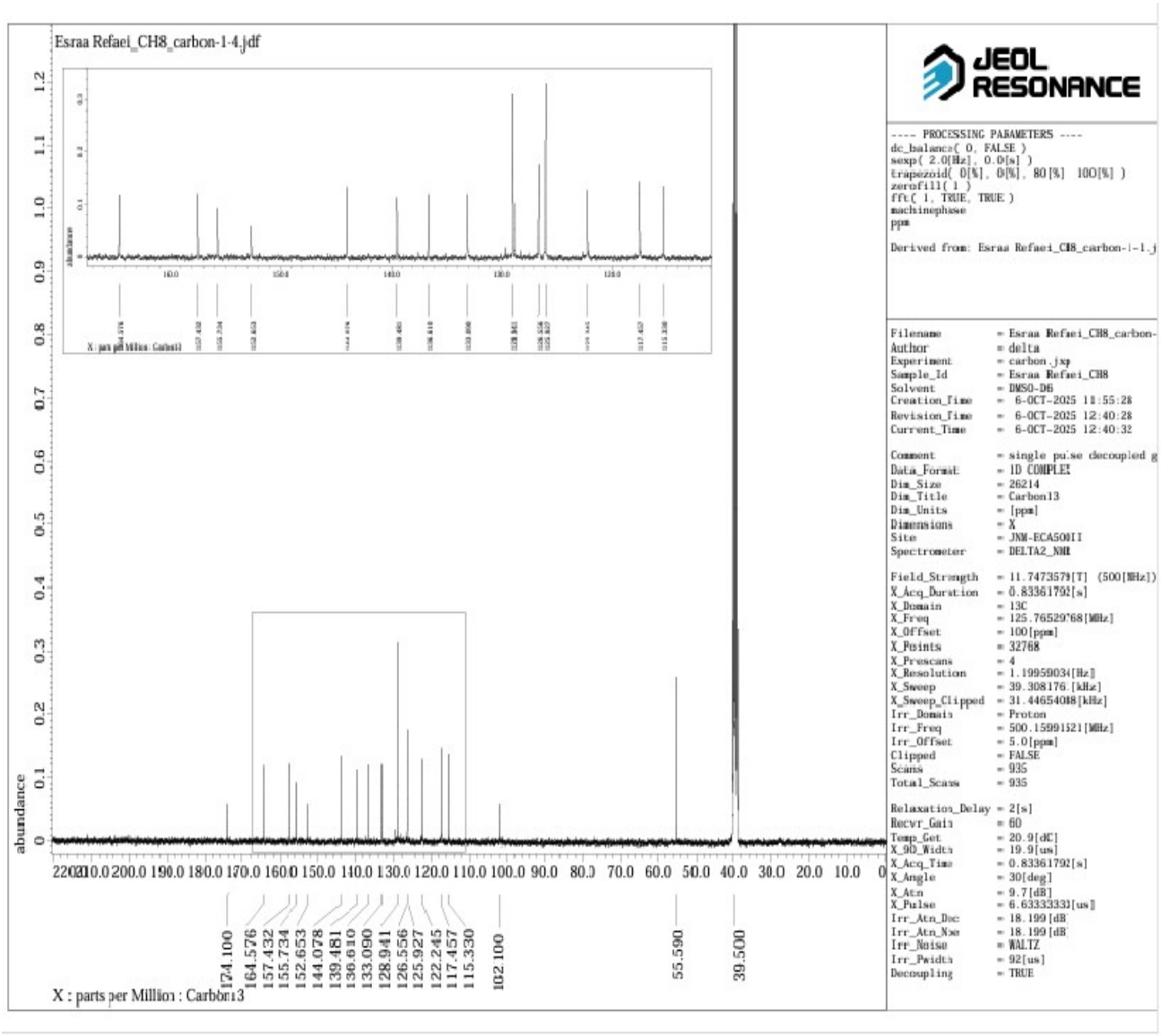
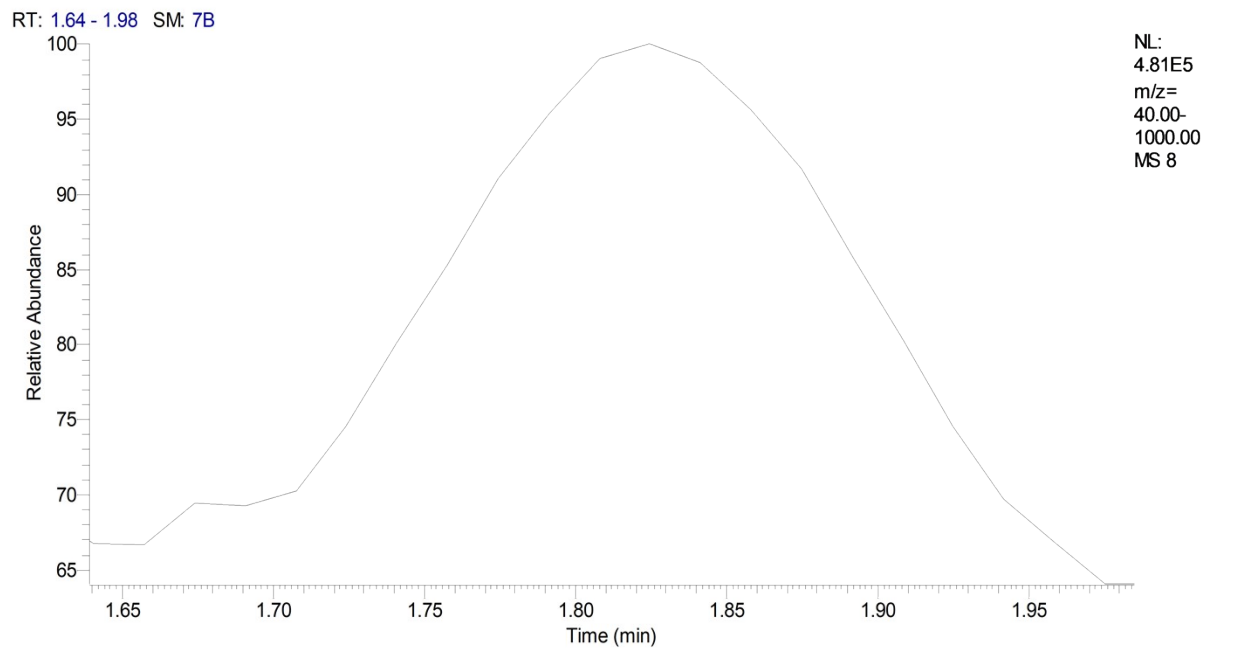
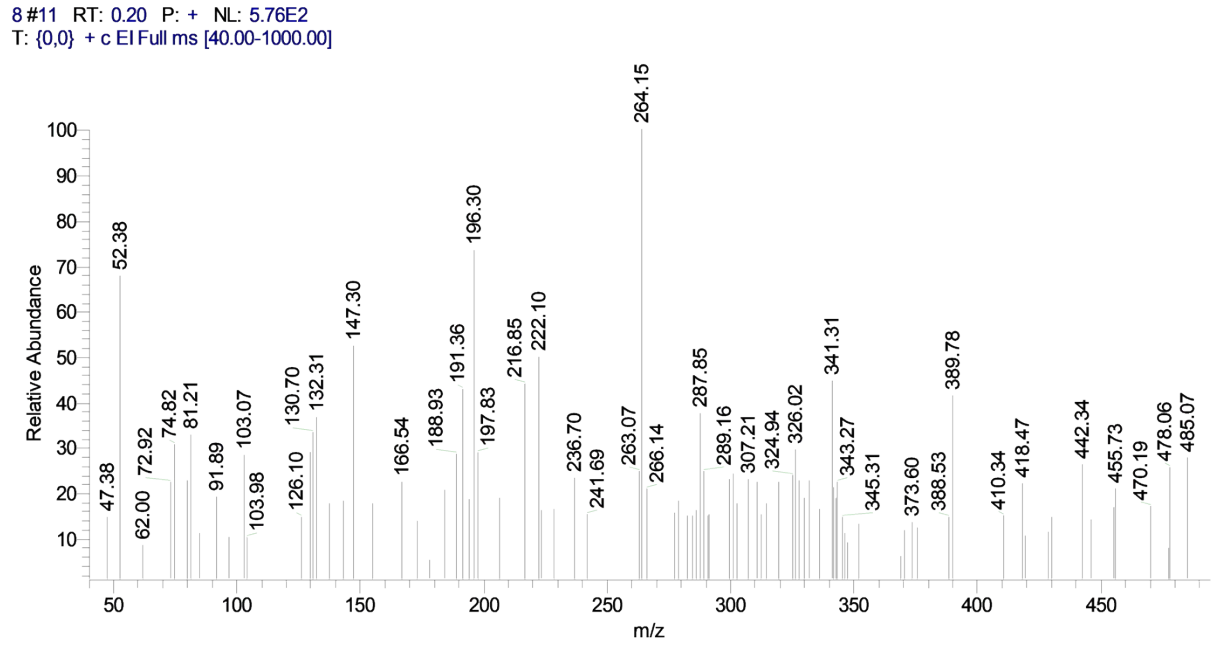


Figure S31. ^{13}CNMR spectrum of compound 8


RT: 1.64 - 1.98 SM: 7B
NL:
4.81E5
m/z=
40.00-
1000.00
MS 8
Relative Abundance
Time (min)
100
95
90
85
80
75
70
65
1.65
1.70
1.75
1.80
1.85
1.90
1.95


8 #11 RT: 0.20 P: + NL: 5.76E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
264.15
52.38
196.30
147.30
222.10
216.85
191.36
132.31
130.70
103.07
81.21
74.82
72.92
62.00
47.38
91.89
103.98
126.10
166.54
188.93
197.83
236.70
241.69
263.07
266.14
287.85
289.16
307.21
324.94
326.02
341.31
343.27
345.31
373.60
388.53
389.78
410.34
418.47
442.34
455.73
470.19
478.06
485.07
100
90
80
70
60
50
40
30
20
10
50
100
150
200
250
300
350
400
450

Figure

S32. Mass spectrum of compound 8

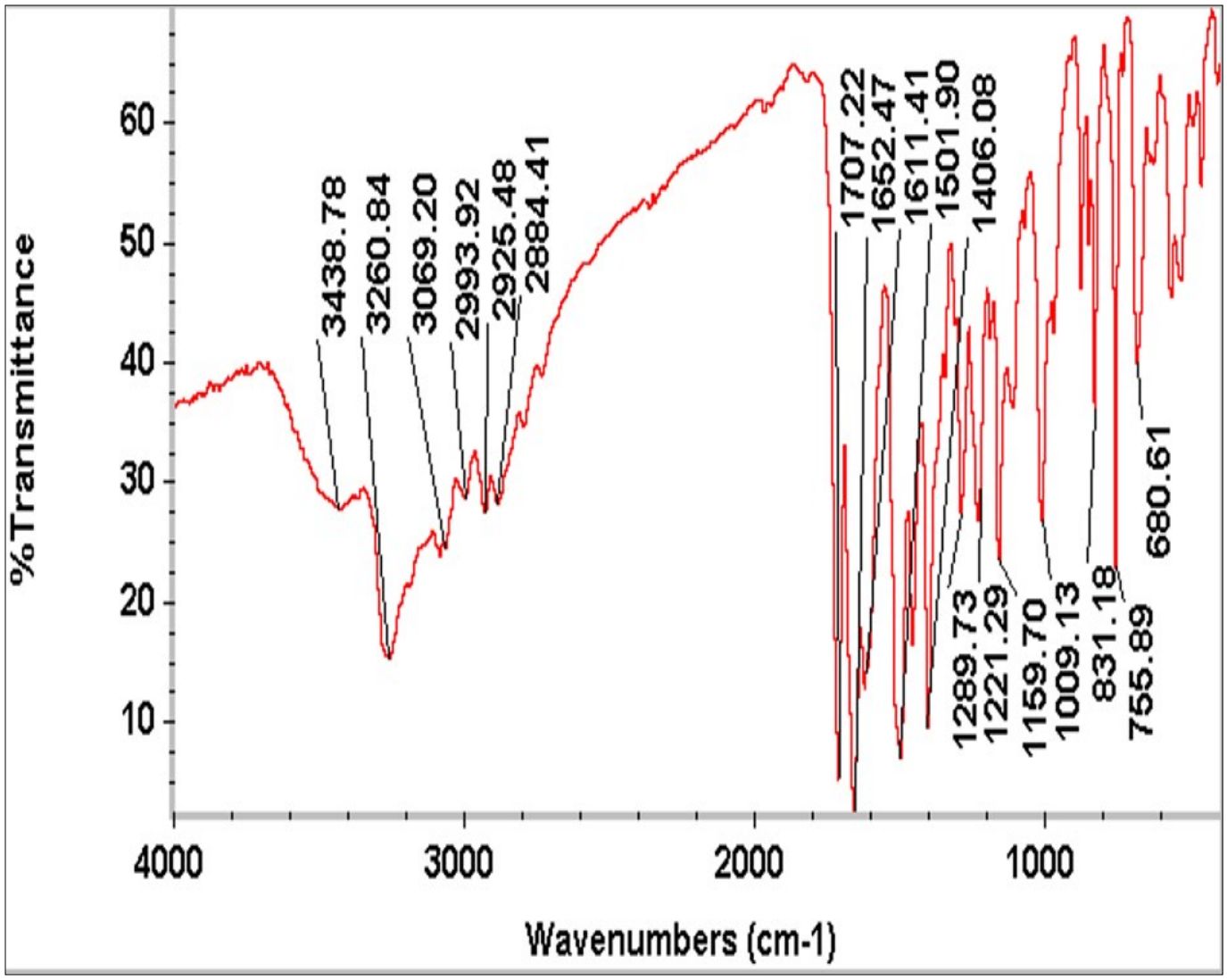


Figure S33. FT-IR spectrum of compound 9

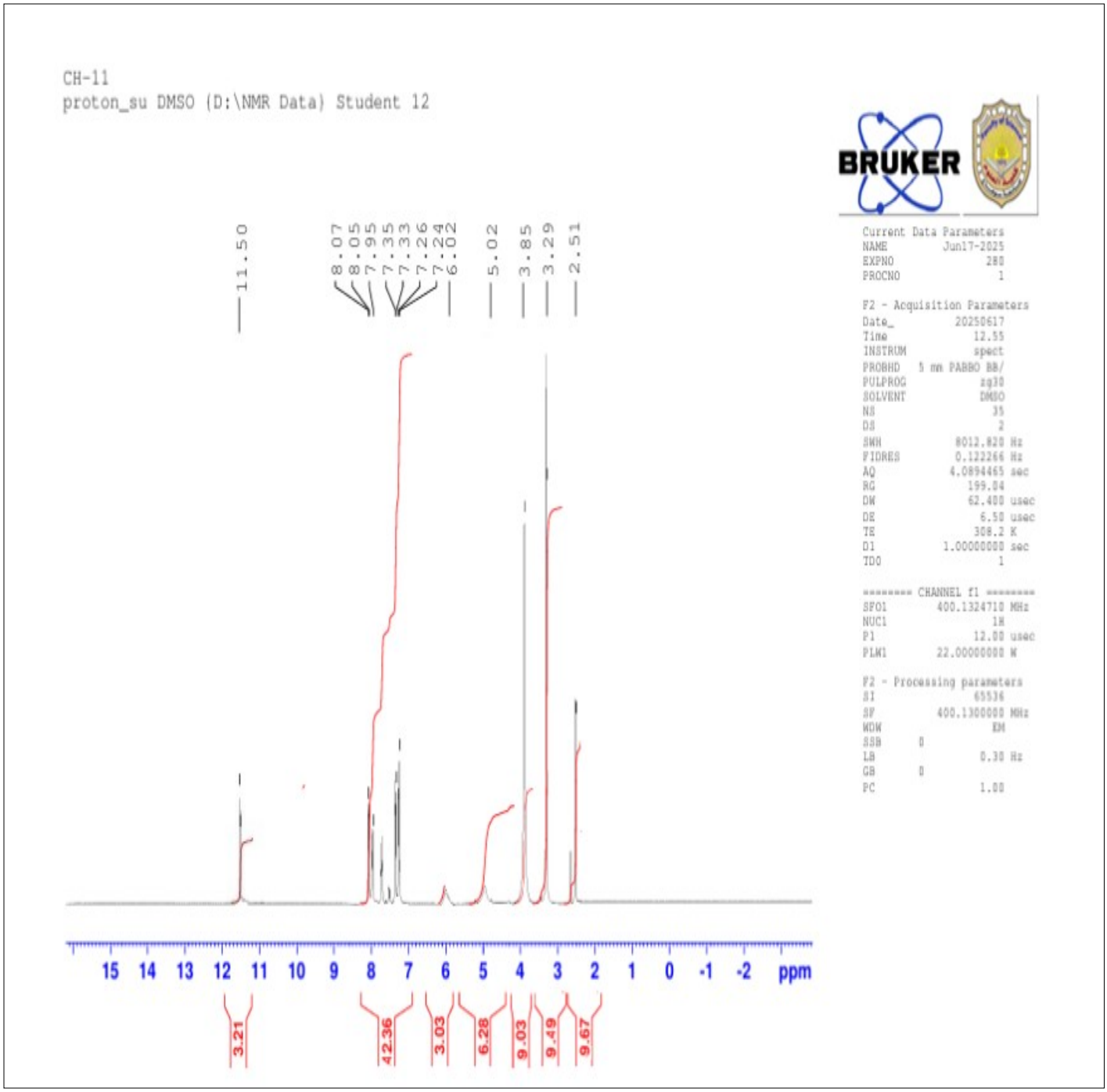
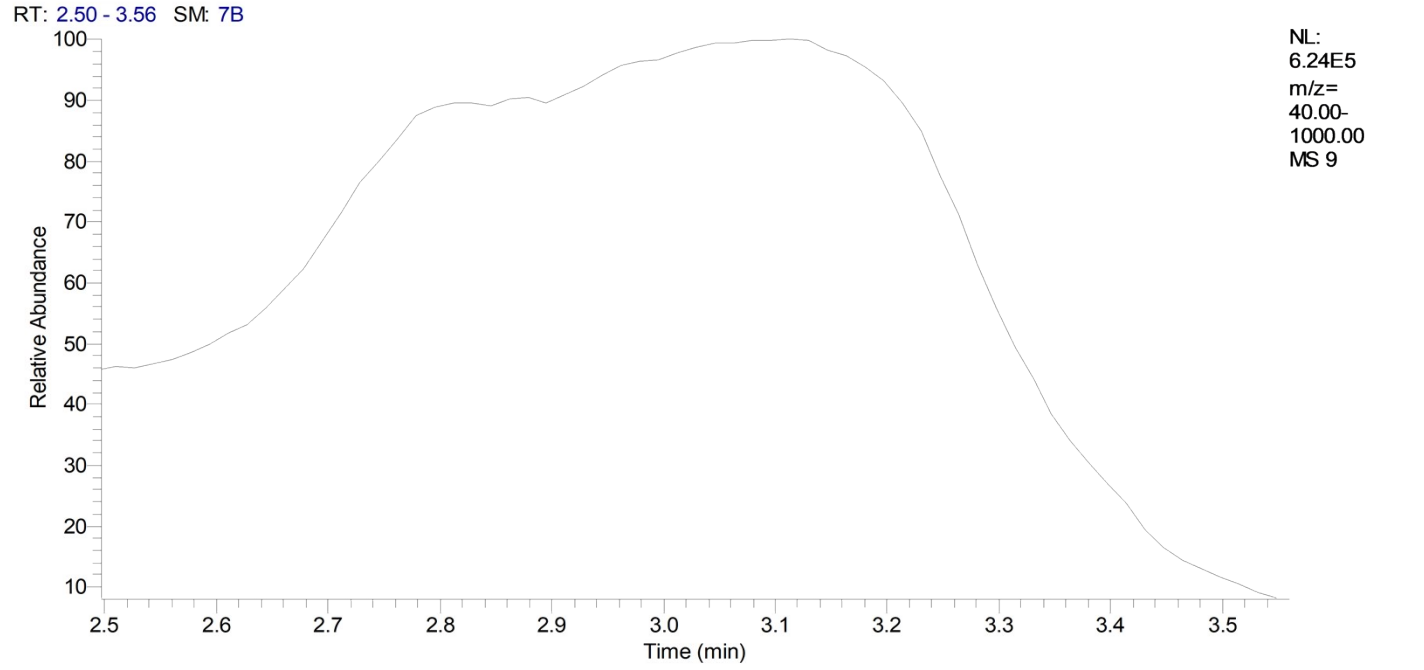


Figure S34. [1]HNMR spectrum of compound 9


RT: 2.50 - 3.56 SM: 7B
NL:
6.24E5
m/z=
40.00-
1000.00
MS 9
Relative Abundance
Time (min)

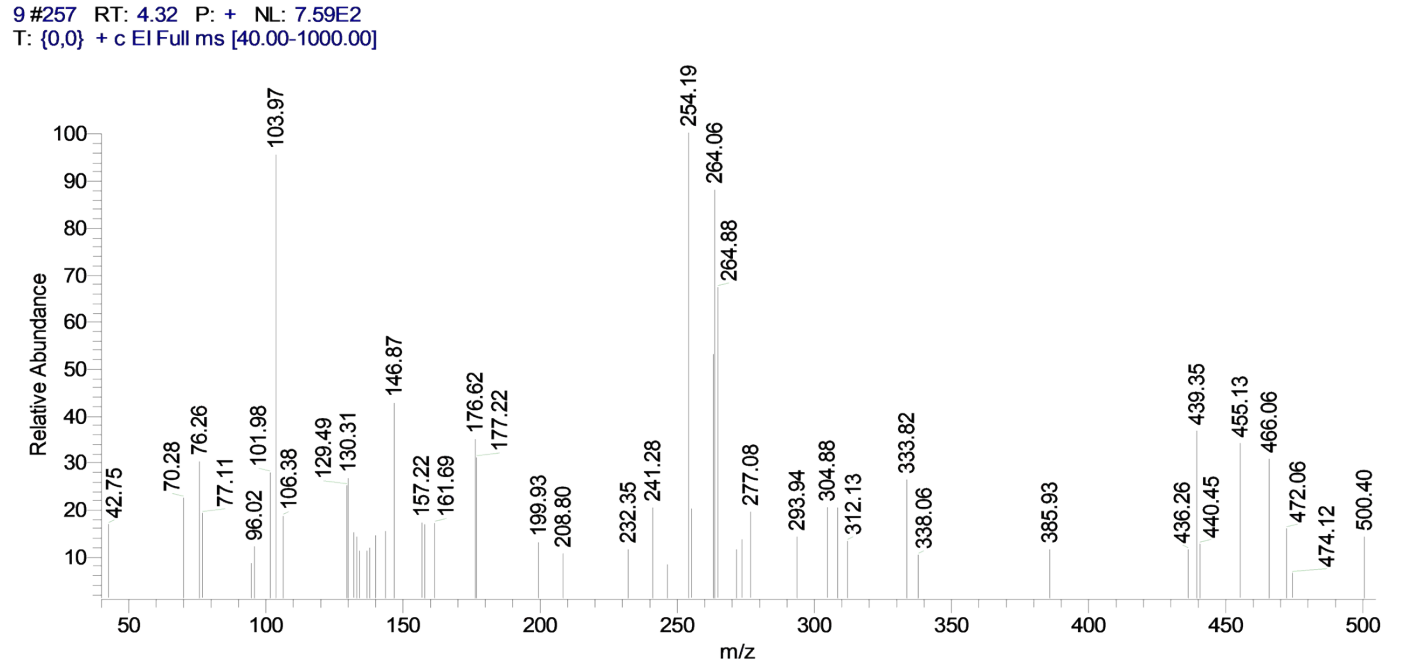

9 #257 RT: 4.32 P: + NL: 7.59E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
42.75
70.28
76.26
77.11
96.02
101.98
103.97
106.38
129.49
130.31
146.87
157.22
161.69
176.62
177.22
199.93
208.80
232.35
241.28
254.19
264.06
264.88
277.08
293.94
304.88
312.13
333.82
338.06
385.93
436.26
439.35
440.45
455.13
466.06
472.06
474.12
500.40

Figure S35. Mass spectrum of compound 9

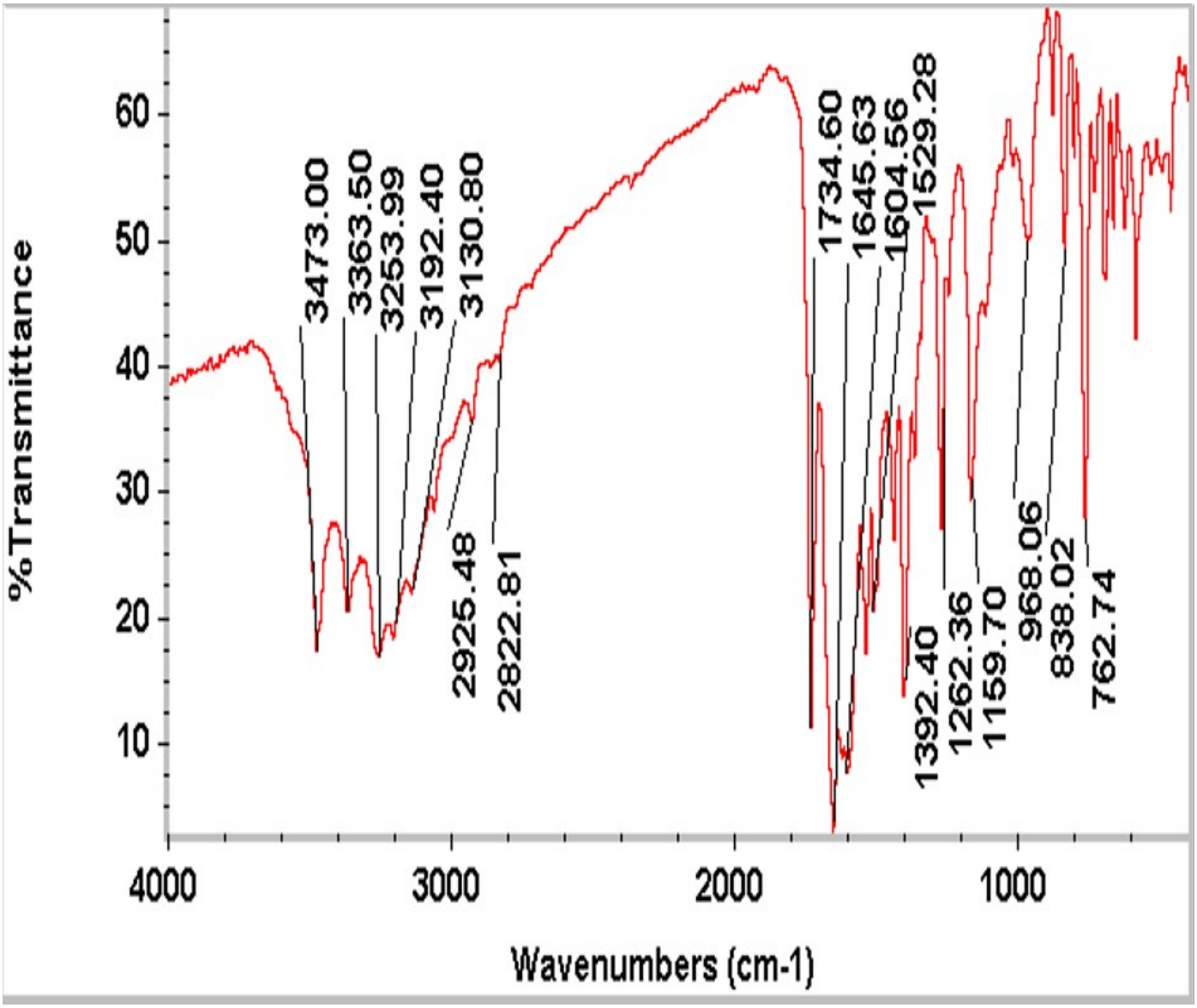


Figure S36. FT-IR spectrum of compound 10

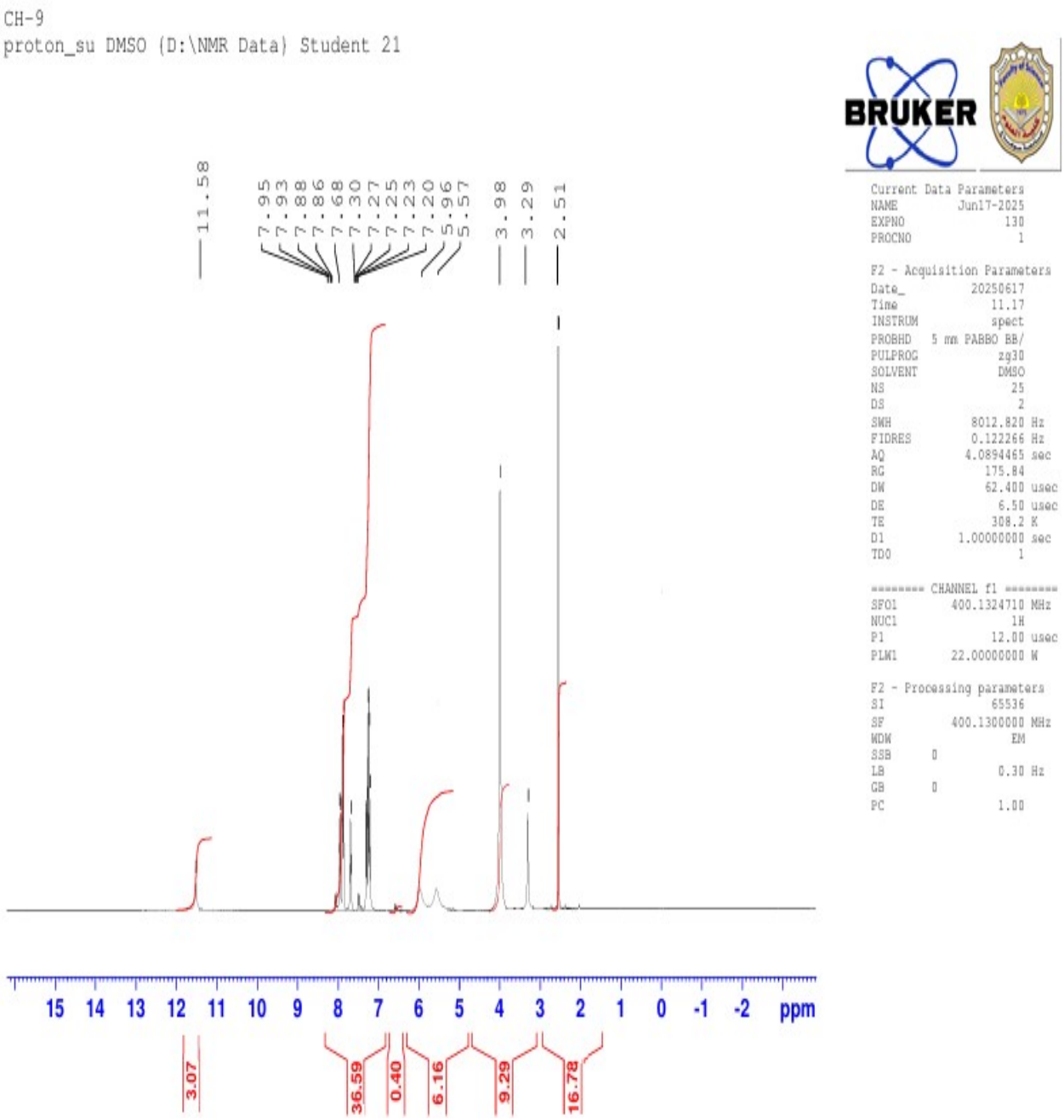
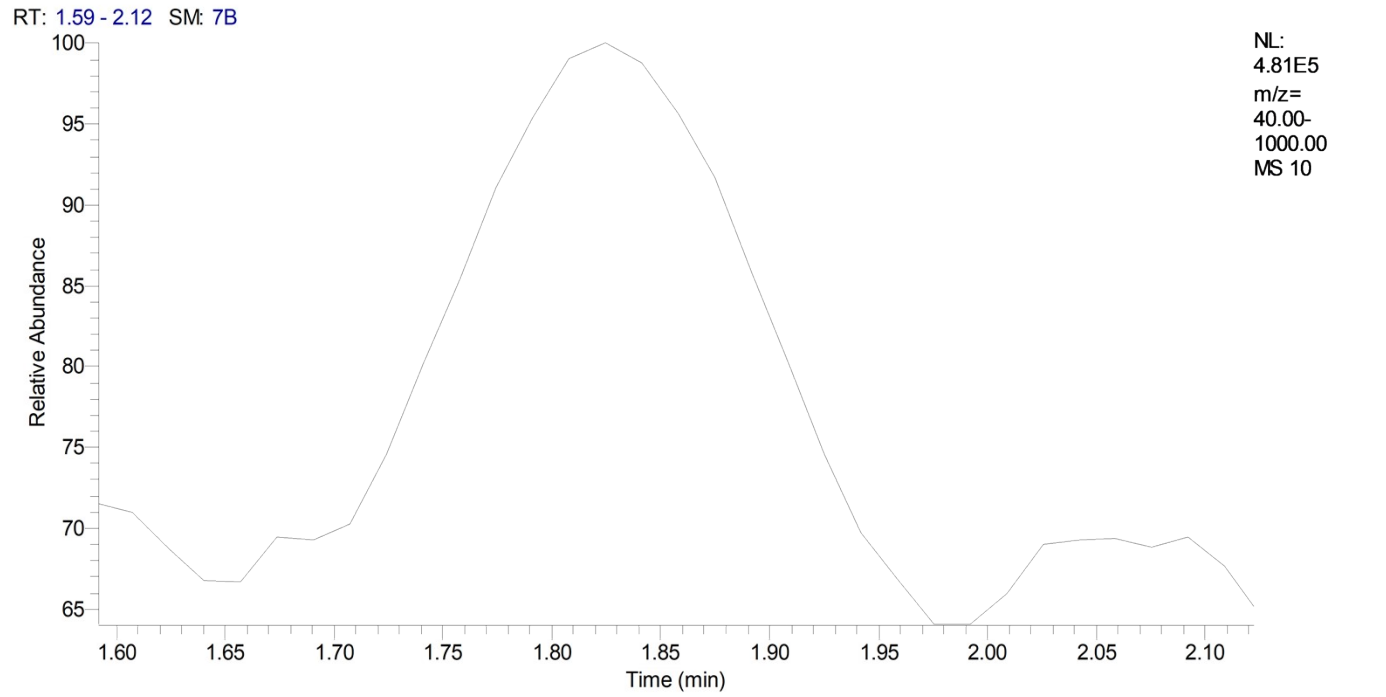


Figure S37. ^{1}HNMR spectrum of compound 10


RT: 1.59 - 2.12 SM: 7B
NL:
4.81E5
m/z=
40.00-
1000.00
MS 10
Relative Abundance
Time (min)

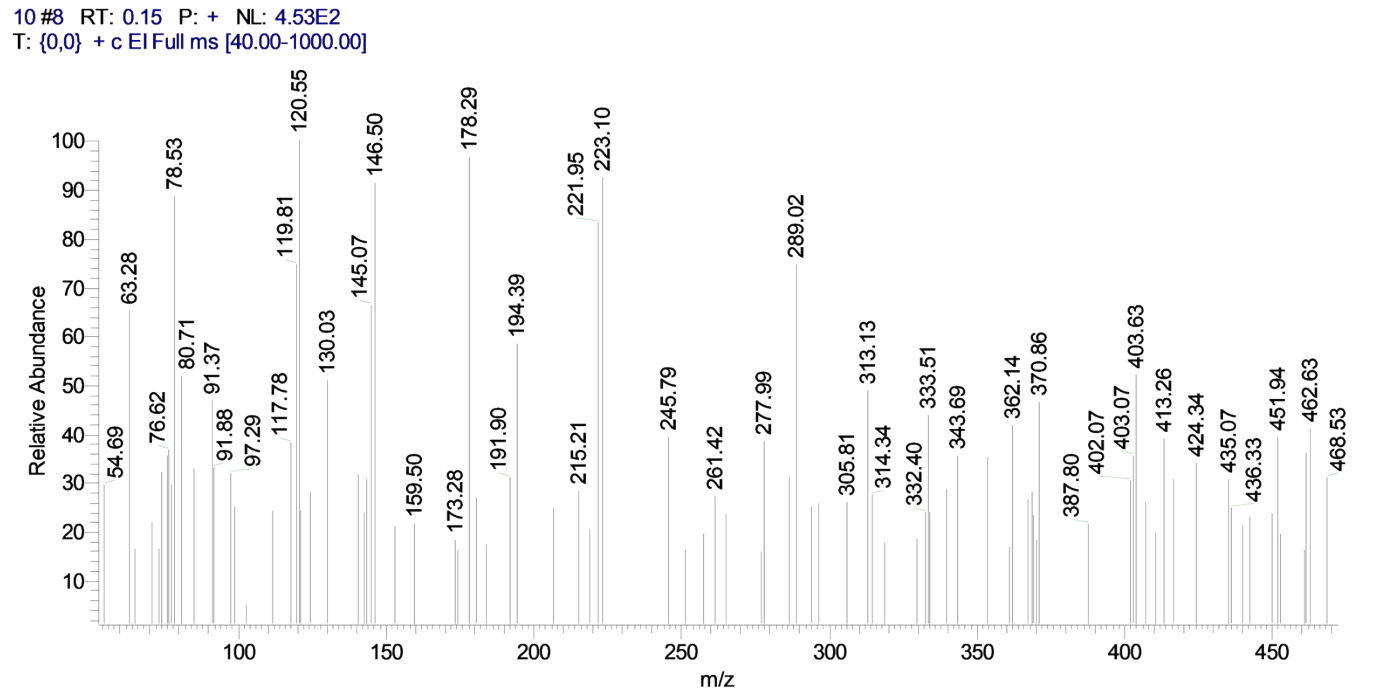

10 #8 RT: 0.15 P: + NL: 4.53E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
54.69
63.28
76.62
78.53
80.71
91.37
91.88
97.29
117.78
119.81
120.55
130.03
145.07
146.50
159.50
173.28
178.29
191.90
194.39
215.21
221.95
223.10
245.79
261.42
277.99
289.02
305.81
313.13
314.34
332.40
333.51
343.69
362.14
370.86
387.80
402.07
403.07
403.63
413.26
424.34
435.07
436.33
451.94
462.63
468.53

Figure S38. Mass spectrum of compound 10

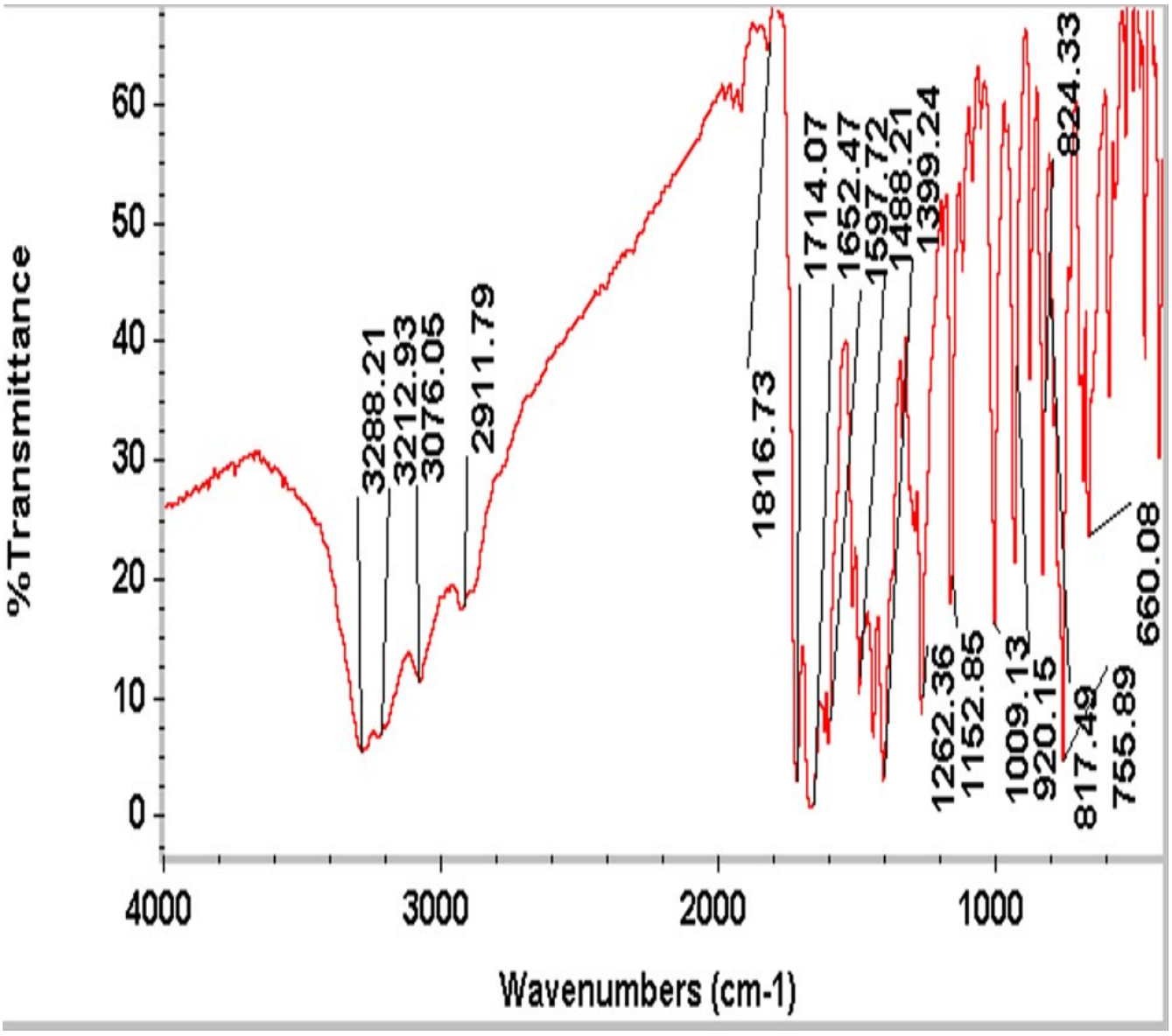


Figure S39. FT-IR spectrum of compound 11

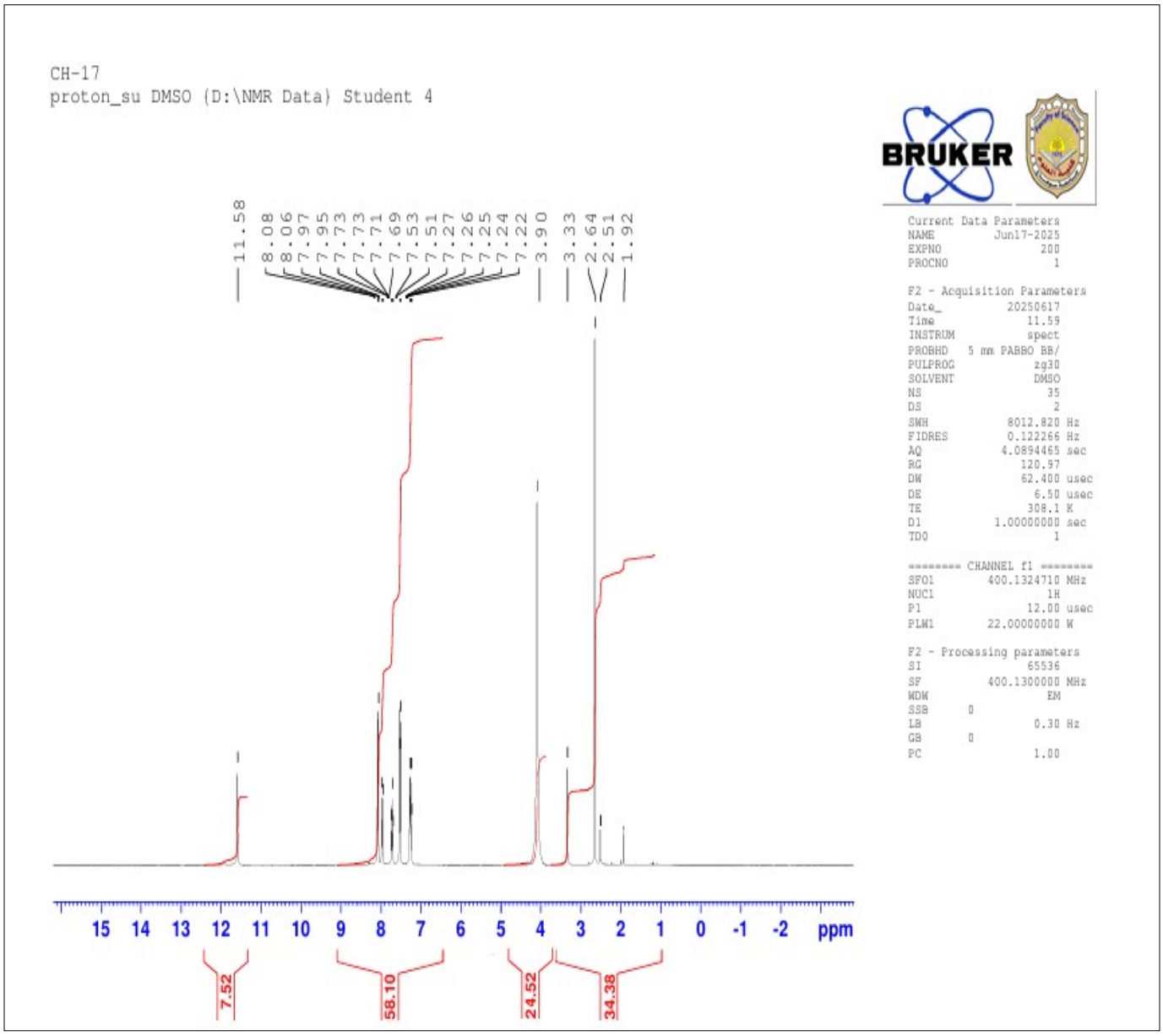


Figure S40. ^{1}HNMR spectrum of compound 11

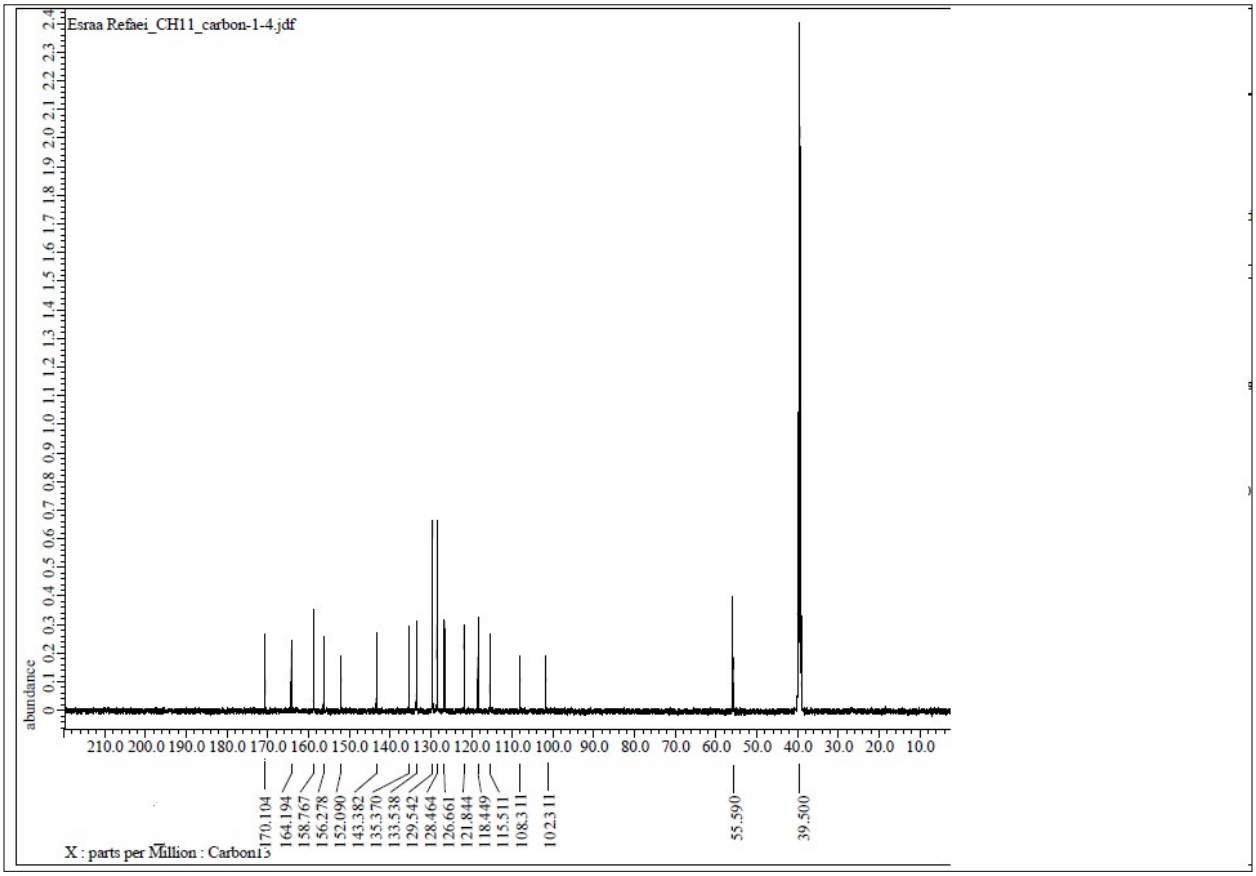
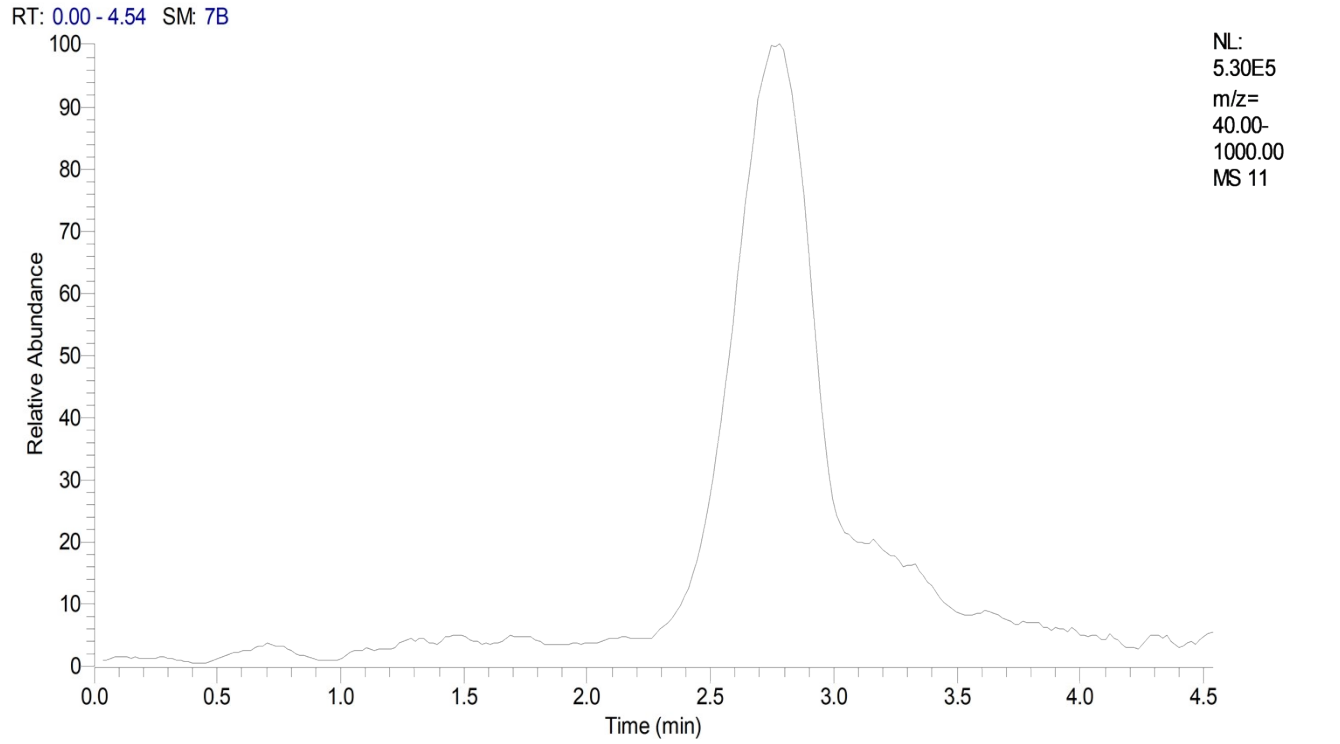


Figure S41. ^{13}CNMR spectrum of compound 11


RT: 0.00 - 4.54 SM: 7B
NL:
5.30E5
m/z=
40.00-
1000.00
MS 11
Relative Abundance
Time (min)

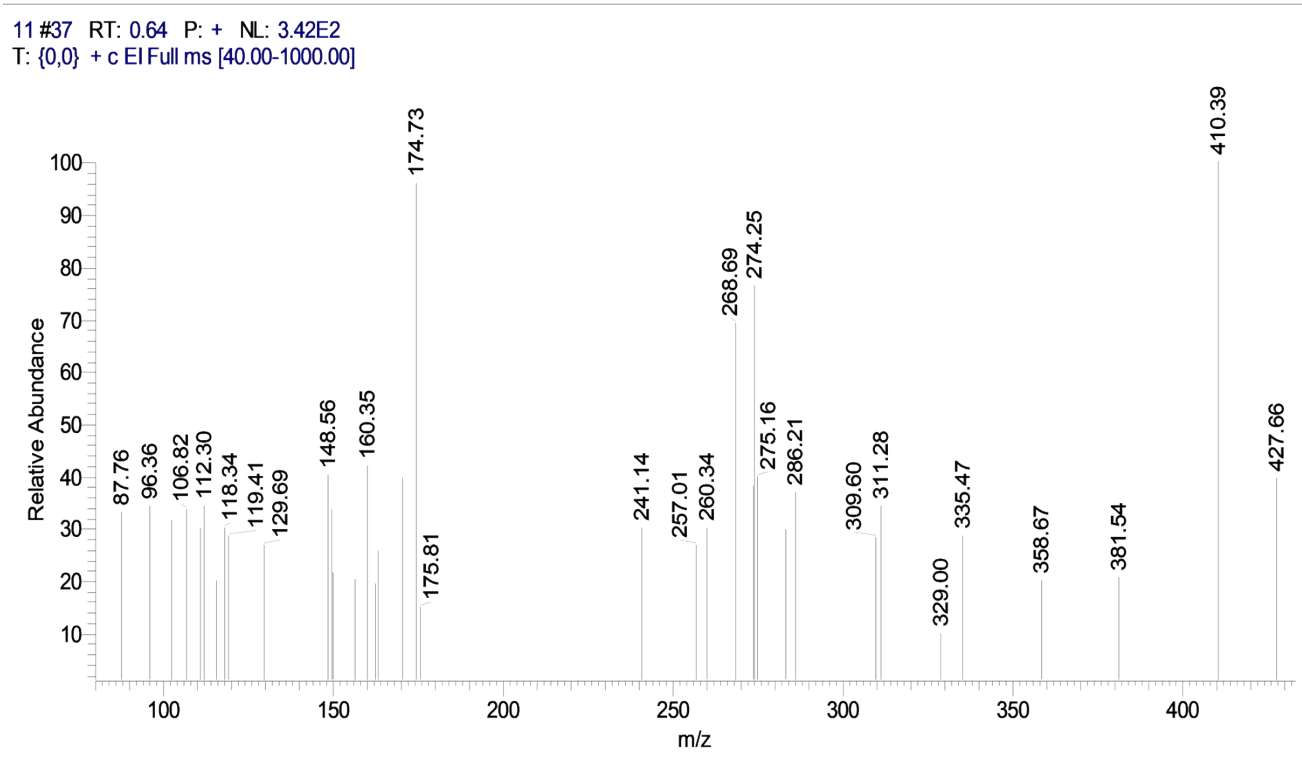

11 #37 RT: 0.64 P: + NL: 3.42E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
87.76
96.36
106.82
112.30
118.34
119.41
129.69
148.56
160.35
174.73
175.81
241.14
257.01
260.34
268.69
274.25
275.16
286.21
309.60
311.28
329.00
335.47
358.67
381.54
410.39
427.66

Figure S42. Mass spectrum of compound 11

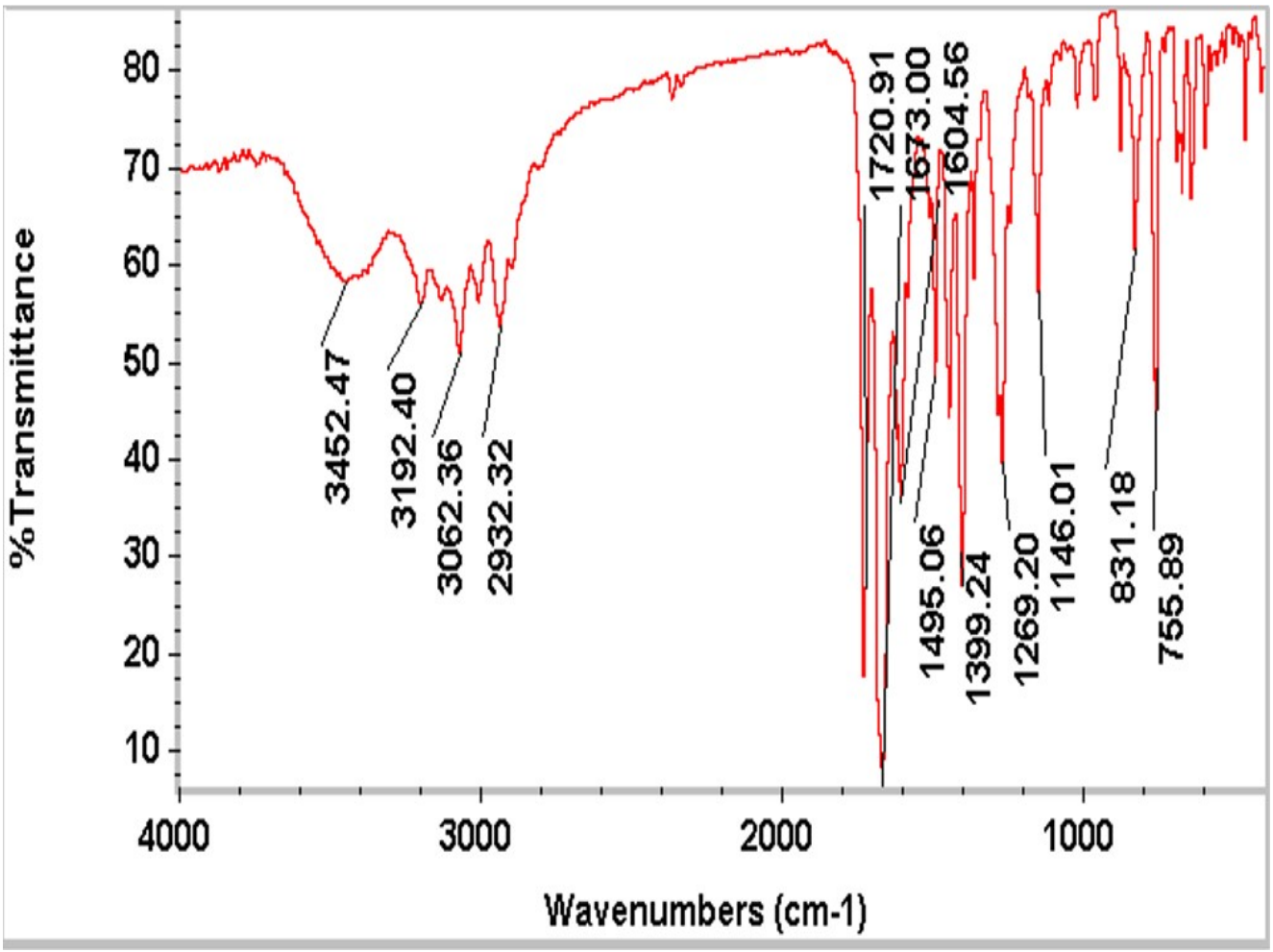


Figure S43. FT-IR spectrum of compound 12

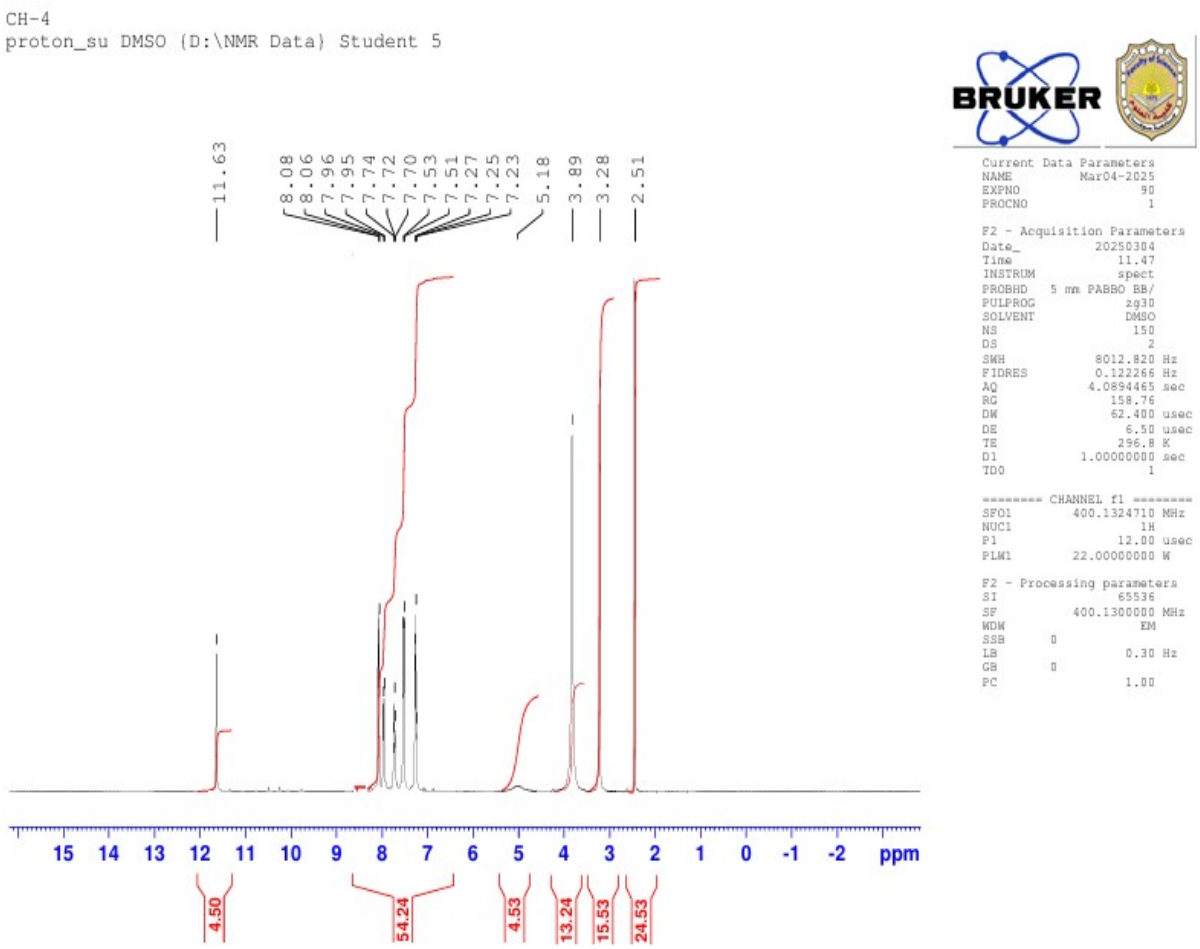


Figure S44. [1]HNMR spectrum of compound 12

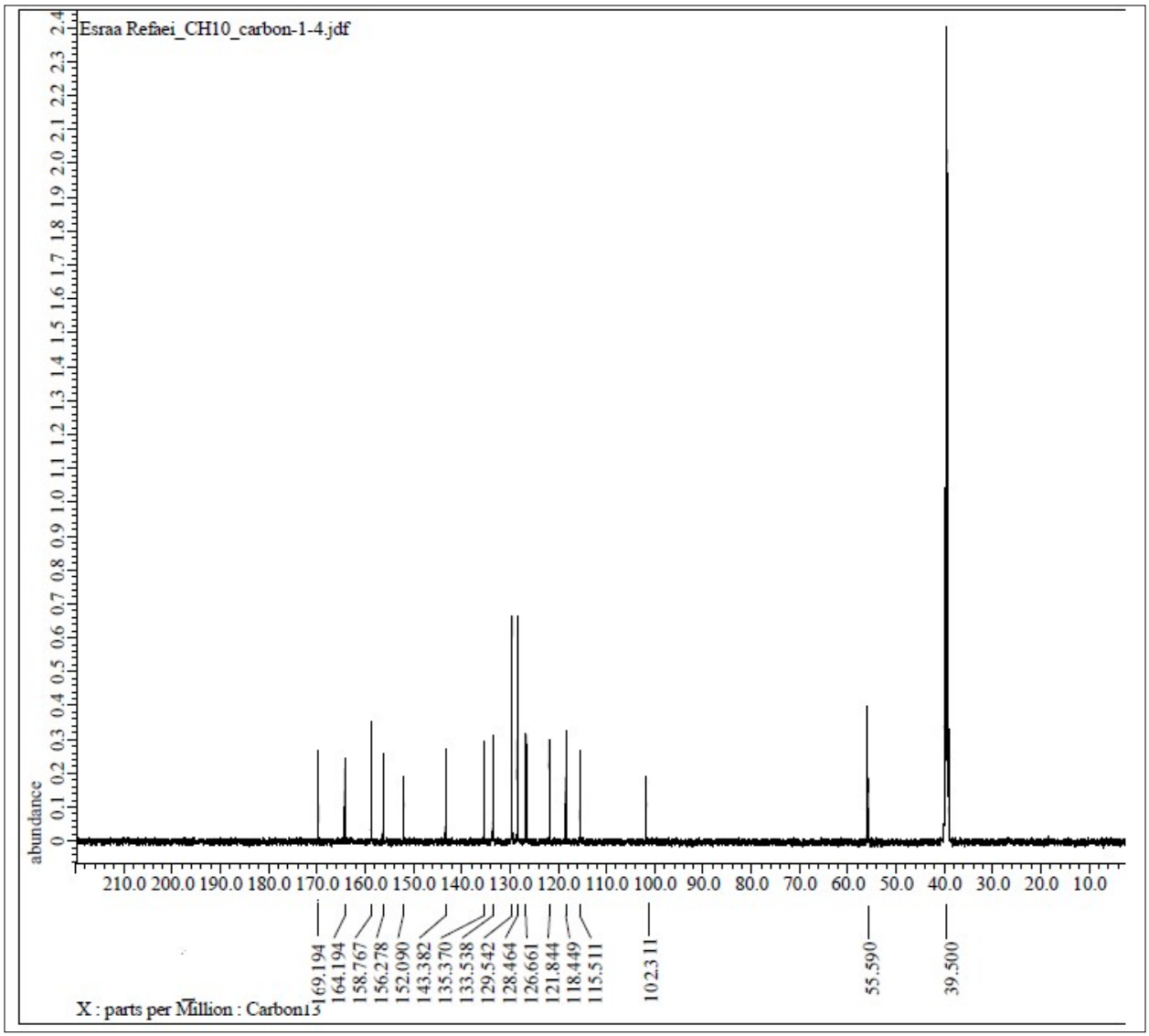


Figure S45. ^{13}CNMR spectrum of compound 12

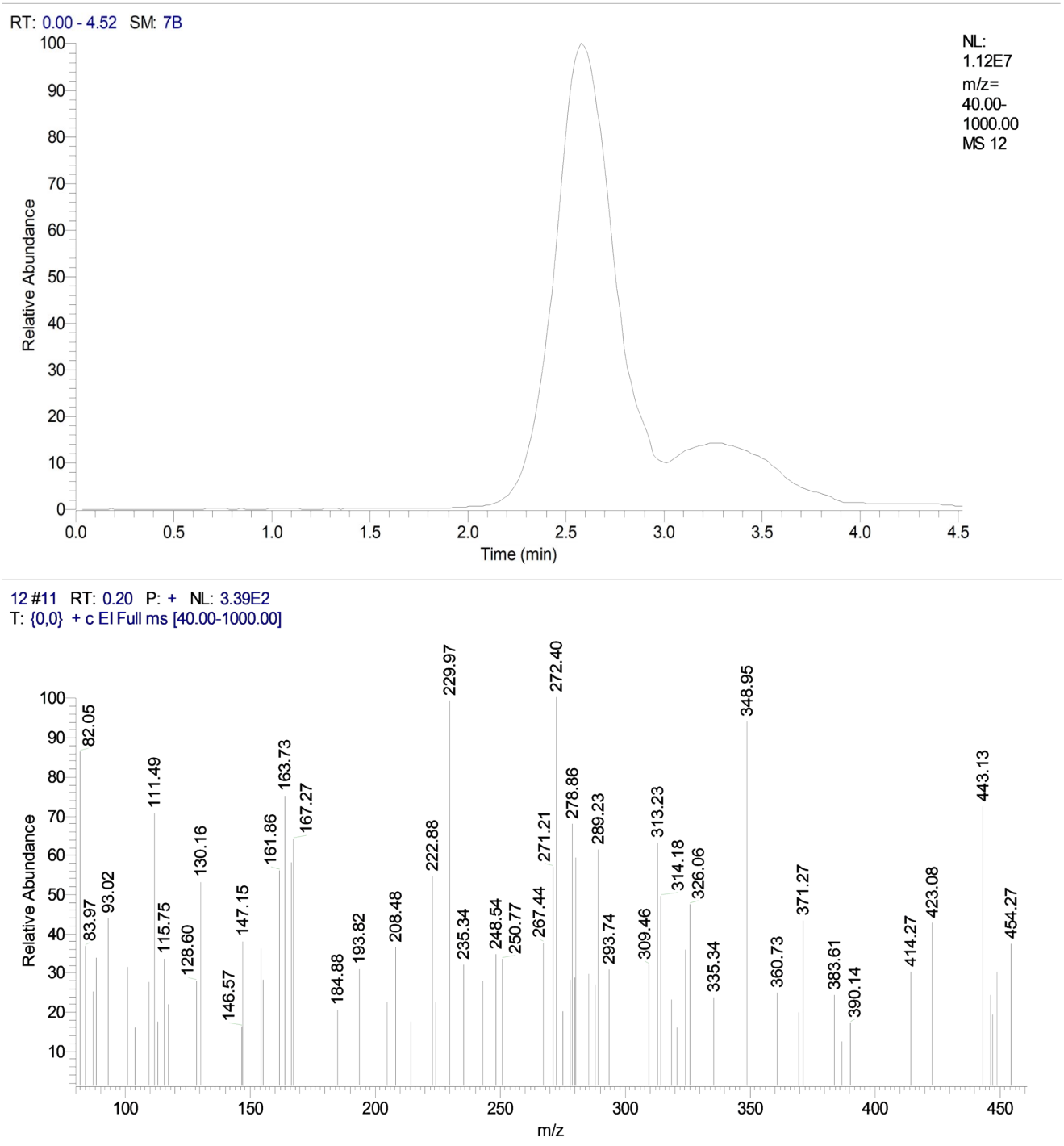


Figure S46. Mass spectrum of compound 12

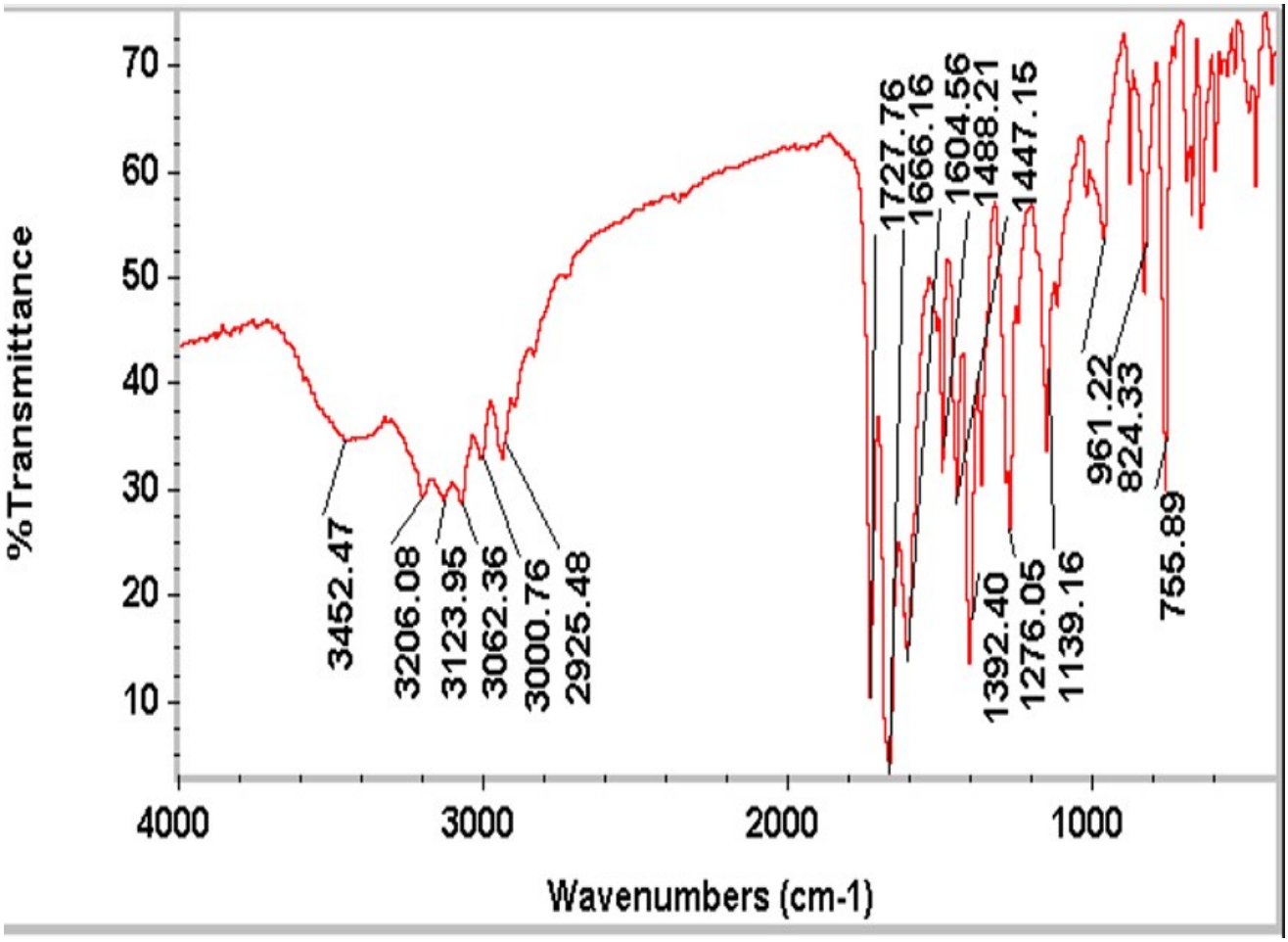


Figure S47.FT- IR spectrum of compound 13

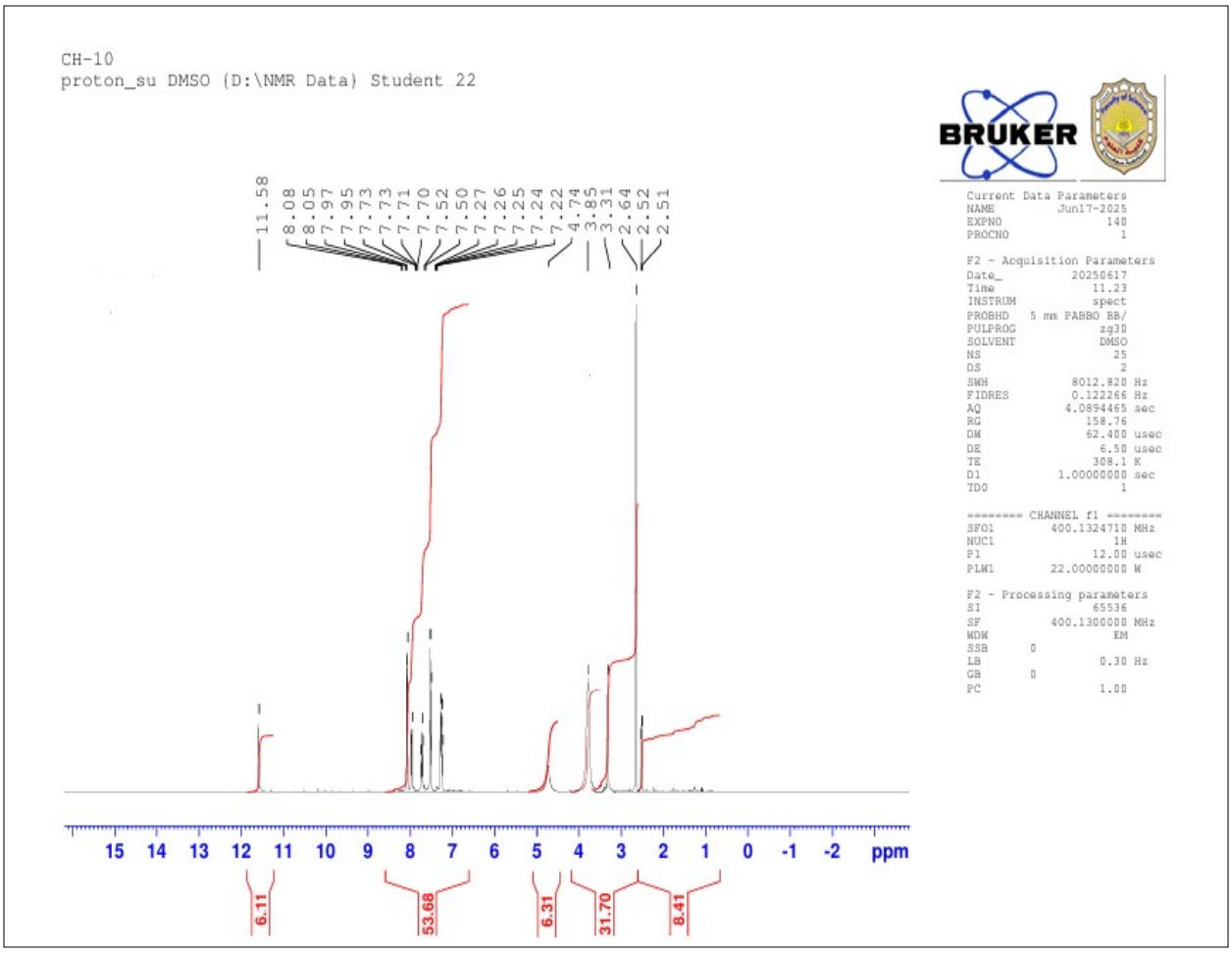


Figure S48. ^{1}HNMR spectrum of compound 13

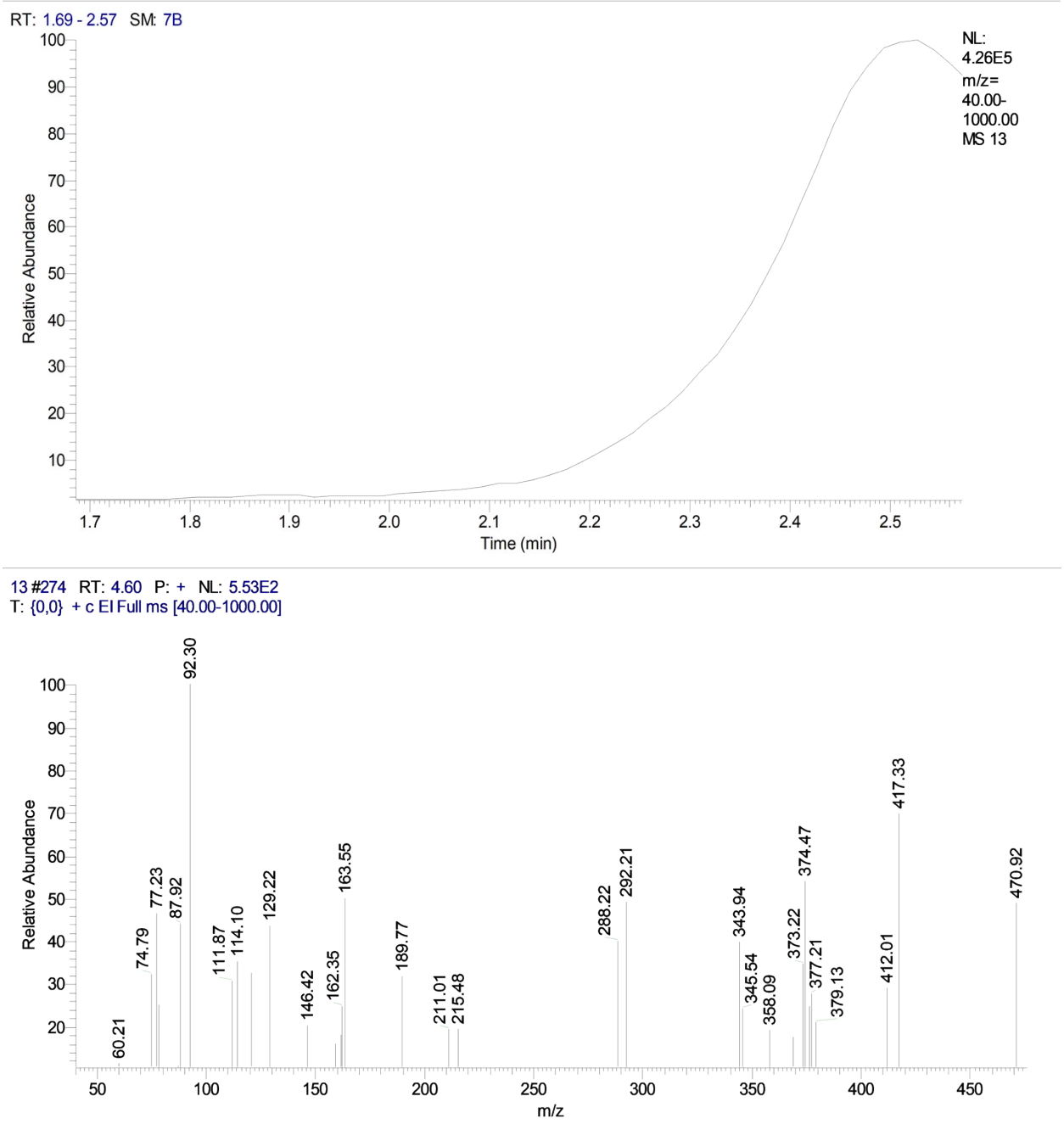


Figure S49. Mass spectrum of compound 13

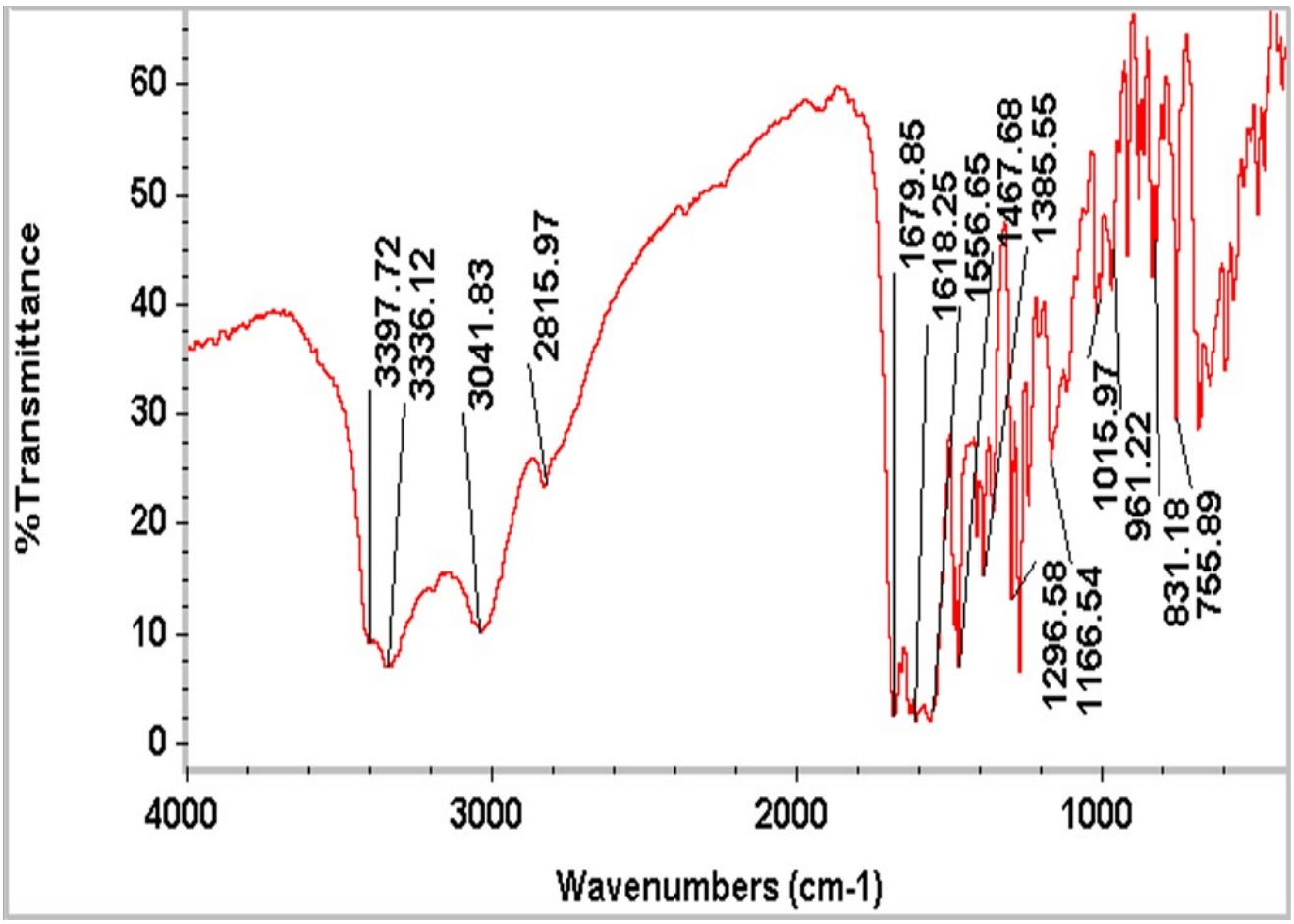


Figure S50. FT-IR spectrum of compound 14

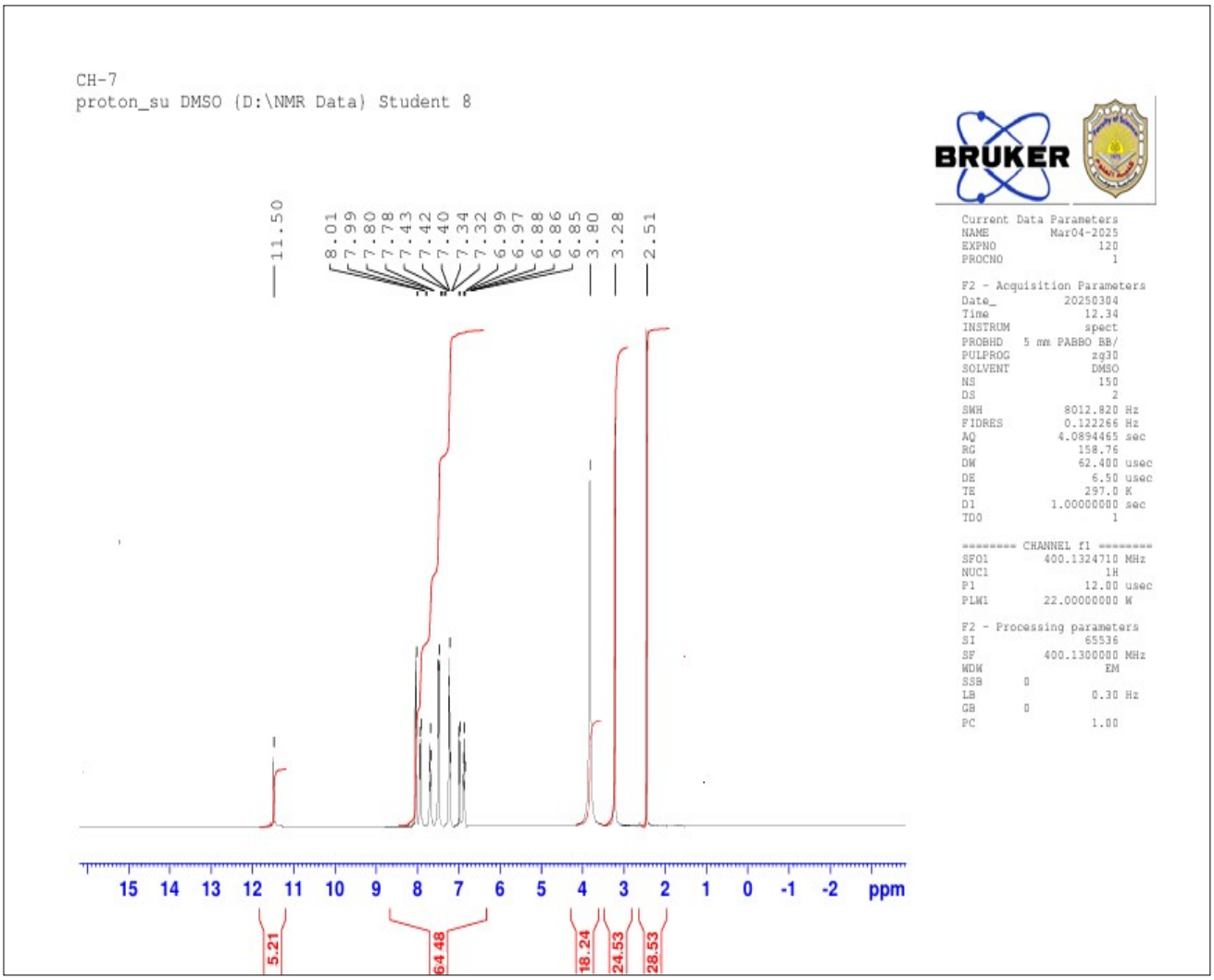


Figure S51. ^{1}HNMR spectrum of compound 14

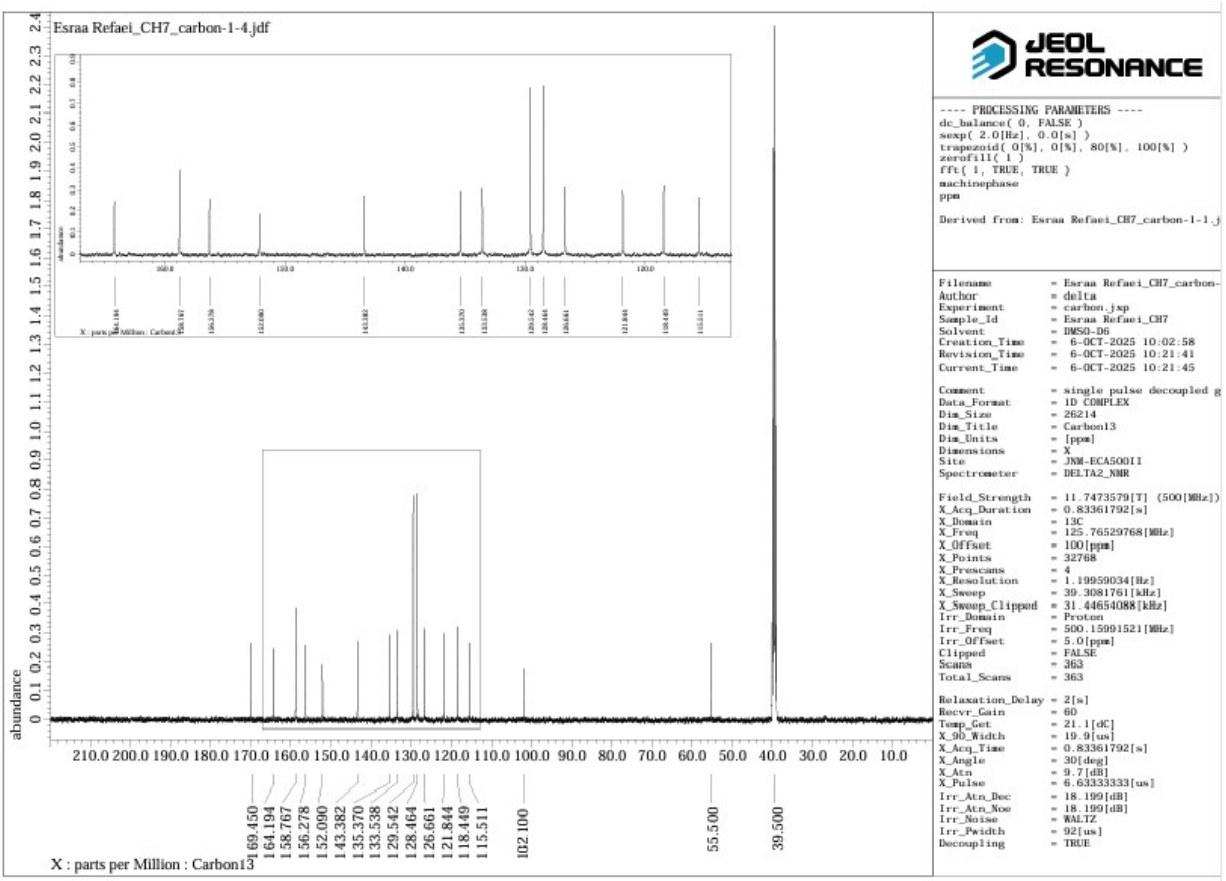
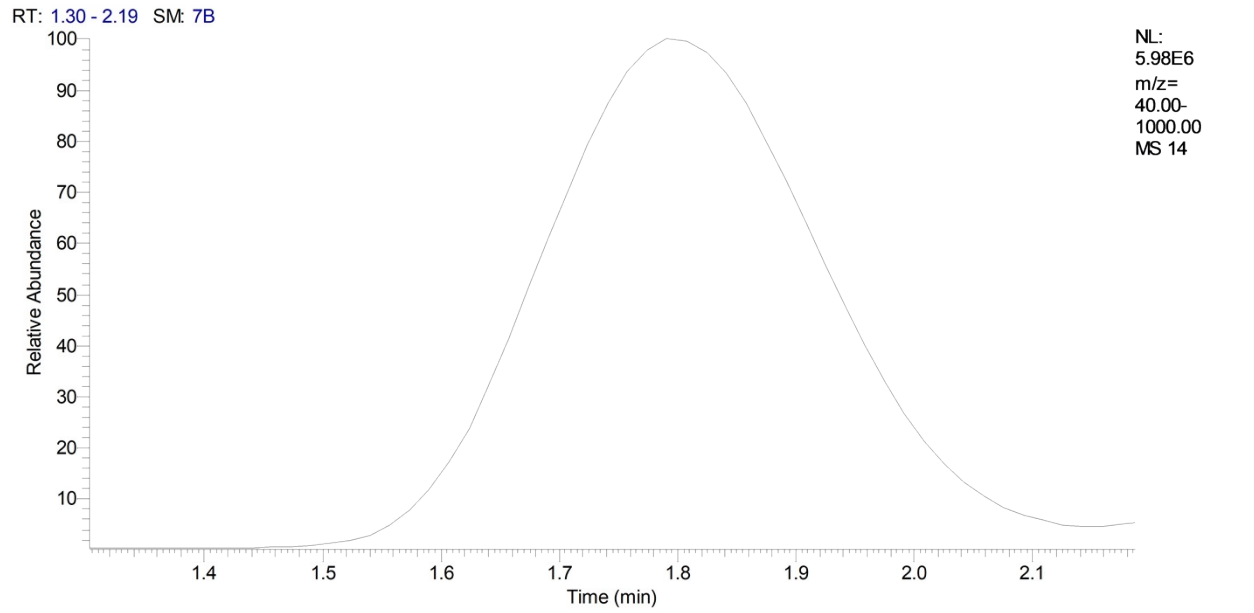


Figure S52. ^{13}CNMR spectrum of compound 14


RT: 1.30 - 2.19 SM: 7B
NL:
5.98E6
m/z=
40.00-
1000.00
MS 14
Relative Abundance
Time (min)

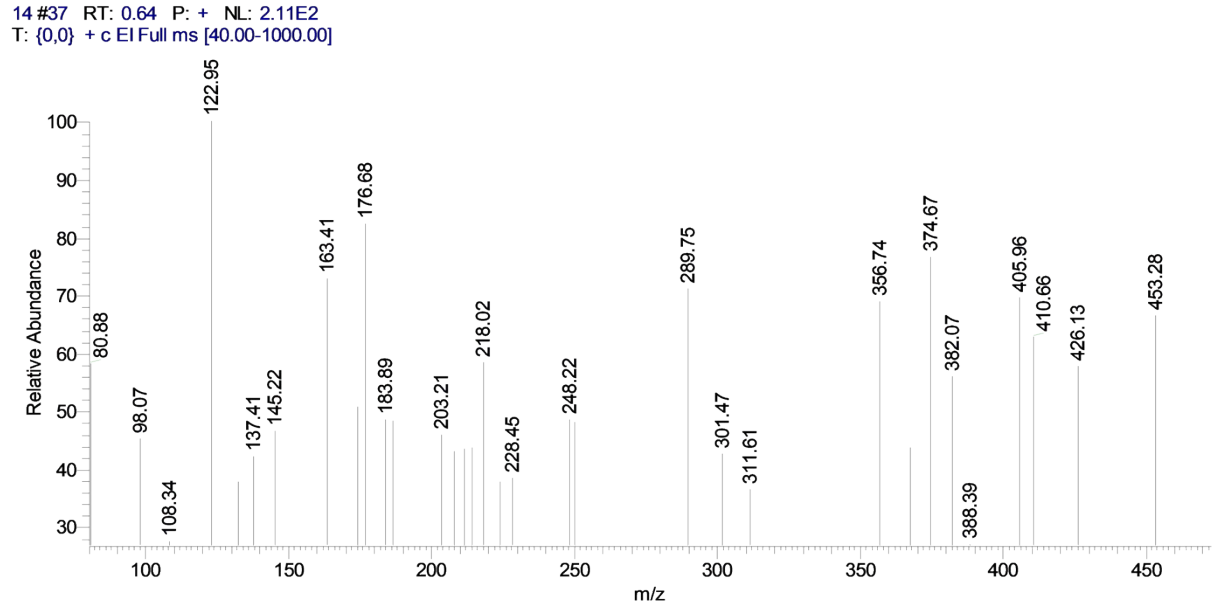

14 #37 RT: 0.64 P: + NL: 2.11E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
122.95
80.88
98.07
108.34
137.41
145.22
163.41
176.68
183.89
203.21
218.02
228.45
248.22
289.75
301.47
311.61
356.74
374.67
382.07
388.39
405.96
410.66
426.13
453.28

Figure S53. Mass spectrum of compound 14

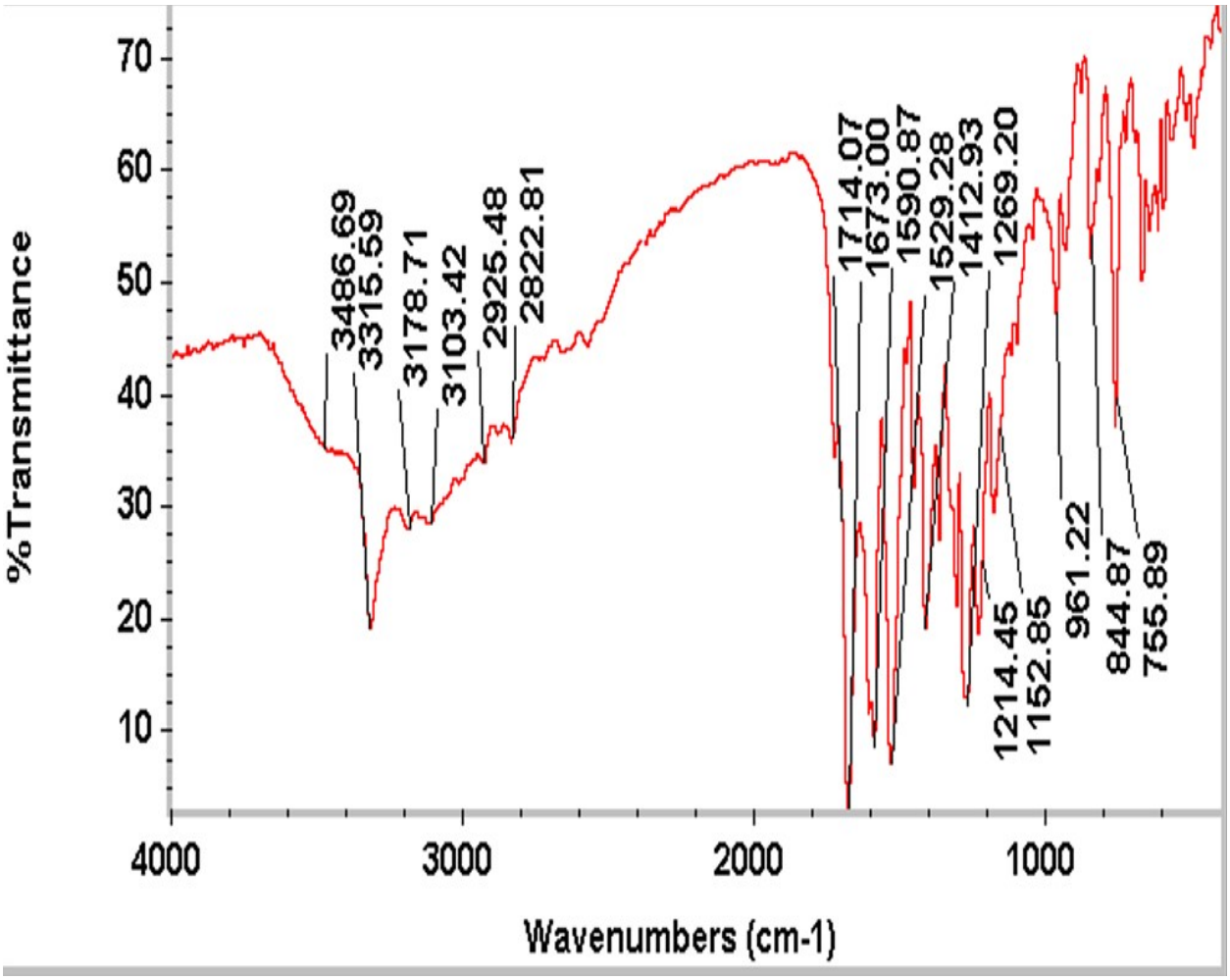


Figure S54.FT- IR spectrum of compound 15

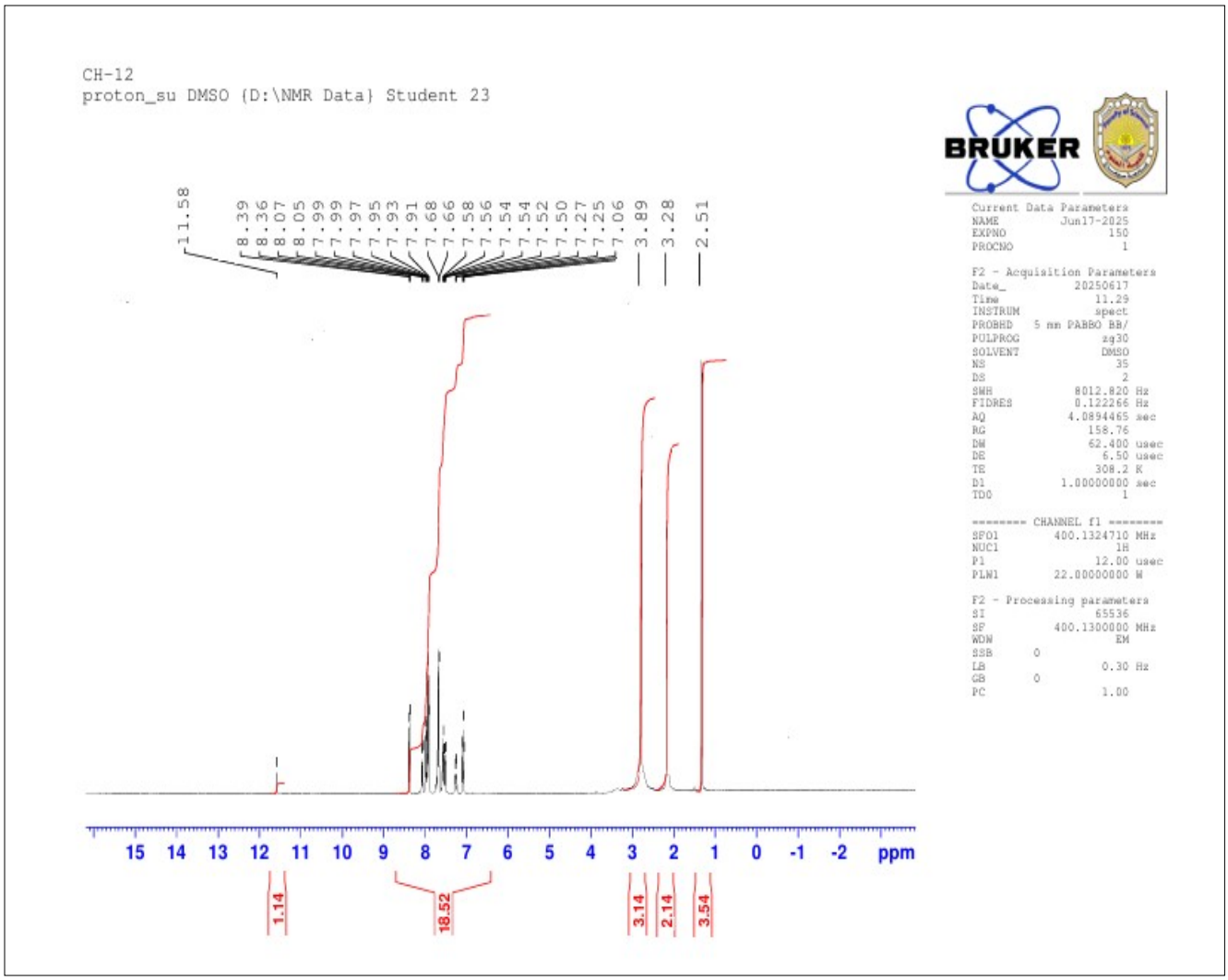


Figure S55. ^{1}HNMR spectrum of compound 15

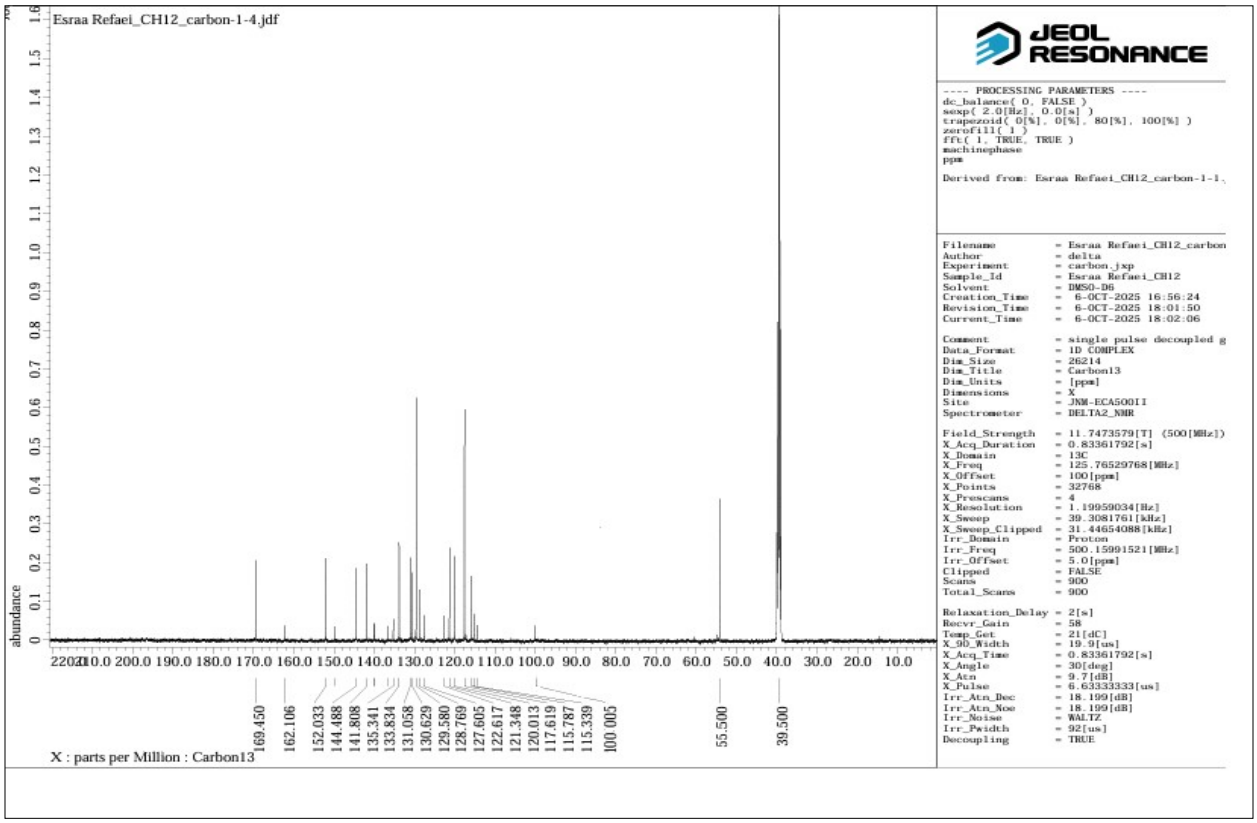
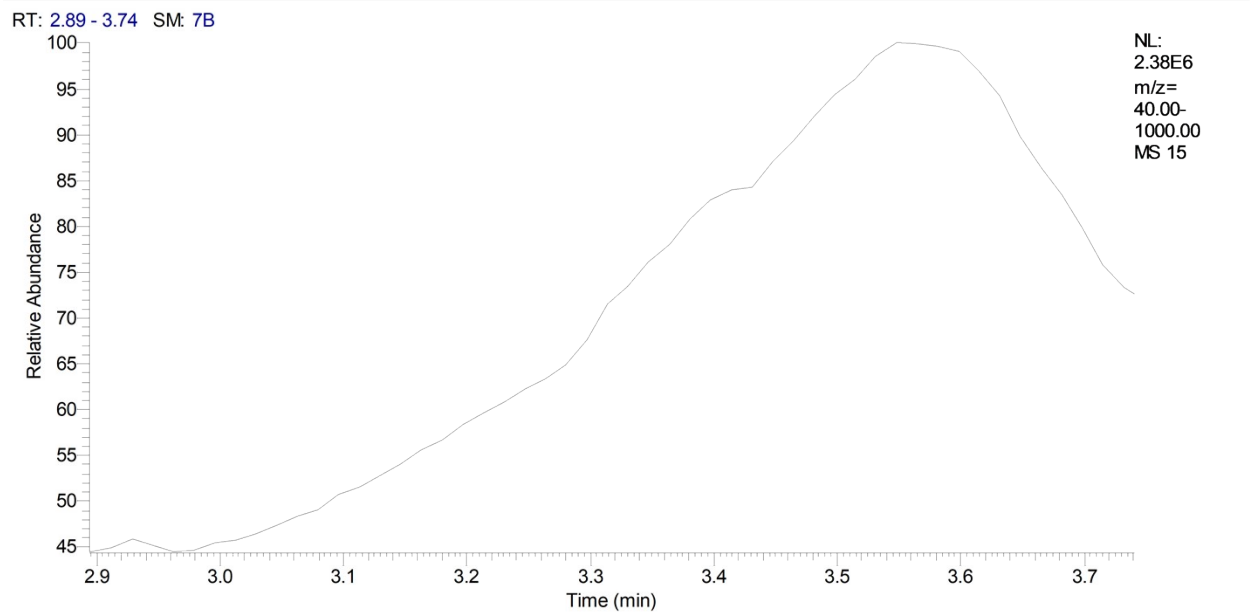


Figure S56. ^{13}CNMR spectrum of compound 15


RT: 2.89 - 3.74 SM: 7B
NL:
2.38E6
m/z=
40.00-
1000.00
MS 15
Relative Abundance
Time (min)

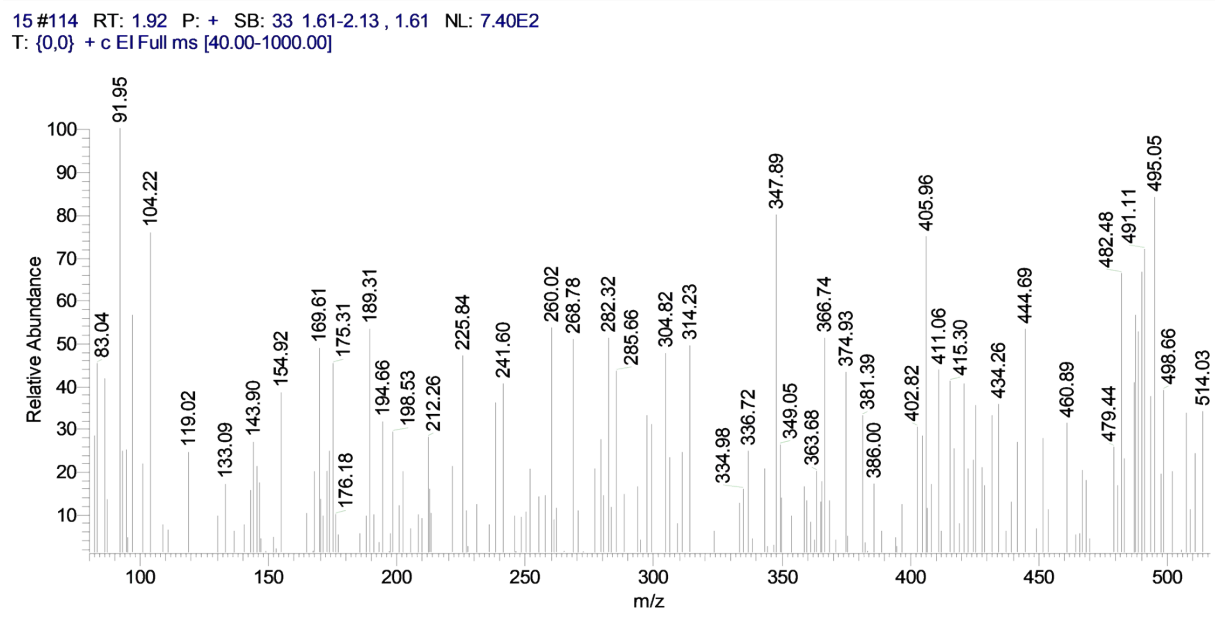

15 #114 RT: 1.92 P: + SB: 33 1.61-2.13 , 1.61 NL: 7.40E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z

Figure S57. Mass spectrum of compound 15