Synthesis, modification of new thiazole nucleus fused quinoxalines and their insecticidal activity targeting the cotton leafworm, *Spodoptera litura*; Design, characterization, *in vivo* bio-evaluation, toxicological effectiveness, and study mode of action

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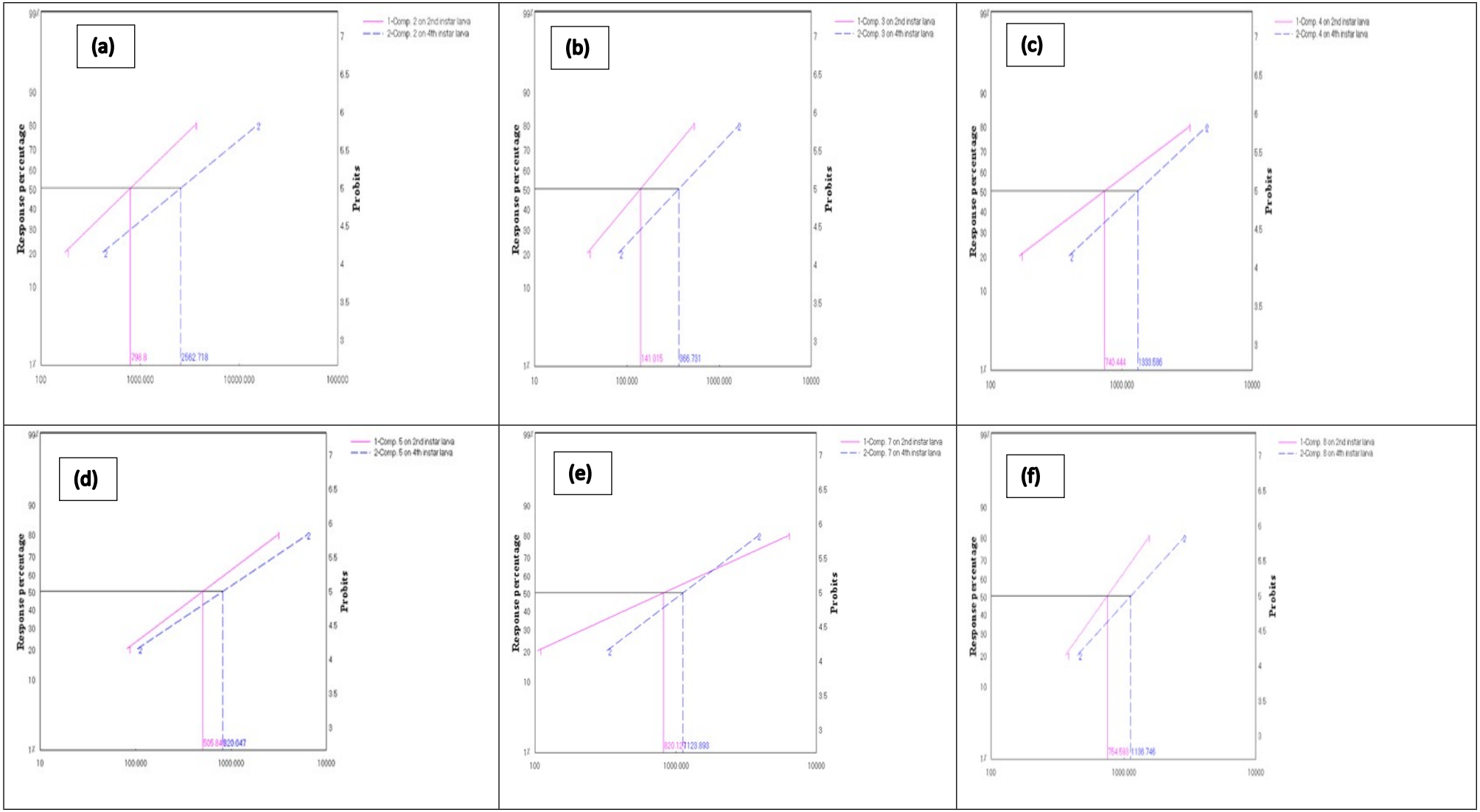

(a)
1-Comp. 2 on 2nd instar larva
2-Comp. 2 on 4th instar larva
Response percentage
Probits
798.8
2662.718
(b)
1-Comp. 3 on 2nd instar larva
2-Comp. 3 on 4th instar larva
Response percentage
Probits
141.015
866.781
(c)
1-Comp. 4 on 2nd instar larva
2-Comp. 4 on 4th instar larva
Response percentage
Probits
740.444
1888.686
(d)
1-Comp. 5 on 2nd instar larva
2-Comp. 5 on 4th instar larva
Response percentage
Probits
505.84
829.047
(e)
1-Comp. 7 on 2nd instar larva
2-Comp. 7 on 4th instar larva
Response percentage
Probits
820.127
1129.893
(f)
1-Comp. 8 on 2nd instar larva
2-Comp. 8 on 4th instar larva
Response percentage
Probits
754.593
1136.746

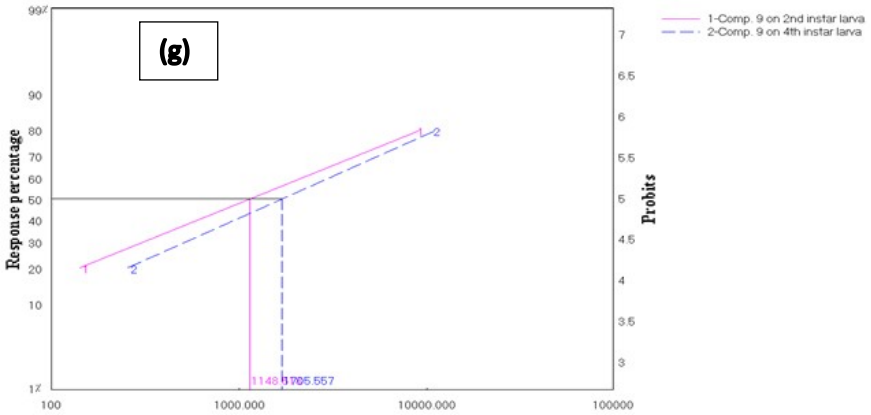
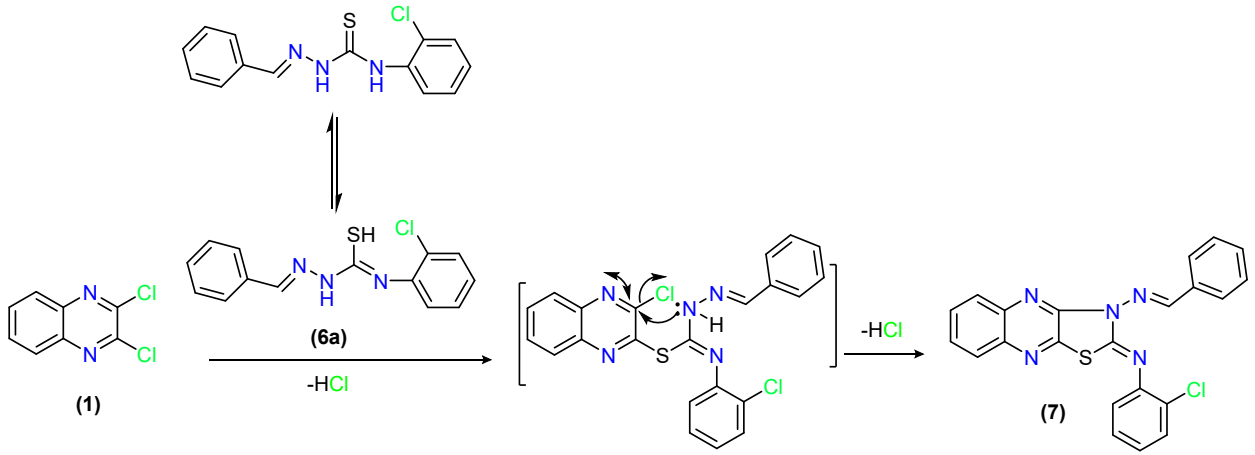


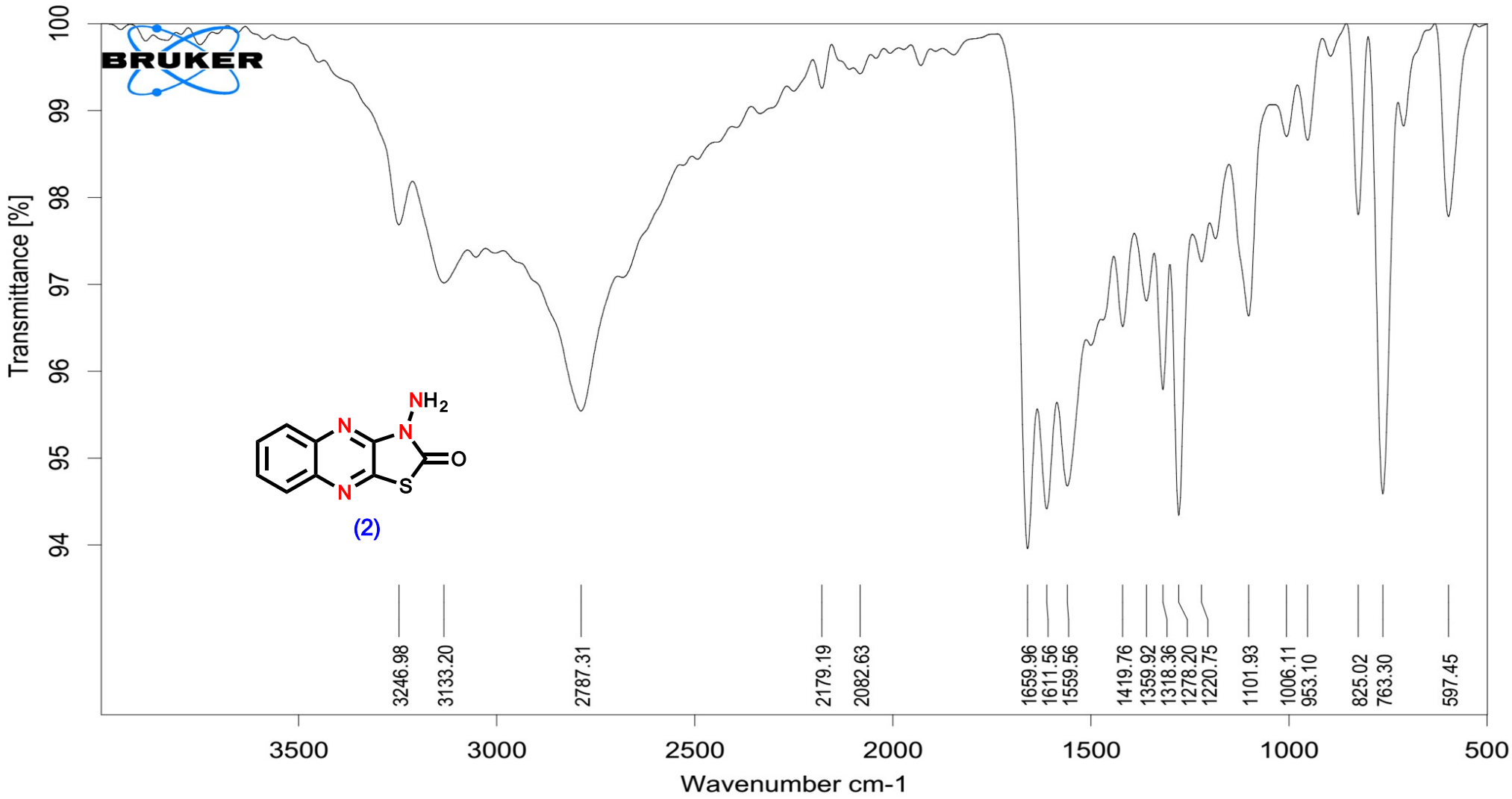
Figure (SI1): Regression lines representing toxicity of tested newly designed quinoxaline derivative **2-5** and **7-9** against 2nd & 4th larval instar of *S. litura* after 5 days from the treatment, where (**a**) compound **2**; (**b**) compound **3**; (**c**) compound **4**; (**d**) compound **5**; (**e**) compound **7**; (**f**) compound **8**; and (**g**) compound **9**

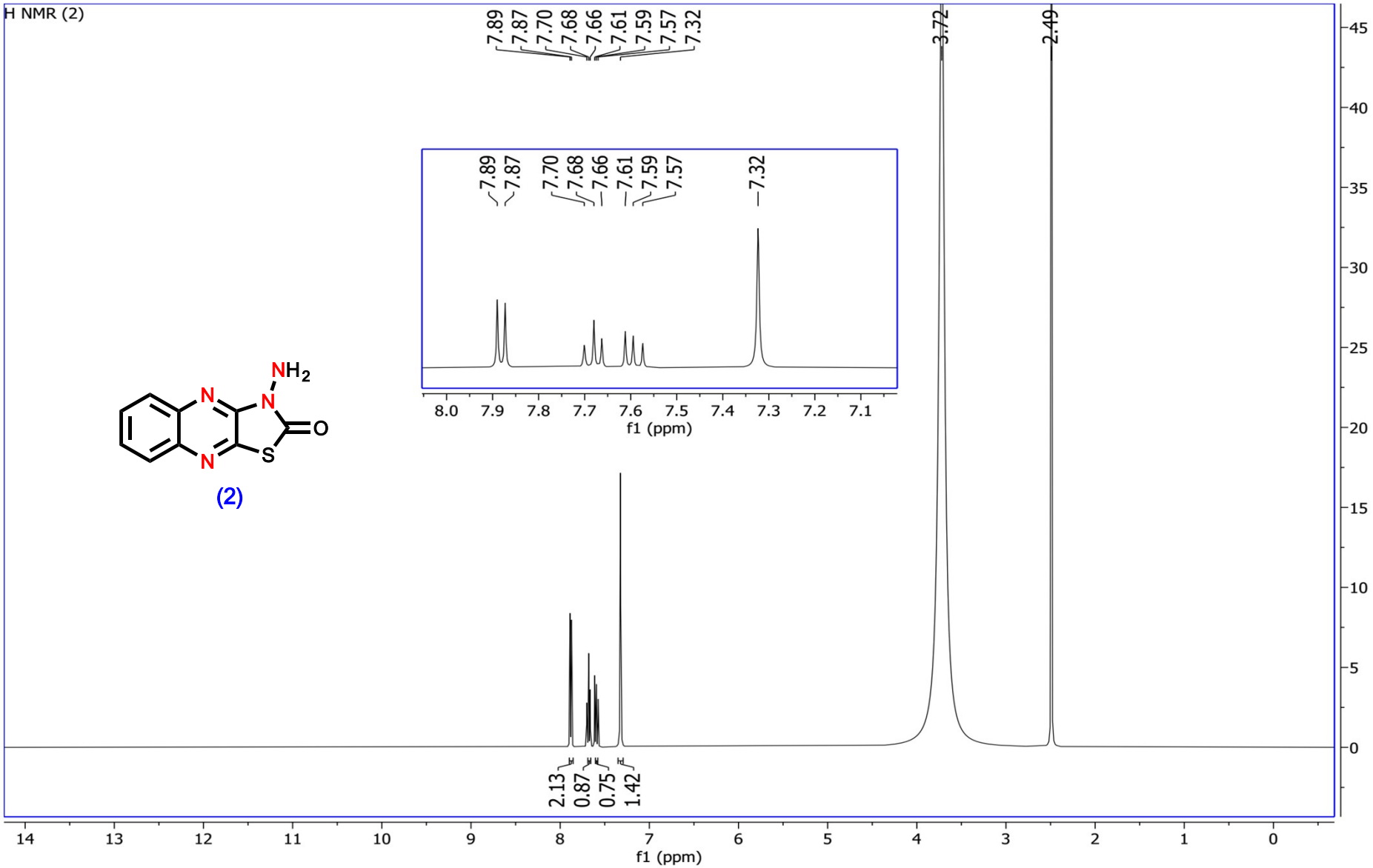
1.1.Chemistry

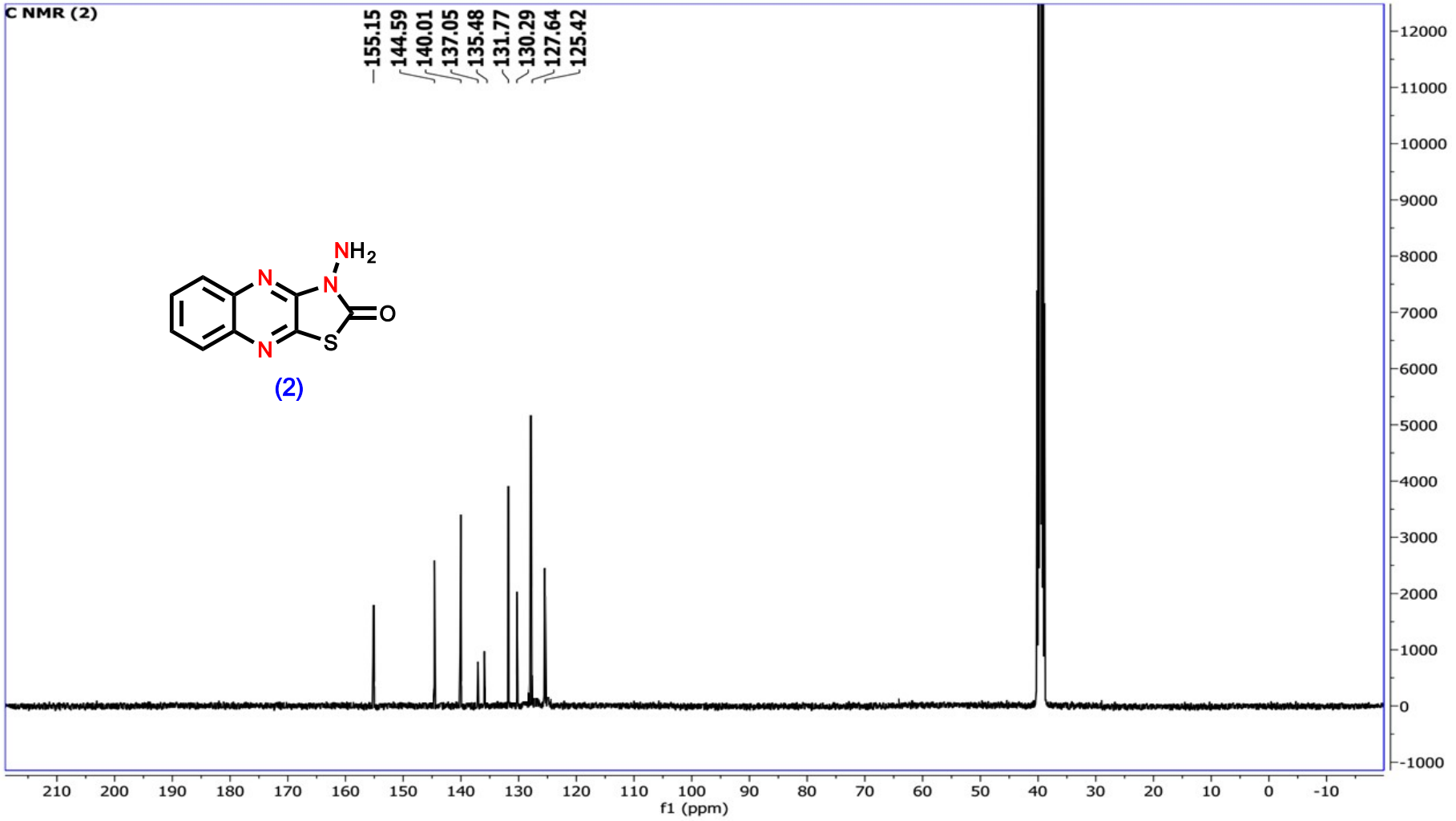
All reagents and chemicals were purchased from Aldrich Chemicals without further purification, while solvents were obtained from Fisher. Melting points (MPs) of the newly designed compounds were measured using open capillaries on a digital Gallen Kamp MFB-595 instrument. IR spectra were acquired using the KBr disc methodology on a Shimadzu 440 spectrophotometer in the range of 400–4000 cm^{-1}. NMR spectra ($^{1}H/^{13}C$) were recorded on a JOEL spectrometer 400/101 MHz using DMSO-d_6 as the solvent, with chemical shifts measured in δ ppm relative to TMS as an internal standard (=0 ppm). The data were presented in the following format: chemical shift, multiplicity (br. = broad, m = multiplet, q = quartet, t = triplet, d = doublet, and s = singlet), coupling constant (*J*) in Hertz (Hz), and integration. Elemental studies were conducted at the Micro Analytical Unit of Cairo University in Cairo. Mass spectra were obtained at 70 eV using the DI-50 unit of a Shimadzu GC/MSQP5050A Spectrometer at the Regional Center for Biotechnology of Al-Azhar University.

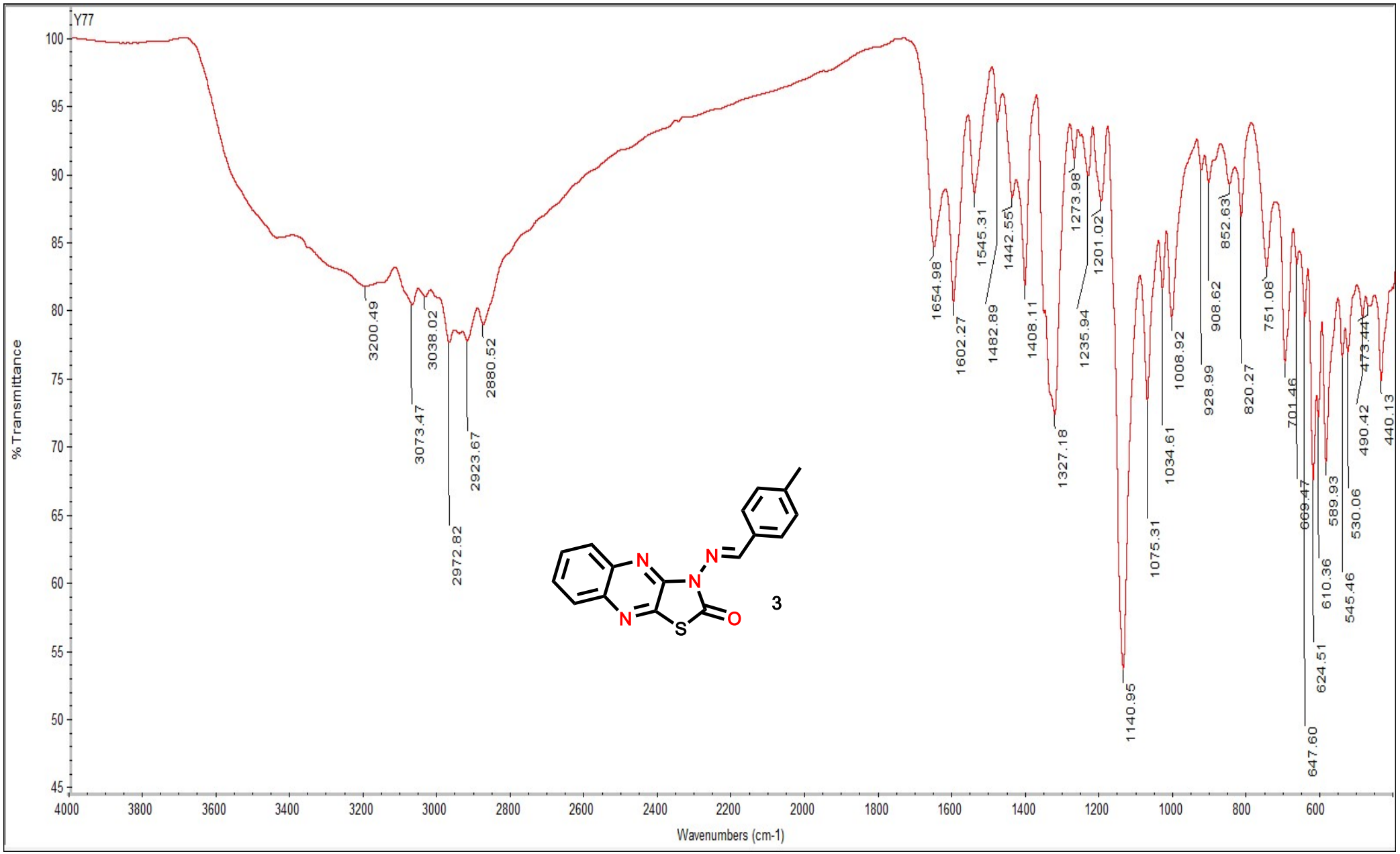


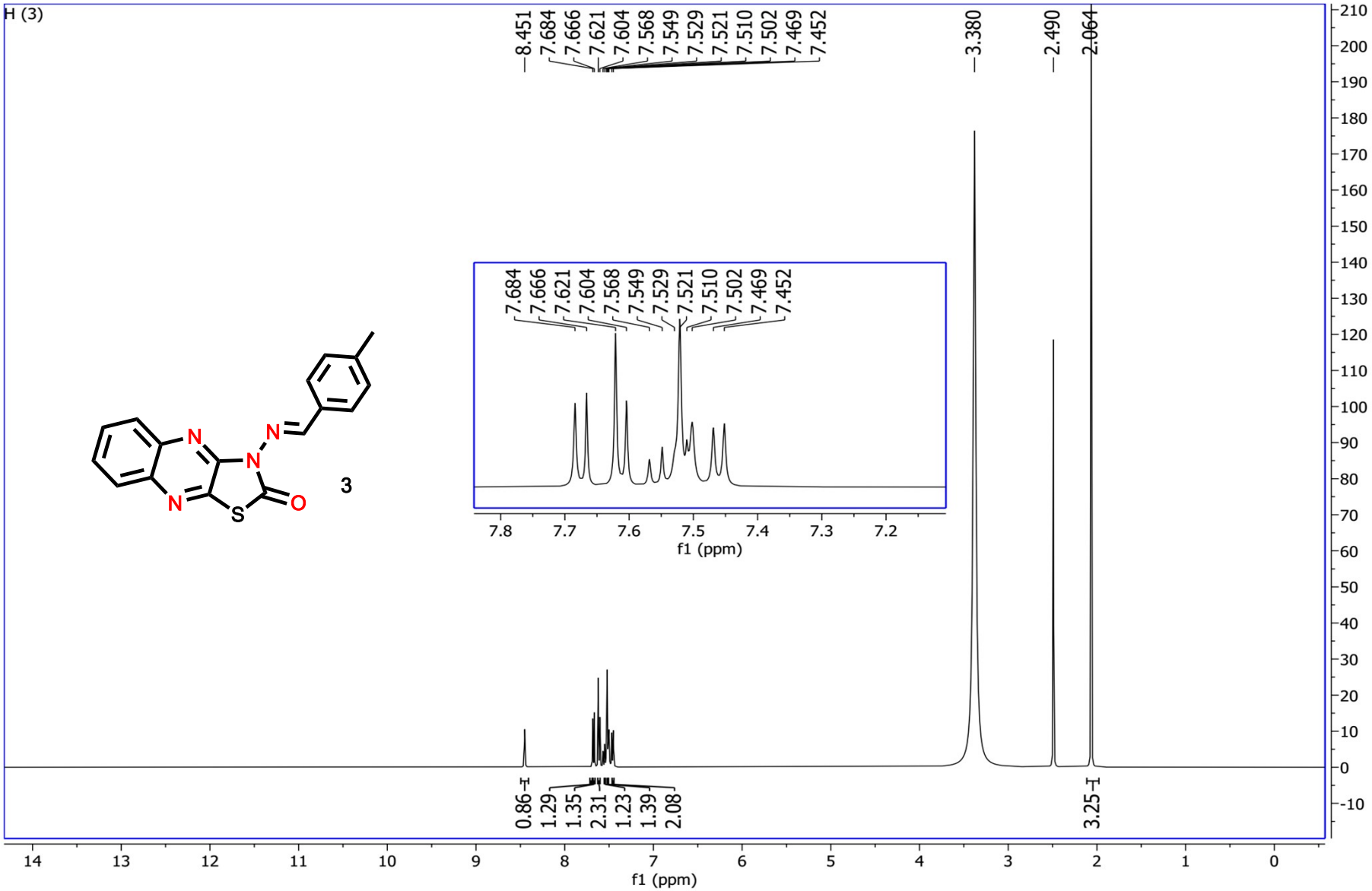
Scheme SI: The mechanismatic equation of bioactive thiazolo-quinoxaline compounds **7**

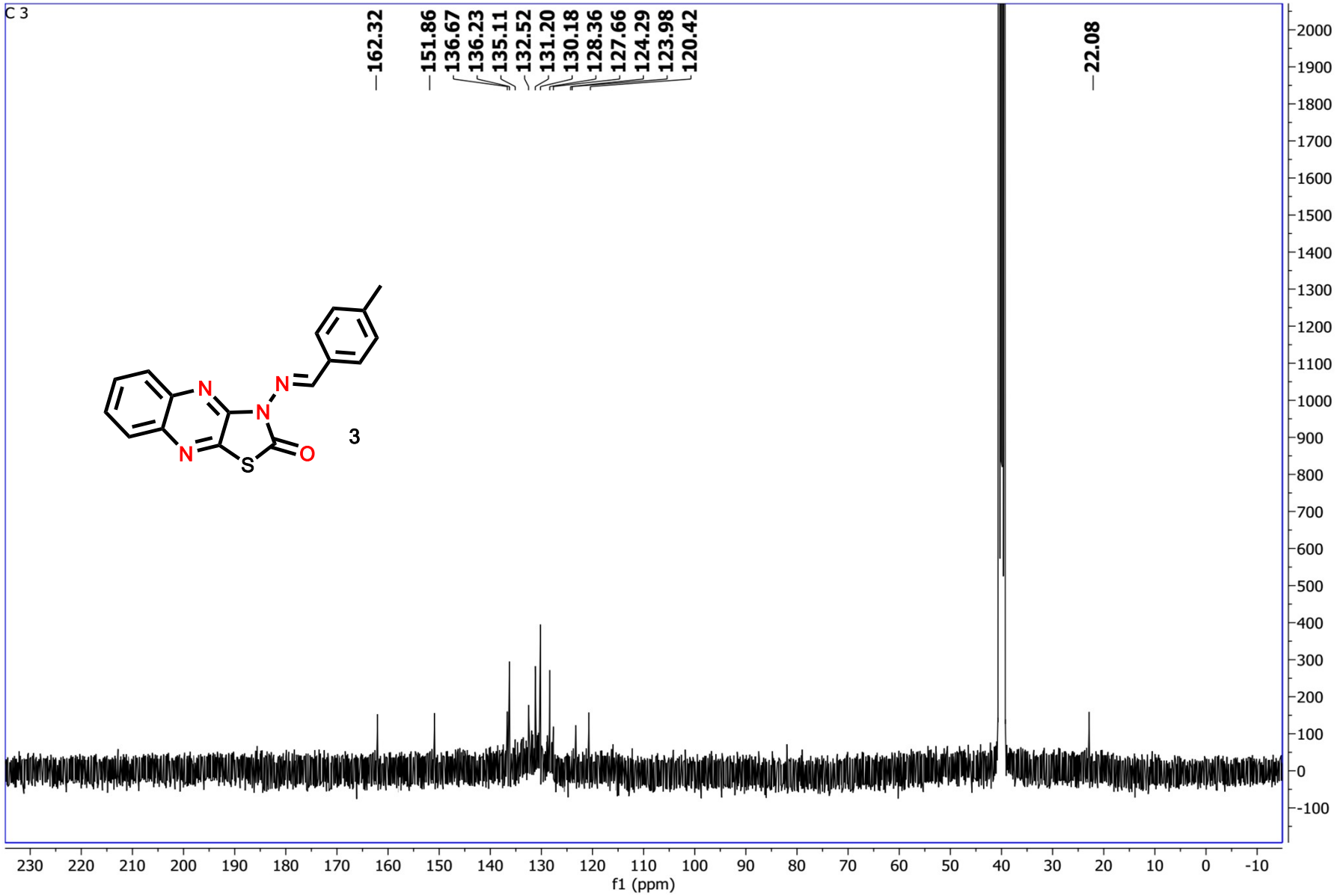

BRUKER
Transmittance [%]
100
99
98
97
96
95
94
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3246.98
3133.20
2787.31
2179.19
2082.63
1659.96
1611.56
1559.56
1419.76
1359.92
1318.36
1278.20
1220.75
1101.93
1006.11
953.10
825.02
763.30
597.45
NH2
N
N
N
S
O
(2)

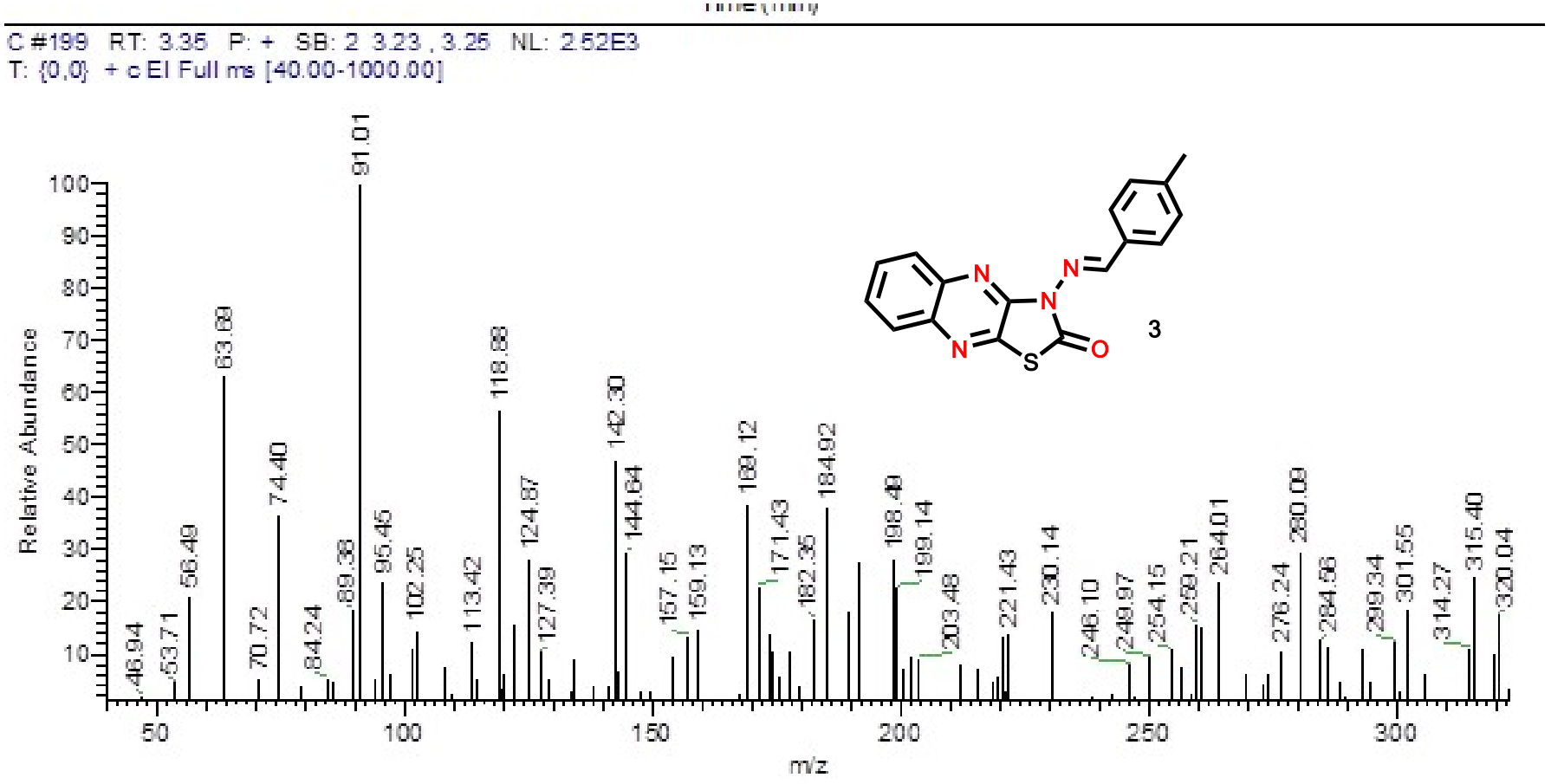

H NMR (2)
7.89
7.87
7.70
7.68
7.66
7.61
7.59
7.57
7.32
3.72
2.49
NH2
N
N
N
S
O
(2)
f1 (ppm)
2.13
0.87
0.75
1.42

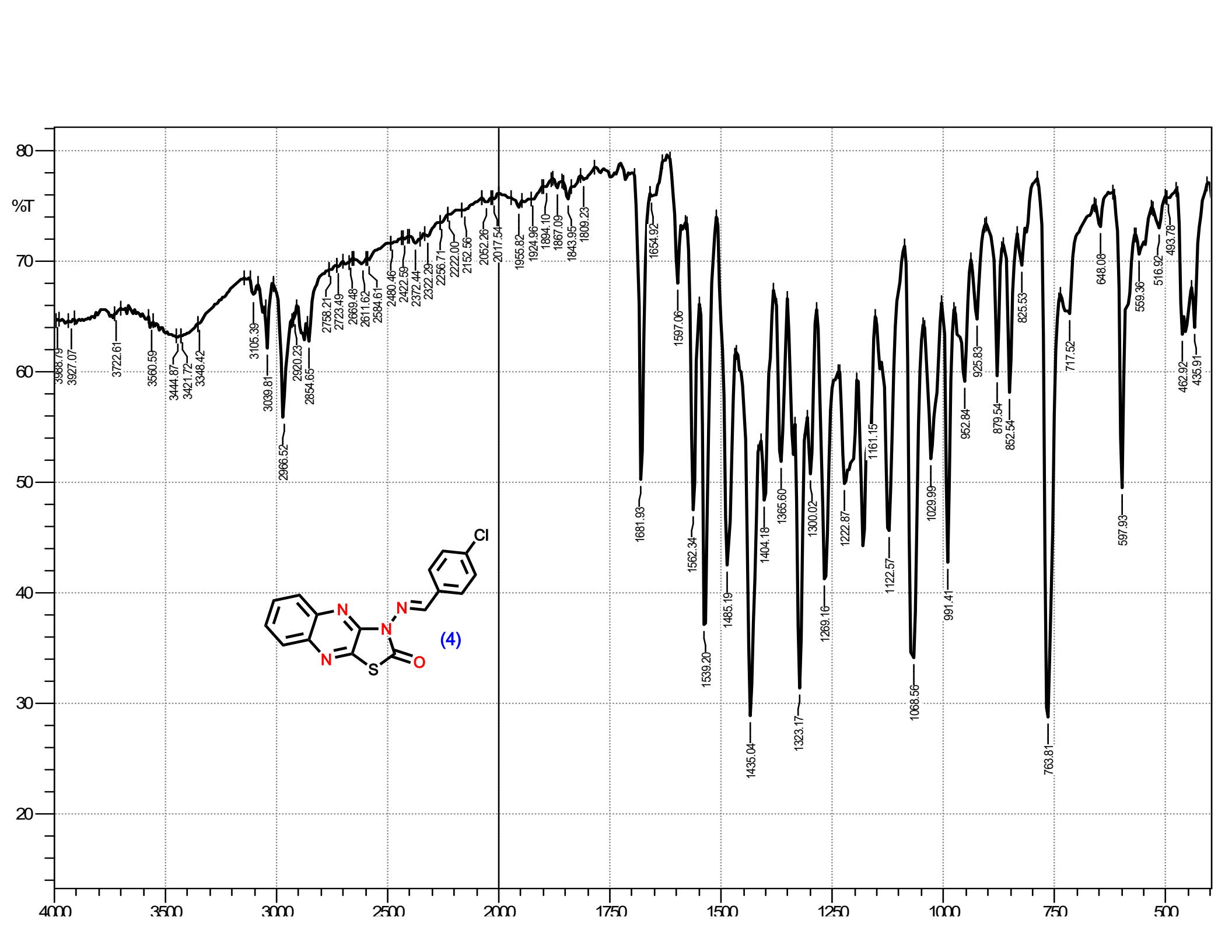

C NMR (2)
155.15
144.59
140.01
137.05
135.48
131.77
130.29
127.64
125.42
NH2
N
N
O
S
N
(2)
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

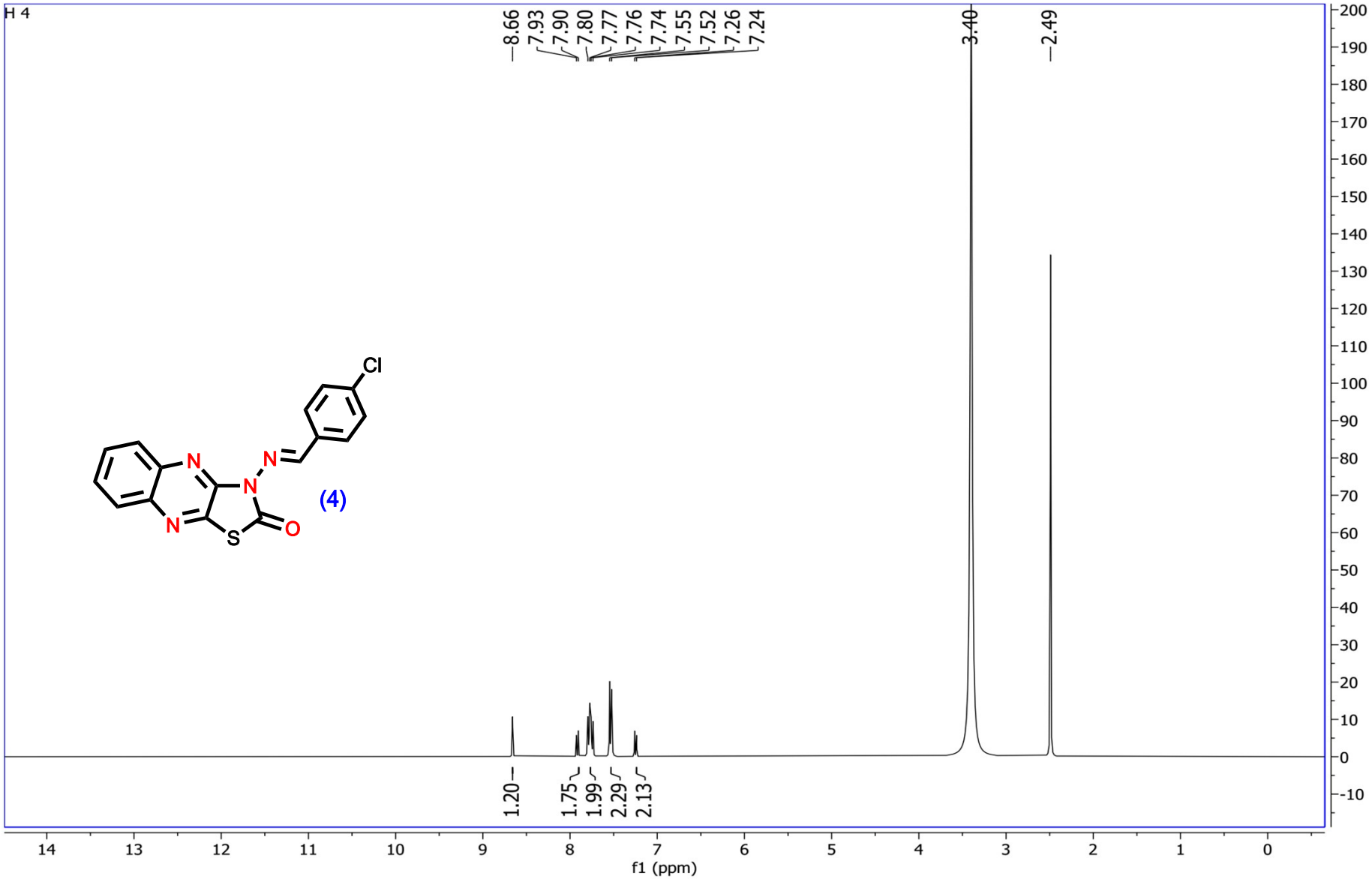

Y77
% Transmittance
Wavenumbers (cm-1)
3200.49
3073.47
3038.02
2972.82
2923.67
2880.52
1654.98
1602.27
1545.31
1482.89
1442.55
1408.11
1327.18
1273.98
1235.94
1201.02
1140.95
1075.31
1034.61
1008.92
928.99
908.62
852.63
820.27
751.08
701.46
669.47
647.60
624.51
610.36
589.93
545.46
530.06
490.42
473.44
440.13
N
N
N
S
O
3

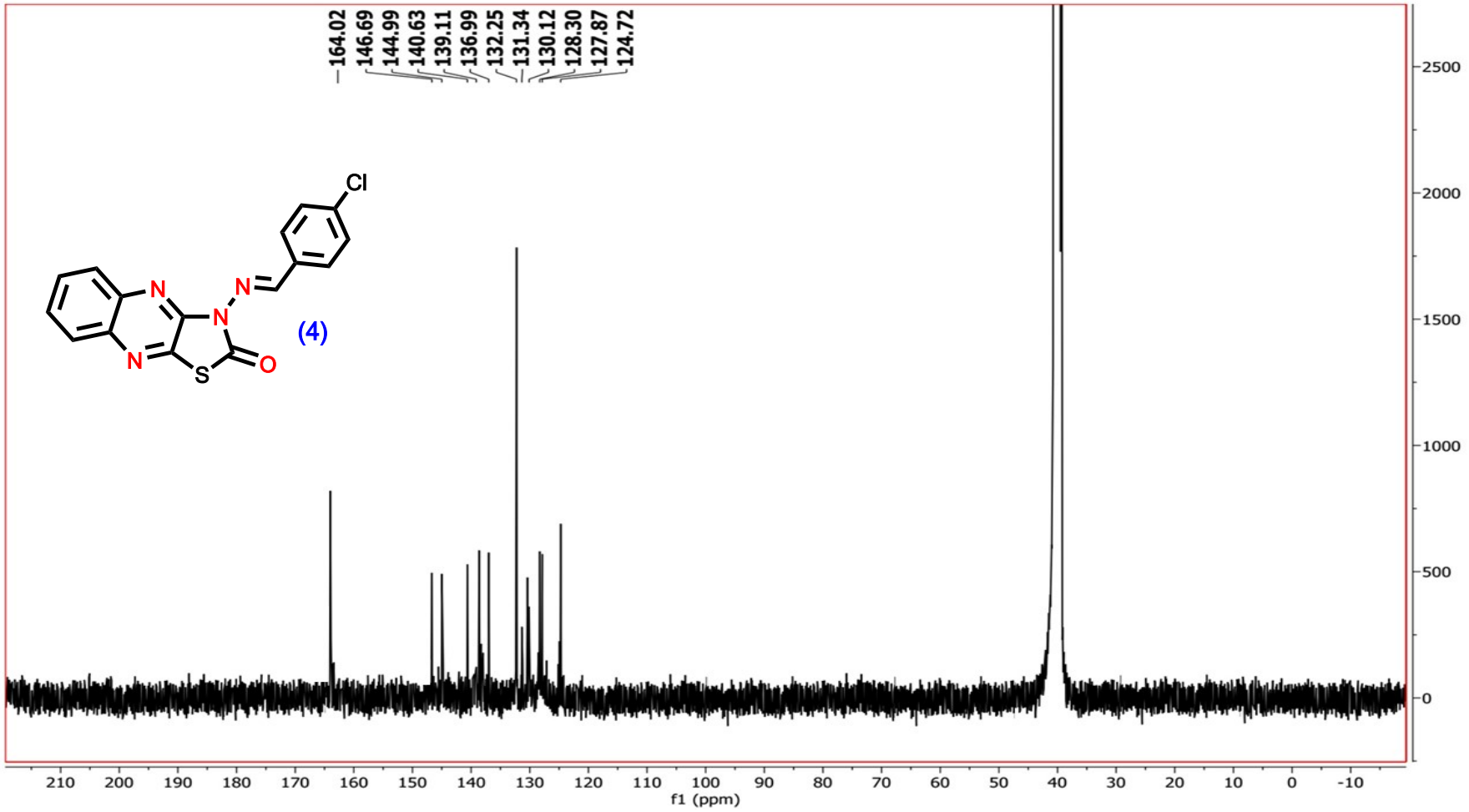

H (3)
8.451
7.684
7.666
7.621
7.604
7.568
7.549
7.529
7.521
7.510
7.502
7.469
7.452
3.380
2.490
2.064
0.86
1.29
1.35
2.31
1.23
1.39
2.08
3.25
f1 (ppm)
3

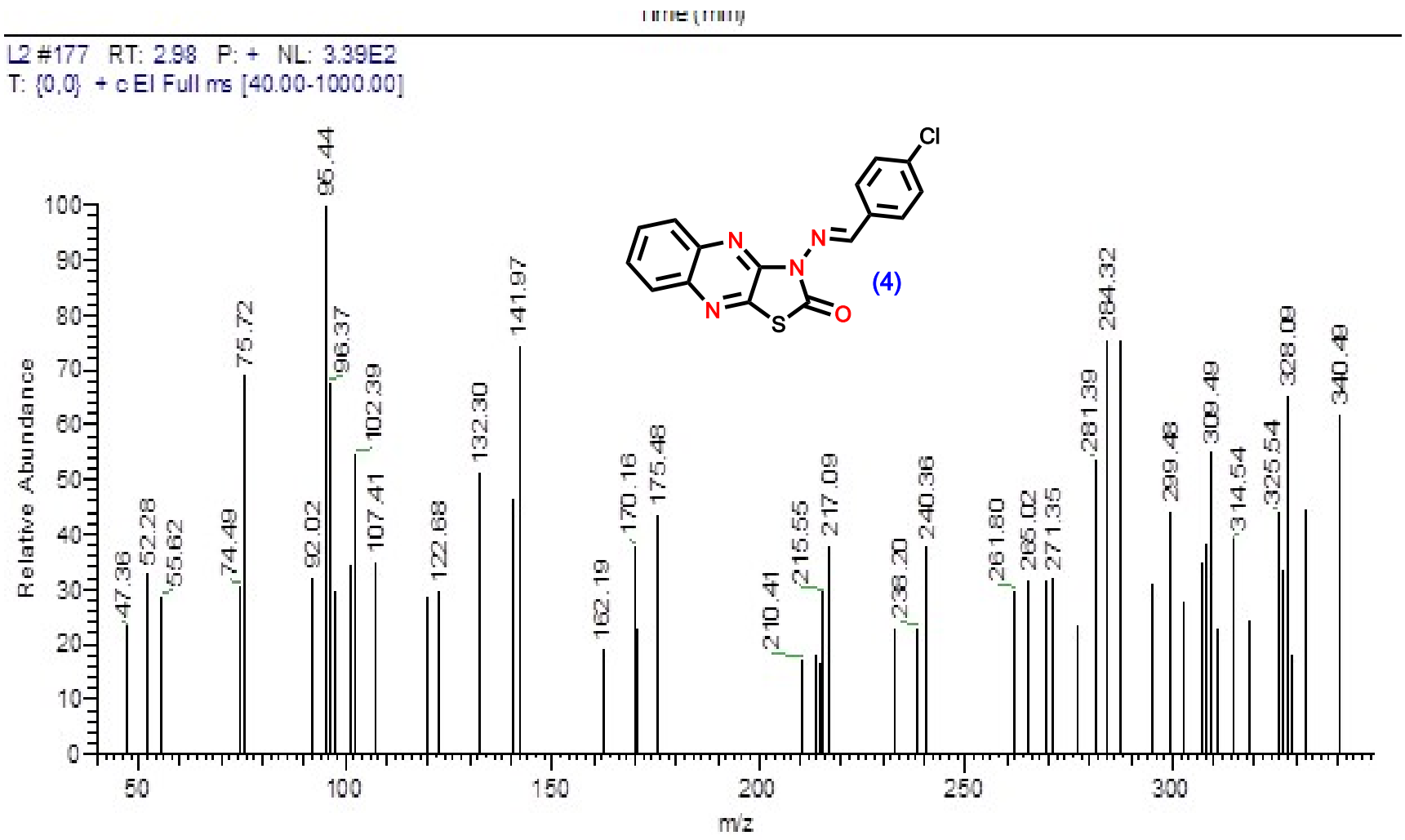

C 3
162.32
151.86
136.67
136.23
135.11
132.52
131.20
130.18
128.36
127.66
124.29
123.98
120.42
22.08
N
N
N
S
O
3
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

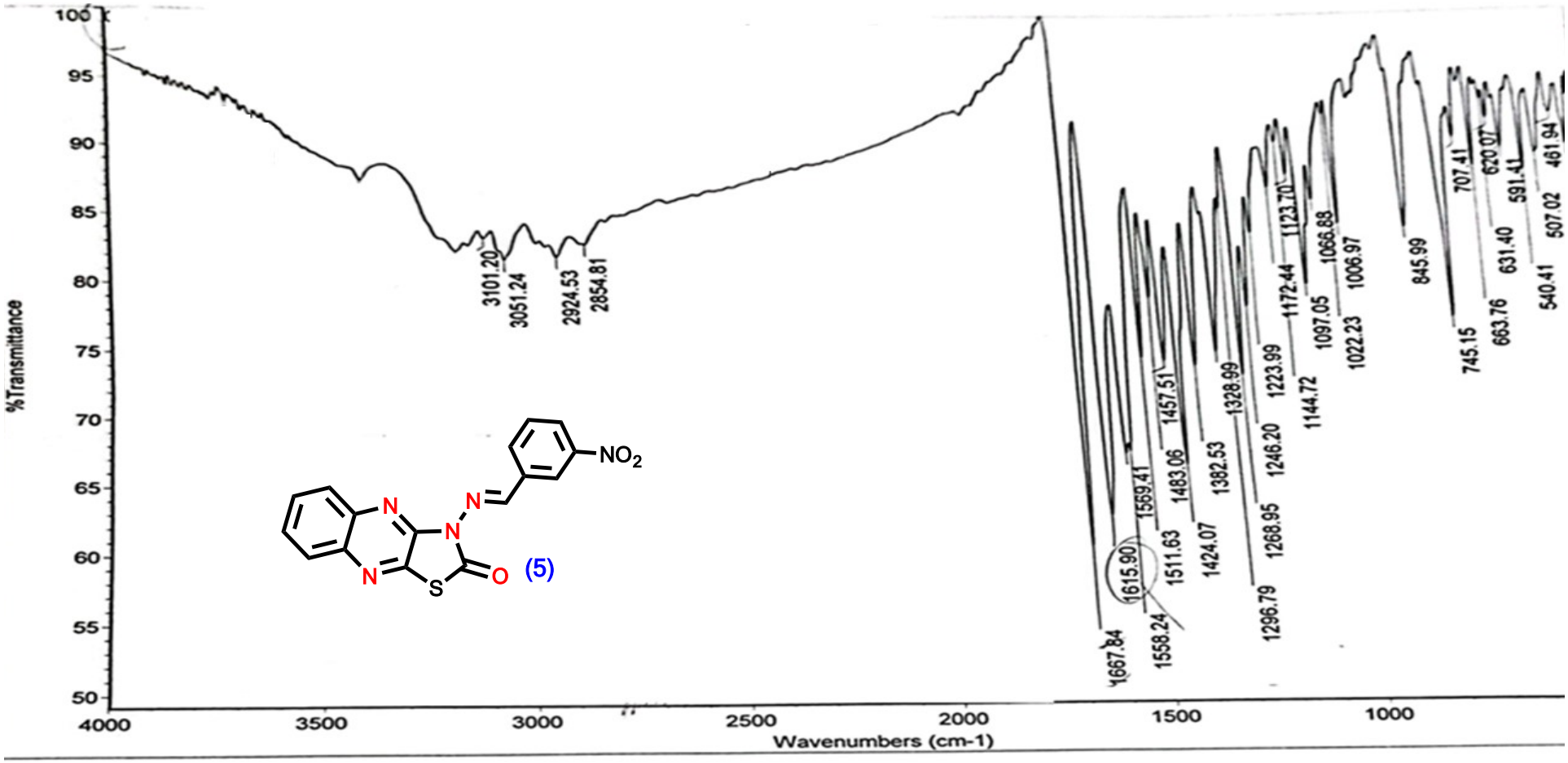

C #199 RT: 3.35 P: + SB: 2 3.23 , 3.25 NL: 2.52E3
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
3
N
N
N
S
O
46.94
53.71
56.49
63.69
70.72
74.40
84.24
89.38
91.01
95.45
102.25
113.42
118.88
124.87
127.39
142.30
144.64
157.15
159.13
169.12
171.43
182.35
184.92
198.49
199.14
203.48
221.43
230.14
246.10
249.97
254.15
259.21
264.01
276.24
280.09
284.96
299.34
301.55
314.27
315.40
320.04

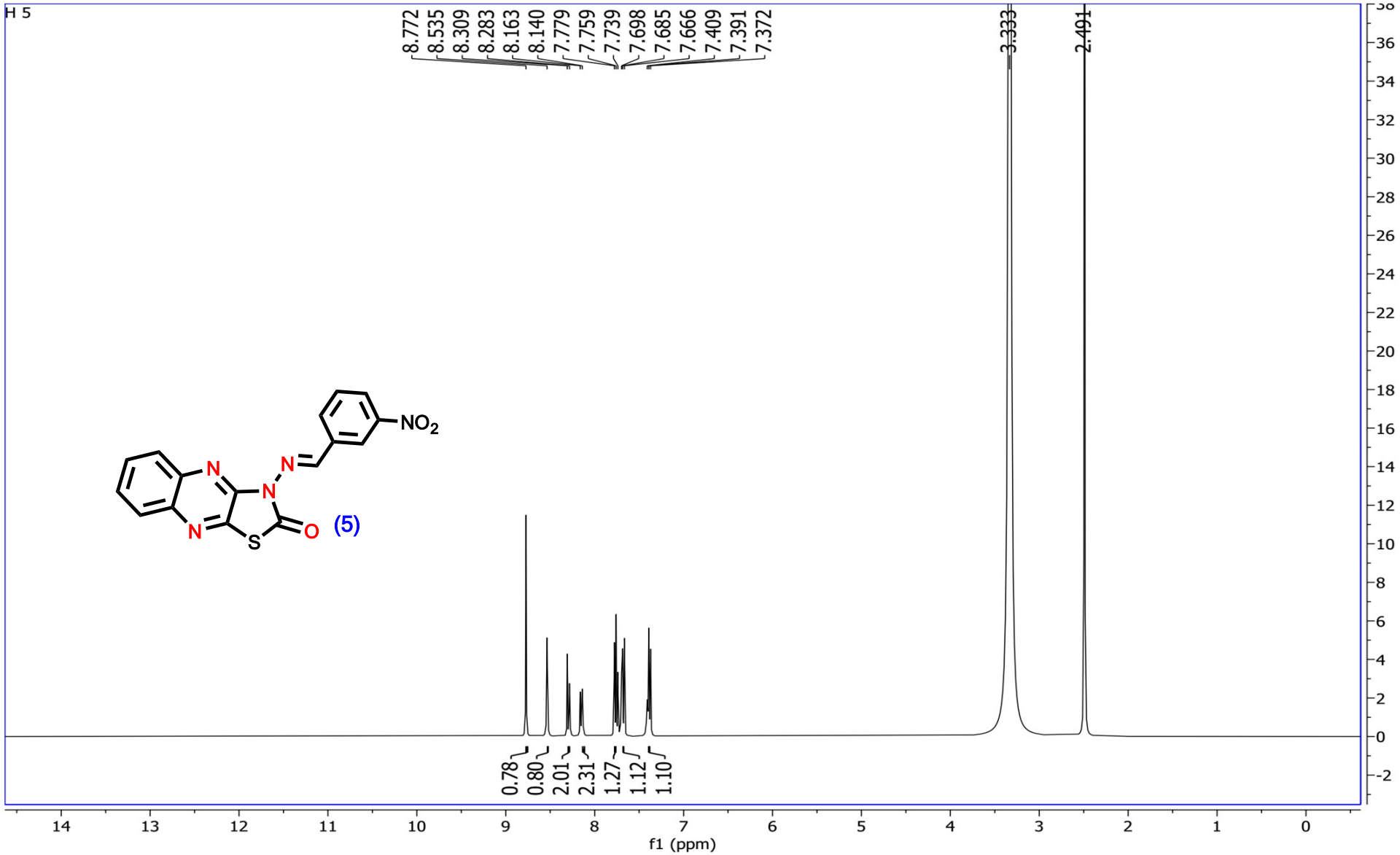

%T
80
70
60
50
40
30
20
4000
3500
3000
2500
2000
1750
1500
1250
1000
750
500
3988.79
3927.07
3722.61
3560.59
3444.87
3421.72
3348.42
3105.39
3039.81
2966.52
2920.23
2854.65
2758.21
2723.49
2669.48
2611.62
2584.61
2480.46
2422.59
2372.44
2322.29
2256.71
2222.00
2152.56
2052.26
2017.54
1955.82
1924.96
1894.10
1867.09
1843.95
1809.23
1681.93
1654.92
1597.06
1562.34
1539.20
1485.19
1435.04
1404.18
1365.60
1323.17
1300.02
1269.16
1222.87
1161.15
1122.57
1068.56
1029.99
991.41
952.84
925.83
879.54
852.54
825.53
763.81
717.52
648.08
597.93
559.36
516.92
493.78
462.92
435.91
Cl
N
N
N
N
S
O
(4)

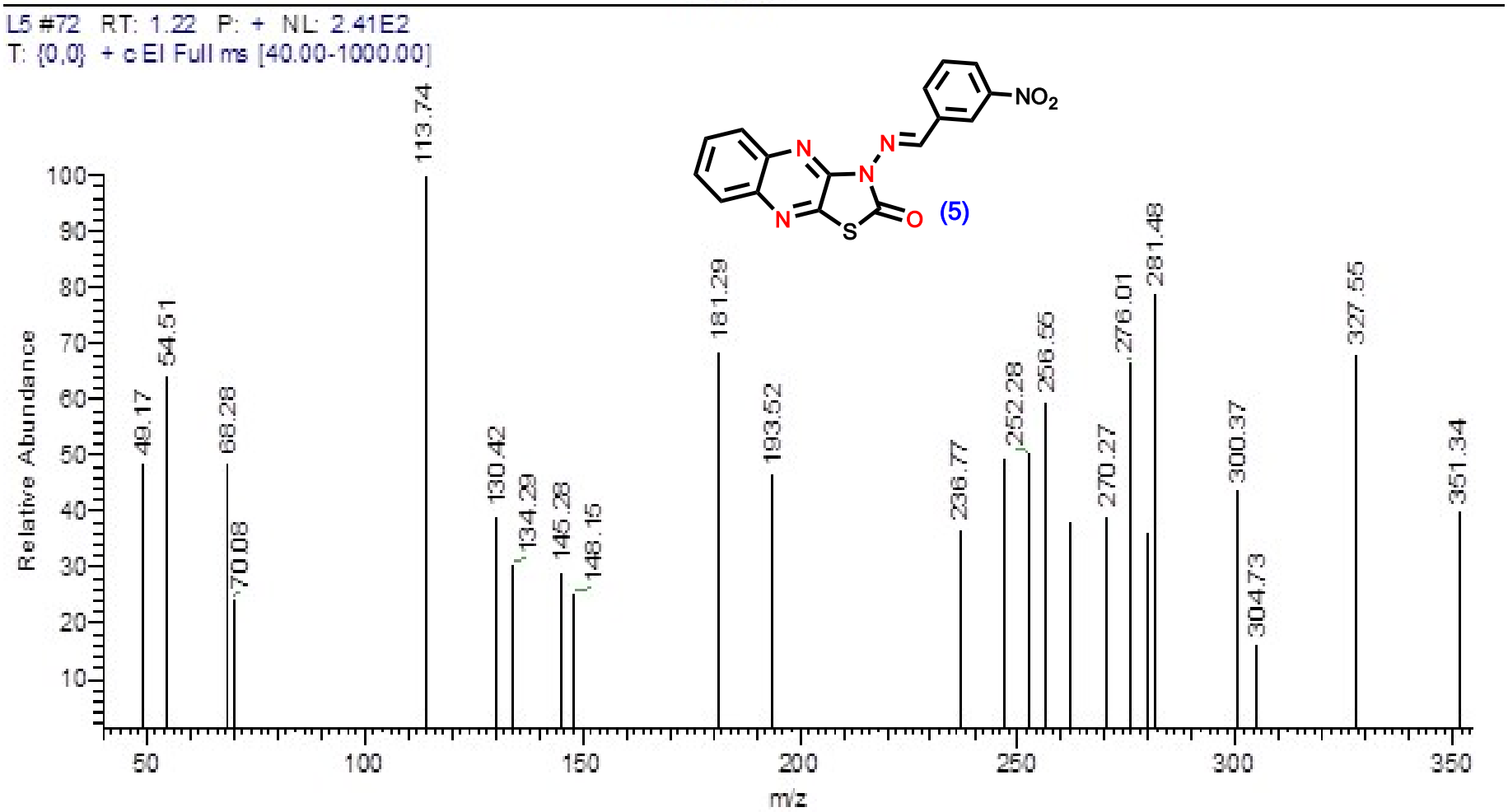

H 4
8.66
7.93
7.90
7.80
7.77
7.76
7.74
7.55
7.52
7.26
7.24
3.40
2.49
Cl
N
N
N
N
S
O
(4)
1.20
1.75
1.99
2.29
2.13
f1 (ppm)

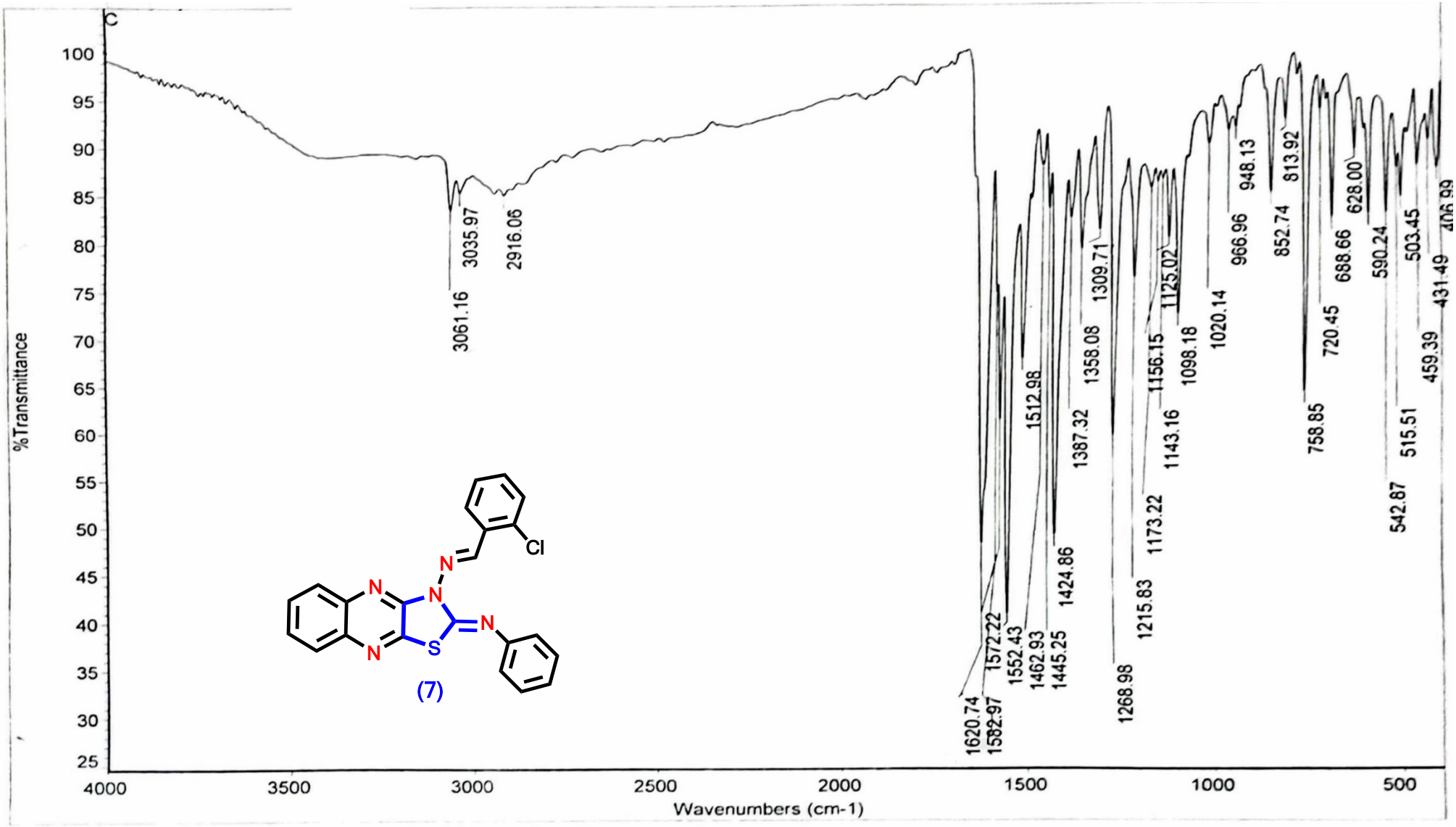

164.02
146.69
144.99
140.63
139.11
136.99
132.25
131.34
130.12
128.30
127.87
124.72
Cl
N
N
N
S
O
(4)
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


L2 #177 RT: 2.98 P: + NL: 3.39E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
(4)
Cl
N
N
N
S
O
95.44
75.72
96.37
102.39
141.97
132.30
107.41
92.02
122.68
74.49
52.28
55.62
47.36
162.19
170.16
175.48
210.41
215.55
217.09
238.20
240.36
261.80
265.02
271.35
281.39
284.32
299.48
309.49
314.54
325.54
328.08
340.40

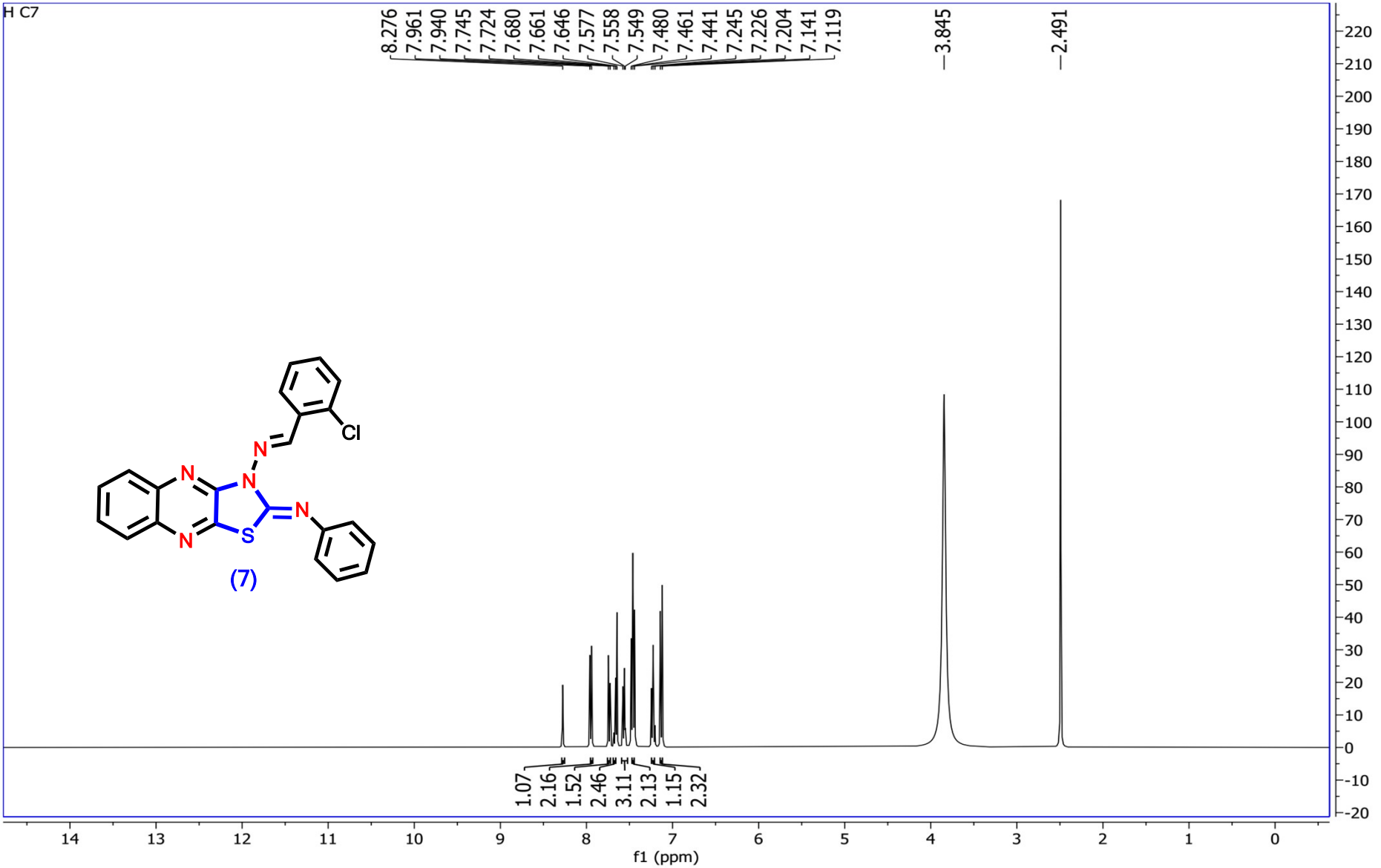

%Transmittance
Wavenumbers (cm-1)
3101.20
3051.24
2924.53
2854.81
1667.84
1615.90
1569.41
1558.24
1511.63
1483.06
1457.51
1424.07
1382.53
1328.99
1296.79
1268.95
1246.20
1223.99
1172.44
1144.72
1123.70
1097.05
1066.88
1022.23
1006.97
845.99
745.15
707.41
663.76
631.40
620.07
591.41
540.41
507.02
461.94
NO2
(5)

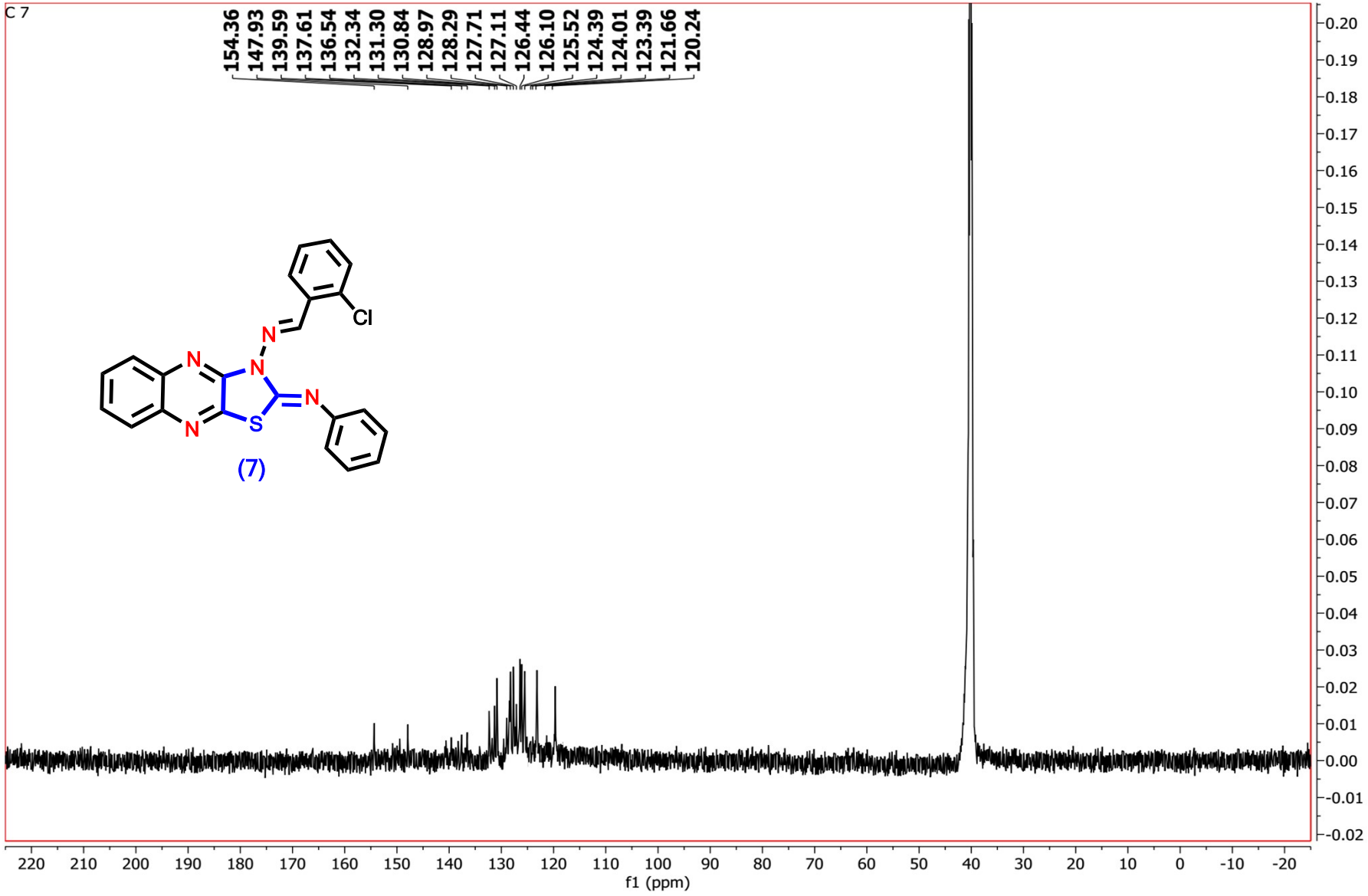

H 5
8.772
8.535
8.309
8.283
8.163
8.140
7.779
7.759
7.739
7.698
7.685
7.666
7.409
7.391
7.372
3.333
2.491
NO2
N
N
N
N
O
S
(5)
0.78
0.80
2.01
2.31
1.27
1.12
1.10
f1 (ppm)

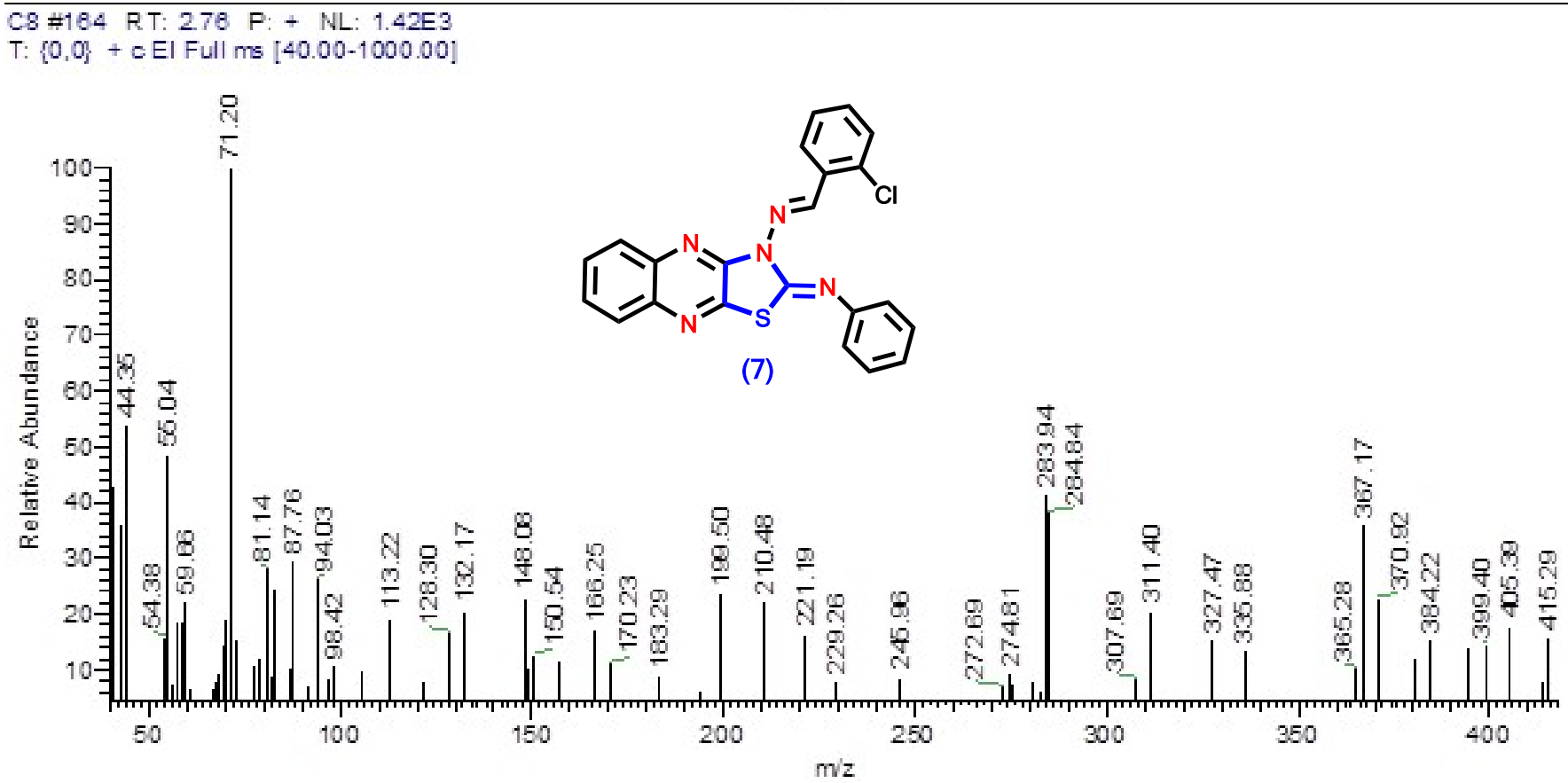

L5 #72 RT: 1.22 P: + NL: 2.41E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
(5)
49.17
54.51
68.28
70.08
113.74
130.42
134.29
145.28
148.15
181.29
193.52
236.77
252.28
256.55
270.27
276.01
281.48
300.37
304.73
327.55
351.34

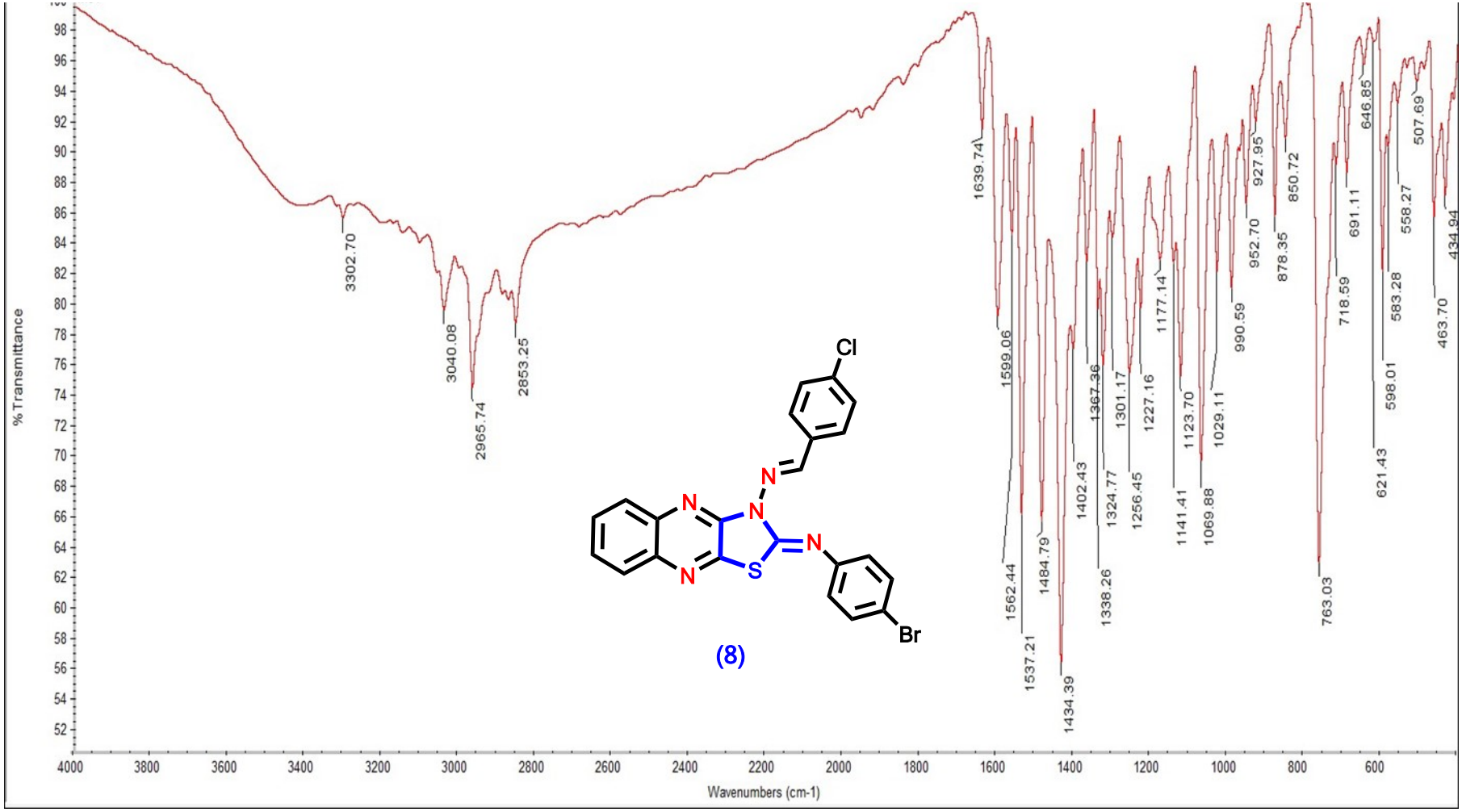

C
%Transmittance
Wavenumbers (cm-1)
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
4000
3500
3000
2500
2000
1500
1000
500
3061.16
3035.97
2916.06
1620.74
1582.97
1572.22
1552.43
1512.98
1462.93
1445.25
1424.86
1387.32
1358.08
1309.71
1268.98
1215.83
1173.22
1156.15
1143.16
1125.02
1098.18
1020.14
966.96
948.13
852.74
813.92
758.85
720.45
688.66
628.00
590.24
542.87
515.51
503.45
459.39
431.49
406.99
Cl
N
N
N
N
S
N

(7)

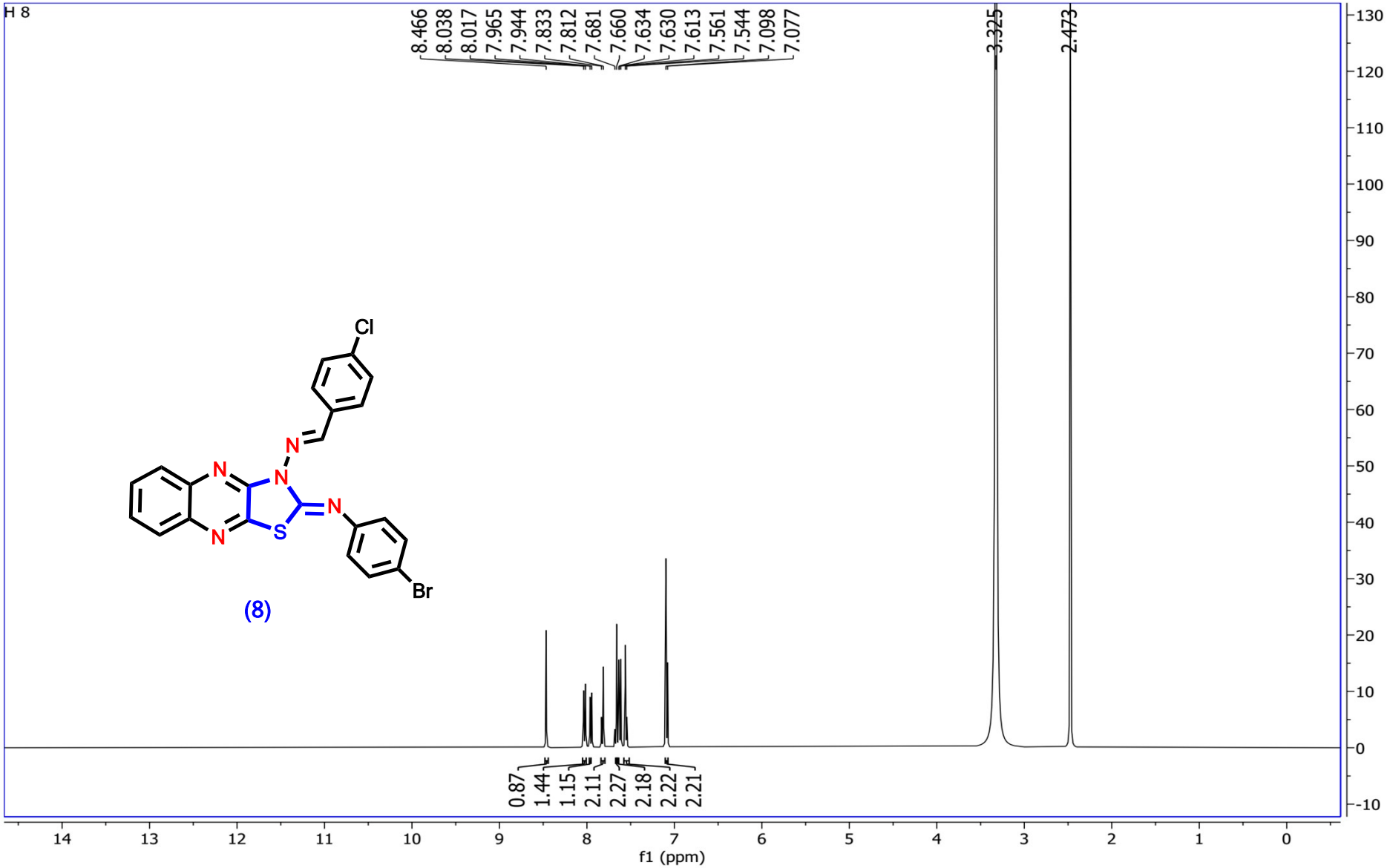

H C7
8.276
7.961
7.940
7.745
7.724
7.680
7.661
7.646
7.577
7.558
7.549
7.480
7.461
7.441
7.245
7.226
7.204
7.141
7.119
3.845
2.491
1.07
2.16
1.52
2.46
3.11
2.13
1.15
2.32
Cl
N
N
N
N
S
(7)
f1 (ppm)

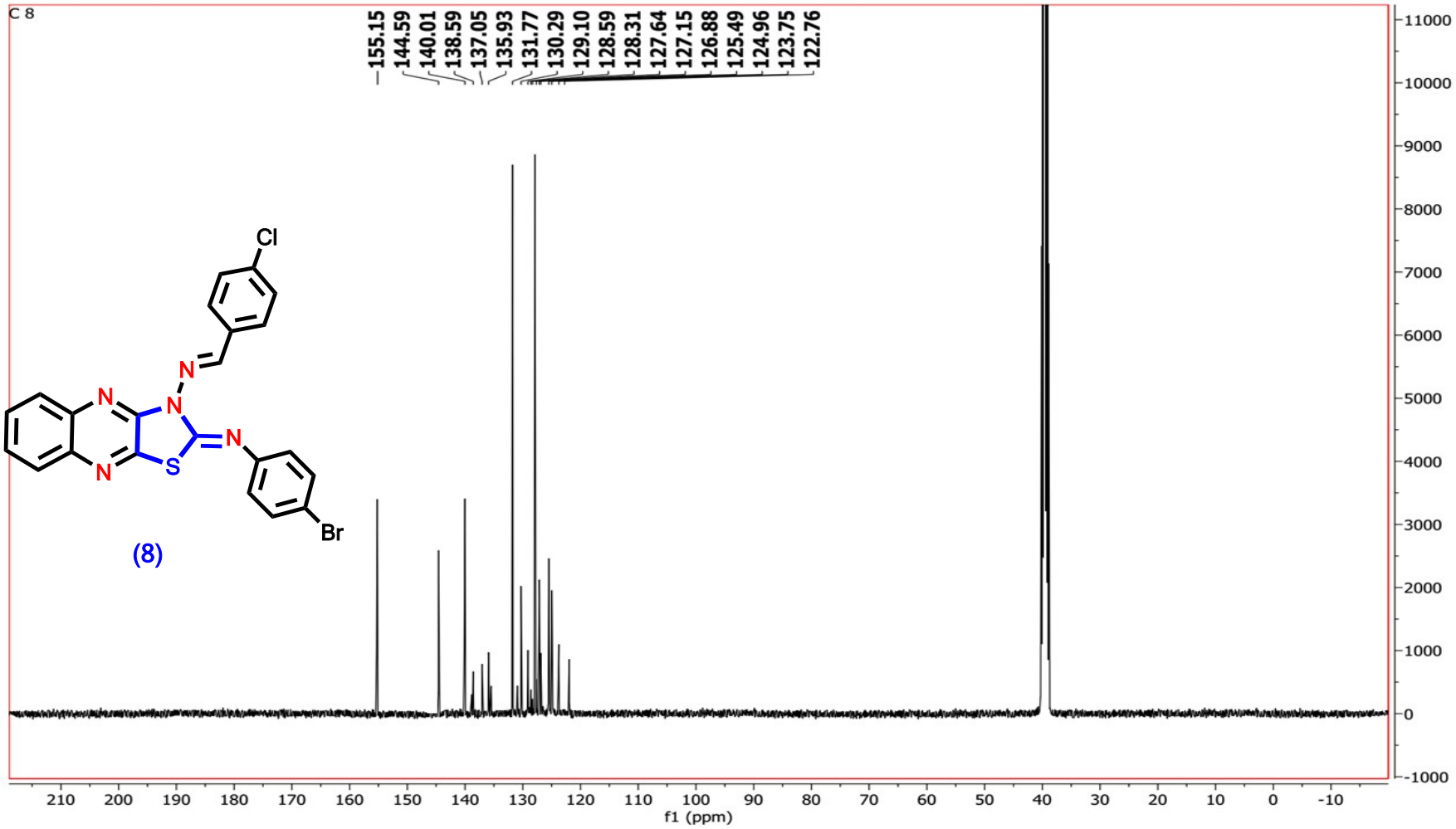

C 7
154.36
147.93
139.59
137.61
136.54
132.34
131.30
130.84
128.97
128.29
127.71
127.11
126.44
126.10
125.52
124.39
124.01
123.39
121.66
120.24
Cl
N
N
N
N
S
N
(7)
f1 (ppm)

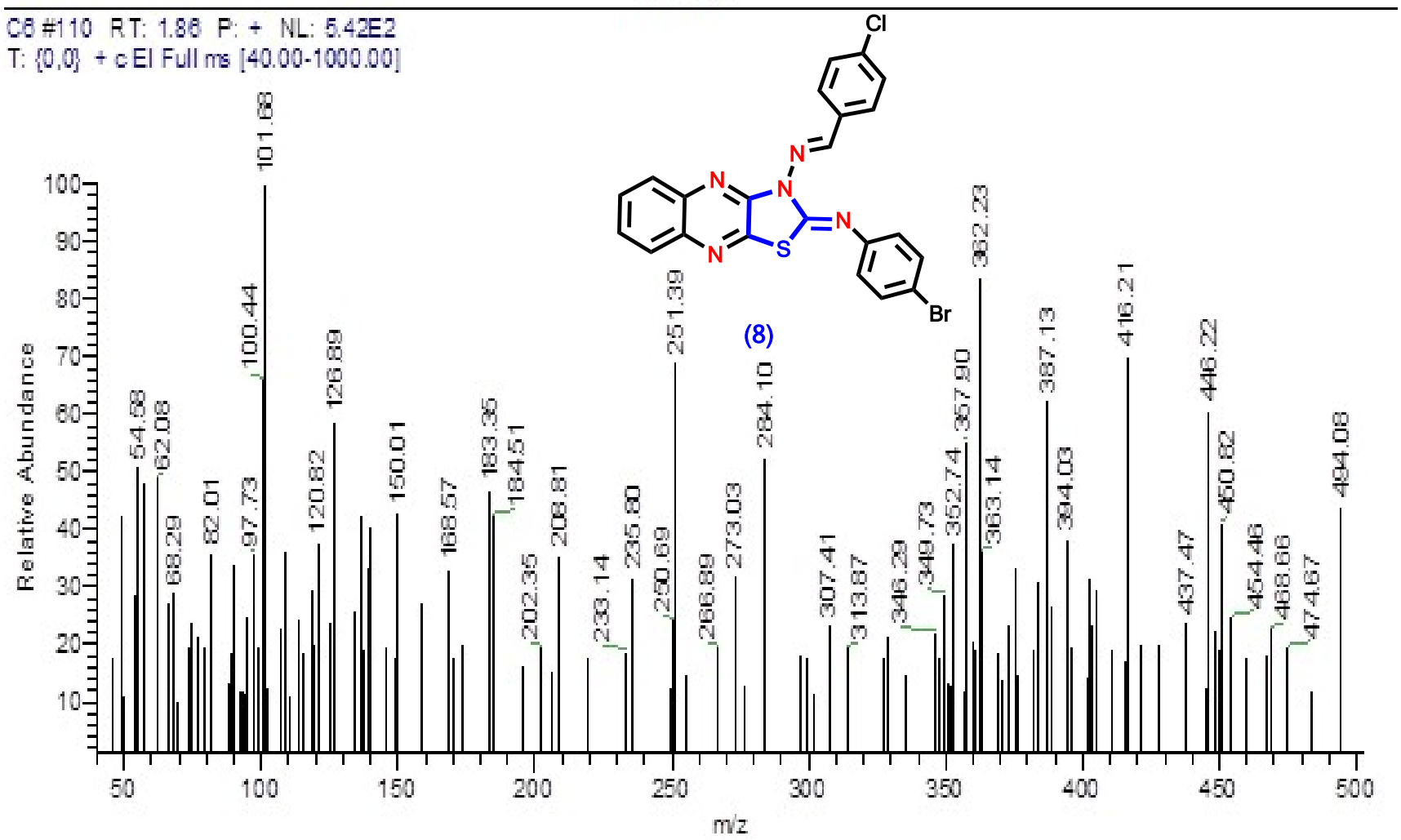

C8 #164 RT: 2.76 P: + NL: 1.42E3
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
(7)
Cl
N
N
N
N
S
71.20
44.35
55.04
54.38
59.06
81.14
87.76
94.03
98.42
113.22
128.30
132.17
148.08
150.54
166.25
170.23
183.29
199.50
210.48
221.19
229.26
245.96
272.69
274.81
283.94
284.84
307.69
311.40
327.47
335.88
365.28
367.17
370.92
384.22
399.40
405.39
415.29

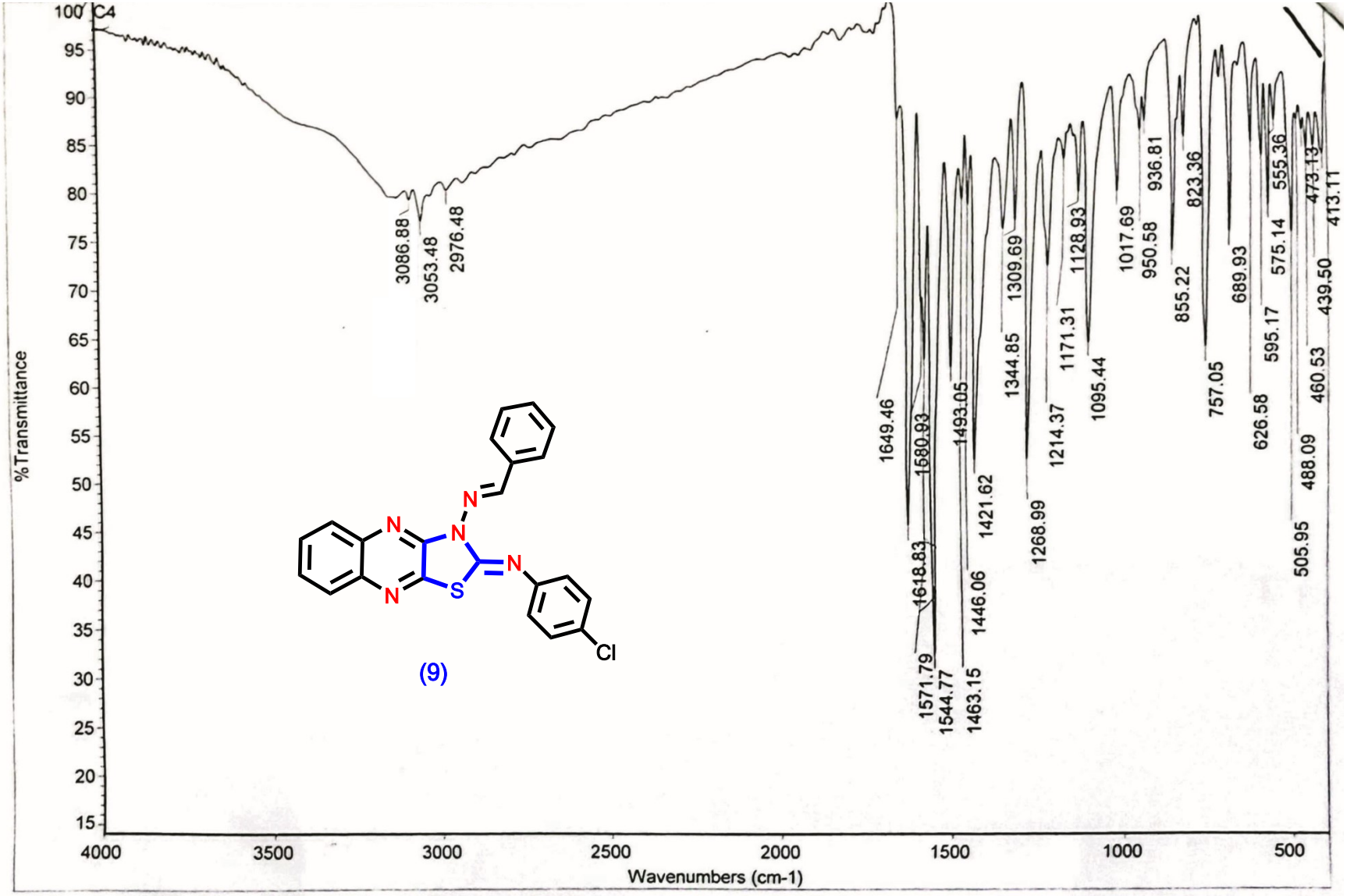

% Transmittance
Wavenumbers (cm-1)
3302.70
3040.08
2965.74
2853.25
1639.74
1599.06
1562.44
1537.21
1484.79
1434.39
1402.43
1367.36
1338.26
1324.77
1301.17
1256.45
1227.16
1177.14
1141.41
1123.70
1069.88
1029.11
990.59
952.70
927.95
878.35
850.72
763.03
718.59
691.11
646.85
621.43
598.01
583.28
558.27
507.69
463.70
434.94
Cl
Br
N
S

(8)

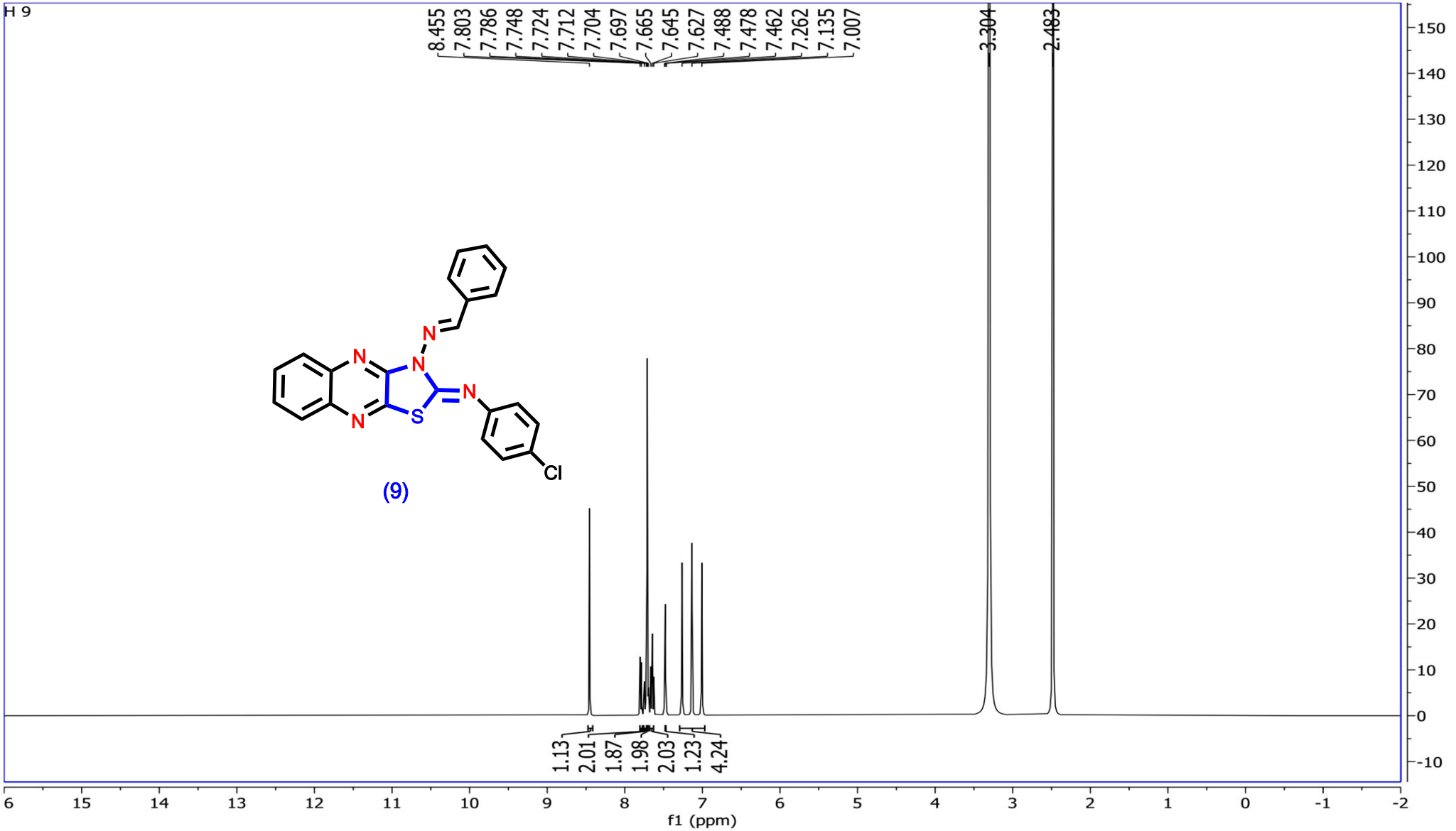

H 8
8.466
8.038
8.017
7.965
7.944
7.833
7.812
7.681
7.660
7.634
7.630
7.613
7.561
7.544
7.098
7.077
3.325
2.473
Cl
N
N
N
N
S
N
Br
(8)
0.87
1.44
1.15
2.11
2.27
2.18
2.22
2.21
f1 (ppm)


C 8
155.15
144.59
140.01
138.59
137.05
135.93
131.77
130.29
129.10
128.59
128.31
127.64
127.15
126.88
125.49
124.96
123.75
122.76
Cl
N
N
N
N
S
Br
(8)
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

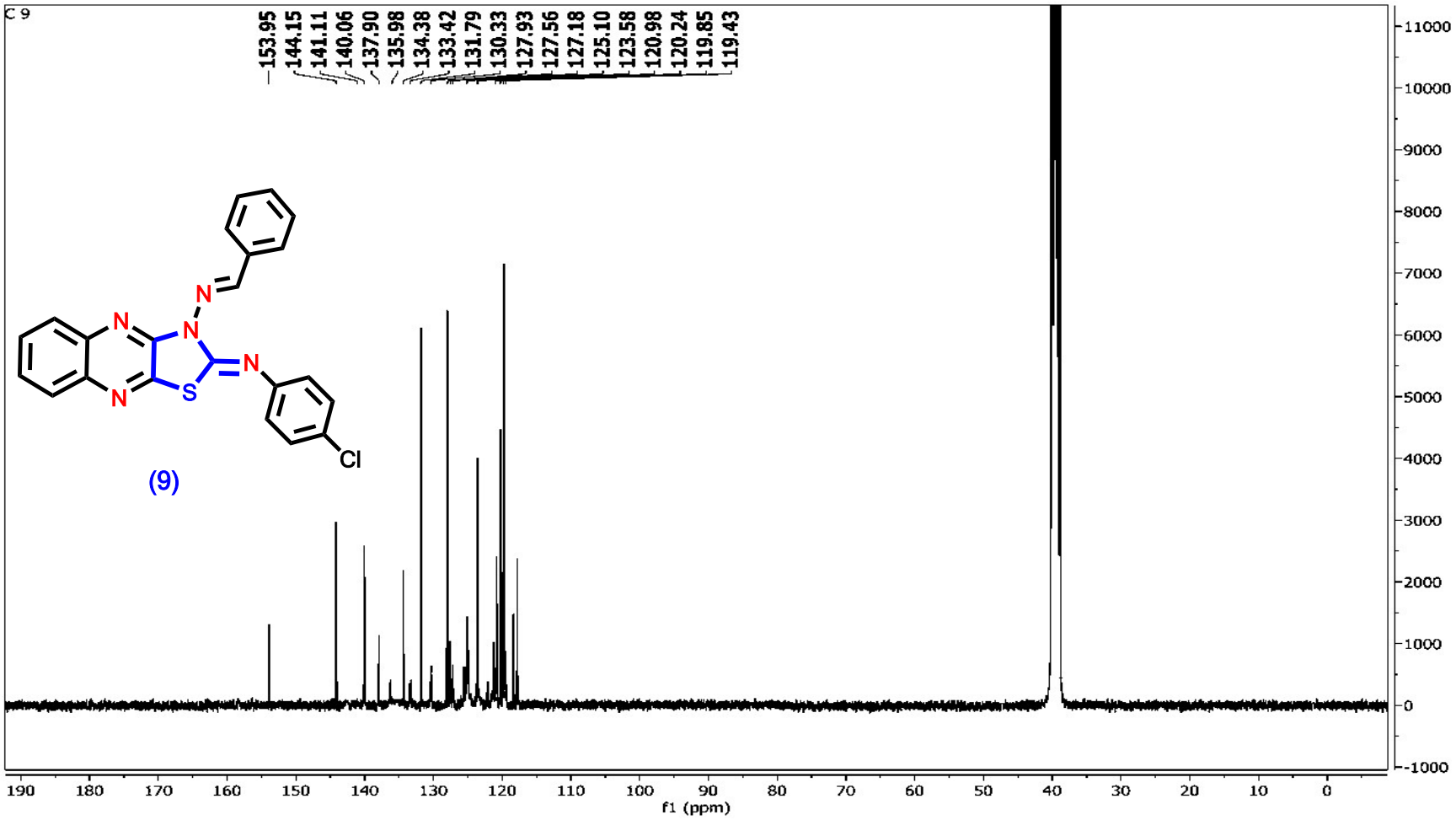

C8 #110 RT: 1.86 P: + NL: 5.42E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
(8)
Cl
Br
N
S
54.58
62.08
68.29
82.01
97.73
100.44
101.68
120.82
126.89
150.01
168.57
183.35
184.51
202.35
208.81
233.14
235.80
251.39
266.89
273.03
284.10
307.41
313.87
346.29
349.73
352.74
357.90
362.23
363.14
387.13
394.03
416.21
437.47
446.22
450.82
454.46
468.66
474.67
494.08

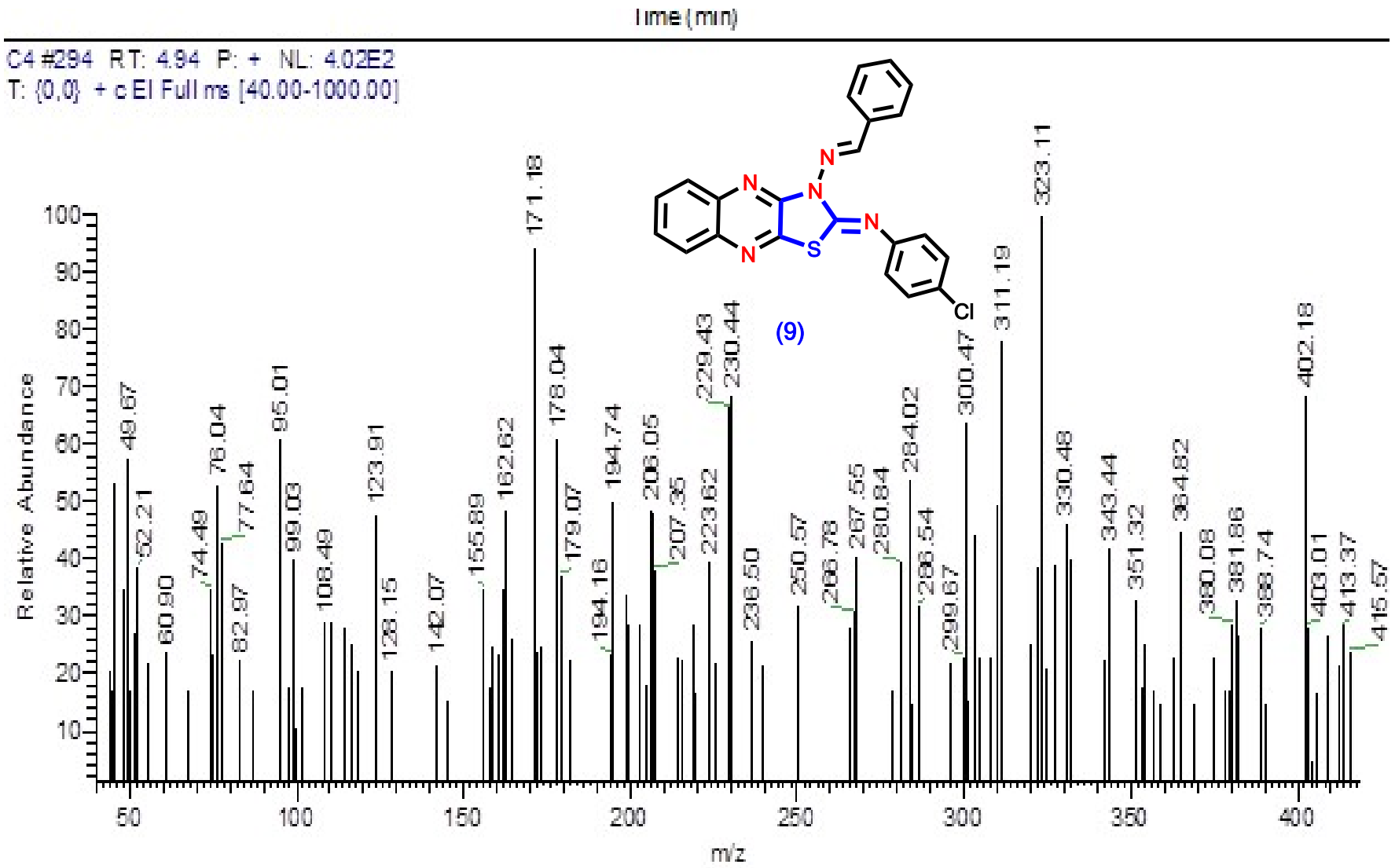

C4
%Transmittance
Wavenumbers (cm-1)
3086.88
3053.48
2976.48
1649.46
1618.83
1680.93
1571.79
1544.77
1493.05
1463.15
1446.06
1421.62
1344.85
1309.69
1268.99
1214.37
1171.31
1128.93
1095.44
1017.69
950.58
936.81
855.22
823.36
757.05
689.93
626.58
595.17
575.14
555.36
505.95
488.09
460.53
439.50
473.13
413.11
N
N
N
N
S
Cl

(9)


H 9
8.455
7.803
7.786
7.748
7.724
7.712
7.704
7.697
7.665
7.645
7.627
7.488
7.478
7.462
7.262
7.135
7.007
3.304
2.483
1.13
2.01
1.87
1.98
2.03
1.23
4.24
f1 (ppm)

(9)


C 9
153.95
144.15
141.11
140.06
137.90
135.98
134.38
133.42
131.79
130.33
127.93
127.56
127.18
125.10
123.58
120.98
120.24
119.85
119.43
N
N
N
N
S
Cl
(9)
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Time (min)
C4 #294 RT: 4.94 P: + NL: 4.02E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
(9)
Cl
N
S
49.67
52.21
60.90
74.48
76.04
77.64
82.97
95.01
99.03
108.49
123.91
128.15
142.07
155.89
162.62
171.18
178.04
179.07
194.16
194.74
206.05
207.35
223.62
229.43
230.44
236.50
250.57
266.78
267.55
280.84
284.02
286.54
299.67
300.47
311.19
323.11
330.48
343.44
351.32
364.82
380.08
381.86
388.74
402.18
403.01
413.37
415.57