

Supplementary material

One-pot synthesis and molecular modeling studies of new bioactive spiro-oxindoles based on uracil derivatives as SARS-CoV-2 inhibitors targeting RNA polymerase and spike glycoprotein

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% of viability for Chloroquine

conc μM/mL	% viability	% viability	% viability		
15	5.597655	6.297361	4.897948	16.79296	5.597655
7.5	4.198241	4.198241	4.198241	12.59472	4.198241
3.75	3.498534	3.498534	4.897948	11.89502	3.965005
1.875	2.798827	4.897948	3.498534	11.19531	3.73177
0.937	3.498534	5.597655	4.897948	13.99414	4.664712
0.468	19.59179	18.89208	23.79003	62.2739	20.75797
0.234	30.08739	33.58593	39.18358	102.8569	34.28563
0.117	81.16599	82.56541	93.76071	257.4921	85.8307
0.0585	100	100	100	300	100
0.029	100	100	100	300	100

D-samar-sispy 4 -1H
D-samar-sispy 4 -1H

11.713

11.063

10.866

9.721

7.666

7.661

7.645

7.640

7.521

7.500

7.166

7.161

3.454

3.343

3.329

3.034

3.028

3.018

3.012

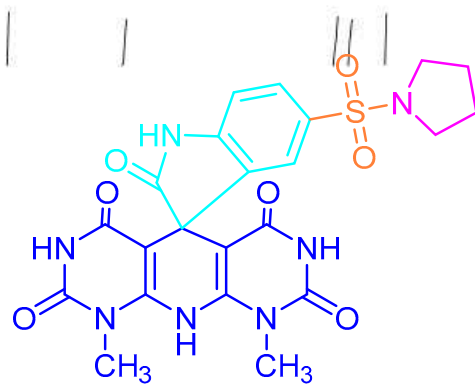
2.500

1.563

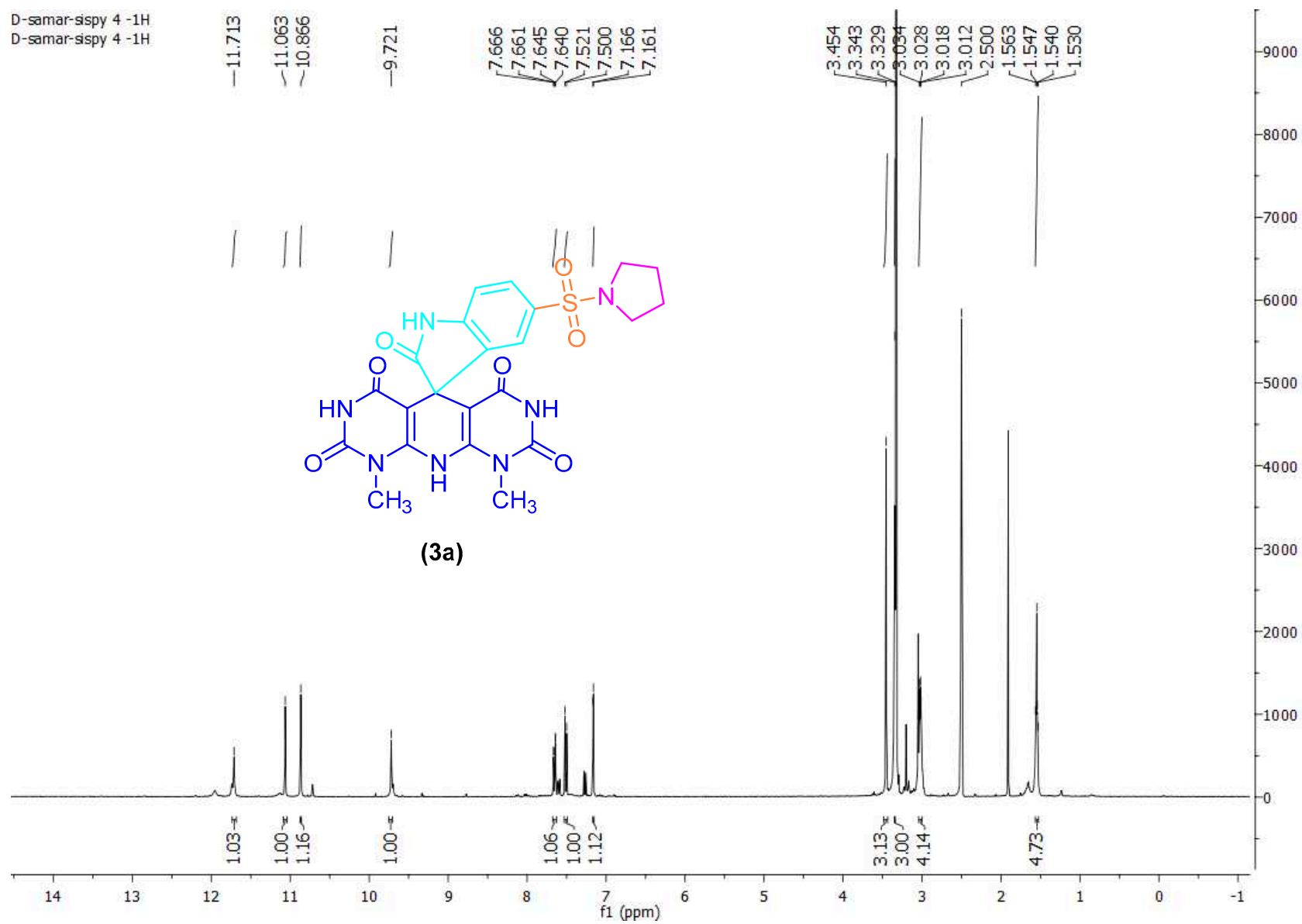
1.547

1.540

1.530

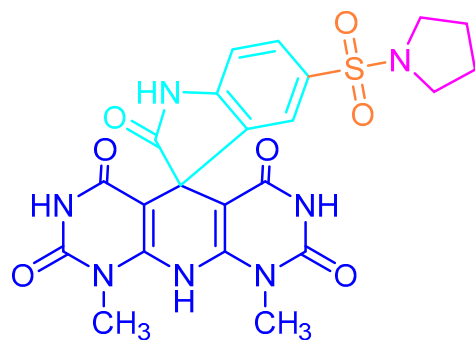


(3a)

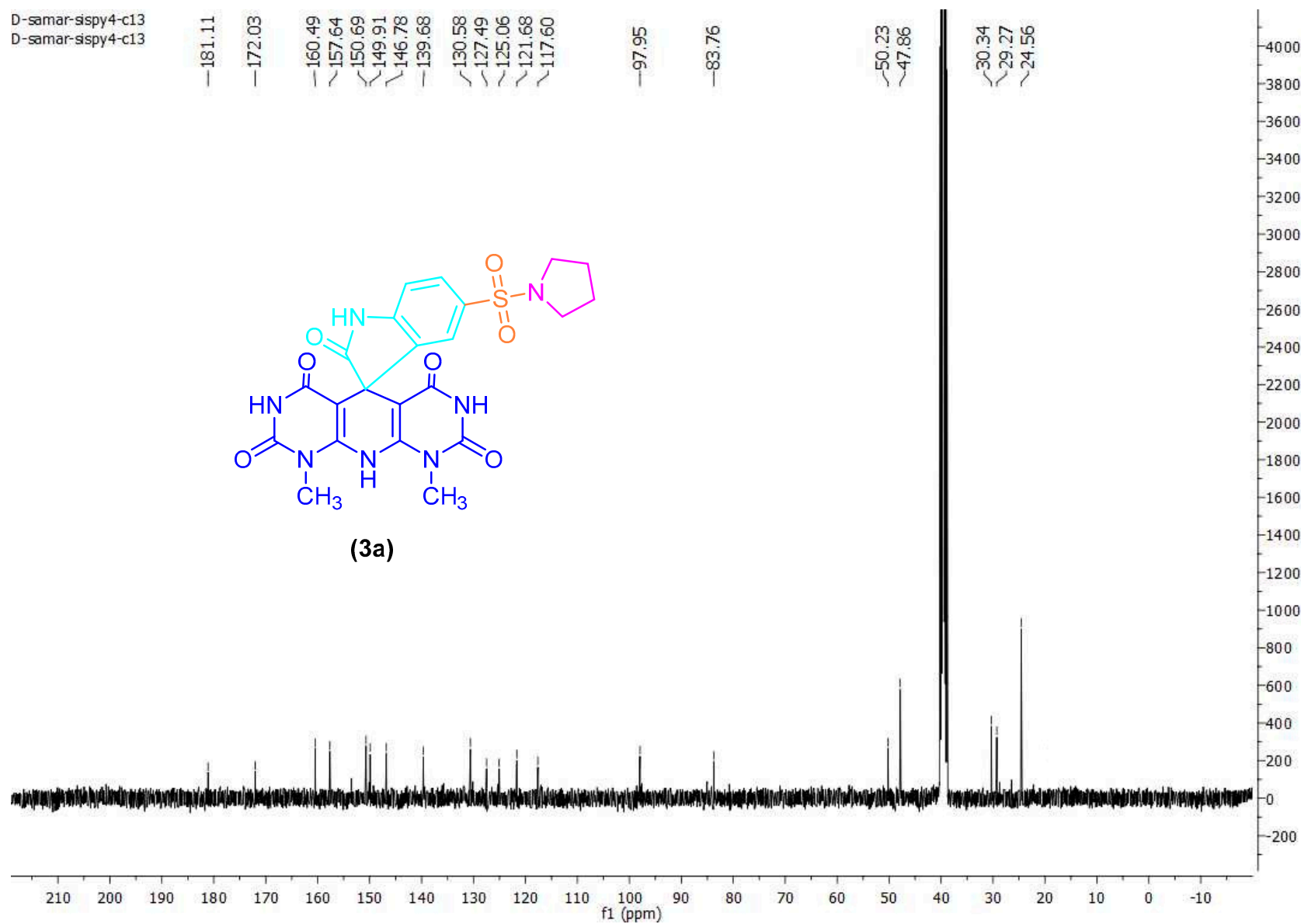


D-samar-sispy4-c13
D-samar-sispy4-c13

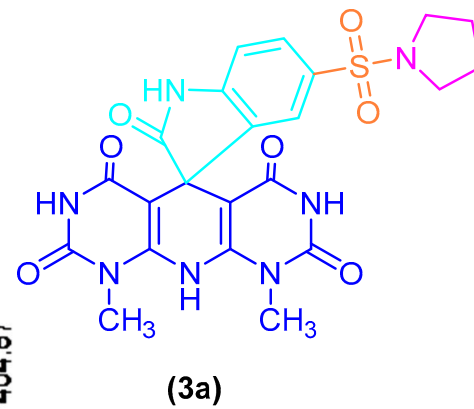
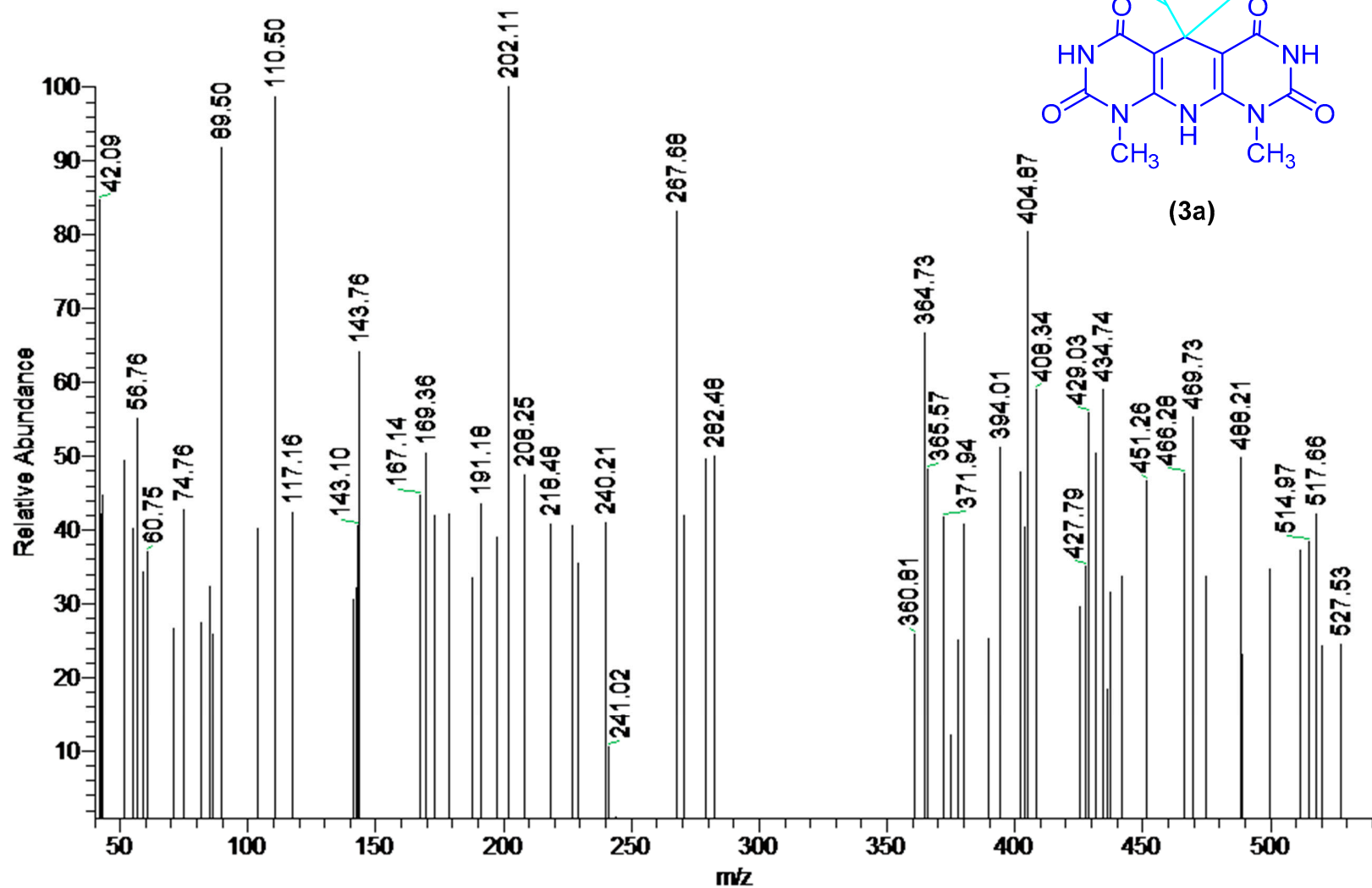
—181.11 —172.03 —160.49 —157.64 —150.69 —149.91 —146.78 —139.68 —130.58 —127.49 —125.06 —121.68 —117.60 —97.95 —83.76 —50.23 —47.86 —30.34 —29.27 —24.56

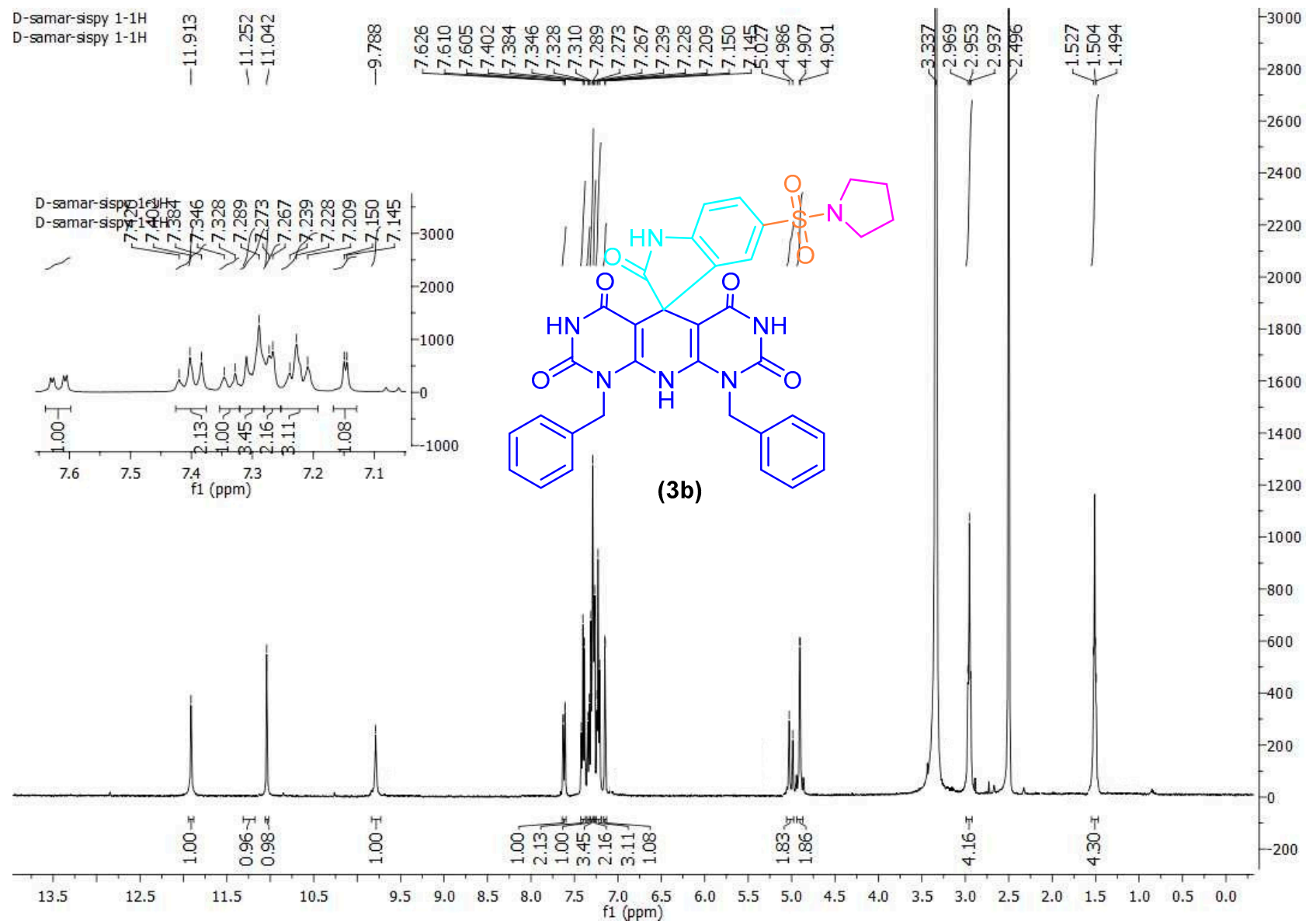


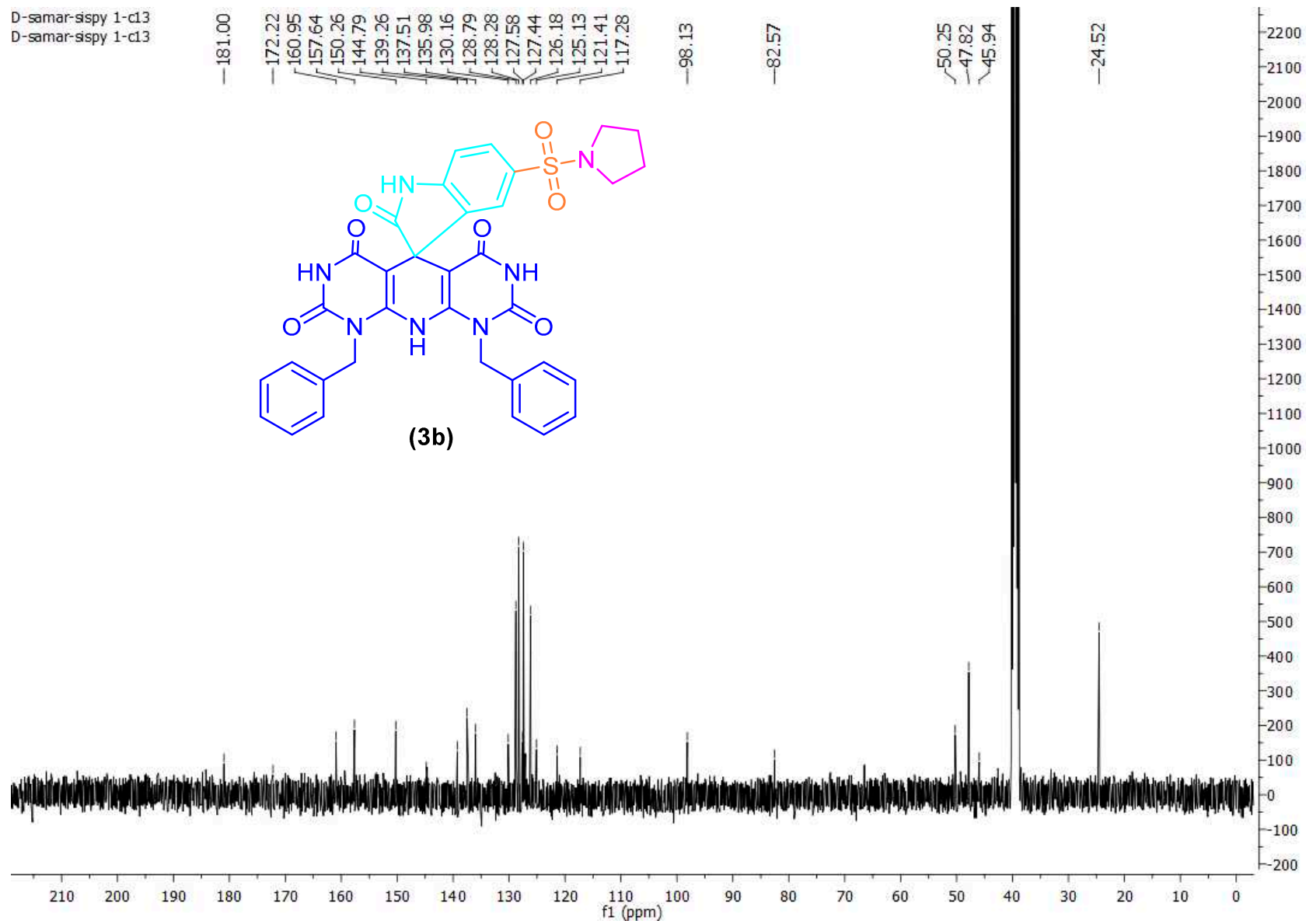
(3a)



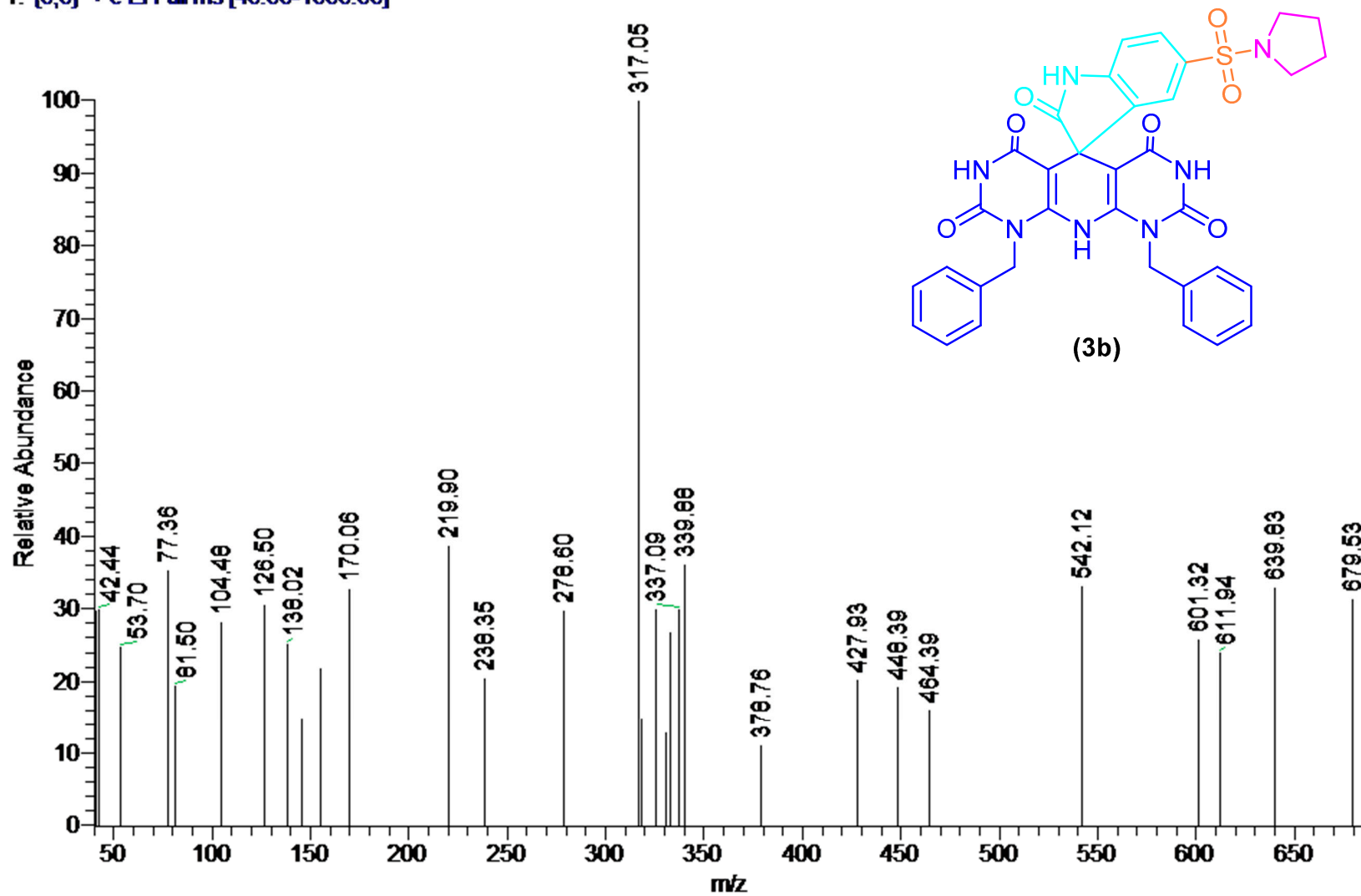
samar-Elkaliopy-sispy4 #235 RT: 3.95 AV: 1 SB: 2 4.45, 4.45 NL: 268E2
T: {0,0} +c EI Full ms [40.00-1000.00]

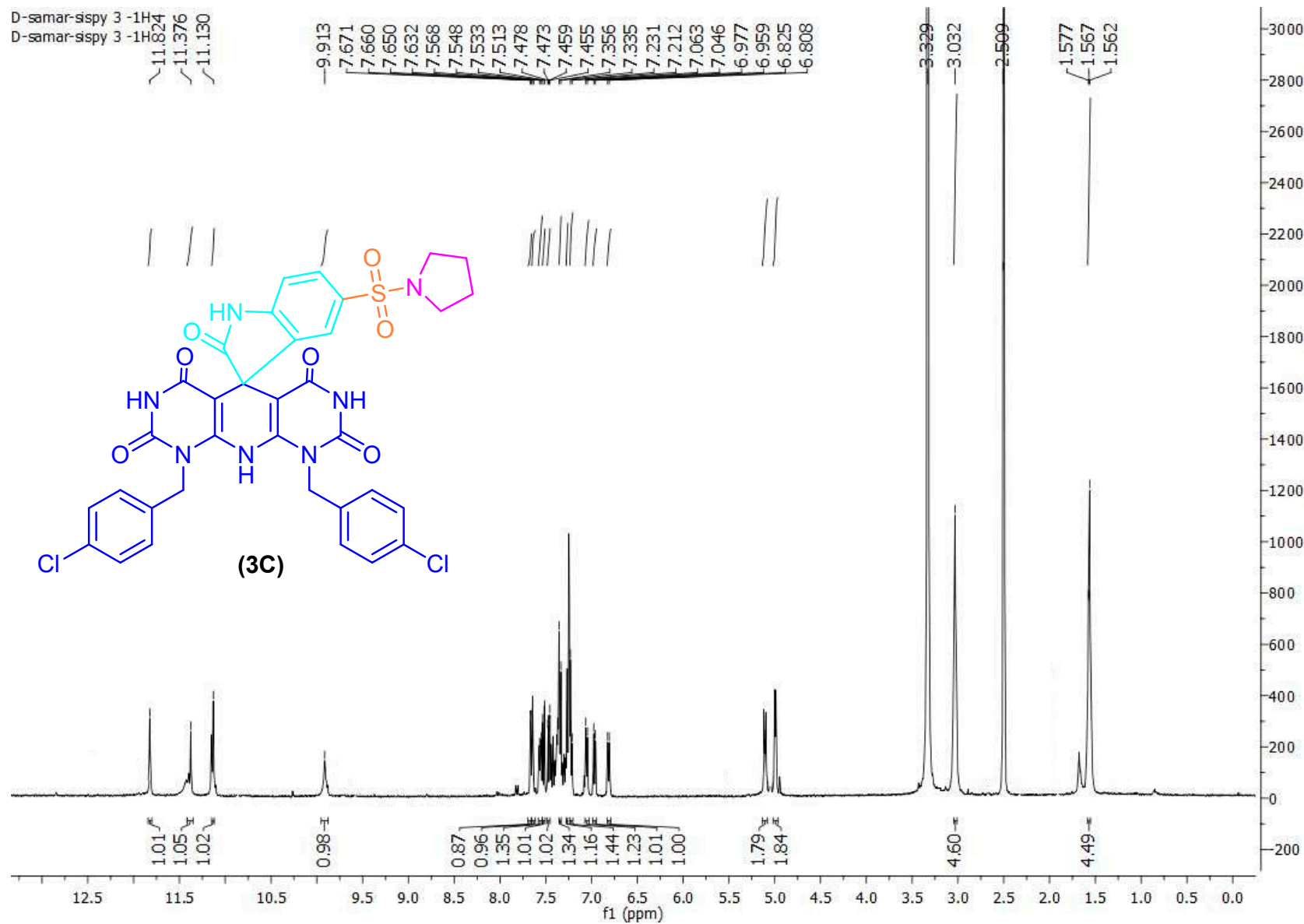






samar-Elkaliopy-sispy1 #237 RT: 3.98 AV: 1 SB: 2 4.45, 4.45 NL: 4.29E2
T: {0,0} + c EI Full ms [40.00-1000.00]





D-samar-sispy 3-1H
D-samar-sispy 3-1H

180.80
166.13
160.75
157.66
150.12
145.15
139.31
134.32
133.32
131.55
130.22
129.58
129.31
128.52
127.19
126.19
125.56

98.41

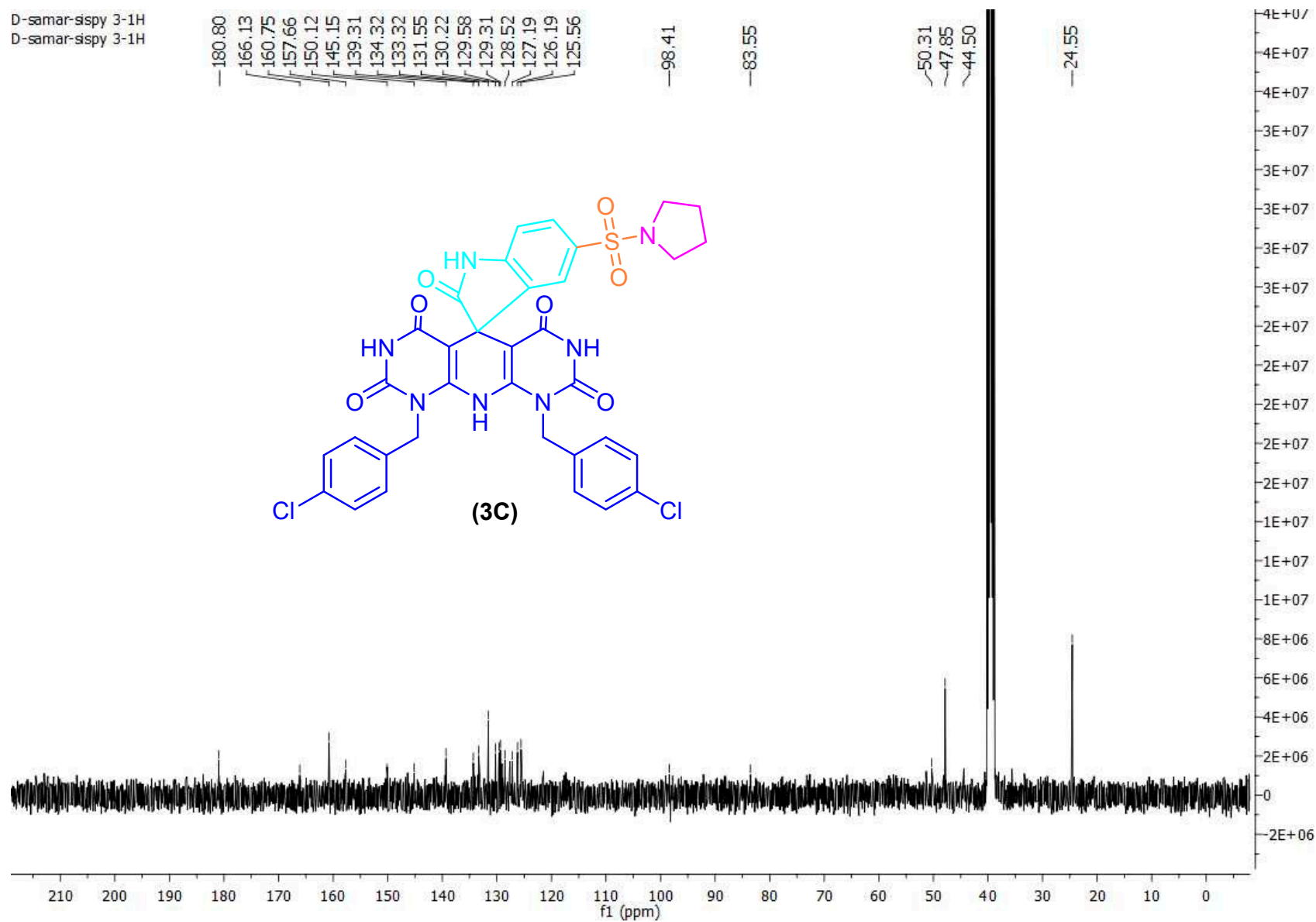
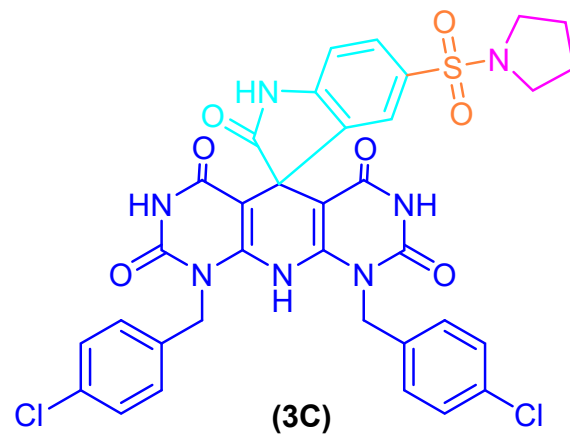
83.55

50.31

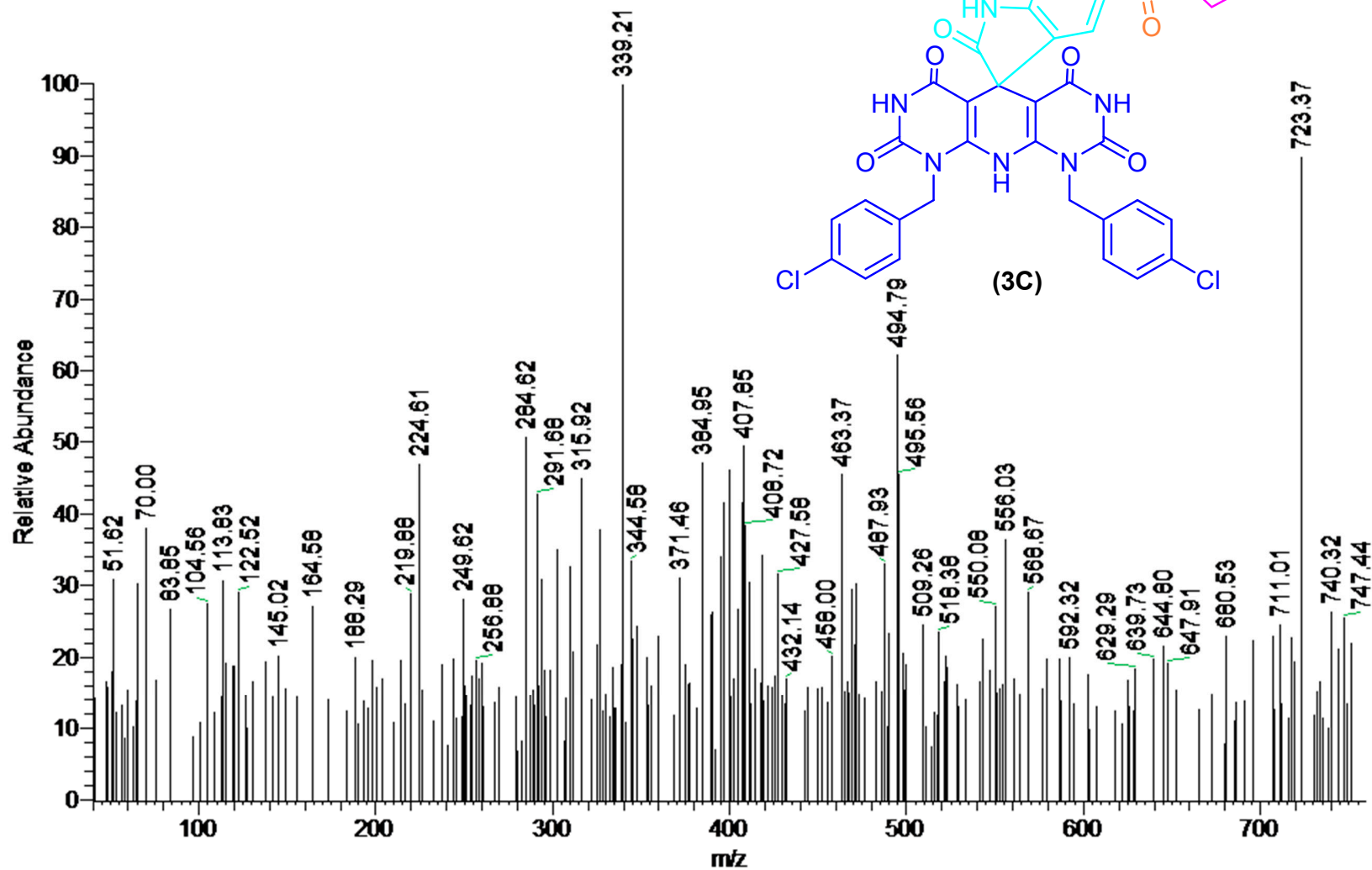
47.85

44.50

24.55



samar-Elkaliopy-sispy3 #63-66 RT: 1.07-1.12 AV: 4 SB: 2 4.45, 4.45 NL: 1.86E2
T: {0,0} +c EI Full ms [40.00-1000.00]



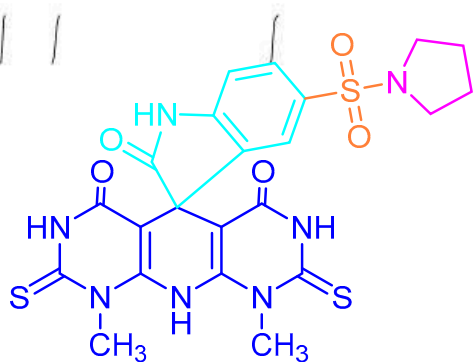
D-samar-sispy 2-1H
D-samar-sispy 2-1H

~12.550
~12.438
~11.944

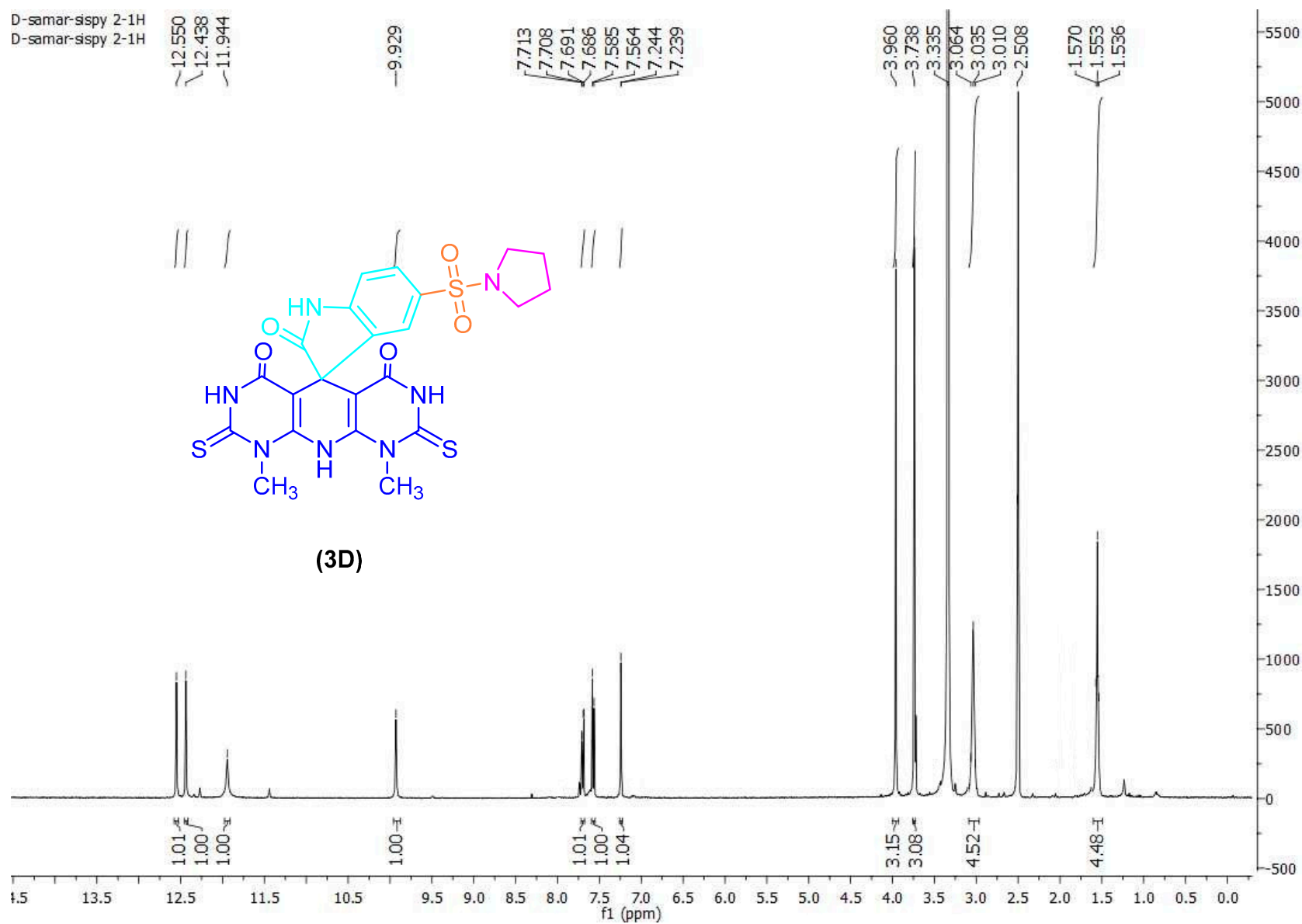
~9.929

7.713
7.708
7.691
7.686
7.585
7.564
7.244
7.239

~3.960
~3.738
3.335
3.064
3.035
3.010
~2.508
1.570
1.553
1.536



(3D)



D-samar-sispy 2-c13
D-samar-sispy 2-c13

180.289
176.319
175.559

157.797
155.274
153.714
147.018
139.504

131.413
128.087
125.164
120.614
118.280

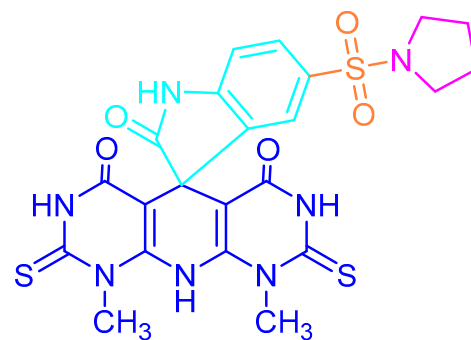
102.228

88.342

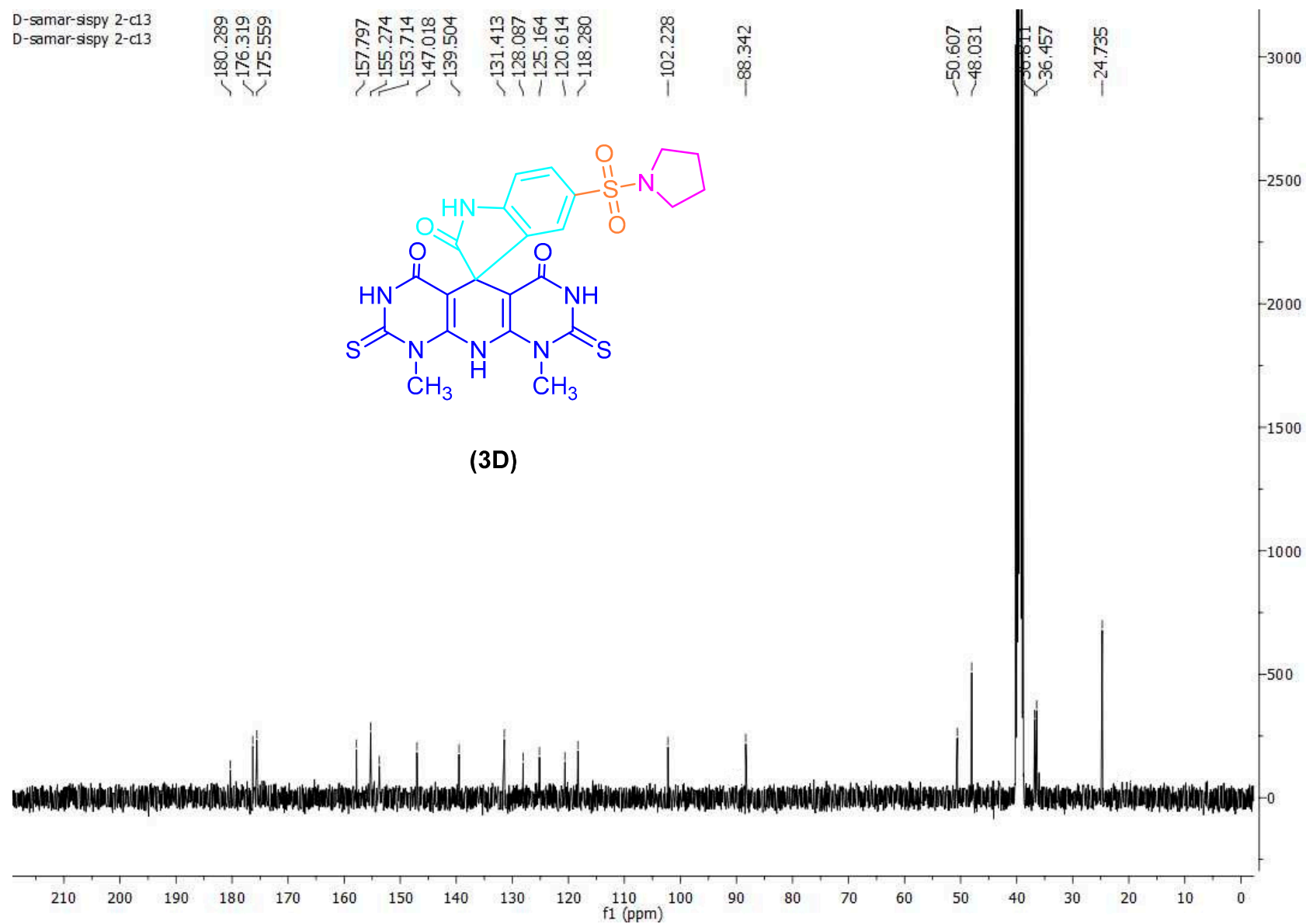
50.607
48.031

36.811
36.457

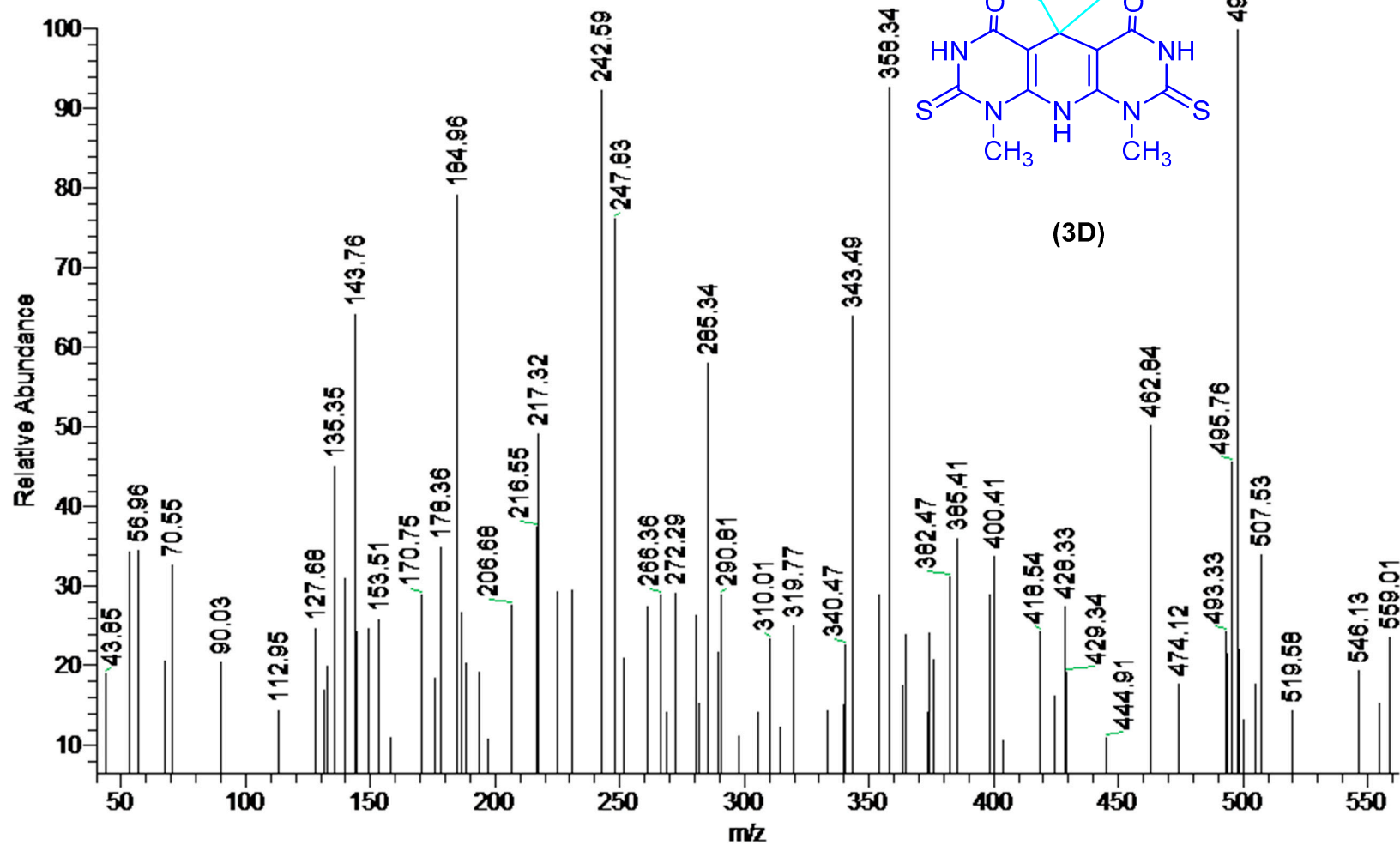
24.735

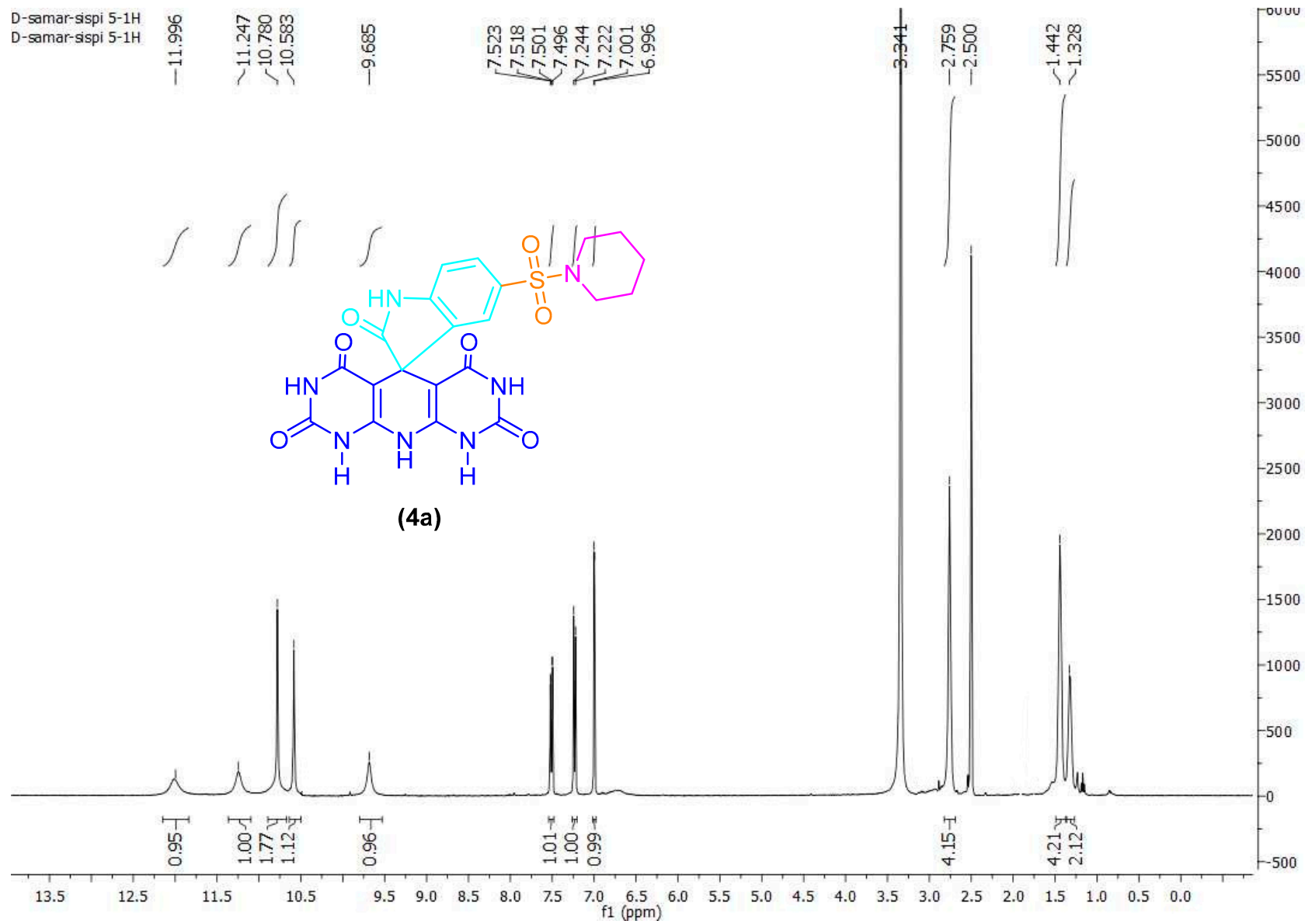


(3D)



samar-Elkaliopy-sispy2 #118 RT: 1.99 AV: 1 SB: 2 4.45, 4.45 NL: 4.65E2
T: {0,0} +c EI Full ms [40.00-1000.00]





D-samar-sispi 5-c13
D-samar-sispi 5-c13

— 180.78

~ 165.81

~ 161.96

~ 158.63

~ 153.67

~ 149.85

~ 145.83

~ 139.39

~ 129.67

~ 127.57

~ 125.38

~ 121.79

~ 116.98

— 97.50

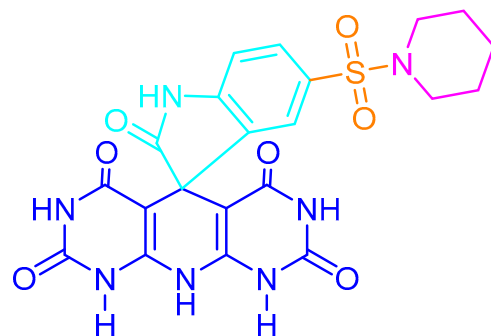
— 82.79

~ 49.05

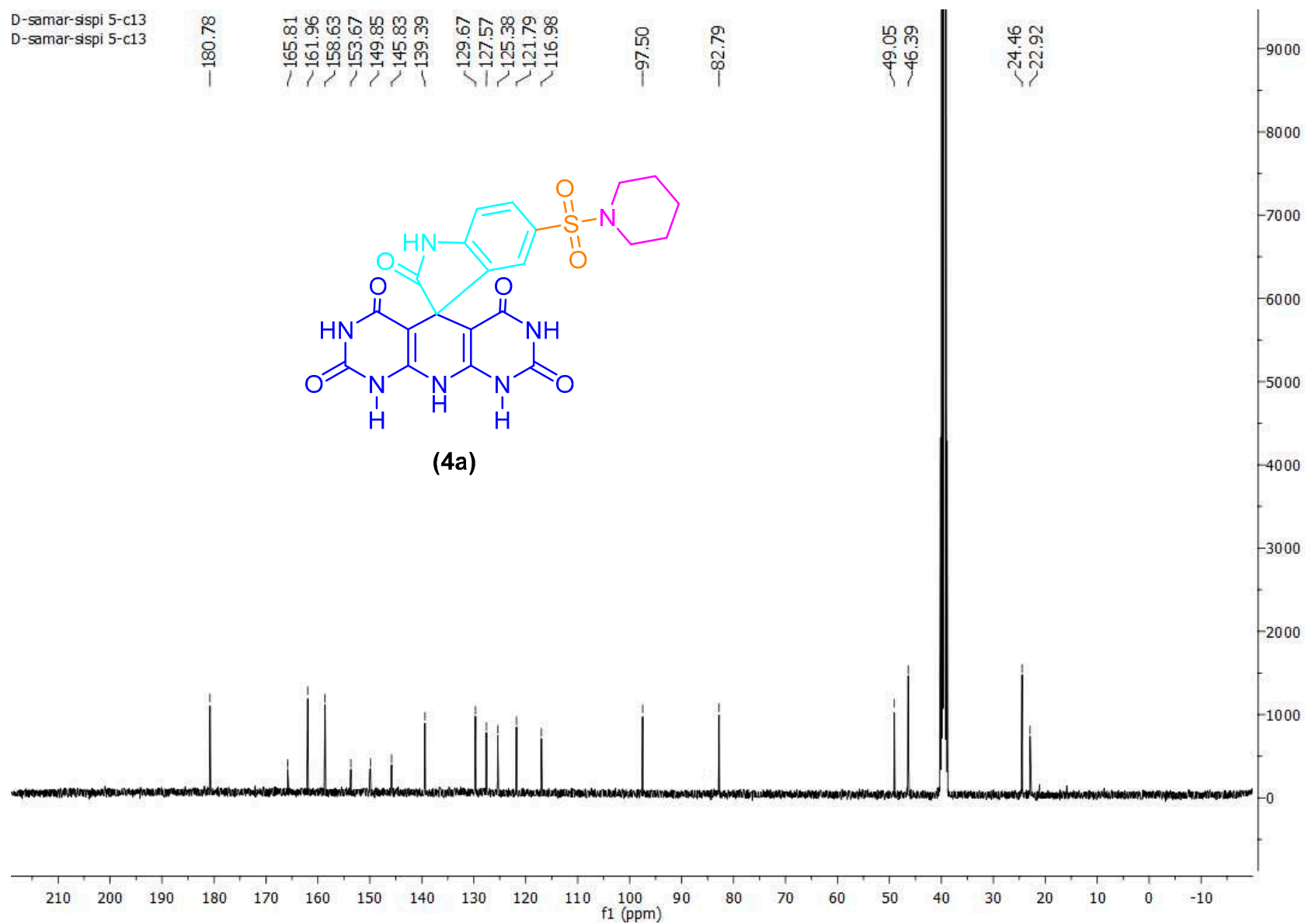
~ 46.39

~ 24.46

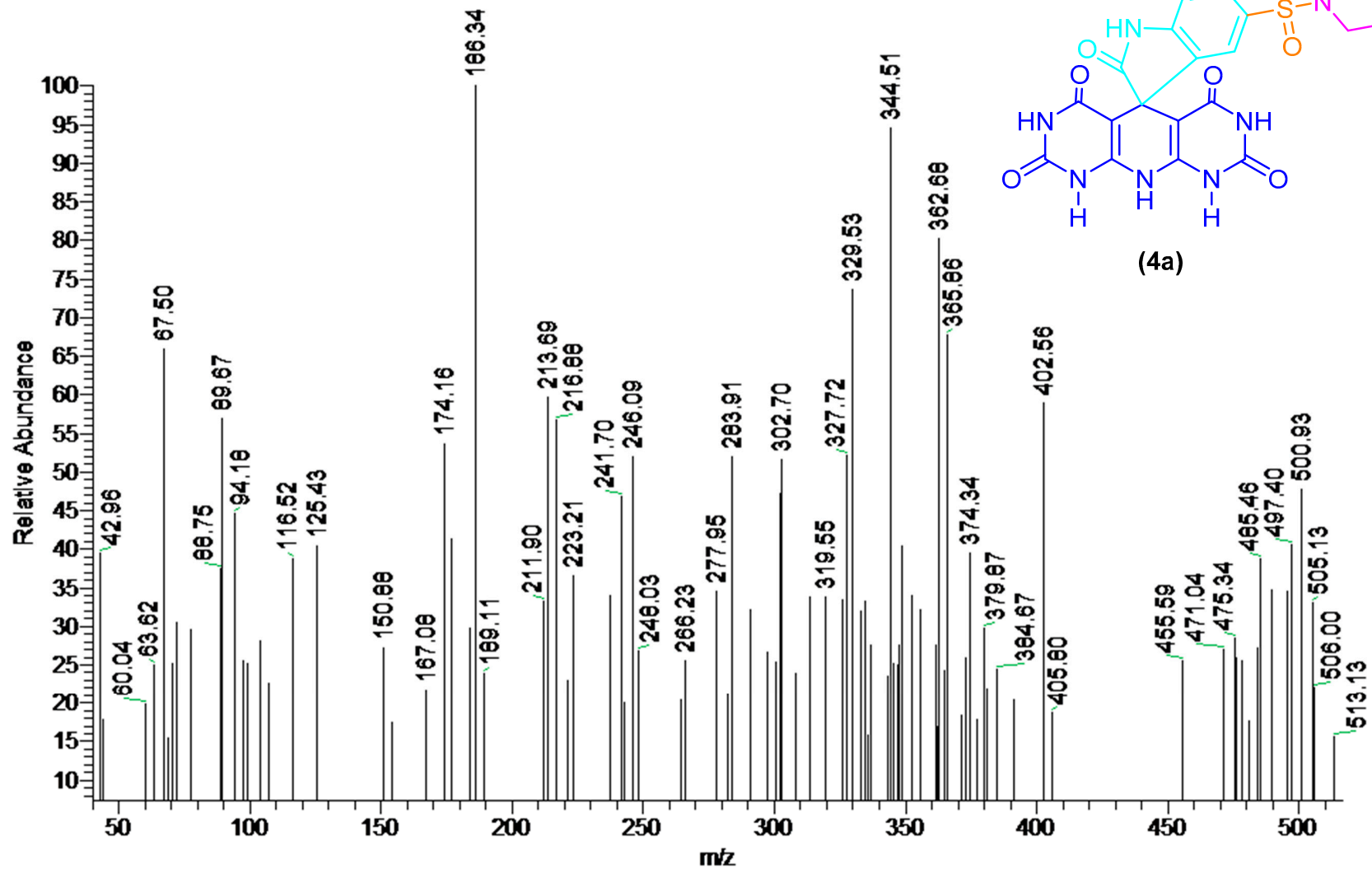
~ 22.92

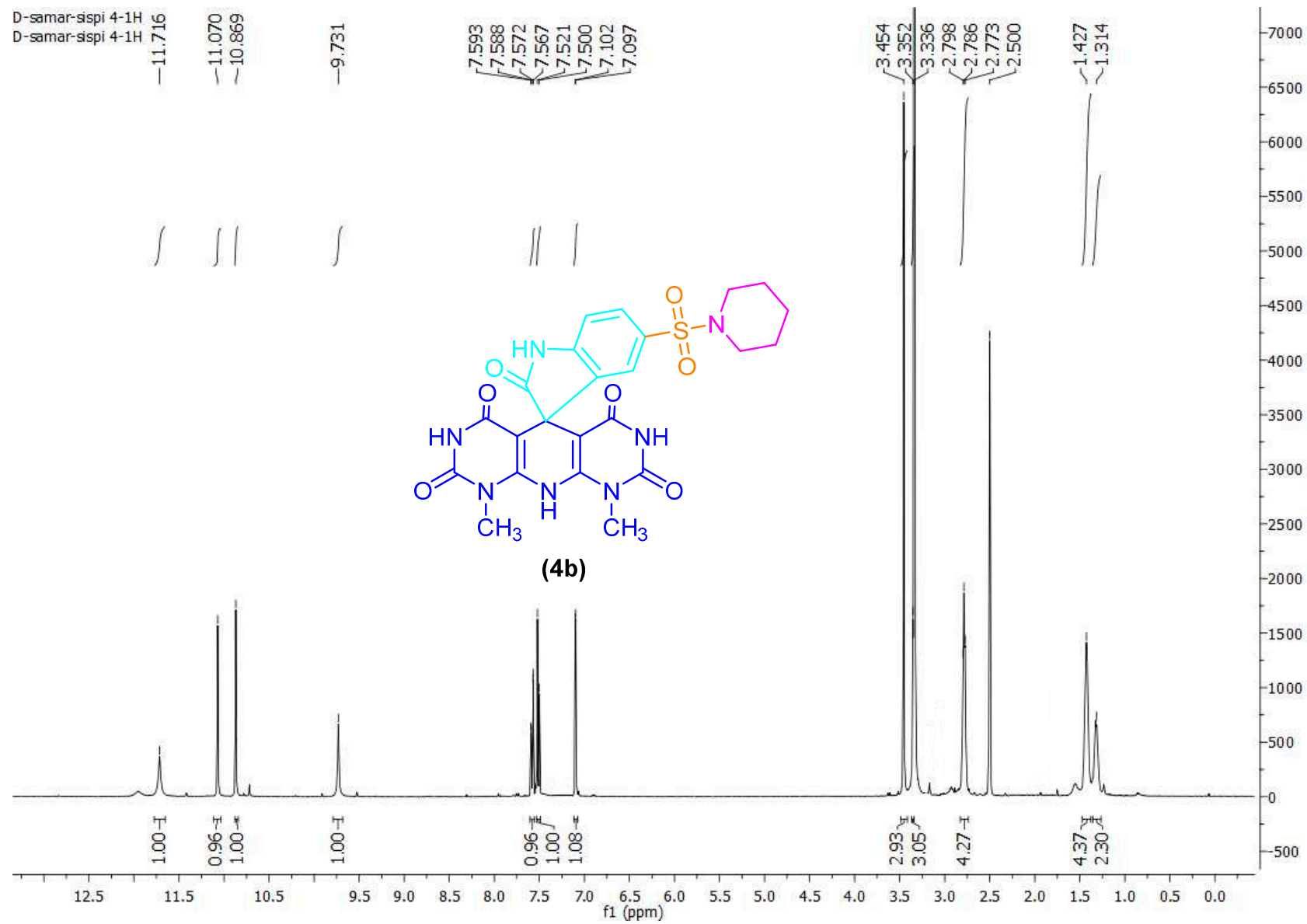


(4a)



samar-Elkaliopy-sispi5 #118 RT: 1.99 AV: 1 SB: 2 4.45, 4.45 NL: 3.60E2
T: {0,0} +c EI Full ms [40.00-1000.00]





D-samar-sispi 4-c13
D-samar-sispi 4-c13

—181.05

—172.05

—160.51

—157.66

—150.69

—149.92

—146.80

—139.66

—130.33

—127.53

—125.30

—121.62

—117.57

—98.09

—83.79

—50.25

—46.38

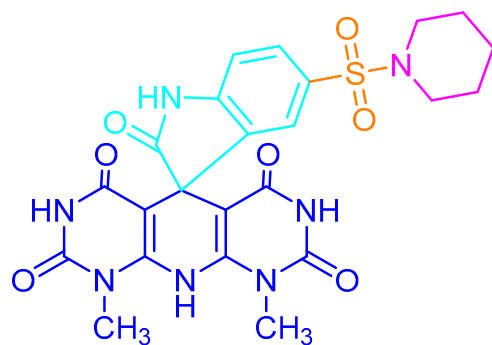
—30.33

—29.29

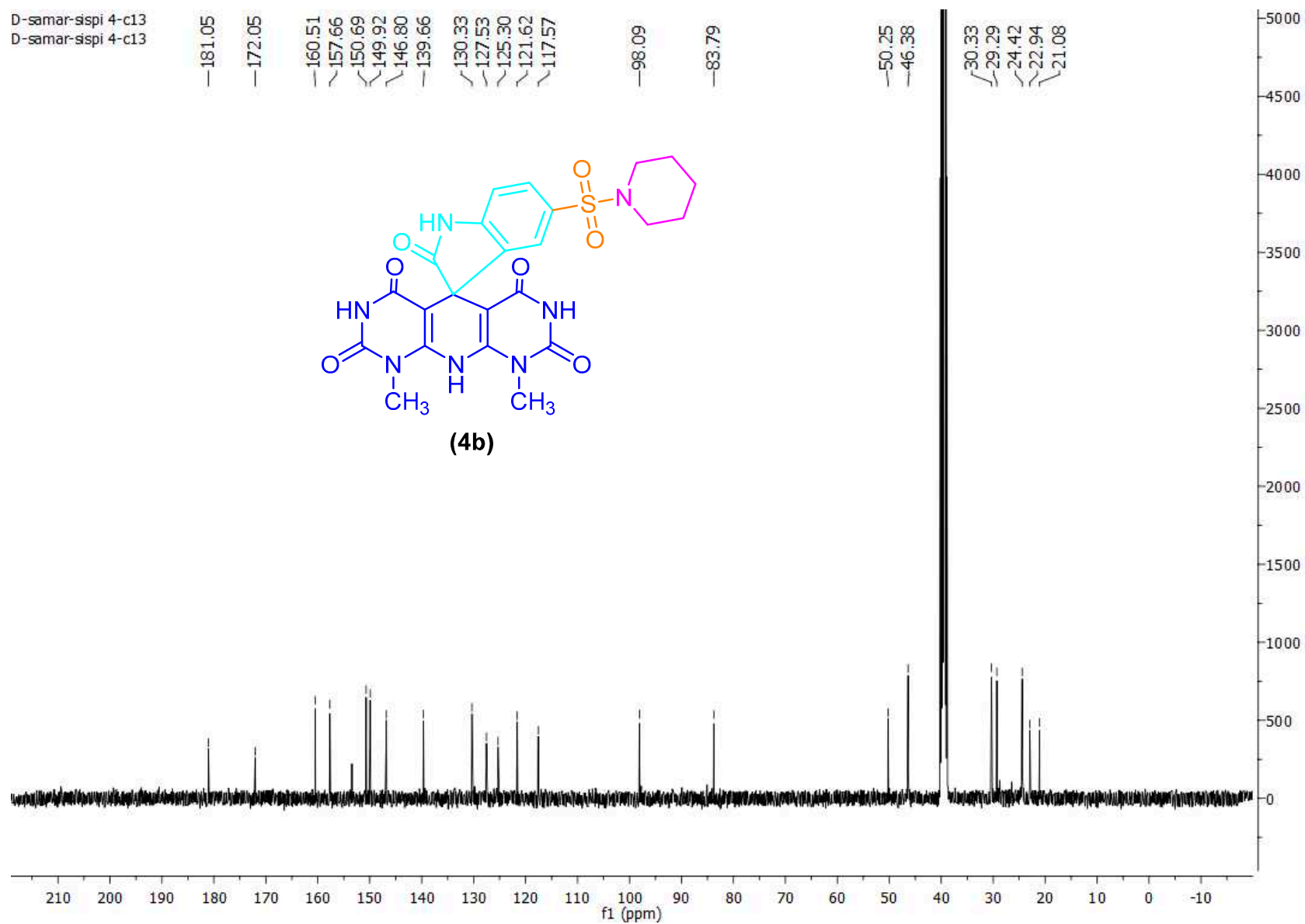
—24.42

—22.94

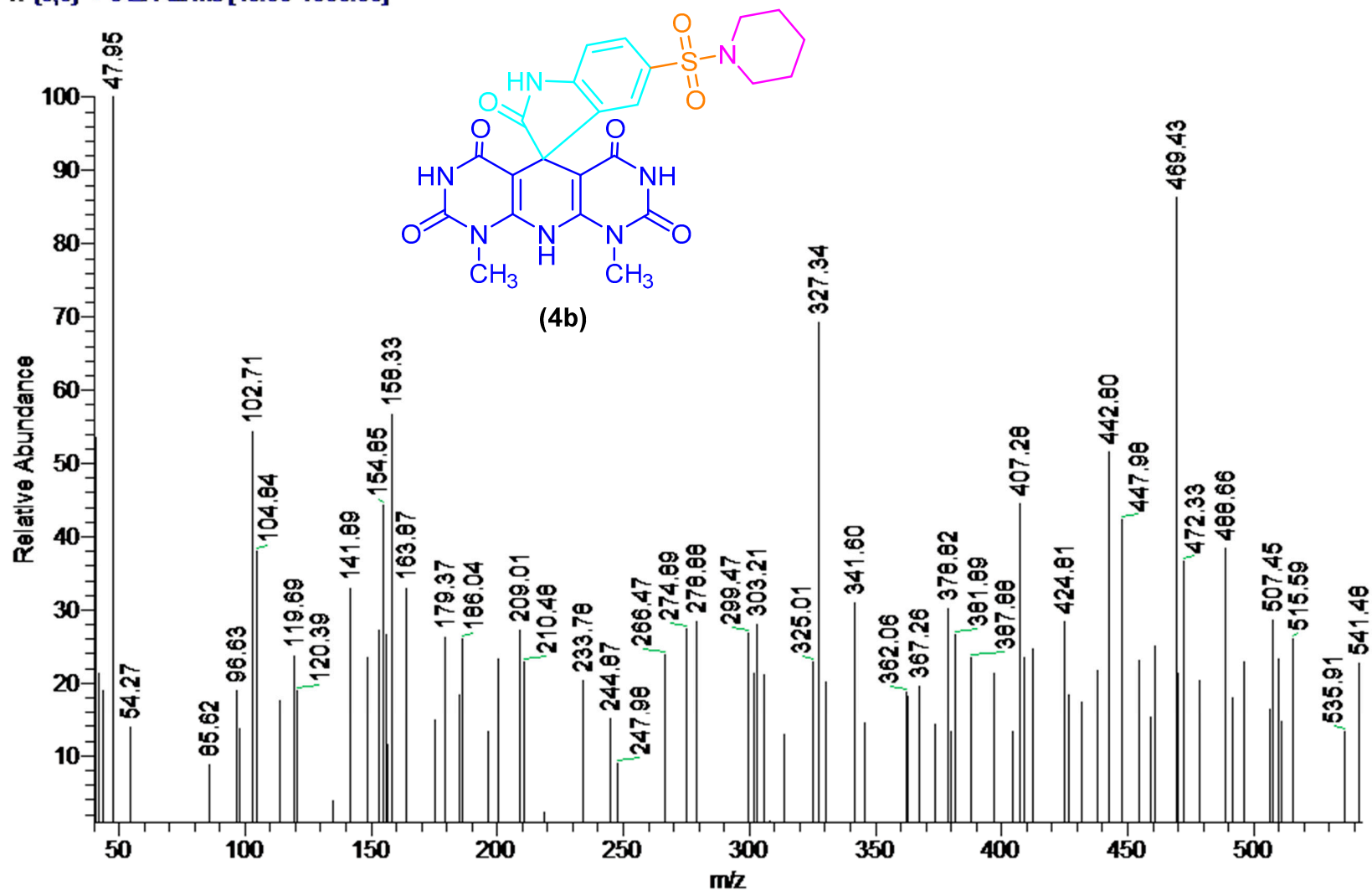
—21.08

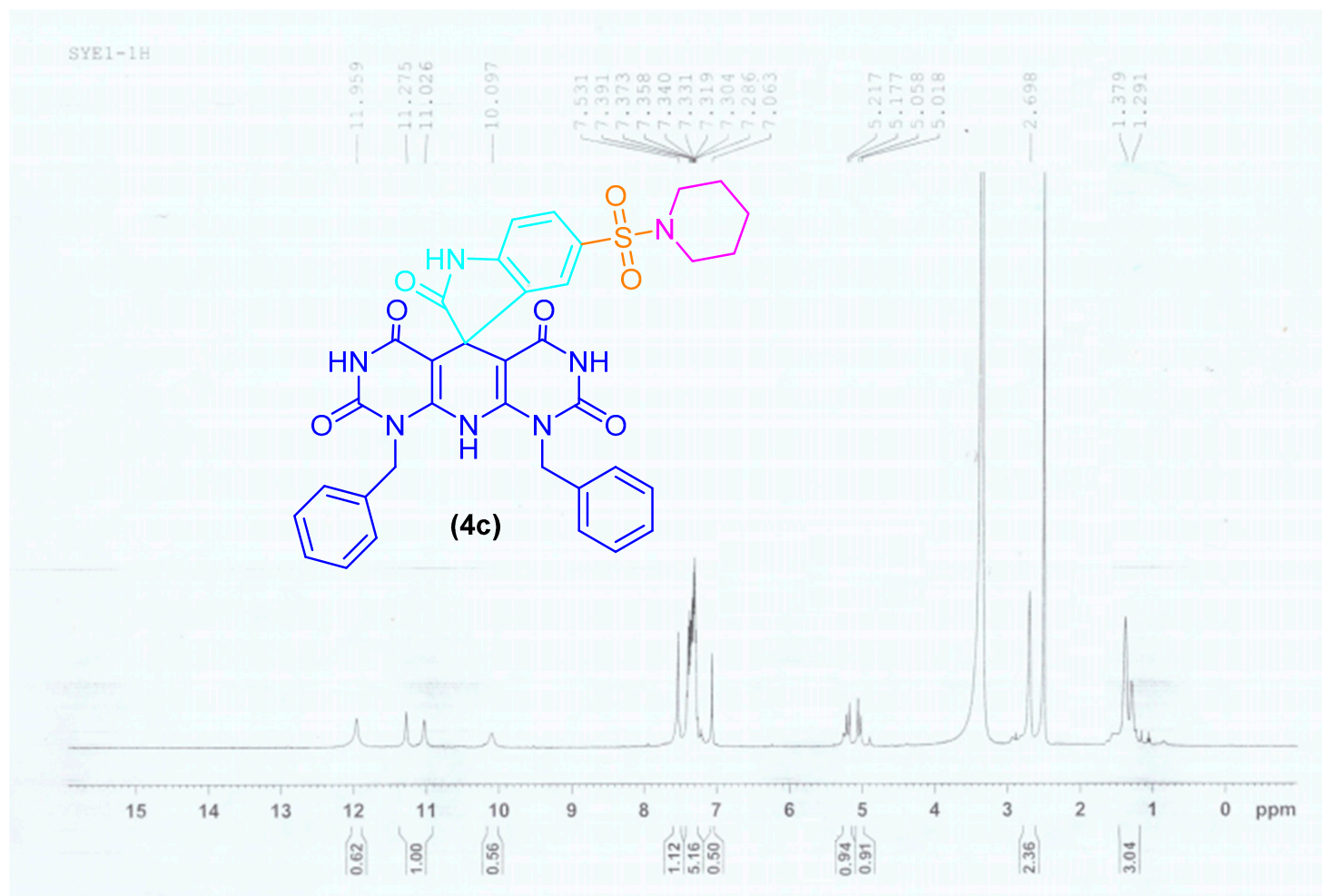


(4b)

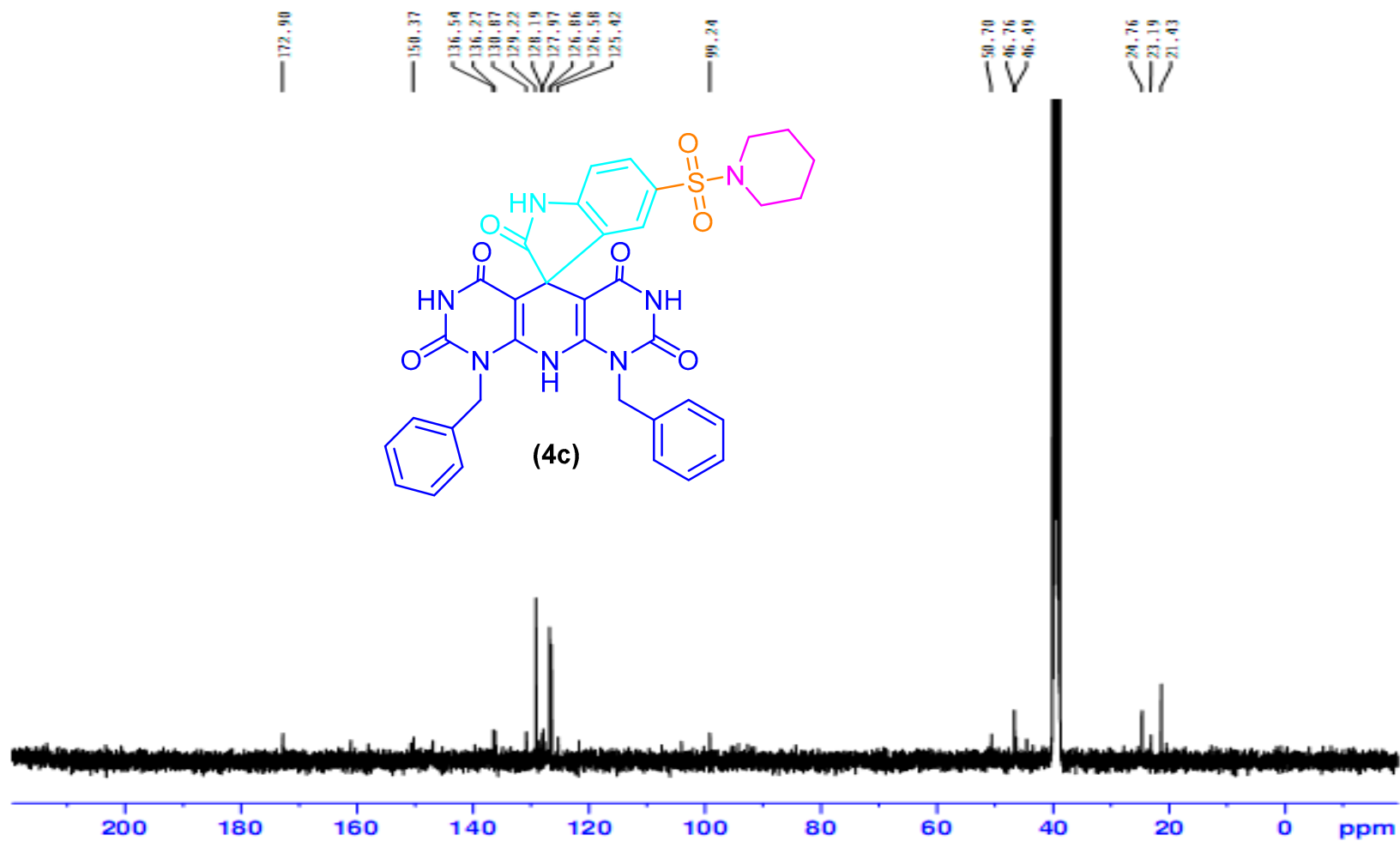


samar-Elkaliopy-sispi4 #157 RT: 2.64 AV: 1 SB: 2 4.45, 4.45 NL: 4.53E2
T: {0,0} +c EI Full ms [40.00-1000.00]

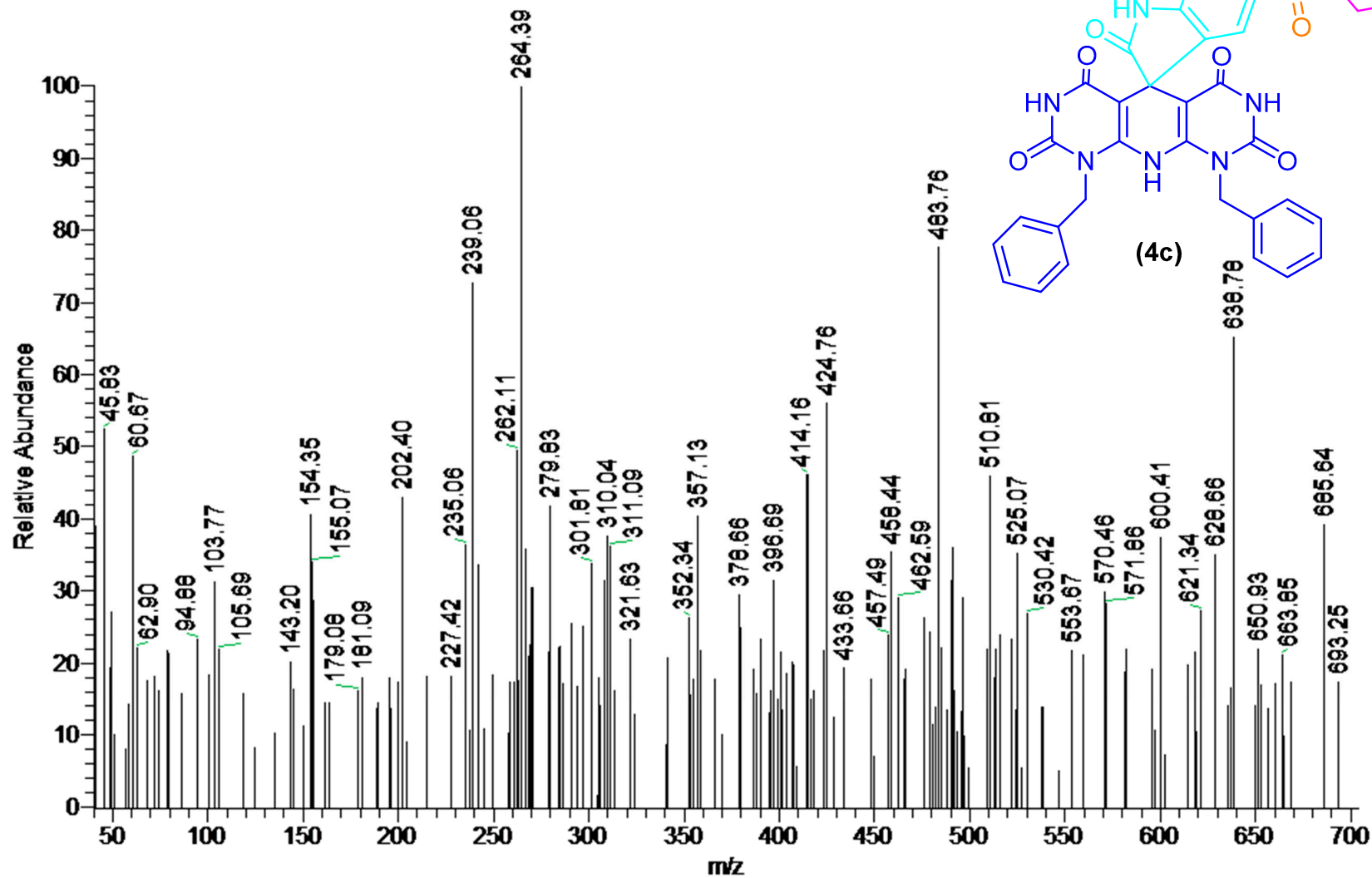


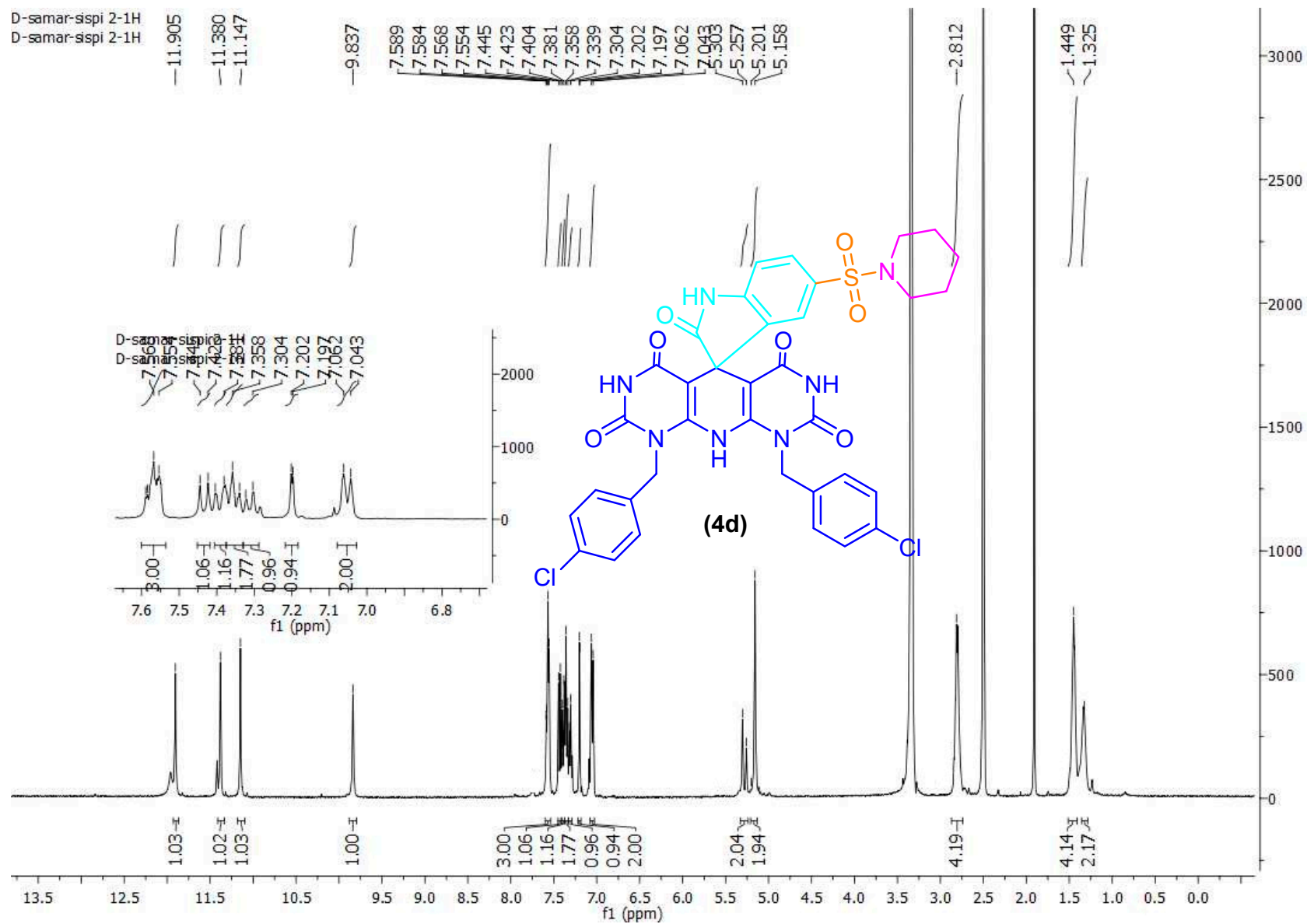


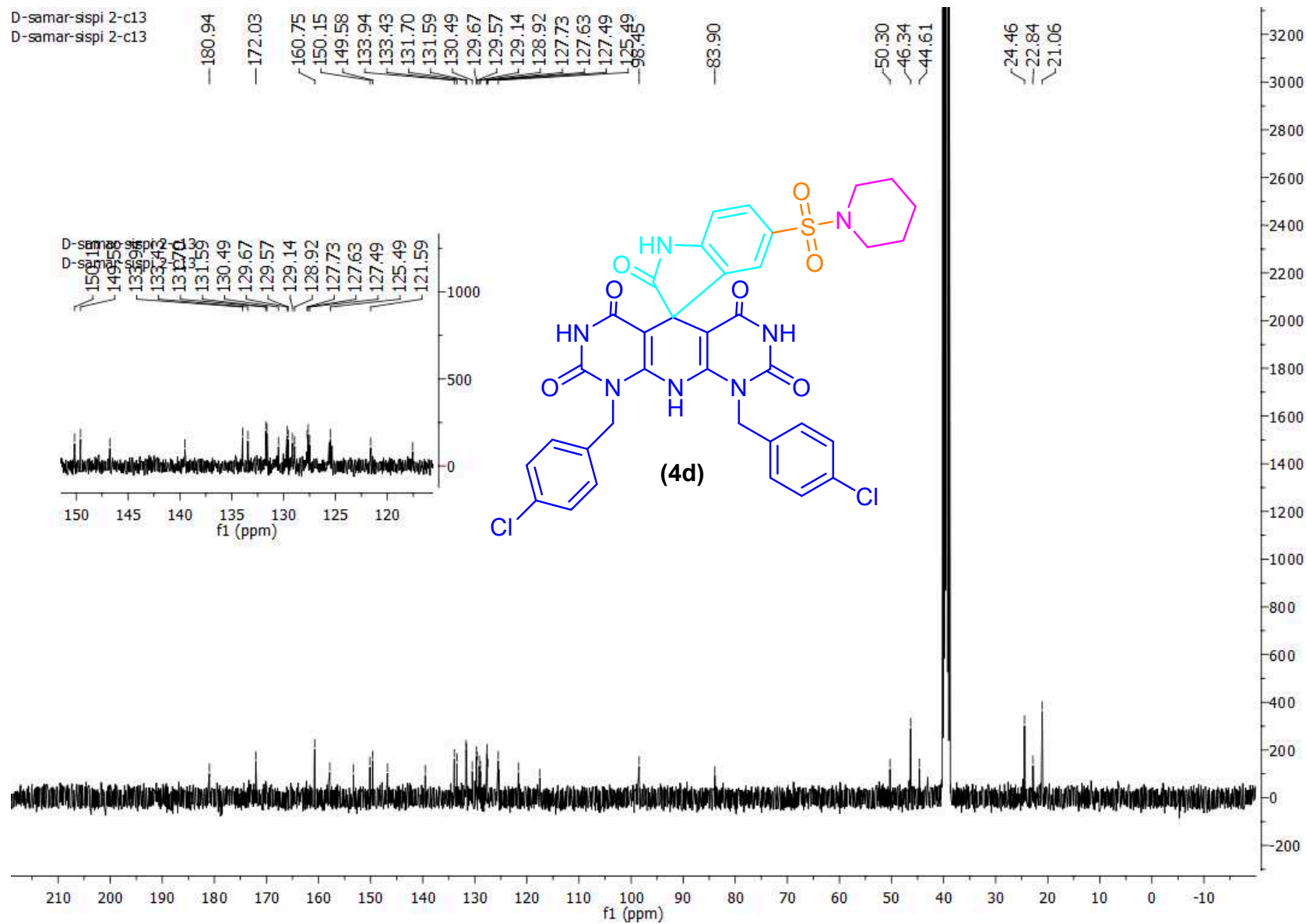
SYE1-c13



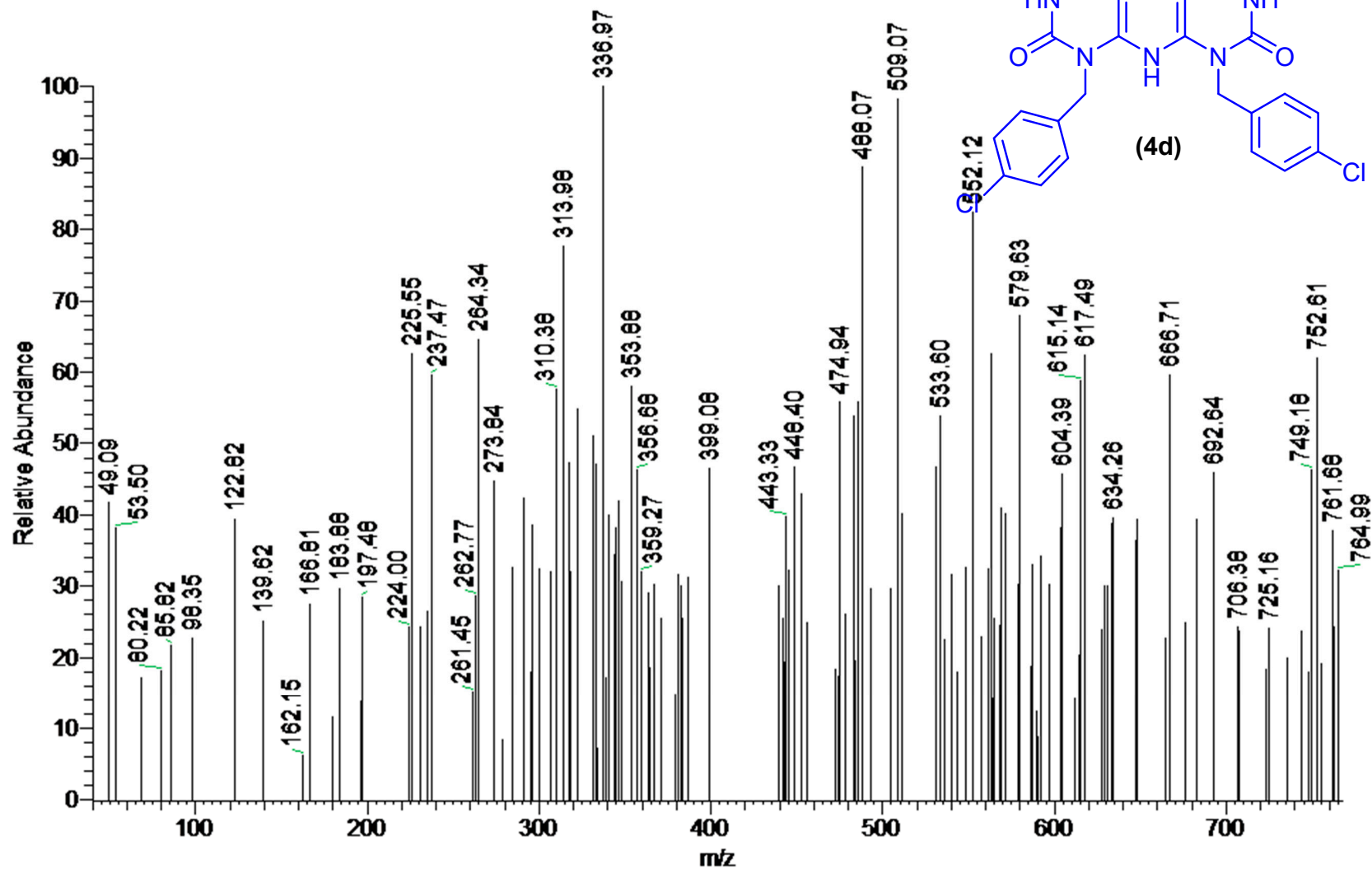
samar-Elkaliopy-sispi1#170 RT: 2.86 AV: 1 SB: 2 4.45, 4.45 NL: 5.60E2
T: {0,0} +c EI Full ms [40.00-1000.00]







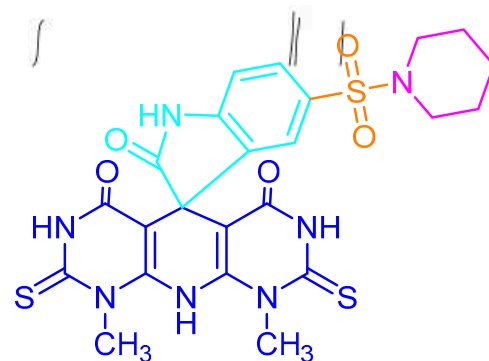
samar-Ekapi2-sispi2 #220 RT: 3.70 AV: 1 SB: 2 4.45, 4.45 NL: 3.26E2
T: {0,0} + c EI Full ms [40.00-1000.00]



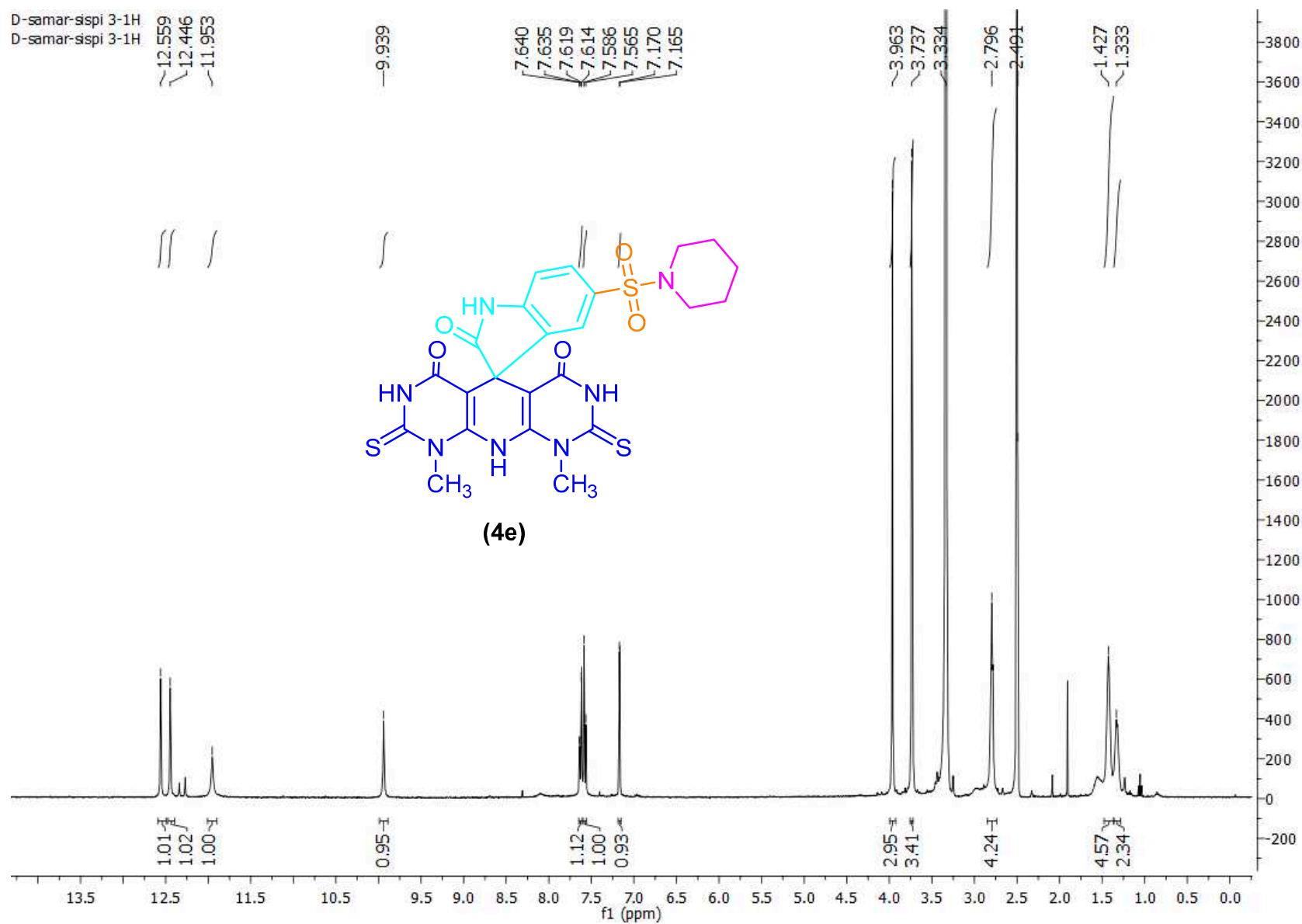
D-samar-sispi 3-1H
D-samar-sispi 3-1H
~12.559
~12.446
~11.953

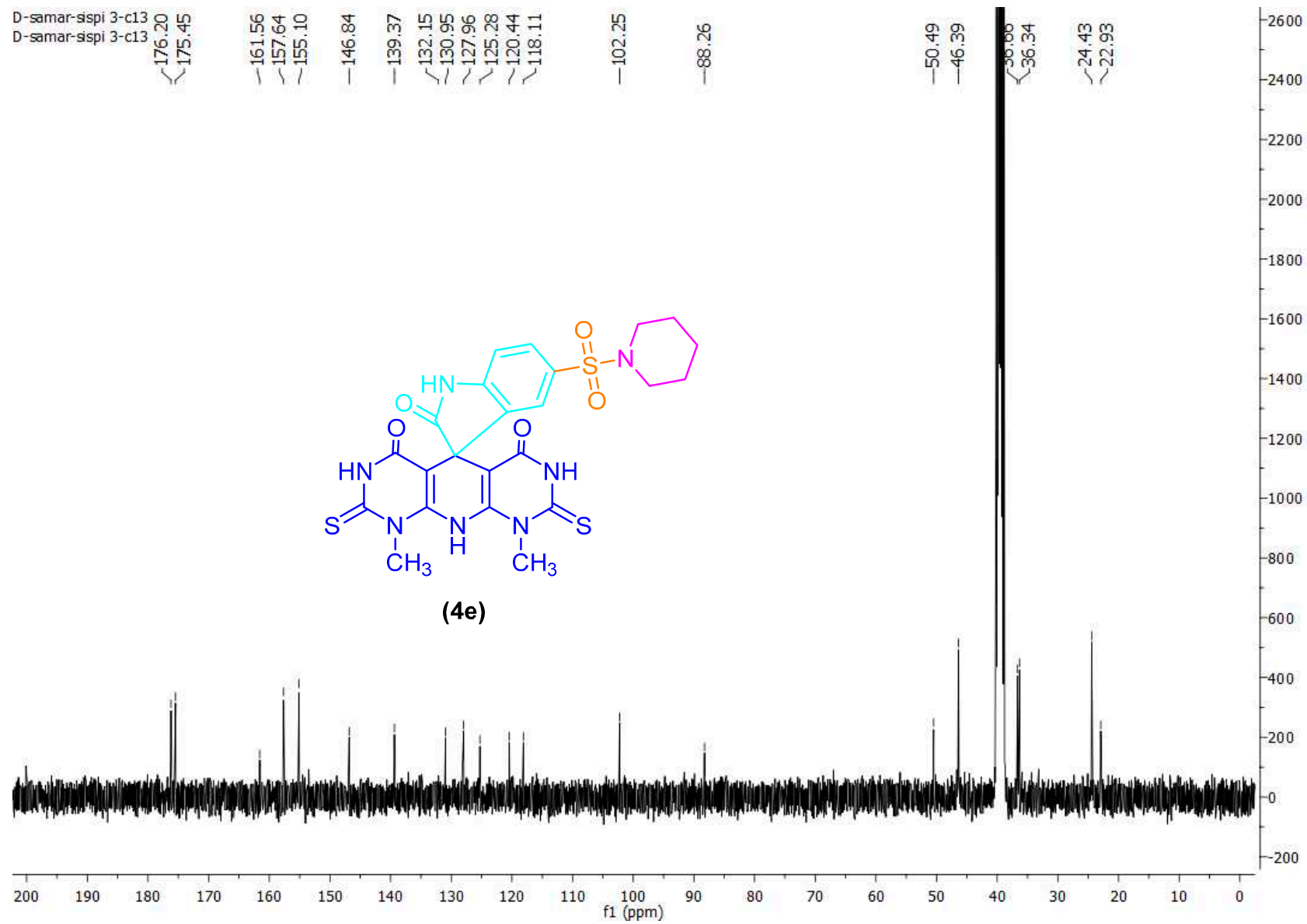
—9.939
7.640
7.635
7.619
7.614
7.586
7.565
7.170
7.165

~3.963
~3.737
3.334
—2.796
2.491
~1.427
~1.333

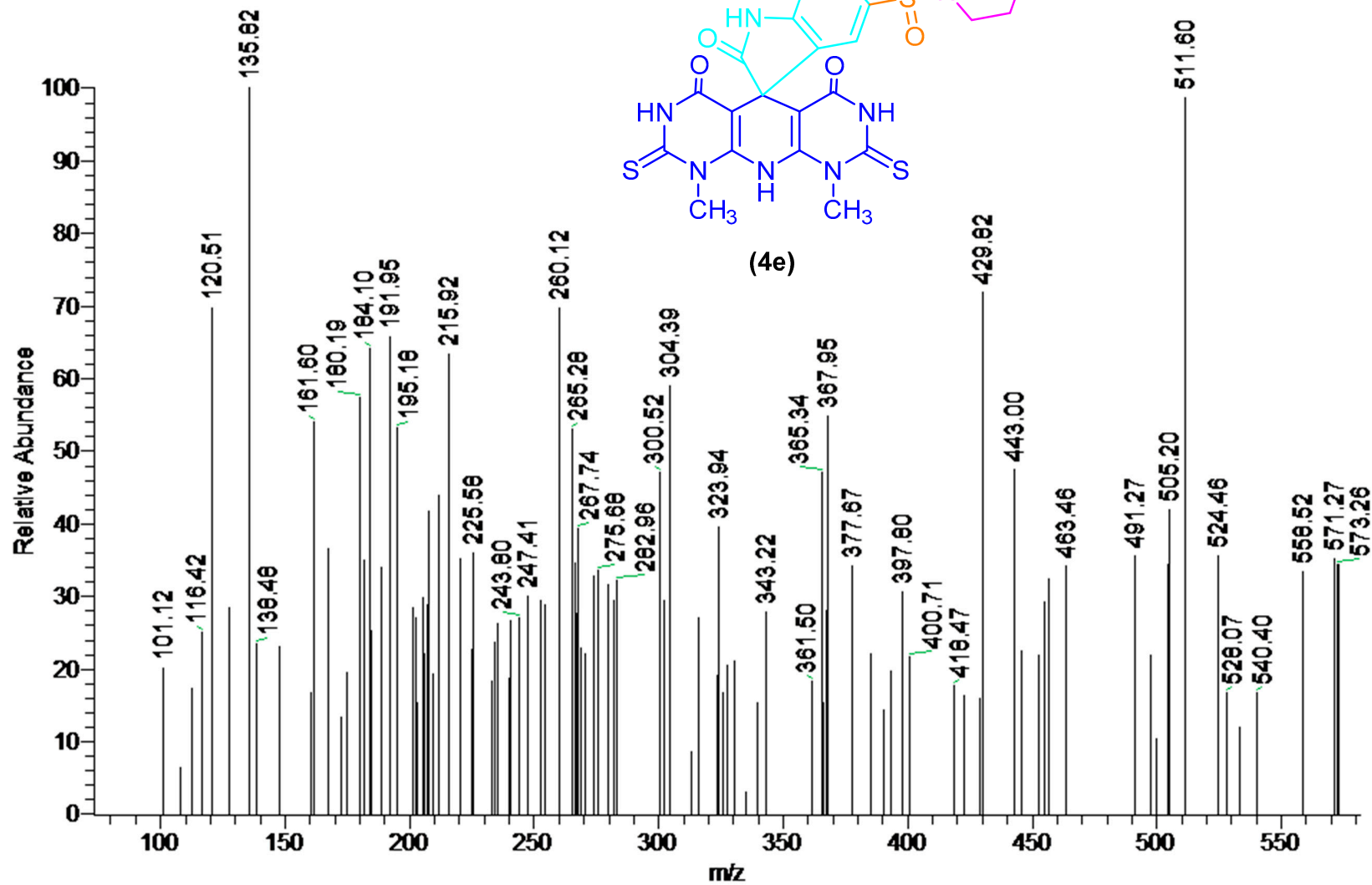


(4e)





samar-Elkaliopy-sispi3 #269 RT: 4.52 AV: 1 SB: 2 4.45, 4.45 NL: 3.62E2
T: {0,0} +c EI Full ms [40.00-1000.00]



D-samar-sism 5 -1H
D-samar-sism 5 -1H

—11.994

~11.257

~10.794

~10.591

—9.684

7.538

7.533

7.517

7.512

7.288

7.267

6.996

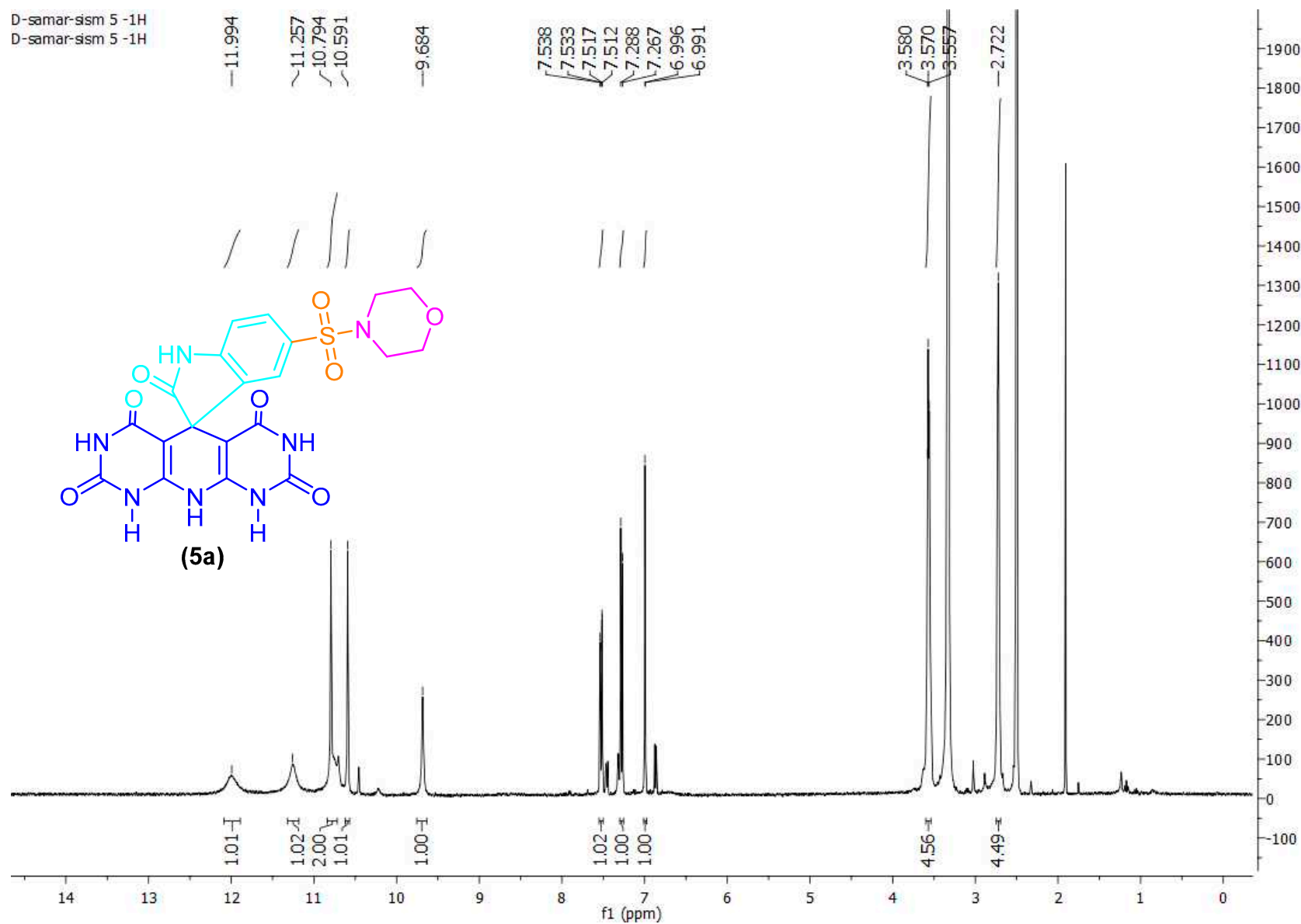
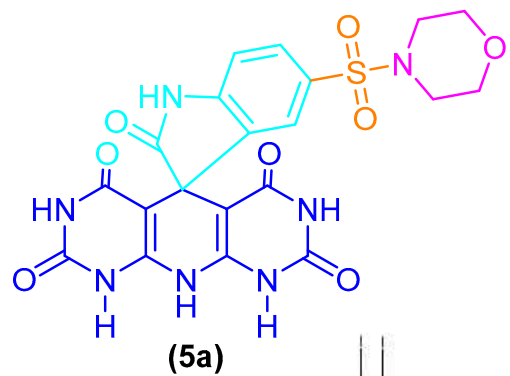
6.991

3.580

3.570

3.557

—2.722



D-samar-sism 5 -c13
D-samar-sism 5 -c13

—180.76

✓161.90

✓158.58

✓152.30

✓150.93

✓149.87

✓145.70

✓139.75

✓128.08

✓127.84

✓125.66

✓121.85

✓117.15

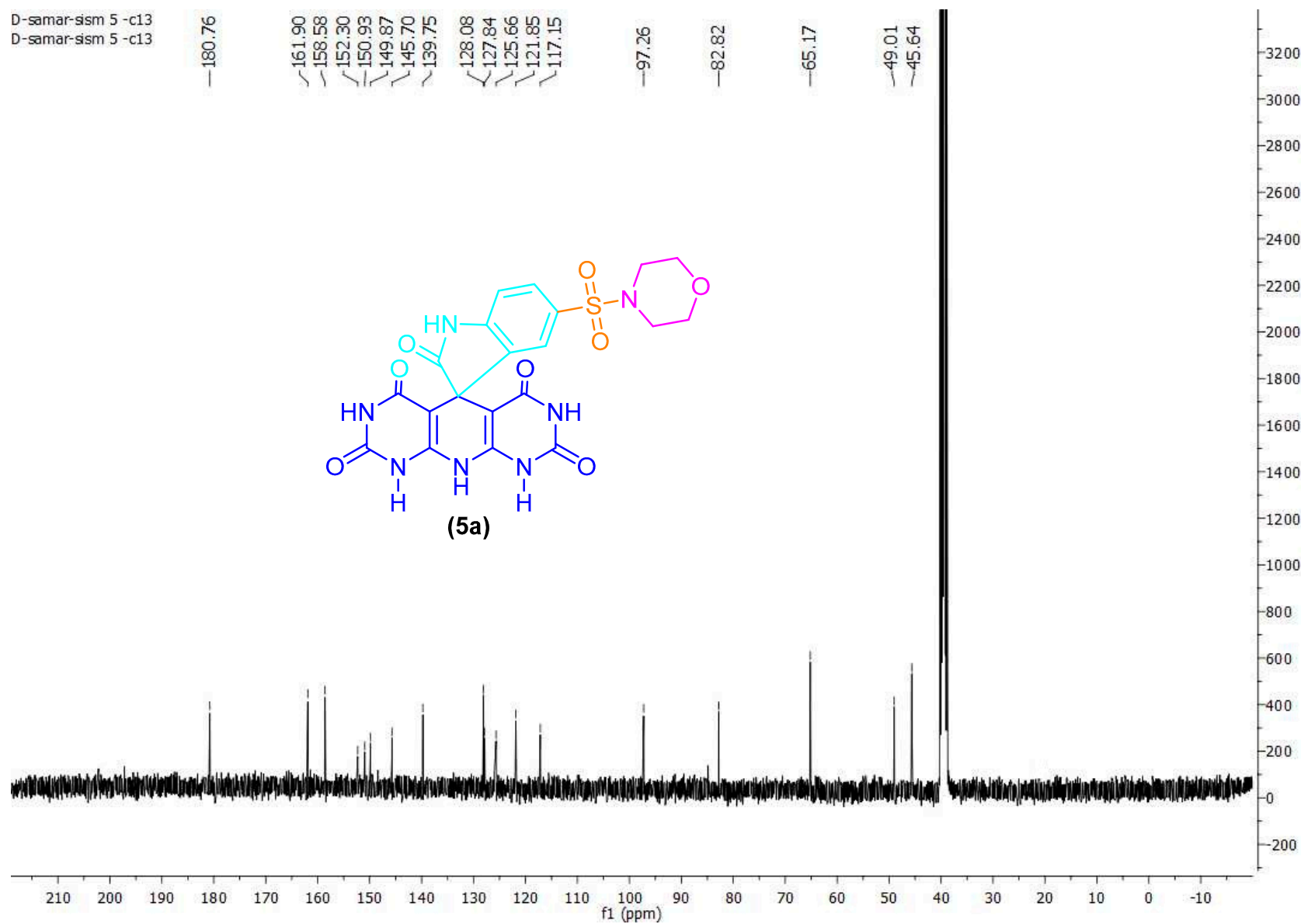
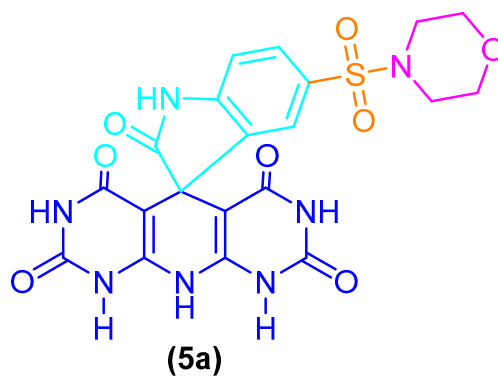
—97.26

—82.82

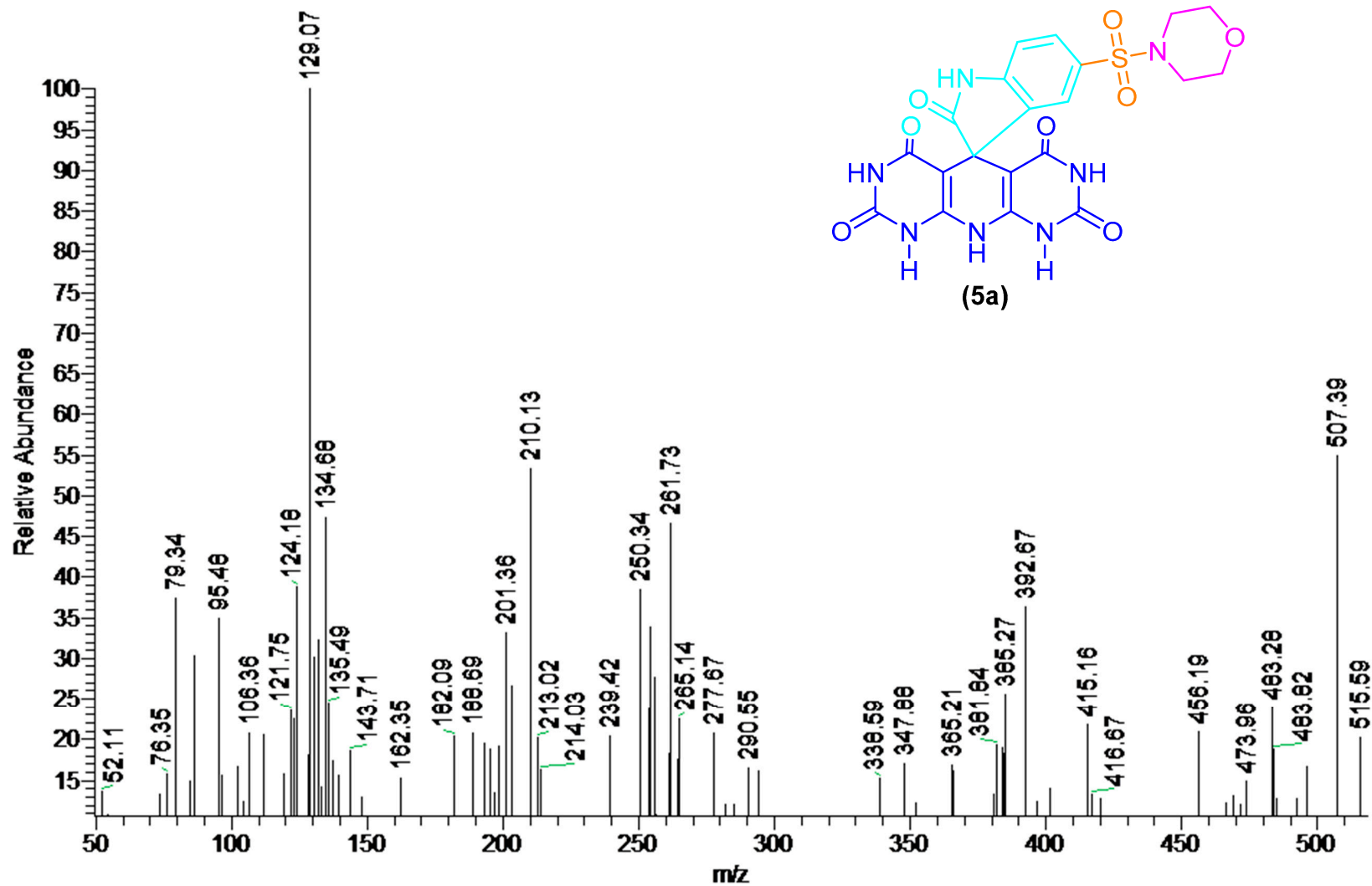
—65.17

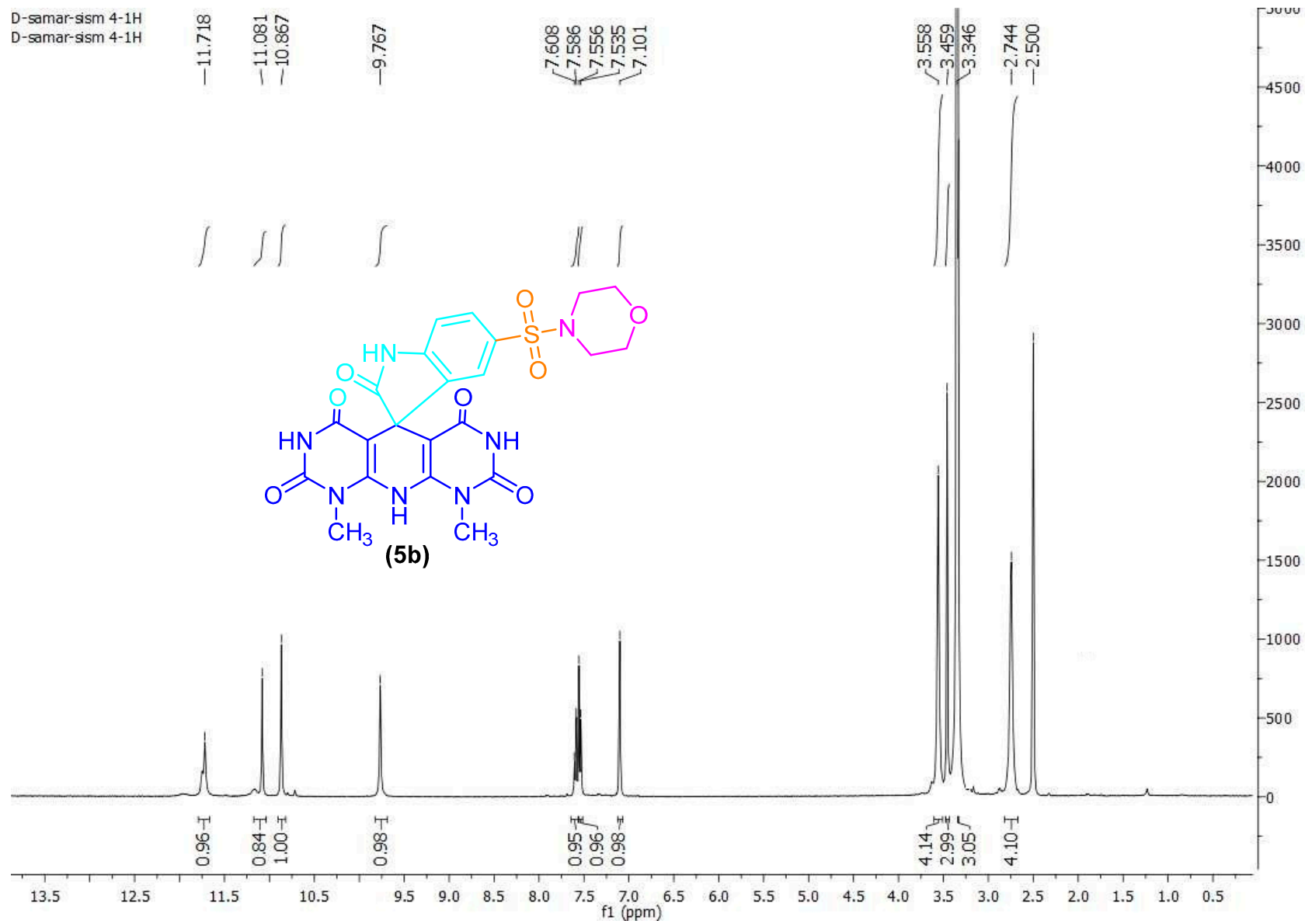
✓49.01

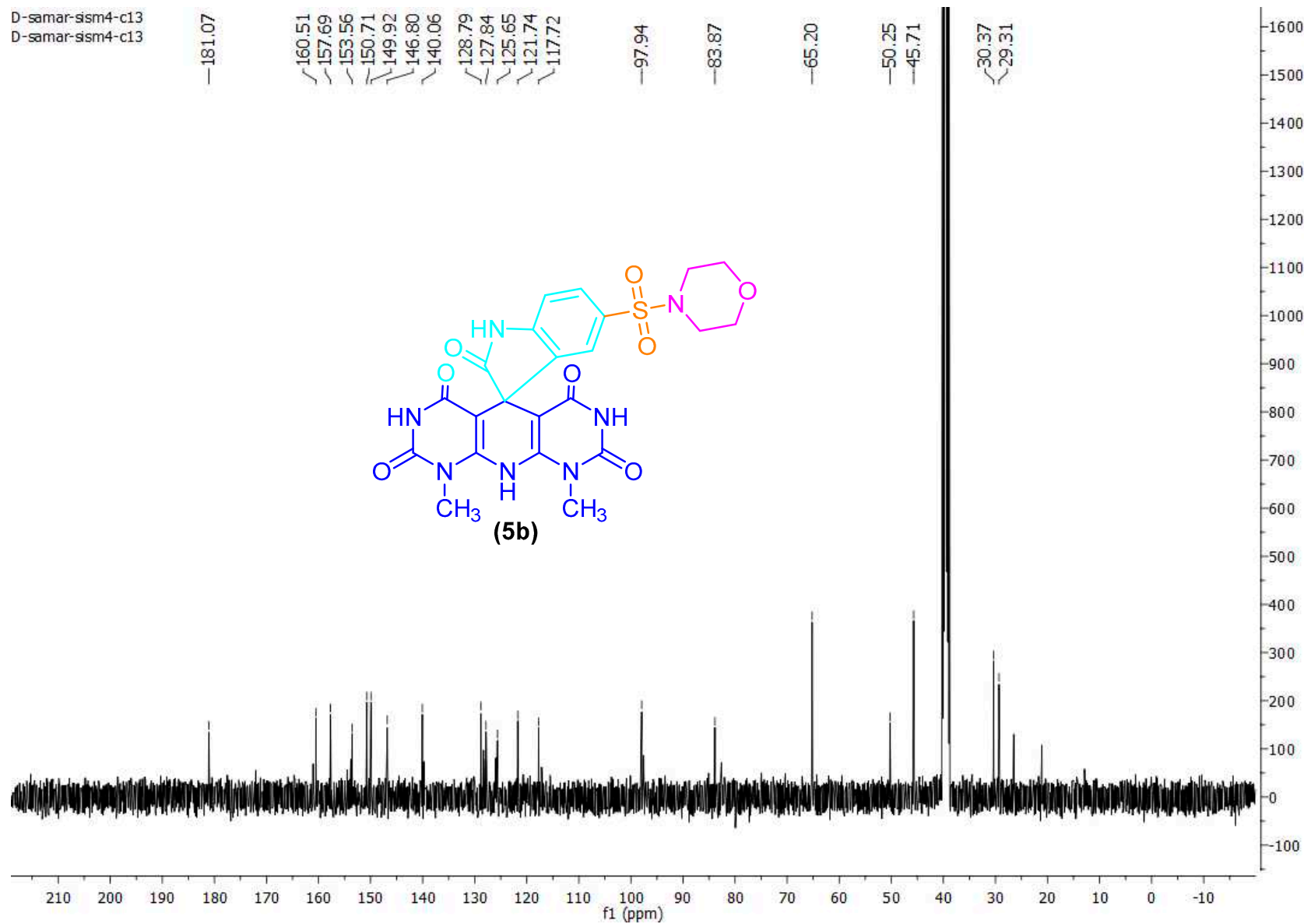
✓45.64



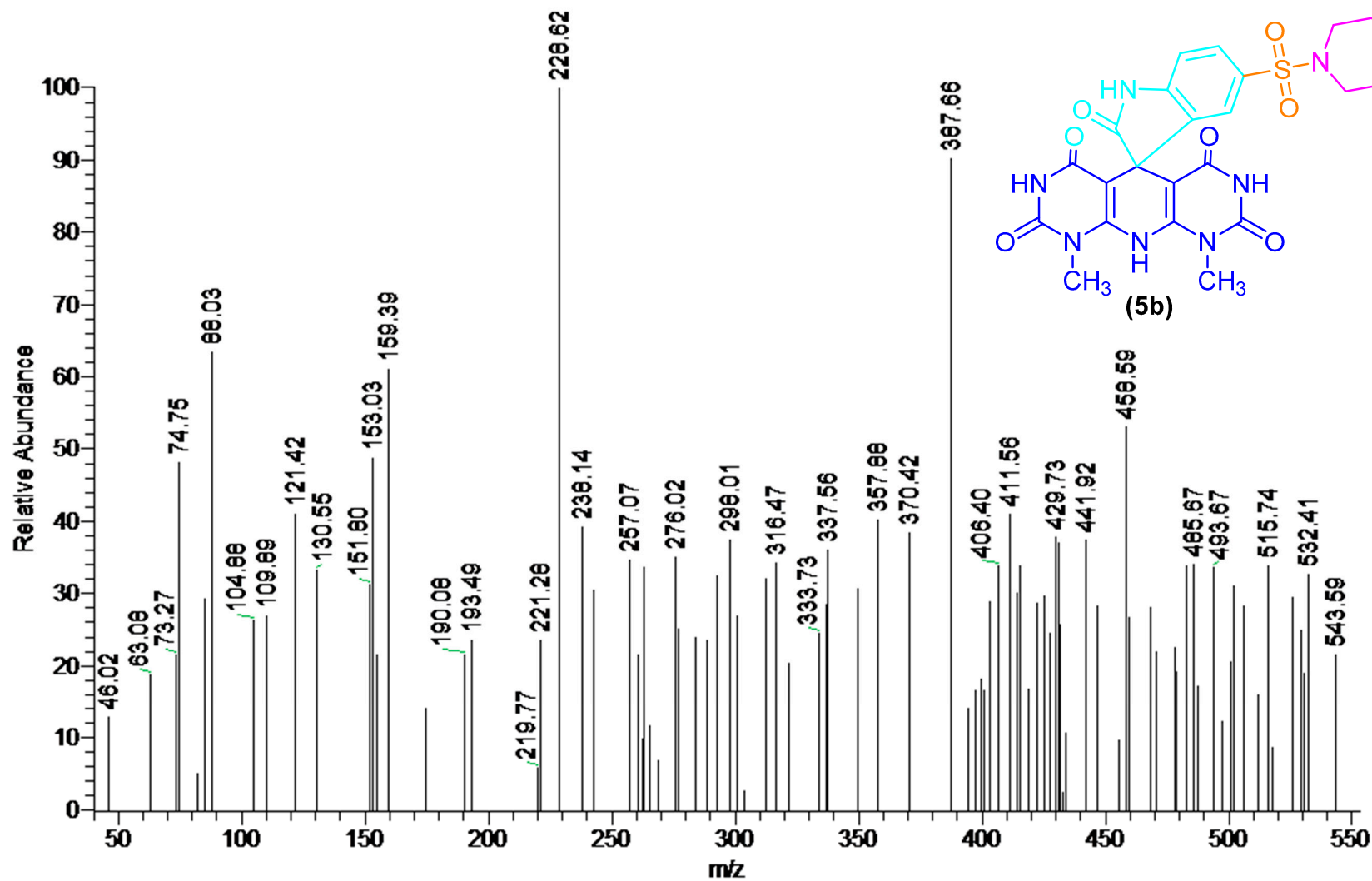
samar-Elkaliopy-sism5 #273 RT: 4.59 AV: 1 SB: 2 4.45, 4.45 NL: 6.12E2
T: {0,0} + c EI Full ms [40.00-1000.00]

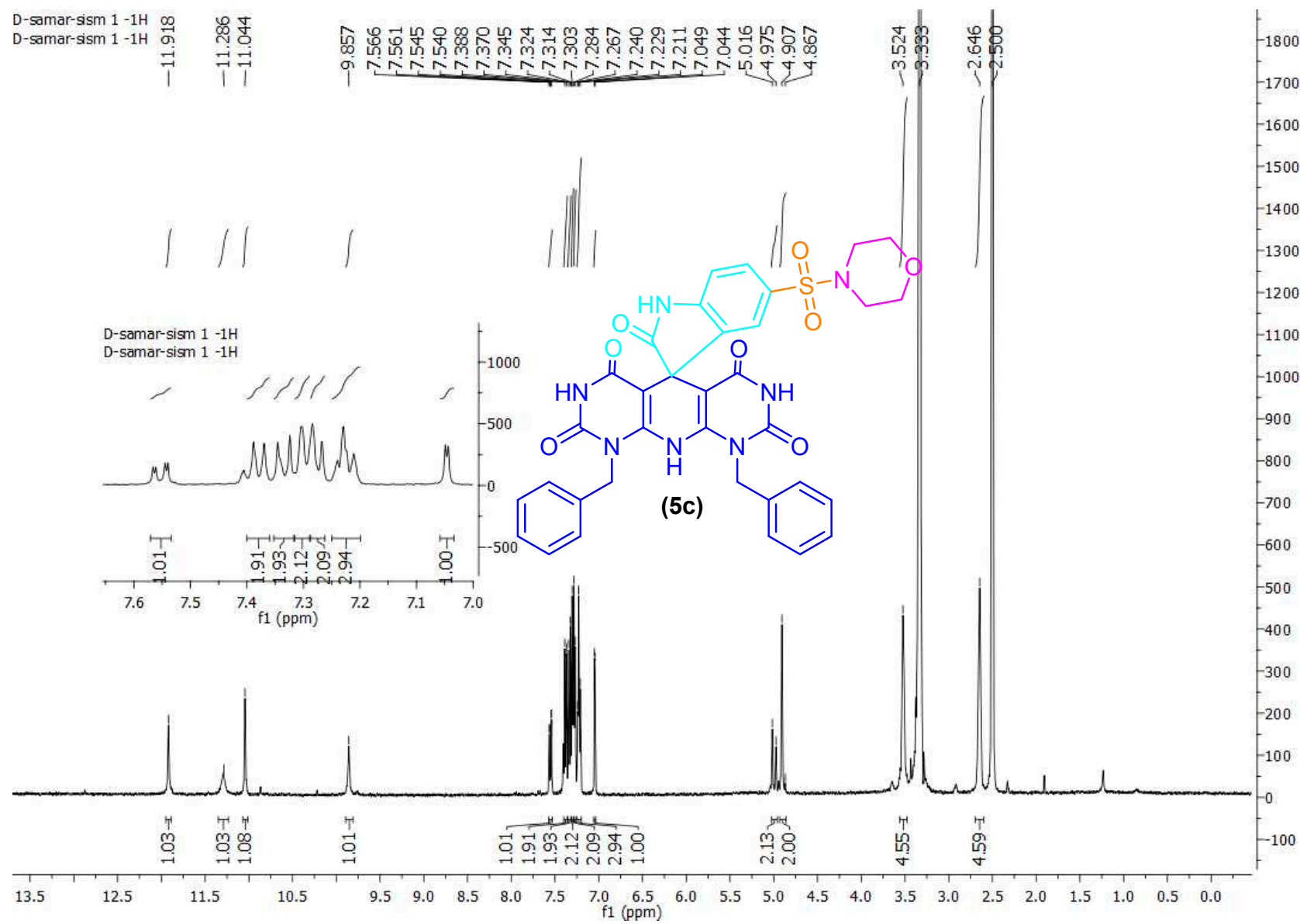


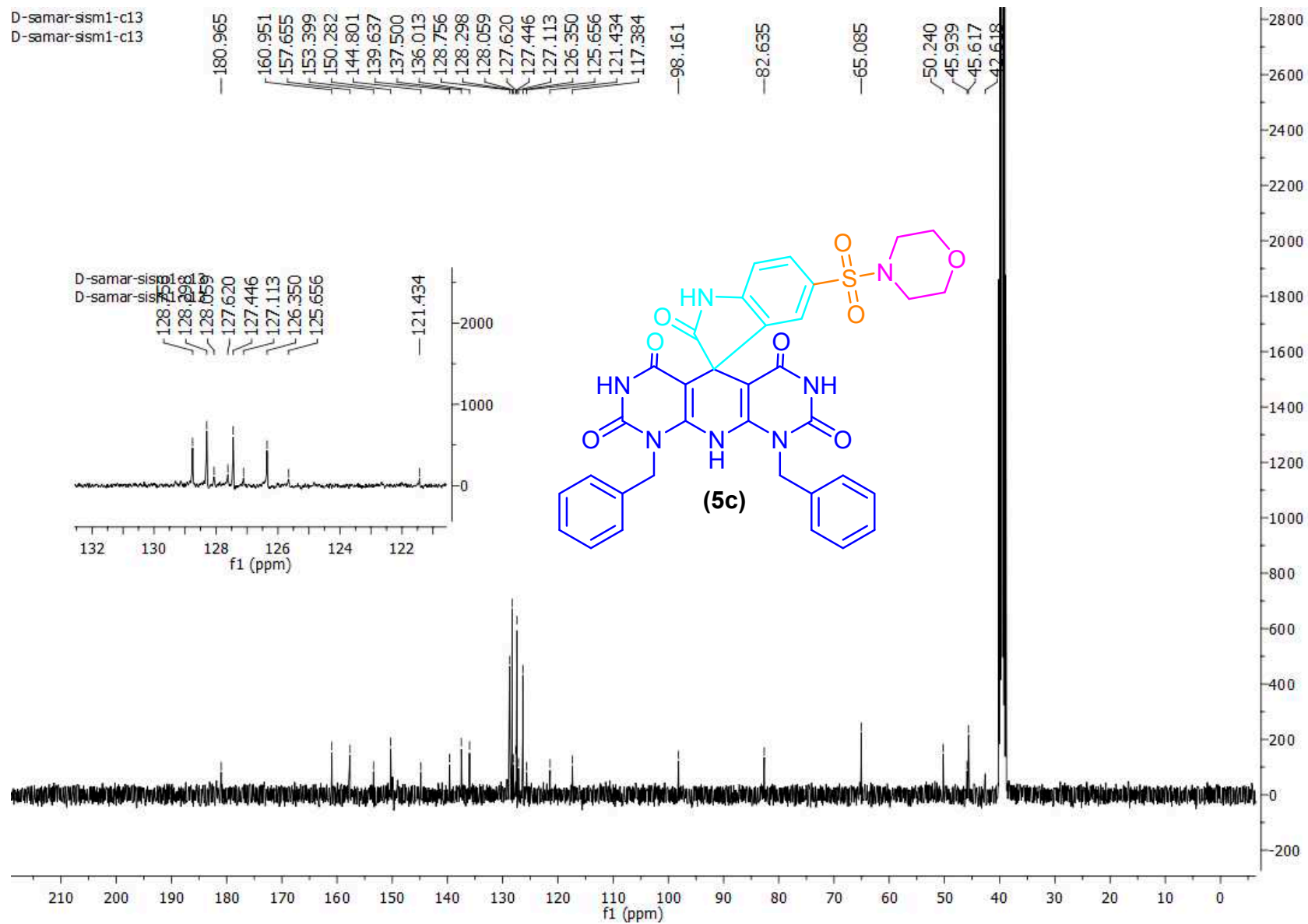




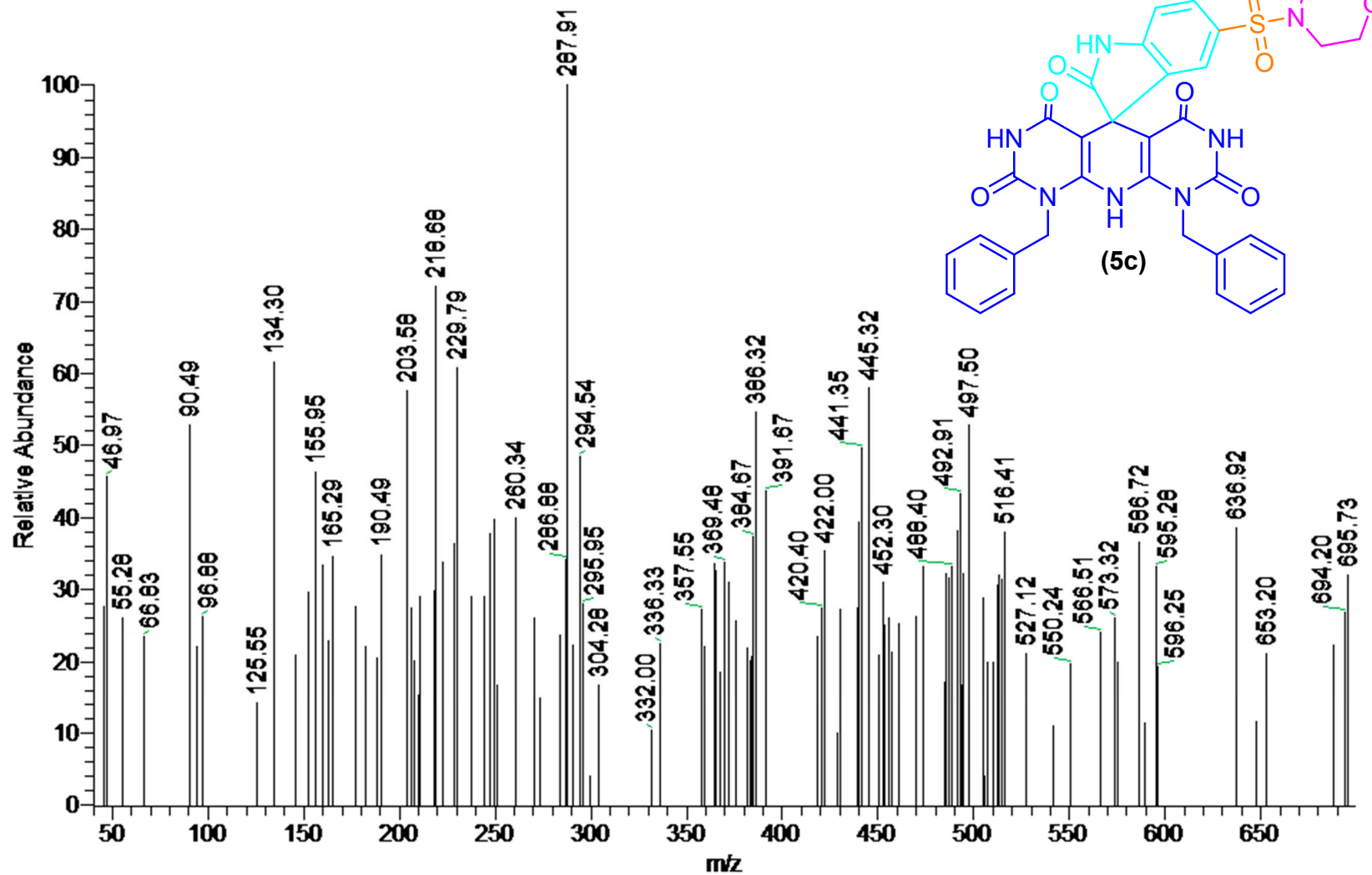
samar-Elkaliopy-sism4 #266 RT: 4.47 AV: 1 SB: 2 4.45, 4.45 NL: 3.99E2
T: {0,0} + c EI Full ms [40.00-1000.00]

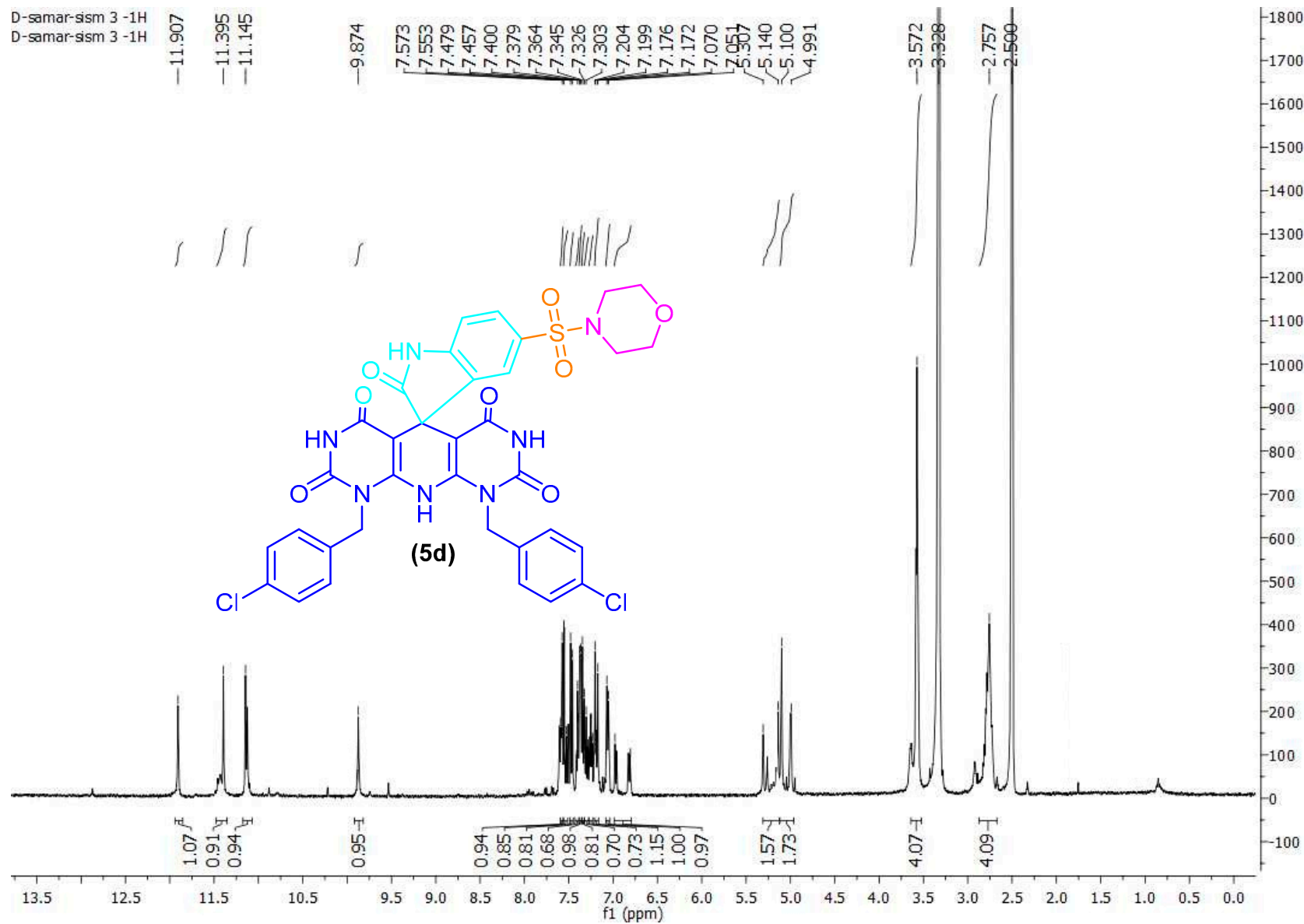






samar-Elkaliopy-sism1 #150 RT: 2.53 AV: 1 SB: 2 4.45, 4.45 NL: 4.01E2
T: {0.0} + c EI Full ms [40.00-1000.00]





D-samar-sism3-c13
D-samar-sism3-c13

180.98
160.76
157.87
157.72
150.15
149.56
146.77
134.31
133.94
133.45
133.31
131.68
131.57
129.57
129.33
129.05
128.48
127.21
126.21
125.67
98.57

83.98

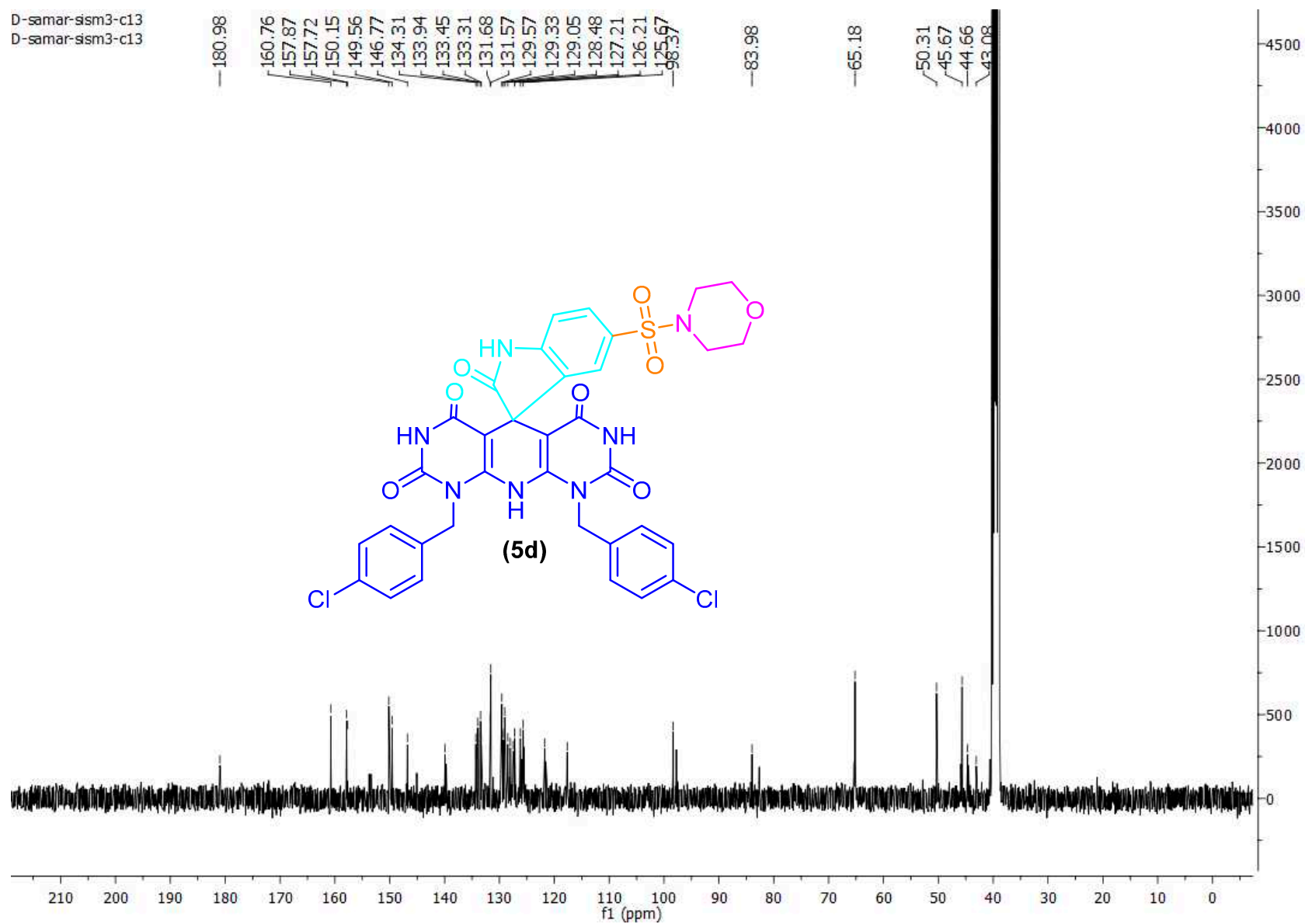
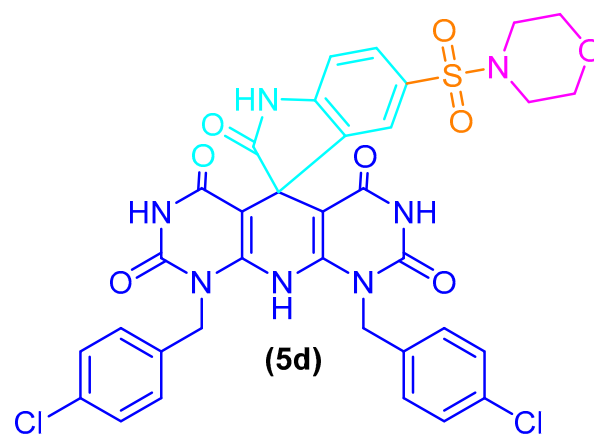
65.18

50.31

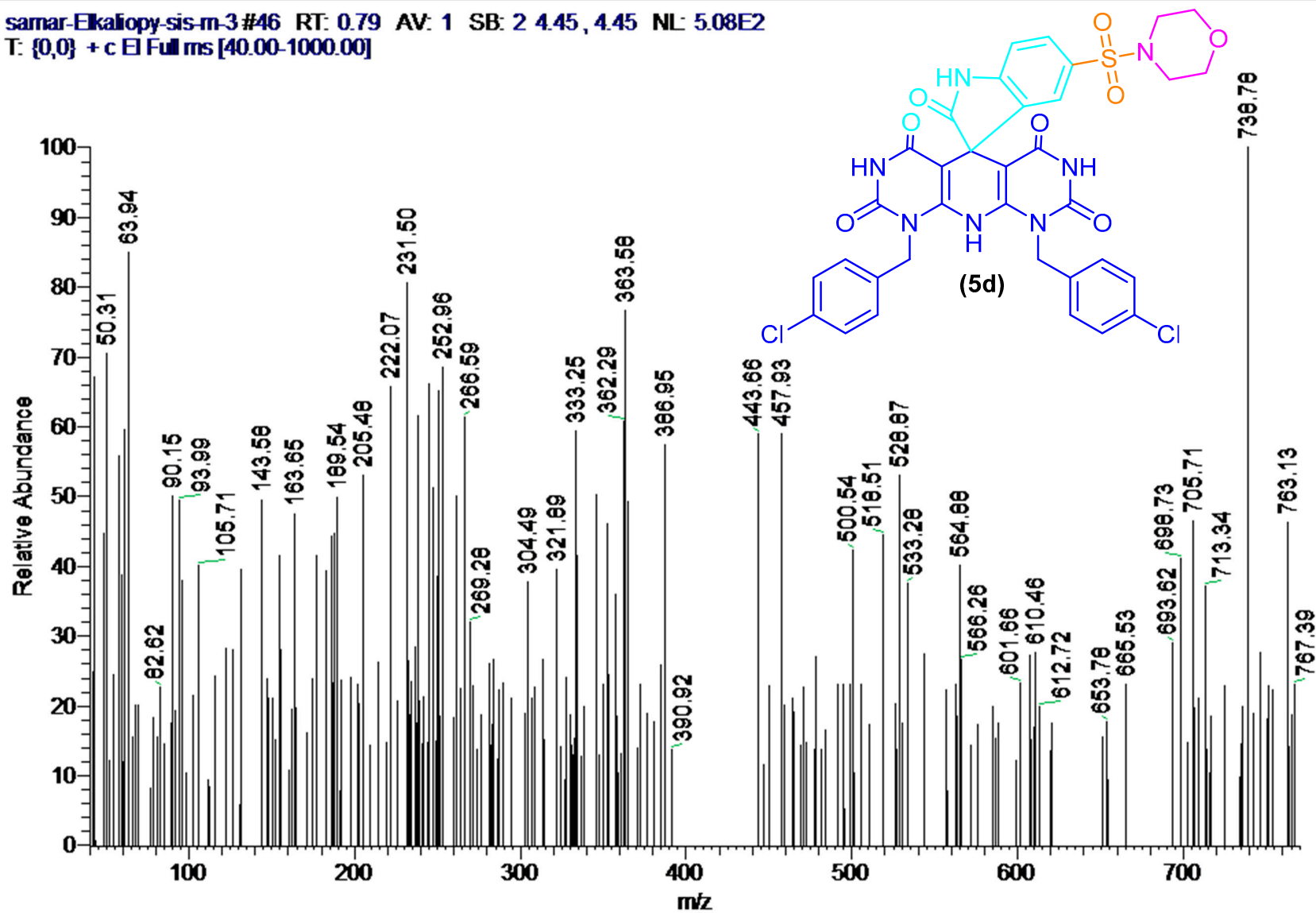
45.67

44.66

43.08



samar-Elkaliopy-sis-m-3 #46 RT: 0.79 AV: 1 SB: 2 4.45, 4.45 NL: 5.08E2
T: {0,0} + c EI Full ms [40.00-1000.00]



D-samar-sism 2 -1H
D-samar-sism 2 -1H

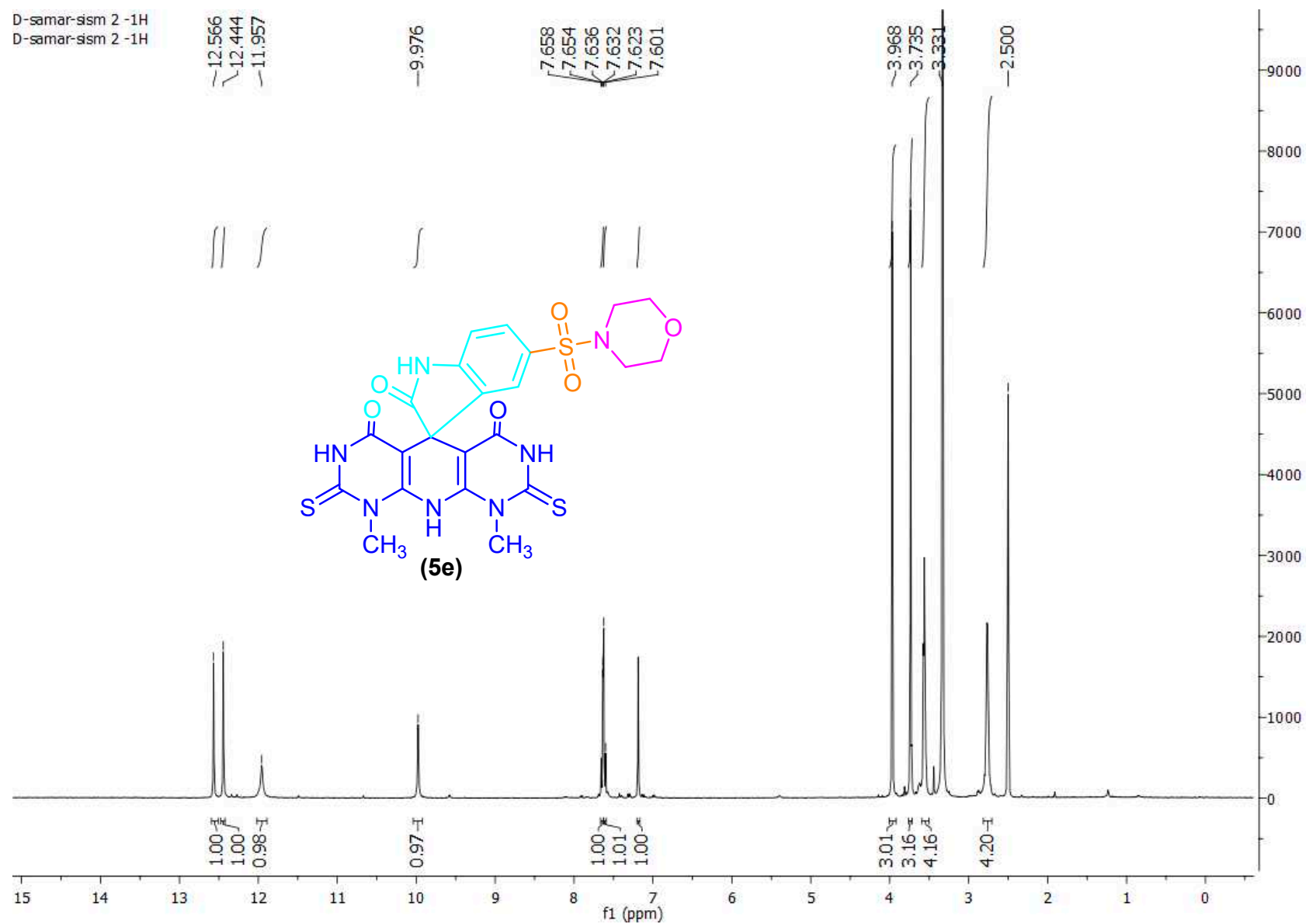
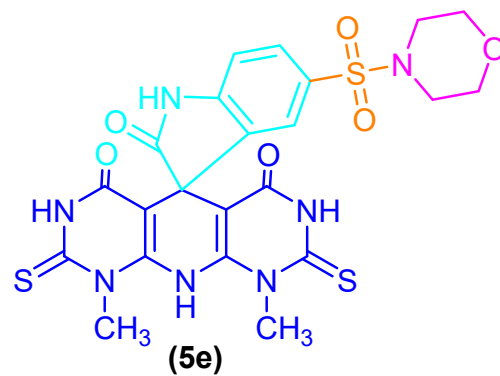
12.566
12.444
11.957

9.976

7.658
7.654
7.636
7.632
7.623
7.601

3.968
3.735
3.331

2.500



D-samar-sism 2 -c13
D-samar-sism 2 -c13

180.07
176.20
175.44

157.61
155.11
153.60
146.82
139.77

129.42
128.23
125.65
120.55
118.24

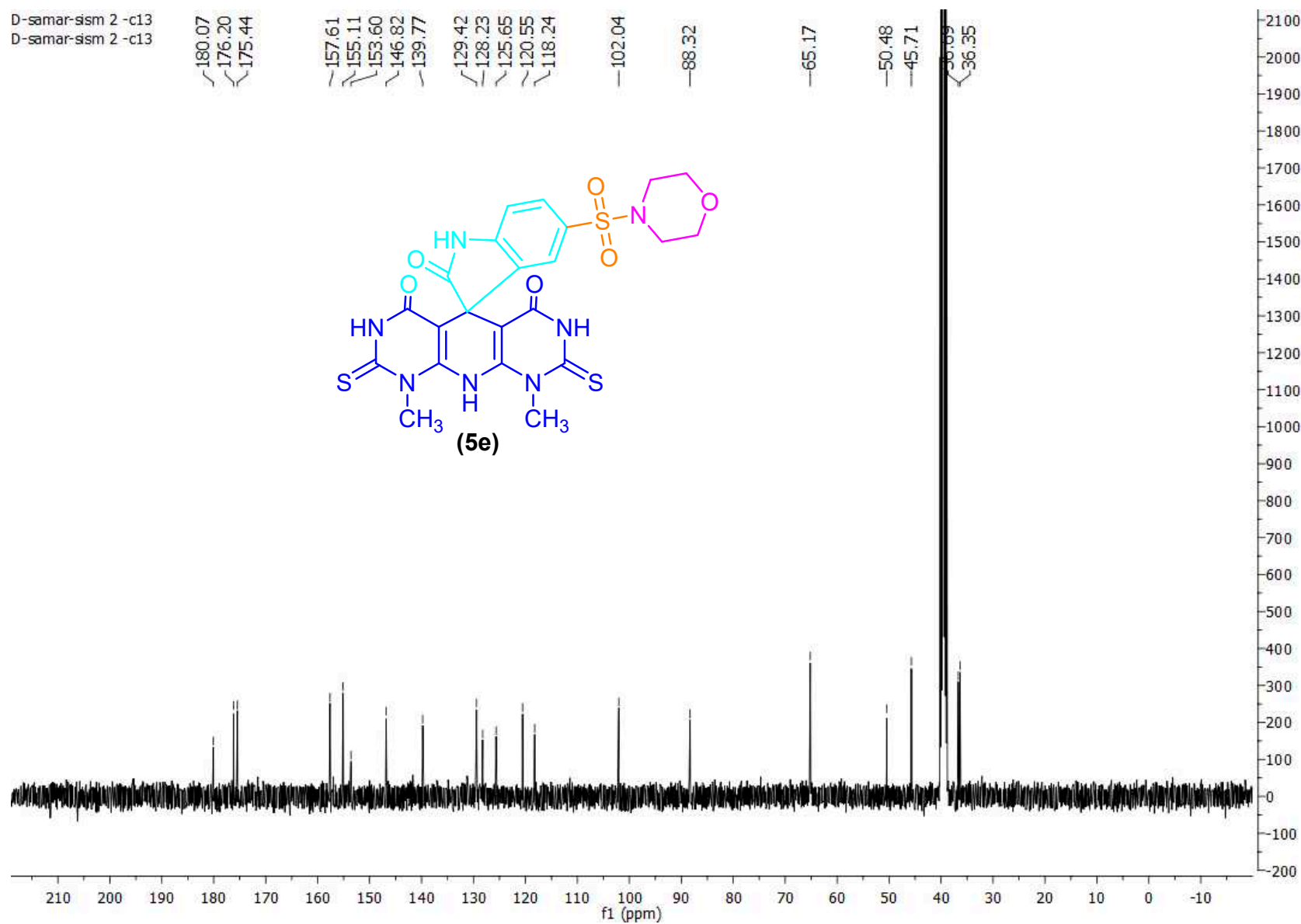
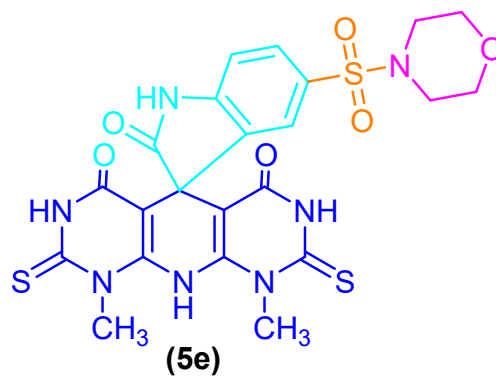
102.04

88.32

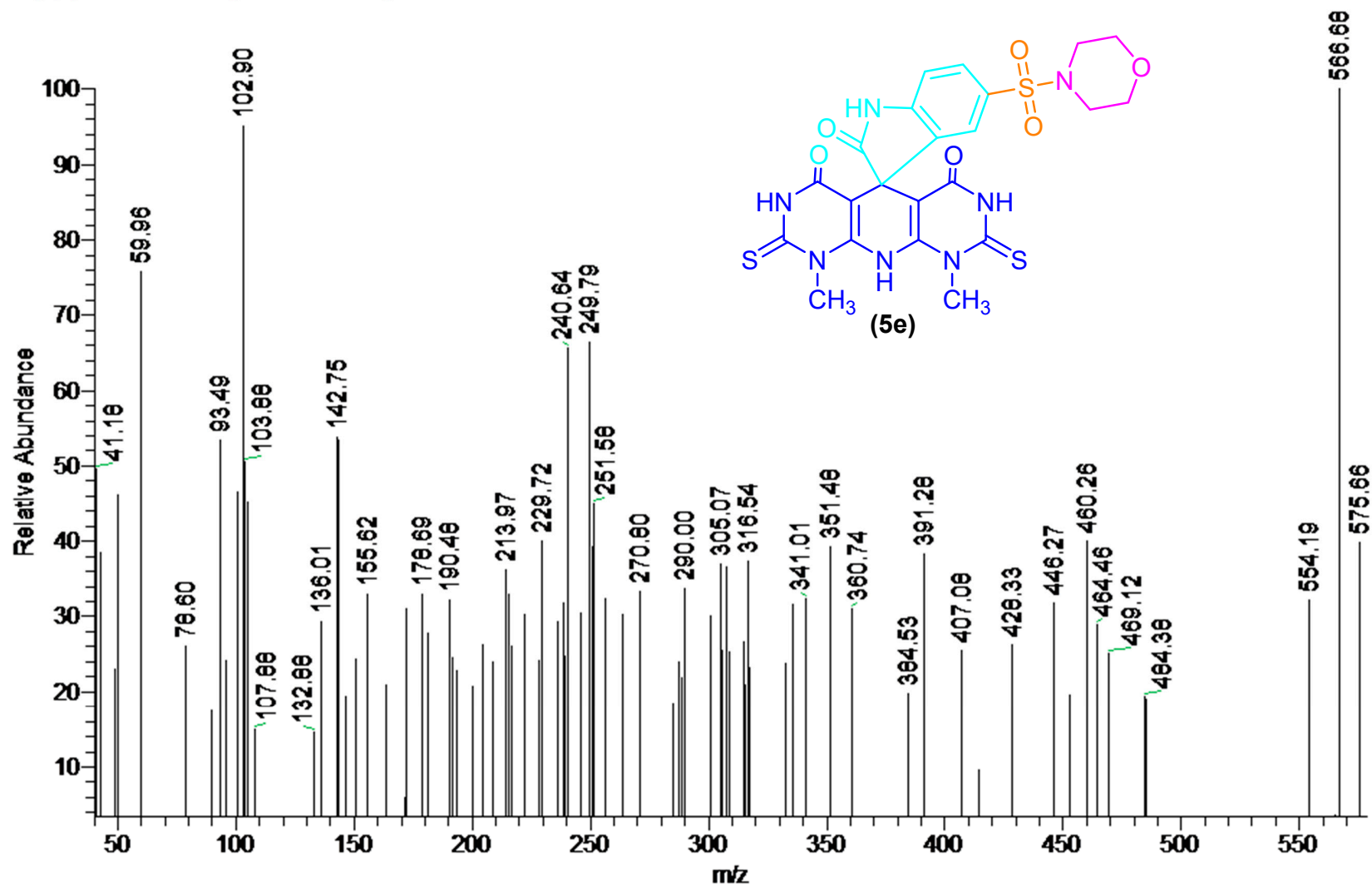
65.17

50.48
45.71

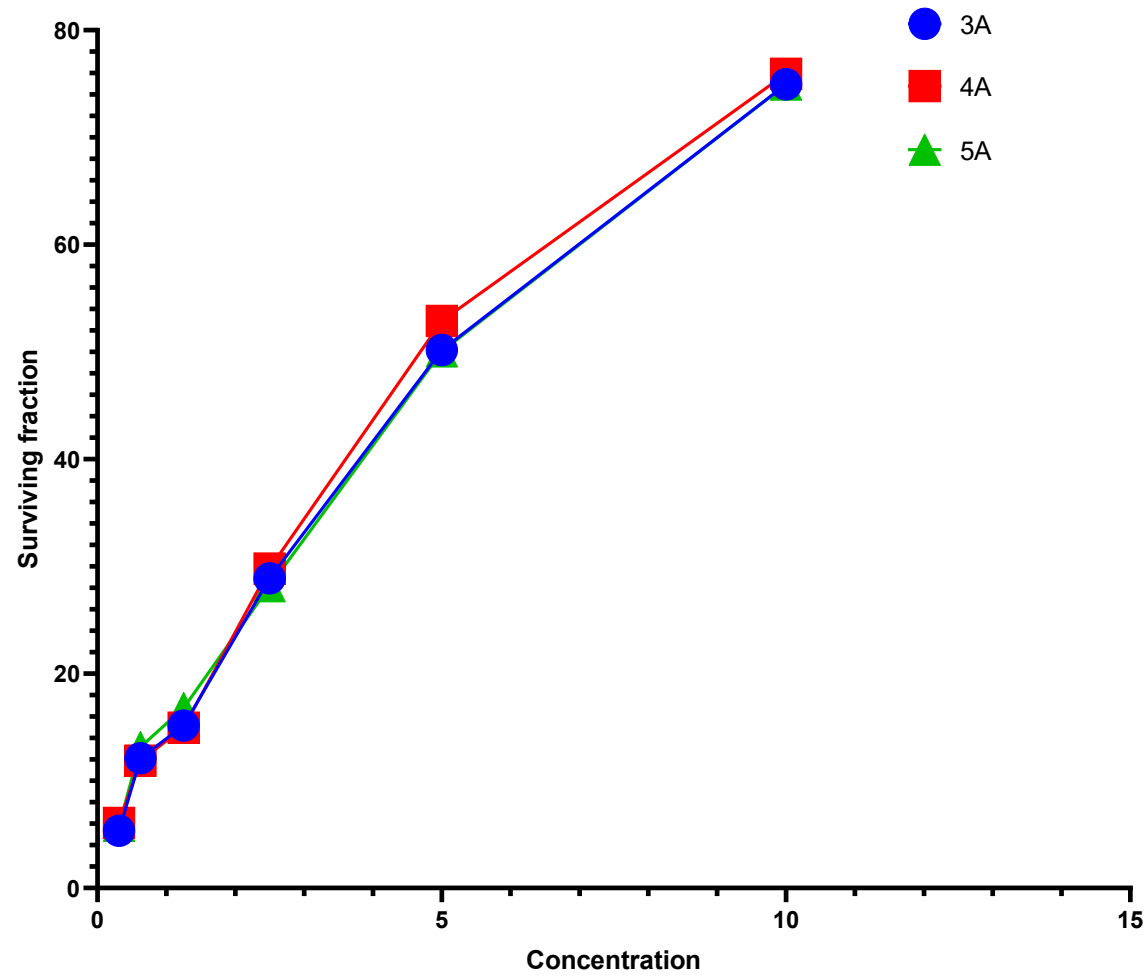
36.69
36.35

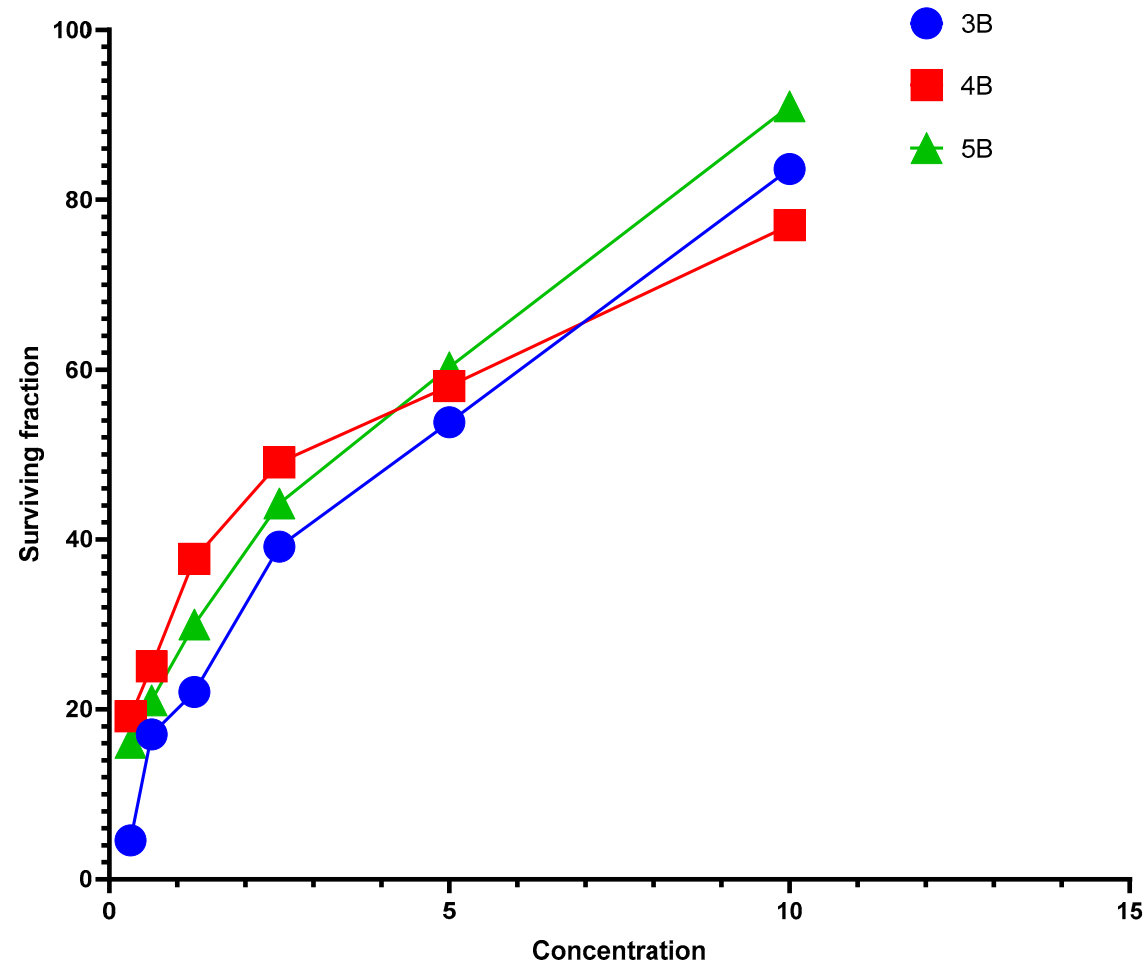


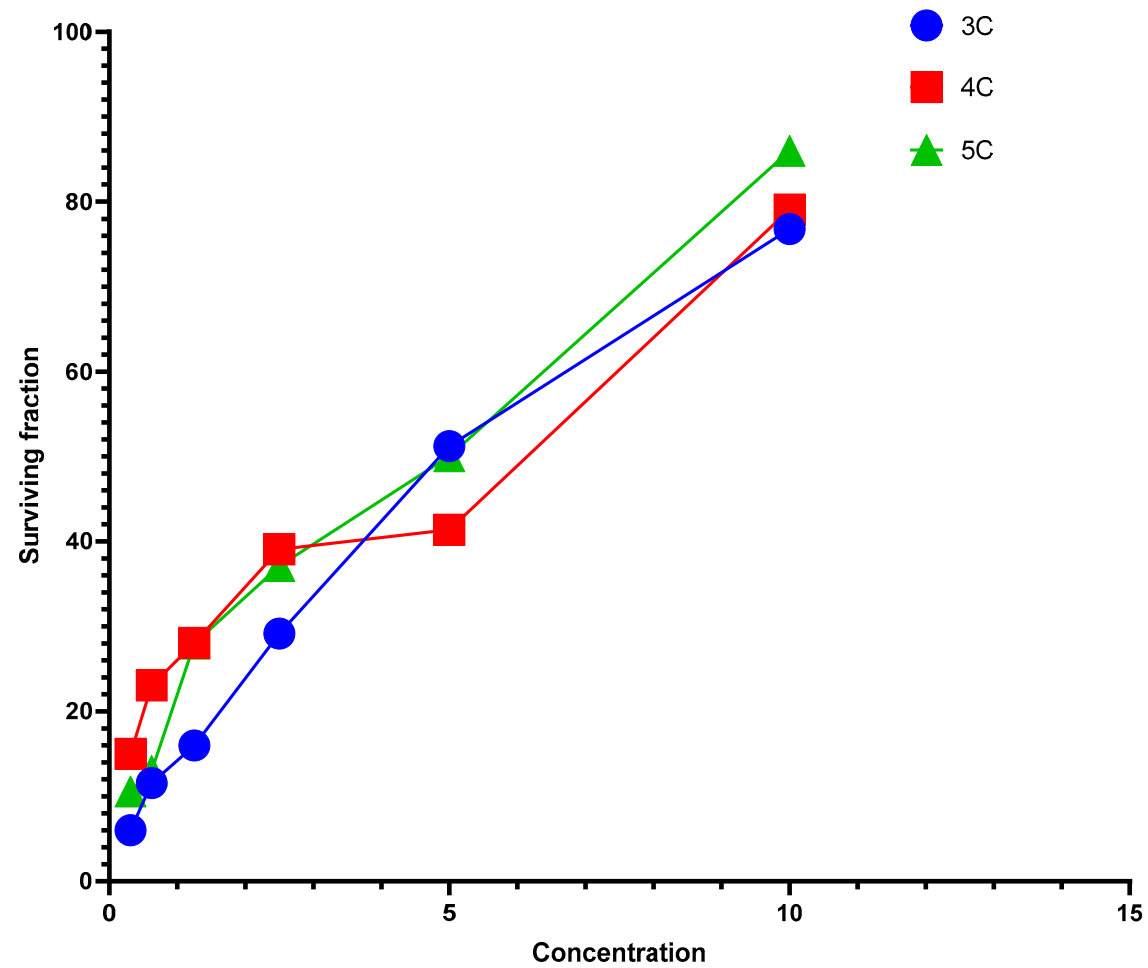
samar-Ekaliopy-sism2 #254 RT: 4.27 AV: 1 SB: 2 4.45, 4.45 NL: 3.27E2
T: {0,0} + c EI Full ms [40.00-1000.00]

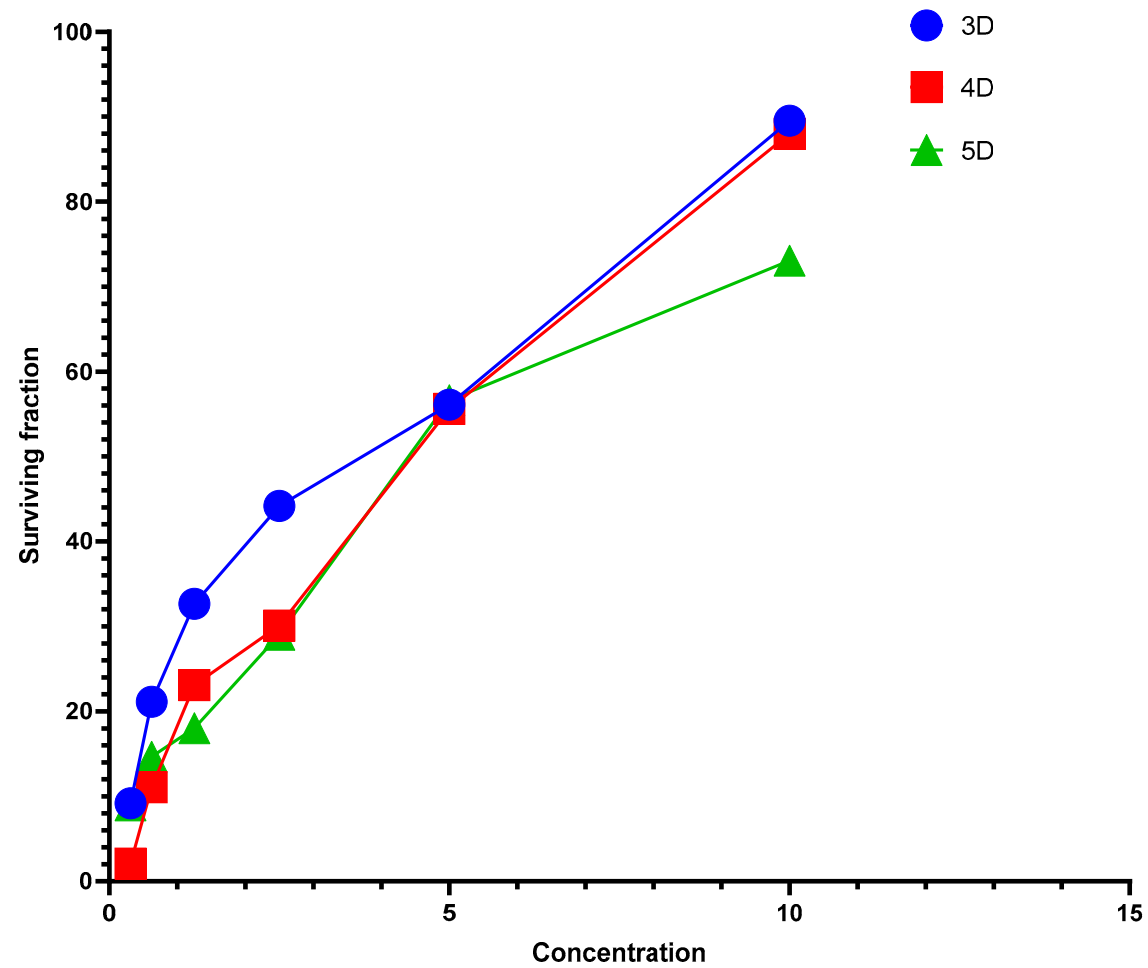


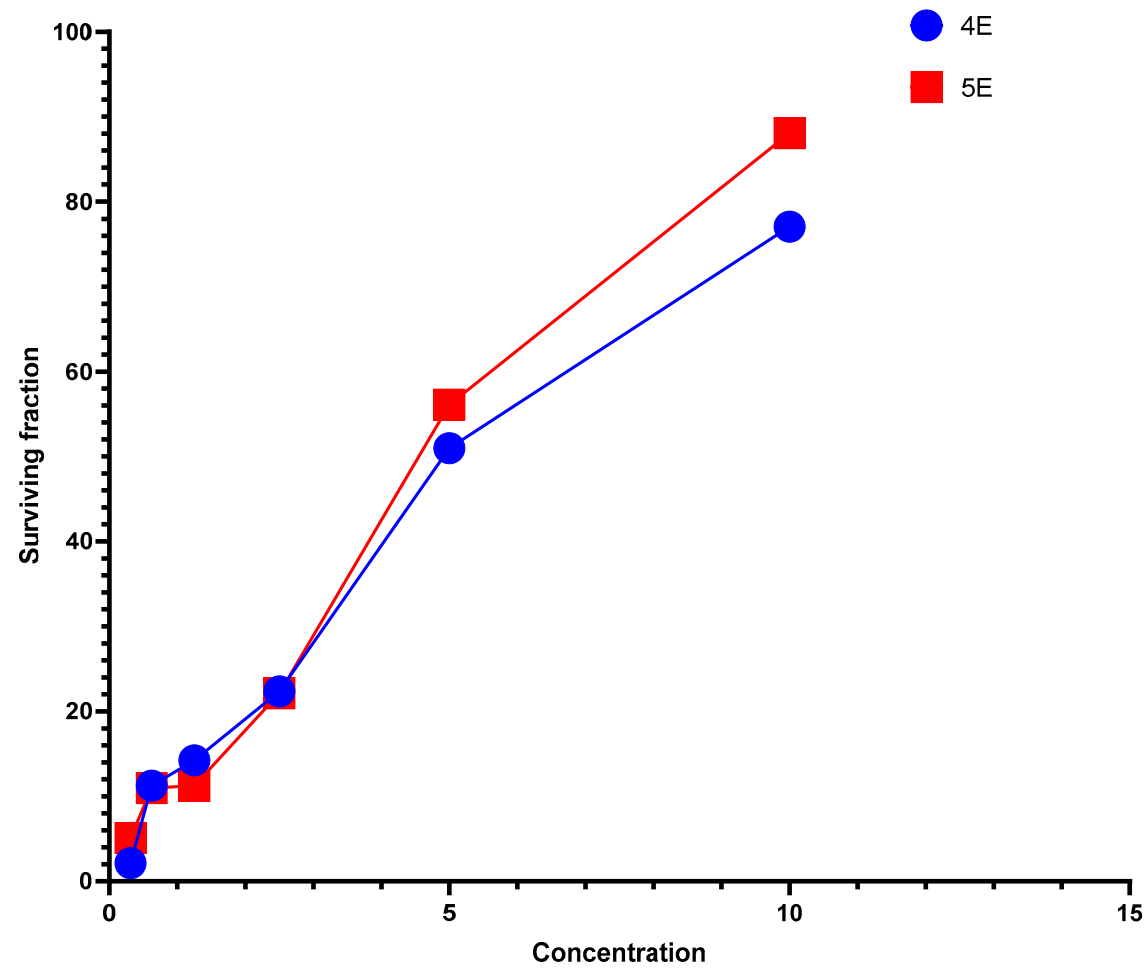
IC₅₀ graphs







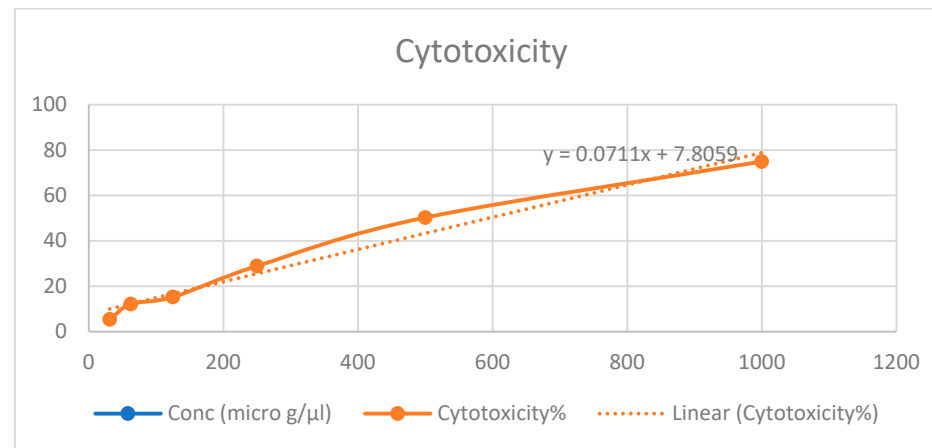




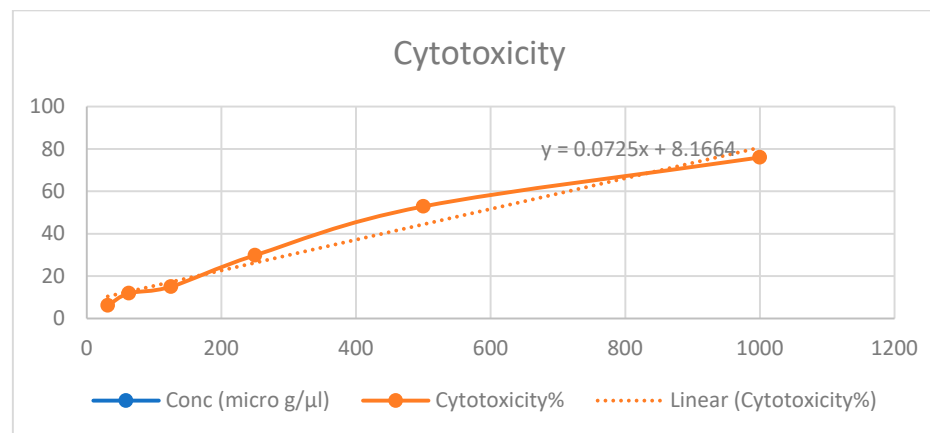
Anti-COVID Cpd report

Cytotoxicity assay:

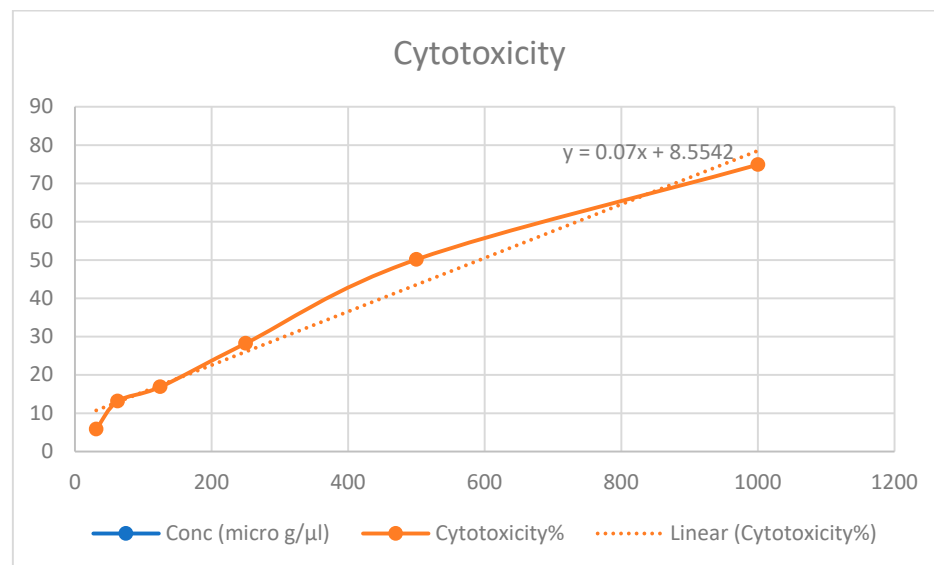
3A	Conc (micro g/μl)	Cytotoxicity%
	1000	74.9480
	500	50.2564
	250	28.876276
	125	15.212
	62.5	12.1323
	31.2	5.35241



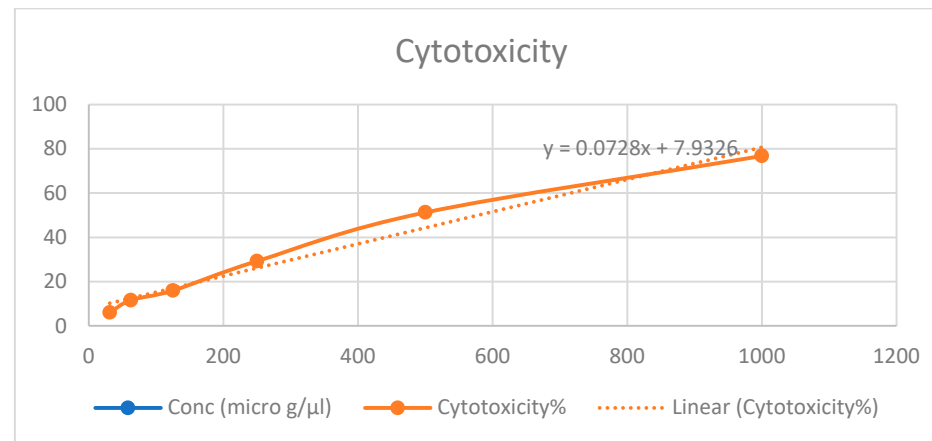
4A	Conc (micro g/μl)	Cytotoxicity%
	1000	75.9821
	500	52.8768
	250	29.78287
	125	14.97829
	62.5	11.87209
	31.2	6.16757



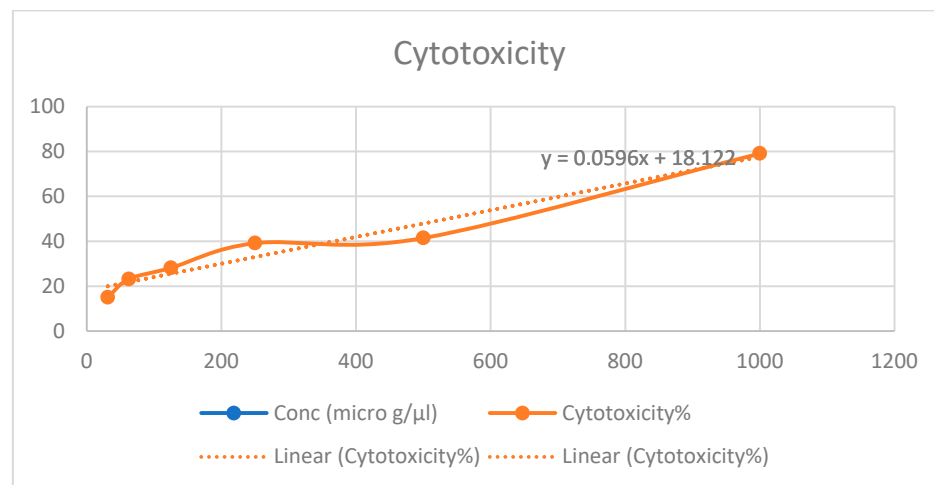
5A	Conc (micro g/μl)	Cytotoxicity%
	1000	74.8721
	500	50.13435
	250	28.23546
	125	16.8754
	62.5	13.12375
	31.2	5.83231



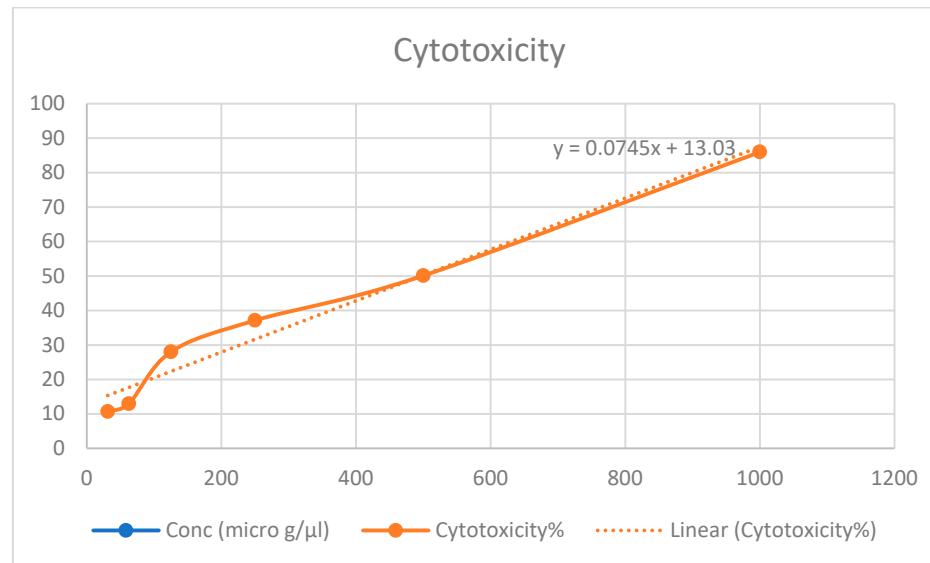
3C	Conc (micro g/μl)	Cytotoxicity%
	1000	76.7863
	500	51.2423
	250	29.2411
	125	15.95432
	62.5	11.6224
	31.2	6.02111



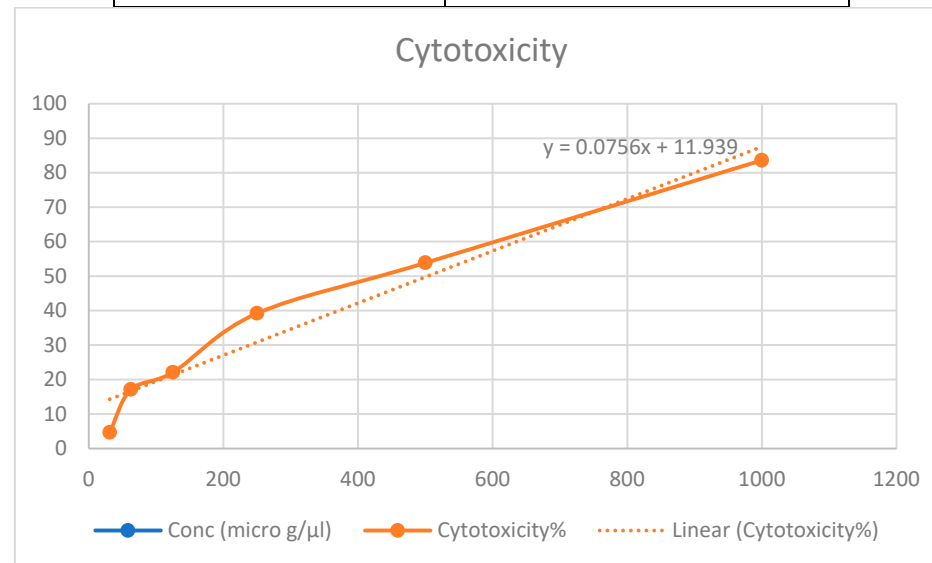
4C	Conc (micro g/μl)	Cytotoxicity%
	1000	79.12321
	500	41.45364
	250	39.12891
	125	28.11989
	62.5	23.12398
	31.2	15.02359



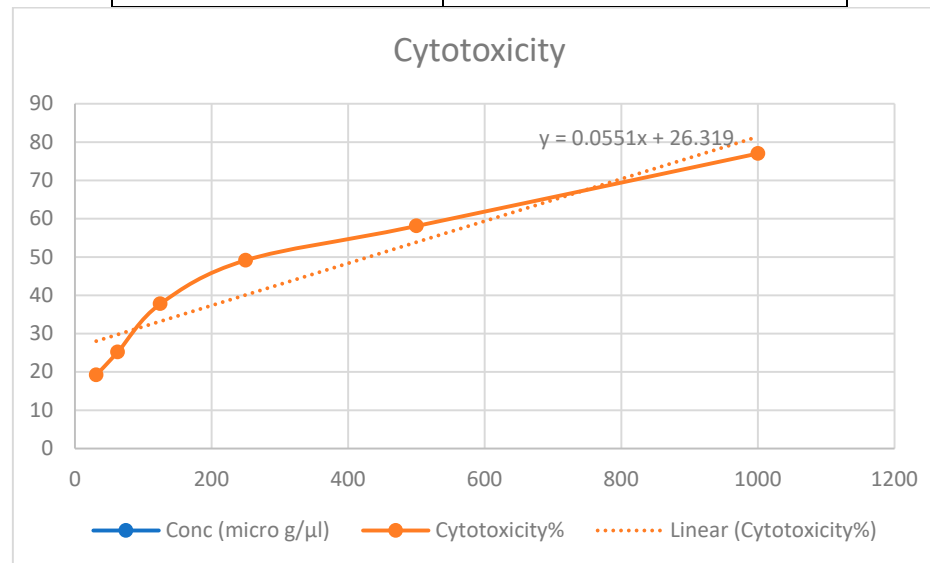
5C	Conc (micro g/μl)	Cytotoxicity%
	1000	85.9899
	500	50.11032
	250	37.12091
	125	28.00918
	62.5	12.97801
	31.2	10.65442



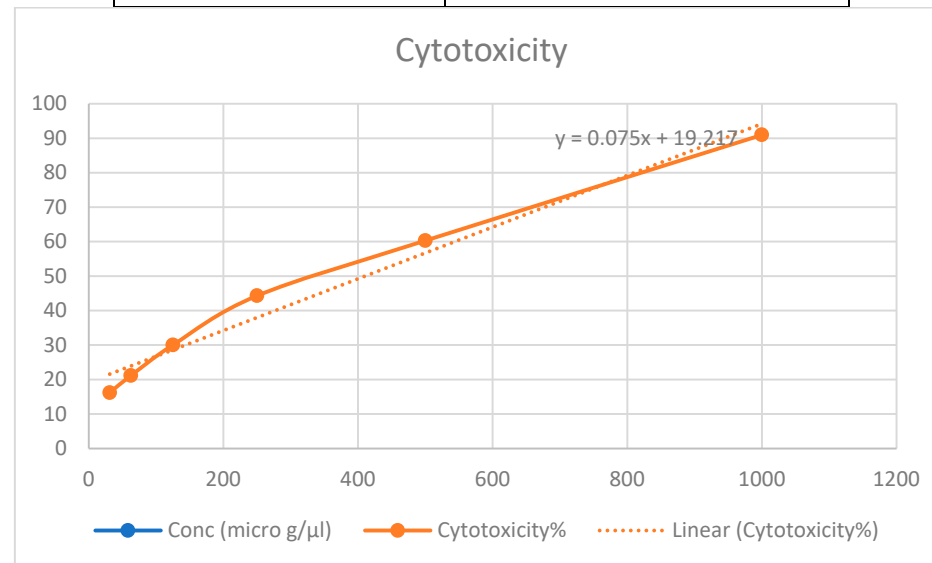
3B	Conc (micro g/μl)	Cytotoxicity%
	1000	83.6251
	500	53.8761
	250	39.1991
	125	22.0918
	62.5	17.1098
	31.2	4.65510



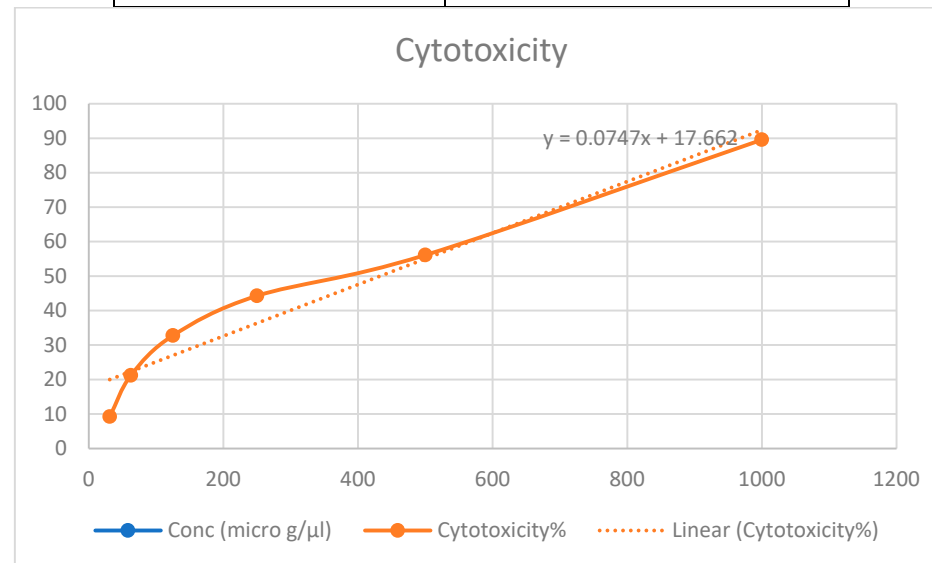
4B	Conc (micro g/μl)	Cytotoxicity%
	1000	77.0009
	500	58.0981
	250	49.1205
	125	37.76181
	62.5	25.1651
	31.2	19.18054



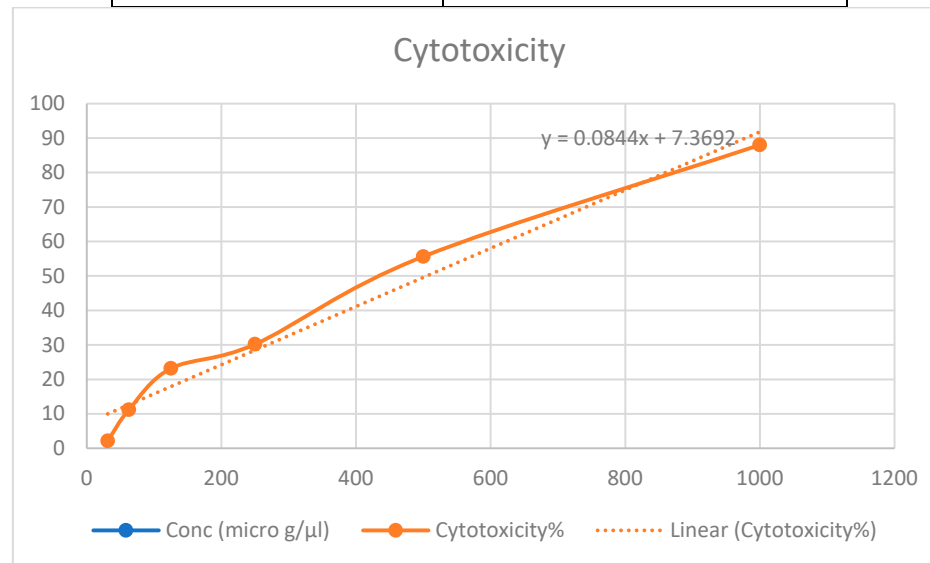
5B	Conc (micro g/μl)	Cytotoxicity%
	1000	90.9826
	500	60.2976
	250	44.2976
	125	30.0092
	62.5	21.14378
	31.2	16.1887



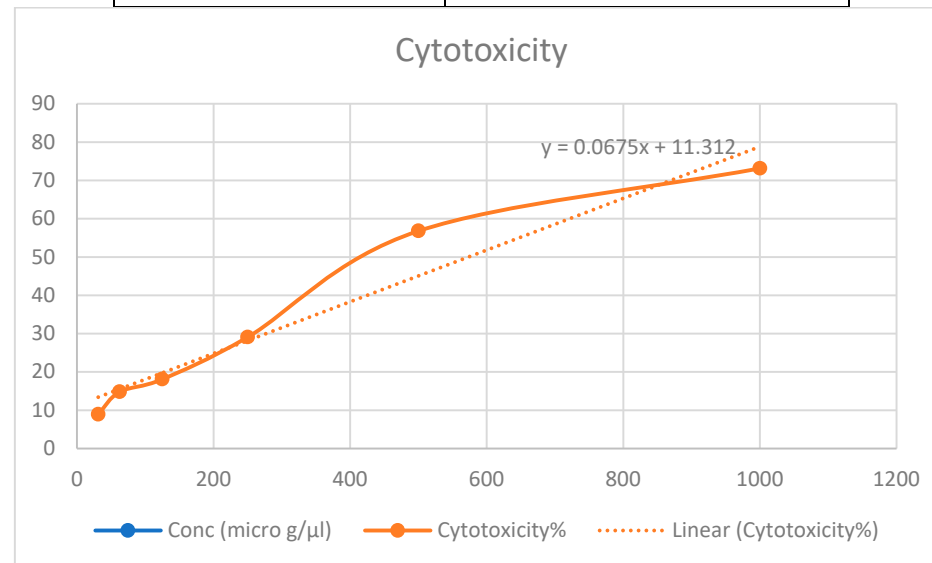
3D	Conc (micro g/μl)	Cytotoxicity%
	1000	89.5618
	500	56.1097
	250	44.2652
	125	32.7651
	62.5	21.1987
	31.2	9.19871



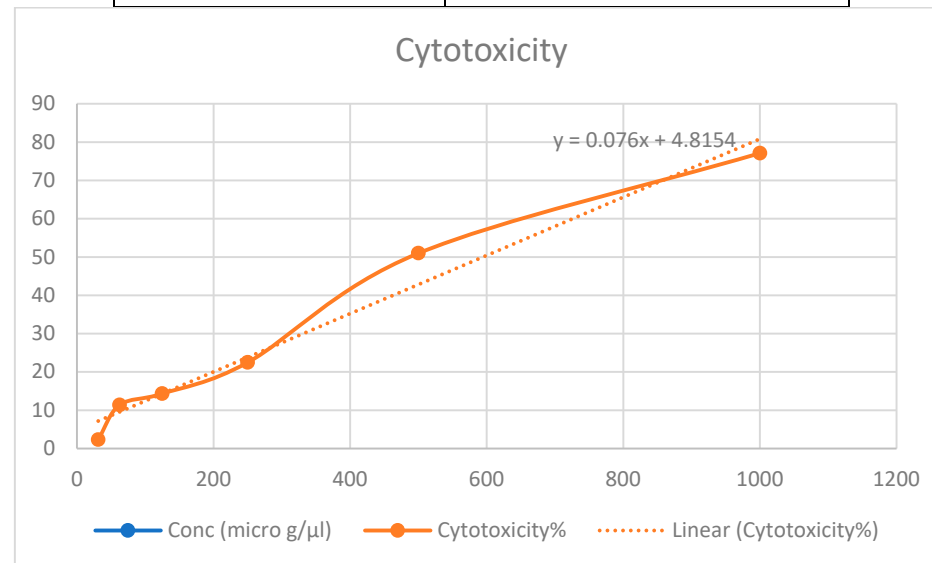
4D	Conc (micro g/ μ l)	Cytotoxicity%
	1000	88.01981
	500	55.66551
	250	30.19711
	125	23.19871
	62.5	11.18711
	31.2	2.187511



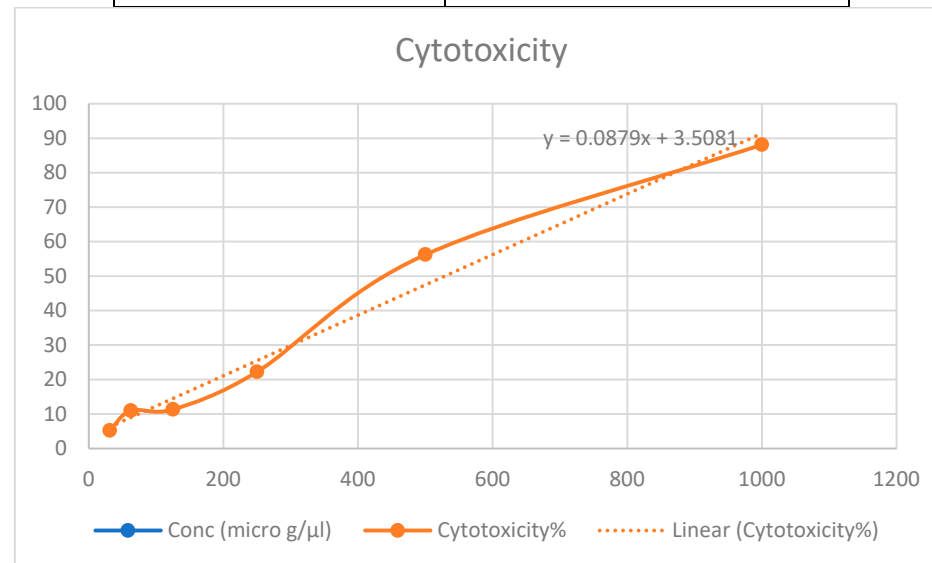
5D	Conc (micro g/μl)	Cytotoxicity%
	1000	73.14226
	500	56.7811
	250	29.0912
	125	18.07912
	62.5	14.7896
	31.2	8.90569



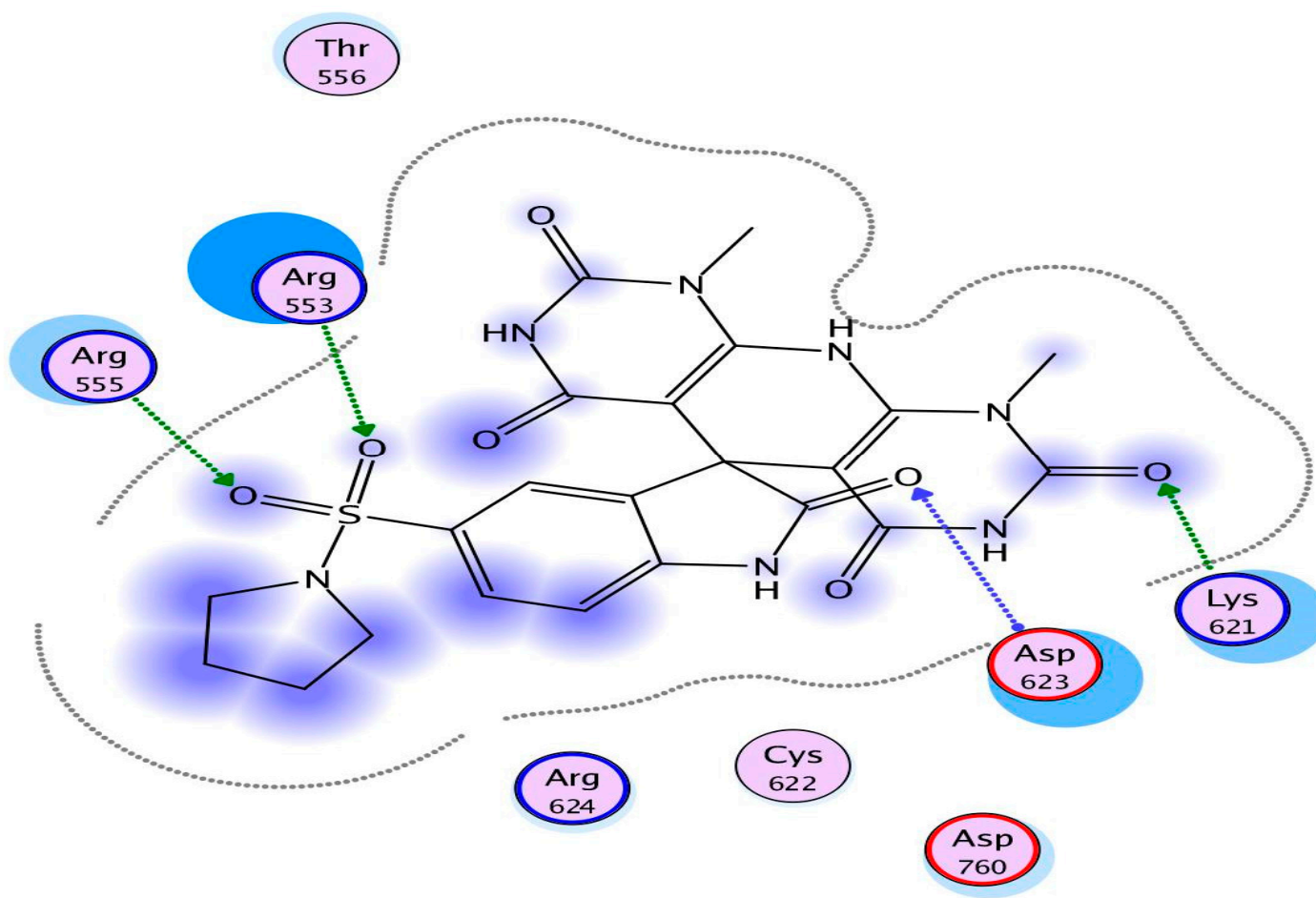
4E	Conc (micro g/μl)	Cytotoxicity%
	1000	77.09444
	500	50.9866
	250	22.45123
	125	14.3221
	62.5	11.3308
	31.2	2.30256



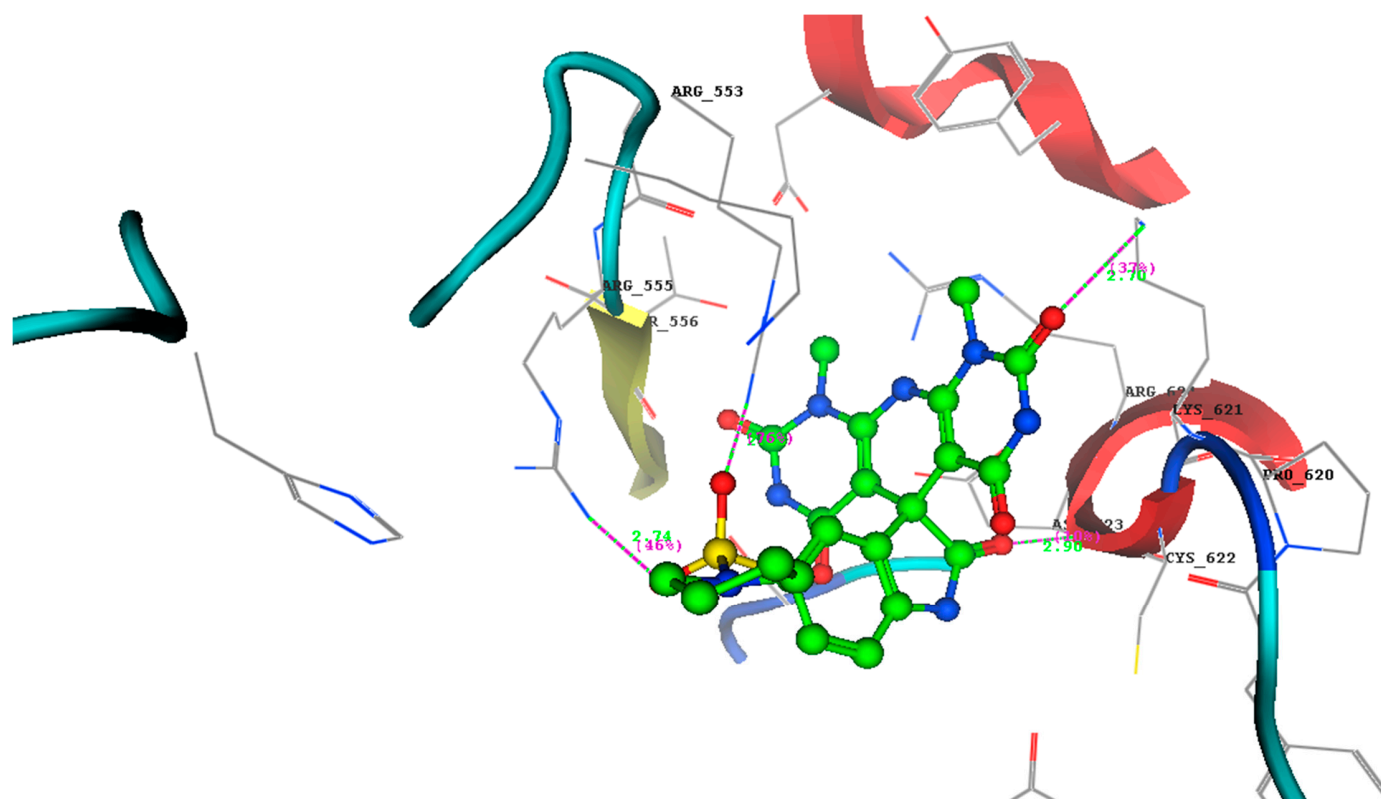
5E	Conc (micro g/μl)	Cytotoxicity%
	1000	88.1425
	500	56.2314
	250	22.2232
	125	11.33456
	62.5	10.98061
	31.2	5.18705



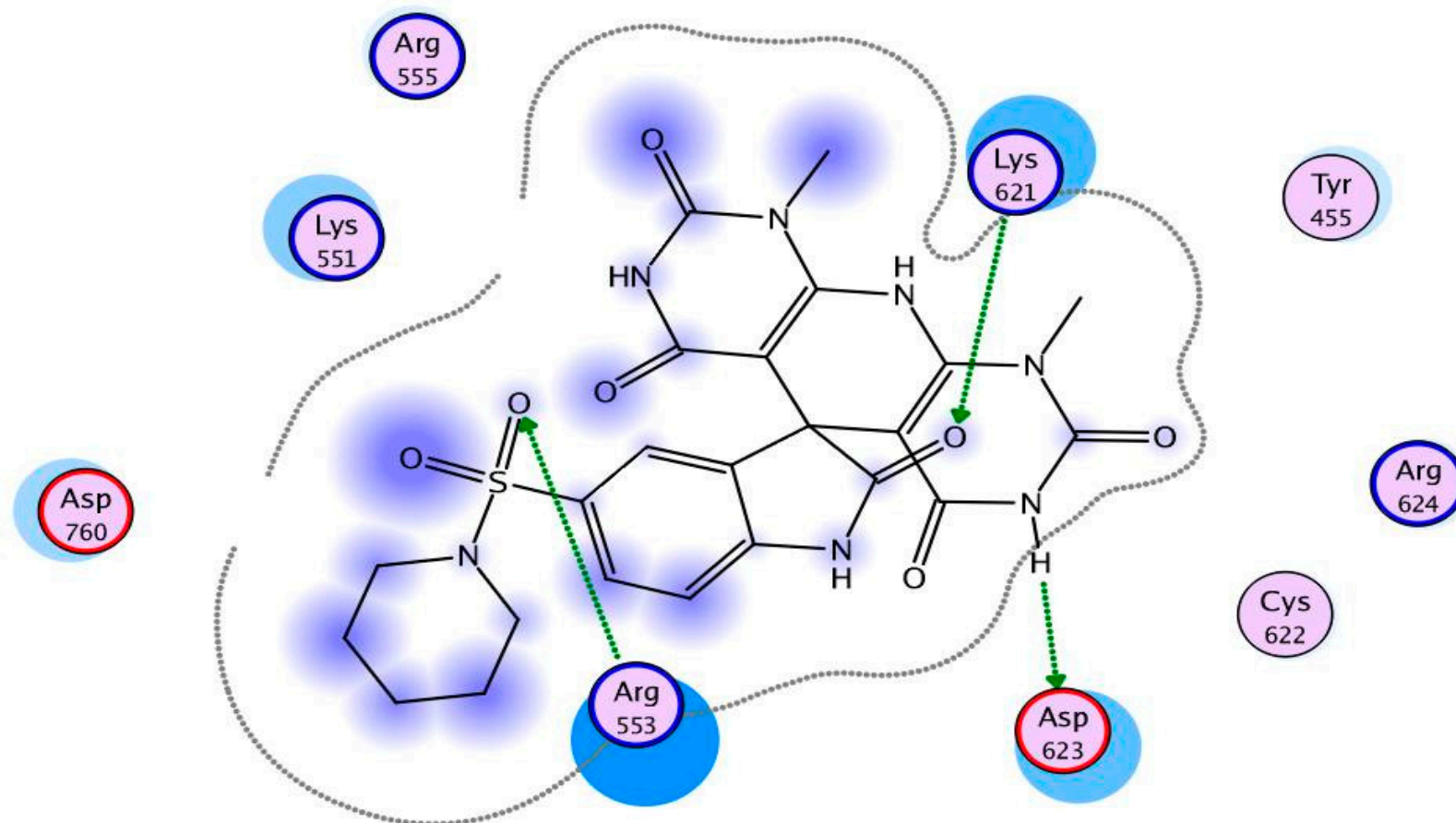
Docking study figures



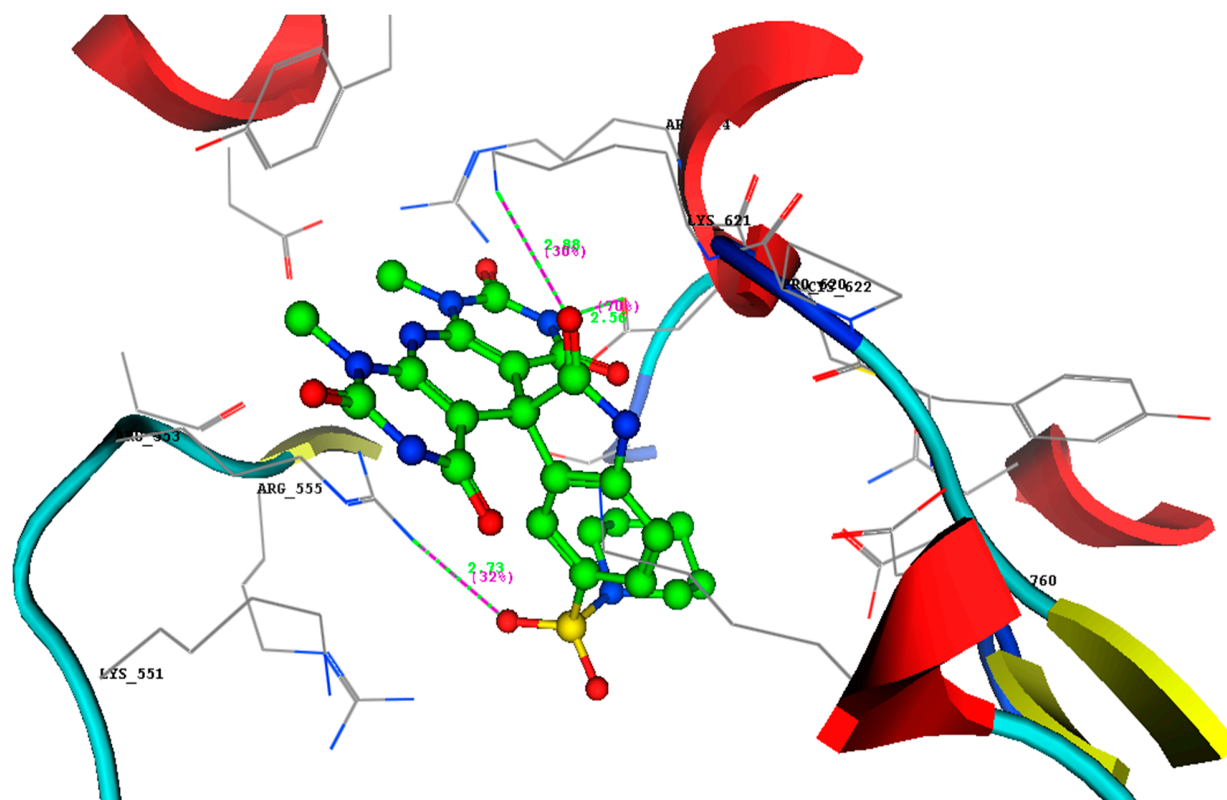
2D structure of compound **3a** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



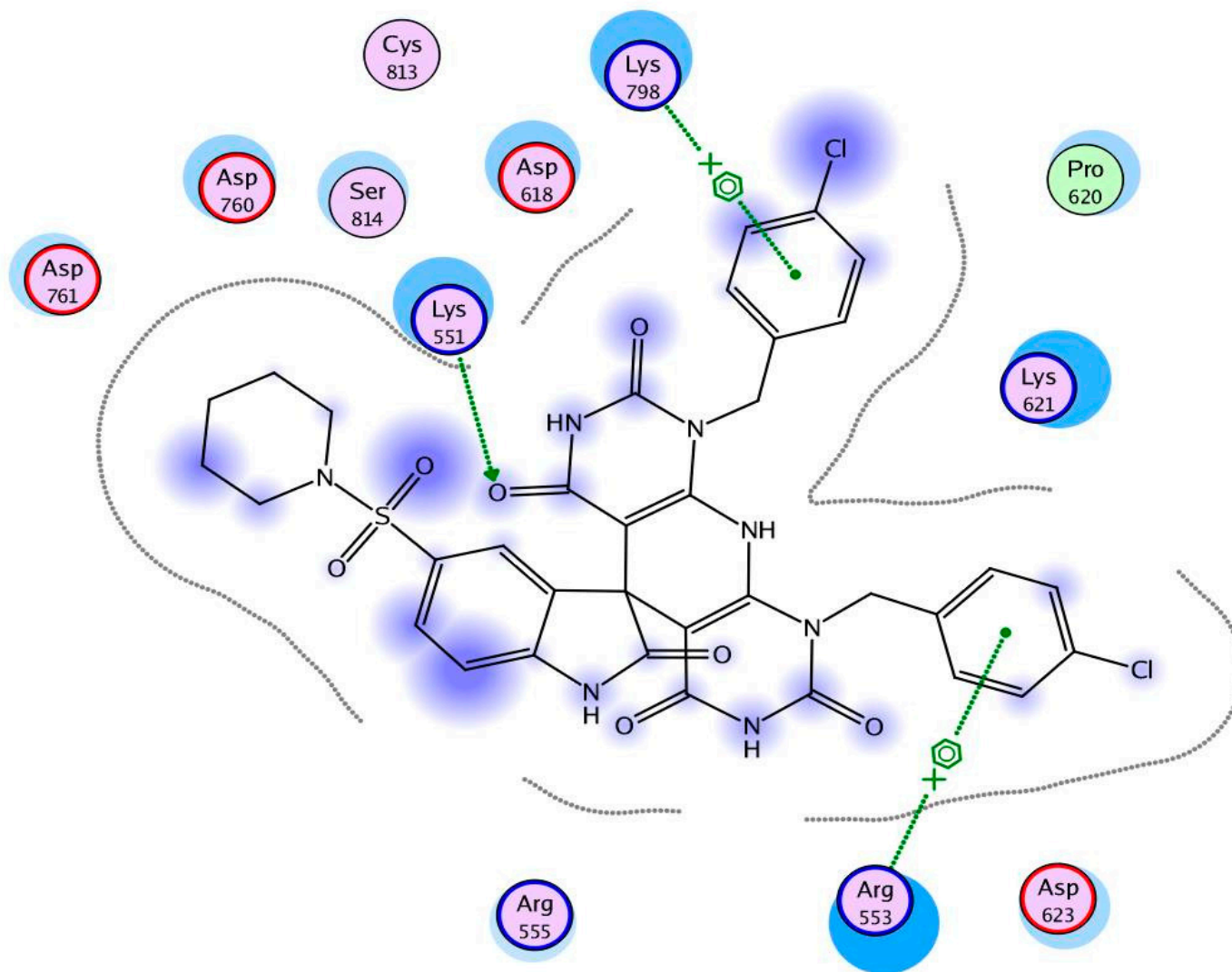
3D structure of compound **3a** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



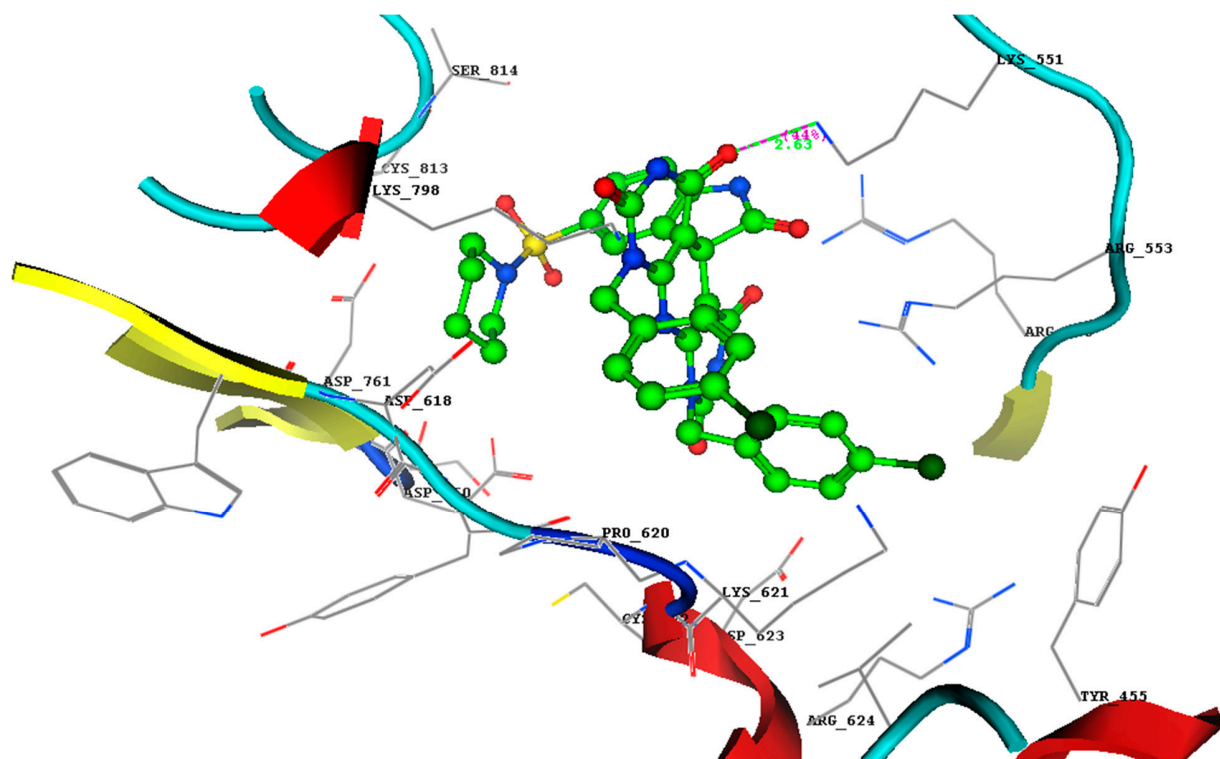
2D structure of compound **4b** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



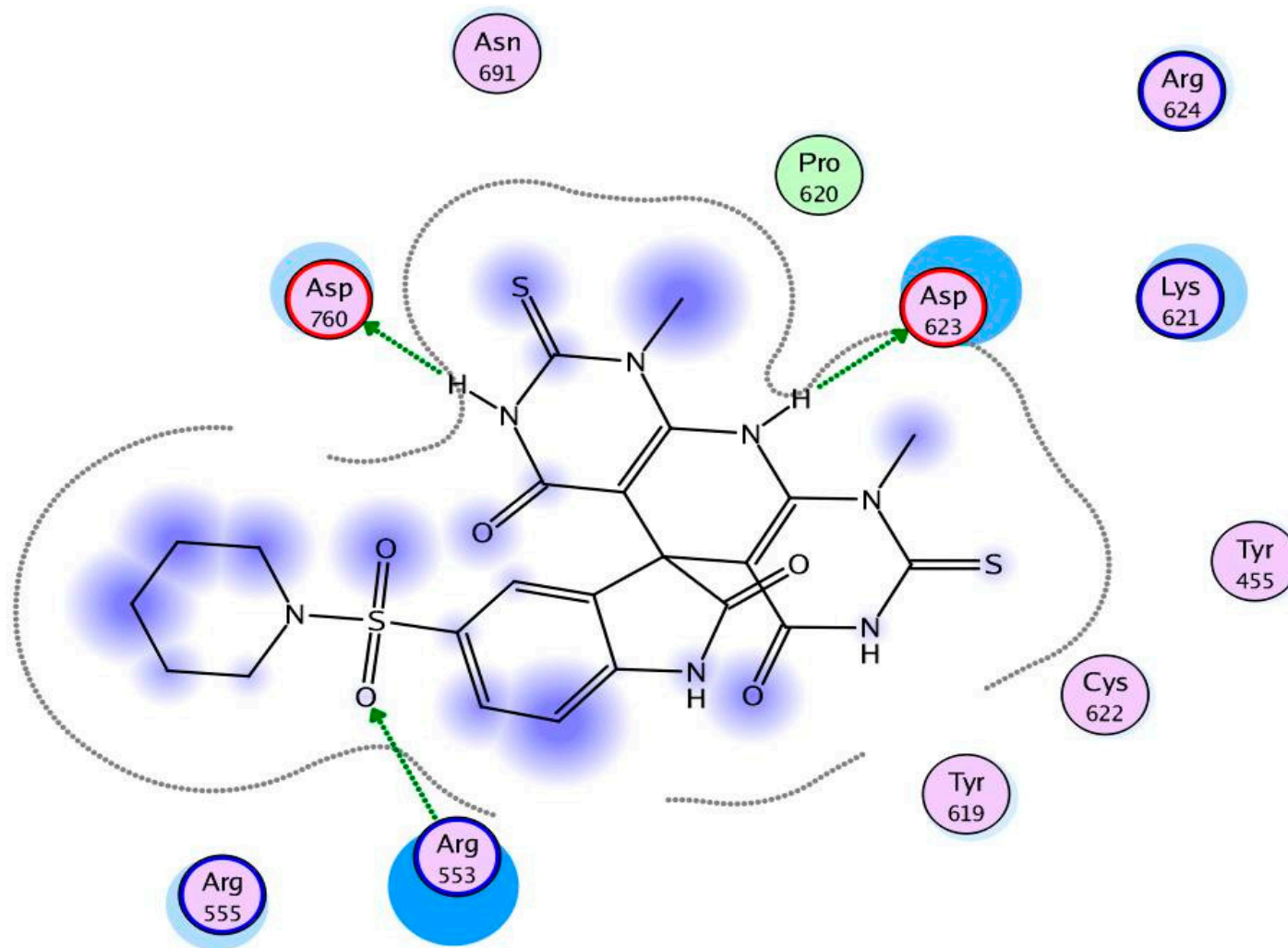
3D structure of compound **4b** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



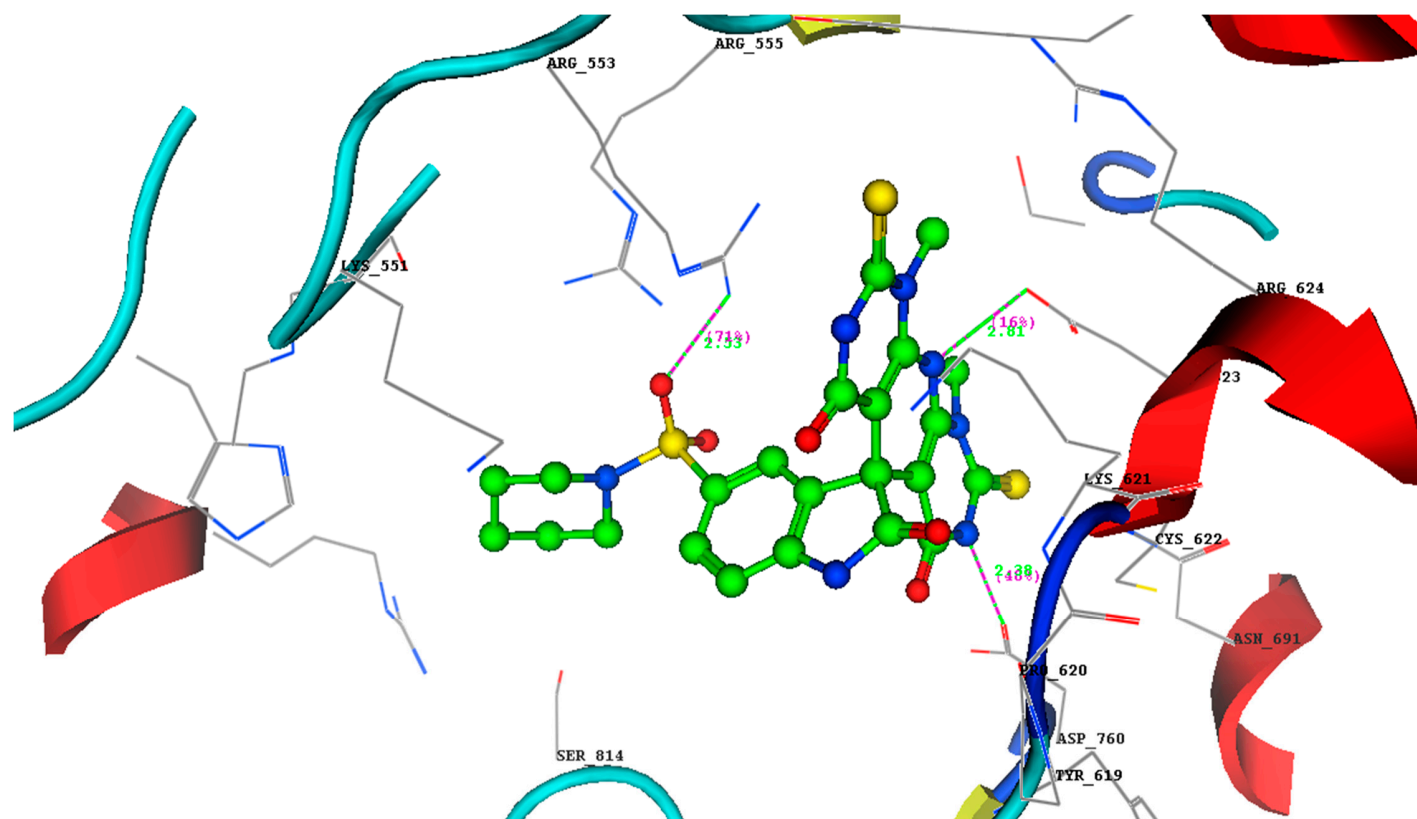
2D structure of compound **4d** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



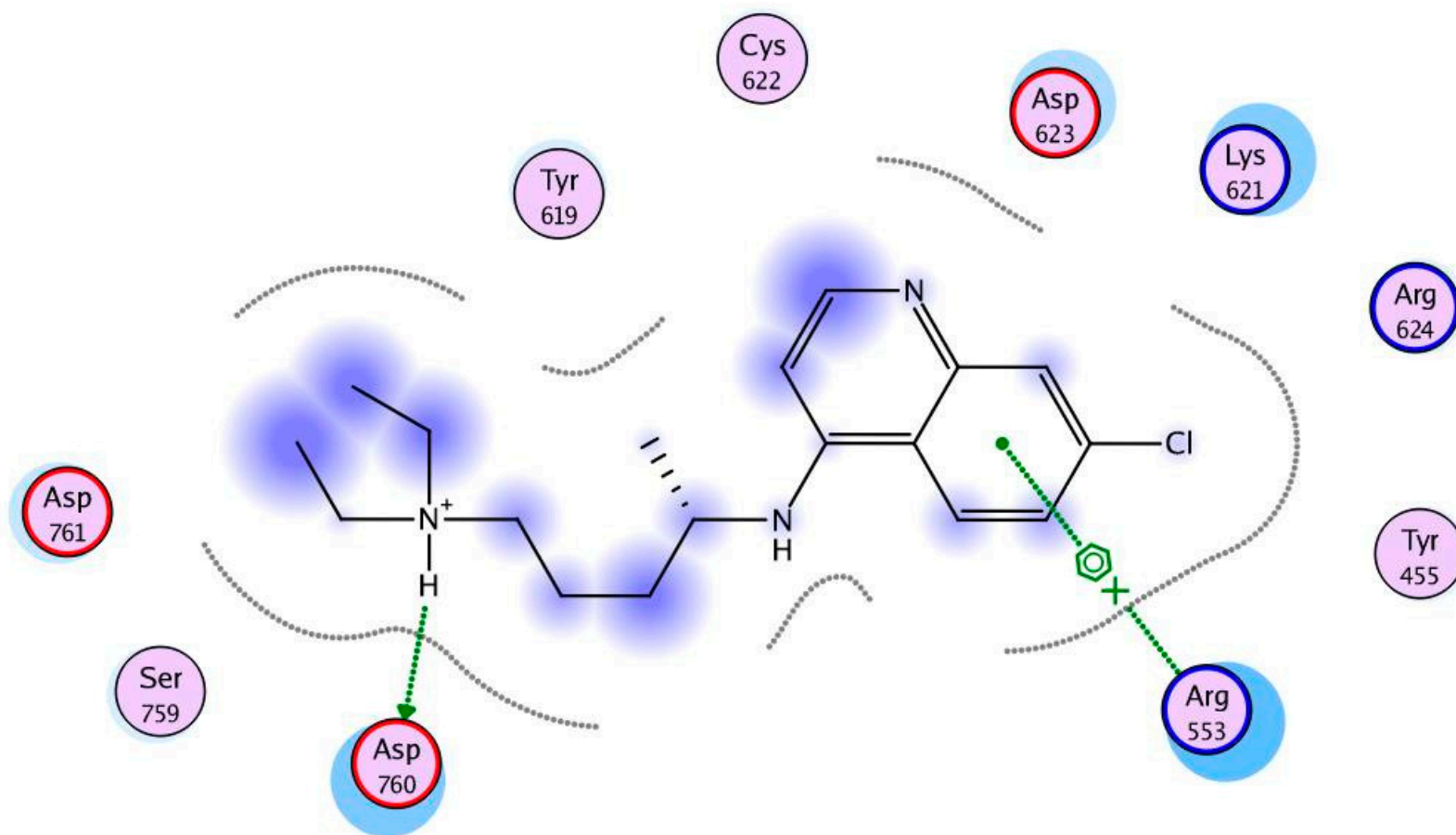
3D structure of compound **4d** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



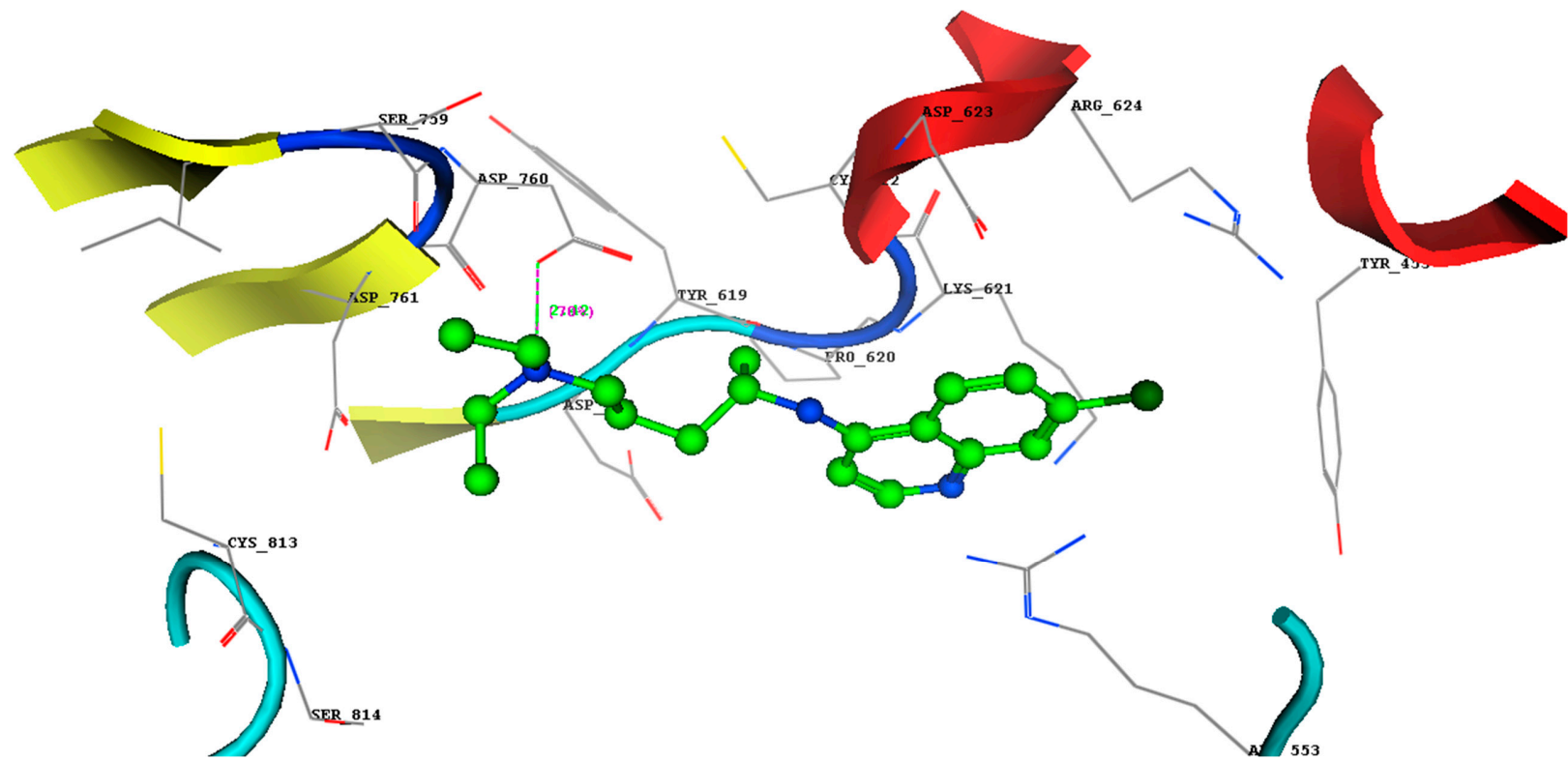
2D structure of compound **4e** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



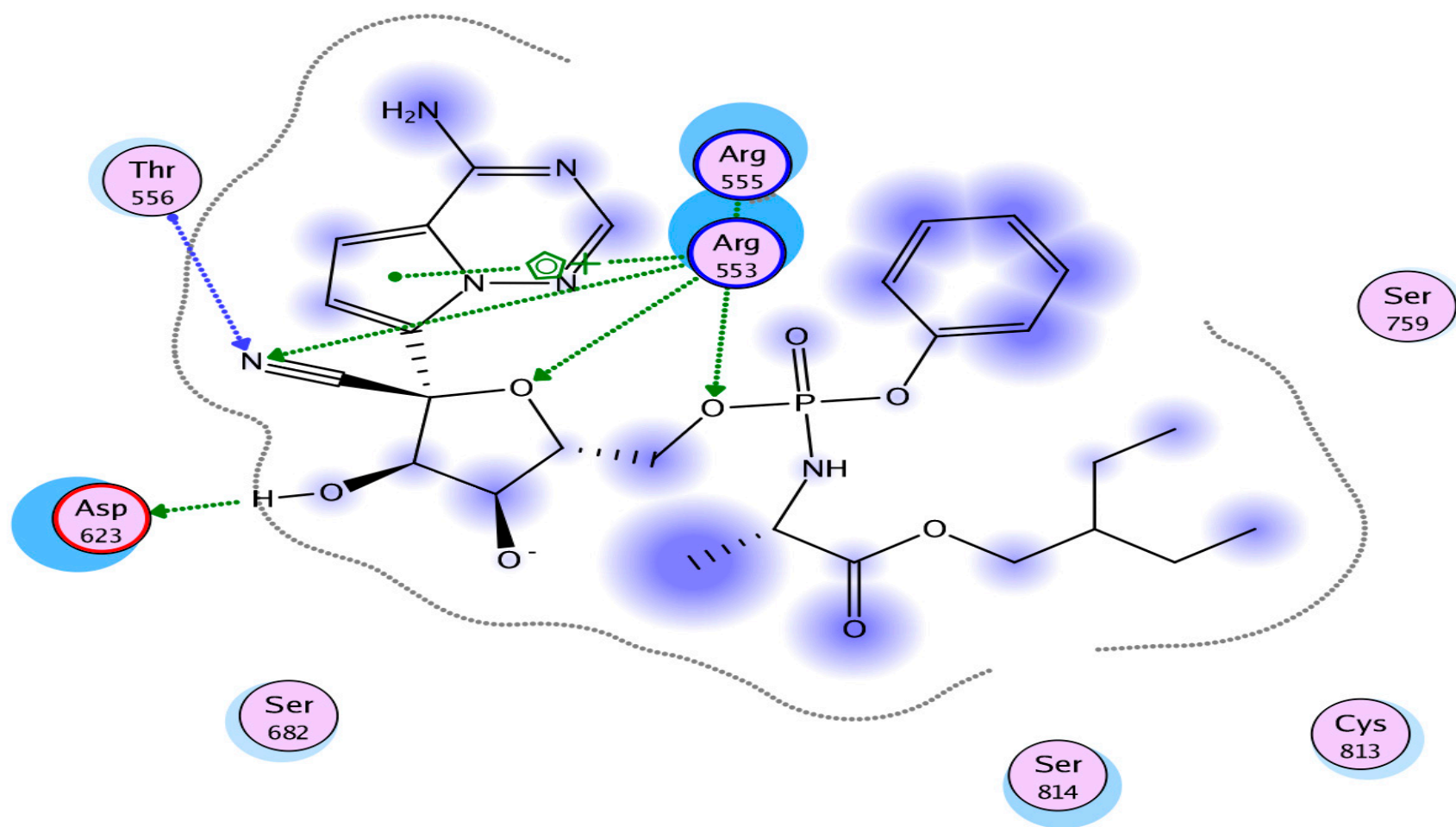
3D structure of compound **4e** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



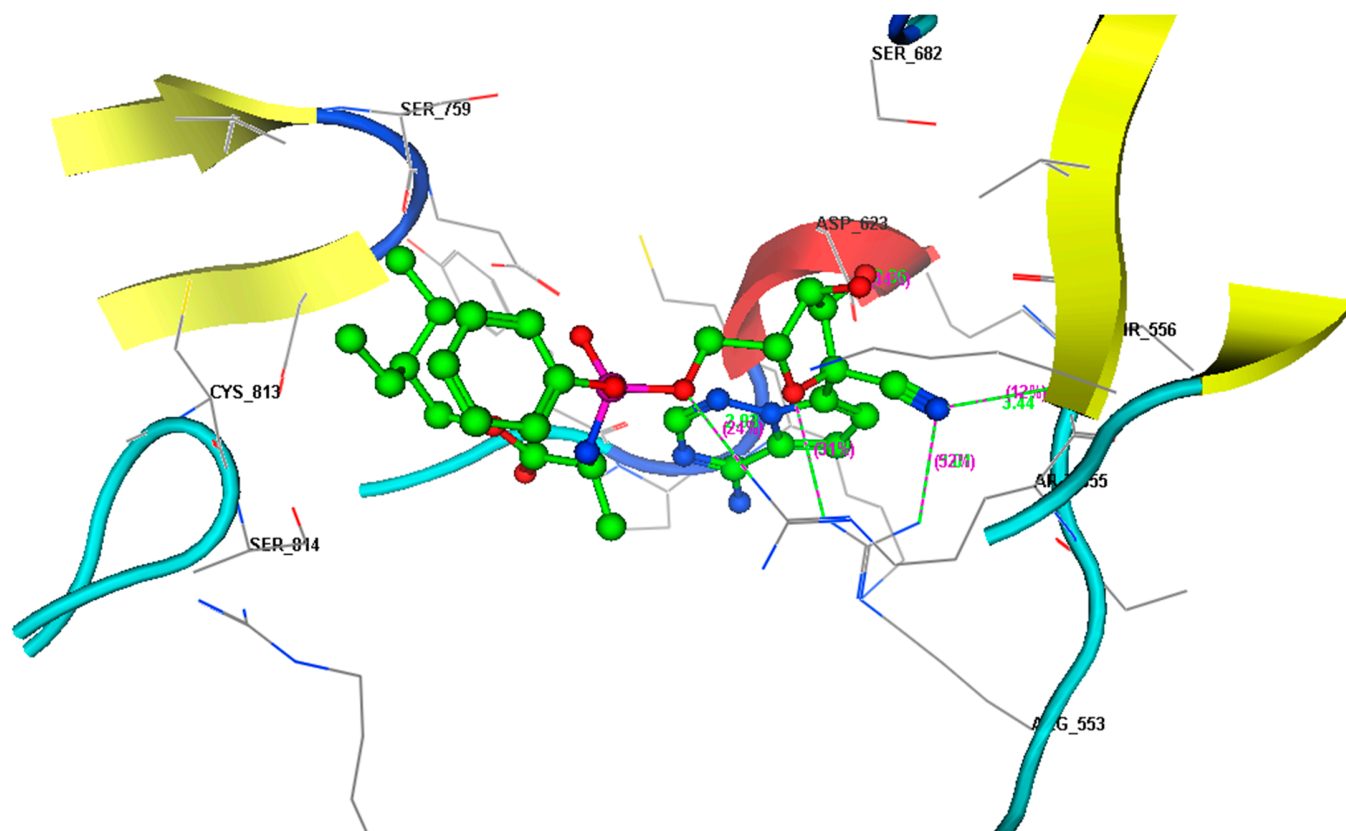
2D structure of **Chloroquine** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



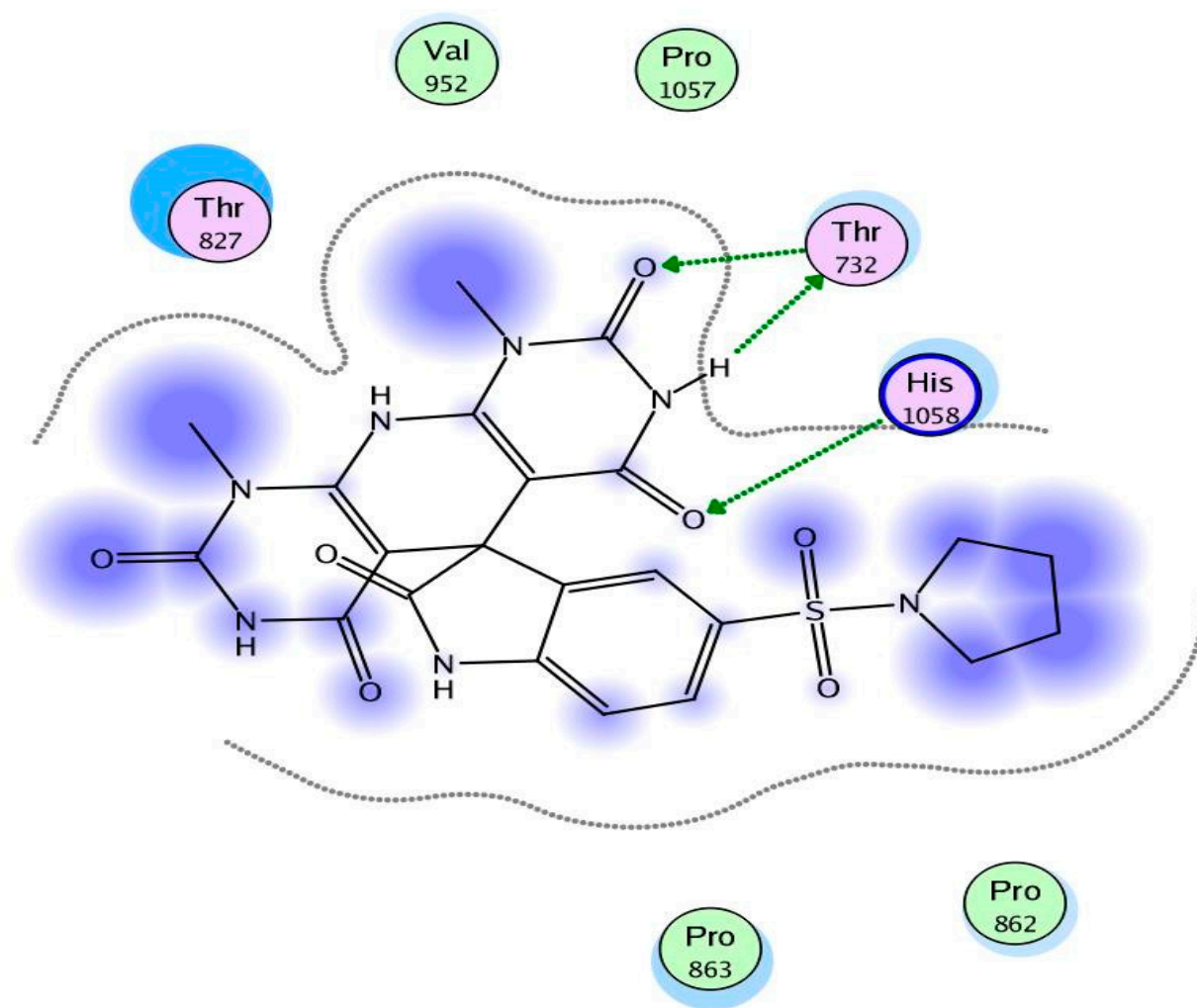
3D structure of **Chloroquine** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



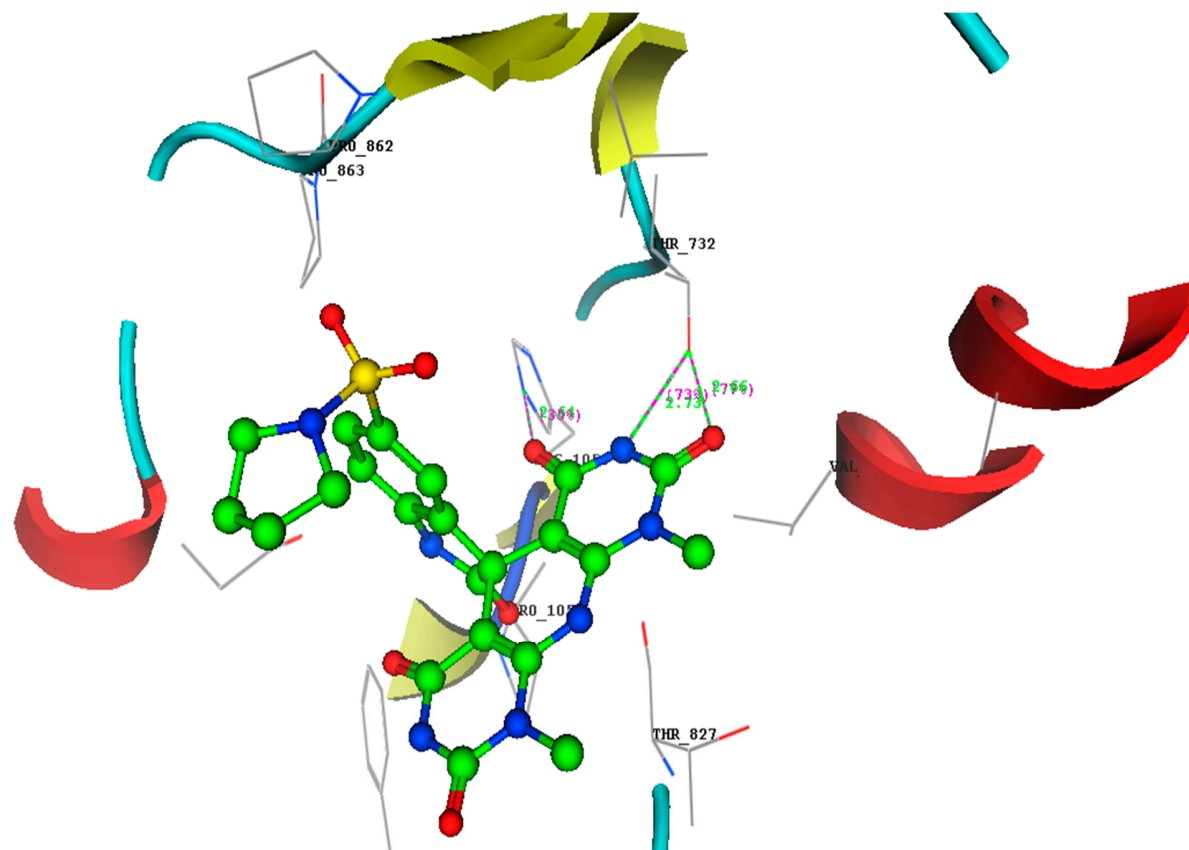
2D structure of **Remdesivir** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



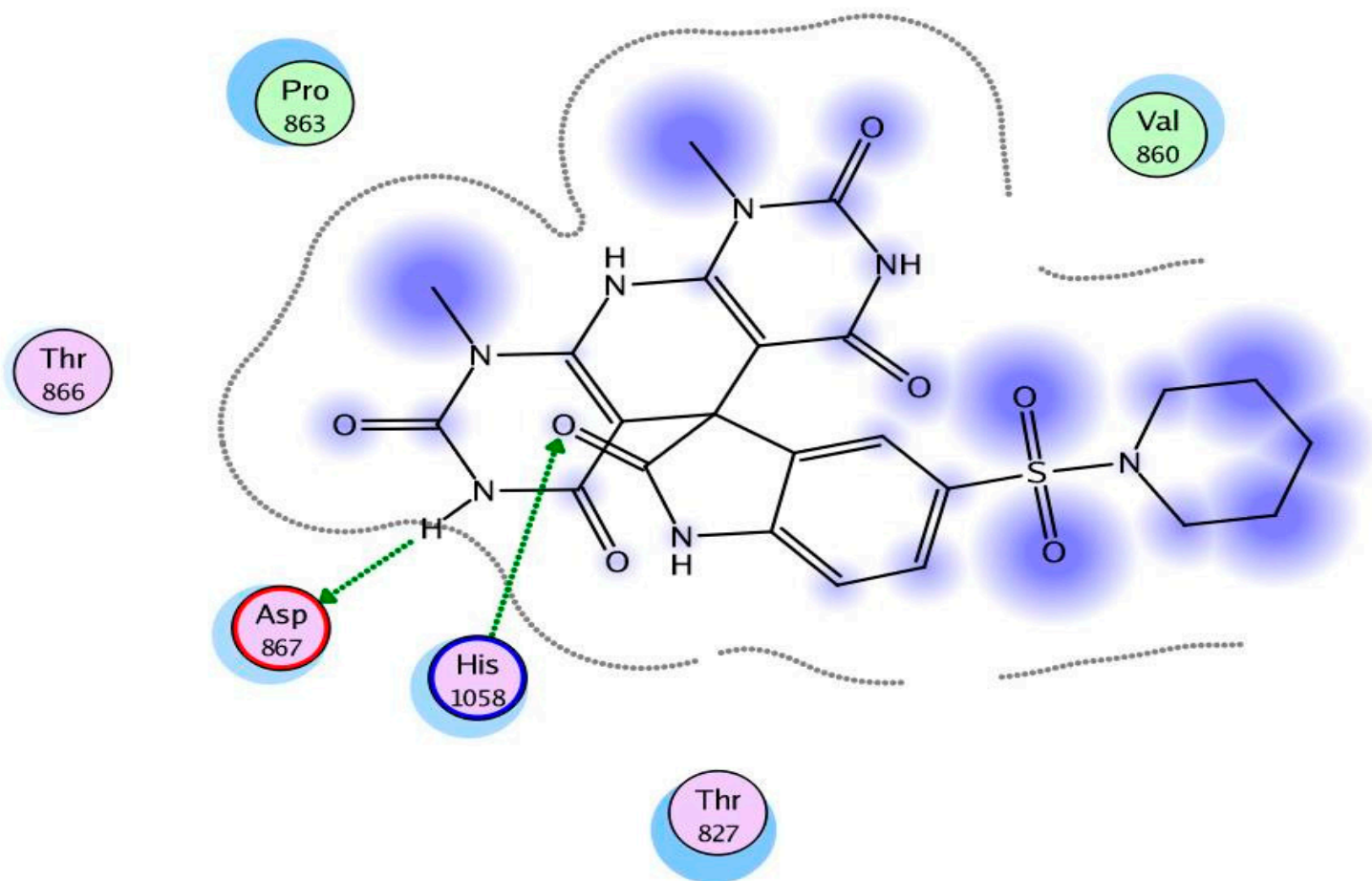
3D structure of **Remdesivir** inside the active site of RNA polymerase (RdRp) (PDB: 6m71)



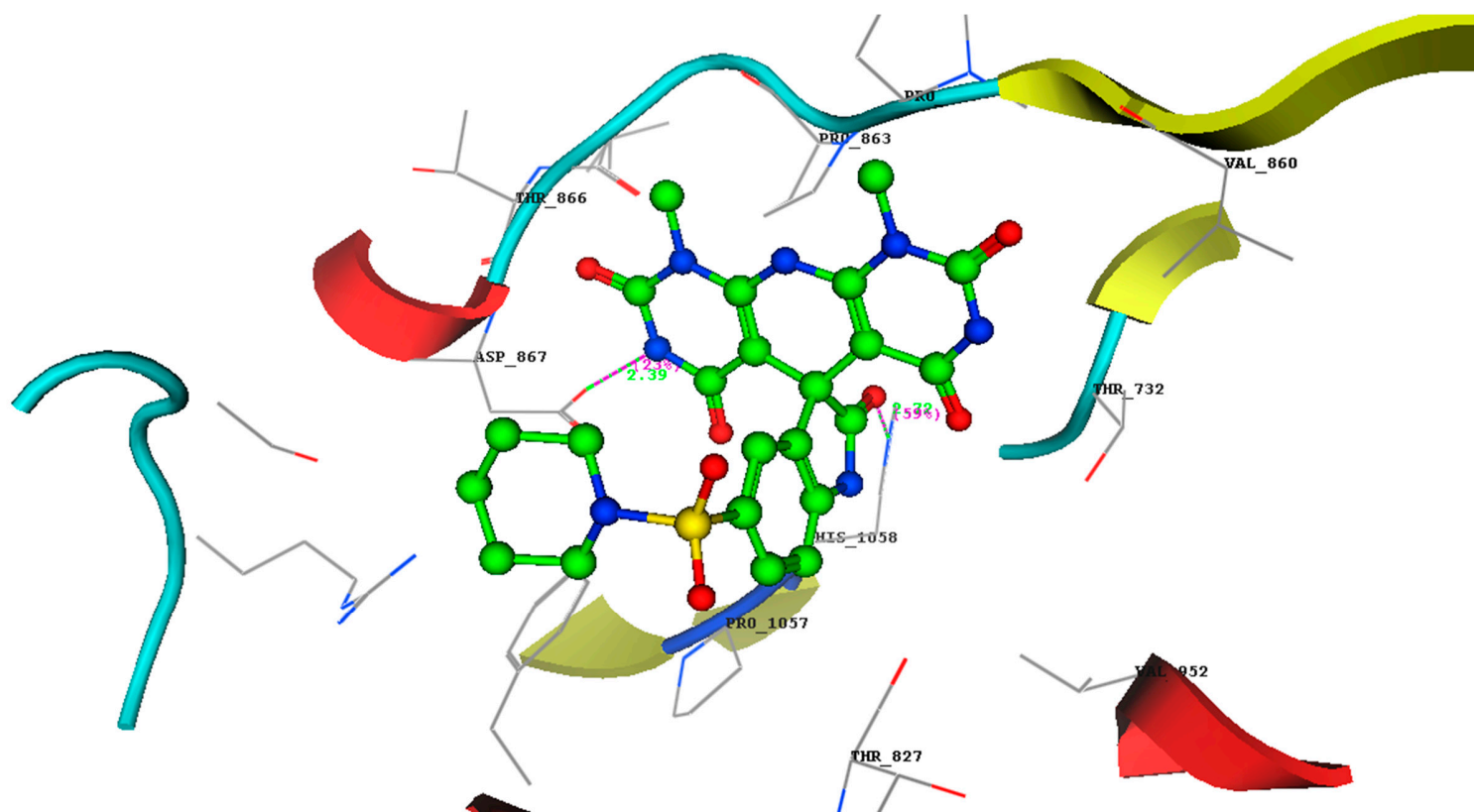
2D structure of compound **3a** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



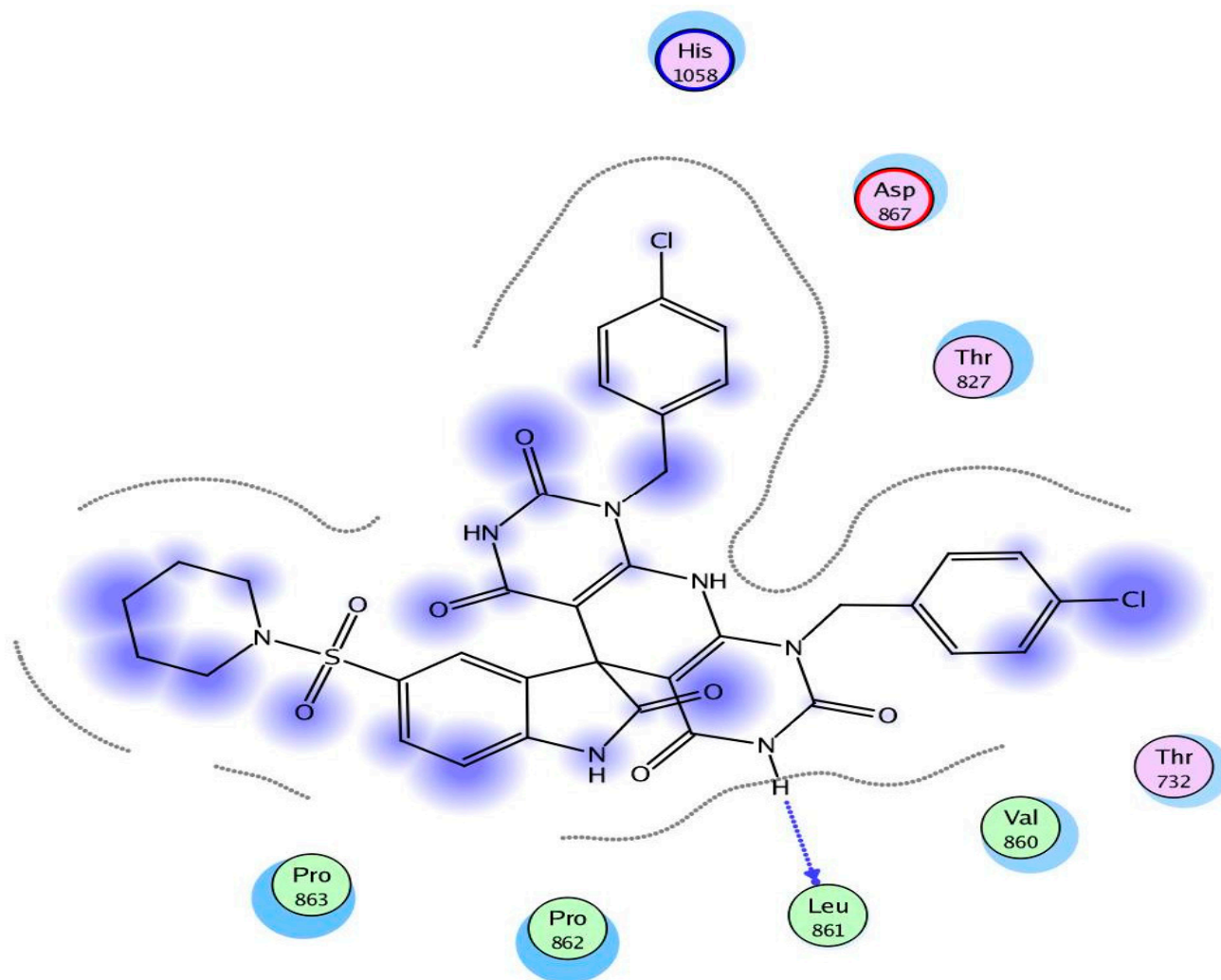
3D structure of compound **3a** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



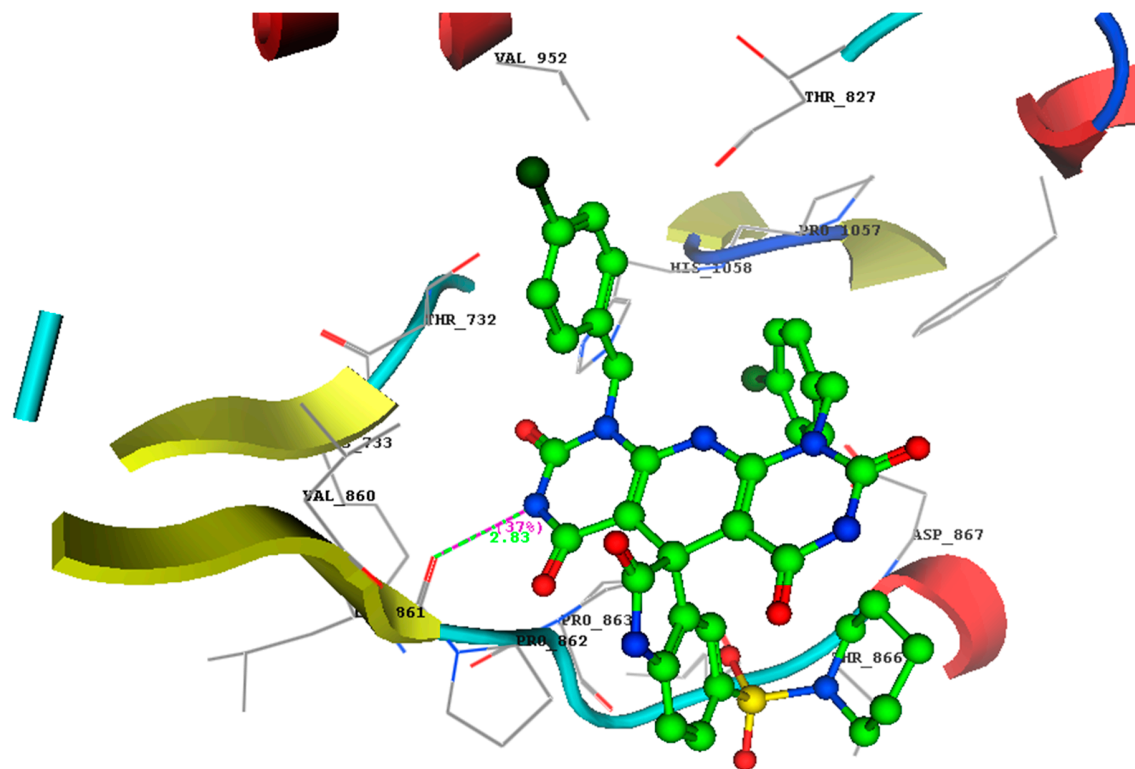
2D structure of compound **4b** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



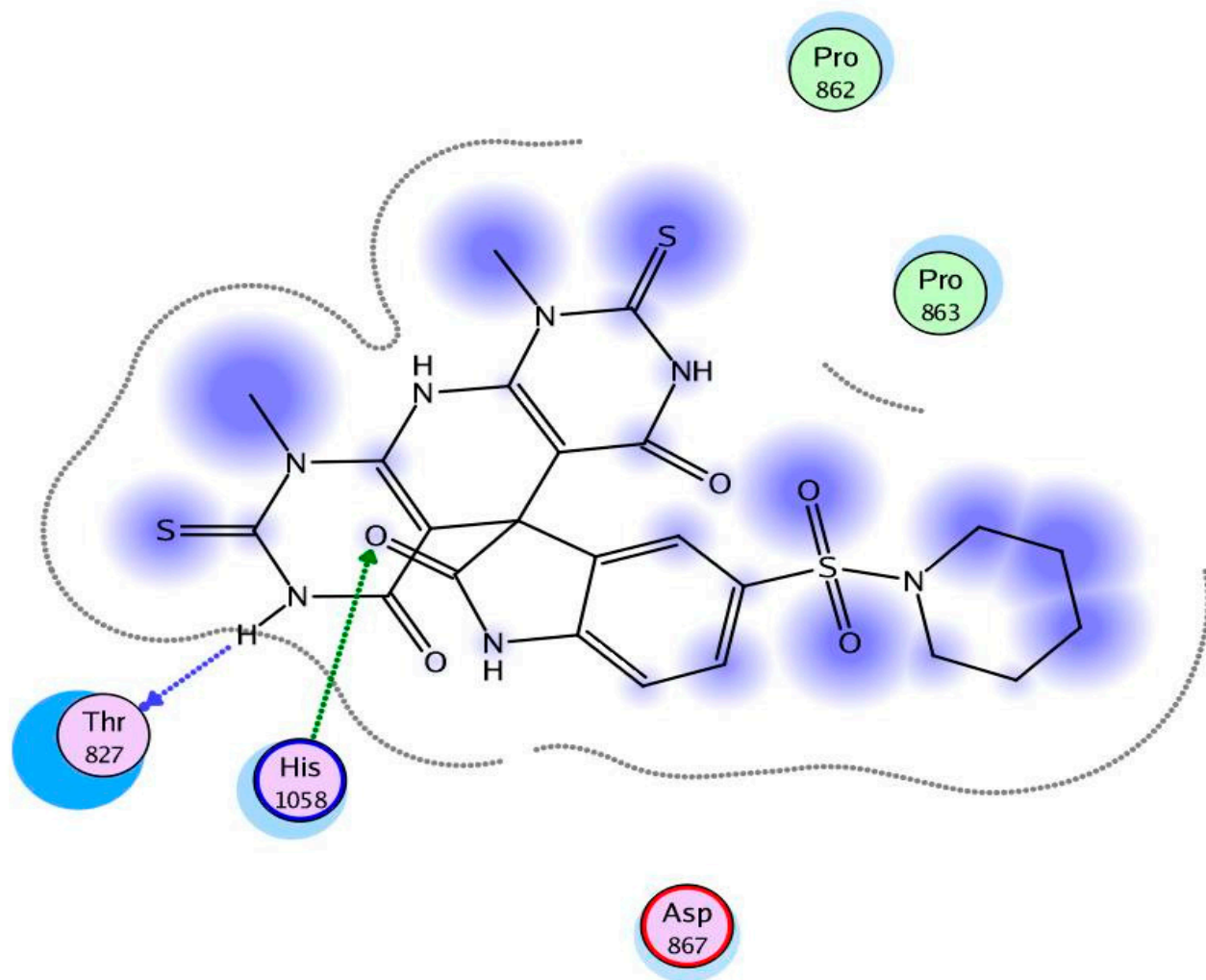
3D structure of compound **4b** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



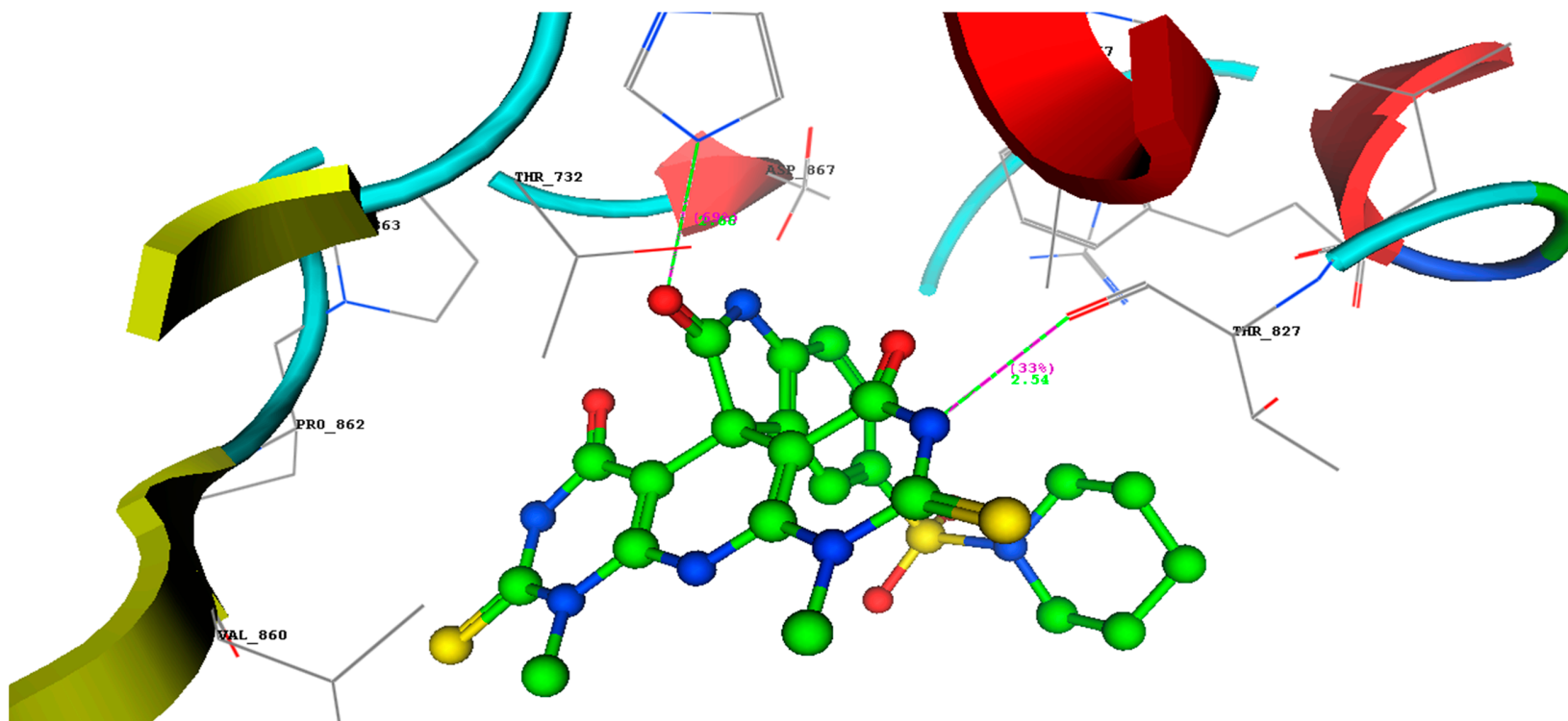
2D structure of compound **4d** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



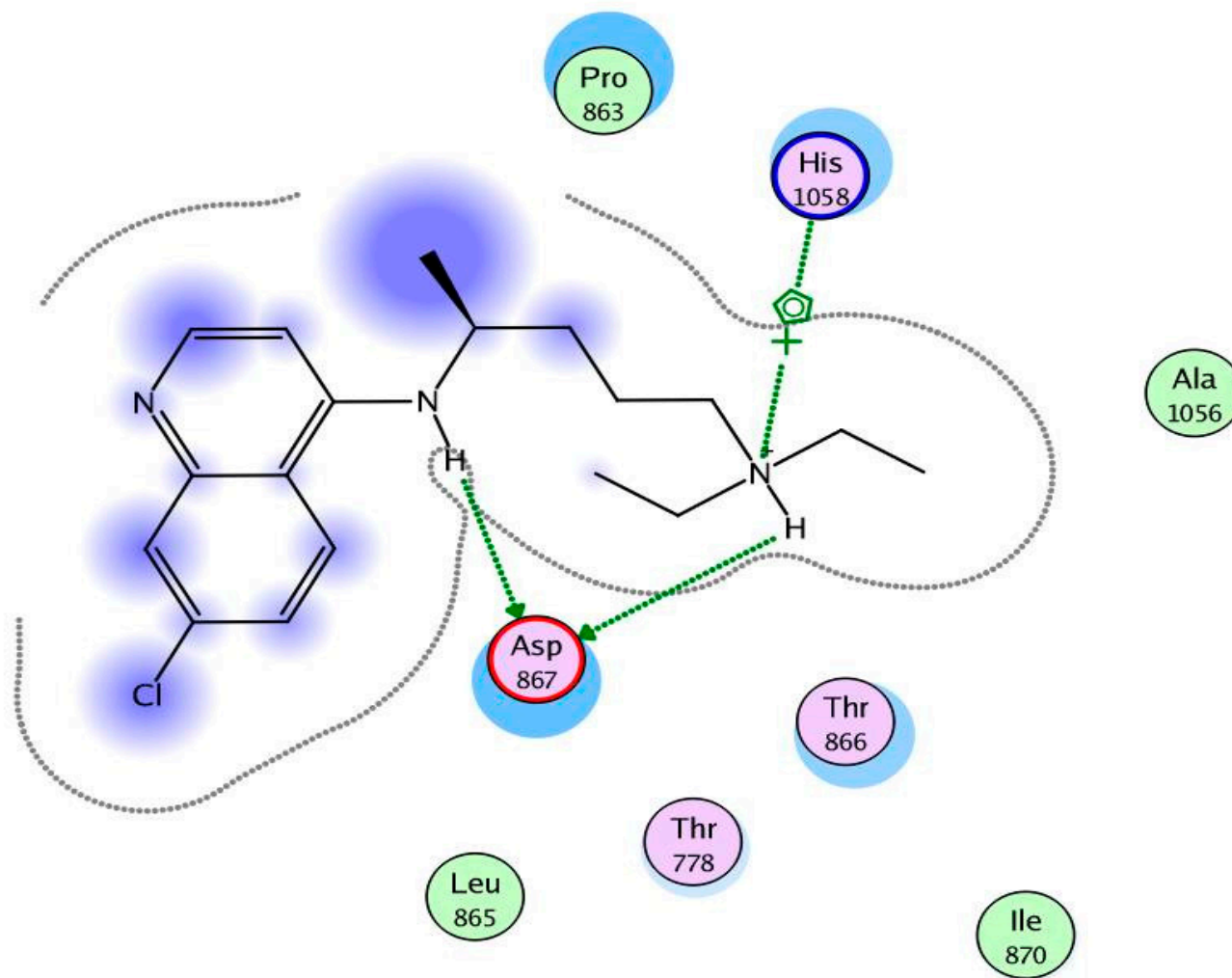
3D structure of compound **4d** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



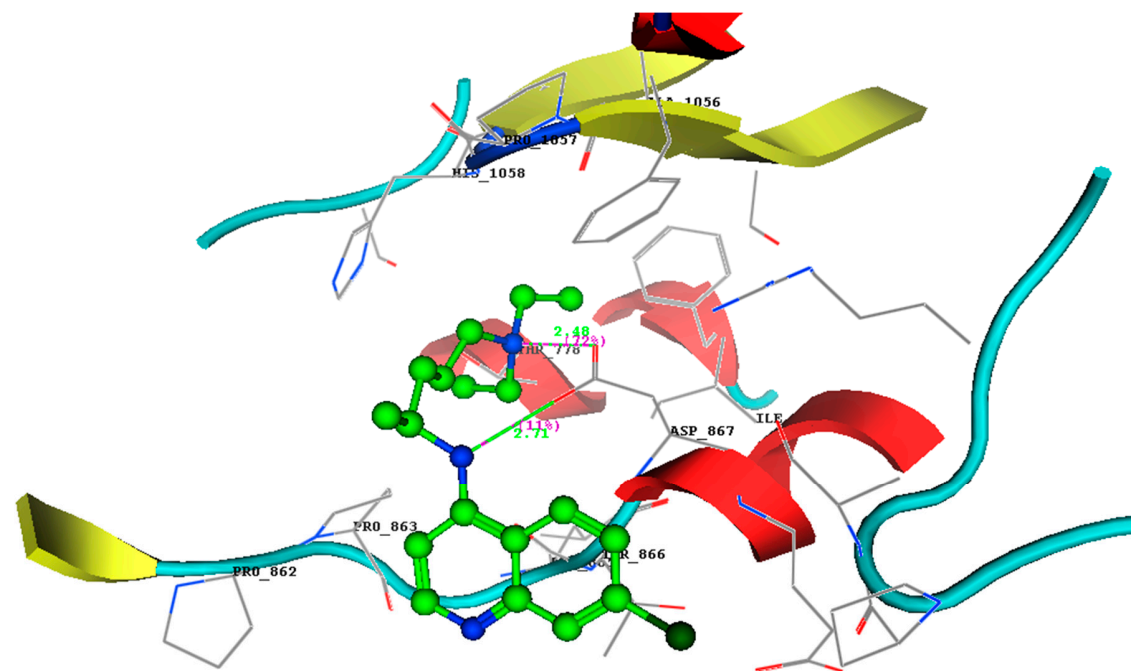
2D structure of compound **4e** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



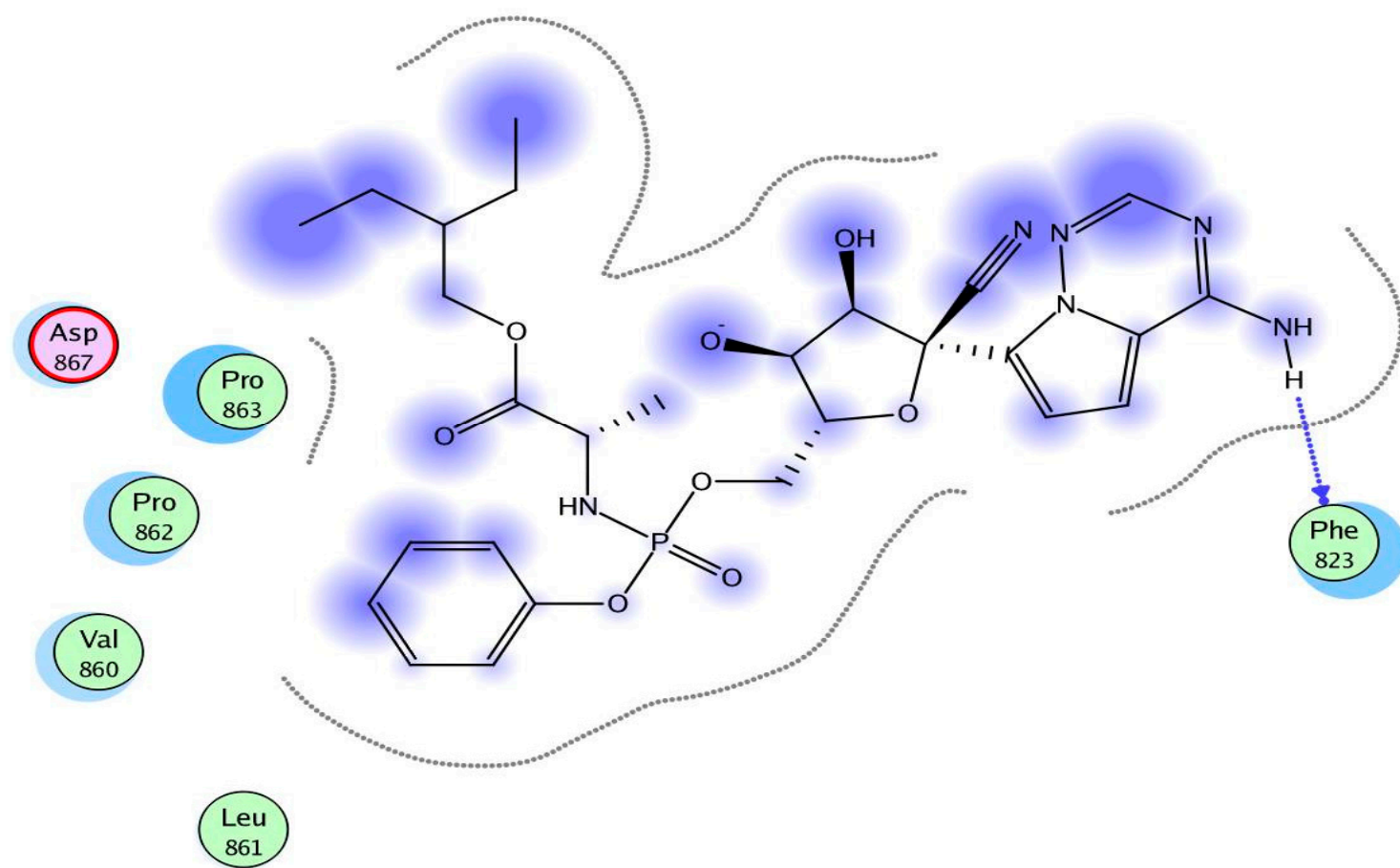
3D structure of compound **4e** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



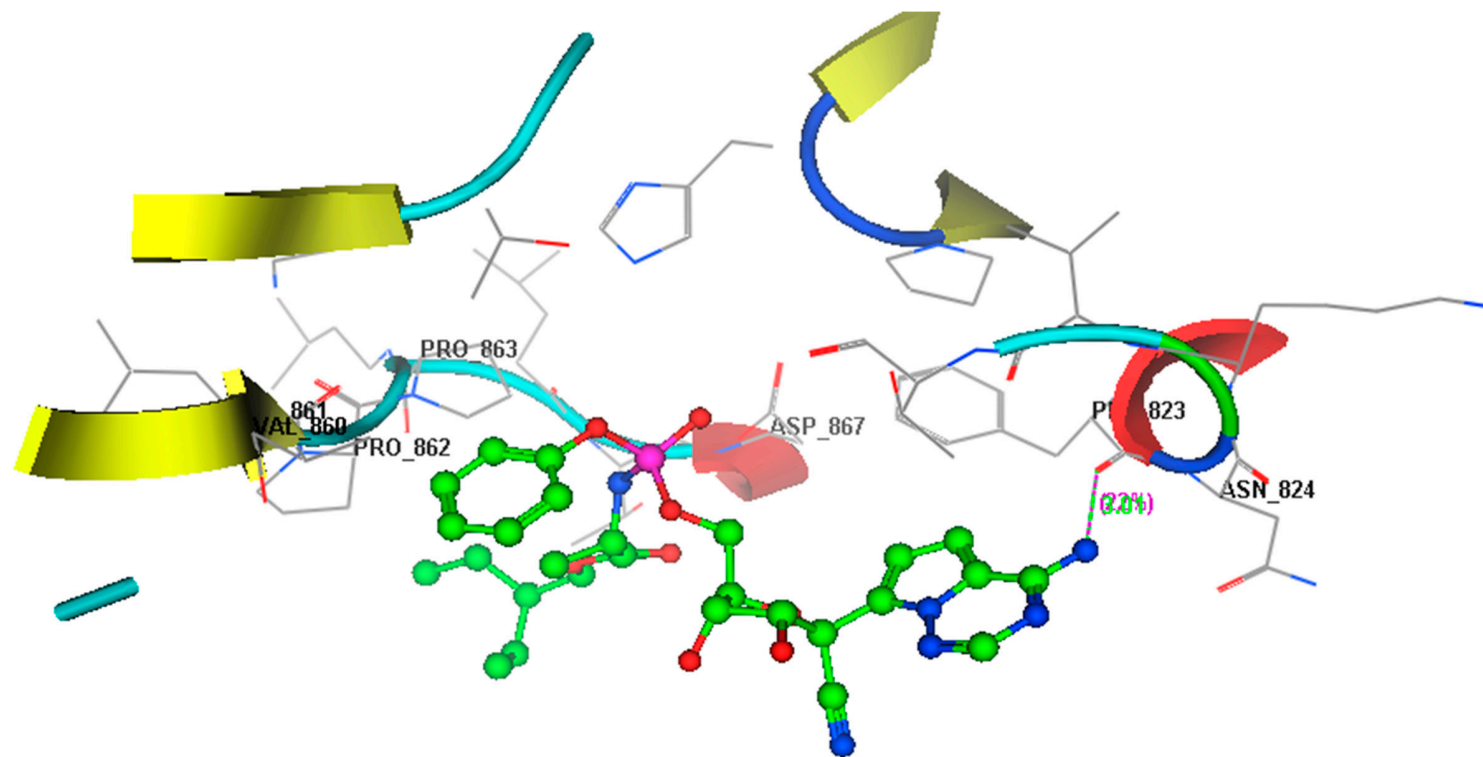
2D structure of **Chloroquine** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



3D structure of **Chloroquine** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



2D structure of **Remdesivir** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)



3D structure of **Remdesivir** inside the active site of spike glycoprotein (SGp) (PDB: 6VXX)