5-Arylideneimidazolones with Amine at Position 3 as Potential Antibiotic Adjuvants against Multidrug Resistant Bacteria

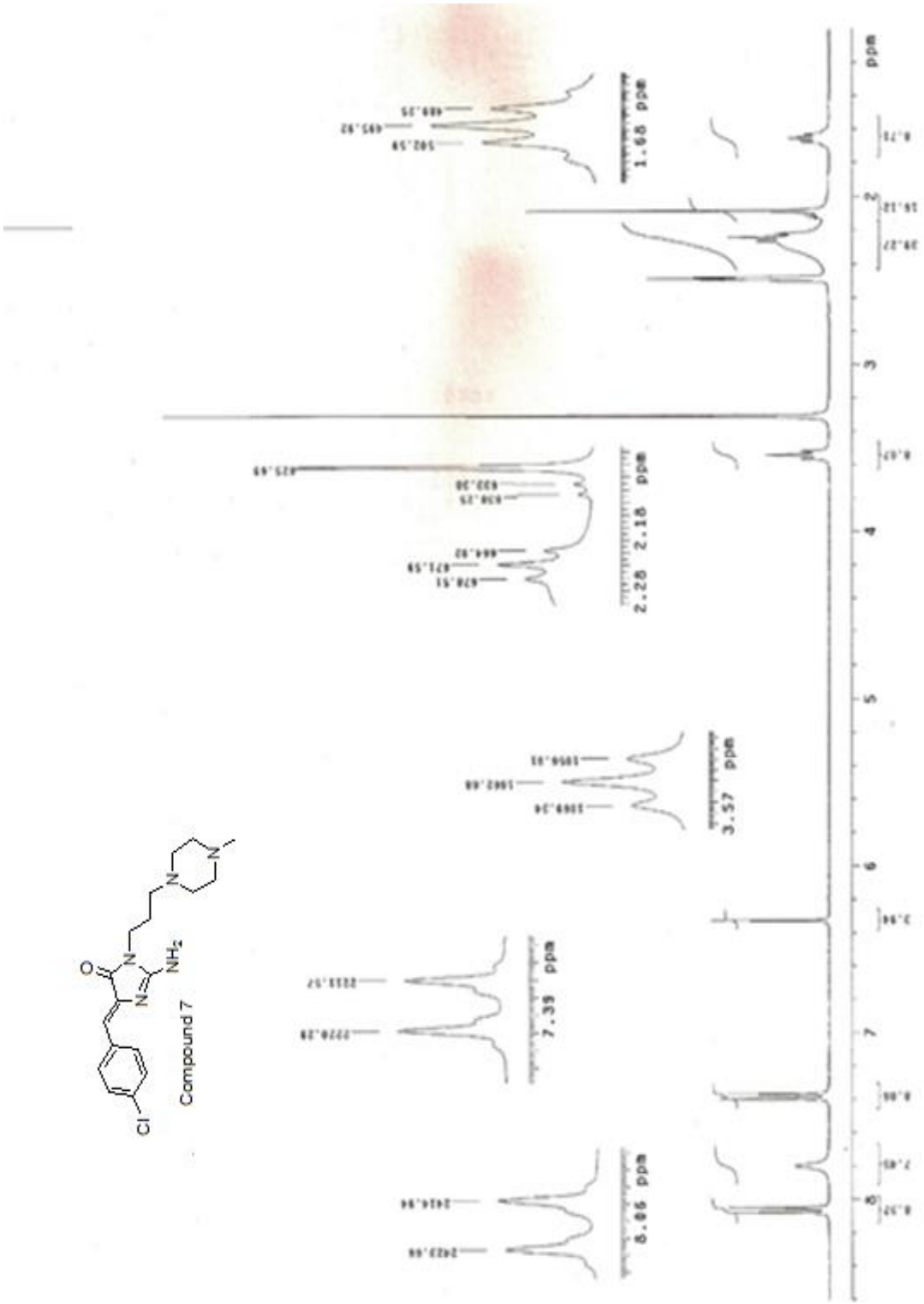
Aneta Kaczor[1], Karolina Witek[1,2,3], Sabina Podlewska[1,4], Joanna Czekajewska[2], Annamaria Lubelska[1], Gniewomir Latacz[1], Ewa Żesławska[5], Wojciech Nitek[6], Sandrine Alibert[3], Jean-Marie Pagès[3], Elżbieta Karczewska[2], Katarzyna Kieć- Kononowicz[1], Jadwiga Handzlik[1,*]

Supplementary

Spectral data for compounds

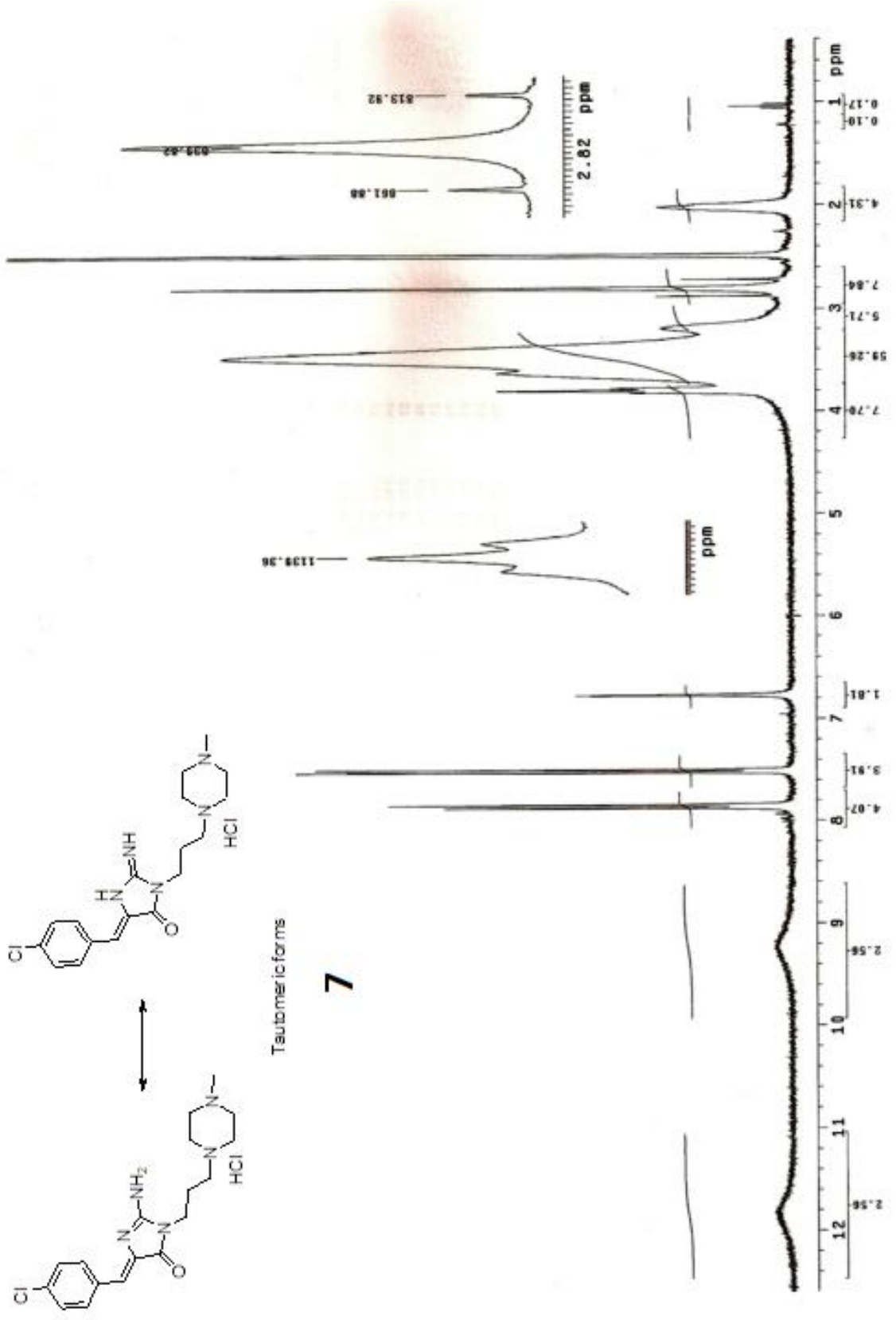
^{1}H NMRs Compounds

Compound 7 (basic form)

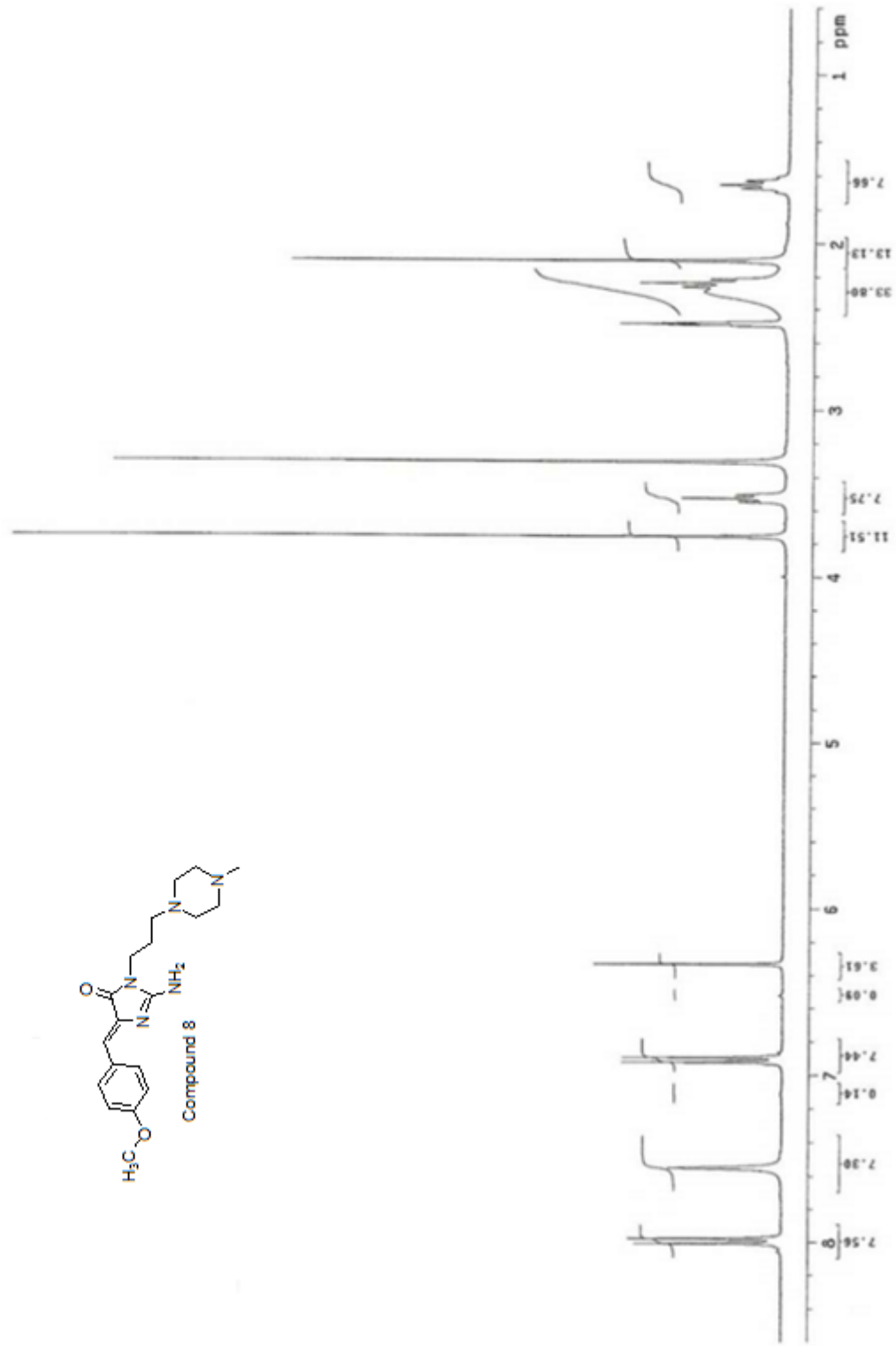


^{1}H-NMR for **7** (DMSO-d_6) δ [ppm]: 1.63 (qu, J=6.67 Hz, 2H, CH_2-$\underline{CH_2}$-CH_2), 2.09 (s, 3H, CH_3), 2.22-2.26 (t def., 10H, Pp, Pp-CH_2), 3.52 (t, J=6.67 Hz, 2H, N3-CH_2), 6.32(s, 1H, CH=C), 7.36 (d, J=8.72Hz, 2H, Ar-3,5-H), 7.80 (br. s, 2H, NH_2), 8.05 (d, J=8.72 Hz, 2H, Ar-2,6-H).

Compound 7 (HCl form)

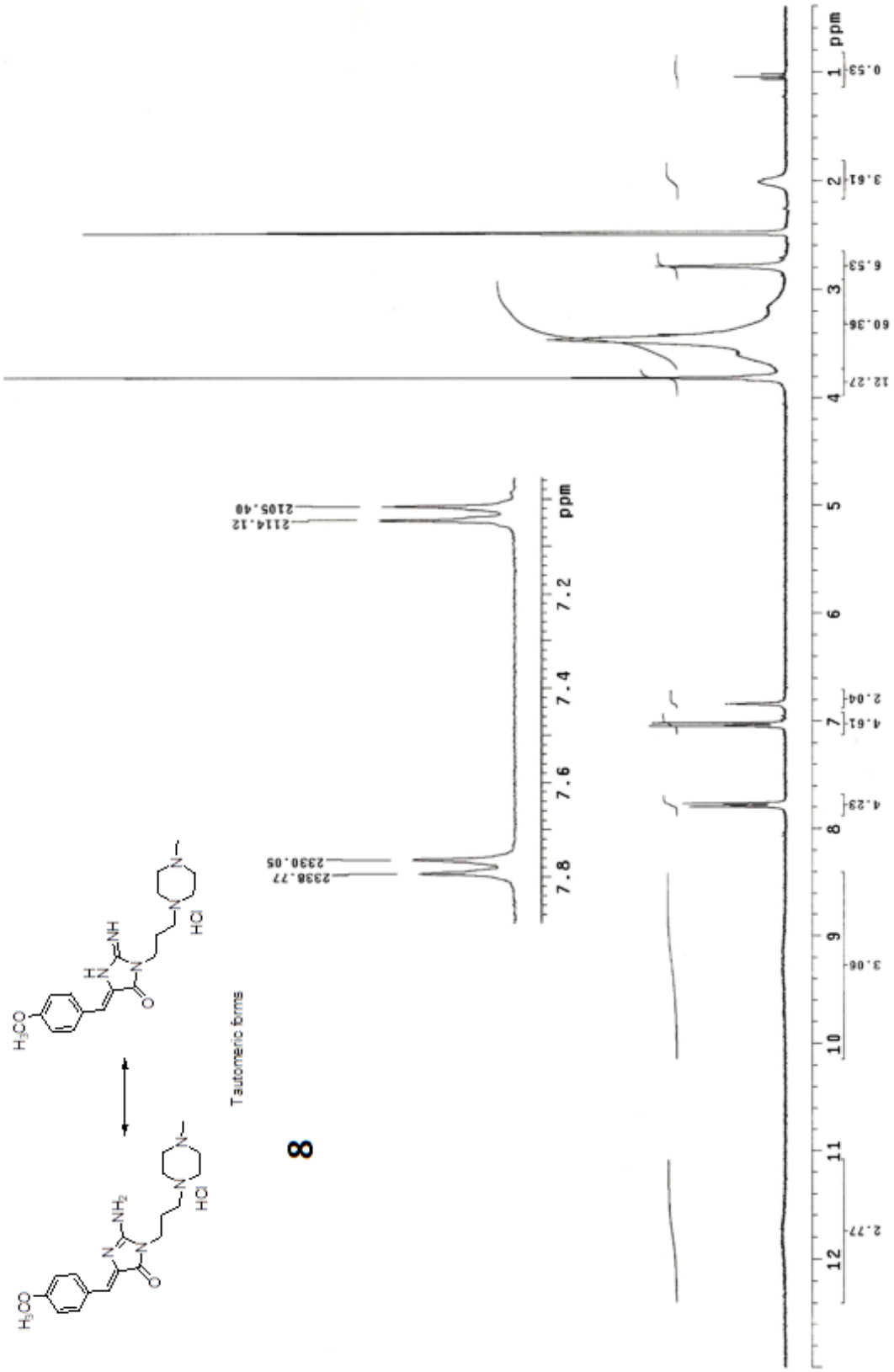


Compound 8 (basic form)

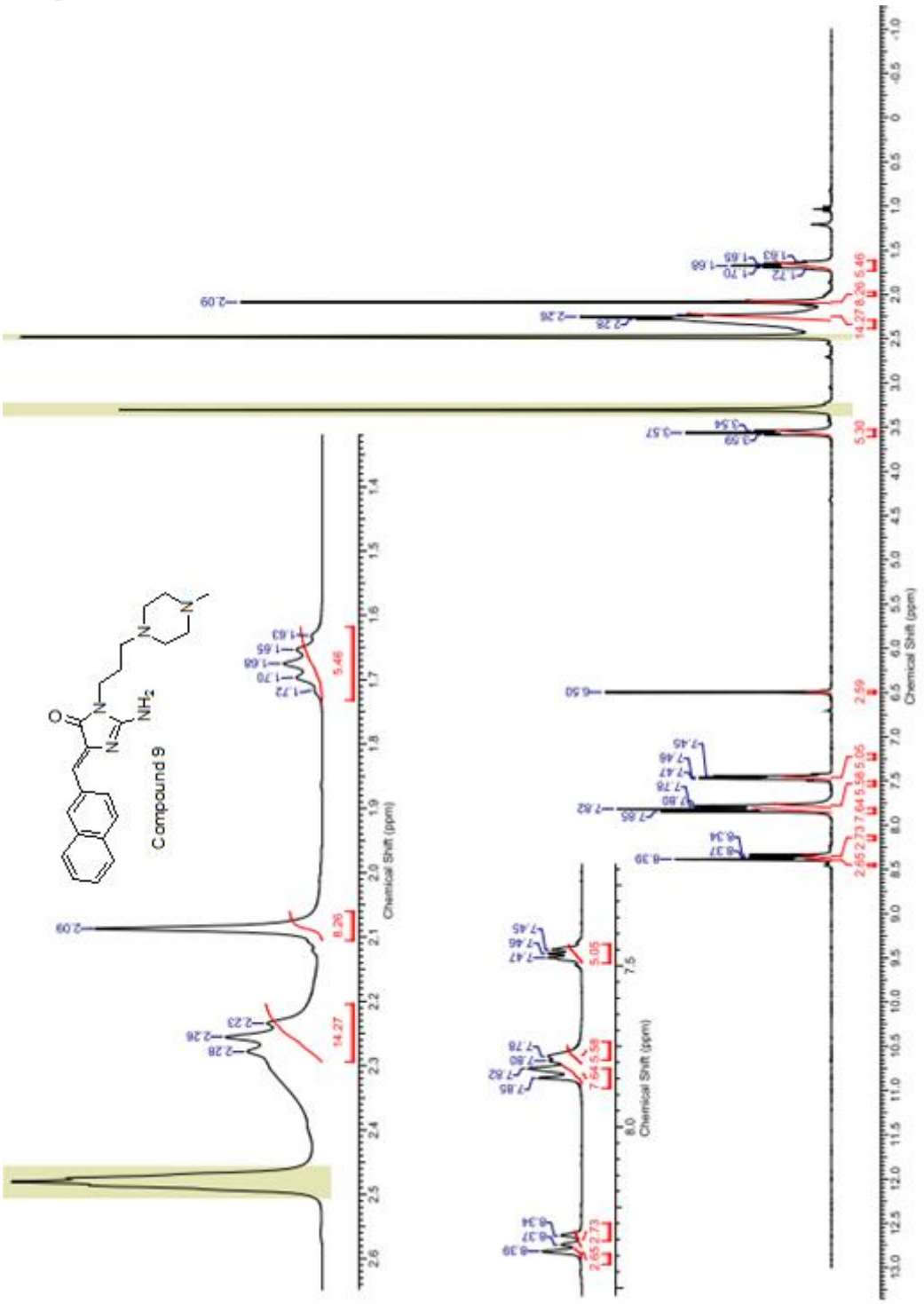


^{1}H-NMR for **8** (DMSO-d_6) δ [ppm]: 1.63 (t, J=6.67 Hz, 2H, CH_2-$\underline{CH_2}$-CH_2), 2.10 (s, 3H, N-CH_3), 2.21-2.40 (m, 8H, Pp, Pp-CH_2), 3.50 (t, J=6.70 Hz, 2H, N3-CH_2), 3.76 (s, 3H, OCH_3), 6.33 (s, 1H, CH=C), 6.89 (d, J=8.98, 2H, Ar-3,5-H), 7.55 (s, 2H, NH_2), 7.98 (d, J=8.72 Hz, 2H, Ar-2,6-H).

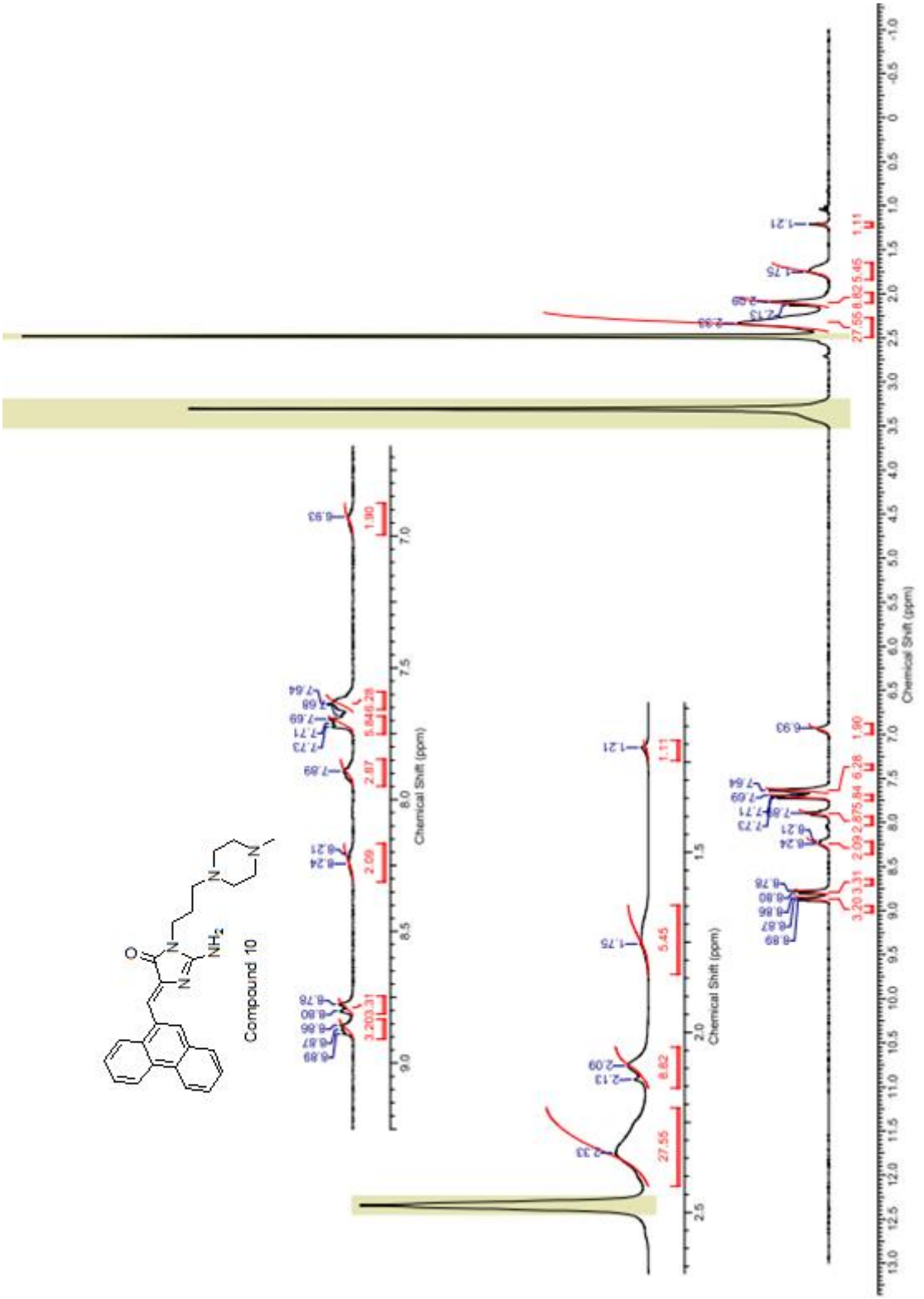
Compound 8 (HCl form)



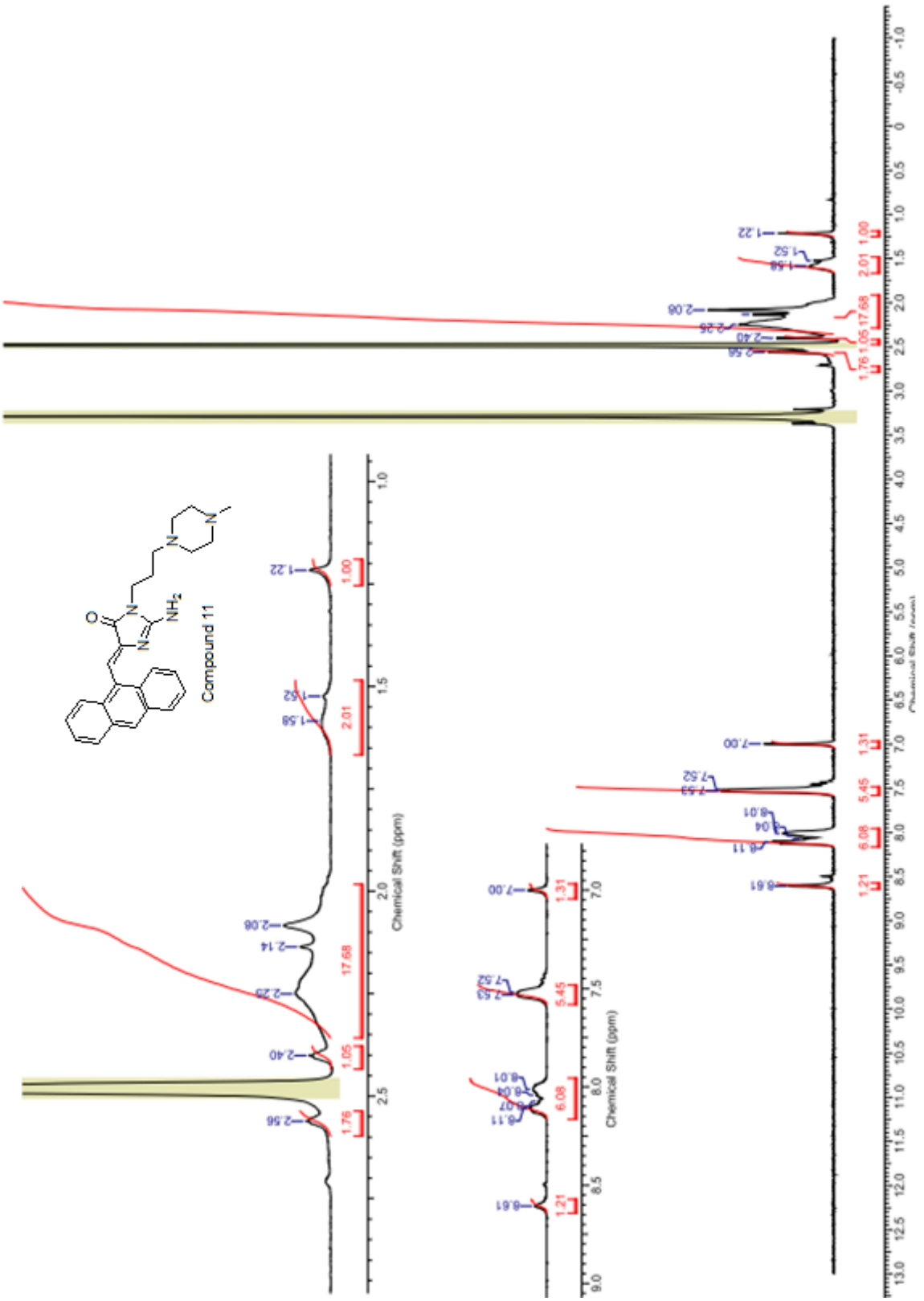
Compound 9



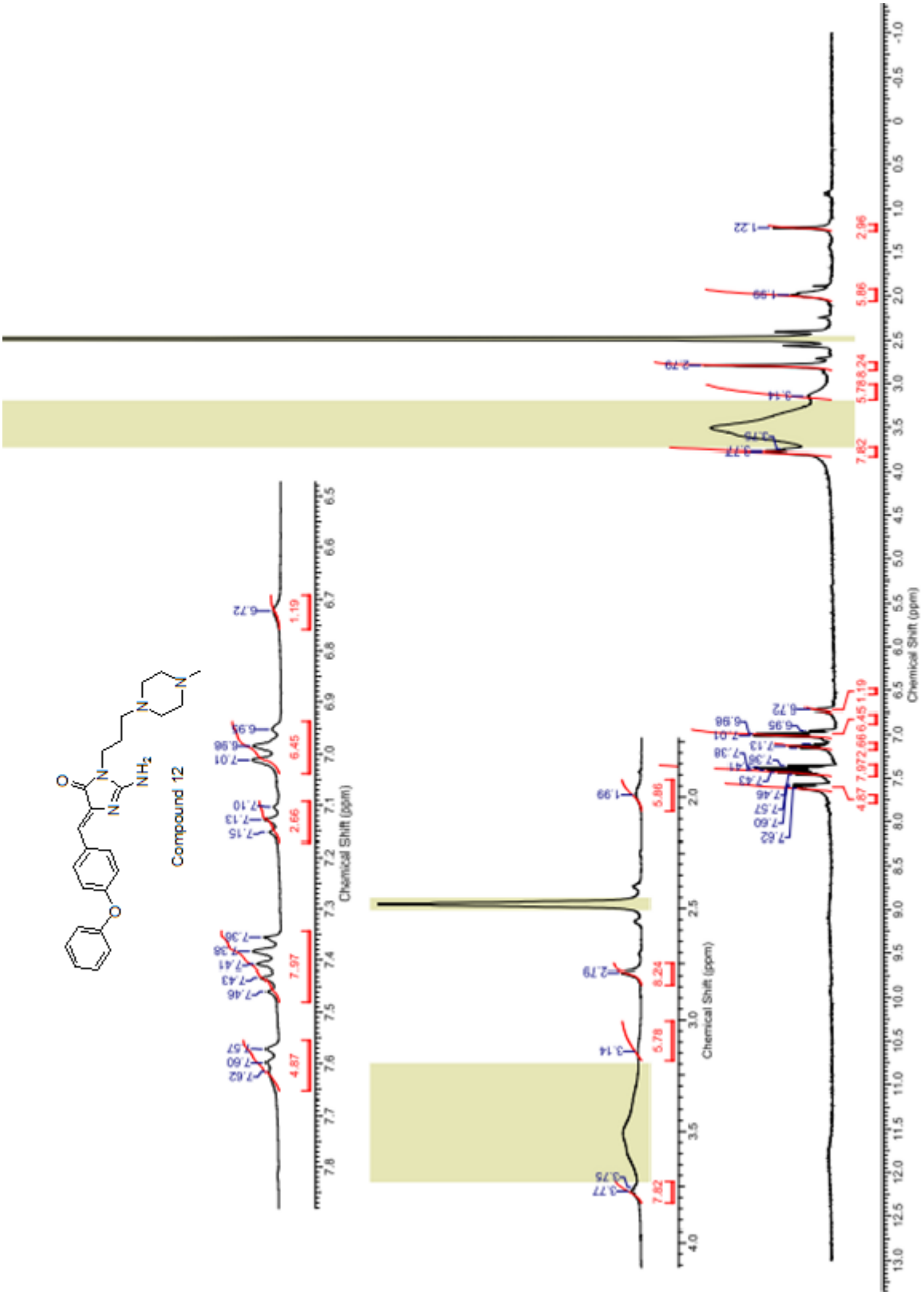
Compound 10



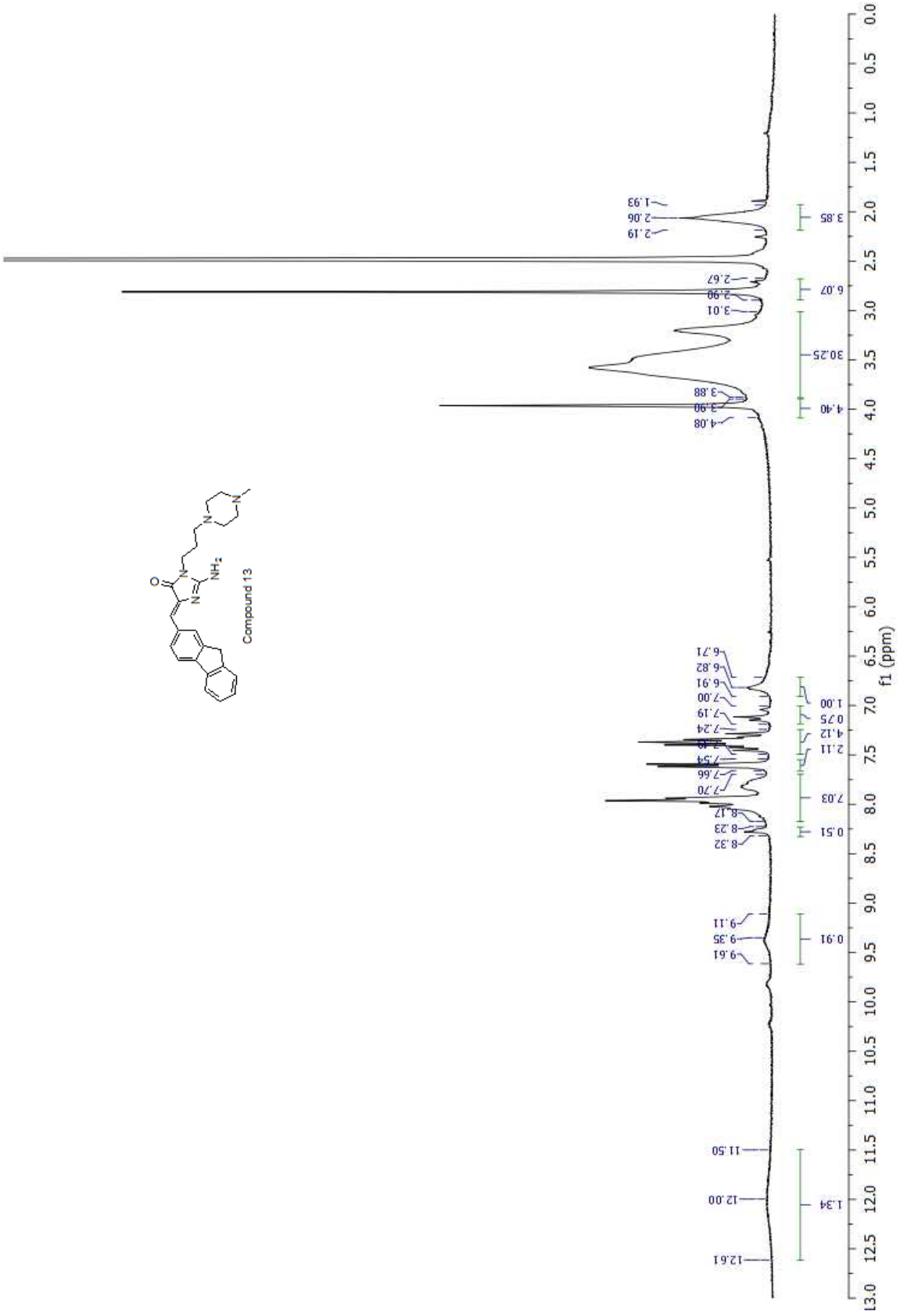
Compound 11



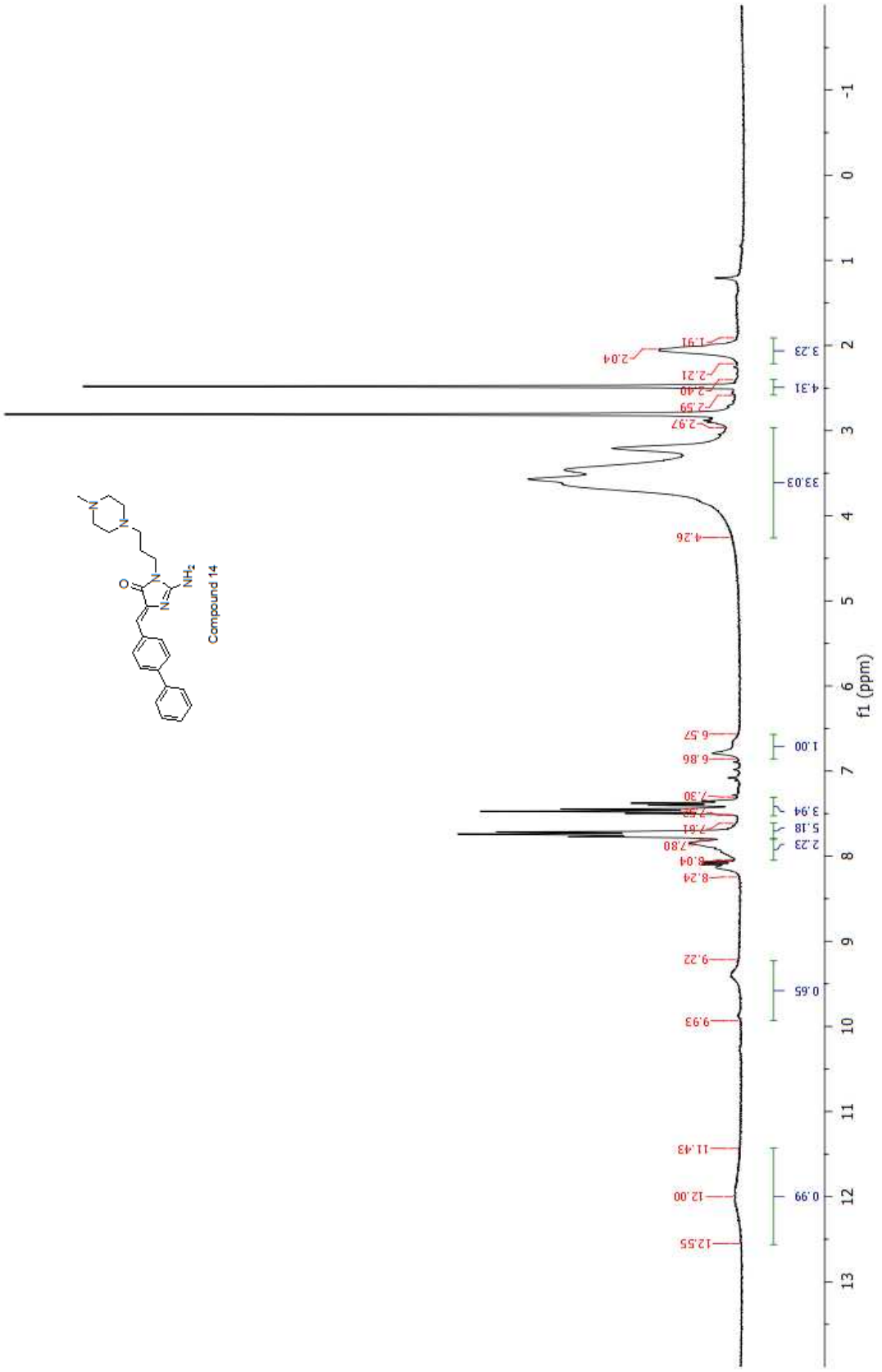
Compound 12


Compound 12
Chemical Shift (ppm)
Chemical Shift (ppm)
Chemical Shift (ppm)

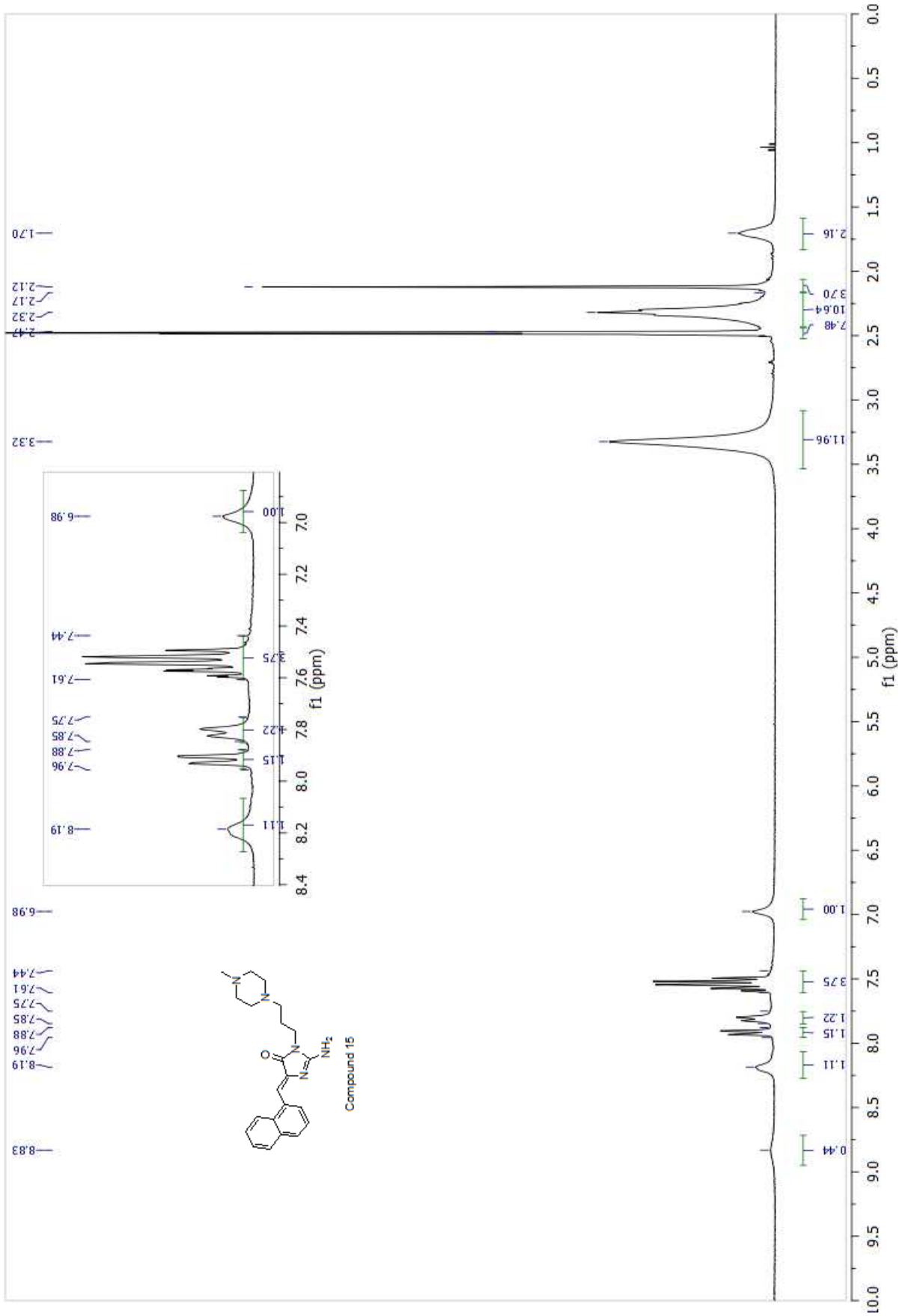
Compound 13



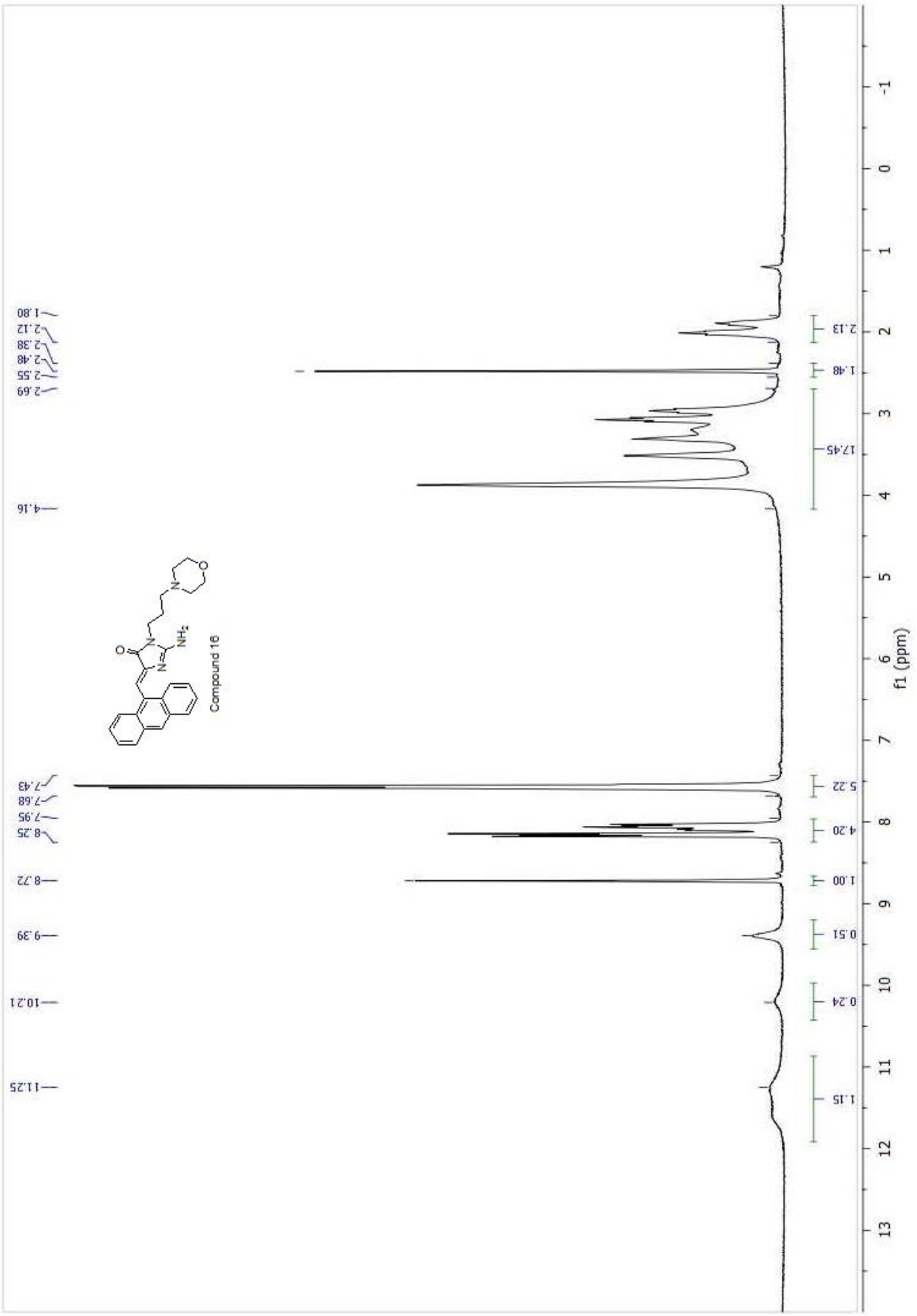
Compound 14



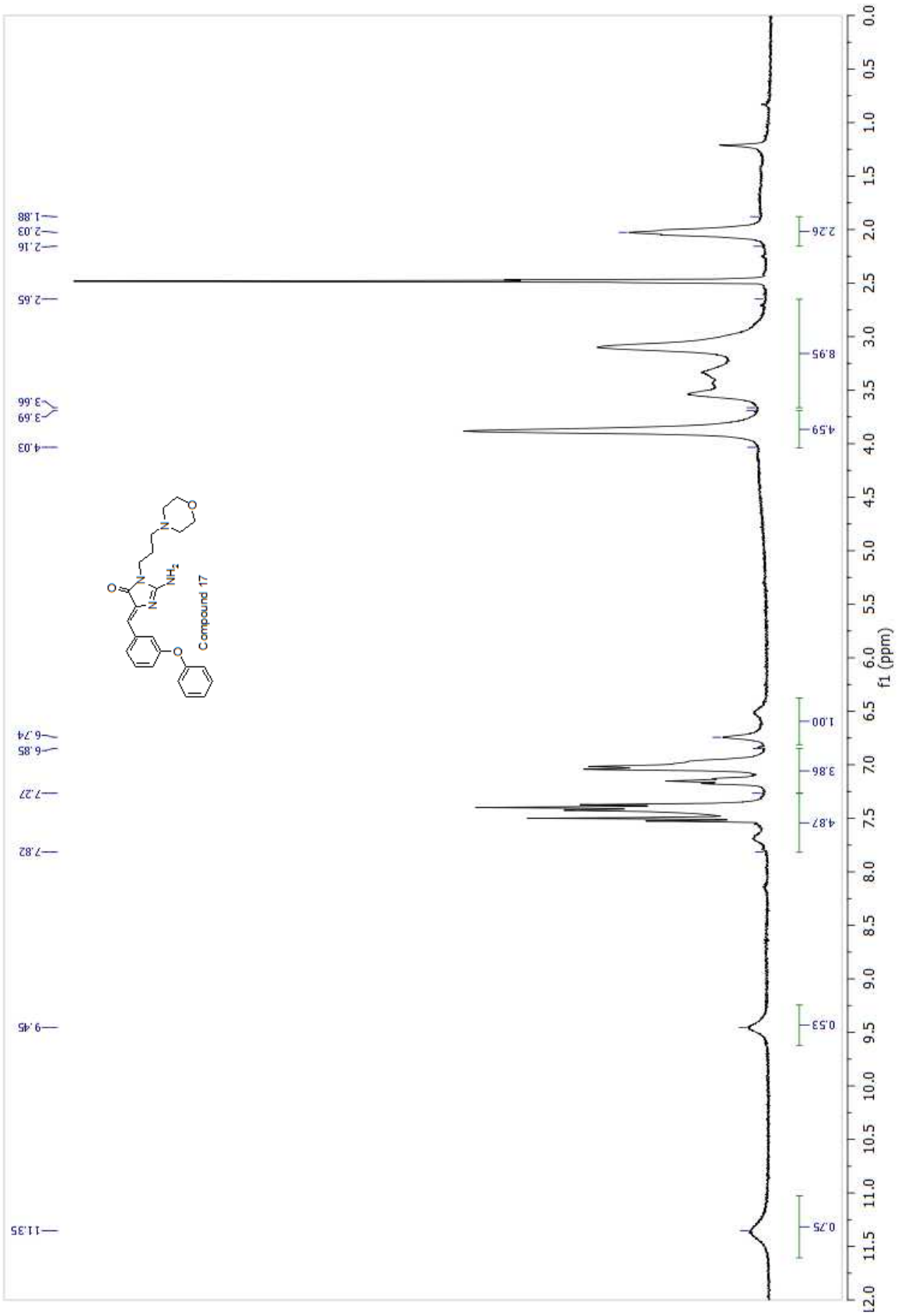
Compound 15



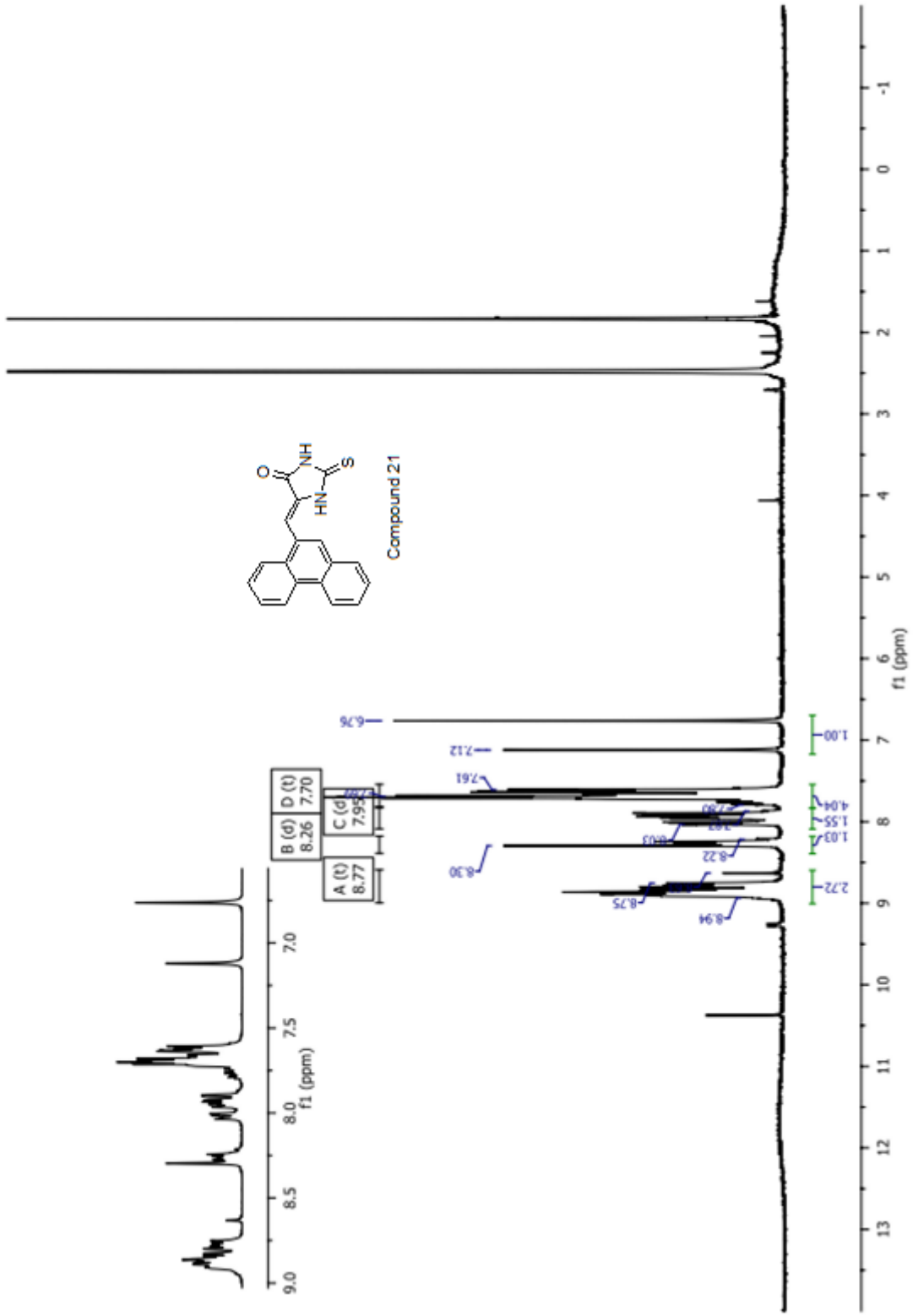
Compound 16


11.25
10.21
9.39
8.72
8.25
7.95
7.68
7.43
4.16
2.69
2.55
2.48
2.38
2.12
1.80
1.15
0.24
0.51
1.00
4.20
5.22
17.45
1.48
2.13
f1 (ppm)
Compound 16

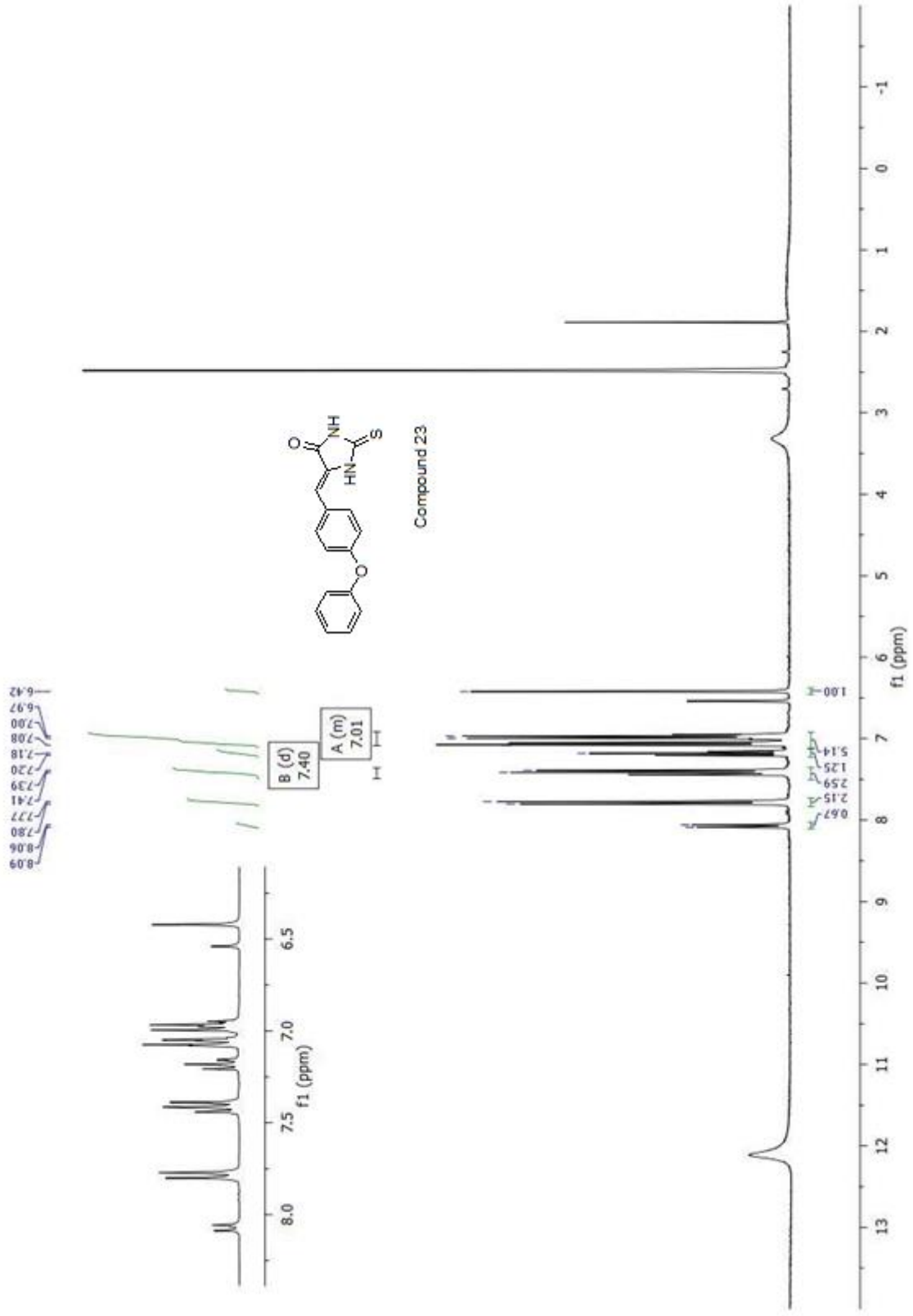
Compound 17


11.35
9.45
7.82
7.27
6.85
6.74
4.03
3.69
3.66
2.65
2.16
2.03
1.88
0.75
0.53
4.87
3.86
1.00
4.59
8.95
2.26
f1 (ppm)
Compound 17

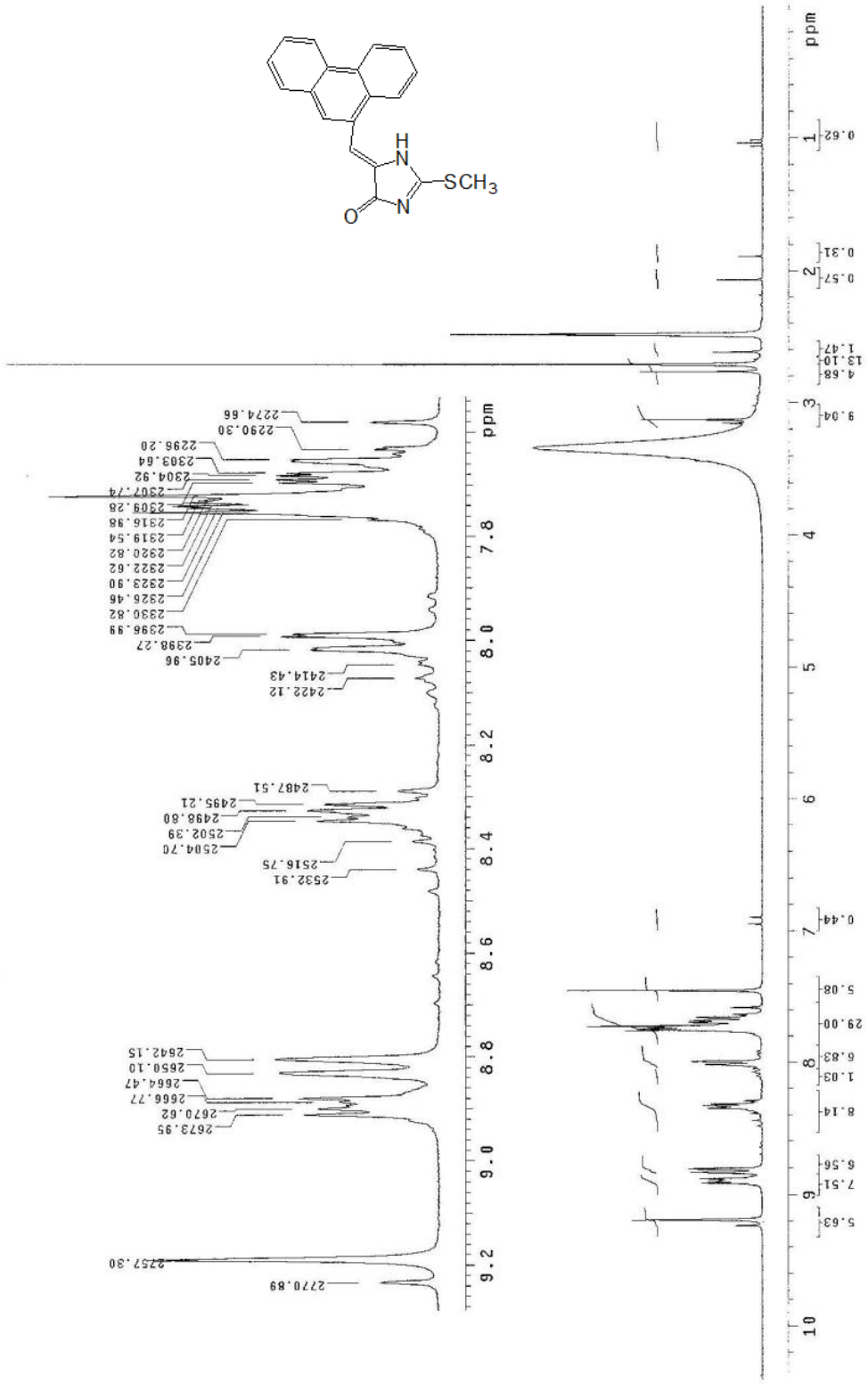
Compound 21



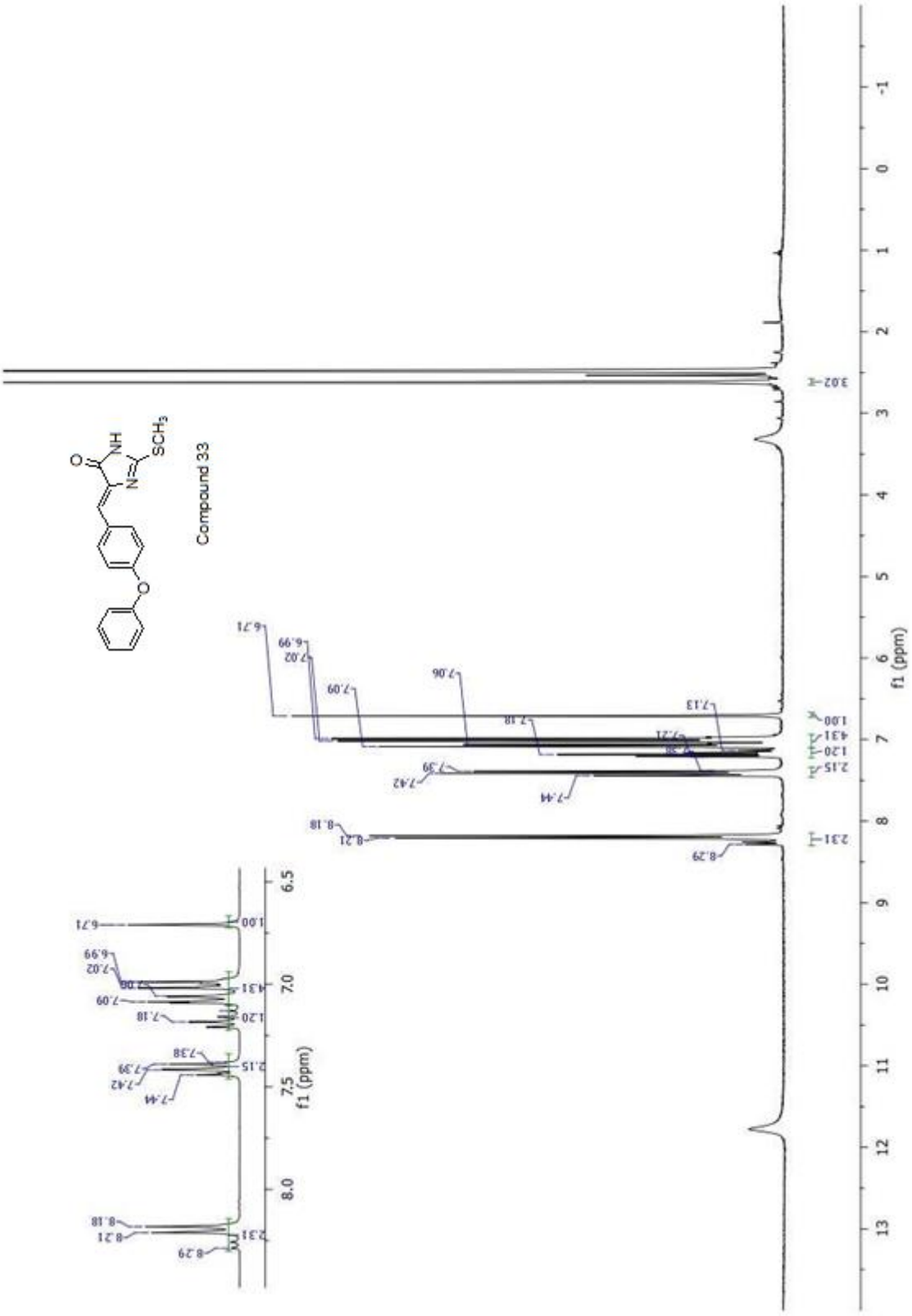
Compound 23



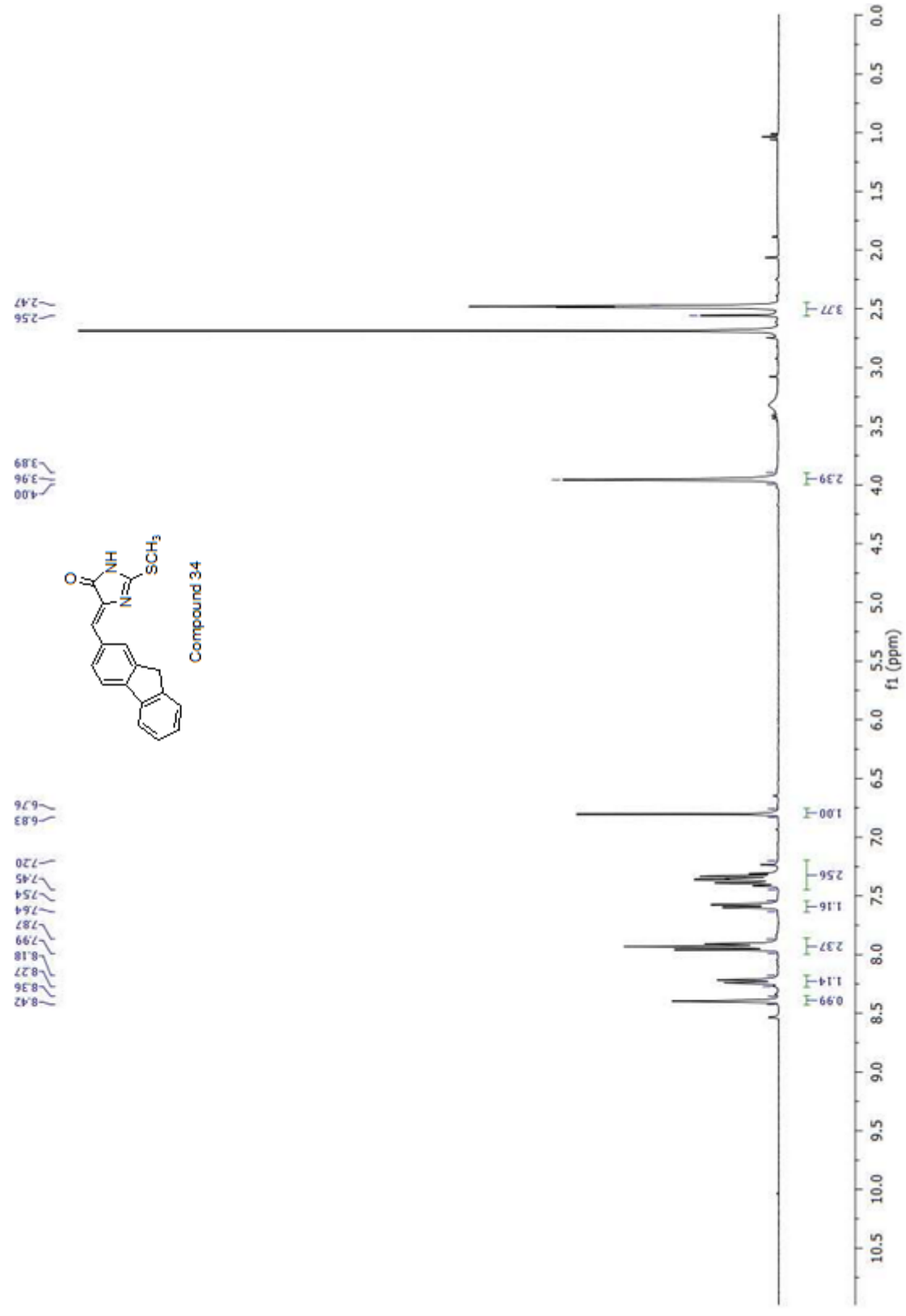
Compound 31


H
N
SCH3
O
N
ppm
9.2
9.0
8.8
8.6
8.4
8.2
8.0
7.8
2257.30
2270.89
2642.15
2650.10
2664.47
2666.77
2670.62
2673.95
2487.51
2495.21
2498.60
2502.39
2504.70
2516.75
2532.91
2405.96
2414.43
2422.12
2274.66
2290.30
2296.20
2303.64
2304.92
2307.74
2309.28
2316.98
2319.54
2320.82
2322.62
2323.90
2326.46
2330.82
2396.99
2398.27

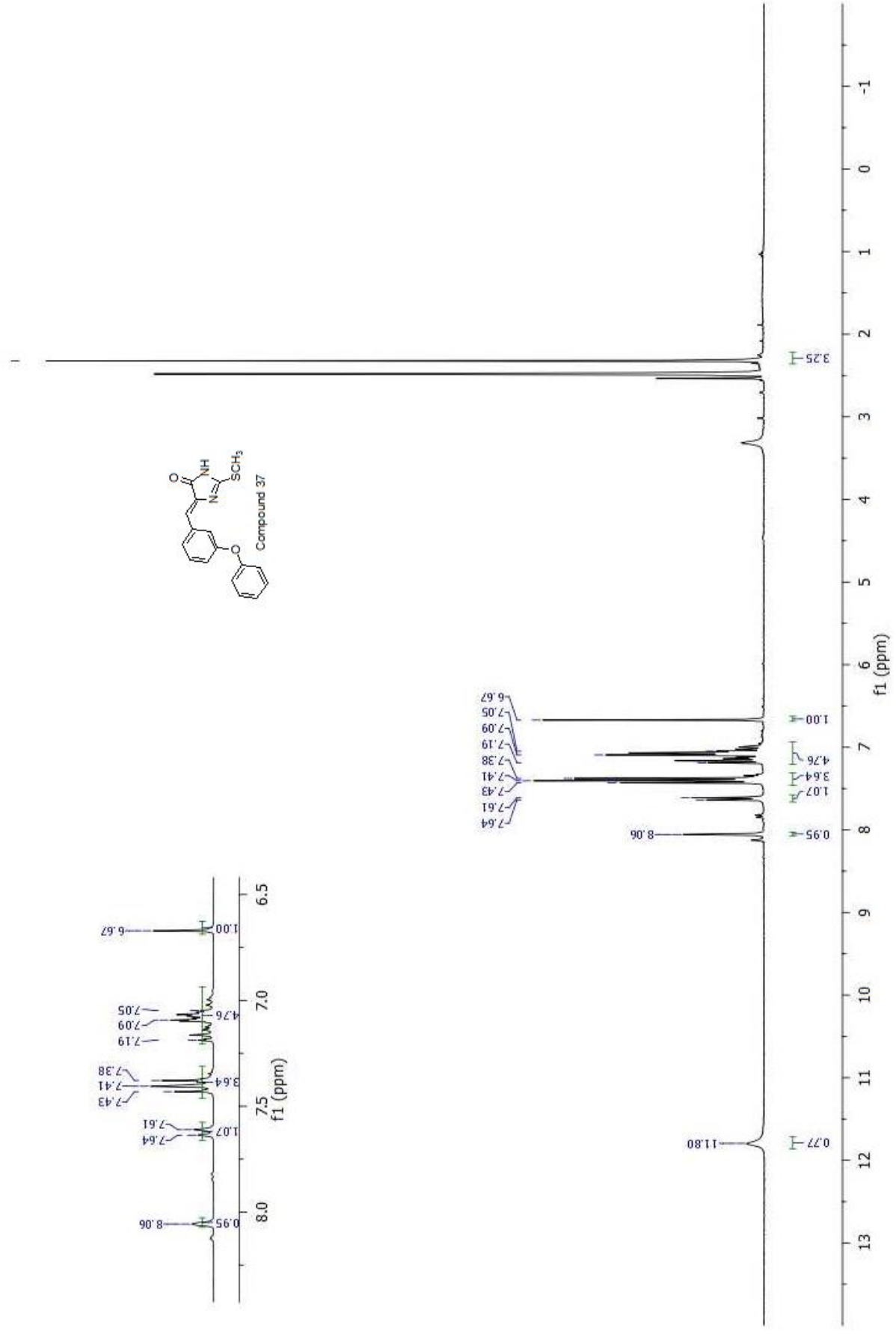
Compound 33


Compound 33
NH
SCH3
O
N
O
f1 (ppm)
8.29
8.21
8.18
7.44
7.42
7.39
7.38
7.21
7.18
7.13
7.09
7.06
7.02
6.99
6.71
3.02
2.31
2.15
1.20
1.31
1.00

Compound 34

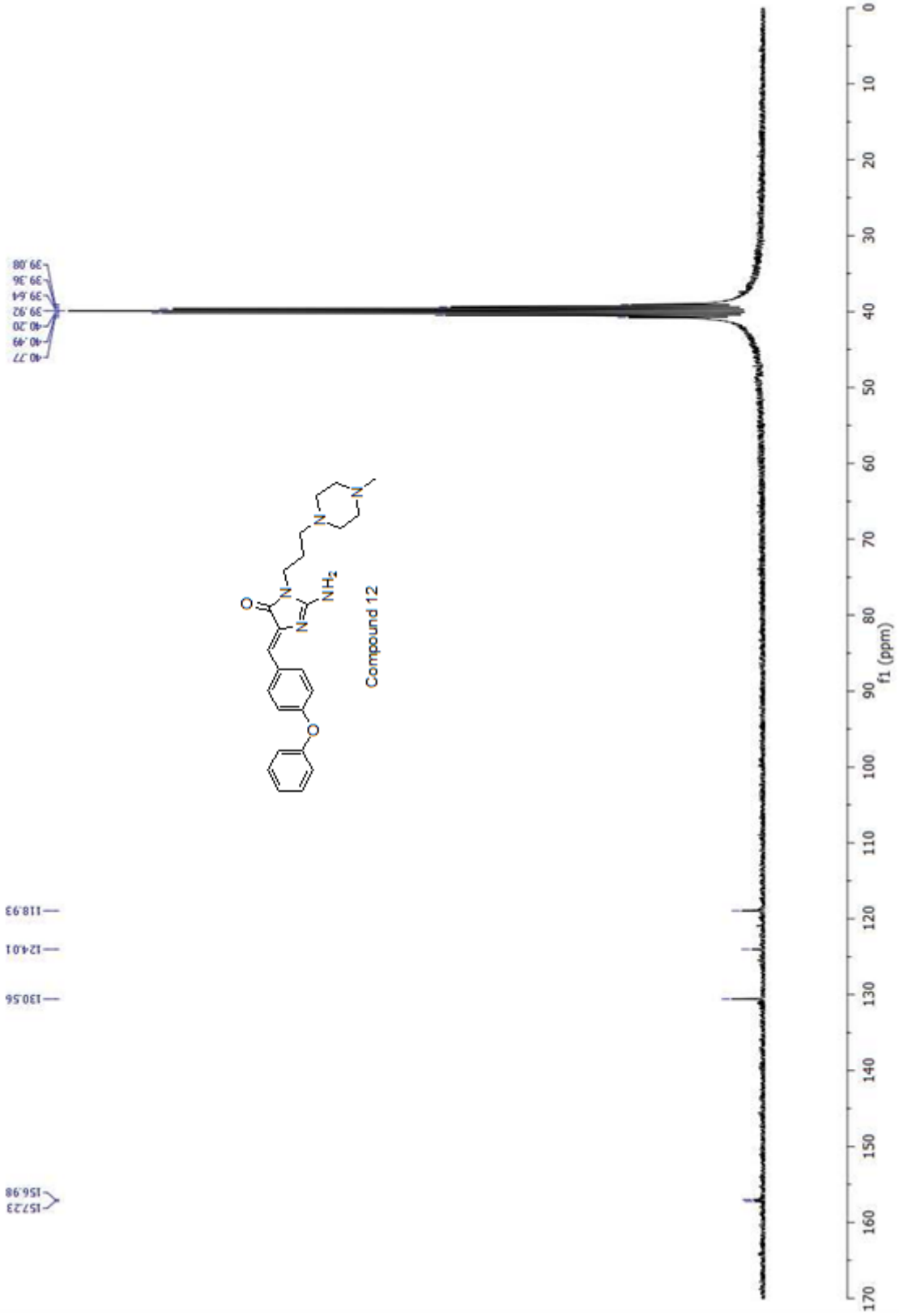


Compound 37

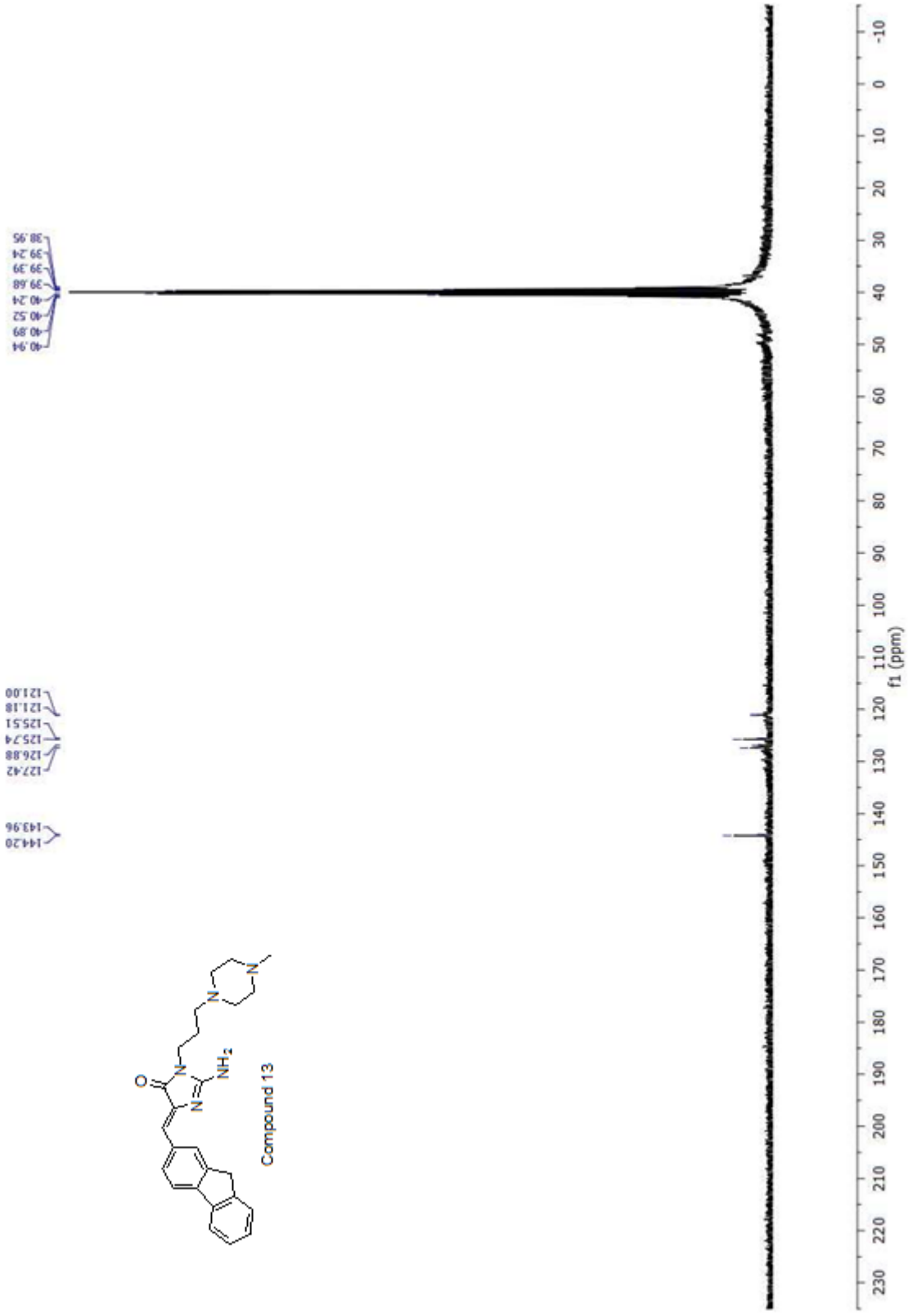


13 C NMRs of selected compounds

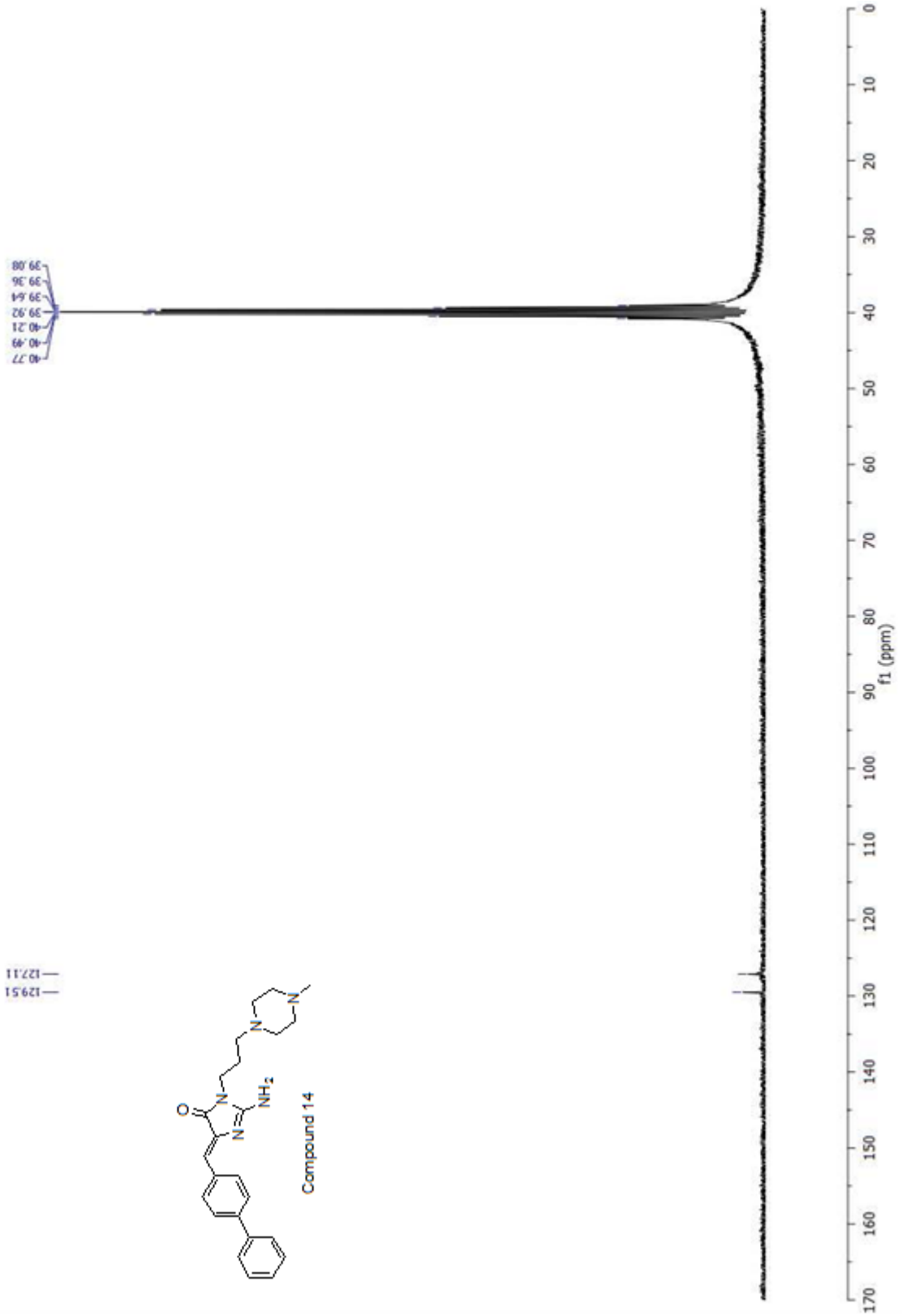
Compound 12



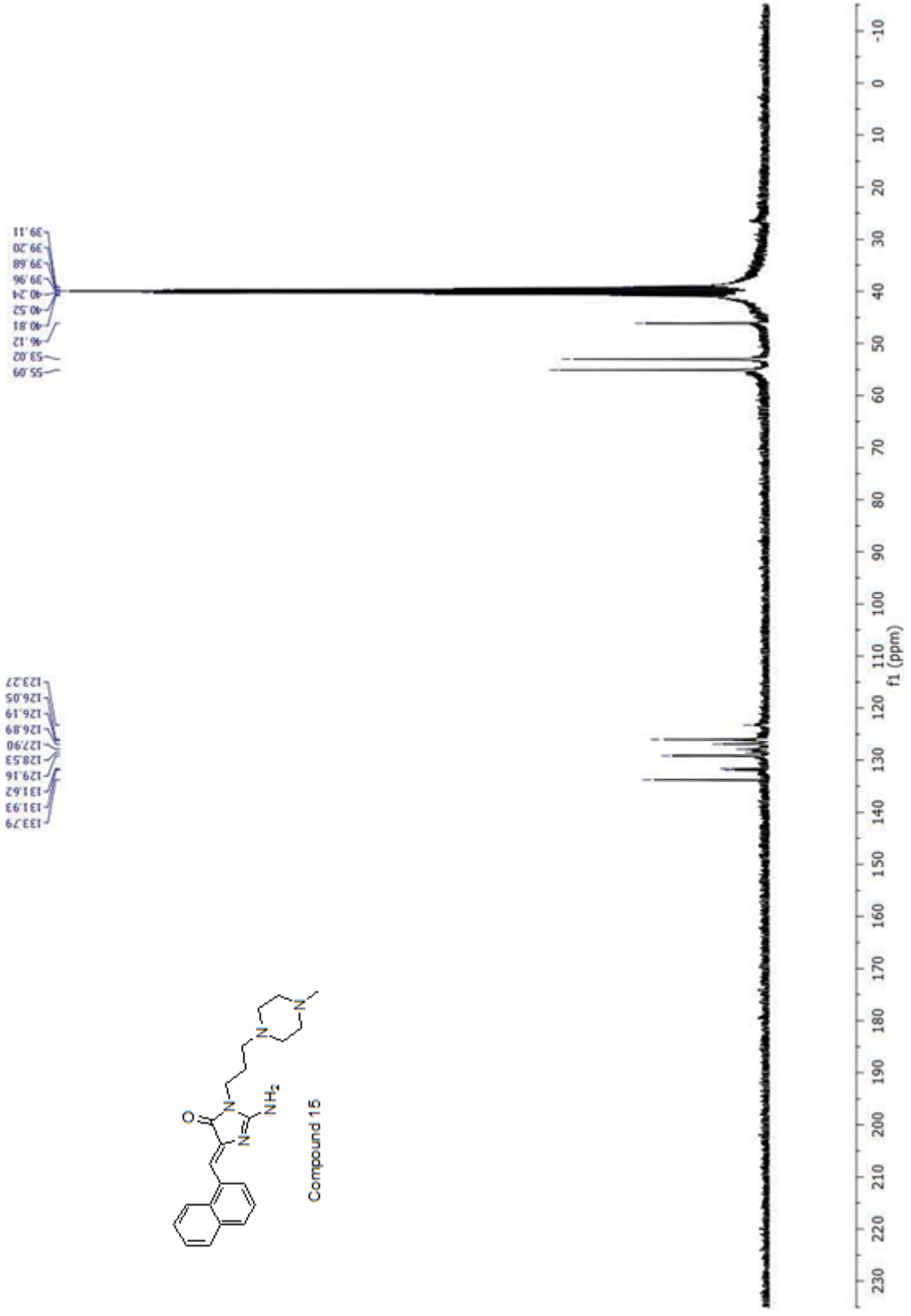
Compound 13


38.95
39.24
39.39
39.68
40.24
40.52
40.89
40.94
121.00
121.18
125.51
125.74
126.88
127.42
143.96
144.20
f1 (ppm)
Compound 13

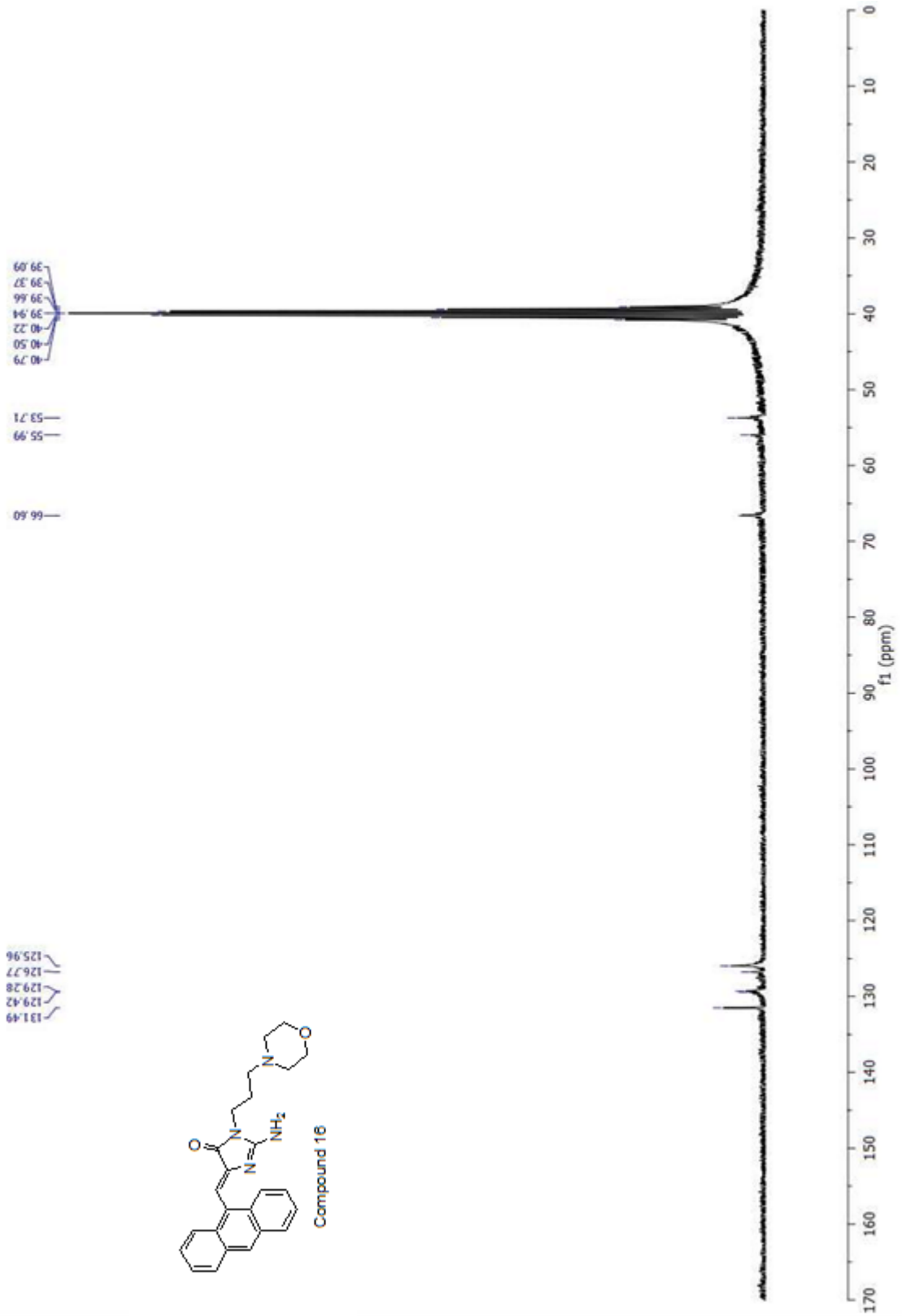
Compound 14



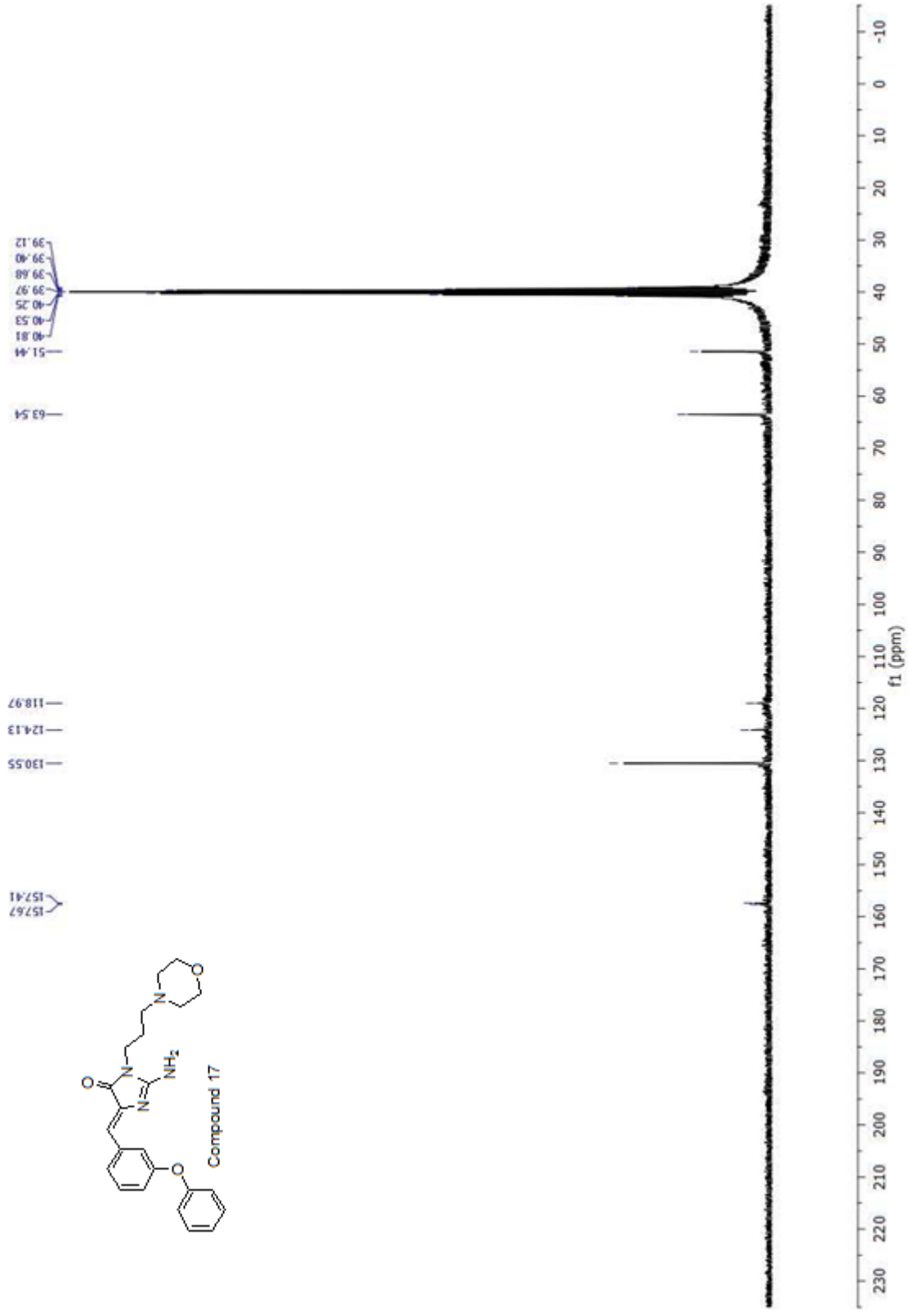
Compound 15



Compound 16

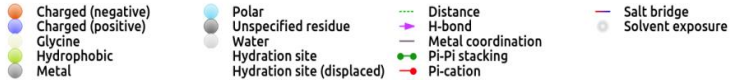

39.09
39.37
39.66
39.94
40.22
40.50
40.79
53.71
55.99
66.60
125.96
126.77
129.28
129.42
131.49
Compound 16
f1 (ppm)

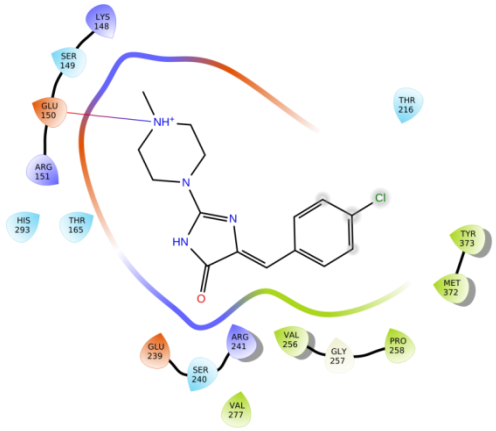
Compound 17


157.67
157.41
130.55
124.13
118.97
63.54
51.44
40.81
40.53
40.25
39.97
39.68
39.40
39.12
f1 (ppm)
Compound 17

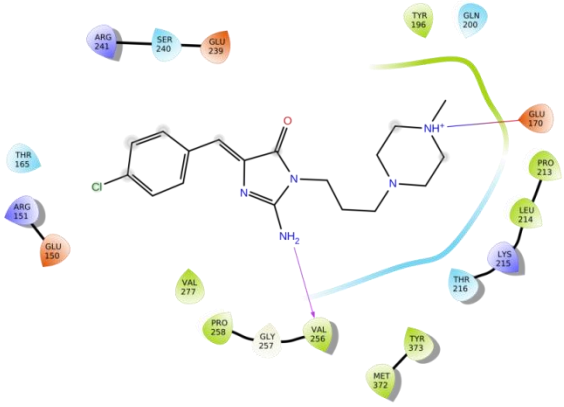
Studies in silico

Ligand interaction diagrams for poses obtained in docking; grid centering at S240.

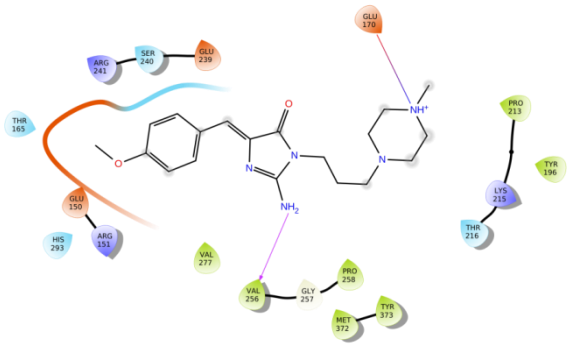




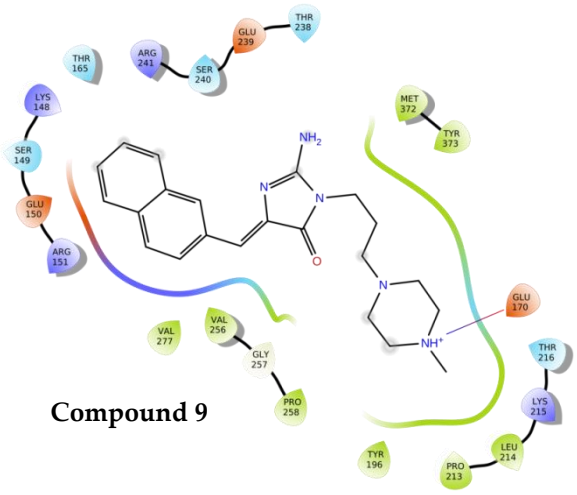
Compound 6



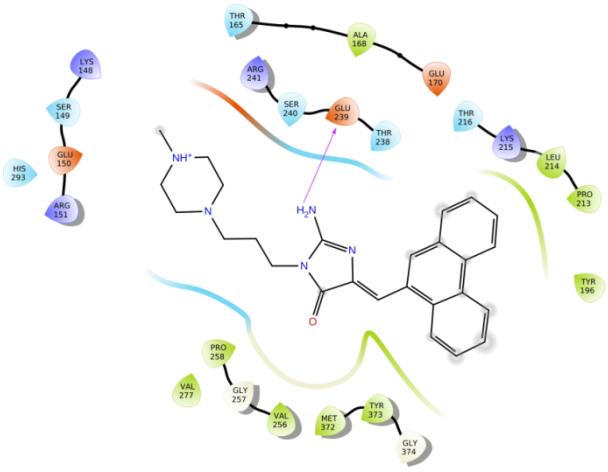
Compound 7



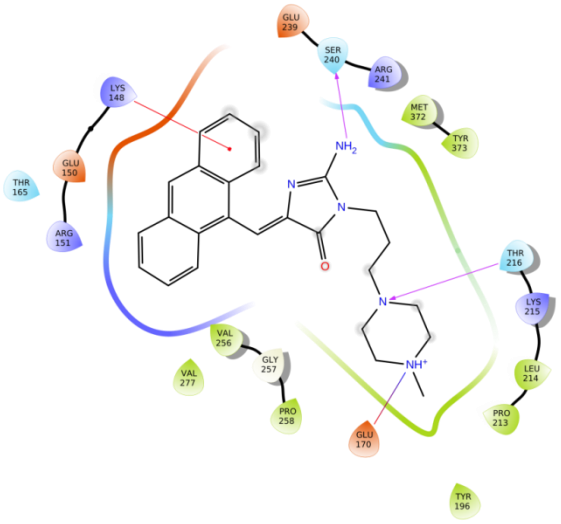
Compound 8



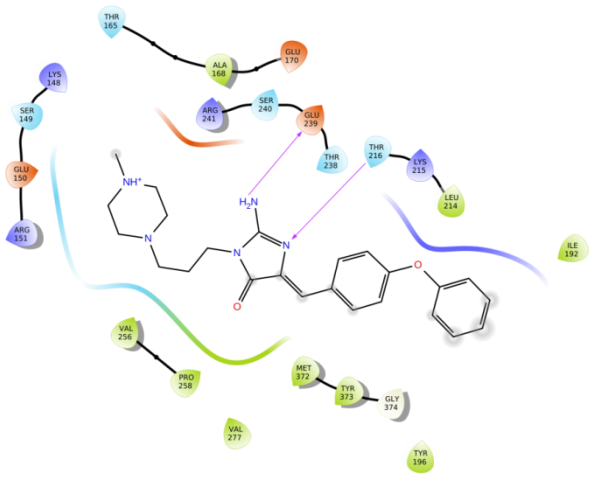
Compound 9



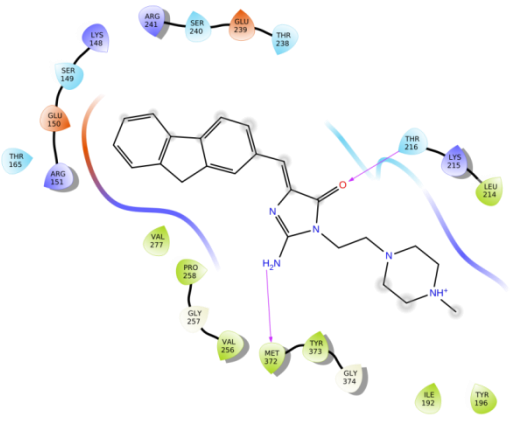
Compound 10



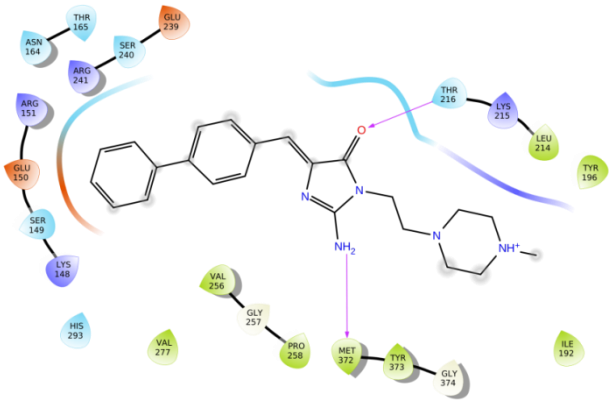
Compound 11



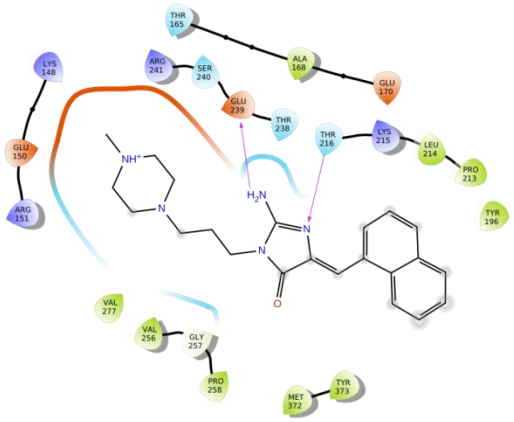
Compound 12



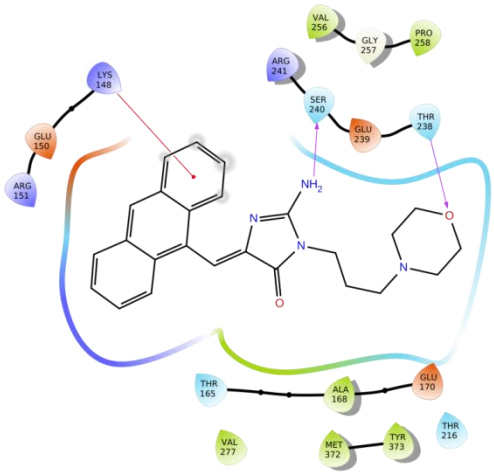
Compound 13



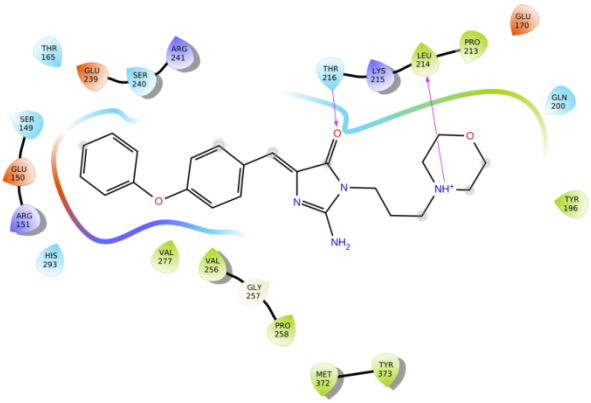
Compound 14



Compound 15

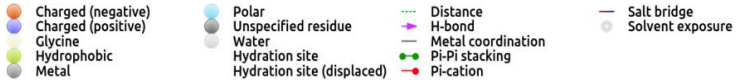


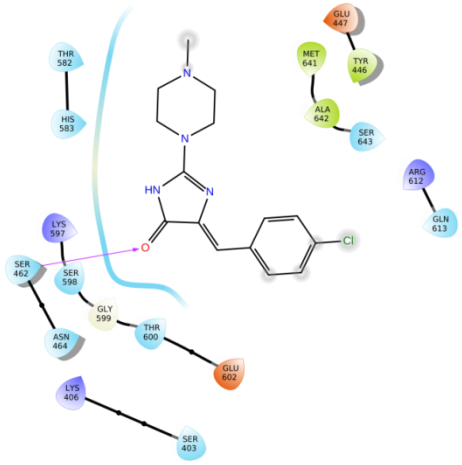
Compound 16



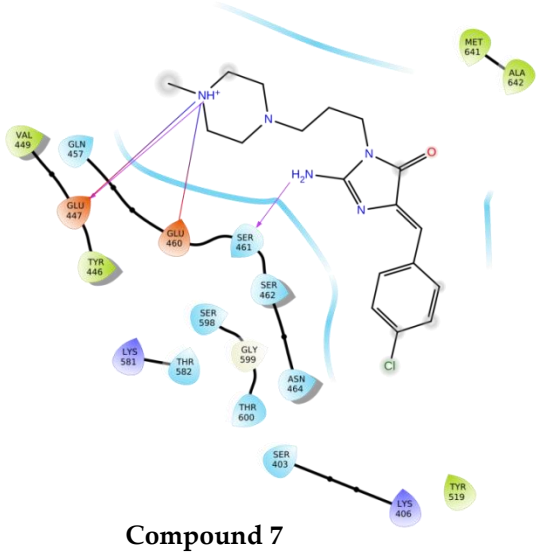
Compound 17

Ligand interaction diagrams for poses obtained in docking; grid centering at S403.

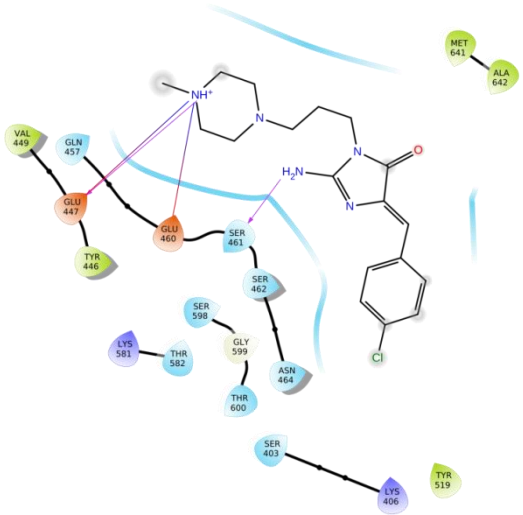




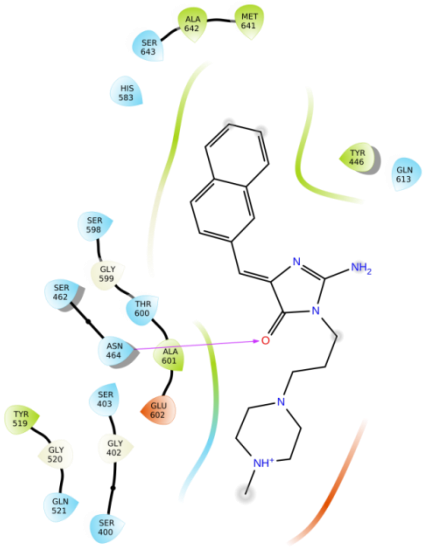
Compound 6



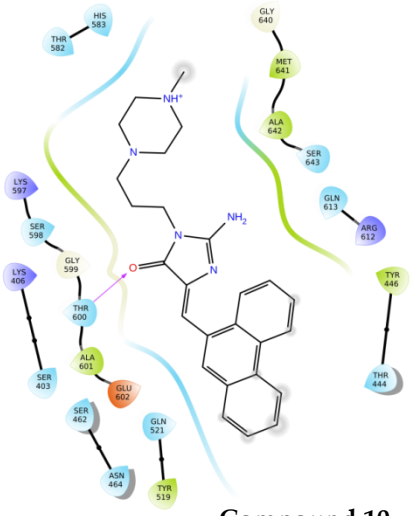
Compound 7



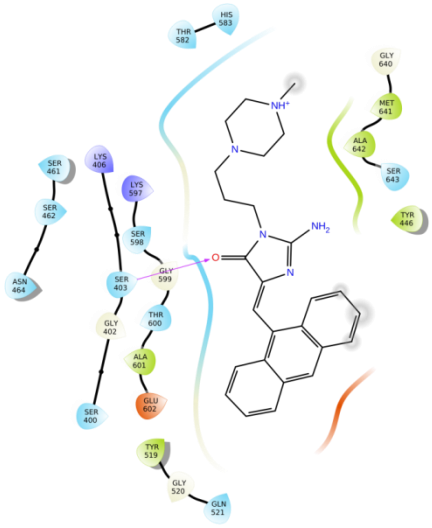
Compound 8



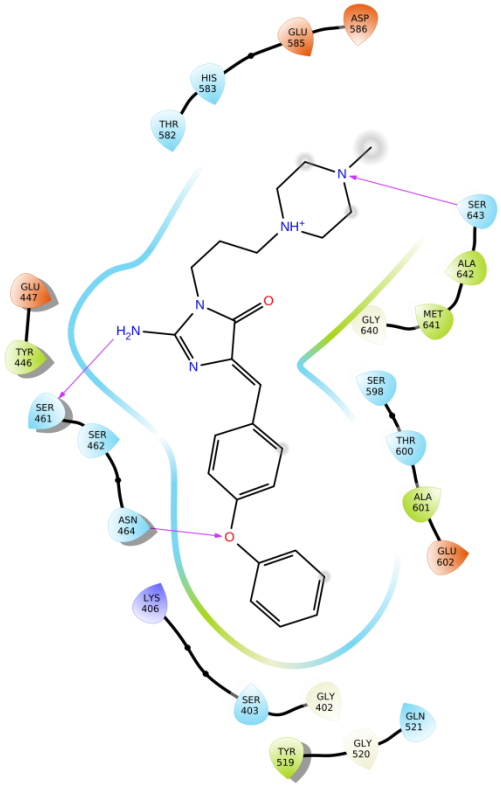
Compound 9



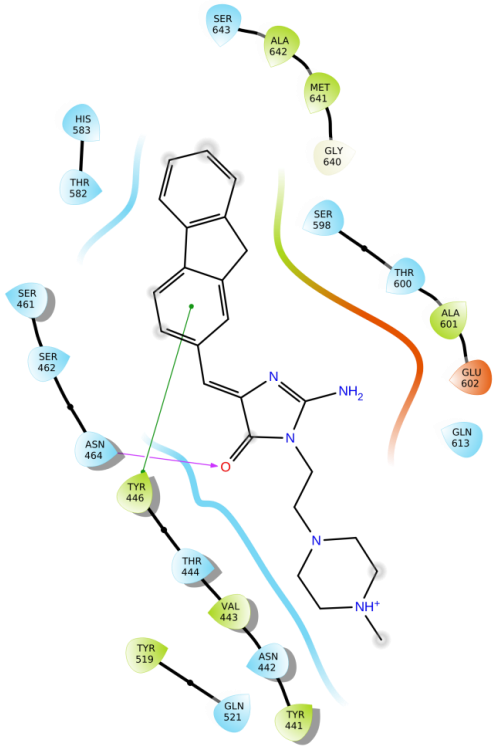
Compound 10



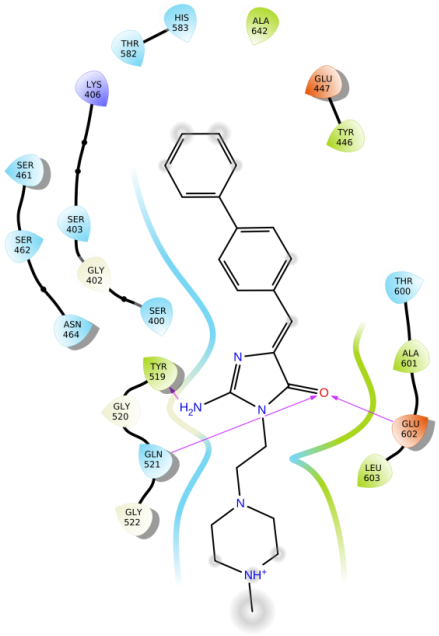
Compound 11



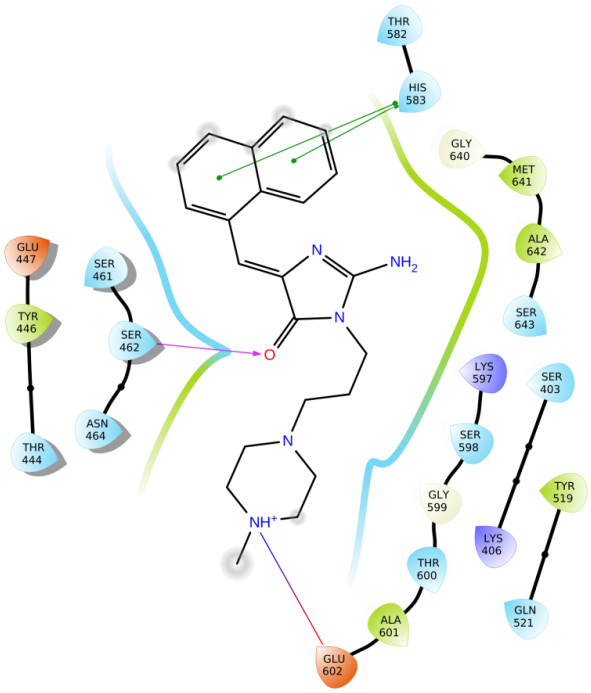
Compound 12



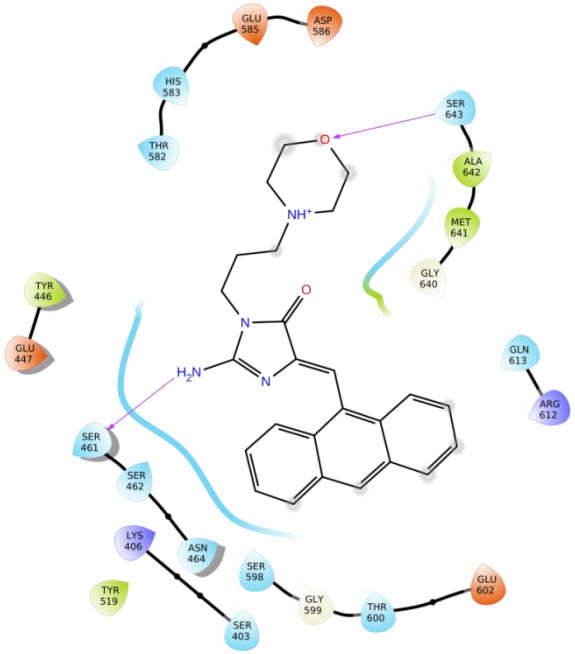
Compound 13



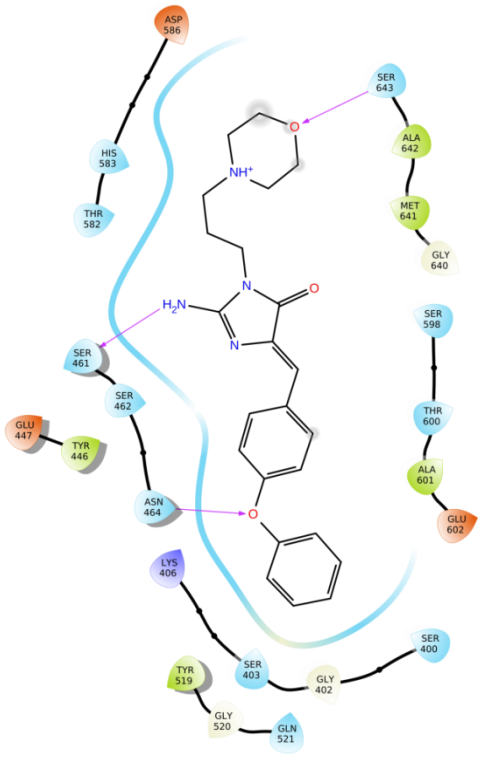
Compound 14



Compound 15

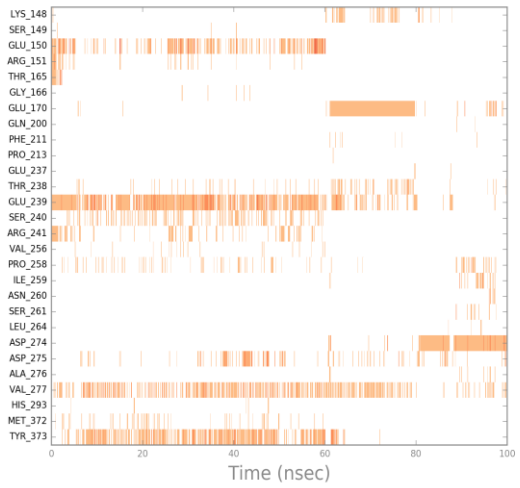


Compound 16

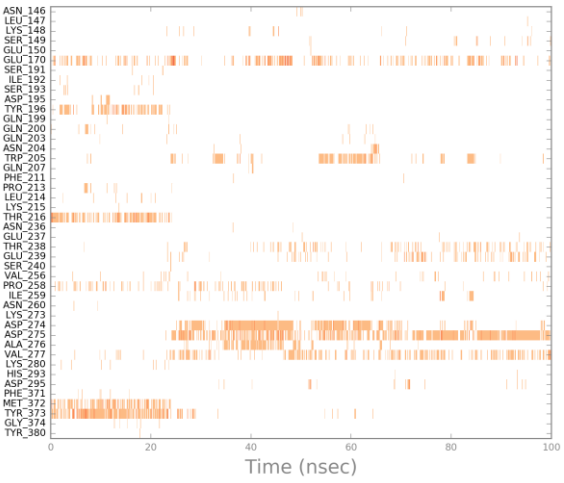


Compound 17

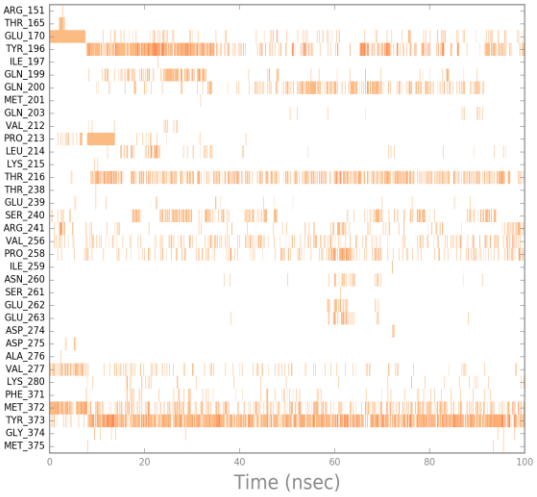
Simulation interaction diagrams from molecular dynamic simulations; grid centering at S240.



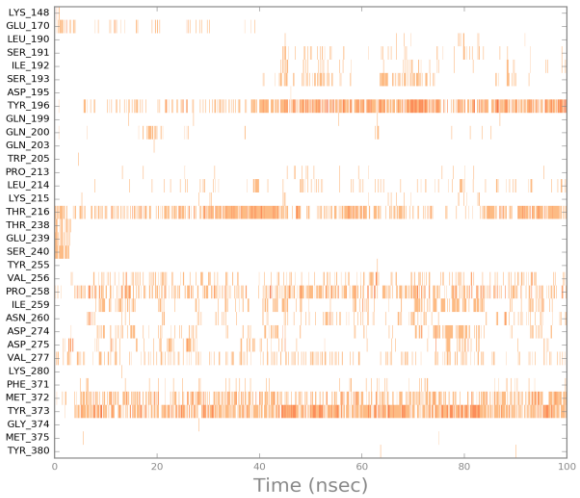
Compound 6



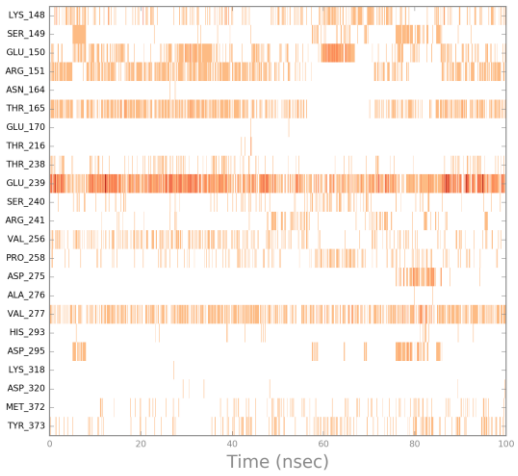
Compound 7



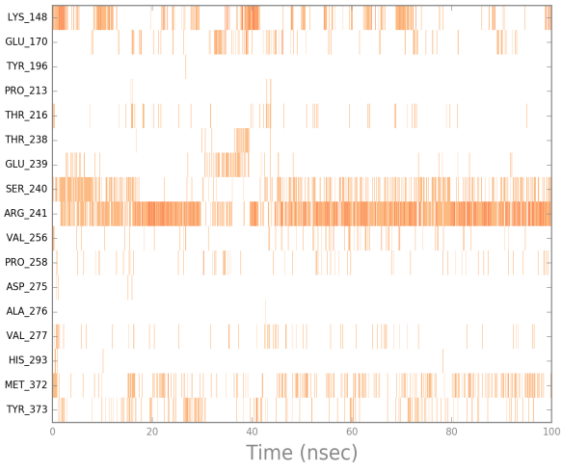
Compound 8



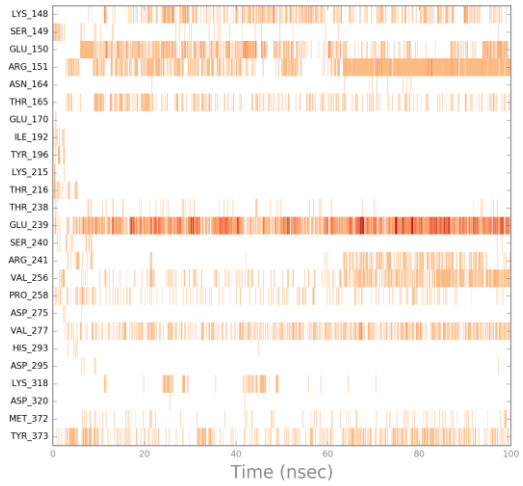
Compound 9



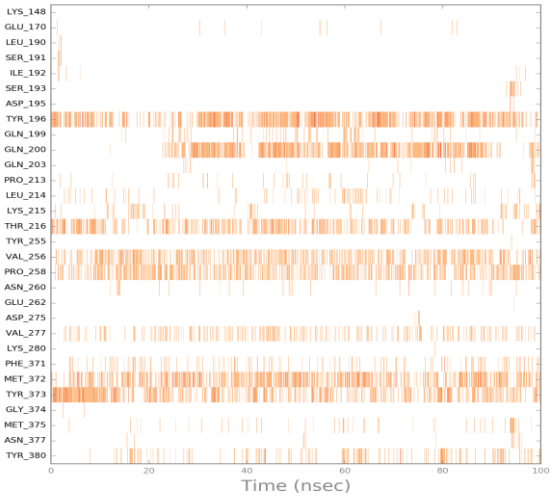
Compound 10



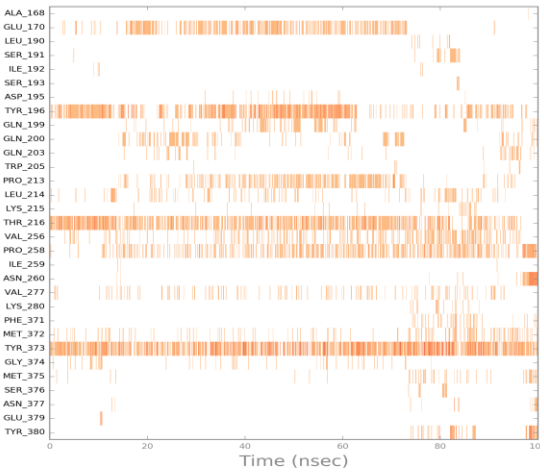
Compound 11



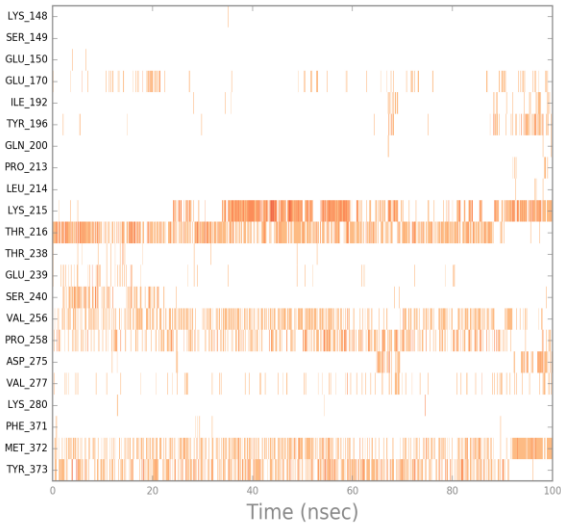
Compound 12



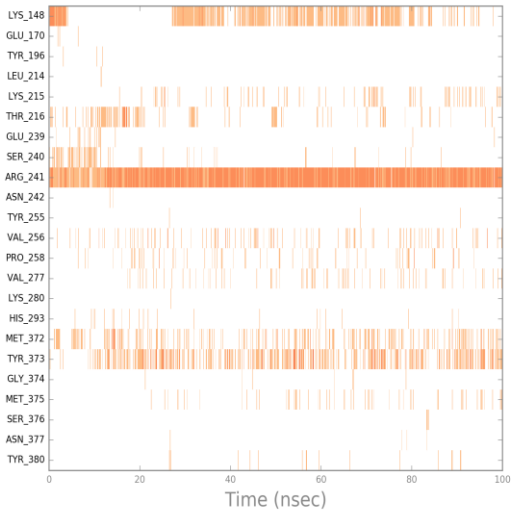
Compound 13



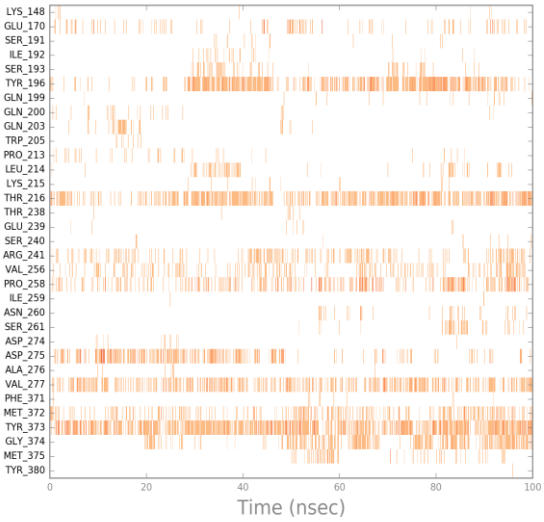
Compound 14



Compound 15

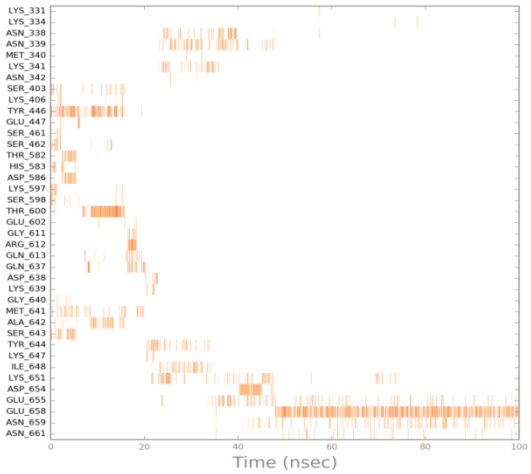


Compound 16

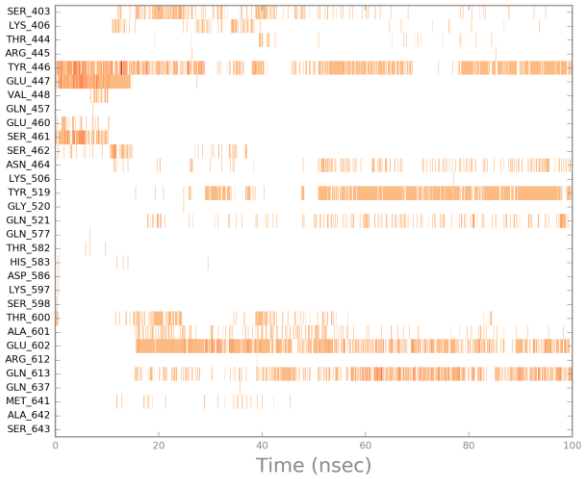


Compound 17

Simulation interaction diagrams from molecular dynamic simulations; grid centering at S403.

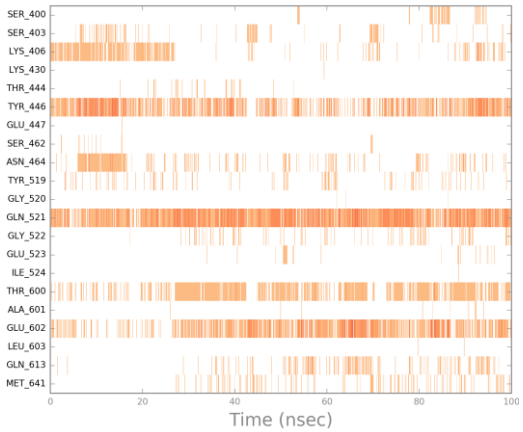


Compound 6

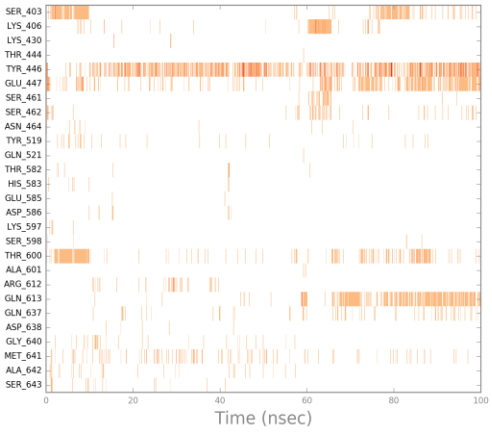


Compound 7

Compound 8 diffused away from the protein during simulation.

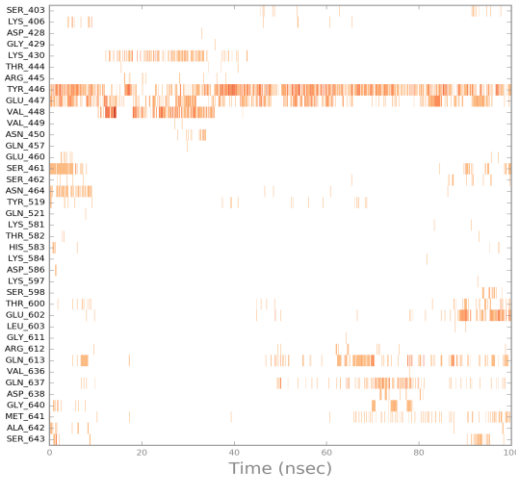


Compound 9

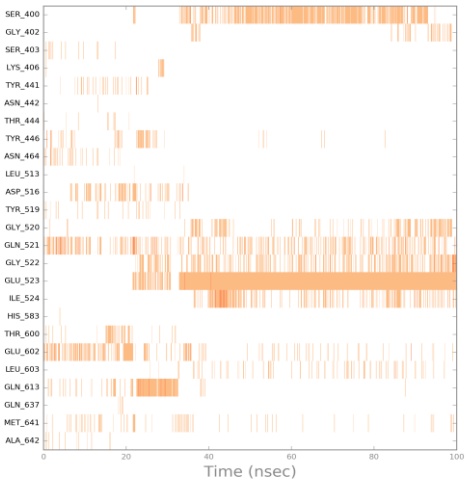


Compound 10

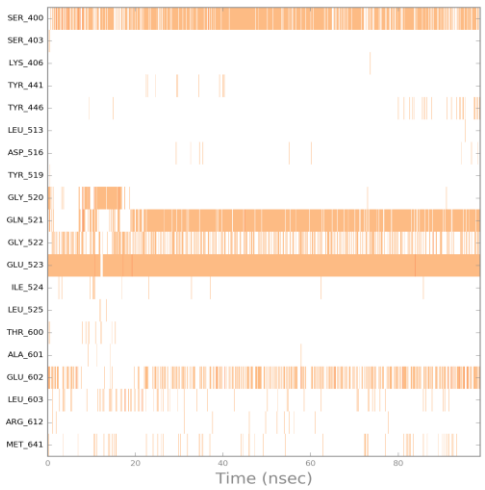
Compound 11 diffused away from the protein during simulation.



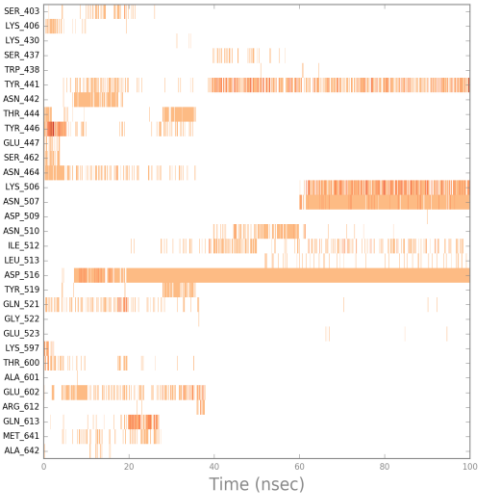
Compound 12



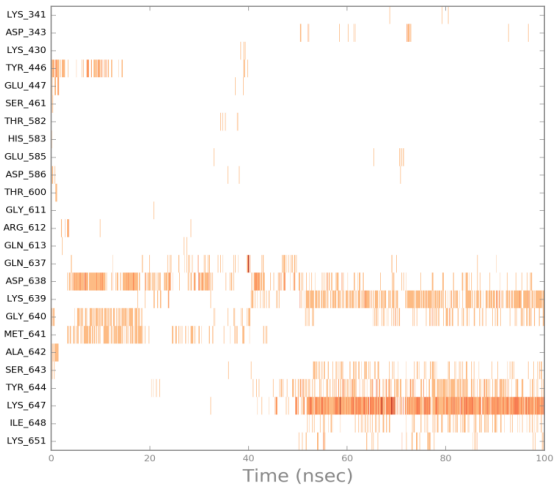
Compound 13



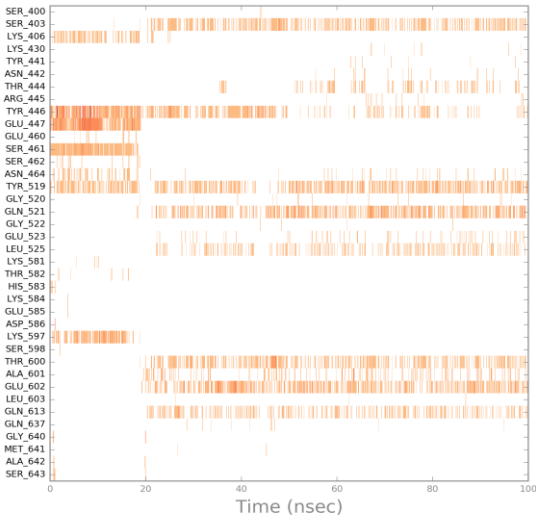
Compound 14



Compound 15



Compound 16



Compound 17